Nages Nagaratnam
Kujan Nagaratnam
Gary Cheuk
Editors

Advanced Age Geriatric Care

A Comprehensive Guide

Springer

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Editors
Nages Nagaratnam
Sydney Medical School
The University of Sydney
Sydney
New South Wales
Australia

Kujan Nagaratnam
Sydney Medical School
The University of Sydney
Sydney
New South Wales
Australia

Gary Cheuk
Rehabilitation and Aged Care Service
Blacktown-Mt Druitt Hospital
Blacktown
New South Wales
Australia

ISBN 978-3-319-96997-8 ISBN 978-3-319-96998-5 (eBook)
https://doi.org/10.1007/978-3-319-96998-5

Library of Congress Control Number: 2018962163

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

The oldest old or those who are over the age of 85 is the fastest growing segment of most developed countries. In the United States, the oldest old is projected to double from 4.3 million to 9.6 million by 2030. The inevitable consequence is that there will be an increase in the prevalence of older persons with chronic diseases, multiple coexisting pathologies and neurodegenerative diseases.

This will pose significant challenges on many levels such as health care, social welfare, transport and residential infrastructures. To a clinician, the care of the oldest old is unique in that it is an area where there is scant clinical evidence to guide practice. The oldest old are often excluded from drug trials, and their treatments are largely based on findings extrapolated from that of the younger old. Furthermore, amongst the oldest old, physiologically they are more diverse than other segments of the population. Their demographic characteristics are unparalleled and different compared to that of the younger old. Several studies have drawn attention to the differing attitudes amongst health professionals towards older persons, and many show prejudice because they are old. As a result, the use of age as a criteria in determining the appropriateness of treatment is of very limited validity.

The increased life expectancy of the population since the early 1900s had been built on the improvement of living conditions, diet, public health and advancement in medical care. With this we have seen a steady decline in the age-specific prevalence of vascular and heart diseases, stroke and even dementia. Older persons nowadays are healthier than their counterparts decades ago. More importantly than in any other age group, the care of the oldest old must be individualised; management decisions should be made taking into consideration the older persons' expressed wishes, quality of life, function and mental capacity.

There is a desperate need for good quality research and data about ageing and age-related problems in the 85 years and older which could help improve their health-care decisions and planning. A proper understanding of the age-related changes in the older person and the ability to distinguish the reversible versus the irreversible conditions are vital to developing appropriate corrective and remedial strategies. Care of the oldest old is a subject in which there is much scope for new writing and debate as this population grows.

Our aim is to create a greater awareness especially amongst the primary care physicians of the complex issues encountered in caring for the oldest old. This book is designed for the primary care physicians, physicians, junior medical officers, specialty nurses and medical students. It is divided into three parts, General Considerations, Chronic Diseases and Geriatric Syndromes. Each chapter provides a summary of important and essential information under the heading of Key Points. Case studies are included in some of the chapters to highlight the principles of management.

Westmead, NSW, Australia
Nages Nagaratnam
The University of Sydney

Westmead, NSW, Australia
Kujan Nagaratnam
The University of Sydney

Blacktown, NSW, Australia
Gary Cheuk
Blacktown-Mt Druitt Hospital

Acknowledgements

We thank Mrs. Sheila Nagaratnam, Mr. Yogan Nagaratnam (for his help in numerous ways), Miss Roshana Kanagaratnam, Prof. Nicholas Manolios and Dr. Lisa Tarlinton for their help.

Disclaimer

Continuous development and research in the fields of medicine, science technology and health care result in on-going changes in the domains of clinical practice as evidence continues to evolve rapidly. We have taken reasonable care and effort to provide material which are current, accurate and balanced at the time of publication.

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We have acknowledged the sources and works of the cited sites at the appropriate locations in the text and references. We have used the source materials in the sense of fair use and extend our apology for any oversight. Readers are advised to cross-reference and confirm points relevant to them.

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Contributors

Dino Benito, Bsc (Psych), MD, FRACP Blacktown Hospital, Hornsby Ku-ring-gai Hospital, The Hills Private, Norwest Private and the Macquarie University Hospital, Sydney, NSW, Australia

Weng Onn Chan, FRANZCO, MPhil Southern Australian Institute of Ophthalmology, University of Adelaide, Adelaide, SA, Australia

Gary Cheuk, MBBS (UNSW), FRACP Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia

Jimmy Chien, BMed, PhD, FRACP Sydney Medical School, The University of Sydney, Sydney, NSW, Australia

Department of Respiratory Sleep Medicine, Westmead Hospital, Westmead, NSW, Australia

Paul Cullen, MBBS, FRANZCP, FPOA Berkeley Vale Private Hospital, Berkeley Vale, NSW, Australia

Derek Davies, MBBS, BSc, FACD Orange Dermatology, Orange, NSW, Australia

Jagit Singh Gilhotra, MBBS, MMed (Clin Epi, Syd), FRANZCO University of Adelaide and The Queen Elizabeth Hospital, Adelaide, SA, Australia

Gail Jamieson, MBBS, FRACP Geriatrician, Sydney, NSW, Australia

Jayasingham Jayamohan, MBBS, MRCP, FRCR, FRANZCR Crown Princess Mary Cancer Centre, Westmead, NSW, Australia

Logan Kanagaratnam, MBBS, FRACP, DDU Royal North Shore, Ryde, North Shore Private and Macquarie University Hospitals, University of Sydney, St. Leonards, NSW, Australia

Vincent Lee, MBBS, FRACP, PhD Renal Department, Westmead Hospital, University of Sydney, Westmead, NSW, Australia

Sydney Medical School, The University of Sydney, Westmead, NSW, Australia

Norwest Private Hospital, Bella Vista, NSW, Australia

Westmead Hospital, Westmead, NSW, Australia

Lucinda Morris, MBBS, FRANZCR Crown Princess Mary Cancer Center, Westmead, NSW, Australia

Vasi Naganathan, MBBS, FRACP, MMed, PhD Centre for Education and Research on Ageing, Faculty of Medicine and Health, The University of Sydney and Ageing and Alzhiemer's Institute, Concord Hospital, Sydney, NSW, Australia

Kujan Nagaratnam, MBBS (UNSW), FRACP, FANZSGM Sydney Medical School, The University of Sydney, Sydney, NSW, Australia

Nages Nagaratnam, OAM, MD, FRACP, FRCPA Sydney Medical School, The University of Sydney, Sydney, NSW, Australia

Sai Adithya Nagaratnam, B Med (Newcastle) Westmead Hospital, Westmead, NSW, Australia

Senan Nagaratnam, MBBS, FRANZCR Alfred Medical Imaging, Sydney, NSW, Australia

Gowrie Pavan, MBBS, FRACGP, DCH Family Medical Practice, Carlingford, NSW, Australia

Latesh Poojara, MBBS, EDIC, FCICM, MM (Clin Epi) Intensive Care Unit, Blacktown Mount Druitt Hospitals, Mount Druitt, NSW, Australia

Arumugam Punnia-Moorthy, PhD Lond, MClinEd, FDSRCS, FFDRCS Formerly Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, The University of Sydney, Sydney, NSW, Australia

Graham Reece, MBBS, FRACP Intensive Care Unit, Blacktown Mount Druitt Hospitals, Mount Druitt, NSW, Australia

Sivagnanavel Senthuran, MBBS, FRCA, FCICM, FANZCA, MClinEpi Department of Intensive Care Medicine, Townsville Hospital, Townsville, QLD, Australia

Sarah So, MBBS Renal Department, Westmead Hospital, University of Sydney, Westmead, NSW, Australia

Jessica Stevenson, BHSc (Nutr), MND Westmead Hospital, Westmead, NSW, Australia

Puma Sundaresan, BSc (Hons), BMBS, FRANZCR, PhD Crown Princess Mary Cancer Centre, Westmead, NSW, Australia

Niluja Thiruthaneeswaran, MBBS, MPH, FRANZCR The University of Sydney, Sydney, NSW, Australia

University of Manchester, Manchester, UK

About the Editors

Nages Nagaratnam, OAM, FRACP, FRCPA is Clinical Associate Professor at the Sydney Medical School, University of Sydney, and was Conjoint Associate Professor in the School of Medicine, College of Health and Science, at the University of Western Sydney, Australia. He graduated and obtained the Doctorate in Medicine from the University of Ceylon and was for many years Consultant Physician in Internal Medicine in Sri Lanka and Senior Physician at the General Hospital, Colombo, the premier teaching hospital. He is a founding Fellow of the National Academy of Sciences of Sri Lanka and was President Section A of the Sri Lanka Association for the Advancement of Science. In Australia, he was a Consultant Physician in Geriatric and Internal Medicine at the Blacktown-Mount Druitt and Westmead Hospitals. He has an almost lifelong commitment to the training and guiding the careers of generation of young doctors. He has authored several scientific publications in both national and international journals. His interests spanned themes from many fields of medicine with continuous clinical research over several years. In the last two decades, his interests are in geriatrics, rehabilitation, stroke and stroke rehabilitation.

Kujan Nagaratnam, MBBS (UNSW), FRACP, FANZSGM graduated in Medicine from the University of New South Wales in 1988. He did his internal medical training and advanced training in geriatric medicine and stroke medicine at Westmead and Royal Prince Alfred Hospitals, Sydney. He obtained his Fellowship of the Royal Australasian College of Physicians (FRACP) in 1997. He held senior staff specialist appointments in general, geriatric medicine and stroke medicine at Westmead Hospital and Blacktown-Mount Druitt Hospitals until 2012. He is also Visiting Consultant Physician at the Norwest Private and Westmead Private Hospitals in Sydney. He is currently the Chairman and Head of the Department of Geriatric Medicine and Stroke Medicine, Norwest Private Hospital, Sydney. His academic interest includes teaching both undergraduate and postgraduate medical students. He is a Clinical Senior Lecturer in Medicine at the University of Sydney. His special interests are stroke medicine, cognitive impairment and dementia, neurological diseases in the elderly and postoperative medical management of elderly patients.

Gary Cheuk, MBBS (UNSW), FRACP graduated from the University of New South Wales in 1985 with honours. He commenced basic physician training in Dunedin (New Zealand) and St George Hospital (Sydney). He underwent advance training in geriatric medicine at Concord and Westmead Hospitals and was granted Fellowship of the Royal Australasian College of Physicians in 1993. In the following year, he became Director of Rehabilitation and Aged Care Service at Blacktown-Mount Druitt Hospital, a position he occupied until 2015. Dr. Cheuk has been involved in undergraduate and postgraduate teaching for many years. Service planning and development are areas of interest for Dr. Cheuk, and he was instrumental in the establishment of the Stroke Unit at Blacktown Hospital and the building of the Rehabilitation Hub at Mount Druitt Hospital. His clinical interests include dementia care, Parkinson's disease and related disorders, stroke medicine and musculoskeletal diseases in older persons.

Part I

General Considerationss

Ageing and Longevity

1

Nages Nagaratnam

Historical Perspective

In ancient Greece, based on the Hippocrates' system of four humours, ageing was attributed to unavoidable loss of body moisture due to the gradual assimilation of innate heat [1]. It was generally believed that the ancient Greeks and Romans died young at the age of 40. This myth was widespread and accepted but is scientifically incorrect, for in calculating the life expectancy, it had not taken into account such factors as infant [2] and maternal mortality rates [3] prevailing at that time. In the past 100 years infant mortality has changed [4]. Once infant mortality was eliminated, the life expectancy at 5 years was 75 for men and 73 for women [5]. The higher mortality rate in the male was related to work, violence or accidental injury and was matched by the high female mortality due to pregnancy and childbirth [3]. Infectious diseases and non-communicable diseases caused deaths equally in men and women [6]. The human mortality rate has improved from the time of the fall of the Roman Empire [7]. Since then life expectancy at birth has improved, and a definite increase was seen from the middle of the nineteenth century [4]. With the discovery of the causes of many diseases, a decline in the mortality rates was evident [8]. This decline was more striking among females than among males [6]. Non-communicable diseases became the principle causes of death throughout the twentieth century, and a female ascendancy arose and extended [3]. Longevity has been associated with occurrence of menopause at a high age and fecundity at an older age [9]. It has been suggested that loss of ovarian hormones instigate immunosenescence which increases mortality and morbidity due to infections and age-related pathologies [3].

N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

Ageing

Ageing is inevitable. In ageing there is a progressive decline or loss of physiological functions at the molecular, cellular and organismal levels [10] leading to increased susceptibility to disease and death [11]. It is the outcome of both environmental and genetic factors, caused by DNA damage and genetic dysregulation [12].

Molecular Causes

Ageing process and increase in the incidence of age-related diseases are closely associated with a decline in mitochondrial function [13]. The mitochondria have a vital role in the ageing process, and age-associated damage may be due to mutagenic damage to nuclear or mitochondrial DNA (mtDNA) [14]. Increase in age-associated accumulation of mtDNA mutations [11] and increased mitochondrial oxidative stress contribute to human ageing [11]. More recent evidence indicate that ageing-associated mtDNA mutations are due to clonal expansion of mtDNA replication errors rather than to damage accumulation [15, 16]. Mitochondrial dysfunction results from clonal expansion of mtDNA mutations [17].

The telomeres have an important role in cell fate and ageing [18]. The telomeres are DNA segments attached to the ends of the chromosomes where the replication enzymes could latch. With each replication, the telomere shortens in all the dividing cells. To compensate for the shortening, the enzyme telomerase adds repeated telomere sequences [19] and reconstructs the telomeres at the chromosome ends [19]. The reconstruction is limited to most somatic cells [18], and most human cells do not maintain sufficient telomerase activity to fully preserve telomeres [20]. The deteriorated telomeres institute a continuous DNA damage response [21] which begins and perpetuates the irreversible growth arrest [22, 23].

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_1

Cellular Senescence

In cellular senescence there is a permanent arrest of cell proliferation [24–27]. It is involved in a number of biological processes and is believed to have important roles in development, tissue repair [26] and susceptibility of tissues to disease [24]. Senescent cells contribute to ageing and age-related diseases [25, 26, 28]. Two types of senescence have been described, telomere-dependent replicative senescence and the other stress-involved premature senescence [25]. When too many critically short telomeres accumulate, cell death (apoptosis) or irreversible growth arrest (cellular senescence) results [18]. Several pathways of cellular senescence have been demonstrated, and telomerase suppression is one such pathway [19].

Physiological and Structural Changes in the Organs

Normal ageing is associated in both physiological and structural changes in the organs and systems. Box 1.1 shows some of the changes that occur in some systems.

Box 1.1. Some Structural Changes with Ageing

Cardiovascular	Cardiac myocytes increase in size, changes in the conducting system, valves sclerosis with calcification, arterial wall thicken with stiffening, endothelial dysfunction
Respiratory	Changes in thoracic cage, airways changes, bronchioles and alveolar ducts
Digestive tract	Neuromuscular degeneration of enteron neurons
Hepatobiliary	Liver volume decreases, decrease in hepatocytes with increase in size of the remaining
Haematopoietic	Dysregulation of mechanisms controlling haemopoiesis occurs
Renal	Renal reserve is reduced with decrease in kidney size and cortical loss
Reproductive	Male: Testicular mass decreases, prostate enlarges Female: Vaginal epithelia thin, cervix shrinks, ovaries become fibrotic
Nervous system	Cerebral atrophy, blood flow reduced, changes in the hippocampus and in white matter
Skin	Structural changes in all structures of the skin
Endocrine	Pancreas: Few morphological changes Thyroid: Number and size of follicles and colloid content decrease, becomes nodular with lymphocytic infiltration
Bone	Structural changes in bone architecture, protein content of bone matrix

Theories of Ageing

Ageing is associated with the gradual loss of function of cells and organs with death as the ultimate outcome resulting from the accumulation of changes over time [29]. Over the years there have been numerous theories on ageing [30]. The evolutionary theories of ageing are now considered by many gerontologists as the basis for the explanation of the ageing process [31]. In humans, modern biological theories can be divided between damage or error theories and programmed theories of ageing, but neither of them are fully satisfactory [32] (Box 1.2). Programmed theories imply that throughout the lifespan from conception, ageing is regulated by biological clocks and deliberately limit their lifespan in order to achieve a direct evolutionary benefit [33, 34]. There are three subcategories, namely, endocrine theory where the biological clocks act through hormones to control the pace of ageing, the programmed longevity theory result from sequential switching on and off of certain genes and the immunological theory, with the immune system programmed to wane leading to increased vulnerability to disease and hence ageing and death [32].

Box 1.2. Theories of Ageing

Programmed theories
- Endocrine theory
- Immunological theory
- Programmed senescence theory

Non-programmed theories (damage theories)
- Wear and tear theory
- Cross-linking theory
- Rate of living theory
- Free radical theory

The thymus may play a significant role in ageing in that, as age advances, it undergoes reduction in size with corresponding reduction in the immune system. This has led to the immune suppression theory. The immune function wanes with age, and the immune system undergoes age-associated changes [35], and the ageing of the immune system is known as immunosenescence. Most of the parameters affected by immunosenescence are largely under genetic control. The genetic component is involved in cell maintenance systems that play an important role in the achievement of longevity. In the elderly alterations occur in the innate/natural and clonotype immunity [36, 37], and the former is largely preserved, whereas the latter reveals appreciable deterioration. These alterations are brought about by the involution of the lymphoid tissue, continuous exposure to a variety of antigens, accumulation of memory/effector T cells and debilitation of the naïve cells [38].

In the course of evolution, the human organism is set to live 40 or 50 years [39]. Presently in a period not foreseen by evolution, the immune system has to be active for longer periods of time. This alterations in the immune system promotes chronic inflammation [40] resulting in damage to the organs late in life which is deleterious for longevity. It is the pathological basis for age-related diseases such as diabetes, cancer, cardiovascular disease and Alzheimer's disease [40]. The pathophysiology of age-related diseases is the result of progressive initiation of inflammatory responses due to continued antigenic stress which involves the immune system throughout life. This immune activity of the innate immune system in later life is evident by the presence of elevated markers of inflammation such as TNF-alpha and interleukin 6(IL-6). The elevation of these markers of inflammation is associated with age-related chronic diseases, disability [41] and death.

Structural damage theories, also referred to as non-programmed ageing theories, are based on evolutionary concepts [33], which suggest that ageing is caused by environmental insults resulting in cumulative damage from the molecular level outwards to the tissues and organs of the body [32]. The lifespan variation between species is explained by differences as to how they resist those processes [33]. The damage theories include the wear and tear theory, cross linking theory, rate of living theory and free radical theory. The wear and tear theory suggests that damage to cells over years eventually wears them out killing them and then the body.

The most widely accepted structural damage theory is the free radical theory of ageing [42]. The term 'free radical' is used to describe any molecule that differs from the conventional molecules in that it has a free electron, a property that makes it to react with normal molecules in a destructive way [43]. They are formed by the cells own metabolic reactions and are also present in the environment [42]. Ageing occurs as a result of the relentless and lifelong attack by these free radicals, derived from oxygen [44] causing damage to the cells which spreads then outwards to involve the tissues and organs.

The mitochondrial electron transport system is constantly generating reactive oxygen species (ROS) [45]. The mitochondrial theory suggests that senescence is the result of damage caused by ROS to the mitochondrial genome in postmitotic cells. Mitochondria are implicated in the fundamental ageing process as well as in the loss of functional characteristics of ageing [46]. In order to ensure mtDNA integrity and mitochondrial function, numerous cellular mtDNAs are wrapped together with proteins and nucleoids to form a shield against ROS and nitrogen species (RONS) [16]. According to Vina et al. [44], all the phenomena expounded by previous theories of ageing such as the loss of immune response, of somatic mutation or catastrophic theory of ageing are explained by these two theories [46].

Other structural damage theories are the molecular cross-linkage theory and somatic DNA damage theory, among others. Not all the DNA damages that are formed in the cells are repaired, for the DNA polymerases and other repair mechanisms cannot keep up with the defects, hence some accumulate [32]. According to the waste accumulation theory, the waste products resulting from normal metabolic processes accumulate and compromises normal cell function.

There has been some debate whether ageing in humans is purposely genetically programmed for living too long creates a evolutionary disadvantage or ageing is non-programmed for there is no such disadvantage [32]. Summarily rejected, programmed ageing is clearly conflicting with the mechanics of the evolution process and is impractical [33]. Recent developments have however strikingly altered this, and programmed mammal ageing now has a better evolutionary basis than non-programmed ageing [33].

Life Expectancy

Life expectancy is the term used to denote the average lifespan of an entire population, and lifespan is the actual length of an individual's life. Life expectancy has increased dramatically, and overall women live longer than men. Today if a man reaches 65, he can reasonably expect to go on to 80 and a woman probably see 84. In Sweden, France, England and Wales, life expectancy at age 85 rose by only 1 year between 1900 and 1960 but by almost 2 years between 1960 and the end of the twentieth century [47].

Certainly, different people age at different rate. Life expectancy is affected by a number of factors, and the significant factors are genetic, gender, diet, life style, exercise and access to health care. In the developed world, the life expectancy will continue to rise, but recent increases in life style diseases such as heart disease, hypertension, diabetes and obesity may slow or reverse this trend. Nevertheless, currently we are living longer. There are a number of reports that ageing has been accompanied by decline in disability at the older ages [46]. Between the years 1980 and 1990, the decline in disability was 0.5–1.0% per year [48], and Liao et al. [49] found a decline of 1.53% per year between 1984 and 1995.

Longevity

The centenarians are increasing in numbers globally [50]. There are different types of ageing, and distinctions must be made between chronological ageing and other forms, namely, biological, social and psychological. Chronological ageing refers to how old the person is. Biological ageing is the physical state as age advances. Social ageing is how the individ-

ual should react socially. The different types may occur singly or in combination and relate to and depict the ageing process.

A study of nonagenarians and centenarians in Switzerland between 1860 and 2001 indicated a strong increase in their numbers as compared to other countries. This was largely attributed to the decline in mortality after the age of 80 as from 1950 [51]. Similarly increasing numbers of centenarians are seen in Japan, New Zealand, France and United States of America [52–54].

Today much research is being done as to why more people are living to their 80s, 90s or 100s. Genes may not be all that matter. There are other factors such as epigenetic, environmental factors and life style factors, and the last furthers longevity at all phases of human development [55]. Proper understanding of the normal age-related changes and their significance is necessary to develop appropriate corrective and remedial strategies. Ageing-related changes must be distinguished from age-related diseases. Ageing-related changes can adversely affect health and functionality (requires therapeutic strategies), predispose to disease (the need for risk evaluation of the older adult) and reciprocally interact with illness resulting in altered disease presentation, response to treatment and outcome.

Socio-environmental factors contribute to the observed decline in mortality and morbidity [47]. Increase in education, nutritional intake, decline in infectious diseases [47], improvement in medical care and better quality of life caused by improved health status have resulted in the overall increase in life expectancy [36]. It is well known that the elderly are susceptible to infectious diseases, autoimmunity and cancer and decreased responsiveness to vaccination directly or indirectly to age-related changes in the immune system [36]. This is also true of age-related diseases such as cardiovascular and neurodegenerative diseases, diabetes and osteoporosis, and in all of these conditions, an immune component is incriminated in their pathogenesis [36].

The development of cancer is almost unavoidable as mammalian organisms age [56]. With advancing age the senescent cells accumulate disrupting the tissue environments and may synergise mutation accumulation increasing the risk of cancer [56]. The increase in frequency of cancer with age may be due to pro-inflammatory status of ageing [57]. This pro-inflammatory condition is referred to as chronic antigenic load which continuously stimulate innate immunity and seems to favour the onset of age-onset diseases such as dementia, atherosclerosis, osteoporosis and neoplasia [57]. With people living longer the frequency of Alzheimer's (AD) and related neurodegenerative conditions increases. Sequential testing by functional magnetic resonance imaging of the brain has shown that the response to tumour necrosis factor inhibitors (TNFi) in patients with rheumatoid arthritis (RA) depends on brain activity [58]. Neuroinflammation has been incriminated in the activation of microglia and astroglia which in turn activate the expression of pro-inflammatory cytokines and chemokines in Alzheimer disease and in a variety of other conditions [59]. Both diseases AD and RA belong to those that accelerate ageing, in those afflicted [36].

Franceschi and Bonafi [60] studied centenarians over a 10-year period to address the biological basis of ageing and longevity. They proposed the term 'inflammaging' for the chronic inflammatory status which characterizes ageing and which is largely under genetic control. They considered inflammaging to be the most important compelling force in age-related pathologies such as dementia, diabetes, atherosclerosis and sarcopenia among others all of which show an inflammatory pathogenesis.

Genetics and Longevity

Very long life beyond 90 years appears to have a strong genetic basis [61]. Genetic factors account for approximately 20–30% of the overall variation in adult lifespan [62, 63, 65, 64]. Genetic influences on lifespan are least before the age of 60 but increase thereafter [62], and heritability is pronounced at the oldest ages [66]. Hjelmborg et al. [62] in a large population-based study of twins in a more than 90-year follow-up found evidence of familial clustering of longevity. A genetic component to longevity was suggested by the clustering of siblings and families with long-lived people.

New research by scientists at the Albert Einstein College of Medicine of Yeshiva University found that the gene variant linked to living a long life – to 90 and beyond – also helps them to retain their memories and think clearly [67]. The 'longevity gene' has been linked with exceptionally long life. According to the researchers, the gene variant alters the cholesterol ester transfer, and this effect may protect against dementia as well as promote longevity [67]. Insulin-like growth factor-1 (IGF-1) affects particularly every cell type in the body, and animal studies have shown that mutations of the genes involving IGF-1 signalling pathway impaired growth but affected longer lifespan [67]. The investigators also reported that female children of centenarians had 35% higher IGF-1 plasma levels than the controls. They concluded that by interfering with IGF-1 signalling, these gene mutations may play a role in extending human lifespan [67]. There are other genetic pathways which may through effects on ageing increase the lifespan, and these include those that affect telomere length, those that regulate DNA repair and nuclear structure, those that regulate cellular stress such as sirtuins and possibly those that regulate inflammatory response [68]. Longevity is associated with some environmental and life style factors interacting with genetic factors [65]. In a population, survival variations among individuals are affected by life style, social and cultural effects [65].

Diet and Longevity

Anti-inflammatory dietary intervention is an important avenue towards promoting healthy ageing, and the aim of this exercise is to diminish innate immune response that contributes to chronic diseases [69]. Rees et al. [70] used a placebo-controlled study design with multiple doses of an EPA-rich fish oil concentrate (EPA, a n-3 fatty acid – eicosapentaenoic acid). The editorial concluded that the *anti-inflammatory dietary intervention* does have a role in promoting healthy ageing, but such interventions should be evaluated for risks.

Dan Buettner [71] in his book *The Blue Zones* recorded five locations in the world with the highest percentage of centenarians, and the five blue zones were Okinawa (Japan), Icara (Greece), Loma Linda (California), Sardinia (Italy) and Nicoya (Costa Rica). He suggested nine life style solutions, namely, physical activity, relieving stress, participation in a religious community, reduction in calories, drinking red wine in moderation, family priority, have a defined goal or purpose and a diet based on beans, whole grains and vegetables.

The most researched study on increasing longevity is dietary restriction. Fairman et al. [72] published evidence of *dietary restriction and low ratio of protein to carbohydrate* extended longevity in malarial vectors. The hormone fibroblast growth factor 21 (FGF21) is increased by diets low in protein and high in carbohydrates in mice, and mice with elevated levels of FGF21 lived longer [73]. Several studies among the elderly have shown that the overall *Mediterranean diet pattern* is associated with longer survival and is more important than single nutrients [74]. Trans fats from partially hydrogenated vegetable oils which is strongly associated with risk of heart disease are absent in traditional Mediterranean diets (MDs) [75]. The traditional MDs include a high intake of cereals, legumes, nuts, vegetables and fruits; a relatively high fat mostly provided by olive oil (it allows the consumption of large quantities of vegetables as legumes in the form of salads and cooked food) [75]; moderate to high fish, low red meat and meat products; moderate alcohol, red wine; and moderate to small amounts of dairy products [76].

Key Points

In ageing there is a progressive decline or loss of physiological functions that occurs at the molecular, cellular and organismal levels [10] leading to increased susceptibility to disease and death [11].

The telomeres have an important role in cell fate and ageing [18].

When too many critically short telomeres accumulate, cell death (apoptosis) or irreversible growth arrest (cellular senescence) results [18].

In humans modern biological theories can be can be divided between damage or error theories and programmed theories of ageing, but neither of them are fully satisfactory [32].

Genetic factors account for approximately 20–30% of the overall variation in adult lifespan [62, 63, 64, 65], and genetic influences on lifespan are least prior to the age of 60 but increase thereafter [62].

Several studies among the elderly have shown that the Mediterranean diet pattern is associated with longer survival and is more important than single nutrients [74].

The most researched to increase longevity is dietary restriction [72], published evidence of dietary restriction and low ratio of protein to carbohydrate extended longevity.

Multiple Choice Questions (MCQs)

1. The following are true relating to ageing process, *except*:
   A. The telomeres have an important role in cell fate and ageing.
   B. To compensate for the shortening, the enzyme telomerase reconstructs the telomeres at the chromosome ends.
   C. Age-associated damage may be due to mutagenic damage to nuclear or mitochondrial DNA.
   D. Telomerase suppression is the only pathway of cellular senescence.
2. The following statements are true regarding theories of ageing, *except*:
   A. The evolutionary theories of ageing are no longer considered as the basis for the explanation of the ageing process.
   B. In humans modern biological theories can be can be divided between damage or error theories and programmed theories of ageing.
   C. Ageing occurs as a result of the relentless and lifelong attack by these free radicals derived from oxygen.
   D. In the immunological theory, the immune system is programmed to wane leading to increased vulnerability to disease and hence ageing and death.
3. The following are true in relation to longevity, *except*:
   A. A genetic component to longevity is suggested by the clustering of siblings and families with long-lived people.
   B. Genetic factors account for approximately 40–50% of the overall variation in adult lifespan.
   C. Several studies among the elderly have shown that the overall Mediterranean diet pattern is associated with longer survival.

D. In mice the fibroblast growth factor 21 (FGF21) is increased by diets low in protein and high in carbohydrates and those with elevated levels of FGF21 lived longer.

Answers to MCQs

1. D
2. A
3. B

References

1. Grignolio A, Franceschi C. Aging/senenscence. History of research into aging/senescence. doi: https://doi.org/10.1002/9780470015902.a0023955. Accessed 9 Apr 2017.
2. Radford B. Human lifespans nearly constant for 2,000 years. http://www.livescience.com/10569-human-lifepans-c0nstant-2-000-years.html. Accessed 30 Mar 2017.
3. Ostan R, Monti D, Gueresi P, Bussolotto M, Franceschi C. Gender, aging and longevity in humans: an update of an intriguing/neglecting scenario paving the way to a gender-specific medicine. Clin Sci. 2016;130(19):1711–25.
4. Pahl KP. Life expectancy in ancient and modern man. Acta Anthropogenet. 1981;5(2):119–28.
5. Rowbotham P, Clayton J. An unsuitable and degraded diet? Part three: Victorian consumption patterns and their health benefits. J R Soc Med. 2008;11:454–62.
6. Bacci L. Longevita Vecchiala Salute. In: Salvini S, editor. La differenza di genere nella longevita: si attenua il vantaggio delle donne. Firenze: Neodemos; 2015. p. 34–8.
7. Boldsen JL, Paine RR. The evolution of human longevity from the Mesolithic to the Middle Ages: an analysis based on skeletal data. http://www.demogr.mpg.de/Papers/Books/Monograph2/the%20evolution.htm. Accessed 30 Mar 2017.
8. Jose MV, Bogaro R. Universal history of mortality. Salud Publica Max. 1989;31(1):3–17.
9. Gagnon A, Smith KR, Tremblay M, Vezina H, Pare PP, Desjrdins B. Is there a trade-off between fertility and longevity? A comparative study women from three large historical data bases accounting for mortality selection. Am J Hum Biol. 2009;4:533–40.
10. Campisi J. Aging cellular senescence and cancer. Annu Rev Physiol. 2013;75:685–705.
11. Lee HC, Wei YH. Mitochondria and aging. Adv Exp Med Biol. 2012;942:311–27.
12. Cellular senescence and pathways in aging. http://wwwrnds-systems.com/research-area/celllar-senescence-and-pathways-in-aging. Accessed 7 Apr 2017.
13. Seo AY, Joseph A-M, Dutta D, Hwang JCY, Aris JP, Leeuwenburgh C. New insights into the role of mitochondria in aging: mitochondrial dynamics and more. J Cell Sci. 2010;123(15):2533–42.
14. Kaeberlein M. Molecular basis of ageing. EMBO Rep. 2007;8(10):907–11.
15. Braticc A, Larsson NG. The role of mitochondria in aging. J Clin Invest. 2013;123(3):951–7.
16. Gaziev AI, Abdullaev S, Podlutsky A. Mitochondrial function and mitochondrial DNA maintenance with advancing age. Biogerontology. 2014;15(5):417–38.
17. DeBalsi KL, Hoff KE, Copeland WC. Role of the mitochondrial DNA replication machinery in mitochondrial DNA mutagenesis, aging and age-related diseases. Ageig Res Rev. 2017;33:89–104.
18. Aubert G, Lansdorp PM. Telomeres and aging. Physiol Rev. 2008;88(2):557–79.
19. Oshimura M, Barrett JC. Multiple pathways to cellular senescence: role of telomerase repressors. Eur J Cancer. 1997;33(5):710–5.
20. Shay JW, Wright WE. Senescence and immortalization: role of telomeres and telomerase. Carcinogenesis. 2005;26(5):867–74.
21. Rodier F, Campisi J. Four faces of cellular senescence. JCB. 2011;192(4):547. https://doi.org/10.1083/jcb.201009004.
22. D'Adda di Fagagna F, Reaper PM, Clay-Farrace L, Fiegler H, Carr P, et al. A DNA damage checkpoint response in telomere-initiated senescence. Nature. 2003;426:194–8.
23. Herbig U, Jobling WA, Chen BO, Chen DJ, Sedivy JM. Telomere shortening triggers senescence of human cells through a pathway involving ATM, p53 and p21(CiP1), but not p16 (INK4a). Mol Cell. 2004;14:501–13. https://doi.org/10.1016/S197-2765(04)00256-4.
24. Burton DGA. Cellular senescence ageing and disease. Age (Dordr). 2009;31(1):1–9.
25. Sikora E, Bielak-Zmijewska A, Mosieniak G. Cellular senescence in ageing, age-related diseases and longevity. Curr Vasc Pharmacol. 2014;12(5):698–706.
26. Van Deursen JM. The role of senescent cells in ageing. Nature. 2014;508:439–46.
27. R&D Systems. Cellular senescence and pathways of ageing. https://www.rndsystems.com/research-area/ce;;u;ar-senescence-and-pathways-in-aging. Accessed 3 Oct 2017.
28. Childs BG, Durik M, Baker DJ, van Deursen JM. Cellular senescence in aging and age-related disease: from mechanisms to therapy. Nat Med. 2015;21(12):1424–35.
29. Harman D. Aging: a theory based on free radical and radiation chemistry. J Gerontol. 1956;11:298–300.
30. Medvedev ZA. An attempt at a rational classification of the theories of ageing. Biol Rev. 1990;65:375–98.
31. Bourg EL. A mini-review of the evolutionary theories of aging. Is it time to accept them. Demographic Res. 2001;4:1–28. Article 1. https://doi.org/10.4054/DemRes.2001.4.1.
32. Jin K. Modern biological theories of aging. Aging Dis. 2010;1(2):72–4.
33. Goldsmith TC. Modern evolutionary mechanics theories and resolving the programmed/non-programmed aging controversy. Biochemistry (Mosc). 2014;79(10):1049–55.
34. Goldsmith TC. Solving the programmed/non-programmed aging conundrum. Curr Aging Sci. 2015;8(1):34–40.
35. Aw D, Silva AB, Palmer DB. Immunosenescence: emerging challenges for an aging population. Immunology. 2007;120(4):435–46.
36. Burkle A, Caselli G, Franceschi C, Mariani E, Sanoni P, Santoni A, et al. Pathophysiology of ageing, longevity and age related diseases. Immun Ageing. 2007;4:4. https://doi.org/10.1186/1742-4933-4-4.
37. Vasto S, Caruso C. Immunity & aging: a new journal looking at ageing from an immunological point of view. Editorial. Immun Aging. 2004. http://www.immunityageing.com/content/1/1/1. Accessed 27 Oct 2010.
38. Moro-Garcia MA, Monso-Arias R, Lopez-Larrea C. Molecular mechanisms involved in the aging of the T-cell immune response. Curr Genomics. 2012;13(8):589–602.
39. Licastro F, Candore G, Leo D, Porcellini E, Colonna-Romano G, Franceschi C, et al. Innate immunity and inflammation in aging: a key for understanding age-related diseases. Immun Aging. 2005;2:8. https://doi.org/10.1186/1742-4933-2-8.
40. Oishi Y, Manabe I. Macrophages in age-related chronic inflammatory diseases. Aging Mechanisms Dis. 2016;2:16018. https://doi.org/10.1038/npjamd.2016.18.
41. Singh T, Newman AB. Inflammatory markers in population study in aging. Aging Res Rev. 2011;10(3):319–29.
42. MacWilliam L. Modern theories of aging. www.macwilliam.net; 2002.
43. Theories of aging. www.ancognitive.com/node/3696. Accessed 3 Oct 2017.

44. Vina J, Borras C, Miquel J. Theories of ageing. IUBMB Life. 2007;59(4–5):249–54.
45. Boveris A, Chance BC. The mitochondrial generation of hydrogen peroxide. General properties and effect of hyperbaric oxygen. Biochem J. 1973;143:707–16.
46. Miquel J, Economos AC, Fleming J, Johnson JE Jr. Mitochondrial role in cell ageing. Exp Gerontol. 1980;15:575–91.
47. Costa DL. Causes of improving health and longevity at older ages: a review of the explanations. Genus. 2005;61(1):21–38.
48. Cutler DM, Richardson E. Measuring the health of the United States population. Brookings papers on economic activity. Microeconomics. 1997;1997:217–71.
49. Liao Y, McGee DL, Cao G, Cooper RS. Recent changes in the health status of the older US population: findings from the 1984 and 1994 supplement on aging. J Am Geriatr Soc. 2001;49(4):443–9.
50. Larkin M. Centenarians point the way to healthy aging. Lancet. 1999;353(9158):1074. https://doi.org/10.1016/S0140-6736(05)76437-0.
51. Robine JM, Paccaud F. Nonagenarians and centenarians in Switzerland,1860–2001: a demographic analysis. J Epidemiol Community Health. 2005;59(1):31–7.
52. Robine JM, Saito Y, Jagger C. The emergence of extremely old people: the case of Japan. Exp Gerontol. 2003;38(7):735–9.
53. Wilkinson TJ, Sainsbury R. The association between mortality and morbidity and age in New Zealand's oldest old. Int J Aging Hum Dev. 1998;46(4):333–43.
54. Ankri J, Pomparo M. Prevalence and incidence of dementia among the very old. Review of literature. Rev Epidmiol et de Sante Pblique. 2003;51(3):349–60.
55. Govindaraj D, Atzmon G. Brazilai N. Genetics, lifestyle and longevity: lessons from centenarians. Appl Transl Genom. 2015. http://di.org/10.1016/j.atg.2015.01.001. Accessed 12 Apr 2017.
56. Campisi J. Cancer aging and cellular senescence. In Vivo. 2000;14(1):183–8.
57. Vasto S, Candore G, Balistreri CR, Caruso M, Colonna-Romano G, Grimaldi MP, et al. Inflammatory networks in ageing, age-related diseases and longevity. Mech Ageing Dev. 2007;128:83–91.
58. Rech J, Hess A, Finzel S, Kreitz S, Sergeeva M, Englbrecht M, et al. Association of brain functional magnetic resonance activity with response to tumour necrosis factor inhibition in rheumatoid arthritis. Arthritis Rheum. 2013;65(2):325–33.
59. O'Callaghan JP, Sriram K, Miller DB. Defining "neuro-inflammation". Ann N Y Acad Sci. 2008;1139:318–30.
60. Franceschi C, Bonafe M. Centenarians as a model for healthy aging. Chem Soc Trans. 2003;31(2):457–61.
61. Newman AB, Murabito JM. The epidemiology of longevity and exceptional survival. Epidemiol Rev. 2013;35(1):181–97.
62. Hjelmborg JB, Iachine I, Skytthe A, Vaupel JW, McGue M, Koskenvuo M, et al. Genetic influence on human lifespan and longevity. Hum Genet. 2006;119:312–21.
63. Herskind A, McGue M, Holm N, Sorensen T, Harvald B, Vaupel J. The heritability of human longevity: a population-based study of 2972 Danish twin pairs born 1870-900. Hum Gent. 1996;97:319–23.
64. Skytthe A, Pedersen N, Kaprio J, Stazi M, Hjelmborg J, Iachine I, et al. Longevity studies in GenomEUtwin. Twin Res. 2003;6(5):448–55.
65. Dato S, Rose G, Crocco P, Monti D, Garagnani P, Franceschi C, et al. The genetics of human longevity: an intricacy of genes, environment, culture and microbiome. Mech Ageing Dev. 2017;165(Pt B):147–55.
66. Brooks-Wilson AR. Genetics of healthy aging and longevity. Hum Genet. 2013;132(12):1323–38.
67. Barzalai N, Suh Y, Atzmo G, Cho M-O. Einstein researchers discover gene mutations linked to longer life spans. http://wwweonstin.yu.edu/news/releases/178/einstin-researchers-discover-gene-mutations-linked-to-longer-lif-spans. Accessed 12 Dec 2016. Based on Hippocrates' system of four humours.
68. Browner WS, Kahn AJ, Ziv E, Reiner AP, Oshima J, Cawthon RM, Hsueh WC, et al. The genetics of longevity. Am J Med. 2004;117(11):851–60.
69. Stephensen CB, Kelley DS. The innate immune system: friend or foe. Editorial. Am J Clin Nutr. 2006;83(2):187–8.
70. Rees D, Miles EA, Banerjee T, Wells SJ, Roynette CE, Wahle KW, et al. Dose-related effects of eicosapentaenoic acid on innate immune function in healthy humans: a comparison of young and older men. Am J Clin Nutr. 2006;83:331–42.
71. Buettner D. The blue zone solutions: eating and living like the World's healthiest people. Washington, DC: Published National Geographic; 2015.
72. Fairman R, Solon-Biet SM, Sullivan M, Lehmann T. The contribution of dietary restriction to extended longevity in the malaria vector Anopheles coluzzi. Parasites Vectors. 2017;10:156. https://doi.org/10.1186/s13071-017-2088-6.
73. Solon-Biet SM, McMahon AC, Ballard JW, Ruohonen K, Wu LE, Cogger VC, et al. The ratio of macronutrients, not calorie intake, dictates cardiometabolic health, aging and longevity in ad libitum-fed mice. Cell Metab. 2014;19(3):418–30.
74. Trichopoulou A. Mediterranean diet: the past and the present. Nutr Metab Cardiovasc Dis. 2001;11(4 Suppl):1–4.
75. Willet WC. The Mediterranean diet: science and practice. Public Health Nutr. 2006;9(1A):105–10.
76. Estruch R, Salas-Salvado J. Towards an even healthier Mediterranean diet. Nutr Metab Cardiovasc Dis. 2013;23(1):1163–6.

End-of-Life Care in Geriatric Population

2

Gary Cheuk and Nages Nagaratnam

Historical Perspective

Over the years there have been striking changes in end-of-life situations [1] such as death with dignity, hospice, palliative care, right to die, physician-assisted death and euthanasia brought about by evolving health systems [1]. End-of-life decisions have become increasingly complex [2] and often involve consideration of psychosocial, spiritual, legal or medical factors [3]. In the Western world, the principle of individual autonomy and informed consent are paramount, whereas in other cultures, the community decision-making is the standard [3]. Since the 1970s the 'right-to-die' movement gained ground and influenced end-of-life care decisions [4]. There is a range of views on euthanasia and assisted suicide. The Netherlands and Belgium legalized euthanasia and assisted suicide in 2002 [5]. In Germany and Switzerland, assisted suicide is allowed under certain circumstances. In France it is against the law [5]. Any constitutional right of terminally ill patients to physician-assisted suicide was without exception rejected in 1997 by the United States Supreme Court [6] and likewise in the Washington v Glucksberg case [7]. In five states however doctors are allowed to provide lethal dose of medicine to the terminally ill [5]. Australian governments continue to resist legalizing euthanasia and assisted suicide [8].

The literature abounds with description of different resuscitation methods. Expired air respiration had been described in the Bible [9], and it was not until 1744 when Tassach revived a coal miner by this technique [10]. The American Indians introduced smoke and Dutch tobacco fumes into the rectum, to stimulate ventilation, and the ancient Chinese immersed their dying victims in hot oil baths [11]. In the sixteenth century, artificial respiration began and progressed with rise and fall of mouth-to-mouth method and ended up in 1958 with confirmation of the supremacy of this technique [12]. Mechanical ventilation using bellows was used in the sixteenth century [9], and by the nineteenth century, both were abandoned. In 1792 James Curry used electrical defibrillation successfully to revive two patients [13]. The history of cardiopulmonary resuscitation (CPR) evolved over many centuries. In 1874 open-chest cardiac massage began and gained ascendancy [12]. It was only after the landmark paper of Kouwenhoven in 1960 that modern technique of CPR [9], an effective means of ventilation, closed-chest cardiac massage, and external defibrillation of the heart, was established [11].

General Considerations

'End -life is defined as the time when health care providers would not be surprised if death occurred within about six weeks' [14]. End-of-life care not only includes terminal care but also, more widely, all conditions that have become progressive and incurable. Terminal care is care of a person in his or her final hours or days before death occurs [15]. The Göteborg H70 longitudinal study of ageing and other studies showed that those who die between 70 and 85 years of age generally were very ill in the months or years before death. In contrast, individuals who live more than 85 years were seen as what has been described as in 'physical, social and mental vitality or healthy ageing' [16]. This would suggest that the oldest old are generally well with a rapid decline compared to the younger who die earlier.

Profile of People of Advanced Age

Risk factors for institutionalization are many, and a large number of the oldest old are in nursing home facilities. In a study of 103 patients aged 90–99 years with an average age of 92 years

G. Cheuk (✉)
Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia
e-mail: gcheuk@optusnet.com.au

N. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_2

and a male to female ratio of 1:3, 55% of the patients hospitalized were from nursing care facilities, and 45% either lived by themselves or with their spouses/relatives who may be their carers [17]. For a female aged 90 or over, the probability of entering a nursing home is 95% and for men 60% [18]. In a retrospective analysis of the profile of people of advanced age, Zhao et al. [19] found that functional and cognitive impairments were higher for those who died around 90 years or older (especially women) compared with those who died aged 85–89 years. Physical impairments and functional limitations have a considerable impact on daily life activities. Disability on activities of daily living (ADL) and instrumental activities of daily living rose from 59.1% before to 85.4% after the age of 90 and cognitive impairment (Mini-Mental State Examination score < 21) from 41.7% to 69.4%, respectively. In spite of the close proximity to death, 60.5% and 67% rated their health positively [19]. The Danish 1905 cohort study involving 2249 nonagenarians found that a high disability level, poor physical and cognitive performance and self-rated health (especially women) predict mortality [20]. Functional and cognitive assessments are an important part of the evaluation of the oldest old. These two studies demonstrated that in the oldest old, physical and cognitive disability predicts mortality, and such factors as smoking and obesity have little relevance.

Although the rates of chronic disease was high in the oldest old, the Newcastle 85+ cohort study found that overall 20%, particularly men, had no difficulty with ADLs, but a substantial proportion require 24-hour care at home or nursing home [21]. In a Swedish study, the ELSA 85 project, a population-based survey of 85-year-olds showed the majoirty have good functional ability and are low users of health care [22].

Chronic Conditions and Mortality in the Oldest Old

In a review of forensic autopsies in 310 patients aged >90 years, the investigators found in 85% death was natural, and the more common causes were ischaemic heart disease (23%), bronchopneumonia (12%), fractures (9%), acute myocardial infarction (8%), cerebrovascular accident (6%) and ruptured aneurysm (5%) and in 19% multifactorial. In 15% the causes were unnatural, and the commonest cause was accident [23]. In another clinical and necropsy study of octogenarians, nonagenarians and centenarians, the cause of death was cardiac (47%), vascular noncardiac (14%) and noncardiac nonvascular (39%) [24]. Deaths due to noncardiac nonvascular causes increased with increasing age [24]. In Australia one-third (seven million) of the population was reported as having at least one of the following chronic conditions, asthma, type 2 diabetes, coronary heart disease, arthritis, osteoporosis, COPD, stroke and hypertension and proportion increased with age [25].

Critical Ill in the Oldest Old

Studies of critically ill oldest old patients (>90 years) admitted to the intensive care unit (ICU) found that very old age was not directly associated with ICU mortality [26]. Death occurred predominantly around 30 days after ICU discharge though higher compared to younger patients, despite the higher risk of dying, ICU care should not be denied to this population [26].

Transition in Place of Care

Data on the oldest old transitions in place of care at end of life are scanty. In a recent study [27], the place of residence or care of the over 85-year-olds less than a year before death and their place of death were examined. It revealed that two-thirds were living in the community when interviewed less than a year before death and less than one-third who had lived at home died there. Care homes were the usual place of death in the majority of people living there (77% in residential homes and 87% in nursing homes), and 15% of deaths in acute hospital came from care homes [27]. In the United States among the people who preferred to die at home, 55% died in the hospital [28]. This was largely attributed to the practice patterns at the hospital [29].

There have been several studies questioning the quality of care in this age group. Rosenwax and colleagues [30] in their study found that 96% of the patients (aged <65 to >75 years) were admitted to hospital during the last year of life with an average of eight admissions. Most of the admissions were during the last 3 months of life and 60% died in hospital. In the age group 75 years or over, 58% had cancer and 42% had non-cancer conditions. Of the patients in their study, 70% of those found suitable for palliative care had at least one visit to the emergency department [30].

End-of-Life Decisions

Current demographic findings predict an increase in the elderly population, more so the very elderly, and this trend is likely to continue. This means there will be greater rates of cognitive decline which strongly require increased awareness of end-of-life decisions and advanced care planning [31]. Many of the older adults do not give thought as to how to handle their end-of-life care [28], and this has led to greater reliance on the primary care providers and medical practitioners when end-of-life decisions are made [32]. End-of-life decisions in Australian medical practice involving active medical practitioners from all Australian states and territories with opportunities to make end-of-life decisions had been studied. It was found that medical end-of-life deci-

sions were made in 30% of all Australian deaths with the explicit intention of ending the patient's life of which 4% were in response to a direct request from the patient [33].

With the advance in medical knowledge and technology over the past few decades, health professionals are confronted with difficult and complex ethical dilemmas. Prager [34] enunciated four principles of medical ethics, 'to do good and don't do bad', patients with capacity have the right to refuse or consent as to their health needs, concerns about the allocation of health-care resources and the respect for the sanctity of human life.

Majority of the elderly would like to be involved in the choice to influence decisions about their care, place of care and cardiopulmonary resuscitation (CPR) [35]. There are three situations that may raise ethical issues. Typically the ethical issues for the elderly include (i) decision-making for those with and without the capacity, (ii) the right to prepare advance directives prior to the advent of incompetency and (iii) the right to use or refuse life-sustaining technologies [36].

(i) The incapacitated patient

Standards of substituted judgement, best interests and advance directives are three existing methods of surrogate decision-making [37, 38]. All of them have limitations [38, 39]. Substituted judgement requires the surrogate to approximately match patients' wishes had he or she were capable of making decisions [39, 40] and would have some insight into patient's preferences when patients' decision-making capacity was intact [39]. The elderly preferred family members as surrogate decision-makers [41] who often have difficulty in making decisions. It is advantageous if the surrogate decision-maker is known ahead and had discussed with the patient his or her preferences [42].

To test patients' preferences by surrogate decision-makers, Uhlmann et al. [43] in their study found that physicians and spouses often did not understand elderly outpatients' resuscitation preferences. In another study neither the physicians nor nurses systematically understood their elderly patient's resuscitation preferences [44]. Hence it is most unlikely that surrogate decision-makers will render proper substituted judgements [43]. There is convincing evidence that the use of substituted judgement has overwhelming weaknesses [8, 40, 45].

Best interest standard expects the surrogate to settle upon a decision which advances patient's best interests and which is what most sensible people would select [46]. Both substituted judgement and best interest standards have problems because of the practical difficulty in obtaining sufficient evidence of patient preferences [39]. In their interpretation of best interests, surrogate decision-makers tend to rely on their own religion and values whereas physicians on the clinical conditions [47].

In the absence of an advance directive – a living will or a power of attorney for health care – the task becomes more arduous than many would think. The number of Australians aged over 65 years is expected to double and the number aged over 85 years is expected to triple by 2040 from 2012 [48]. 227,300 Australians are diagnosed with dementia according to statistics at 2008 [49]. About 45% of the patients with dementia are in nursing homes. The progression of dementia over many years has been categorized as mild, moderate or severe. The clinical picture of Alzheimer's dementia may vary from mild impairment of memory to severe loss of intellectual function, and it is the severity of the dementia that determines the ability to make competent decisions. This means that not everyone with the diagnosis of Alzheimer's disease is severely incapacitated [50] and it must not necessarily be presumed that the elderly with Alzheimer's disease is incapable of providing informed consent [51] indent. The physician must determine whether the patients' preserved cognitive abilities are sufficient for him or her to make satisfactory discernment in relation to the particular point at issue [52]. Even in cases of disputable competency, it is important in patients with Alzheimer's disease to distinguish these areas that maintain competency from those areas in which they do not [51].

(ii) Advanced care directives (ACD) allows individuals ways to exercise their health-care preferences should they become incompetent to make decisions in the future. An important aspect of ACD is the issue of decision-making capacity, that is, the ability to understand the nature and consequences of the decision to be made and to communicate that decision in some way [31]. Another issue is that decision-making should be informed, providing factual information and determining the ability to understand the information provided. The general principles governing informed decision-making for medical treatment or for its refusal also apply to ACD [31].

There are two types of directives: (a) instrumental directives also referred to as living wills or end-of-life instructions and (b) proxy directives also referred to as power of attorney for health care. The living will is a voluntarily created document that declares patient's intention and signed by the patient and witnessed by two adults. The living will not be binding unless the physician caring for the patient's care certifies that death is imminent and death-delaying procedures will only prolong the dying process [53]. The proxy directive, the durable power of attorney for health care, is a document where the patient can designate a surrogate. The surrogate has the legal right and responsibility to make decisions on patient's health care which include initiation and termination of medical procedures and life support systems, among others [53].

Best way to ensure that the patient's desires concerning medical treatment will be respected is a combined document which includes both a living will and power of attorney for health care [54]. An advance directive only comes to effect when the individual is incompetent to make health-care decisions and the competent individual can change or destroy their advanced directive at any time [55].

(iii) With the availability of advance technologies such as mechanical ventilators, kidney dialysis, artificial nutrition and hydration, advance and complex resuscitative techniques among others pose serious personal decisions. Patients and physicians are responsible for medical end-life-decisions.

Cardiopulmonary Resuscitation(CPR) in the Elderly

In the elderly especially those who are disabled and chronically ill, CPR should not be considered as binding as a final endeavour to prolong life whatever the circumstances [56]. Age by itself is not an important determinant of the outcome from CPR but on other factors such as physical and mental function, presence of comorbidities, mechanism of arrest, inactivity and dependency among others [57] (Box 2.1). If ventricular fibrillation/ventricular tachycardia is the presenting rhythm in the elderly survival after out of hospital, cardiac arrest is reasonable [58]. In the nonhospital setting, survival to 1 month after cardiac arrest is less than 5% with rates considerably lower in the elderly with comorbidities [59].

Box 2.1. Indicators of Poor Outcome of CPR in the Elderly

Underlying medical condition
Comorbidities
Mechanism of arrest
Physical disability and mental impairment
Inactivity and dependency
Homebound

Information source: Gordon and Hurowitz [56], Beer [57]

Very often patients and their families have limited understanding of the procedure and overestimate its usefulness [60]. Physicians should not presume their patient's wishes. Physicians can decide which patient is for CPR or who is not after discussion with the family or surrogate decision-maker (Box 2.2) Physicians often do not understand their elderly patients' preferences for resuscitation [43] and do not routinely discuss CPR with their elderly patients [60]. Physicians should communicate and document the usefulness of CPR in the event of cardiac arrest which should be regularly reviewed especially if there is a change in the patient's clinical status [56, 57]. Elderly patients' wishes regarding resuscitation have been found to be inconsistent [57, 60]. Many want CPR, others would want only comfort care especially the very sick inpatients [61], and still others those with severe congestive heart failure do not want to be resuscitated [62]. In one study less than quarter of the patients had discussed preference for CPR with their physicians, and in those who had not discussed their preferences for resuscitation, 58% were not interested in doing so, and 25% did not want resuscitation [63]. In terminal illness CPR is not indicated [64].

Box 2.2. Physician's Role in CPR in the Elderly

Physicians can decide which patient is suitable for CPR or who is not.
Physicians' decision to resuscitate or not to should be made after discussion with family or surrogate decision-maker.
In the vulnerable elderly patient, physicians should estimate, communicate and document the usefulness of CPR in the event of cardiac arrest.
Should discuss with older patients and recognize their decision-making capacity.
Should where appropriate to share responsibility for decisions.
Resuscitation status should be regularly reviewed more so if there is a change in the patient's clinical status.

Information sources: Gordon and Hurowitz [56]; Beer [57]

Artificial Nutrition and Hydration

One of the most difficult decisions to make by the physician and family members is the decision about artificial nutrition and hydration. Artificial nutrition and hydration constitutes a form of medical care [65]. Severely demented patients need only care to make them comfortable. Although bioethical literature argues that feeding tubes are not mandatory [66, 67], some families will entreat or demand life-sustaining treatment like placement of feeding tubes. Some surrogate decision-makers and family members because of their religious beliefs or other personal reasons, dictate that sustenance must never be withheld [68, 69]. In patients with advanced dementia with difficulty in swallowing or refusal of food or water by mouth, the decision sometimes is made to insert a feeding tube [70], and the use of percutaneous endoscopic

gastrostomy (PEG) tubes has increased in frequency. Many opt for feeding tubes with the belief it will prolong life and prevent aspiration. Feeding tubes do not solve the problem of aspiration pneumonia because often patients inhale their own saliva and medical evidence questions whether feeding tubes improve the quality of life or even prolong life [71]. However, the decision-makers have to justify that continuing treatment will only add to the patient's ordeal and decidedly override whatever gain he or she may derive from continued life. Rarely subcutaneous fluids (hypodermoclysis) may be tried for patients with severe symptomatic thirst [64].

Intercurrent Illnesses

It is ethically appropriate not to treat intercurrent illnesses in this group of patients except with measures required for comfort [72]. The handling of intercurrent illness in this category of patients should be made prospectively before the onset or threat to life [72]. It is not uncommon for family members or surrogate decision-makers to strongly request or demand that the severely demented patient in the aged care facility is hospitalized for treatment of the intercurrent illness, intensive care and resuscitation. Rather than delegate the responsibility to relative and surrogates, the chronically ill patient should be encouraged to determine their treatment, for example, by advanced directives [73] and physician-patient discussions [74]. It is not unusual for spouses to overestimate patients' preferences [43]. It will be more appropriate to have earlier and more complete discussions of a broad range of options for the care of patients at the end of life [75]. It is not an uncommon practice in intensive care units to withhold or withdraw therapy in patients who are unlikely to survive [76]. It has been advocated that a number of factors should be considered before a decision to withhold or withdraw therapy is made, factors such as medical comorbidities, pre- and post-ICU quality of life, families' wishes and predicted mortality [76]. Morphine and other opioids are used only for specific conditions to relief pain or shortness of breath [64]. General nursing should be strictly adhered to and includes regular attention to general hygiene and mouth care, bowel and bladder care and use of pressure-relieving cushions to prevent skin breakdown [64].

Palliative Care

Palliative care is an active care that improves the quality of life of patients and their families confronted by life-threatening illnesses through control of pain and social, psychological and spiritual problems [15]. Palliative care services should embrace the needs of a wide spectrum of patients, those with multiple chronic symptoms, increasing frailty [77] and other physical, psychosocial vulnerability, and spiritual problems [15, 78, 79]. It should be available in all settings and at any point from diagnosis through to death and to all patients regardless of age, diagnosis and location [80]. The Ontario Coroner stipulated four conditions that has to be satisfied for palliative care interventions to be legal, the care intended solely to relieve suffering, administered in response to suffering or signs of suffering, it must be appropriate with that suffering and it cannot be a deliberative infliction of death, and documentation is essential with progressive increase in the doses [64].

Clinical Relevance

Older patients and their families should be made to understand their preferences in making and acting on the decisive issues.

Typically the ethical issues for the elderly include decision-making, to prepare advance directives and the right to use or refuse life-sustaining technologies [36].

The physician must determine whether the patients' preserved cognitive abilities are sufficient for him or her to make satisfactory discernment in relation to the particular point at issue.

There are two types of directives: (i) instrumental directives also referred to as living wills or end-of-life instructions and (ii) proxy directives also referred to as power of attorney for health care.

Standards of substituted judgement, best interests and advance directives are three existing methods of surrogate decision-making [38].

Medical end-life-decisions may include non-treatment decisions, withholding or withdrawing parenteral hydration and nutrition, relieving pain and the use of drug that might shorten life.

In the elderly especially those who are disabled and chronically ill, CPR should not be considered as binding as a final endeavour to prolong life whatever the circumstances may be [56].

Artificial nutrition and hydration constitutes a form of medical care [65], and severely demented patients need only care to make them comfortable.

Decision-makers have to justify that continuing treatment will only add to the patient's ordeal and decidedly override whatever gain he or she may derive from continued life.

It is ethically appropriate not to treat intercurrent illnesses in this group of patients except with measures required for comfort [72].

The handling of intercurrent illness in this category of patients should be made prospectively before the onset or threat to life [72].

Palliative care services should include a wide spectrum of patients [77].

Multiple Choice Questions (MCQs)

1. In an incapacitated patient, the following are true, *except*:
   A. An advance directive only comes to effect when the individual is incompetent.
   B. Patients and physicians are responsible for medical end-of-life decisions.
   C. It is appropriate not to treat intercurrent illness in severely demented patients.
   D. In advanced dementia, feeding tubes do solve the problem of aspiration pneumonia.
2. The following are indicators of poor outcome of CPR in the elderly, *except*:
   A. Mechanism of arrest.
   B. Physical disability and mental impairment.
   C. Age is an important determinant.
   D. Presence of co-morbidities.

Answers to MCQs

1. D
2. C

References

1. Mackleprang RW, Mackelprang RD. Historical and contemporary issues in end-of-life decisions: implications for social work. Soc Work. 2005;50(4):315–24.
2. Luptak M. Social work and end-of-life care for older people: a historical perspective. Health Soc Work. 2004;29(1):7–15.
3. American Psychological Association. End-of-life issues and care. http://www.apa.org/topics/death/end-of-life.aspx. Accessed 16 Aug 2017.
4. McCormick AJ. Self-determination, the right to die, and culture: a literature view. Soc Work. 2011;56(2):119–28.
5. Guardian staff. Euthanasia and assisted suicide laws around the world. www.theguardian.com/society/2014/Jul/17/euthanasia. Accessed 16 Aug 2017.
6. Mariner WK. Physician assisted suicide and the Supreme Court: putting constitutional claim at rest. Am J Public Health. 1997;87(12):2058–62.
7. Kamisar Y. Foreword: can Glucksberg survive Lawrence? Another look at the end of life and personal autonomy. Mich Law Rev. 2008;106(8):1453–78.
8. McGee A. Why Australia hesitates to legalise euthanasia. the conversation.com/why-australia-hesitates-to-legalise-euthanasia.2015. Accessed 16 Aug 2017.
9. Hurt R. Modern cardiopulmonary resuscitation-not so new after all. J Roy Soc Med. 2005;98(7):327–31.
10. Dagi F. Exhortations to resuscitate in the 18th century. In: Atkinson RS, Boulton TB, editors. The history of anaesthesia. London: RSM Press; 1989. p. 359–67.
11. Hermreck AS. The history of cardiopulmonary resuscitation. Am J Surg. 1988;156. http://www.americanjournalofsurgery.com/article/S0002-9610(88)80521-X/pdf. Accessed 14 Aug 2017.
12. DeBard ML. The history of cardiopulmonary resuscitation. Ann Emerg Med. 1980;9(5):73–5.
13. Curry J. Popular observations on apparent death from drowning, suffocation etc. London: Lae; 1972.
14. American Psychologist Association. End of life care fact sheet. http://www.apc.org/pi/acds/programs/eol/end-of-lifr-factssheet.aspx. Retrieved 30 August 2018.
15. British Geriatric Society. Palliative and end of life care for older people. http://www.bgs.org.uk/index.php/topresources/publication-find/goodpractice/368-palliative.care. Accessed 30 July 2014.
16. Hessler RM, Eriksson BG, Dey D, Steen B. The compression of morbidity debate in aging: an empirical test using the gerontological and geriatric population studies in Goteborg, Sweden (H70). Arch Gerontol Geriatr. 2003;37(3):213–22.
17. Nagaratnam N, Gayagay G Jr. Validation of the cumulative illness rating scale (CIRS) in hospitalized nonagenarians. Arch Gerontol Geriatr. 2007;44:29–36.
18. Liu Z. The probability of nursing home use for a lifetime. Working paper no.16. Australian Institute of Health and Welfare, Welfare Division, Canberra; 1998.
19. Zhao J, Barclay S, Farquhar M, Kinmonth AL, Brayne C, Fleming J, et al. The oldest old in the last year of life: population based findings from Cambridge City over -75s Cohort Study participants aged 85 and older at death. J Am Geriatr Soc. 2010;58:1–11.
20. Nybo H, Petersen HC, Gaist D, Jeune B, Andersen K, McGue M, et al. Predictors of mortality in 2,249 nonagenarians –the Danish 1905-Cohort Survey. JAGS. 2003;51:1365–73.
21. Jagger C, Collerton J, Davies K, Bond J. Capability and dependency in Newcastle 85+ cohort study. Projections on future needs. BMC Geriatr. 2011;11(1):21. https://doi.org/10.1186/1471-2318-11-21.
22. Dong H-J. Health maintenance in very old age. Medical conditions, functional outcome and nutritional status. Linkoping; 2014. www.diva-portal.org/smash/record.jsf?pid=diva2%3A.:703502/dswld=-1817.
23. John SM, Koelmeyer TD. The forensic pathology of nonagenarians and centenarians: do they die of old age? (The Auckland experience). Am J Forensic Med Path. 2001;22:150–4.
24. Roberts W, Shirani J. Comparison of cardiac findings at necropsy in octagenarians, nonagenarians and centenarians. Am J Cardiol. 1998;82(5):627–31.
25. AIHW. Risk factors contributing to chronic disease. Ca.no.PHE157. Canberra: AIHW; 2012.
26. Rellos K, Falagas ME, Vardakas KZ, Sermaides G. Michalopoulos.. Outcome of critically ill oldest-old patients (aged 90 and older) admitted to the intensive care unit. J Am Geriatr Soc. 2006;54(1):110–4.
27. Fleming J, Zhao J, Farquar M, Brayne C, Barcly S, Cambridge City over -75s Cohort(CC75C) Study, et al. Place of death for the oldest old: >85 year olds in the CC75C population –based cohort. Br J Gen Pract. 2010;60(573):171–9.
28. Fink-Samnick E. The evolution of end-of-life care. Ethical implications for case management. Prof Case Manage. 2016;21(4):180–92. https://doi.org/10.1097/NCM.0000000000000159.
29. The Dartmouth atlas of health care. End-of-life care. http://www.dartmouthatlas.org/keyissue.aspx?con=2944.
30. Rosenwax LK, McNamara BA, Murray K, McCabe RJ, Aoun SM, Currow DC. Hospital and emergency department use in the last year of life: a baseline for future modifications to end of life care. MJA. 2011;194:570–3.
31. Cartwright CM, Parker MH. Advance care planning and end of life decision making. Aust Fam Phys. 2004;33:815–8.
32. Institute of Medicine. Dying in America: improving quality and honouring individual preferences near the end of life. Washington, DC: The National Academics Press.
33. Kuhse H, Singer P, Baume P, Clark M, Rickard M. End-of-life decisions in Australian medical practice. Med J Aust. 1997;166(4):191–6.
34. Prager K. As quoted by Leslie Knownlton. Ethical issues in the care of the elderly. Geriartric Times. 2002;3. http://www.geriatrictimes.com/g020301.html. Retrieved 30 Nov 2005.

35. Foley KM. Pain, physician assisted dying and euthanasia. Pain. 1995;4:163–78.
36. Mueller PS, Hook C, Fleming KC. Ethical issues in geriatrics: a guide for clinicians. Mayo Clin Proc. 2004;79:554–62.
37. Stanford Encyclopedia of Philosophy. Advance directive and substituted decision-making. 2009. Platostanfordedu/entries/advance-directives/. Accessed 29 Dec 2017.
38. Tunzi M. A new standard for incapacitated patient decision making: the clinical standard of surrogate empowerment. J Clin Ethics. 2012;23(4):316–30.
39. Docker C. Limitations of the best interests and substituted judgement standards. Dying in dignity. Mensa Sig News J. 3(1). http://www.euthanasia.cc/bi.html. Retreived 26 Dec 2013.
40. Torke AM, Alexander GC, Lantos J. Substituted judgement: the limitations of autonomy in surrogate decision making. J Gen Intern Med. 2008;23:1514–7.
41. High DM. Surrogate decision making. Who will make decisions for me when I can't? Clin Geriatr Med. 1994;10(3):445–62.
42. Kane R. Long term care. In: Encyclopedia of social work. Silver Springs: National Association of Social Workers; 1987. p. 59–92.
43. Uhlmann RF, Pearlman RA, Cain KC. Physicians' and spouses' predictions of elderly patients' resuscitation preferences. J Gerontol. 1988;43(5):M115–21.
44. Uhlmann RF, Pearlman RA, Cain KC. Understanding of elderly patients' resuscitation preferences by physicians and nurses. West J Med. 1989;150(6):705–7.
45. Seckler A, Meier D, Mulvihill M, Paris BE. Substituted judgement. How accurate are proxy prediction? Ann Int Med. 1991;115(2):92–8.
46. Deathright HJ. Culture, medicine, politics and the right to die. Oxford: Westview Press; 1994.
47. Chidwick P, Sibbald R, Hawryluck L. Best interests at end of life: an updated review of decisions made by the consent and capacity Board of Ontario. J Crit Care. 2013;28(1):22–7.
48. Australian Bureau of Stastics. 3222.0-Population Projections, Australia, 2012(base) to 2101. http://www.abs.gov.au/ausstats/abs@.nsf/lookup/3222.0Media%20Release12012%20(base)%20to202101. Accessed 20 August 2018.
49. NSW Health Fact Sheet –Dementia update 1 August 2004.
50. Lowernkoff EL. Legal issues of geriatric patients: competency and decision making, GeriatricTimes. 2005. http://www.cmellc.com/geriatrichmps/g011133.html.
51. Kane MN. Consent and competency in elders with Alzheimer's disease. Am J Alz Dis. 1998;13(4):179–88.
52. Freedman M, Stuss DT, Gordon M. Assessment of competency: the role of neurobehavioural deficits. Review. Ann Int Med. 1991;15:203–8.
53. Ilangovan K. Advanced directives: personalizing your end -of -life care decisions. website: http://www.amsa.org/dd/livingwill.cfm accessed on 4/15/2009.
54. Silverman HJ, Vinicky JK, Gasner MR. Advance directives: implications for critical care. Critical Care Med. 1992;20:1027–31.
55. Canadian Association of Critical Care Nurses. Advanced directives. website: http://www.caccn.ca/en/publiations/position_stateents/ps1999.html. Acessed on 15 Apr 2009.
56. Gordon M, Hurowitz E. Cardiopulmonary resuscitation in the elderly: balancing technology and humanity. Can Med Assoc J. 1985;132:743–4.
57. Beer C. End of life care for the elderly people admitted to hospital. Review. Aust J Ageing. 2004;23:58–62.
58. Bonnin MJ, Pepe PE, Clark PS Jr. Survival in the elderly after out-of-hospital cardiac arrest. Crit Care Med. 1993;21(11):1645–50.
59. Orenstein D. CPR death highlights end of life decision. Brown University News and Events. http://www.brown.edu/press.releases/2013/03/cpr. Accessed 19 June 2013.
60. Frank C, Heyland DK, Chen B, Faquhar D, Meyers K, Iwaasa K. Determining resuscitation preferences of elderly inpatients: a review of the literature. CMAJ. 2003;169(8):795–9.
61. Somogyi-Zalud E, Zhong Z, Lynn J, Hamel M. Elderly persons' last six months of life: findings from the hospitalized elderly longitudinal project. J Am Geriatr Soc. 2000;48:S131–9.
62. Krumholz H, Phillips R, Hamel M, Teno JM, Bellamy P, Breste SK, et al. Resuscitation preferences among patients with severe congestive heart failure. Results from SUPPORT project. Circulation. 1998;98:648–55.
63. Hofmann JC, Wenger NS, Davis RB, Teno J, Connors AF Jr, Derbeins N, et al. Patient preferences for communication with physicians about end-of-life decisions. SUPPORT investigators. Study to understand prognosis and preference for outcome and risks of treatment. Ann Intern Med. 1997;127(1):1–12.
64. Department of Health & Human Services, Tasmania. http://wwwdhhs.tasgov.au/_data/assets/pdf_file/0006/47049/Clinical_Decision_Makers_EOL_Final290909_PLSubComm.pdf. Retrieved 31 July 2014.
65. Weir RF, Gostin L. Decisions to abate life –sustaining treatment for non-autonomous patients: ethical standards and legal liability for physicians after Cruzan. JAMA. 1990;264:1846–53.
66. Lynn J, Childress J. Must patients always be given food and water? In: Lynn J, editor. By no extraordinary means. Bloomington: Indiana University Press; 1986. p. 47–60.
67. Steinbrook R, Lo B. Artificial feeding-solid ground, not a slippery slope. N Engl J Med. 1988;318:286–90.
68. Ouslander JG, Tymchuk AJ, Krynski MD. Decisions about enteral tube feeding among the elderly. J Am Geriatr Soc. 1993;41:70–7.
69. Mitchell SL, Lawson PM. Decision-making has long –term tube-feeding in cognitive impaired elderly people. CMAJ. 1999;160:1705–9.
70. Gillick MR. Rethinking the role of tube feeding in patients with advanced dementia. N Engl J Med. 2000;242:207–10.
71. Senior Journal. Feeding tubes may not help in severe dementia (Alzheimer's)- yet use varies widely. website: http://seniorjournal.com/NEWS/Alzheimer's/3-07%2D%2D7tubes.htm. Accessed on 17 Apr 2009.
72. Alzheimer's Association National Bard of Directors. May 1988. Website: http://www.alz.org/AboutUs/PositionStatements/overview.asp.
73. Corke CF, Lavery JF, Gibson AM. Choosing life support for suddenly severely ill elderly relatives. Crit Care Resusc. 2005;7:81–6.
74. Rosenfeld KE, Wenger N, Kagawa -Singer M. End of life decision making. J Gen Intern Med. 2000;15:620–5.
75. Cherniack EP. Increasing use of DNR orders in the elderly world wide: whose choice is it? J Med Ethics. 2002;28(5):303–7.
76. Ho KM, Liang J. Withholding and withdrawal of therapy in New Zealand intensive care units (ICUs): a survey of clinical directors. Anaesth Intensive Care. 2004;32(6):781–6.
77. The National Council for Palliative Care. The palliative care needs of older people. Briefing bulletin no:14. www.ncpc.org.uk (January 2005).
78. Kite S. Palliative care for older people. Age Ageing. 2006;35(5):459–60.
79. Gatto M. Palliative Care Hartford Institute of Nursing. http://consultgerirn.org/topics/palliative_care /want_to_know_more. Retrieved 20 July 2014.
80. House of Commons Select Committee. Fifth report of session. United Kingdom. 2014-15.

Elderly Abuse and Neglect

3

Kujan Nagaratnam and Nages Nagaratnam

Historical Perspective

Elderly abuse is known to occur for more than a thousand years. The ancient Romans and Greeks and conditions in the mediaeval period recorded that old age was gloomy, and intergenerational support was unpredictable and was severely influenced by economic conditions [1]. Hence in mediaeval times, the common advice to older persons was not to pass their assets to their children too early to avoid abuse [1]. The lives of England's elderly did not improve even after the development of the Poor Laws and workhouses [1]. The first record of elderly abuse was made by British scientists in 1975 who referred to 'granny battering' in their journals [2]. In the United States the National Elder Abuse Incidence Study in 1996 revealed that over half a million Americans over the age of 60 years were victims of elderly abuse [2].

General Considerations

Elderly abuse has been defined as acts directed towards the elderly that results in physical, psychological, sexual abuse and financial exploitation [3] or acts of omissions such as neglect. Elder abuse is a widespread problem [4], and the elderly are particularly prone to abuse and is increasing with the growing elderly population [5]. As many as 2.5 million older people in United States are abused each year [6], and approximately 1 to 2 million Americans aged 65 or older have been abused or neglected [7]. In a review of medical records of veterans, the prevalence of elder abuse/neglect was higher in the 80 years and older and in Caucasian and African American veterans [8]. It frequently goes unrecognised, and there is a lack of awareness of the problem, and even when detected the management can be difficult. A research study in the community in the inner London Borough of Tower Hamlets revealed 84% of general practitioners had a case of elder abuse [9]. In another Scandinavian report, 25% of the general practitioners were aware of patients subjected to verified or suspected elder abuse [10]. About 4% of Australian nurses and little more than half of Canadian nurses had knowledge of some form of elder abuse [11]. Although nurses are able to recognise situations of elder abuse, they are reluctant to act, and this has been attributed to the lack of confidence and knowledge [12]. Women are at higher risk of abuse than men [13]. Highest prevalence have been reported from developed countries with Spain having 44.6% and lower estimates from 13.5% to 28.8% from developing countries [14].

It is only a little over a decade that it is recognised, and its significance confirmed as a social, medical and legal problem in Australian communities [15]. It has generally been estimated, both in Australian and overseas studies, that around 3–5% of the people aged 65 years and over suffer from some type of abuse [16, 17]. The overall prevalence estimated in Western Australia is 0.58% [18]. Elder abuse is associated with increased mortality [19].

Risk Factors

One in four vulnerable elders are at risk of abuse and only a small proportion of them are detected [20]. Risk factors associated with vulnerability among older persons include ageing, poor health, impaired cognition [4, 22] and lack of family, financial and community support. Other risk factors include dependency [23], social isolation, substance abuse, faith-based factors [24], alcohol abuse and history of domestic violence [4]. Elder abuse most commonly occurs in

K. Nagaratnam · N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney,
Sydney, NSW, Australia
e-mail: kujan@nagaratnam.net; nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_3

residential and institutional settings, and those responsible are known to the victim [25] (Box 3.1). The elderly are often abused by the people with whom they live [6]. Abusers are most often family members, and some 90% are committed by a family member [22] including spouses, son, daughter, brother or friend and should be seen in the context of domestic violence. This often extends from psychological neglect to physical violence and causes an enormous burden of suffering. Dependent elders are particularly susceptible to mistreatment [23]. According to Vida et al. [26] in a retrospective review, found that certain situations indicated a higher risk and in their findings included situation of living with non-spouse family, friends or other non-supervised setting. They also recorded widowhood, divorce or separation correlated with abuse. Clinician's reluctance to report victims and their lack of awareness of warning signs are factors for underreporting [27]. Although the reports of elder abuse to official agencies have increased, only 2% of the reported cases are by physicians [28].

Box 3.1. Risk Factors

Ageing, poor health and impaired cognition [4, 22].
Lack of family, financial and community support.
Other risk factors include dependency [23].
Social isolation, substance abuse, faith-based factors [24], alcohol abuse and history of domestic violence [4].
Most commonly occurs in residential and institutional settings [25].

Types of Abuse

Two basic types have been recognised, abuse and neglect. The former is an act of commission with active involvement of the abuser, and the latter, neglect, is used as a general label for acts of omission with only a passive involvement of the abuser [29]. The National Centre on Elder Abuse [7] recognises seven types of abuse, namely, physical, financial, psychological, sexual, social, violation of basic rights and neglect.

Physical abuse

Physical abuse can take various forms such as inflicting pain and injury and includes hitting, slapping, pushing, burning, extreme forms of restraint and sexual assault. It also includes the inappropriate use of restraints or confinement and drugs [30].

Financial abuse

This may include misuse or misappropriation of the elderly person's material, for example, property, money and valuables [31].

Psychological abuse

Psychological abuse has a wide spectrum from verbal insults and humiliation to that of violence, isolation and deprivation [31].

Sexual abuse

Any sexual activity such as involving sex acts, viewing sex acts or disrobing where the elderly person has not given consent or incapable of giving consent is sexual abuse [30].

Violation of basic rights

Older persons have the right to care, participation, independence, dignity and self-fulfilment [32].

Neglect

Neglect includes abandonment and failure to provide adequate food, shelter, clothing and medical or dental care and also prevention of others to provide such care [31]. When a caregiver deliberately or wilfully abdicates his or her duty-bound commitments towards the older persons, it is active neglect [28]. When the caregiver un-wilfully fails to provide [28] due to ignorance concerning accepted caregiver procedures, it is passive neglect.

Identification of Abuse

Awareness of the risk factors and clinical manifestations [27] and a high degree of suspicion will provide early detection of elder mistreatment. Special attention to 'hidden' signals and certain situations may signal high risk [26]. Injury out of proportion to explanation given may signal elder abuse [25, 32]. Avoiding confrontation [33], carer's or relative's defiance of outside intervention, averse to leave older person alone with health professional and increased dependency on the carer of elderly victim or the perpetrator [27] for example, cognitive impairment, stroke; alcoholism, drugs [35] , substance abuse [34] mental illness make them more susceptible[23] should raise suspicion of abuse.

Clinical Evidence

1. Physical mistreatment – injuries [36] (bruises, burns, cuts), bed sores, unusual fractures, marks on wrists (restraint), implausible explanation for injuries [33], etc.
2. Psychological mistreatment – sudden changes in behaviour, fear of speaking for oneself or in the presence of caregiver, fear, shame and embarrassment [36]
3. Financial mistreatment – material abuse, changes in will, large withdrawals or closing of bank accounts [35]
4. Health status [21] – alcohol and history of domestic violence [4]
5. Carer behaviour – threatening remarks, aggressive behaviour, attitude of indifference, problems with alcohol and drugs [35]

Screening and Intervention

Screening is the most important of the primary intervention strategies for the detection of elder abuse [37]. This is followed by thorough abuse assessment, and there are several screening tools [38] and techniques available. The Elder Assessment Instrument (EAI) is suitable for all clinical settings [22]. Fulmer et al. [39] composed and validated the EAI, a 41-item screening tool comprising 7 subscales. A detailed history, thorough physical examination, appropriate laboratory tests and radiological assessment are essential [5] . The specific type of abuse and issues of safety and vulnerability are identified [22].

In Australia according to the Aged Care Act 1997, mandatory reporting for elder abuse only applies to provide residential aged care of incident of alleged or suspected reportable assaults. The latter refers to any unlawful sexual contact with a resident of an aged care home or unreasonable use of force on a resident of an aged care home [40]. Intervention strategies can take a wide range of services. Specific interventions noted are respite care, advocacy and counselling services [41]. Intervention appropriate for addressing the problems arising from abuse may include one or more of the following actions: (i) Once suspected elder mistreatment should be reported to adult protective services [4, 42], (ii) the need for crisis intervention, (iii) clinical strategies to stop abuse include moving the victim into hospital, nursing home and care facility [8], and (iv) decreasing the stress of caregiving and other family stressors in less acute cases [42]. (Algorithm 3.1).

Efforts to Respond to and Prevent Elder Abuse

These include (i) caregiving support, (ii) psychological support for the abused, (iii) self-help groups, (iv) mandatory reporting of abuse to authority, (v) safe houses and emergency shelter and (vi) help lines to provide information and referral [43].

Clinical Relevance

Risk factors associated with vulnerability among older persons include impaired cognition, poor health and lack of family, financial and community support [4, 22].

Abusers are most often family members [22].

Abuse can be physical, financial, psychological, sexual, social or neglect [7].

The primary care physician is in a unique position to detect abuse for he has a long-standing relationship with the patient and knowledge of present and past medical problems.

Elder abuse is often difficult to detect without obvious signs of physical injury.

Physicians and other professionals should have the knowledge, awareness as well as a high index of suspicion of abuse and increased diagnostic vigilance.

Physicians and other professionals should have knowledge of the various forms and indicators of abuse.

Screening is the most important of the primary intervention strategies for the detection of elder abuse [38] followed by thorough abuse assessment.

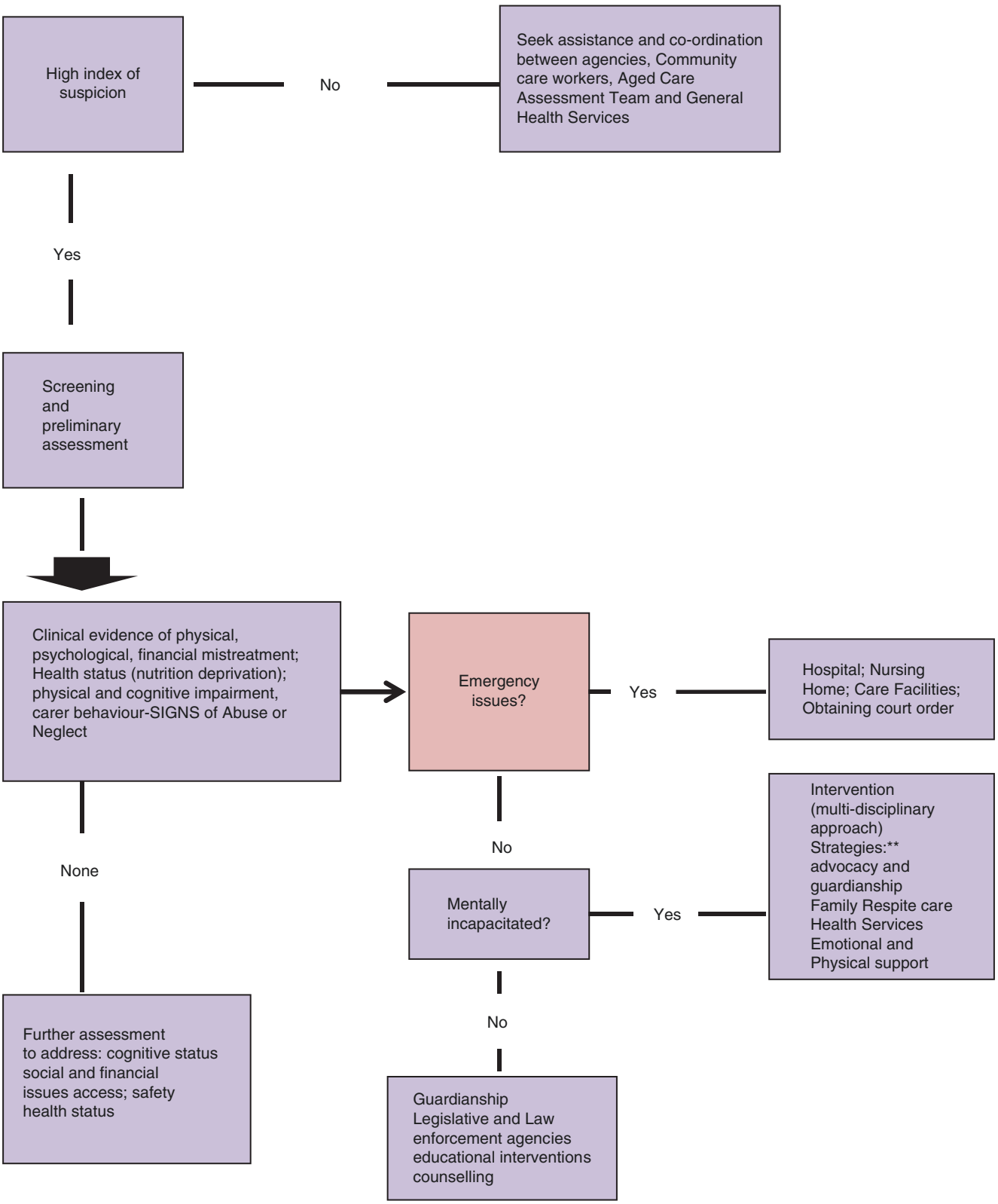
Intervention strategies involve a wide range of services.

Short Answer Questions(SAQs)

1. List five types of elderly abuse.

Answers to SAQ

1. Physical, financial, sexual, neglect and psychological



Algorithm 3.1 Screening of patient suspected of being abused. Special attention to 'hidden' signals and certain situations may signal high risk [26]. Vide identification of abuse (above). (Sources of information: Elderly Crime Victims Resource Center [35], Australian Society of Geriatric Medicine [44], *The Merck Manual of Geriatrics* [45],** James [46], Mills [47], Wolfe [48])

Multiple Choice Questions (MCQs)

1. The following is related to elderly abuse are true, *except*:
   A. Abusers are most commonly family members.
   B. Relatives' defiance of outside interference is a hidden signal of abuse.
   C. Many professional do not find it difficult to comprehend sexual abuse as a form of violence where elderly people are involved.
   D. Elderly men spouses are abused twice as often as elderly wives.
2. The following are 'hidden signals' in the identification of elder abuse, *except*:
   A. Injury out of proportion to explanation given.
   B. Increased dependency.
   C. Abusers are not financially dependent on the victim.
   D. Carers' defiance of outside intervention.

Answers to MCQs

1. C
2. A

References

1. Meridian Aging Project. The history of elder abuse and financial abuse. http://www.meridianaging.com/news/the-history-of%2D%2Delder-abuse-and-financial-abuse . Accessed 20 Jan 2017.
2. Rocketswag. Elderly abuse history. http://www.rocketswag.com/elderly/elderly-abuse/Elderly-Abuse-History.html. Accessed 20 Jan 2017.
3. Capezuti E, Brush BL, Lawson WT 3rd. Reporting elder mistreatment. Gerontol Nurs. 1997;23(7):24–32.
4. Swagerty DL Jr, Takahashi PY, Evans JM. Elder mistreatment. Am Fam Physician. 1999;59(10):2804–8.
5. Chen AL, Koval KJ. Elder abuse: the role of the orthopaedic surgeon in diagnosis and management. J Am Acad Orthop Surg. 2002;10(1):25–31.
6. Kleinschmidt KC. Elder abuse: a review. Ann Emerg Med. 1997;30(4):463–72.
7. National Center for Elder Abuse. Elder abuse prevalence and incidence. Washington, DC: National Center for Elder Abuse; 2005.
8. Moon A, Lawson K, Carpiac M, Spaziano E. Elder abuse and neglect among veterans in Greater Los Angeles: prevalence, types and intervention outcomes. J Gerontol Soc Work. 2006;46(3–4):187–204.
9. McCreadie C, Bennett G, Tinker A. General practitioners knowledge and experience of the abuse of older people in the community: report of an exploratory research study in the inner London borough Tower Hamlets. Br J Gen Pract. 1998;48:1687–8.
10. Saveman BJ, Sandvide A. Swedish general practitioner awareness of older people patients at risk of actually suffering from elder abuse. Scand J Caring Sci. 2001;15:244–9.
11. Trevitt C, Gallagher E. Elder abuse in Canada and Australia: implications for nurses. Int J Nurs tud. 1996;33:651–9.
12. Bond C. Education and multidisciplinary approach are key to addressing elder abuse. Prof Nurse. 2004;20(4):38–41.
13. Wei GS, Herbers JE Jr. Reporting elder abuse: a medical, legal and ethical overview. J Am Med Womens Assoc. 2004;59(4):248–54.
14. Sooryanarayana R, Choo WY, Hari NN. A review on the prevalence and assessment of elder abuse in the community. Trauma Violence Abuse. 2013;14(4):316–25.
15. Kurrle SE. Elder abuse. Aust Fam Physician. 2004;35:807–12.
16. McCallum J. Abuse and neglect of older persons: maximizing and minimizing the problem' in Conference Proceedings. Crime and older people. Australian Institute of Criminology. 1994.
17. Sadler PM. What helps? Elder abuse interventions and research. Aust Soc Work. 1994;47(4):27–36.
18. Boldy D,Wells M, Horner B, Davey M, Kingsley B. Elder abuse in Western Australia. Report of a Survey conducted for the Department for Community Development- Senior' Interests.
19. Lachs MS, William CS, O'Brien S, Pilleer KA, Charlson ME. The mortality of elder mistreatment. J Am Med Assoc. 1998;280:428–32.
20. Cooper C, Selwood A, Livingston G. The prevalence of elder abuse or neglect: a systematic review. Age Aging. 2008;37(2):151–60.
21. Killick C, Taylor BJ. Professional decision making on elder abuse: systemic narrative review. J Elder Abuse Negl. 2009;21(3):211–38.
22. Stark S. Elder abuse: screening intervention and prevention. Nursing. 2012;42:24–2926.
23. Quinn MJ. Undue influence and elder abuse: recognition and intervention strategies. Geriatr Nurs. 2002;23(1):11–6.
24. Bond J. Prevention of elder abuse project and the respect for Seniors Campaign. Primary interventions: literature review; June 2010.
25. Marshall CE, Benton D, Brazier JM. Elder abuse: using clinical tools to identify clues of mistreatment. Geriatrics. 2000;55(2):42. -4,47-50
26. Vida S, Monks RC, Des Rosiers P. Prevalence and correlates of elder abuse and neglect in a geriatric psychiatric service. Can J Psychiatr. 2002;47(5):459–67.
27. Levine JM. Elder neglect and abuse. A primer for primary care physicians. Geriatrics. 2003;58(10):37–40.
28. Ahmad M, Lachs MS. Elder abuse and neglect. What physician's can and should do. Clev Clin J Med. 2002;69(10):801–8.
29. McCallum J, Matusz S, Graycar A. Abuse of the elders at home. The range of the problem. National Centre for Epidemiology and Population Health. 1990, Canberra.
30. McGarry J, Simpson C. Identifying reporting and preventing elder abuse in the practice setting. Nurs Stand. 2008;22(46):49–55.
31. Kurle S. Position statement No 1. Elder Abuse. Revised 2003. Aust J Ageing 2004;23(1):310–41.
32. Preventing abuse-rights of older persons website: http://www.aged.rights.asu.au/prevent/definition.html.
33. Hirsch CH, Loewy R. The management of elder mistreatment: the physician's role. Wien Klin Wochenschr. 2001;113(10):384–92.
34. Pillemer AK, Mueller -Johnson UK, Mock ES, Suitorr JJ, Lachs MS. Intervention to prevent elder mistreatment. Handbook of aging and violence prevention. Atlanta: Springer; 2008. p. 241–54.
35. Elder Crime Victims Resource Center, New York City, Department of Aging. Elder abuse hurts. In more ways than one. http://www.nyc.gov/html/dfta/downloads/pdf/elder_abuse/elder_abuse.pdf. Retrieved 12 June 2013.
36. Benton D, Marshall C. Elder abuse. Clin Geriatr Med. 1991;7(4):831–45.
37. Kurrle S, Naughton G. Review of elder abuse and neglect in Australia. J Elder Abuse and Neglect. 2008;20(2):108–25.
38. Cohen M. Screening tools for the identification of elder abuse. JOCM. 2011;18(6):261–70.
39. Fulmer T, Guadagno L, Dyer CB, Connolly MT. Progress in elder abuse screening and assessment instruments. Am J Geri Soc. 2004;52:197–304.
40. Ageing and Age Care. Guide for aged care staff-Compulsory reporting. Agedcare. health.gov.au/ensuring-quality/aged-care-quality-and-compliance/compulsory-reporting-for-providers/guide-for-aged-care-staff-compulsory-reporting. Accessed 23 Apr 2018.

41. Boldy D, Harner B, Crouchley K, et al. Addressing elder abuse: Western Australia. Case Study http://cra.curtin.edu.au/local/docs/AJA. Elder Abuse Article.pdf retrieved 22 Nov 2013.
42. Lachs MS, Fulmer T. Recognizing elder abuse and neglect. Clin Geriatr Med. 1993;9(3):665–81.
43. World Health Organisation. Elder abuse. Fact sheet .2017. www.who.int/mediacentre/factsheets/fs357/en/. Accessed 31 Dec 2017.
44. Australian Society of Geriatric Medicine. Position statement No.1 –elder abuse Revised 2003.
45. Merck Manual of Geriatrics. Chapter 111 Elder Abuse and Neglect. 1408–16.
46. James M. Abuse and neglect of older people. http://www.aifs.gov.au/institute/pubs/fml/fm37mj.html.
47. Mills TJ. Elder abuse treatment & management. Medscape. 2015. http://emedicine.medscape.com/article/805727-treatment. Accessed 24 Jan 2017.
48. Wolfe DA. Elder abuse intervention: lessons from child abuse and domestic violence initiatives. www.nbcbi.nim.nih.gov/books/NBK.9873/.

Decision-Making Capacity and Consent in the Older Adult

4

Gail Jamieson

Historical Perspective

It is well known and documented that during the times of the Egyptian civilisation and that of the Greeks and Romans, physician-directed intervention had to have prior approval from the patient, but the principle of consent is relatively new [1, 2]. The Ottoman judges had consent documents called *riza senedi* which were physician-patient contracts which protected the physician if the patient died, but it is not clear whether the patient was properly informed or not [3]. The contracts, which related to Islamic law rather than to modern civil law [3, 4], divided medical history in relation to terms 'information' and 'consent' into three epochs. The first is from 500 years BC to the nineteenth century AC, when formal consent was not required. 1957 marked the introduction of the term 'informed consent'. Historically it is due to the developments in healthcare law and ethics that influenced the origin of the doctrine of informed consent and the origins of the concept of decisional capacity [5].

Life expectancy is increasing, and this trend will continue. Worldwide many are living to their 80s and 90s [6], and those living to a 100 have doubled [7]. Age is the most important risk factor for cognitive impairment [8, 9], and as the percentage of population of older adults increase so will the number of people with impaired cognition. In dealing with older adults with cognitive impairment, the question of capacity to make decisions in various areas of their lives will arise due to any condition or treatment [10]. There is a greater risk of older adults making errors in complex decision-making due to decline in their cognitive abilities [11]. The major areas that this becomes a practical issue for the physician are with regard to medical and dental consent (including advanced care planning) and lifestyle decisions (including services and accommodation). In addition, the physician is frequently asked by their legal colleagues to assess an older person's capacity to make financial decisions and execute legal documents (enduring guardian and power of attorney appointments, making of a will or entering into a contract).

General Consideration

The terms competency and capacity are frequently used interchangeably [12, 13], and it is important to have an understanding of these terms and how they are being used when interpreting literature as well as clinical and legal reports. Historically, decision-making capacity is clinically determined by physician's assessment, whereas competence and incompetence are legal designations, determined by the courts [14, 15]. Capacity denotes a person's ability to understand, maintain and communicate, appreciate and manipulate information [13] in order to come to a decision in the context of making a specific choice. It refers to the process of decision-making. Competency is a legal judgement often informed by an assessment of capacity, as to whether a person has a legal right to make his or her own decisions [16]. As this chapter is aimed at clinicians, the term capacity will be used throughout.

Capacity to make one's own decisions is fundamental to the ethical principle of respect of autonomy [17–20], and an adult is presumed to have capacity until proven otherwise [21]. There are a number of situations in which capacity can be impaired, and the elderly are a high-risk group. Physicians working in aged care must therefore be skilled in evaluating the possibility of impaired decision-making capacity in their patients [12] and be able to document their assessment and how conclusions were derived [14]. During this process they need to identify any ways to potentially enhance a person's capacity. A clinician needs to balance respect for autonomy with a duty to protect, ensuring patients do what is in their best interests and are not denied treatment and protection due to a disability (e.g. refuse treatment or care because they have no insight into their illness or how that affects their function).

G. Jamieson
Geriatrician, Sydney, NSW, Australia

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_4

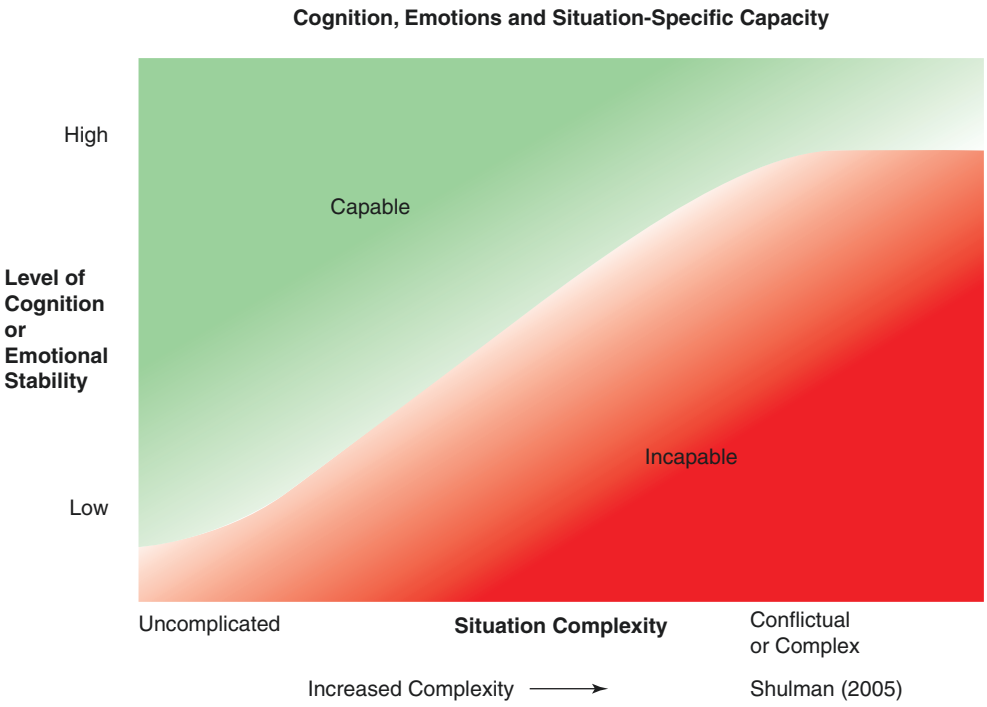


Fig. 4.1 Cognition, emotion and situation-specific capacity. (Reproduced with permission from Shulman et al. [26])

Capacity can fluctuate over time depending on a person's mental state, which can vary for a variety of physiological and psychological reasons [22]. Thus capacity is not a fixed state [23]. Any diagnosis or treatment that compromises mentation may be associated with impaired capacity, for example, dementia, delirium and stroke, as well as anxiety, depression and psychosis. Lack of insight amongst psychiatric patients is thought to be a strong predictor of lack of decision-making capacity [14]. A diagnosis or score on a particular test does not equate to impaired capacity. It rather alerts to the fact that there could be impairment, and this needs to be evaluated if there is concern regarding a particular decision that needs to be made in relation to the person. Normal ageing is frequently associated with less flexible thinking and declining retrieval memory, but it is unlikely to affect decision-making capacity. The situation in which the decision is being made can also influence capacity. For example, a person may be able to make a decision in a non-threatening environment, but be unable to do so if there is a lot of conflict surrounding the decision (deciding where they should live when adult children are in conflict over this).

There are a number of different types of decisions that the physician may be asked to assess an older person's capacity to make. These include medical and dental consent, making of advanced directives, lifestyle (e.g. general living arrangements, accommodation, services) [24, 25] as well as legal and financial (e.g. managing financial affairs, giving power of attorney, making a will). In view of the fact that capacity is decision specific, an assessment of incapacity in one area cannot be extrapolated to another Fig 4.1.

Determining Decision-Making Capacity

It is vital to keep in mind that capacity is not an all-or-nothing phenomenon. It is decision specific [27] and there are a number factors which may affect a person's capacity (Box 4.1). Law and ethics have agreed that in order to have capacity, a person requires the following [28]:

1. Understanding – the need to comprehend information given about a particular issue.
2. Appreciation – the ability to see how the particular problem relates to themselves and their own particular situation.
3. Reasoning – the ability to recognise options, and the consequences of those various options (i.e. appreciate risks and benefits), and to show logical, rational thought processes in coming to a decision.
4. Ability to communicate their decision – verbal or non-verbal.
5. These basic principles are applied to all types of decisions, from informed consent to medical treatment, managing finances or making of a will (Box 4.1).

Box 4.1. Factors Affecting Capacity Specific to the

1. **Decision** itself (e.g. complexity, risks, consequences)
2. **Circumstances** in which the decision is made (e.g. conflict, dependency, presence of supports)
3. **Person** themselves (e.g. underlying illness causing temporary or fluctuating impairment of decision-making processes, emotional state, own values and beliefs)

Consequently all these things need to be taken into account when performing a capacity assessment.

Conducting the Assessment

Assessing someone's capacity to make a decision is essentially an assessment of the person's thought processes in coming to a particular decision and integrating that with information gathering regarding the decision, circumstances of that decision and the person themselves. This enables a clinical judgement as to the person's capacity to be made. Documentation of all these components is important.

Firstly, the specific decision for which capacity is to be assessed has to be determined (i.e. answer the question 'capacity to do what?'). Clarification is obtained by interviewing the agency or person requesting the assessment. This is followed with a review of the individual's understanding of the reason for visiting the doctor. The person must be told the purpose of the evaluation if they are not aware, and any relevant information to making an informed decision about the task needs to be conveyed to them [29].

The assessment should be done face-to-face [28], and it is useful to begin with general conversation, (which can provide significant clinical information), before moving onto a more structured interview, so as to put the person at ease. The framework for more directed questions is built around the four components required for a person to have capacity (understanding, appreciation, reasoning, communication), as well as exploring the factors that are known to affect capacity (in relation to the decision itself, the circumstances of the decision and the person). Comment should be made as to any things that could be made to enhance a person's capacity in a particular situation (e.g. providing a nonthreatening environment, explaining things in a quiet setting, with no distractions or in the morning before issues of fatigue set in). Although there are no widely accepted standardised instruments for capacity assessment [30], published question sets are readily available and include simple questions that can be used to guide clinical assessments [31–33].

The components of a capacity assessment should include the following.

1. **Overall Assessment of Cognitive Ability and Mental State**

As already stated a diagnosis or score on a specific test does not equate with someone having capacity or not; however it is a predictive factor, and doing an overall assessment of cognition allows you to identify cognitive deficits that need to be specifically addressed during the rest of the assessment. Other aspects of mental state examination need to be assessed to identify any mood disturbance, anxiety, phobias and delusional ideas that may affect the persons thought processes regarding a particular decision.

A Standard Cognitive Test (e.g. MMSE, MoCA, Addenbrooke's cognitive assessment) should be performed followed by more in-depth testing of specific areas involved in decision-making such as language, attention, memory and frontal lobe function (initiation, planning, organisation). Areas specific to the issue at hand also need to be explored in more depth – e.g. arithmetic and value of money if the question is around ability to manage finances.

In addition to the score on a test, it is useful to make a comment on the way the person approaches the test and how they come up with answers (e.g. were their thought processes slow or fast, did they approach tasks in an ordered logical way or disordered). Any degree of dysphasia needs to be explored to ensure further communication with the patient during the assessment is tailored to the patients' needs.

Multiple formal capacity assessment tools have been developed in an endeavour to enhance the reliability and validity of capacity evaluations including the Hopkins Competency Assessment Test (HCAT) [34], Aid to Capacity Evaluation (ACE) and MacArthur Competence Assessment Tool (MacAT) [30], amongst others. As with standard cognitive assessment tools, capacity tools do not give a definitive answer, however, they can be a useful adjunct in circumstances where there is disagreement amongst professionals or in matters that are to be referred to the courts [12]. While they all have their limitations, they are also a useful reference for the clinician to guide relevant questions and how they should be asked. In addition detailed neuropsychological testing is helpful if there is still uncertainty as to a person's capacity. This may arise, for example, when a person performs well on assessment tools, but their decisions do not appear to be congruent with social norms.

2. **Semi-Structured Interview**

The goal of this is to assess the four basic skill requirements for capacity in relation to the particular issue [13, 28].

I. Understanding

This involves establishing the person's understanding of the facts (This is influenced by language skills, memory, attention and processing speed) [36]. Any additional facts relevant to the issue need to be disclosed, for example, in the case of consent to medical treatment informing the person of their options, risks and benefits of each, as well as that of no treatment. Reassessment of their understanding can follow by asking them to explain things back in their own words. Mere repetition of what was said does not imply understanding.

II. Appreciation

An understanding of the person's insight into their illness and functional status needs to be sought, and their ability to see how that impacts on the particular decision. Can they personalise the issue? (comprehension, abstract reasoning, insight and delusional ideation contribute to this skill) [36].

Does the person understand how the issue relates personally to them? For example, if they do not believe that they have an illness, they will not be able to make informed decisions around management. If delusional ideas, such as medication is poisonous, are driving their decision to refuse to take their diabetic medicine, then again they do not appreciate their situation.

III. Reasoning

The person's choice and views need to be elicited, as well as how they came to those explored. They need to demonstrate logical and rational thought processes in coming to a particular choice. (This is influenced by memory and executive functions – abstract reasoning, concept formation, problem solving and ability to shift set.) [36].

Why did they choose one option over another? Are they consistent in their choices and views? Open-ended questions should be used initially; however more specific questioning for clarification, especially if the person has significant cognitive impairment, often needs to follow.

IV. Communication

The person's ability to express preferred choice. This may be by verbal or non-verbal means [13].

3. **Factual Corroborative Information**

Without the facts surrounding the decision, you cannot make a judgement regarding the person's capacity. It is essential to establish if the person's reporting of the 'facts' is accurate. For example, with regard to medical and lifestyle decisions, you need to check the person is functioning as they report. When it comes to such things as financial issues and making of wills, it is relevant that they have some idea of what their estate contains and who their family members are. It's important to establish whether all the complexities of their situation have been relayed.

Corroborative information, including relevant history of events that may indicate cognitive impairment is present, is important. For example, lack of follow through with plans indicating frontal lobe dysfunction, frequent presentations to lawyers with change of instructions (with no clear explanation) would raise doubt as to the persons capacity around that issue.

In making a final judgement on capacity, all this information is integrated with the context in which the decision is to be made [28], as the threshold for capacity to make a particular decision will vary depending on issues related to the three factors outlined in Box 4.1 (i) the decision (e.g. degree of risk associated with it), (ii) the circumstances (e.g. complexity of persons affairs, presence of any conflict) and (iii) the person (e.g. underlying values and beliefs).

For example, a person may be able to consent to medications but be unable to consent to a limb amputation (as they are unable to understand the risks and appreciate how it will affect their future function, e.g. ability to live at home). A person with a simple estate may be able to make a will, whereas someone with the same degree of cognitive impairment but a more complex estate may not. That is the threshold for having capacity is higher in high-risk, complex situations (Fig. 4.1).

Writing Up the Assessment

When writing up the assessment, keep in mind the principles of the four basic skills required for capacity (understanding, appreciation, reasoning, communication), as well as the factors that can influence capacity (specific to the decision, the circumstances and the person) [28].

It is imperative only to make a judgement in areas that have specifically been addressed. For example, if someone has been reviewed regarding their ability to consent to medical treatment, the outcome of this assessment cannot be extrapolated to management of finances. If another issue is brought up after the consultation then another appointment needs to be made to address that specific issue.

Explaining how the conclusion was arrived at is vital. In other words the clinician's reasoning needs to be evident to the reader. It is often helpful to record relevant examples of the actual questions the patient had been asked, as well as their responses [12]. If you are using historical events or the person's behaviour or presentation as evidence, this needs to be explained explicitly (e.g. not maintaining basic personal hygiene over the last 6 months despite agreeing that this is a problem and promising to address it by accepting supports indicates an inability to follow through with tasks). Observation

and comment on factors that may have impacted on the person's performance and participation in testing should be noted, as well as how these could potentially be modified to enhance a person's capacity. For example, if they have any physical deficits such as poor hearing and vision, fatigability or emotional issues, including interpersonal relations, impacting their decision-making ability.

Practical Problems Encountered

Dysphasic Patient

This can be an issue after a stroke, as well as with progression of neurodegenerative diseases. Conventional assessments are highly language oriented and do not give an accurate picture of a dysphasic patient's ability. Making an assessment can be very challenging in these circumstances. Until guidelines for reliable criteria are established, the clinician should assess the patient in a global way and not just on one aspect of the patient's symptomatology [35]. This includes careful observation of their behaviour and responses to varying situations, which can then be interpreted. Any limitations to the assessment need to be explicitly relayed.

Unco-operative Patient

There is no full proof way of getting around the unco-operative patient. There may be any number of reasons why they are unco-operative, and an attempt to understand these is imperative. It may be that they believe that they do not have a problem and cannot see the point of testing, or that they feel vulnerable and are frightened as to the consequences of participating and having, what they view, as an 'adverse finding'. Often if given time, an opportunity to build up a sense of trust and to allay any unfounded fears, the patient will agree. Explaining to the person that the idea of an assessment is also to find out their strengths to guide how they can be used to overcome difficulties is helpful. If the situation is urgent and the risks to the patient deemed high, explaining to them that an assessment will need to be made anyway, and it is better for them to participate in the process to ensure they can have their say can also increase co-operation, even if only partially.

Informed Consent

It is required by law to obtain informed consent from patients before commencing treatment [12]. The doctor must ensure that all decisions made complies with the patient's interests [22] especially those who are vulnerable. Informed consent is a legal transaction that incorporates the individual's right to make autonomous decisions in medical settings [36]. It is a process of communication between the physician and patient regarding treatment plans, and capacity is only one of the components of informed consent.

Legitimate informed consent can only be obtained if three conditions are met [37]. Firstly the person has to have the capacity to make the decision [15, 34], secondly the person must be provided with adequate information about the issue [29] and understand the medical procedure proposed and thirdly they must be free to choose without pressure.

There are many interactions between physician and patient for which consent is implied, rather than explicitly given. Implied consent refers to consent being granted by gestures, signs, actions (or inaction) and statements that are construed as agreement, for example, holding out an arm to have blood pressure taken.

What to Do When a Person Lacks Capacity

Clearly it depends on the significance and urgency of what the particular issue is. Laws surrounding various types of decisions in each state differ in detail but are similar in principle.

In all situations the first step is to identify and address any reversible factors that may be contributing to the impairment. For example, in the case of a delirium, treat and wait for resolution. If there is conflict or stressors that can be addressed, attempt to resolve these and then reassess the patient's capacity.

Once it is clear there are no reversible factors, or the decision needs to be made prior to factors being able to be reversed, then the course of action will depend on the type of decision.

(i) Medical

In a medical, emergency treatment can be provided without consent in order to save a person's life or prevent serious damage to a person's health [21].

If the situation is not an emergency, then identify a 'person responsible' who is then able to act as a substitute decision-maker. A person responsible can be a legally appointed guardian, a spouse or partner or other relatives or friends with a close relationship to the person. The exact hierarchy of who is 'person responsible' does vary slightly in each state [21].

If no 'person responsible' is identified (e.g. homeless person, no known relatives or friends) and the treatment is considered major (e.g. surgical procedure, psychotropic medication), then referral to the guardianship body in the particular state is required to obtain consent [21].

Referral to the relevant guardianship body would also be required if the person is objecting to the proposed treatment, (as a person responsible cannot consent if someone is objecting to treatment), or if there is disagreement amongst the persons responsible of the same hierarchy, or amongst the treating health professionals and person responsible (i.e. the health professionals do not think the person responsible is acting in the best interests of the patient).

(ii) Lifestyle

In most circumstances there are informal support systems surrounding a person to enable these decisions to be made. Services and decisions about such things as where someone should live are usually sorted out on an informal basis with family and friends assisting. Referral to a guardianship body for a formally appointed substitute decision-maker for specific lifestyle decisions is only required if, once again, the person is objecting to a proposed course of action (e.g. residential care in a situation where there is felt to be no other option by those around them due to severe risk to the person's health or safety), or if there is significant disagreement amongst family and friends to the point where the person's welfare is at risk.

(iii) Managing Finances

Identify if the person has a power of attorney in place that remains valid once the person has lost capacity. If so then this can be activated. If not, explore if they wish to appoint a power of attorney and assess if they have the capacity to do so (remembering that capacity is decision specific, so a person may not be able to manage their finances themselves, but they may retain the capacity to appoint someone else to do that for them). Otherwise establish if things can be managed informally (e.g. family member already co-signatory on bank accounts, direct debits in place, able to access accounts to pay bills electronically, etc.), ensuring there are no issues of exploitation evident. If informal management is not possible, then an application to the relevant judicial body (e.g. court or tribunal) to appoint a financial manager formally would need to be made.

(iv) Legal Documents

The person simply cannot execute those documents if they are deemed not to have capacity to do so (e.g. enduring guardian, enduring power of attorney, making a will or entering into a contract) (Algorithm 4.1).

Conclusion

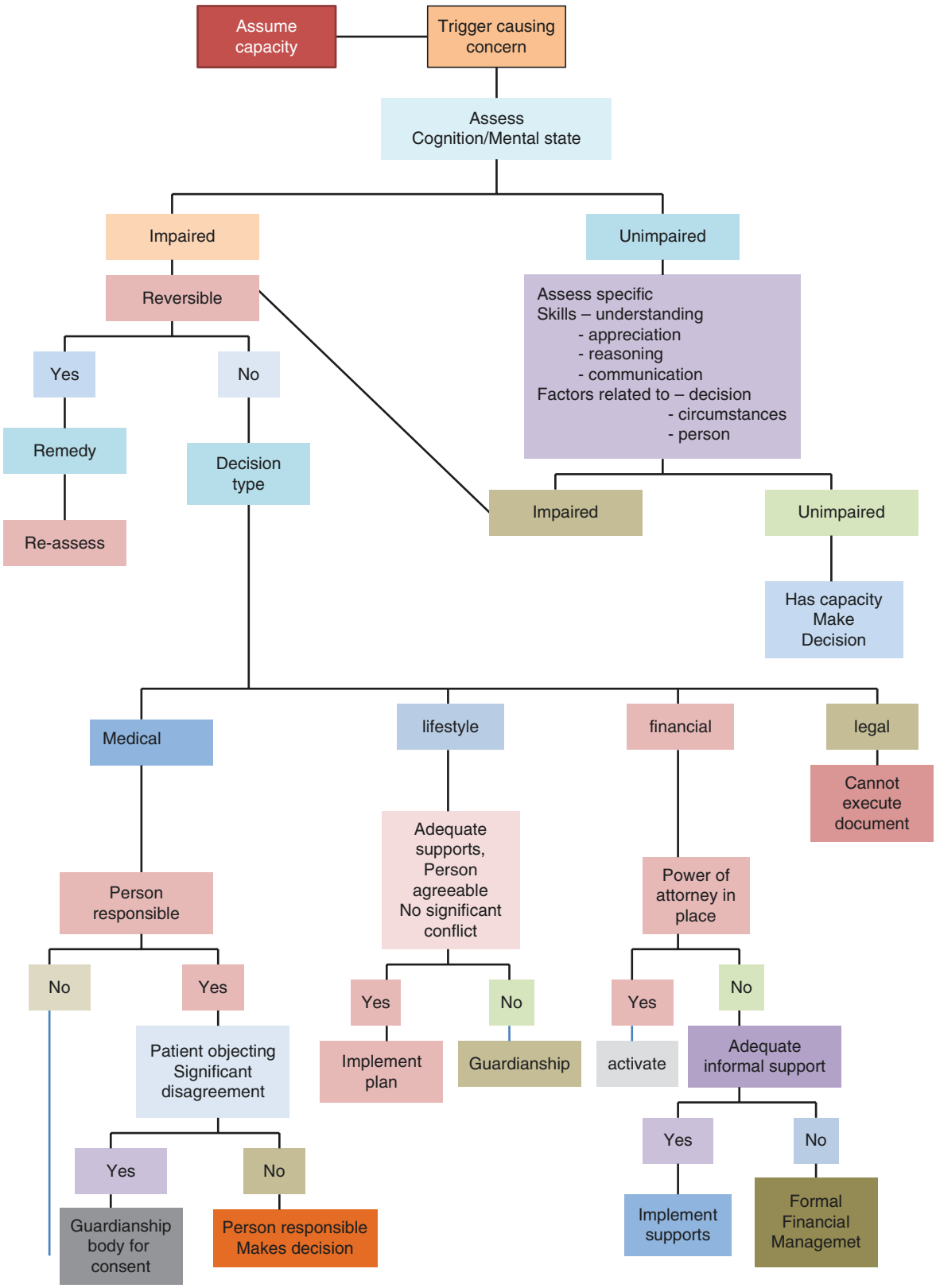
Physicians managing elderly patients, while encouraging and supporting independence and self-determination, must be skilled in identifying those whose capacity is impaired and ensure that they are not denied treatment or protection. It must be remembered that capacity is decision and situation specific and can fluctuate over time depending on the underlying cause of impairment. A structured approach to assessment and documentation of findings based on principles is imperative. Ethical dilemmas frequently arise and while at times, the situation can be complex and confusing, going back to first principles, as with other clinical problems, can assist in gaining a degree of clarity.

Clinical Relevance

- Assessment of the patient's capacity for decision-making should begin with the assumption of capacity.
- Capacity is not an all-or-nothing phenomenon, but rather task and situation specific and can fluctuate over time [22].
- Decision-making capacity cannot be presumed to be present or absent on the basis of the patient's diagnosis or score on a particular test.
- Four skills required for decision-making capacity are understanding, appreciation, reasoning and communication.
- Factors affecting decision-making capacity may relate to the decision, the circumstances and the person.
- Assessment for capacity should focus on the cognitive processes.
- Physicians should use a structured approach to assessment and documentation of findings.
- The doctor must ensure all decisions made comply with the patient's interests especially in the case of the vulnerable [22].
- Informed consent requires that the patient
  - (i) Is provided with the necessary information and understands the treatment proposed
  - (ii) Is free to choose without pressure
  - (iii) Has the capacity to make the decision [15, 34]

Multiple Choice Questions (MCQs)

1. The following are true when assessing for capacity, EXCEPT:
   - A. In patients with depression, there may be time-specific impairment of capacity.
   - B. Patients with Alzheimer's disease and other dementias have a high rate of incapacity, and everyone with the diagnosis is incapacitated.
   - C. A stroke in people with long-term cognitive problems of sufficient severity can interfere with capacity.



Algorithm 4.1 What to do when the patient lacks capacity

D. In everyday life competency is rarely a fixed state and can fluctuate.

2. The following are true, EXCEPT:
   A. It is required by law to obtain informed consent from patients before commencing treatment.
   B. Physicians should be encouraged to use a structured approach to assessment.
   C. Decision-making capacity can be presumed to be present or absent on the basis of the patient's diagnosis.
   D. Assessment of the patient's capacity for decision-making should begin with the assumption that the individual has capacity.

Answers to MCQs

1. B
2. C

References

1. Mallardi V. The origin of informed consent. Acta Otorhinolaryngol Ital. 2005;25(5):312–27.
2. Kour NW, Rauff A. Informed patient consent historical perspective and a clinician's view. Singap Med J. 1992;33(1):44–6.
3. Kara MA, Aksoy S. On the Ottoman consent documents for medical interventions and the modern concept of informed consent. Saudi Med J. 2006;27(9):2306–10.
4. Lutterbach J, Weissenberger C, Hitzer K, Hlmes A. On past practices and future directions of informed consent in (radiation) oncology. Strahlenther Onkol. 2004;180(8):469–77.
5. Standford Encyclopedia of Philosophy. Decision-making capacity. 2011. https://plato.stanford.edu/entries/decision-capacity. Accessed 12 July 2017.
6. World Health Organisation. Facts about aging. www.who.int/ageing/about/facts/eu. Accessed 8 July 2017.
7. Christensen J, Willingham V. Live to 100. Number of centenarians doubled. Edition. cnn.com/2014/06/04/health/centenarian-death/index.html. Accessed 67 July 2017.
8. www.cdc.gov/aging/pdf/cognitive_impairment/cogimp_poicy_inall.pdf. Accessed 8 July 2017.
9. Harada CN, Love MCN, Triebel K. Normal cognitive aging. Clin Geriatr Med. 2013;29(4):737–52.
10. Karlawish J. Assessment of decision-making capacity in adults. 2017 UpToDate. http://www.uptodate.com/contents/assessment-of-decision-making-capacity-in-adults. Accessed 8 July 2017.
11. Denburg NL, Cole CA, Hernandez M, Yamada TH, Tranel D, Bechara A, et al. The orbitofrontal cortex, eal-world decision making and normal aging. Ann N Y Acad Sci. 2007;1121:480–98.
12. Appelbaum PS. Assessment of patients' competence to consent to treatment. N Engl J Med. 2007;357:1834–40.
13. Life in the fast lane. Capacity and competence. https://lifeinthe.fastlane.com.ccc/capacity-and-competence. Accessed 8 July 2017.
14. Jones RC, Holden T. A guide to assessing decision making capacity. Cleve Clin J Med. 2004;71:971–5.
15. Lowenkopf EL. Legal issues of geriatric patients: competency and decision making. Geriatric Times. 2001;2(9). http://www.cmellc.com/geriatrictimes/g011133.html. Retreived on 1 April 2009.
16. Jones. A guide to assessing decision making capacity. Clev J Med. 2004;1–5.
17. Varelius J. The value of autonomy in medical ethics. Med Health Care Philos. 2008;9(3):377–88.
18. Coggon J, Miola J. Autonomy, liberty and medical decision- making. Camb Law. 2011;70(3):523–47.
19. Reid KI. Respect for patents' autonomy. J Am Dent Assoc. 2000;140(4):470–4.
20. Entwistle VA, Carter SM, Cribb A, McCaffery K. Supporting patent autonomy: the importance of clinician patient relationships. J Gen Intern Med. 2010;25(7):741–5.
21. Stewart C, Kerridge I, Parker M. The Australian medico-legal handbook. 1st ed. Marrickville: Church Livingstone Elsevier; 2007.
22. Zabow T. Will and curators-decision –making in adults with impaired capacity. CME. 2012;30(4). http://www.cmej.org.za/index.php/c,ej/article/niew/2404/2276. Accessed on 20 Oct 2013.
23. Kelly TB. Paternalism and marginally competent: an ethical dilemma. No easy answers. J Gerontol Social Work. 1994;23(1/2):67–84.
24. Freedman M, Stuss DT, Gordon M. Assessment of competency: the role of neurobehavioural deficits. Ann Int Med. 1991;115:2–3-208.
25. Moye J, Marson DC. Assessment of decision –making capacity in older adults: an emerging area of practice and research. Focus. 2009;7:88–97.
26. Shulman K, Cohen C, Kirsh F, Hull I, Champine P. Assessment of testamentary capacity and vulnerability to undue influence. Am J Psychiatr. 2007;164:5.
27. NSW Government –Justice. Section 2-what is capacity. http://www.justice.nsw.gov.au/diversityservices/Pages/Diversv/ds_capacity_tool/ds_capa_whatis.aspx. Accessed 11 July 2017.
28. Uptodate Assessment of decision making capacity in older adults. www.uptodate.com/contents/assessment-of-decision-making-capacity-in-adults. Accessed 23 Sept 2017.
29. Venesy BA. A clinician's guide to decision making capacity and ethically sound medical decisions. Am J Phys Med Rehabil. 1994;73(3):26.
30. Marson DC, Schmitt FA, Ingram KK, Harrell LE. Detemining the competency of Alzheimer patients to consent to treatment and research. Alzheimer Dis Assoc Disord. 1994;8(Suppl 4):5–18.
31. Grisso T, Appelbaum PS. MacArthur competence assessment tool for treatment (MacCAT-T). Sarsota: Professional Resource Press; 1998.
32. Etchells E, Darzins P, Silberfeld M, Singer PA, McKenny J, Naghe G, et al. Assessment of patient capacity to consent to treatment. J Gen Intern Med. 1999;14:27–4.
33. Sturman ED. The capacity to consent to treatment and research: a review of standardized assessment tools. Clin Psychol Rev. 2005;25:954–74.
34. Janofsky JS. Assessing competency in the elderly. Geriatrics. 1990;45(10):45–8.
35. Nagaratnam N, McNeil C. Dementia in the severely aphasic: global aphasia without hemiparesis-a stroke subtype simulating dementia. Am J Alz Dis. 1999;14:74–8.
36. McAuliffe J. Presentation guardianship division training Mar 2016 – capacity assessment a neuropsychologists perspective. Balmain
37. Kitamura T. Assessment of psychiatric patients' competency to give informed consent: legal safeguard of civil right to autonomous decision-making. Psychiatry Clin Neurosci. 2000;54(5):515–22.

Comprehensive Geriatric Assessment

5

Gary Cheuk

Historical Perspective

The word "geriatrics" comes from two Greek words "iatros", a healer, and "geros", an old man. Ignatz Nascher was the first to coin the word geriatrics and advocate for the formation of a new branch of medicine for old people [1]. In 1935 Dr. Marjory Warren, a physician and deputy medical director of West Middlesex Hospital, Isleworth, Middlesex, was given the responsibility for the adjacent workhouse with 714 chronically ill patients [2]. She systematically reviewed them and was able to discharge a large number to their homes or residential care by providing active rehabilitation and proper equipment [3]. She attributed this high number of chronically ill to a number of reasons, including poor diagnosis, the lack of proper treatment and supervision and the lack of multidisciplinary teamwork [2]. This was the beginning of the first geriatric unit in the United Kingdom based upon comprehensive assessment and early rehabilitation by a multidisciplinary team [4] and the development of geriatric medicine as a specialty [5]. In her writings, Dr. Warren stressed the importance of multidisciplinary teams, early ambulation, active involvement in daily activities [6] and a holistic approach to older patients [7]. This still forms the basic principles of CGA today.

Comprehensive Geriatric Assessment

Comprehensive geriatric assessment (CGA) is a process where the complex physical, functional, cognitive, psychosocial and rehabilitation needs of a frail older person are identified and a plan of management instituted. Geriatric evaluation and management (GEM) describes a similar process with a specific therapy component as part of the management plan. A team-based approach is essential with input from general practitioners, geriatric medicine specialists, physiotherapists, occupational therapists, social workers, speech therapists and, where applicable, staff working in aged care facilities and other community care staff. CGA has been applied in a number of settings. These include inpatient geriatric and management unit (GEMU), inpatient consultative service such as orthogeriatric service, domiciliary care, outpatient service and in chronic aged care facilities. The practice of CGA varies according to the setting. For example, in the primary care setting, the process could be initiated by the general practitioner with input from a practice nurse. In the acute hospital setting, older persons in GEMU often have blanket referrals to the multidisciplinary team, which includes geriatricians, physiotherapists, occupational therapists and social workers with other personnel involved as appropriate. In the outpatient setting, it is often performed by geriatricians or nurse practitioners, whilst in the domiciliary setting, older persons are often assessed by a single aged care worker with the involvement of other disciplines where appropriate. CGA commonly involves a number of contacts with the subjects over a period of time, that is, it is a process rather than a single interaction with one or more health-care providers. It is imperative that frail older persons and their families and significant others are central to the process of assessment and care planning. Indeed, no assessment is complete without involving the older persons' families and carers in the identification of issues and in the formulation of care plans. As this process often involves more than one health-care professional, it is important that documentation is structured and presented in a way which enables the effective transfer of clinical information across different settings and between service providers.

CGA was promoted and practised based on the observation of and advocacy by pioneers in the practice of geriatric medicine before there was any credible evidence to support its cost-effectiveness, similar to the development of coronary care units in medicine. There is significant variation in the model, composition of the multidisciplinary team and intensity of intervention. It is practised in a number of different

G. Cheuk (✉)
Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia
e-mail: gcheuk@optusnet.com.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_5

care settings, such as inpatient geriatric evaluation and management unit (GEMU), inpatient geriatric consultative service (IGCS), inpatient rehabilitation, domiciliary assessment programme and outpatient service. This makes the evaluation of the effectiveness of CGA very challenging.

A meta-analysis of 28 trials by Stuck et al. in 1993 showed that the odds ratios of remaining at home versus death or admission to a nursing home are higher for subjects who were randomised to comprehensive geriatric assessment in GEMU, hospital post-discharge assessment and domiciliary assessment [8]. There is also some evidence that GEMU improves physical and cognitive function in follow-up, but there is no clear evidence of benefit in mortality and prevention of hospital admissions [8]. Covariate analysis showed that programmes with direct control over interventions and long-term ambulatory care follow-up are more likely to be effective [8]. Patients managed in inpatient geriatric assessment units are less likely to experience decline in health-related quality of life at 3 months [9]. In the latest updated review in the Cochrane Database, older patients who received CGA are more likely to be alive and living in their homes after follow-up of 3–12 months. CGA decreases the likelihood of participants being admitted to nursing homes but makes no difference in their mortality, physical or cognitive function at follow-up [10].

In the care of the oldest old, CGA is being employed increasingly in the determination of appropriate medical intervention. CGA has been shown to influence treatment decisions in the management of solid-organ malignancy in 21–49% of cases [11]. Functional impairment, malnutrition and co-morbidities are independently associated with chemotoxicity and/or survival [11]. CGA was also shown to be useful in a small study to predict death or hospitalisation within 3 months of transcatheter aortic valve implantation [12]. CGA can also be used in the review of treatment and identify potential subjects for deprescribing in the oldest old who are most at risk of adverse drug events and reactions.

Instruments Used in CGA

It is beyond the scope of this chapter to review instruments used in CGA. There are certainly many validated instruments to screen and document cognitive function, abilities to perform personal and instrumental activities of daily living, behavioural and psychological symptoms, depression, falls risk and continence. The choice of instruments should take into consideration of the patient's education and cultural background, settings where the assessment occurs, the nature of presentation and the purpose of the assessment. For example, it would be inappropriate to use Folstein's mini-mental examination for patients with little education, from a cultural and linguistic diverse background or suspected frontal lobe impairment. Whilst it is not mandatory to do so, the benefit of using structured instruments in the assessment of older persons is to enable fairly uniform documentation and transfer of information and may assist in avoiding duplication of assessment, which often is a cause for complaint when an older person is assessed by a number of health professionals (Table 5.1).

Table 5.1 Domains and examples of instruments used in CGA

Domains	Context	Instruments
Basic activities of daily living (ADL)	Ability to self-care, basic mobility and continence	Barthel index [13]
Instrumental ADL	Ability to shop, cook, housekeeping and manage finance	Lawton and Brody [14]
Social activity and support	Extent of social network and engagement in community activities	Lubben social network scale [15]
Cognition	Alertness, orientation, attention and ability to perform complex tasks	Folstein mini-mental state examination [16], Addenbrooke's cognitive examination [17, 18], Rowland's universal dementia assessment scale [19]
Mental health	The degree the person feels depressed, anxious	Geriatric depression scale [20]
Mobility	Assessment of gait, balance and risk of falls	Tinetti performance-oriented mobility assessment [21], timed up and go test [22]
Nutrition	Current nutritional status and risk of malnutrition	Mini-nutritional assessment [23]

Screening in the Elderly

According to the World Health Organization (1974), the purpose of screening in geriatrics is preventive care, "to keep the elderly in good health and happiness in their own houses for as long as possible" [24]. To achieve this, the initial assessment and screen should determine any acute and chronic medical issues and review of their treatment, levels of functional and psychosocial well-being, home environment and the strengths and deficits in an individual as well as the presence of harmful life-style behaviours such as smoking, excessive alcohol use or sedentary life-style followed by the development of intervention or management plan. A review of the vaccination status should also be performed. The subject should also be encouraged to develop or review existing advance care plans. There is paucity of data in the benefit of specific disease-oriented screening in the oldest old. The goal of treating the oldest old should be to preserve function and improve the quality of life rather than to prolong life [25].

With increasing years, there is an increasing frequency of disorders involving all organ systems resulting in increasing co-morbidity. The presence of disability also increases with age, with 40% of those aged between 65 and 69 reporting a disability. This rises to 88% in those aged 90 or over [26]. The syndrome of frailty, which can be defined as a state of increased vulnerability to stressors due to decreased physiologic reserves, also increases with ageing with as many as 40% of people aged 80 or over are frail [27]. The combination of increasing co-morbidity, frailty and disability of older persons contributes to the complexity and often difficulties in prioritising intervention in an older person. The fragmentation of the health care, long-term care and social welfare systems and the prevalence of ageism contribute to the challenges in addressing the care needs of the oldest old.

Primary care physicians are the best placed to commence comprehensive geriatric assessment as well as to co-ordinate the implementation of care plans. In a large majority of the elderly, the care provided is by the primary care physicians. Many of the elderly are brought to assessment by their families. It is well known that it is the family member who has noticed functional deficits before the deficits are evident by normal psychometric tests in the elderly. The American College of Physicians recommends that primary care physicians incorporate within their routine medical management of older patients procedures for measuring functional deficits [28]. The Affordable Care Act in the United States also provides for yearly "wellness" examination with key preventive services to enrollees [25]. In Australia, the Medicare Benefits Schedule has set payments for primary care physicians for annual assessments of people aged 75 or over including medical, functional, psychological and social/environment components [29]. Primary care physicians should also screen for the presence of geriatric syndromes such as cognitive impairment, falls/immobility, depression and incontinence. The World Health Organization has developed a toolkit for the use by primary care physicians which covers the main elements of health screening for older persons [30]. Following the screening by the primary care physicians, a referral to a specialist aged care service may be required especially for persons who suffer from one of the geriatric syndromes, are frail or suffer from multiple co-morbidities.

Geriatric Assessment Team

This is followed by a referral to a geriatric assessment team (a multidisciplinary team), which determines the current status – physical, mental and psychosocial health:

(i) His or her ability to function independently.
(ii) Living arrangements.
(iii) Access to and needs for support services.
(iv) Identify current problems and predict course of illness and likely problems.
(v) Establish connection between older person and resources.
(vi) Follow up and ongoing monitoring and to determine what extent the connection between the older person and resources has or has not addressed the problem.

The OUTCOME of the comprehensive assessment is the development of the 'CARE PLAN' which lists the problems identified and suggests specific interventions (e.g. specialist services) or actions required (Algorithm 5.1).

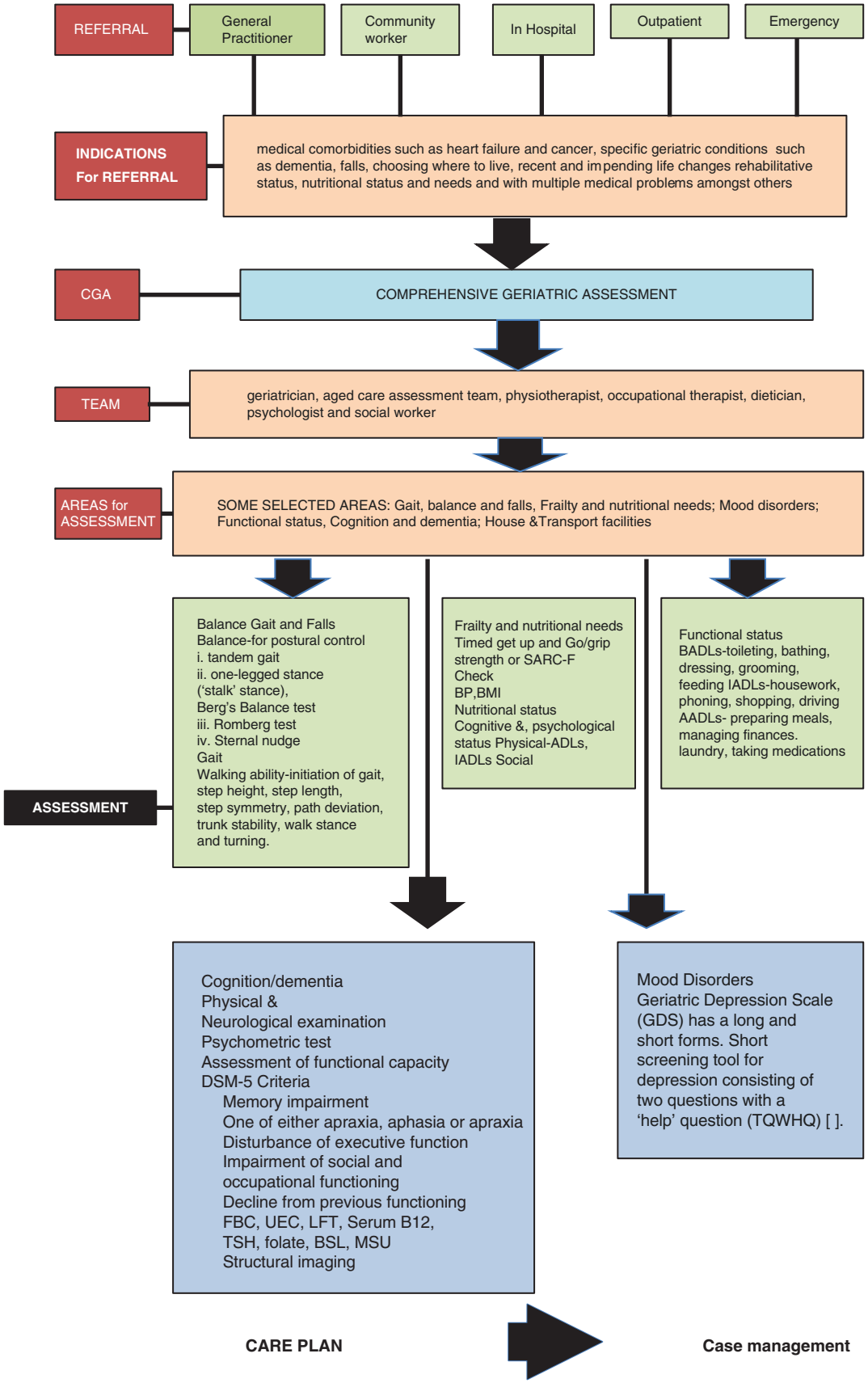
Clinical Relevance

Comprehensive geriatric assessment by a multidisciplinary team is the cornerstone of geriatric medicine.
The incidence of multiple co-morbidities, frailty and disability increases with age and is a predictor of poor outcomes.
Comprehensive geriatric assessment increases the likelihood of an older person being alive and living in their own homes.
The older person and his/her significant other should be central to the process of assessment.
Primary care physicians and health care professionals are best placed to screen for geriatric syndromes, provide life-style counselling and make referrals to specialist aged care service.
Comprehensive geriatric assessment is being applied in other fields of medicine to determine appropriate therapy.

Case Study

An 88-year-old man who lives at home with his wife suffers from dementia. He is independent in his personal activities of daily living but requires assistance with housekeeping and meal preparation. He has a history of ischaemic heart disease with previous coronary artery stent, Type II diabetes mellitus and hypertension. He was being treated with chemotherapy (docetaxel) and immune checkpoint inhibitor (ipilimumab) therapy for metastatic carcinoma of prostate from October last year, with a pretreatment prostate-specific antigen (PSA) level of >500 ng/ml. This was complicated by immune colitis, requiring high-dose prednisone, which in turn caused instability of his diabetes, necessitating the commencement of insulin. He presented with decreased oral intake and mobility.

He was asymptomatic of his known skeletal metastases but since the commencement of chemotherapy has been complaining of paraesthesia of his limbs and altered taste.



Algorithm 5.1 A practical approach to comprehensive geriatric assessment and management. (Information sources: Ward, 2017; Ellis et al. [10]; Yesavage et al. [20]; Dupee [31]; Mohd-Sidik et al. [32]; Brit Geriatr Soc [33]; Walston and Fried [34])

On assessment, he was stable haemodynamically and cognitively intact. He was found to be malnourished with decreased mobility. There was evidence of peripheral neuropathy and chronic venous stasis. He was cognitively intact. Due to his impaired mobility, he has become functionally incontinent or both urine and faeces. His repeat PSA was 150 ng/ml.

Issues: Appropriateness of continuing therapy for metastatic disease, which is causing non-specific symptoms but has significant side effects.

Outcomes: Patient's medications were rationalised, and he was given rehabilitation following which will be reviewed by his oncologist to seek further information of prognosis with or without treatment.

Multiple Choice Questions (MCQs)

1. The following in relation to comprehensive geriatric assessment are true, EXCEPT:
   A. Comprehensive geriatric assessment is carried out most successfully by a multidisciplinary team.
   B. Medicare Benefits Schedule does not have set requirements for payments to primary care physicians for assessments.
   C. The outcome of the comprehensive assessment is the development of the care plan.
   D. A comprehensive screen consisting of a group of targeted instruments would be useful to assess functional deficits methodically.

Answers to MCQs

1. B

References

1. Barton A. History of the development of Geriatric Medicine in the UK. Postgrad Med J. 2003;79:229–34.
2. Kong TK. Dr Marjory Warren: the mother of geriatrics. J Hong Kong Geriatric Soc. 2000;10(2):102–5.
3. British Geriatric Society. Marjory Warren. 2013. http://www.bgs.org.uk/geriatricmedicinearchive/bgsarchive/biographies/marjory-warren. Accessed 16 July 2017.
4. Warren MW. The evolution of a geriatric unit from a public assistance institution. 1935-1947. Proc R Soc Medicine. 1948;41:337.
5. Ritch A. History of geriatric medicine: from Hippocrates to Marjory Warren. J R Coll Physicians Edinb. 2012;42(4):368–74.
6. St John PD, Hogan DB. The relevance of Marjory Warren's writings today. Gerontologist. 2014;54(1):21–9.
7. Mathews DA. Dr Marjory Warren and the origins of British geriatrics. J Am Geriatric Soc. 1984;32(4):253–8.
8. Stuck AE, et al. Comprehensive Geriatric Assessment: a meta-analysis of controlled trials. Lancet. 1993;342:1032–6.
9. Ekerstad N, Karusin BW, Ivanoff SD, Landahl S, Anderson D, Heintz E, et al. Is acute care of frail elderly patients in a comprehensive geriatric assessment unit superior to conventional acute medical care? Clin Intern Aging. 2017;12:1–9.
10. Ellis G, Whitehead M, O'Neill D, Langhorne P, Robinson D. Comprehensive geriatric assessment for older adults admitted to hospital. Cochrane Database Syst Rev. 2014; https://doi.org/10.1002/14651858.CD006211.pub2. Accessed 17 July 2017.
11. Caillet P, Laurent M, Bastuji-Garin S, Liuu E, Culne S, Lagrange J-L, et al. Optimal management of elderly cancer patients: usefulness of the comprehensive geriatric assessment. Clin interv Aging. 2014;9:1645–60.
12. Ungar A, Mannarin G, van der Valde N, Baan J, Thibodeau MP, Masson J-B, et al. Comprehensive Geriatric Assessment in patients undergoing transcatheter aortic valve implantation-result from the CGA-TAVI multi-centre registry. BMC Cardiovasc Disord. 2018;18(1):1.
13. Mahoney FI, Barthel DW. Functional evaluation-barthel index. Md State Med J. 1965;14:61–5.
14. Lawton MR, Brody EM. Assessment of older people: self -maintaining and instrumental activities of daily living. Gerontologist. 1969;9:179–86.
15. Lubben JE. Assessing social network among elderly population. Fam Community Health. 1988;11(3):842–52.
16. Folstein MF, Folstein SE, PL MH. "Mini-mental status". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189–98.
17. Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR. A brief cognitive test battery to differentiate Alzheimer's and fronto-temporal dementia. Neurology. 2000;55(11):1613–20.
18. Hodge JR, Larner JH. Addenbrooke's cognitive examination: ACE, ACER, ACE III, ACE app and M ACE. In: Cognitive screening instruments. A practical approach. Cham: Springer; 2017. p. 109–37.
19. Storey J, Rowland JT, Basic D, Conforti DA, Dickson HG. The Rowland Universal Dementia Assessment Scale: a multicultural cognitive assessment scale. Int Psychgeriatr. 2004;16(1):13–31.
20. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and validation of a Geriatric Depression Screening Scale. A preliminary report. J Psch Res. 1983;17(1):37–49.
21. O'Keefe S. Deconditioning in old age. https://doi.org/10.13140/2.1.3889.1846 or Deconditioning in old age. In: Ekerdt DK, editors. Book: Encyclopaedia of aging, Macmillan: Reference USA. p. 2005–9.
22. Mathias S, Nayak USL, Issacs R. Balance in elderly patients, the "get up and go" test. Arch Phys Med Rehabil. 1986;14(6):387–9.
23. Rubenstein LZ, Harker JO. Screening for under-nutrition in geriatric practice: developing the short form mini-nutritional assessment (MNA-SF). J Gerontol. 2001;56A:M366–72.
24. World Health Organiszation. 1974. http://apps.who.ont/iris/bitstream/handle/10665/43030/9241592184.pdf?sequence=1.
25. Nicholas JA, Hall WA. Screening and preventive services for older adults. Mt Sinai J Med. 2011;78(4):498–509.
26. ABS 2009. http://www.abs.gov.au/ausstats/abs@.nsf/Previousproducts/4430.0Main%20Features22009.
27. Fried L, Ferrucci L, Durer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty and co-morbidity: implications for improved targeting and care. Journal of Gerontology: Medical Science. 2004;59(3):255–63.
28. Almy TP, et al. Subcommittee. American College of Physicians, Health and Public Policy Committee. Position Paper 1. Comprehensive functional assessment for elderly patients. Ann Intern Med. 1988;70–2.

29. Medicare benefit schedule book. November 2000 ed. Canberra: Department of Health and Aged Care; 2000.
30. www.who.int/ageing/publications/AF_PHC_Centretoolkit.pdf.
31. Ward KT. Comprehensive geriatric assessment. Uptodate. http://www.uptodate.com/content/comprehensive-geriatric-assessment. Accessed 16 July 2017.
32. Dupee R. Geriatric assessment. 2. Aging.ocw.tufts.edu/data/42/490303.pdf. Assessed 24 Apr 2018.
33. Mohd-sidik S, Aroll B, Goodyear-Smith F, Zain AM. Screening for depression with a brief questionnaire in a primary care setting: validation of two questions with help question (Malay version). Int J Psychiatry Med. 2011;41(2):143–54.
34. British Geriatric Society. Comprehensive assessment of the frail older patient. http://www.bgs.org.uk/good-practice-guides/resources/goodpractice/gpgassessment. Accessed 6 Jan 2017.
35. Walston JD, Fried LP. Frailty and its implications for care. In: Morrison RS, Meir DE, editors. Geriatric palliative care. New York: Oxford University Press; 2003.

Long-Term Care, Nursing Homes and Support Services

6

Kujan Nagaratnam and Nages Nagaratnam

Historical Perspective

In Britain in the early seventeenth century, workhouses were institutions that provided non-residential relief for return of work [1]. It was only after 1723 they formed part of Britain's societal system [1]. The treatment of the poor barely changed till 1834, when the Poor Law Amendment Act was passed [2]. The medical care in the workhouses were abhorrent until 1870 [3]. In about the 1850s, improvement began as a result of pressure from Joseph Rogers, a medical officer, Florence Nightingale and the journal, *The Lancet* [3]. Subsequently in 1894, the *British Medical Journal* began a drive to expose the poor conditions that still existed in the workhouse infirmaries [3]. Prior to admission to the workhouse patients are means tested and where applicable will be required to contribute to their maintenance in the infirmary [3].

In the United States soon after the Civil War, there were no age restrictions to institutions for long-term care, and the elderly, insane, inebriated and homeless ended their days in the almshouses [4]. By 1880 one-third of the inmates in the national almshouses were the elderly [4]. In the beginning of the nineteenth century, women and church groups began to create special housing for the elderly individuals of their own ethnic and religious background [4]. Soon after almshouses were debarred for payments resulting in the aged seeking asylum in private work houses for long-term care [4], and by 1920, 70% of the residents in almshouses were the elderly [5]. The Medical Facilities Survey and Construction Act of 1954 allowed the development of public institutions for the needy elderly and provided support for both private and public nursing homes [4].

K. Nagaratnam · N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: kujan@nagaratnam.net; nages@nagaratnam.net

In Australia formal aged care developed in an ad hoc way [6]. Between 1890 and 1900, places called asylums were used to house the destitute elderly who received basic support of food and water [7]. In 1962 with the introduction of the Commonwealth nursing home benefit, the provision of nursing homes was initiated largely by the profit sector [7]. Between 1963 and 1971, there was a rapid growth of nursing homes [7]. In 1985 a group of citizens in Victoria founded the Melbourne District Nursing Service with the object of looking after the disadvantage sick at their homes, and since then nursing service had spread to other states and territories [8].

General Considerations

Globally, in pre-industrial societies, very few older persons, disabled or otherwise, live alone. The percentage of elderly living alone in Denmark and Sweden is 42% compared to 17–19% in Spain, Greece and Portugal [9]. Most developed countries have accepted the chronological age of 65 years to define 'elderly 'or 'older person' [10]. The elderly have been categorised as young old between the ages of 65 and 74 years, old between 75 and 84 years and the oldest old those 85 years or over [11]. The older group those above 85 years is said to be a rapidly growing segment of the population and is expected to grow by nearly 4% per annum in Australia [12]. In the United States, the oldest old is projected to double from 4.3 million in 2000 to 9.6 million in 2030 [13].

Life expectancy or longevity has increased dramatically, and overall women live longer than men. Life expectancy is affected by several factors, and the significant factors are genetic, gender, diet, lifestyle, activity and access to health care. The centenarians are increasing in numbers globally [14]. A study of nonagenarians and centenarians in Switzerland between 1860 and 2001 indicated a strong increase in their numbers as compared to other

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countries. This was largely attributed to the decline in mortality after the age of 80 from 1950 [15]. Similar increasing numbers of centenarians are seen in Japan, New Zealand, France and the United States [16, 17]. Celebrated octogenarians like Winston Churchill, Charlie Chaplin and Katharine Hepburn demonstrate that life need not stop being vigorous, exciting and creative after the arbitrary point. Sri Kantha [18] identified 34 scientists who became centenarians in the twentieth century. He separated them into two groups. One group belonged to those who were active in research even in their late 90s. In contrast, the other group retired from active involvement in science in the nominal 65–70 years and then continued to live until 100. The centenarian scientist Hillebrand published most of his 300-odd papers after the official 'retirement' and even co-authored a paper at the age of 100 [18]. One way of postponing or thwarting the onset of age-related diseases is by studying the centenarians to find out why they are able to withstand diseases which affect the general population at a much younger age [19].

Disability and Disease

According to Australian data, 70% of the elderly aged 80 years and over have a handicap, and 41% are severely handicapped as revealed by the Survey of Disability, Ageing and Carers by the Australian Bureau of Statistics in 1993. Despite the fact that the life expectancy has increased, there has been little change in the overall expectancy of life with disability [20]. In a retrospective analysis of the profile of people of advanced age, Zhao et al. [21] recorded the functional and cognitive impairments were higher for those who died around 90 years or older (especially women) compared with those who died aged 85–89 years. Physical impairments and functional limitations have a considerable impact on daily life activities. The Danish 1905-Cohort Study involving 2249 nonagenarians recorded a high disability level, poor physical and cognitive performance and self-rated health (especially women) predict mortality [22]. Functional and cognitive assessments are an important part of the evaluation of the elderly. These two studies demonstrated that in the oldest old, physical and cognitive disabilities predict mortality, and such factors as smoking and obesity have little relevance.

The oldest-old age group is a rapidly growing segment worldwide. There is an increasing frequency of several diseases virtually involving all organs co-existing in older people leading to increasing morbidity [23]. The disease of one organ often affecting another compounding both, heralding debility and if not corrected, may lead to death. There is an increase in the needs for health and long-term care in these groups which are often entangled by countless and complex clinical problems requiring different health-care needs and increasing health-care costs [24]. Elderly people are particularly vulnerable and require a wide spectrum of services.

The oldest old may have on an average a better health with a rapid terminal decline relative to those who die earlier [25]. According to the Goteborg H70 longitudinal study of ageing and other studies, those who die between 70 and 85 years of age generally are very ill in the months or years before death. In contrast, individuals who live more than 85 years were seen as what has been described as in 'physical, social and mental vitality or healthy ageing' [26].

Data on the oldest-old transitions in place of care at end of life are scanty [27]. Fleming et al. [27] examined the place of residence or care of the over 85 years old less than a year before death and their place of death. They found that two-thirds were living in the community when interviewed less than a year before death and less than one-third who had lived at home died there. Care homes were the usual address of most people dying there (77% in residential homes and 87% in nursing homes), and 15% of deaths in acute hospital came from care homes. Harris et al. [28] reported a mortality rate of 6% for patients from the community as compared to 12% from a sheltered environment. In another study, the figures were 11% and 18%, respectively, and there were no significant differences in these rates between nonagenarians according to the source of residence or referral mode [29].

Studies of critically ill oldest-old patients (>90 years) admitted to the intensive care unit (ICU) found that very old age was not directly associated with ICU mortality [30, 31]. Death occurred predominantly around 3 months after ICU discharge, and prior limitation of activity was associated with the risk of dying, and ICU care should not be denied to this population [30].

Long-Term Care

People in this group at some stage in their life will find it demanding to look after themselves at home. The demand for care services may present itself after a sudden illness or accident, after a stay in hospital or may happen gradually. The general aim of aged care services is to keep old people in their own homes rather than a residential accommodation or in hospital [32]. This is accomplished by providing the form of service most befitting to the need of the elderly person. There has been an increase in the needs for health care and long-term care in these groups and are often compli-

cated by innumerable and complex clinical problems requiring different health-care needs and increasing health-care costs [24].

Risk factors for institutionalization are many, and a large number of the oldest old are in nursing home facilities. For a female aged 90 years or over, the probability of entering a nursing home is 95% and for men 60% [33]. Long-term care (LTC) typifies a variety of services that include medical and non-medical care to people with a chronic illness or disability [34] and people with different degrees of physical and mental impairment. LTC includes a wide range of services that entail medical, personal and social needs met in an array of locations and settings.

Numerous services are available to the ageing population in the community before entering a nursing home. Based upon the level of care and types of services, there are four main categories of services provided, namely, (i) independent living communities/retirement communities, (ii) assisted living facilities, (iii) continuing care retirement communities and (iv) skilled care/nursing homes.

Nursing Homes

At some stage in one's life, the prospect of living in a nursing home is significantly higher. By the age of 90 years, the probability increases to 60% for men and 95% for women [33]. All nursing homes provide a high level of care and are funded by the Commonwealth Government in Australia [32].They are staffed by registered and enrolled nurses and nursing assistants. Nursing homes are generally suitable for persons who require 24-h nursing care such as those with medical conditions or in the later stage of dementia.

Hostels provide low level of care and are funded by the Commonwealth Government [32]. They are appropriate for persons who are mobile and require assistance with activities of daily living such as personal hygiene and dressing and instrumental activities of daily living such as cooking, laundry, shopping and supervision of medication.

In Australia before a person can enter an aged care facility, he or she must be assessed by the Aged Care Assessment Team (ACAT). ACAT is usually based in a hospital or community centre and includes a doctor, social worker, physiotherapist, occupational therapist or other allied health personnel. Following an appointment, a member of the ACAT will visit the prospective resident either in his or her home or in hospital. ACAT will determine the level of care, low level (hostel) or high level (nursing home) care. ACAT can also assess whether a person is suitable for home care packages [35] (Box 6.1).

Box 6.1. Functions of Aged Care Assessment Team
Assessment** for

(i) High level of care (nursing homes)
(ii) Low level of care(hostels)
(iii) Community Aged Care Package (CACP)
(iv) Extended Aged Care in the Home (EACH)
Approve for transition care
Arrange for respite care
Refer to community care services

**Not required for Home and Community Care (HACC) or for retirement villages

After assessment, the person assessed is not under any obligation to enter the nursing care facility. In the case of an individual who does not have the mental capacity, the decision can be made by the his or her legal guardian. The assessment for residential care is valid indefinitely, whereas the level of home care packages may require reassessment if the person's care needs changes. Following the assessment based on the assessment data, the needs of the individual are identified and then translated into services and settings for long-term care.

Long stay refers to accommodations that are for unlimited period of time. Short stay refers to short-lived stays up to a maximum of 90 days per year. There are two types of short stay. Short-stay respite services provide a caregiver a breather from caregiver duties. This can take the form of either care in day centre, a short stay in a residential aged care facility or support in the individual's home for a few hours a week. The other short stay is the supportive care services which provide help to regain confidence, improve independence and strength especially following a stay in hospital. Also known as transition care [36], it can be either high-level or low-level care depending on the individual's needs, and usually it is up to 12 weeks. Hospice care is for individuals who are not expected to live for more than 6 months [37] and are provided in the individual's home, nursing home, assisted living centres or hospitals.

Support Services

The Commonwealth provides payments and supports chiefly to the aged in the way of age pensions, rent assistance, residential services, public housing, medical and pharmaceutical benefits, community care, hospital and home support and acute care [32].

Community Care Services

The Commonwealth Government is involved in providing funding for nursing homes and community services for the aged [32]. These services provide basic needs and ensure safety and independence of individuals within the recipient's home or in different locations around the individual's communities. There is a wide variety of community services which include meal programmes, day care, transportation and other services (see Box 6.2).

Box 6.2. Community Support Services
Meals on wheels
Transportation
Caregiver respite
Foot care
Home maintenance and repair
Housing
Home help
Security

Clinical Relevance
Analysis of the profile of people of advanced age, functional and cognitive impairments were higher for those who died around 90 years or older (especially women) compared with those who died aged 85–89 years [21].

Care homes were the usual address of most people dying, 77% in residential homes and 87% in nursing homes and 15% of deaths in acute hospital came from care homes [27].

Long-term care (LTC) typifies a variety of services that include medical and non-medical care to people with a chronic illness or disability [34].

LTC includes a wide range of services that entails medical, personal and social needs met in an array of locations and settings.

ACAT will determine the level of care, low-level (hostel) or high-level (nursing home) care.

ACAT can also assess whether a person is suitable for Home and Community Care [35].

Multiple Choice Questions (MCQs)

1. The following in relation to long-term care for the elderly are true, EXCEPT:
   A. About 70% of the elderly 80 years and over have a handicap and 41% severely handicapped.
   B. The demand for care services can happen gradually or after a sudden illness, accident or stay in hospital.
   C. By the age of 90 years, the probability of entering a nursing home for permanent care is 95% for men and 60% for women.
   D. There are a wide variety of services available to old people.
2. The following factors portend institutionalization for the elderly are true EXCEPT:
   A. Multiple co-morbidities
   B. Behavioural and psychiatric symptoms
   C. Safety concerns
   D. Unable to sleep

Answers to MCQs
1. C
2. D

Short-Answer Questions (SAQs)

1. List four functions of the Aged Care Assessment Team (ACAT).
2. List four community services.

Answers to SAQs
1. (i) Assess for different levels of care.
   (ii) Approve for transitional care.
   (iii) Arrange for respite care.
   (iv) Refer to community care services.
2. (i) Meal-on-wheels
   (ii) Caregiver respite
   (iii) Home maintenance and repair
   (iv) Domestic assistance

References

1. BBC History Magazine. The rise and fall of the workhouse. http://www.historyextra.com/workhouse. Accessed 14 Apr 2017.
2. Londonist. Punished for being poor: London's forgotten workhouses. http://londonist.com/204/04/punished-for-being-poor-londons-forgotten-workhouses. Accessed 14 Apr 2017.
3. Higginbotham P. Medical care in the workhouse. http://www.workhouses.org.uk/life/medical.shtml. Accessed 14 Apr 2017.
4. FATE. Foundation Aiding The Elderly. The history of nursing homes www.4fate.org/history.pdf.
5. Rincon del Rio. The history of nursing homes: from alms houses to skilled nursing. http://rincodelrio.com/info-for-seniors/th-history-of-nursing-homes-from-almshouses-to-skilled-nursing/. Accessed 28 Jan 2017.
6. Brown L, Nepal B, Thurech L. Aged care in Australia. Past Present and Future. www.natsem.canberra.edu.au/storage/Brown9620-9620ged%20%20-%20past%0resent%20future. Accessed 18 Apr 2017.
7. Aged Care in Australia_ introduction. www.slideshoare.net/goodburn/aged-cae-inaustraliaintroductionfeb08. Accessed 16 Apr 2017.
8. Australian Bureau of Statistics. Home nursing in Australia. www.abs.gov.au/ausstats/abs@.nsf/09/911b5af721818795ca2569de0024eda?OpenDocument. Accessed 20 Apr 2017.
9. Long-term care around the globe-history of long-tem care. http://www.medicine.jrank.org/page/1056/Long-Term-Care-Arnd-Globe-History-Long-Term-Care.html. Accessed 28 Jan 2007.
10. World Health Organisation. Definition of older or elderly person. www.who/int/healthinfo/survey/ageingdef-older/en/index/html. Retreived 25 Jan 2010.
11. Balducci L, Cohen HJ, Engstrom PF, Ettinger DS, Hater J, Gordon LI, et al. Senior adult oncology, clinical practice guidelines in oncology. J Natl Campr Canc Netw. 2005;3:72–5.
12. Australlian Institute of Health and Welfare. Australia's welfare 1997: services assistance. Canberra: Australian Institute of Health and Wealth; 1997.
13. Gundrum JD, Go R, Kwong R. Cancer in the oldest old population in the United States: current statistics and projections. J Clin Oncol 2009;27 No: 1555 (May 20 supplment):9553.
14. Larkin M. Centenarians point the way to healthy ageing. Lancet. 1999;353:1074.
15. Robine J-M, Paccaud F. Nonagenarians and centenarians in Switzerland,1860-2001: a demographic analysis. J Epidemiol Community Health. 2005;59:31–7.
16. Robine J-M, Sato Y, Jagger C. The emergence of extremely old people: the case in Japan. Exp Gerontol. 2003;38:735–9.
17. AnionA J, Poupard M. Prevalence and incidence of dementia among the very old. Review of the literature. Revue d'Epidemiologie et de Sante Publique. 2003;51:349–60.
18. Sri Kantha S. Centenarians scientists: an unusual cluster newly formed in the 20th century. Med Hypothesis. 2001;57(6):750–63. Harcourt Publishers Limited
19. Barzilai N, Gabriely I, Gabriely M, Iankowitz N, Sorkin JD. Offspring of centenarians have favourable lipid profile. J Am Geriatr Soc. 2001;49(1):76–9.
20. Australian Institute of Health and Welfare. Australia health, 1996. Canberra: Australian Institute of Health and Welfare; 1998. p. 68–9.
21. Zhao J, Barclay S, Farquar M, Kinmouth AL, Brayne C, Fleming J, et al. The oldest old in the last year of life: population based findings from Cambridge City over 75s cohort study participants aged 85 and older at death. J Am Geriatr Soc. 2010;58:1–11.
22. Nybo H, Petersen HC, Gaist D, Jeune B, Andersen K, McGue M, et al. Predictors of mortality in 2,249 nonagenarians-the Danish 1905 Cohort Survey. J Am Geriatr Soc. 2003;51:1365–73.
23. Solichova D, Melichar B, Blaha V, Klejna M, Vavrova J, Pallicka V, et al. Biochemical profile and survival in nonagenarians. Clin Biochem. 2001;34:563–9.
24. Callahan D. Controlling the costs of health care for the elderly; fair means or foul. N Engl J Med. 1996;335:744–6.
25. Hitt R, Young -Xu Y, Silier M, Peris T. Centenarians:' the older you get the healthier you have been. Lancet. 1999;354:662.
26. Hessler RM, Eriksson BG, Dey D, Steen G, Sundh V, Steen B, et al. The compression of morbidity debate in aging: an empirical test using the gerontological and geriatric populations. Studies in Goteborg, Sweden (H70). Arch Gerontol Geriatr. 2003;37:213–22.
27. Fleming J, Zhao J, Fraquar M, Bryne C, Barclay S. Place of death for the oldest old: >85 years old in the CC75CC population-based cohort. Br J Gen Pract. 2010;60:e171–9.
28. Harris JH, Finucane PM, Healy DC, Bakarich AC. Use of in patient hospital services by people aged 90-99 years. Med J Aust. 1997;167:417–20.
29. Nagaratnam N, Gayagay G Jr. Validation of the cumulative illness rating scale (CIRS) in hospitalised nonagenarians. Arch Geront Geriatr. 2007;44:29–36.
30. Rellos K, Falagas ME, Vardakas KZ, Sermaides GS, Michalopoulos A. Outcome of critically ill oldest-old patients (aged 90 and older) admitted to the intensive care unit. J Am Geriatr Soc. 2006;54(1):110–4.
31. Somme D, Maillet JM, Gissbrecht M, Novra A, Ract C, Fagin JY. Critically ill old and oldest old patients in intensive care short and long term outcomes. Intensive Care Med. 2003;29(12):211–5.
32. McIntosh G, Phillips J. 'Caring for the elderly'-an overview of aged care support and services in Australia. http://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/Publications_Archive.archive/agedcare. Accessed 28 Jan 2017.
33. Liu Z. The probability of nursing home care over a life time. Canberra. Australian Institute of Health and Welfare. Wellfare Diversion Working Paper No: 10. 1998.
34. Doty P, Liu K, Weiner J. An overview of long term care. Health CareFinan Rev. 1985 spring;(3):69–78.
35. Aged Care Assessment Teams, Australian Government, The Department of Health. Updated 22 Aug 2013.
36. Myaged care-after-hospital care (transition care). www.myaged-care.gov.au/after-hospital-care-transition-care. Accessed 22 Apr 2018.
37. Harris PS, Stalam T, Archi LA, Harold JE, Craig T, Teno J, et al. Can hospices predict which patients will die within six months. J Palliat Med. 2014;17(8):984–898.

Immune System, Immunosenescence and Immunisation in the Elderly

7

Nages Nagaratnam and Sai Adithya Nagaratnam

Historical Perspective

The prehistoric people interpreted disease through the spirits they believed in. The ancient Egyptians, the Greeks and the Romans also had supernatural approaches to disease and had strong belief in their gods [1].They believed that disease was a punishment by the gods for their sinful acts. Between then and the nineteenth century, disease was attributed to an imbalance or a change in one of the four humours, blood, phlegm, yellow bile and black bile [2]. In 430 BC the Athenian Thucydides described the plague of Athens and recorded that those who recovered from the disease attended to the sick and dying for they knew from their experience they will not be attacked a second time [3]. The word immunity was derived from the Latin words *immunis* and i*mmunitas* initially in Rome, meaning exemption from military service or duty [4]. Around 60 BC the poet Marcus Annaeus Lucanus used the term 'immunes' in his epic poem *Pharsalia* to describe the North African Psylli tribe's resistance to snakebite venom [4, 5].

In the ninth century, an Islamic physician Al-Razi distinguished smallpox from measles [1]. Modern scientific methods were applied during the renaissance and thereafter, based on careful observation and recording of patient's symptoms [1]. Edward Jenner (1749–1823) in 1796 inserted pus from a cowpox pustule into the arm of an 8-year-old boy, James Phipps. He subsequently proved that Phipps was immune to smallpox having been inoculated with cowpox. He later coined the word vaccine from the Latin word 'vacca' for cow [6]. Ilya Mechnikov was the first to recognise the contribution of phagocytosis to the generation of immunity [7]. In 1908 he was awarded together with Paul Ehrlich the Nobel Prize for Physiology or Medicine. Robert Koch a country physician identified the organism responsible for tuberculosis. Louis Pasteur's work together with that of Koch's led firmly to establishing the germ theory of diseases [7]. Pasteur created vaccinations for rabies and anthrax. The first realistic approach to the treatment of infectious diseases was the discovery of diphtheria toxin by Emil von Behring and Shibasaburō Kitasato in the 1890s [8]. Behring was awarded the Nobel Prize in Physiology or Medicine in 1901 for his work on serum therapy.

The earliest recognised attempt to induce immunity to an infectious disease was around 1000 AD in China by drying and inhaling crusts of smallpox lesions [3]. Mithridates VI, king of Pontus, lived between the second and first century BC, and the origin of active immunotherapy may have begun then. Mithridates consumed small doses of various types of poisons in order to develop immunity against them should someone try to kill him by this means [9].

General Considerations

The immune system is a complex process which responds to the invasion by viruses, bacteria and other pathogens by systemic inflammation. The immune system is divided into two categories, namely, innate and adaptive (Fig. 7.1), and more recently attention has been drawn to the interface between the two [10]. The former refers to non-specific mechanisms and includes physical barriers, physiological barriers and phagocytic cells. The natural killer cells (NK cells), neutrophils and macrophages are components of the natural innate immune system [11]. The innate immune system does not require previous experience to carry out its functions [12]. When the innate immune defences are avoided or overpowered, the adaptive immune system responds [12].

The adaptive immunity is more complex and is comprised of T and B cells and consists of two arms, cellular immunity (mediated by T cells) and humoral immunity (mediated by

N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

S. A. Nagaratnam
Westmead Hospital, Westmead, NSW, Australia
e-mail: sai@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_7

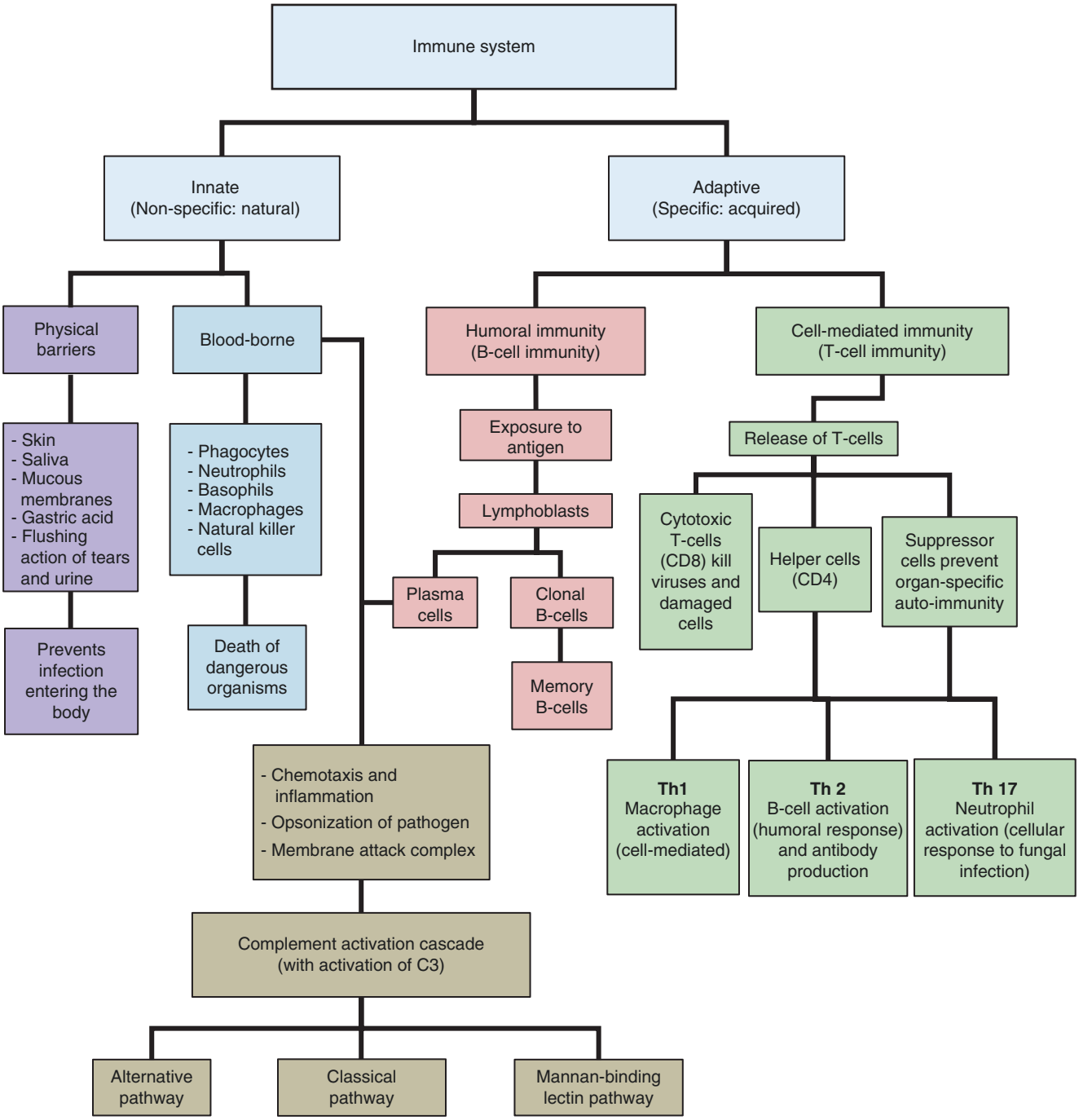

Fig. 7.1 The immune system. (Adapted with the permission of Virtual Medical Centre. Other sources Chaudhry [12], Troow and Daha [17], Rus et al. [18])

B cells) [12]. The T cells are specialised in the thymus gland and plays an important role in adaptive immunity via cellular immunity and B cell-mediated humoral immunity [13]. T cells have to be activated by functional antigen-presenting cells (APCs) to initiate adaptive immune response [10]. Both T and B cells are directed against specific antigens [12]. The T cells are released as cytotoxic T cells (CD8+), helper T cells (CD4+) and suppressor T cells. T cells play a significant role in the prevention of organ-specific autoimmunity and allograft rejection [14]. The helper T cells activate B cells to secrete antibodies, activate macrophages to destroy ingested microbes and activate cytotoxic T cells to kill infected target cells [15]. Once activated to become an effector cell, the helper cell helps to activate other cells, and it is the innate immune responses that determine what kind of helper T cell will develop into [15]. Th1, which secretes IL 2

and IFN 8, play an important role in macrophage activation, Th2, which secretes IL 4,516[d]10, in B cell activation and antibody production and Th17 which secretes IL222[d]147, in fungal infections [12].

Two classes of major histocompatibility complex (MHC), the MHC I and MHC II, play vital roles in adaptive immunity [16]. Both present peptides on the cell surface for the recognition by T cells {16}. MHC I found on the surface of all nucleated cells allows cytotoxic CD8(+) T cells to destroy cells infected with virus or damaged cells. MHC II expressed by antigen-presenting cells (APCs) display an array of peptides to the T cell receptors of helper CD4(+) T cells [17] and initiate an antigen-specific response.

The mechanism mediated by the antibody called humoral immune response is brought about by antibodies that bind to the antigens and promote their destruction. The mature B cell when it leaves the bone marrow is not as yet exposed to self-antigen and requires signals from helper T cells (Th2) to make antibody. After activation of the B cells, they differentiate into plasma cells which secrete abundant amounts of antibodies [12]. Each plasma cell is specific for a specific antibody [12]. Following clonal expansion of an activated B cell is the memory B cell which functions in a similar way to that of memory T cells. Unlike the innate immune system, the adaptive immune system requires prior experience. To make future responses against a specific antigen more effective, a relative amount will be retained as 'memory' which provides adequate immune protection against recurring pathogen in the domain [18]. The term *repertoire* is used to refer to the collection of cells that respond to a specific pathogen [18].

During analysis of T cell responses to pathogens, T cell receptor (TCR) nucleotide sequences are created [18]. The capacity to distinguish the body's own cells (self-antigen) from that produced by invaders (non-self-antigen) is made by way of the T cell receptors (TCR) or B cell receptors (BCR). The third complementary-determining region (CDR3) is the most significant region of the TCR and whose nucleotide sequence is unique to each cell clone [18].

The complement system heightens the strength and actions of innate immune response and is a major component of the innate immune system [19] defending against all foreign pathogens via complement fragments that take part in chemotaxis, opsonisation and activation of the leucocytes [20]. The complement system is also involved in tissue regeneration and clearance of immune complexes and dead cells [19, 20]. It is also closely involved in the adaptive B and T cell responses [21]. There are three pathways through which complement can be activated on pathogen surfaces [12]. The three pathways are the classical pathway, the mannan-binding lectin pathway (MB-lectin pathway) and the alternative pathway. A protease called C3 convertase is generated in each of these pathways through a series of reactions and is bound covalently on the pathogen surface [22]. The C3 convertases cleave C3 to generate C3a a peptide mediator of inflammation and C3b. The C3b binds the C3 convertase to form C5 convertase to produce C5a, another peptide mediator of inflammation [22].

Immunosenescence

The ageing of the immune system is known as immunosenescence. It affects both innate and adaptive immunity [23]. Immunosenescence affects the innate immunity, the NK cells, polymorphonuclear leucocytes and macrophages which are part of the natural immune system [11, 24, 25]. Adaptive immunity with ageing is characterised by a reduced humoral response as well as a decrease in cell-mediated immune function [26]. In the elderly alterations occur in the innate/natural and clonal-type immunity, and the former is largely preserved [11, 27], whereas the clonic compartment undergoes appreciable alterations [11, 27–29].

The alterations in the innate immune system associated with ageing have been shown to affect the natural killer (NK) cells. The natural killer (NK) cells whose role is to target virally infected, tumerogenic or other abnormal cells increase in numbers with increasing age [30] to compensate for their impaired function [10], but their toxicity and that of the antigen-presenting dendritic cells diminish with age [31–33] with reduced production of cytokines and chemokines by the activated NK cells [26, 31, 34]. Similar increases are seen in the other NKT-related cells. NKT cells exhibit features of both T and NK cells. The function of the NK cells is controlled by diverse families of antigen receptors, the most prominent among them is the killer cell immunoglobulin-like receptor (KIR) [30]. There is a decline in their phagocytic capacity [24, 25]. Macrophages play an important role in the initiation of inflammatory responses, elimination of pathogens, manipulation of adaptive immune response and reparation of damaged tissue [35]. Wound healing is impaired, but it is offset by relocation of young macrophages [10]. There seems to be a decline in the number of phagocytes in the aged host with reduction in their bacterial activity [36, 37].

The alterations to the clonal-type immunity are brought about by involution of the lymphoid tissue, continuous exposure to a variety of antigens, reduced number of dendritic cells, debilitation of the naïve cells and accumulation of memory/effector T cells [27]. The accumulation of late differentiated effector T cells commonly associated with cytomegalovirus (CMV) infection results in a decline in their ability of the adaptive immune mechanism to respond to novel antigens [33]. The composition of T cell subsets is altered by CMV infection resulting in an increased number of CD8+ and CD57+ subsets in CMV-positive individuals [28], and the clonal expansion of CMV-specific CD8+ cells increases with age [28]. The

T cell activation and susceptibility to apoptosis are decreased in aged individuals and are due to CD28 which is an important receptor [28]. CD8+ and CD28- population is increased with age and CMV positivity [28].

In the aged, the age-dependent decline in immunity has been attributed to the functional activity of the haematopoietic stem cells (HSC) [38], and there is evidence to suggest that there is a decline in function with ageing [39]. HSC gives rise to all the components of the immune system, lymphoid as well as myeloid and with ageing an inclination towards myeloid lineage. Haematopoietic stem cells lose their capacity to self-renewal due to accumulation of oxidative damage to DNA by ageing [40] and are distinct from thymic changes [10].

Replicative senescence and degenerative changes associated with involution of the thymus are two mechanisms whereby age has an effect on host immunity [10]. Replicative senescence suppresses tumorigenesis, and there is indirect evidence that it contributes to ageing [41]. The senescence of clonotypic immunity is mostly the result of the T cells [11]. The T cell function begins to decline from birth with involution of the thymus and lifelong chronic antigenic stimulation. There is a progressive age-dependent decline of virgin T cells (CD 95), and the immune function of the elderly is weakened by exhaustion of the CD95- virgin cells and replaced by large clonal expansion of memory CD28- T cells [42]. In advanced age EBV and CMV induce different CD8+ T cells both in quality and in quantity [11]. The age-dependent expansion of CD28- T cells mostly positive for pro-inflammatory cytokines underscores the importance of chronic antigenic stimulation [43] in the pathogenesis of the main immunological changes with ageing (Box 7.1).

Box 7.1. Pathophysiology of Immunosenescence

Immunosenescence affects both innate and adaptive immunity.

Innate Immunity

Affects the natural killer (NK) cells; increase in numbers to compensate for impaired function [21].
Dendritic cells diminish with age [29–31].
Reduced number of phagocytes with reduced phagocytic capacity [34].
Decline in function of haematopoietic stem cells (HSC) with inclination towards myeloid lineage.

Adaptive Immunity

Reduced humoral response [24].
Decrease in cell-mediated functions [24].
Accumulation of memory/effector T cells [25].
CD8+ CD28− T cells increase with age [28].

Age-Related Diseases

Most of the parameters are largely under genetic control [44]. The susceptibility of the elderly to infectious diseases, autoimmunity and cancer and in their decreased responsiveness to vaccination is directly or indirectly related to age-related changes of the immune system [11]. It has been suggested that age-related diseases are due at least in part to dysregulation of the function of the immune system [45]. There is a high incidence of infection in the elderly, and the outcomes are severe [46]. Several pathologies such as dementia, atherosclerosis, and cancer all of which share an inflammatory pathogenesis may be the result of such immunological alterations with ageing [46].

The genetic component is involved in the achievement of longevity. In the course of evolution, the human organism is set to live 40–50 years [47]. Presently in a period not foreseen by evolution, the immune system has to be active for longer periods of time. The genetic component appears to control the functioning of the innate/inflammatory and clonotypic responses and necessarily the inflammatory state in later life [48, 49]. Although inflammatory genotypes are important in early life, excessive production of inflammatory molecules may be detrimental and cause immune-related inflammatory diseases [47].

The major driving force of immunosenescence seems to be the lifelong chronic antigen load [11, 39] which leads to chronic inflammatory status [28] resulting in damage to the organs later in life and is deleterious for longevity [11]. Chronic antigenic overload (virus, bacteria, fungi, toxins, mutated cells) results in a pro-inflammatory condition that continuously stimulates innate immunity and seems to incline towards the onset of age-related disease where immune and autoimmune factors play an important role [28]. The immune activity of the innate immune system in later life is evident by the presence of elevated markers of inflammation such as TNF-alpha and interleukin-6 (IL-6) [50]. The elevation of these markers of inflammation is associated with disability and death [51].

Immunisation in the Elderly

Nutrition including protein malnutrition and deficiency of vitamins and free elements may underlie many immune deficits attributed to ageing [52, 53]. The elderly have a greater susceptibility to infection due to age-related decline in immune responses [33]. The frequency and severity of infectious diseases are increased in the elderly [28]. Cytomegalovirus (CMV) is the leading cause of mortality in immunosuppressed individuals, and the immune system plays a vital role in controlling it by decreasing its effect on the individual [54]. The elderly have increased rates of infection and multiple co-morbidities. An intact cell-mediated

immunity is essential to generate the humoral response to vaccination which is distinctly diminished in some of the elderly [10]. The ability of the immune system to produce specific antibodies and memory cells in response to stimulation with an antigen is referred to as active immunisation. The ability of the elderly to produce antibodies in response to vaccination is not clearly understood. Active immunisation by vaccine administration in the elderly is safe and effective even in the presence of illness [55].

It is well documented that diseases such as tuberculosis, pneumonia and bacteraemia have an increased incidence and increased fatality rate in the elderly [55]. The elderly are at greater risk of vaccine-preventable diseases [56]. Vaccine-preventable diseases contribute significantly to increased mortality and morbidity among the elderly [57, 58]. And older adults with co-morbidities are at high risk of complications [56]. Despite the beneficial effects of vaccination, vaccination rates remain low among the elderly [57]. In the USA, the majority of deaths from influenza occur in over 60 years old, yet only 60% of the older adults are immunised against influenza [56].

Older adults require vaccination against the following diseases, namely, seasonal influenza, pneumococcal disease, shingles, tetanus, diphtheria and pertussis. It is recommended that adults above the age of 50 have influenza vaccination and every ten-yearly tetanus-diphtheria and adults above 65 for one-time pneumococcal vaccination who are either healthy or have medical conditions [56]. The elderly especially the bedridden and those in institutions are at increased risk of severe disease. The oldest old in a recent study was shown to be 16 times more likely to die of influenza-related disease [59] and 32 times more likely to die of influenza-related pneumonia than those between the ages of 65 and 69. In the USA, more than 90% of the influenza-related annual deaths occurred in those 65 years or older [60].

The influenza viruses have two external viral glycoproteins, namely, haemagglutinin (HA) and neuraminidase (NA), which permit the virus to attach and infect the susceptible host [61]. There are three major subtypes of HA (H1, H2, H3) and two subtypes of NA (N1 and N2) [62]. Changes in the antigenicity occur annually with influenza. Mutations of HA and NA within the type of influenza virus are known as 'antigenic drift', a continuous process for both A and B viruses [61]. It can be substantial and has led to extensive epidemics and severe outbreaks. With increasing age there is decreasing vaccine effectiveness due to the decline in immune function resulting in waning of vaccine-induced immunity [63].

Influenza vaccination is recommended to (i) all elderly above the age of 65 years, (ii) to all those in residential and long-term care facilities and (iii) to all suffering from chronic pulmonary and immune-depressed patients. The only contraindication to vaccination is hypersensitivity to hen's eggs. Yearly vaccination is recommended. A recent development of live attenuated influenza A virus given intranasally has shown promising results. Influenza vaccination is recommended for residents in aged care facilities and healthcare carers [56, 64].

To improve their efficacy, new vaccines are being developed such as intradermal and high-dose vaccines for influenza [33]. Pneumonia in the oldest old often follows influenza. Since influenza frequently causes secondary bacterial pneumonia, it is recommended that patients who are at high risk should be encouraged to have pneumococcal vaccine. It includes elderly with chronic heart and lung disease, diabetes, asplenism and malignancy. Revaccination should be considered after 6 years. Pneumococcal vaccine is given after 6 years with the current 20-valent polysaccharide [64] vaccine and to include all adults with asthma and all smokers [58]. For those above the age of 60, a single vaccination with current live herpes zoster vaccine is recommended [58]. Herpes zoster affects 20–30% of adults with more than 50% occurring in those above the age of 60, and 40% develop post-herpetic neuralgia [64]. Hepatitis B vaccination should be encouraged in non-immune adults [65]. Tetanus vaccination and revaccination are recommended to older people exposed to the agent. It is fatal in at least 32% of people over the age of 80 years [55]. Certain subsets of the elderly may require vaccinations for hepatitis A, hepatitis B, meningococcal disease, varicella and measles, mumps and rubella (MMR) [56].

Clinical Relevance

The ageing of the immune system is known as immunosenescence.

With ageing there are alterations to the immune system [11, 25] and the capacity to respond to infection.

The elderly have a greater susceptibility to infection due to age-related decline in immune responses [31], and the elderly are at greater risk of vaccine-preventable diseases.

Active immunisation by vaccine administration in the elderly is safe and effective even in the presence of illness [53].

Older adults require vaccination against the following diseases, namely, seasonal influenza, pneumococcal disease, shingles, tetanus, diphtheria and pertussis.

Certain subsets of the elderly may require vaccinations for hepatitis A, hepatitis B, meningococcal disease, varicella and measles, mumps and rubella (MMR).

All elderly above the age of 65 in residential and long-term facilities and those with chronic pulmonary, cardiovascular, malignant and metabolic diseases should be offered vaccination.

Multiple Choice Questions (MCQs)

1. The following in relation to the immune system in the older adult are true EXCEPT:
   A. With ageing there is a reduced humoral response as well as a decrease in cell-mediated immune function.
   B. With increasing age there is an increase in the absolute number of total CD3+ T cells involving CD4+ and CD8+ subsets and a reduction of B cells.
   C. In the elderly alterations occur in the innate/natural and clonal-type immunity, and the former is largely preserved.
   D. The major driving force of immunosenescence seems to be the lifelong chronic antigen load.
2. The following are true in relation to immunisation for the elderly, EXCEPT:
   A. The elderly are at a greater risk of vaccine-preventable diseases.
   B. There is decreased responsiveness to vaccination in the elderly.
   C. Hepatitis B vaccination should be encouraged in non-immune adults.
   D. For those above the age of 60, vaccination with current live herpes zoster vaccine is not recommended.

Answers to MCQs

1. B
2. D

References

1. Medicine through time. Disease and infection. Revision guide. History-help.wikia.com/wiki/Medicine_Through_Time_Disease_and_Infection_Revision_Guide. Accessed 29 Dec 2016.
2. http://en.wikipedia.org/wiki/Four_humors.
3. Gherardi E.The concept of Immunity. History and applications. Immunology Course Medical School, University of Pavia. http://nfs.unipv.it/minf/dispense/immunology/immun.html.
4. Silverstein AM, Bialasiewicz AA. A history of theories of acquired immunity. Cell Immunol. 1980;51:151–67.
5. Silverstein AM. History of immunology. Academic Press. http://www.amazon.com/gp/reader/012643770X.
6. Jenner E (1749–1923). http://www.bbc.co.uk/history/historc_figures/jenner _edward.shtml. Accessed 29 Dec 2016.
7. Greenberg S. A concise history of immunology. www.columbia.edu/etc/hs/medical/pathophys/immunology/readings/Concise-History-Immunology.pdf. Accessed 28 Dec 2016.
8. www.coloumbia.edu/itc/hs/medical/pathophys/immunology/readings/Concise-HistoryImmunology.pdf. Accessed 29 Dec 2016.
9. Ancient Origins. Mithridates VI of Pontus: the poison king of Pontus and aggravation to Rome. http://www.ancient-origins.net/history-famous-people/mithridates-vi-pontus-poison-king-ponts-and-aggravation-rome-005907. Accessed on 29 Dec 2016.
10. Castle SC. Clinical relevance of age-related immune dysfunction. Clin Infect Dis. 2000;31(2):578–83.
11. Burkle A, Casell G, Franceschi C, Mariani E, Sansoni P, Sansoni A, et al. Pathophysiology of ageing, longevity and age related disease. Immunity Aging. 2007;4(4) https://doi.org/10.1186/1742-4933-4-4.
12. Chaudhry S. Introduction to immunology. McMaster pathophysiology. Review. http://www.pathophys.org/immunology/. Accessed 25 Nov 2016.
13. Gruver AL, Hudson LL, Sempowski GD. Immunosenescence of ageing. J Pathol. 2007;211(2):144–56.
14. McHugh RS, Shevach EM. The role of suppressor T cells in regulation of immune responses. J Allergy Clin Immunol. 2002;140(5):93–702.
15. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walker P. Helper T cells and lymphocyte activation. In: Molecular biology of the cell. 4th ed. New York: Garland Science; 2002.
16. Wieczorek M, Abuairous ET, Sticht J, Alvaro-Beniti M, Stolzenberg S, Noe F, et al. Major histocompatibility complex (MHC) Class I and MHC Class II proteins: conformational plasticity in antigen presentation. Front Immunol. 2017;8:292. https://www.ncbi.nim.gov/pmc/articles/PMC5355494/. Accessed 9 Jan 2018.
17. Jones EY, Fugger L, Strominger JL, Siebold C. MHC class II proteins and disease :a structural perspective. Nat Rev Immunol. 2006;6:271–82.
18. Yassai MB, Naumov YN, Naumova EN, Gorski J. A clonotype nomenclature for T cell receptors. Immunogenetics. 2009;61(7):493–502.
19. Troow LA, Daha MR. Role of complement in innate immunity and host defense. Immunol Lett. 2011;138(1):35–7.
20. Rus H, Cudrici C, Niculescu F. The role of the complement system in innate immunity. Immunol Res. 2005;33(2):103–12.
21. Le Friec Gaelle KC. Complement: coming a full circle. Arch Immunol Ther Exp. 2009;57(6):393–407.
22. Janeway CA Jr, Travers P, Walport M, Shlomchi KM. Immunobiology: the immune system in health and disease. 5th ed. New York: Garand Science; 2001.
23. Ongradi J, Stercz B, Kovesdi V, Vertes L. Immunosenescence and vaccination of the elderly. I age-related immune impairment. Acta Microbiol Immunol Hung. 2009;56(3):199–210.
24. Gomez CR, Boehmer ED, Kovacs EJ. The aging innate immune system. Curr Opin Immunol. 2005;17:457–62.
25. Plackett TP, Boehmer ED, Faunce DE, Kovacs EJ. Aging and innate immune cells. J Leukoc Biol. 2004;76:291–9.
26. Weiskopf D, Weinberger B. Grubeck-Loebenstein B. The aging immune system. Transpl Int. 2009;22(11):1041–50.
27. Franceschi CS, Bonafe M. Centenarians as a model for healthy aging. Biochem Soc Trans. 2003;3192:457–61.
28. Vasto S, Colonna-Romano G, Larbi A, WikbyA CC, Pawelec G. Role of persistent CMV infection in in figuring T cell immunity in the elderly. Immun Ageing. 2007;4:2. https://doi.org/10.1186/1742-4933-42.
29. Pawelec G, Barnett Y, Forsey R, Frasca D, Globerson A, McLeod J, et al. T cells and ageing Front Biosci. 2002;7:d1056–183.
30. Rea IM. Belfast nonagenarians: nature or nurture ? Immunological cardiovascular and genetic factors. Immun Ageing. 2010;7:6. http://www.immunity.ageing.com/content/7/1/6. Accessed on 25 Oct 2010.
31. Mocchegiani E, Malavolta M. NK and NKT cell functions in immunosenescence. Aging Cell. 2004;3(4):17–184.
32. Uyemura K, Castle SC, Makinodan T. The frail elderly: role of dendritic cells in the susceptibility of infection. Mec Ageing Dev. 2002;123:955–62.
33. Grubeck-Loebenstein B, Della Bella S, Iorio AM, Michel JP, Pawelec G, Solana R. Immunosenescence and vaccine failure in the elderly. Aging Clin Exp Res. 2009;21(13):201–9.
34. Solana R, Mariani E. NK and NKT cells in human senescence. Vaccine. 2000;18:1613–20.

35. Plowden J, Renshaw-Hoelscher M, Engleman C, Katz J, Samhara S. Innate immunity in ageing: impact on macrophage function. Aging Cell. 2004;3(4):161–7.
36. Lord JM, Butcher S, Killampali V, Lascelles D, Salmon M. Neutrophil ageing and immunosenescence. Mech Ageing Dev. 2002;122(14):1521–35.
37. Strout RD, Sutters J. Immunosenescence and macrophage functional plasticity: dysregulation of macrophage function by age associated microenvironmental changes. Immunol Rev. 2005;205:60–71.
38. Aw D, Silva AB, Palmer DB. Immunosenescence: emerging challenges for the ageing population. Immunology. 2007;120(4):435–46.
39. Geiger H, Van Zant G. The aging of lympho-hematopoietic stem cells. Nat Immunol. 2002;3:32–3.
40. Ito K, Hirao F, Arai S, Matsuoka S, Takubo K, Hamaguchi J, et al. Regulation of oxidative stress by ATM is required for self renewal of haemopoietic stem cells. Nature. 2004;431:997–1002.
41. Campisi J. The biology of replicative senescence. Eur J Cancer. 1997;33(5):703–9.
42. Innovita Research Foundatuion. Aging immune system. http://www.innovitaresearch.org/news/09080601.html. Accessed on 27 Oct 2010.
43. Effros RB. Loss of CD28 expression on T lymphocytes: a marker of replicative senescence. Dev Comp Immunol. 1997;21(6):471–8.
44. Franceschi CS, Valensin F, Fagnoni C, Barbi C, Bonafi M. Biomarkers of immunosenescence within an voluntary perspective: the challenge of heterogeneity and the role antigenic load. Exp Gerontol. 1999;34:911–21.
45. Lang PO, Mithchell WA, Lapenna A, Pitts D, Aspinali R. Immunological pathogenesis of main age-related diseases and frailty: role of immunosenescence. Eur Geriatr Med. 2010;1(2):112–21.
46. Gavazzi G, Krause KH. Aging and infections. Lancet Infect Dis. 2002;2:659–66.
47. Vasto S, Caruso C. Immunity & aging: a new journal looking at ageing from an immunological point of view. Editorial. Immun Aging. 2004; http://www.immunityageing.com/content/1/1/1. Accessed 27 Oct 2010.
48. Capri M, Salvioli S, Sevini F, Valensin S, Celeni L, Monti D, et al. The genetics of human longevity. Ann N Y Acad Sci. 2006;1007:252–7.
49. Candore G, Colonna-Romano G, Balistreri CR, Di Carlo D, Grimaldi MP, Listi F, et al. Breaking of longevity: role of innate immune system. Rejuvenation Res. 2006;9:143–8.
50. Bruunsgaard H, Pedersen M, Pedersen BK. Aging and proinflammatory cytokines. Curr Opin Hemstol. 2001;8:131–6.
51. Kritchevsky SB, Cesari M, Pahor M. Inflammatory markers and cardiovascular health in older adults. Cardiovasc Res. 2005;66:265–75.
52. Wardwell L, Chapman-Novakofski K, Herrel S, Woods J. Nutrient intake and immune function of elderly people. J Am Diet Assoc. 2008;108(12):2005–12.
53. Mazari L, Lesourd B. Nutritional influences on immune response in health ages persons. Mech Ageing Dev. 1998;64:25–40.
54. Wreghitt TG, Teare EL, Sule O, Devi R, Rice P. Cytomegalovirus infection in immunocompetent patients. Clin Infect Dis. 2003;37:1603–6.
55. Cattaneo AG. Active immunization in the elderly. gerogogi.net/editoriali/active immunization.html. Accessed 23 Nov 2010.
56. Greenberg SA. Immunizations for older adults. Best practices in nursing care to older adults. The Hartford Institute for Geriatric Nursing. New York University College of Nursing. www.hartfordign.org. 2012.
57. Bader MS. Immunization for the elderly. Am J Med Sci. 2007;334(6):481–6.
58. Vaughin JA, Miller RA. Update on immunizations in adults. Am Fam Physician. 2011;84(1):1015–20.
59. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson KJ, et al. Mortality associated with influenza and respiratory syncytial virus in the US. JAMA. 2003;28992:179–86.
60. Centers for Diseases Control and Prevention. Influenza. www.cdc.gov/vaccines/pubs/pinkbook/flu.html. Accessed 6 Dec 2016.
61. MHS UBUTU. Influenza. www.mhs.co.za/Medical Forum/Conditions Search/Conditions/Influenza/ Basicinfo.asp. Accessed 6 Dec 2016.
62. Tang JW, Shetty N, Lam TTY. Infuenza. Antimicrobe. www.antimicrobe.org/vii.asp. Accessed 6 Dec 2016.
63. Wensteliger B, Herndler-Brandsteler D, Schwaniinger A, Weiskopf D, Grubeck-Loebenstein B. Biology of immune response to vaccine in elderly persons. Clin Infect Dis. 2008;46:1078–84.
64. Australian and New Zealand Society for Geriatric Medicine Position Statement No 7. Immunisation of older people-Revision Number 2; 2011.
65. Pham H, Geraci SA, Burton MJ. CDC advisory committee on immunization practices: adult immunizations: update on recommendations. Am J Med. 2011;124(8):698–701.

Ortho-geriatric Care

8

Dino Benito

Historical Perspective

Hip fractures are life-changing events that can potentially have devastating effects particularly in the geriatric population. Beyond the morbidity associated with the actual fracture, it confers a considerable mortality risk and functional impairment. A person's quality of life can substantially deteriorate after a hip fracture. A significant proportion of these patients will have ongoing pain and permanent disability or require institutional care.

Surgery remains the definitive treatment for patients with hip fractures. In an effort to improve outcomes, the ortho-geriatric model of care was developed. Ortho-geriatric care is defined as collaborative care for older patients with orthopaedic disorders involving orthopaedic services and medical programmes catering for older people [1].

Michael Bertrand Devas invented what he called "geriatric orthopaedics" [2]. He was an orthopaedic surgeon in the UK who famously said "I am only a carpenter and I need a physician to tell me what's wrong with the patient". In 1963, he started the world's first geriatric orthopaedic unit in Hastings where surgeons and geriatricians worked together, conducting joint ward rounds [3].

Descriptive studies of the ortho-geriatric model of care at that time managed to demonstrate shorter length of stay and greater proportion of discharging back to their normal homes rather than institution [4]. A healthy scepticism of the robustness of the evidence behind it prevailed until the publication of the British Orthopaedic Association and British Geriatric Society Blue Book in 2003 and its further revision in 2007 [5]. It took over 40 years before the establishment of evidence-based standards to care for older patients with fragility fractures. This included implementing the ortho-geriatric model of care and physician involvement in high-risk surgical patients.

D. Benito
Blacktown Hospital, Hornsby Ku-ring-gai Hospital, The Hills Private, Norwest Private and the Macquarie University Hospital, Sydney, NSW, Australia

Australia in the 1980s was one of the first regions outside of the UK to describe and implement the principles of an ortho-geriatric model of care [6]. However, an audit of public hospitals in Australia and New Zealand in 2014 still showed marked variability in services offering care for patients with hip fractures [7]. In efforts to improve upon outcomes and standardize care, the Australia New Zealand Hip Fracture Registry (ANZHFR) was started, and an annual report has been published since 2012 on care activity directed to hip fracture patients across facilities [8]. Presently, the ortho-geriatric model of care is the standard around the world in managing patients with hip fractures with a strong evidence base to support its implementation.

This clear benefit in the geriatrician's involvement in the overall management of hip fractures has opened new opportunities for the subspecialty. Geriatrician involvement in the management of other fragility fractures particularly the vertebral, wrist, pelvis, sacrum and ankle has been endorsed [1]. Admittedly, the benefit is still not as established as the evidence for hip fractures in the scientific literature, but expert opinion and clinical experience have alluded to its utility [6, 9]. The practice of the comprehensive geriatric assessment is also thought to be beneficial and is increasing the geriatrician's role in the management of older people involved in major trauma and preoperative care of patients undergoing elective joint replacement and spine surgery [9].

The Osteoporotic Hip Fracture

Osteoporosis

Osteoporosis is a condition where the bones weaken and lose their structural integrity. It is the most common bone disease in humans, mostly affecting older females but also is represented in males. It is characterized by low bone mass, deterioration of bone tissue and disruption of bone architecture, compromised bone strength and an increase in the risk of fracture [10]. The World Health Organization (WHO) defines

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_8

osteoporosis as a bone mineral density (BMD) at the hip or lumbar spine that is less than or equal to 2.5 standard deviations below the mean BMD of a young adult reference population [9].

By age 18–25, an individual would have achieved peak bone mass. This is largely determined by genetic factors but, to a degree, is also determined by external factors including nutrition, general health and physical activity [10]. Bone health is a dynamic process that involves constant remodelling which ensures that older bone is removed and replaced by new bone maintaining structural integrity [11]. Factors that alter this balance lead to bone loss and eventual osteoporosis. Menopause and advancing age are the two leading factors that predispose people to osteoporosis.

A strong force is normally needed to cause a fracture in healthy individual. Our bodies should be able to sustain a fall from a standing height without a fracture. In the setting of osteoporosis, a less than significant event, like a fall from a standing height or less, can cause a fragility fracture. There are three fractures sites typical of a fragility fracture: Colles fracture of the wrist, vertebral crush fractures and hip fractures.

Hip Fracture

The hip joint is one of the most important joints in the human body. It is a ball and socket synovial joint where the acetabulum forms the socket and the femoral head is the ball that facilitates a great range of motion. The term hip fracture is a general term used to describe a fracture of the hip joint but mostly of the proximal femur.

An estimated 19,000 people aged 50 and over are hospitalized with a hip fracture every year in Australia, 71% occurred in individuals over 80 and 72% of hip fractures were in women [12]. Although the rate of hip fractures is decreasing over time, the actual number continues to increase due to the increasing number of older adults in Australia [12].

There are three general categories of hip fractures depending on their anatomical location: femoral neck fractures, intertrochanteric fractures and sub-trochanteric fractures [13]. Each category is having their own unique challenges that dictate care and management.

Femoral neck fractures are located in the area distal to the femoral head but proximal to the greater and lesser trochanters. These are considered intracapsular fractures because they are located within the capsule of the hip joint. This anatomical characteristic has an important healing implication because marked displacement can disrupt blood supply to the femoral head and can increase the incidence of non-union and osteonecrosis of the femoral head [13].

Intertrochanteric fractures are fractures in the well-vascularized metaphyseal region between the greater and lesser trochanter. These are extracapsular fractures that do not interfere with the blood supply to the femoral head. It is however associated with a different complication profile that includes mal-union, shortening of the femur and imperfect gait because of the deforming forces of the fracture itself [14].

The last category is a fracture in the area distal to the lesser trochanter. These are called sub-trochanteric fractures and are quite distinct from the two previous proximal fractures. The sub-trochanteric region of the femur is an area of great stress concentration and is subject to deforming forces because of muscular insertions [15]. Interestingly, there is also an increase association between long-term bisphosphonate use and sub-trochanteric fractures [16]. It is hypothesized to result from long-term suppression of bone remodelling.

Femoral neck and intertrochanteric fractures account for 90% of hip fractures [13]. They occur at approximately the same frequency in patients between the ages of 65 and 99 years [17]. The remaining 5–10% is accounted for by sub-trochanteric fractures.

Risk Factors

The major risk factors for hip fractures by far remain osteoporosis and falls. In an elderly individual, the combination of both, compounded by other environmental factors, leads to an injury with potential life-changing outcomes.

There are certain factors that increase the risk of developing osteoporosis. Medical conditions such as the malignancies, autoimmune disease, rheumatoid arthritis, chronic renal failure, airways disease and eating disorders increase the risk [12]. Part of the risk involves the medications we use to treat them: example of which include glucocorticoids (steroids), aromatase inhibitors (for breast cancer) and androgen deprivation therapy (for prostate cancer) [12]. There are also modifiable risk factors including vitamin D and calcium deficiencies, smoking, general malnutrition and physical inactivity. Non-modifiable risk factors include a strong family history, older age and genetic predisposition [12].

Factors that increase falls risk increase the chances of an elderly patient from falling over. Intrinsic risk factors include muscle weakness (sarcopenia), visual impairment, poor balance, cognitive impairment, medications, older age and osteoporosis itself. Extrinsic factors include bad footwear, unfamiliar environment, poor lighting, tripping hazards and clutter.

Independent of falls and osteoporosis, other factors have been identified as risks for having hip fractures. Low socioeconomic status has been associated with a higher incidence of hip fractures. Being female is associated with threefold risk [17].

General Outcomes

The incidence of death and major disability is substantially increased after a hip fracture. Previously considered a palliative procedure because of its high risk of mortality and morbidity, outcomes have improved in recent years mostly due to care improvement strategies that are spearheaded by the ortho-geriatric model of care.

Despite the more recent reduction, hip fracture mortality remains a significant issue. Death from hip fractures can be immediate, stemming from the actual fall or even in association with the in-hospital stay when they develop acute complications. Beyond that, it can also lead to a progressive deterioration in an individual's health causing increased risk of death over a period of time. Rates can vary depending on geographical location, but the 30-day mortality rate was in the order of 4.3–9.3%, and the 1-year mortality rate was 18.8–32.5% [18, 19]. General trends seem to reflect that this is declining, but there is still a marked discrepancy, typically showing higher rates in the male population. Certain factors also confer a higher risk of mortality including nursing home residents, the elderly, diagnosis of cognitive impairment, individuals with poor baseline mobility and individuals treated nonoperatively [18].

Hip fractures can also cause disability that can lead to functional dependence. For patients who survive to 6 months, close to half of patients recover their pre-fracture ability to walk and ability to perform activities of daily living; and a quarter recover their pre-fracture ability to perform instrumental activities of daily living [20]. But overall, after a year, only 54% of surviving patients can walk unaided, and only 40% can perform independently their activities of daily living [20].

In Australia, the rates were in keeping with the global trend including in-hospital mortality and the declining incidence of hip fractures. In-hospital mortality rate from a hip fracture was 6%; males (9%) were almost twice as likely to die as female (5%) [21]. Almost 11% of patients with a hip fracture were discharged into a residential aged care facility where this has not been their usual place of residence [21]. This is a surrogate marker of disability, requiring assistance in performing their activities of daily living.

Diagnosing Hip Fractures

Achieving an accurate diagnosis as soon as possible is very important when a hip fracture is being considered. Without a diagnosis, it is impossible to come up with a proper management plan. Missing the diagnosis entirely can also expose an individual to significant consequence. Most hip fractures are readily diagnosed on the basis of a history, physical examination and standard radiographs. However, in the elderly, there are instances that more than the basic imaging is needed to confirm the diagnosis.

History

There is still variability in how patients with hip fractures present. The common denominator is trauma to the pelvic area. In a young person, this is commonly associated with high-velocity impacts like a motor vehicle accident. In the elderly population, this is most often associated with a fall.

Patients with a hip fracture will have pain referred to the groin, buttock and leg and extending to the upper knee. They will also be unable to weight bear, and predictably, pain is worsened with attempts at movement and weight bearing. In certain situations, a stress fracture should be considered if there is significant hip pain without antecedent trauma. The pain in this situation can be insidious and progresses to a point of consistency even without any activity. All things considered, when an elderly person complains of significant hip pain in the proper context, a hip fracture should be considered until proven otherwise.

Physical Examination

Trauma from a fall should trigger not only an examination of the hip but also screening for any other associated injury. Focusing on the hip examination, bruising may or may not be evident on depending on the intensity of the trauma. On further inspection, a patient lying in the supine position would normally have a deformity of the leg in external rotation and abduction and appears to be shortened. Note that a deformity may not be evident when dealing with a stress fracture or a non-displaced fracture.

Pain is normally elicited when testing for passive range of motion particularly on external and internal rotation. Pain is further aggravated when applying an axial load on the affected extremity. The heel percussion test also produces pain and patients are unable to perform an active straight leg raise. There is tenderness on deep palpation of the inguinal area most notable around the area of the femoral neck. Sensation and distal pulses should also be assessed and documented.

Diagnostic Imaging

Plain radiography Plain film radiography is the initial imaging investigation that is organized. Most hip injuries will be identified in a plain film including fractures and dislocations. Hip radiographs have an estimated sensitivity of between 90% and 98%, and the initial films will therefore miss only small proportion of hip fractures [22], assuming that the proper films have been taken.

Computed tomography (CT) If the clinical suspicion remains high and the plain radiographs remain non-diagnostic, a computed tomography image of the hip is indicated. Although it is a good imaging modality for bone, a major limitation that limits its sensitivity is its inability to detect marrow changes (oedema), which occur in the hip fracture adjacent to the fracture line [22].

Magnetic resonance imaging (MRI) MRI is usually considered to be the reference standard, as numerous studies have found MRI to have the highest accuracy (100% sensitivity and between 93% and 100% specificity, depending on experience and skill of radiologist interpreting the images) [22]. Its utility is most useful in imaging for non-displaced fractures, insufficiency fractures and stress or incomplete fractures of the femoral neck that is not seen on plain radiographs. It also has the advantage of detecting bone contusion and muscle and sciatic nerve injury [22].

Radionuclide Tc-99m bone scan Its clinical utility is mainly in the setting of a suspected fracture with non-diagnostic plain radiographs where an MRI or a CT is not available. The limiting issue is its low sensitivity, meaning 2–25% of those who have a fracture could be missed [22].

Ultrasonography The sensitivity of an ultrasound in this setting is 100% and its specificity is 65% [22]. This means none of the patients with a fracture would have been missed; however with its low specificity, 35% of those who tested positive do not have a fracture. An advantage is that it can detect soft tissue haematoma, as well as partial or complete muscle and tendon tear. However, technically the procedure is difficult in the setting where pain is an issue.

Ortho-geriatric Models of Care

A fractured hip is typically considered a surgical problem. However, treating a patient with a hip fracture, collaborative work with a physician looking into the context of their medical background and susceptibilities has shown improved outcomes. There are four recognized models of ortho-geriatric care [6].

The reactive consultation model This is the conventional approach where older patients with a hip fracture are cared for by the orthopaedic surgeons and referred to a geriatrician on an as-needed basis. This is not the recommended model of care anymore because this has led to higher inpatient mortality and increased length of stay [23].

The ortho-geriatric liaison model In this model of care, patients with hip fractures are still admitted under the orthopaedic surgeon. However there is regular geriatrician review in the orthopaedic ward, and there is a multidisciplinary team meeting where care plans are discussed. This model compared to usual care has shown to reduce inpatient mortality and length of stay [24]. Continuity of care and ensuring regular review are still not perfect considering the liaison nature of the relationship of the two treating teams.

The perioperative geriatric rehabilitation unit model This model involves shared care acutely with the orthopaedic and anaesthetic team that manages the patient with a hip fracture perioperatively. This is then followed by an early postoperative discharge to a geriatric rehabilitation unit for continuing care. This has led to reduced length of stay [25], but continuity of care was a major concern because of needing to transfer to another ward. There is also concern that the lack of geriatrician involvement in the acute setting may compromise care, and this is where the patient is considered most vulnerable.

The joint model of care This is where the care of a patient with a hip fracture is jointly shared between a geriatrician and an orthopaedic surgeon in a dedicated ortho-geriatric ward. This model ensures that from the time of admission, there is always medical support from a medical team well versed in the care of the elderly. This model has been shown to reduce inpatient mortality [23] and reduced length of stay [26]. This has also led to a reduction in time to surgery and fewer postoperative complication rates [26]. This model of care is supported and is considered standard of care.

Preoperative Care

It is a recognized challenge to expedite the care of patients with hip fractures. The initial challenge is their presentation, which is usually because of a traumatic event like a fall. It is necessary to make sure that there has been an exhaustive review of the extent of the injury. Secondly, the population of hip fracture patients usually has a raft of comorbidities that need to be optimized prior to anaesthesia and major surgery.

Timing of Surgery

The timing of surgery is one of the most important markers of a patient's outcome following a hip fracture. Functional recovery is delayed because of longer non-weight-bearing status and longer fasting in preparation for surgery. Complication rates also increase the longer surgery is withheld [13]. However, failure to stabilize and optimize patients appropriately before surgery also has its own associated risk and negative outcome. This makes timing of surgery crucial; it is recommended that patients with hip fractures be consid-

ered for early surgery if they are medically stable within the window of 48 h [22].

Unnecessary delay does not fall within expected standard of care for patients with hip fractures. It is although acknowledged that in some instances, there will be unavoidable and legitimate reasons for delay. It is considered reasonable to delay up to 72 h in certain situations where patients need more intensive stabilization for their comorbidities, but generally delays beyond this should be avoided [22].

Antibiotic Prophylaxis

Surgical site infection is an avoidable complication, and minimizing its risk is a marker of good care. Gram-positive organisms like *Staphylococcus aureus* are common organisms found on skin; it asymptomatically colonizes 30% of the human population [27]. It is also, however, the most common isolated organism in hip fracture patients with surgical site infections. It is recommended that prophylactic antibiotic be used to prevent wound infections after an orthopaedic procedure.

It has been shown that single-dose antibiotic prophylaxis significantly reduces deep and superficial surgical site infection and even reduces the incidence of urinary and respiratory tract infection [17]. The choice of antibiotics should always be guided by local bacterial aetiology and susceptibility, paying attention to the risk of resistant organisms like methicillin-resistant *Staphylococcus aureus* [28]. This should also be guided by the relative safety of the drug in relation to its side effects profile and its cost-effectiveness.

It is recommended to use a first-generation cephalosporin (cefazolin 2 g IV) 60 minutes before skin incision. For patients known to be colonized or infected with methicillin-resistant *S. aureus*, vancomycin 15 mg/kg should be administered in addition to cefazolin, whereas patients with immediate hypersensitivity to penicillins and cephalosporins, vancomycin 15 mg/kg should be used instead [28]. If there is any suspicion of a pre-existing infection, appropriate cultures should be taken prior to administration of antibiotics.

Multiple-dose prophylaxis was shown to have a similar effect compared to single-dose prophylaxis on reducing deep surgical site infection. However similar reduction in incidence of urinary and respiratory tract infections was not confirmed [27]. Repeat intraoperative doses should be considered in situations where there was prolonged (>4 h) surgery and if major blood loss has occurred following fluid resuscitation [27]. Urinary catheters are commonly used in hip replacement surgery. This should not affect decisions to continue antibiotics because this practice is not supported by evidence and can potentially cause adverse effects.

Analgesia

Surgically addressing the hip fracture is the most effective way to address pain, and this is one of the main incentives to expedite surgery. Pain can be severe, however, while waiting for the operative procedure. By same token, pain after the surgery can be limiting for functional recovery. In patients with hip fractures, it is crucial therefore to ensure that patients have adequate analgesia.

Analgesia in this setting can be systemic or local, and there may be advantage in its combined use. Systemic analgesia comes in a spectrum from over-the-counter paracetamol to the highly potent opioids. The use of nerve blocks in hip fractures remains low but is becoming more common and expected standard of care [22]. The main limiting factors identified in this setting are the need for trained staff and timely access to appropriate equipment.

It is recommended that patients with hip fractures be provided with adequate pain relief on presentation in the emergency department. As first line, they should be offered paracetamol every 6 h unless contraindicated. If this is not adequate, they should be offered additional opioids and be closely monitored for its associated side effects. Depending on resource and local experience, nerve blocks should be considered acknowledging its value in reducing systemic analgesia use and its adverse effects [29]. In the elderly, the use of non-steroidal anti-inflammatory drugs should be used with caution particularly in patients with coexisting comorbidities including diabetes, chronic renal failure and previous GI bleeding.

Venous Thromboembolism Prophylaxis

Venous thromboembolism (VTE) is another complication that causes significant mortality and morbidity in patients with hip fractures. The combination of older age, immobilization, trauma, major surgery and inherent comorbid factors increases the risk of developing a VTE in this setting.

Thromboembolic prophylaxis is a routine aspect of care for patients with hip fractures significantly reducing the incidence of venous thromboembolism. It is recommended that patients undergoing hip fracture surgery receive intervention to prevent a VTE rather for a minimum of 10–14 days [30]. Interventions to prevent a VTE include low molecular weight heparin (LMWH), fondaparinux, low-dose unfractionated heparin (LDUH), adjusted-dose vitamin K antagonist, aspirin or an intermittent pneumatic compression device (IPCD) [30].

Among all the interventions to prevent a VTE, the use of LMWH is preferred [30]. LMWH have been shown to be more effective than LDUH in reducing the risk of asymptomatic DVT. It is recommended to start LMWH ≥12 h before surgery, irrespective of the use of concomitant IPCD [30].

This becomes very important if there is anticipated delay in the timing of surgery. Postoperatively, VTE thromboembolism prophylaxis should continue for at least a minimum of 10–14 days as mentioned. Further recommendation to extend this in the outpatient period for up to 35 days from the day of surgery until mobility has returned back to normal [30].

Special considerations should be given to patients undergoing hip fracture surgery with significant risk of bleeding. It is recommended to use IPCD for mechanical prophylaxis rather than pharmacologic treatment as long as a reasonable risk and benefit assessment has been had [30]. Efforts should be made to achieve 18 h of daily compliance for an IPCD.

Delirium Prevention

Delirium is an acute disorder of attention and cognition. Patients with hip fractures have been specifically identified as highly at risk for developing a delirium. This highly vulnerable set of patients also includes patients who are >65, patients with known diagnosis of cognitive impairment and patients with severe comorbid medical illness [31].

Developing delirium in older patients (>65) who have hip fractures was noted to be an independent predictor of poor outcomes [32]. Patients who had postoperative delirium had a significantly longer length of hospitalization. They also had significantly higher rates of mortality at 1 year, were less likely to recover their pre-fracture level of ambulation and were more likely to show a decline in level of independence in basic activities of daily living at the 1-year follow-up [32].

A comprehensive geriatric assessment in the context of the ortho-geriatric model of care has been shown to reduce the risk of developing delirium in this at-risk population [33]. This puts the emphasis on early consultation with a geriatrician and to facilitate multidisciplinary care. The Australian delirium clinical care standard also highlighted the prompt assessment of patients with hip fractures [31]. It incorporated the need for an assessment by a clinician competent in delirium diagnosis and in using a validated diagnostic tool to support the diagnosis.

Once a delirium has developed, unfortunately there is little evidence that any intervention can improve outcome. This stresses the importance of prevention and the need to do basic medical interventions appropriately. Interventions for preventing delirium include medication review; correction of dehydration, malnutrition and constipation; oxygen therapy; regular reorientation and reassurance; activities for stimulating cognition; nondrug measures to help promote sleep; and assistance for patients who usually wear hearing and visual aids [34].

Perioperative Care

Anaesthesia

In order to surgically address a hip fracture, it is necessary for a patient to receive some form of anaesthesia for the procedure. Part of the assessment of operative risk is to determine the most appropriate form of anaesthesia. This will include a careful consideration of the patient's comorbidities, patient's preference and local expertise. The choice of anaesthesia is between a general anaesthesia and a regional anaesthesia.

Several outcome measures have been reviewed to see if there was any difference between a general and a regional anaesthetic used in hip fracture surgical procedures [35]. The measures reviewed included mortality in 1 month and the incidence of specific medical complications like myocardial infarction, cerebrovascular accident, delirium and pneumonia. There was no significant evidence that one was better than the other, noting that the available data were considered of low quality to formally base a recommendation [35].

Given the limited evidence, it becomes important to consider patient preference after extensive discussion of potential risks and benefits of both general and regional anaesthetics. The decision should also reflect the experience of the anaesthetists that will be involved in the procedure [29].

Surgical Intervention

Returning patients to their previous level of function is the overall goal of hip fracture treatment. Once patients have been assessed and medically optimized, the next important steps will be timely surgery and early mobilization. Once a decision has been made to operate, the aim primarily should be to allow patients to fully weight bear without restrictions in the immediate postoperative period.

The type of surgery depends on generally two main things: the type of fracture and the inherent characteristic of the patient. Firstly, the type of the fracture is carefully considered. This will involve looking at the location of the fracture, the bone quality surrounding it and the level of displacement and comminution. Inherent patient characteristics that are considered include the patient's age, baseline mobility, premorbid function and ability to take part in postoperative rehabilitation.

The two main surgical options for the treatment of a hip fracture are replacement arthroplasty and internal fixation. Replacement arthroplasty involves removing all of the damaged bone and replacing it with an orthopaedic prosthesis. The hip joint has two components, the ball and socket, and

this is used to characterize the nature of replacement arthroplasties. Replacement arthroplasties can be a total hip replacement or a hemiarthroplasty. Total hip replacement involves removing both the ball (femoral head) and the natural socket in the hip and replacing it with prosthesis. A hemiarthroplasty, on the other hand, is similar to a total hip replacement but only involves half of the hip, replacing only the femoral head with prosthesis. Internal fixation involves returning the bone fragments to an acceptable position and then holding it with pins, screws, rods or plates while it heals.

Femoral neck fracture Femoral neck fractures are also referred to as intracapsular fractures (within the capsule of the hip joint). Internal fixation is only generally considered appropriate in impacted, non-displaced or minimally displaced neck of femur fractures particularly in the young (<70). Note that the blood supply of the femoral head travels in a retrograde direction [13]. As such, the incidence of non-union and osteonecrosis of the femoral head is much higher in displaced fractures.

It is recommended to perform replacement arthroplasty (total hip replacement or hemiarthroplasty) in patients with a displaced femoral neck fracture (intracapsular fracture) [13]. There is evidence of variable quality to show that a total hip replacement is better than a hemiarthroplasty when it comes to functional outcome. However, there was no clear difference between the two in terms of mortality, reoperation rate, failure to regain mobility and length of hospital stay [22]. It is therefore recommended that a patient with a displaced femoral neck fracture (intracapsular fracture) is offered a total hip replacement if the patient was able to walk independently outdoors with no more use of a stick, is not cognitively impaired and is medically fit for anaesthesia and the procedure [29].

Use of bone cement Polymethyl methacrylate (PMMA) is commonly known as bone cement [22]. It acts as space filler that creates a tight space, which holds the implant against bone. It secures the implant and reduces the need for revision secondary to loosening of the prosthesis. The exact aetiology of bone cement syndrome is poorly understood. Cemented arthroplasty was shown to be associated with less pain and better mobility at 12 months compared to uncemented arthroplasty. Therefore the recommendation favoured the use of cemented arthroplasties in the treatment of hip fractures [22].

Intertrochanteric and sub-trochanteric fractures These fractures are considered extracapsular fractures. Intertrochanteric fractures, as the name implies, are fractures between the greater and lesser trochanter. Sub-trochanteric fractures are fractures distal to the lesser trochanter up to 5 cm below. There is no disruption of the blood flow to the femoral head in extracapsular fractures, and this becomes a very important surgical consideration [13].

The main goal of surgically treating extracapsular fractures is to stabilize the intact femoral head and neck onto the shaft of the femur. The femoral head is stabilized by inserting screws up the neck onto the head. The screws are then fixed to a plate on the outside of the bone (extramedullary fixation) or to a nail inserted into the middle of the femoral shaft (intramedullary fixation). The nail can either be short (a third of the femur) or long (spanning the entire length of the femur). Commonly, extramedullary fixation is called a sliding hip screw, and intramedullary fixation is called an intramedullary nail.

With regard to the operative management of intertrochanteric fractures, there was no significant difference in mortality, rate of reoperation, mobility outcome, infection or length of hospital stay with extramedullary compared to intramedullary fixation [22]. However there was a significant increase in the incidence of operative or postoperative fracture of the femur with intramedullary compared to extramedullary fixation (low-quality evidence). This prompted the NICE guideline to recommend extramedullary fixation over intramedullary fixation [22]. However the committee reviewing local recommendations in Australia and New Zealand was not convinced; it could recommend one over the other recommending both extramedullary and intramedullary fixation as suitable for operative management of intertrochanteric fractures [29].

For sub-trochanteric fractures, it was noted that there was no significant difference in reoperation, infection and mortality with intramedullary compared to extramedullary fixation. However, there was a significant decrease in non-union with intramedullary fixation compared to the extramedullary approach [22]. Local guidelines are in agreement with the NICE guideline in recommending intramedullary fixation for sub-trochanteric fractures [29].

Appropriately skilled team There has been significant discussion whether the seniority of surgeon affects outcomes in the operative management of hip fractures [22]. Although seniority is often associated with greater knowledge, skills and experience, it might not necessarily reflect specific expertise in hip fracture management. It was also noted that outcomes are associated beyond the skills of one surgeon. It stresses the importance of team effort from surgeons, anaesthetists, theatre staff, geriatrician, nursing staff and allied health considered as an appropriately skilled team. The recommendation is to schedule hip fracture surgery on a planned list or planned trauma list where an appropriately skilled team is available to undertake the procedure [29].

Postoperative Care

Early Mobilization

The restoration of mobility is perhaps one of the important goals of hip fracture surgery. Any delay in mobilizing after a hip fracture has been associated with poorer outcomes including development of delirium, postoperative pneumonia and increased length of stay [36]. This is consistent with previous efforts to decrease delay in timing of surgery and minimize any restriction to weight-bearing status.

Early mobilization with a physiotherapist has been shown to be safe and effective in promoting recovery and unrestricted weight bearing after surgery did not result in increased mechanical complications [37]. It is therefore recommended as standard of care to offer a patient a physiotherapy assessment in view of mobilization day after surgery unless it is medically or surgically contraindicated. It is also recommended that mobilization be offered at least once a day ensuring that there is access to regular physiotherapy review [29].

Postoperative Pain Relief

Continuing mobilization will depend on adequate pain relief, and this will enhance participation in any effort to promote recovery. Pain levels should be routinely reviewed, using pain scores wherever available to have an objective guide on whether it is being addressed appropriately. The regular use of paracetamol is encouraged with the addition of opioid analgesia regularly or PRN carefully considered. Patients who are cognitively impaired are highly vulnerable because they might not be able to communicate pain levels, but it should be assumed that they are still in need of pain relief.

Discharge Planning and Rehabilitation

The reward for the overall investment in hip fracture surgery is bringing back patients to their former functional state living in their usual residence. Early supported discharge from hospital should be considered when patients on continuing review have been deemed medically stable. At the least, the patient should be able to transfer and mobilize for short distances. There should be a plan to continue to support in the community in keeping with the goals of the multidisciplinary team until the patient has achieved their full rehabilitation potential as discussed with the patient, carer and family [29]. If the patient is unable to meet the criteria for early supported discharge, patients should be considered for inpatient rehabilitation until further improvement is achieved.

Impact of Osteoporotic Hip Fractures in the Very Old

General trends would reflect that the age-adjusted incidence rate of osteoporotic hip fracture is decreasing. However with an ever-growing ageing population, the actual number of hip fractures in the vulnerable elderly population continues to increase [21]. The management of hip fractures in itself is expensive [38]. It is not just the surgical procedure that is costly, but there is an indirect price associated with rehabilitation, outpatient visits, temporary support and accommodation during the recovery period.

But beyond the economic burden, the true cost of a hip fracture is the mortality, pain and disability that are associated with it. Surviving a preventable life event like this should be a clear focus for healthcare providers. Quality of life is very important particularly in the very old. Losing functional independence is a significant source of emotional distress in this age group. Depending on other people for the most basic of tasks and needing to move to a residential facility are a major blow to self-respect and one's dignity. This is perhaps unquantifiable cost that is at stake when we make healthcare-related decisions in the management of osteoporotic hip fractures.

Clinical Relevance

Osteoporotic hip fractures lead to significant mortality and morbidity particularly in the vulnerable elderly population.

Ortho-geriatric care, defined as collaborative care for older patients with orthopaedic disorders involving orthopaedic services and medical programmes catering for older people, has been shown to improve outcomes.

Osteoporosis and falls remain the most significant risk factors associated with hip fractures.

Achieving an accurate diagnosis as soon as possible is very important when a hip fracture is being considered.

The restoration of mobility and functional independence are perhaps the important goals of hip fracture surgery.

Multiple Choice Questions (MCQs)

1. What is the optimal time to operate on a patient with a hip fracture?
   A. Immediately upon presentation after a fall
   B. Early surgery within the window of 48 h
   C. Electively 48–96 h post fall
   D. After failing a trial of immobilization of 96 h

2. What is the primary aim of surgery?
   A. Pain control
   B. Full weight bearing without restriction post operatively
   C. Haemostasis
   D. Full range of motion of the hip

Answers to MCQs

1. B
2. B

References

1. ANZSGM. Orthogeriatric care revised 2010. http://www.anzsgm.org//documents/PositionStatementNo5-OrthogeriaticCareRevision2010.pdf. Accessed June 2017.
2. BMJ. 1999;318:946.
3. Devas M. Geriatric orthopaedics. BMJ. 2004;1:190–2.
4. Briggs R. Orthogeriatric care and its effects on outcome. J R Soc Med. 1993;86(10):560–2.
5. British Orthopaedic Association. The care of fragility fracture patients. London: BOA; 2007.
6. Sabharwal S, Wilson H. Orthogeriatrics in the management of frail older patients with a fragility fracture. Osteoporos Int. 2015;26:2387–99.
7. Australian and New Zealand Hip fracture registry. Australian and New Zealand facility level audit of hospitals performing surgery for hip fracture. http://anzhfr.org/wp-content/uploads/2016/07/ANZHFR_FLA_Report_2015_Final.pdf. Accessed June 2017.
8. Australian and New Zealand Hip Fracture Registry. ANZHFR Bi-National annual report for hip fracture care 2017. http://anzhfr.org/wp-content/uploads/2017/08/ANZHFR-Annual-Report-2017.pdf. Accessed June 2017.
9. Aw D, Sahato O. Orthogeriatrics moving forward. Age Ageing. 2014;43(3):301–5.
10. Cosman F, de Beur S, LeBoff M, Lewiecki E, Tanner B, Randall S, Lindsay R. Clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2014;25:2359–81.
11. Khosla S, Riggs B. Pathophysiology of age-related bone loss and osteoporosis. Endocrinol Metab Clin N Am. 2005;34:1015–30.
12. Australian Institute of Health and Welfare. Estimating the prevalence of osteoporosis. Cat. no. PHE 178. Canberra: AIHW; 2014. Accessed June 2017.
13. Zuckerman J. Hip fracture. N Engl J Med. 1996;334:1519–25.
14. Ahn J, Bernstein J. In brief: fractures in brief: intertrochanteric hip fractures. Clin Orthop Relat Res. 468:1450–2.
15. Barbosa de Toledo Lourenco P, Pires R. Subtrochanteric fractures of the femur: update. Revista Brasileira de Ortopedia (English Edition). 2016;51:246–53.
16. Shane E, Burr D, Abrahamsen B, Alder RA, Brown TD, Chang AM, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2010;25:2267–94.
17. Karagas M, Lu-Yao G, Barrett J, Beach M, Baron J. Heterogeneity of hip fracture: age, sex and geographic patterns of femoral neck and trochanteric fractures among the US elderly. Am J Epidemiol. 1996;143:677–82.
18. Mariconda M, Costa G, Cerbasi S, Recano P, Aitanti E, Gambacorta M. The determinants of mortality and morbidity during the year following fracture of the hip: a prospective study. Bone Joint J. 2015;97-B:383.
19. Brauer C, Coca-Perraillon M, Cutler D, Rosen A. Incidence and mortality of hip fractures in the United States. JAMA. 2009;302:1573.
20. Morrison R, Chassin M, Siu A. The medical consultant's role in caring for patients with hip fracture. Ann Intern Med. 1998;128:1010.
21. Australian Institute of Health and Welfare. The problem of osteoporotic hip fracture in Australia. Bulletin 76 AUS 121. Canberra: AIHW; 2010. http://www.aihw.gov.au/publication-detail/?id=6442468333. Accessed June 2017.
22. National Clinical Guideline Centre. The management of hip fracture in adults. London: National Clinical Guideline Centre; 2011. www.ncgc.ac.uk. Accessed June 2017.
23. Vidan M, Serra JA, Moreno C, Riquelme G, Ortiz J. Efficacy of a comprehensive geriatric intervention in older patients hospitalized for hip fracture: a randomized, controlled trial. J Am Geriatr Soc. 2005;53:1476–82.
24. Fisher A, Davis W, Rubenach E, Sivakumaran S, Smith N, Budge M. Outcomes for older patients with hip fractures: the impact of orthopedic and geriatric medicine cocare. J Orthop Trauma. 2006;20:172–8.
25. Stenvall M, Olofsson B, Nyberg L, Lundstrom M, Gustafson Y. Improved performance in activities of daily living and mobility after a multidisciplinary postoperative rehabilitation in older people with femoral neck fracture: a randomized controlled trial with 1-year follow-up. J Rehabil Med. 2007;39:232–8.
26. British Geriatric Society. Orthogeriatric models of care. 2007. http://www.bgs.org.uk/index.php/topresources/publicationfind/goodpractice/371-orthogeriatricmodels. Accessed June 2017.
27. Gillespie W, Walenkamp G. Antibiotic prophylaxis for surgery for proximal femoral and other closed long bone fractures. Cochrane Database Syst Rev. 2010;(3):CD000244.
28. Surgical prophylaxis for orthopaedic surgery. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2017.
29. Australian and New Zealand Hip Fracture Registry (ANZHFR) Steering Group. Australian and New Zealand guideline for hip fracture care: improving outcomes in hip fracture management of adults. Sydney: Australian and New Zealand Hip Fracture Registry Steering Group; 2014.
30. Falck-Ytter Y, Francis C, Johanson N, Curley C, Dahl O, Schulman S, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141:e278S–325S.
31. Australian Commission on Safety and Quality in Health Care. Delirium clinical care standard. Sydney: ACSQHC; 2016. Accessed June 2017.
32. Edelstein D, Aharonoff G, Karp A, Capla E, Zuckerman J, Koval K. Effect of postoperative delirium on outcome after hip fracture. Clin Orthop Relat Res. 2004;422:195–200.
33. Shields L, Henderson V, Caslake R. Comprehensive geriatric assessment for prevention of delirium after hip fracture: a systematic review of randomized controlled trials. J Am Geriatr Soc. 2017;65:1559–65.
34. Clinical Epidemiology and Health Service Evaluation Unit. Clinical practice guidelines for the management of delirium in older people. Melbourne: Victorian Government Department of Human Services on behalf of AHMAC; 2006;
35. Guay J, Parker M, Gajendragadkar P, Kopp S. Anaesthesia for hip fracture surgery in adults. Cochrane Database Syst Rev, 2016;(2):CD000521.
36. Kamel H, Iqbal M, Mogallapu R, Maas D, Hoffmann R. Time to ambulation after hip fracture surgery: relation to hospitalization outcomes. J Gerontol A Biol Sci Med Sci. 2003;58:1042–5.
37. Koval K, Friend K, Aharonoff G, Zuckerman J. Weight bearing after hip fractures: a prospective series of 596 geriatric hip fracture patients. J Orthop Trauma. 1996;10:526–630.
38. Burge R, Worley D, Johanson A, Bhattacharya S, Bose U. The cost of osteoporotic fractures in the UK projections for 2000–2020. J Med Econ. 2001;4:51–62.

Geriatric Anaesthesia

9

Sivagnanavel Senthuran and Nages Nagaratnam

Historical Perspective

Throughout history, there has been a continuous search for a remedy to relieve pain. According to the Bible, God created Eve from one of Adam's ribs by putting him to sleep [1]. The ancient Romans and Greeks used various methods such as inhalation of fumes of hemp and carbon dioxide and the use of mandragora, amongst others, to dull consciousness and produce sleep [2]. The word 'anaesthesia' of Greek derivation signifies loss or lack of feeling of sensation, and the word 'anaesthesia' in relation to surgery dates from 1846 [2, 3]. It was this year the pain of surgery was eliminated [4] when William Morton, a young dentist, administered ether to a patient before extracting a tooth and proved that ether was safe and effective anaesthesia when inhaled in proper dose [4]. Arthur Ernest Guedel, a US-born anaesthetist, gave a thorough description of nitrous oxide and was amongst the pioneers of cuffed endotracheal tubes [5] which led the way to provide positive pressure ventilation [4]. Today, innovations in science and engineering in combination with a systems approach to safety and training have made anaesthesia safer than flying.

Demographic and Other Characteristics of the Very Old

The very old suffer from chronic illnesses and increased disability, frailty, hospitalisation and institutionalisation. There is an increasing incidence of cardiovascular diseases with increasing age such as heart failure, hypertension and ischaemic heart disease. The elderly are inclined to develop heart failure due to age-related changes in the cardiovascular system and high prevalence of hypertension and coronary heart disease [6]. The Framingham study showed that heart failure increased with age. The prevalence of heart failure in age groups 60–69, 70–79 and >80 years was 2.3%, 4.9% and 9.1%, respectively [7]. In the elderly, COPD occurs with increasing frequency and severity and is associated with cardiovascular comorbidity. The elderly are more prone to develop pneumonia due to the decreased ability to mount an immune reaction with age which is termed immunosenescence.

Impact of Age-Related Structural and Functional Changes

Age-related changes must be distinguished from age-related diseases. The very old demonstrate a reduction in physiological reserve and an inability of organ systems to respond to illness and surgical stress [8, 9].

Cardiovascular

A variety of alterations in cardiovascular physiology [10] (Box 9.1) make the elderly more vulnerable to cardiac morbidity. There is a loss of myocytes with hypertrophy of remaining cells [11]. The left ventricular diastolic filling rate decreases to 50% of the peak rate by the age of 80 [12]. The elderly patient compensates poorly for hypovolaemia due to diastolic dysfunction and decreased vascular compliance [13]. Calcification of the fibrous skeleton involves the valvular apparatus and conduction system [14]. The elderly patient is prone to conduction delay and atrial and ventricular ectopy due to fibrosis or calcification of the conduction pathways [15]. The incidence of cardiac arrhythmias increases with age both at rest and on exercise [16]. There is blunting of the beta-adrenergic responsiveness [9, 17, 18]. The cardiac output is however maintained despite reduced early diastolic filling through the use of the Frank-Starling mechanism [13–15].

S. Senthuran (✉)
Department of Intensive Care Medicine, Townsville Hospital, Townsville, QLD, Australia

N. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_9

There is a loss of arterial compliance with ageing contributing to left ventricular hypertrophy and systolic hypertension [14].

Box 9.1. Age-Related Changes Which May Affect Cardiovascular Performance
Diastolic dysfunction
Blunting of the beta-adrenergic responsiveness
Fibrotic involvement of conduction pathways
Resetting of baroreceptor reflex
Increased stiffness and decreased vascular compliance
Elevated levels of catecholamines

Information sources; Pugh andWei [14]; Priebe [9]

Respiratory

There are age-related changes in the anatomy, physiology and immunology of the respiratory system that impact on perioperative assessment and postoperative care (Box 9.2). Anatomically, there are loss of thoracic intervertebral disk spaces and increased kyphosis, which results in stiffening of the chest wall and a decrease in vital capacity as well as in the fraction of exhaled volume in 1 s (FEV1). There are also loss of lung elasticity and reduction in alveolar surface area which together result in homogenous enlargement of air spaces and has been referred to as 'senile emphysema'. Physiological changes of ageing include increased air trapping and hyperinflation due to changes in the lung parenchyma. Lung hyper-expansion, in turn, flattens the diaphragm altering the length-tension relationship of its muscle fibres resulting in weaker cough and decreased respiratory efficiency. Impairment in gas exchange occurs due to ventilation-perfusion mismatch (especially in the supine position) and a decline in alveolar surface area which affects oxygen diffusion. The elderly also have a reduced response to hypoxia and hypercapnia due to changes in central ventilatory control possibly related to reduced number of medullary ventral respiratory neurons. Immunological changes include an imbalanced increase in pro-inflammatory cytokines (e.g. IL-1, TNF-a) even in the absence of a threat and a more blunted response to infection or injury. Toll-like receptors which are important in the initiation of the innate immune response are reduced in expression as is the cytotoxic ability of alveolar macrophages. The adaptive immune response is also impaired with decreased T cell activation and reduced antibody-secreting ability of B cells. Thus the elderly are more vulnerable to respiratory infections from a variety of pathogens [19].

Box 9.2. Age-Related Changes Which May Affect Respiratory Performance
Stiffening of the chest wall.
Increase in functional residual capacity and residual volume.
A decline in the diffusion capacity.
Increase in pulmonary vascular stiffness, vascular pressures and resistance due to changes in pulmonary vasculature.
Ventilation control diminishes.

Information sources: Taylor and Johnson [20]; Oyarzun [21]

Pharmacokinetics and Pharmacodynamics

Many of the age-related physiological changes in the function and composition of the body result in many pharmacokinetic changes in the elderly [22]. With advancing age, there is a reduction in the total body water and lean body mass with a relative increase in body fat [23–27]. The decrease in the water content of the body with ageing results in water-soluble drugs having a smaller volume of distribution [27] and higher serum levels for drugs such as lithium and aminoglycosides. An increase in the fat content, however, results in an increase in volume distribution and the half-life of fat-soluble drugs [22, 27] such as diazepam. There is a progressive decline in counter-regulatory mechanisms (impaired homeostasis) in old age, and age-related changes in pharmacodynamics occur at the receptor site or signal transduction level [28]. In old age, the pharmacodynamic changes alter the sensitivity of drugs [26]. Some drug effects are augmented. There is now evidence to suggest that there is altered 'sensitivity' at the receptor site to a given concentration of the drug in the elderly. Enhanced sensitivity to warfarin, for example, is the probable reason for its increased toxicity [29].

Liver

Due to 20–50% reduction in the blood flow and 20–30% decrease in liver mass with increasing age [30], first-pass

metabolism is reduced [31]. With ageing, there is a decline in the intrinsic metabolic activity of hepatic parenchyma and hepato-biliary function, with shifts in the expression of a variety of proteins resulting in a moderate reduction in Phase 1 metabolism of many drugs [22, 32]. Phase 2, however, is unchanged with ageing. Conjugation and oxidative reactions by the hepatic microsomal enzymes are involved in drug metabolism [24, 33]. Conjugation, reduction and hydrolysis are not altered [29]. Oxidative metabolism through cytochrome P450 system decreases with ageing [34]. The elderly exhibit a decline in the hepatic clearance of certain drugs with increased frequency of adverse drug reactions and this has been attributed to a decrease in liver volume rather than to a reduction in Phase 1 metabolism [32].

Renal

In the elderly, the most important pharmacokinetic change is the decline in the excretory capacity of the kidney, and this is much more clinically significant than the decline of hepatic drug metabolism El [25]. The glomerular filtration rate, renal plasma flow and associated tubular function decline with age [35]. The renal function declines linearly from the age of 30 and mirrors the decline in drug excretion with age. Such decrease in drug clearance increases the blood levels and toxic effects of the drug [36].

Management of Anaesthesia

Anaesthetic techniques can be broadly categorised into general anaesthesia, regional anaesthesia (e.g. spinal, epidural, peripheral nerve blocks) and local anaesthesia (infiltration of surgical field). The choice of technique is based on several factors such as surgical procedure (e.g. laparotomies require muscle relaxation and cannot be done under regional anaesthesia alone in comparison to caesarean sections which are usually done under spinal anaesthesia only), coexisting disease and the need to minimise postoperative complications (e.g. epidural analgesia may be performed with local anaesthesia and no opiate in those with severe sleep apnoea and right heart failure) and patient preferences (e.g. frail patients with multiple comorbidities undergoing cataract surgery often receive only local anaesthesia topically).

General Anaesthesia

General anaesthesia aims to achieve a deep enough level of sedation, analgesia and muscle relaxation to allow surgery. Though historically this was accomplished with a high dose of a single volatile agent (ether, halothane, etc.), modern techniques rely on use of low doses of individual drugs specific to each aim: sedation is achieved with short-acting volatiles such as sevoflurane, and analgesia is achieved with potent but short-acting opioids such as fentanyl and muscle relaxation with agents such as rocuronium or cisatracurium.

Though the conduct of anaesthesia is nuanced and dependent on the surgical procedure and patient factors, broad principles affecting the management of the elderly are outlined in the table below [37] (Table 9.1).

Age-related changes such as depletion of neurotransmitters, reduced neuronal density and reduced innervation of skeletal muscles may cause a reduction in anaesthetic requirements [38].

Regional anaesthetic techniques may be suitable for certain operations usually involving the limbs or extremities. They can also be used in combination with general anaesthesia for postoperative analgesia. Non-randomised studies and propensity score matched reviews have suggested that older patients undergoing general anaesthesia for hip surgery have a higher incidence death, stroke, respiratory failure and intensive care unit admission [39]. Problems with using regional techniques include surgical acceptance of having a semi-awake patient, the risk of failure of the block, the limitations on operative time imposed by the duration of the block and need for specific skills in performing the technique avoiding complications like nerve injury. The very old may also have a higher incidence of delirium or dementia, and it can be challenging to obtain consent for the procedure or win their co-operation for positioning for the block.

Risk Scoring and Assessment

There are several risk assessment systems that have evolved for different types of surgery. These systems can be specific for certain types of surgery (e.g. EuroSCORE for cardiac surgical risk assessment) and particular diseases (e.g. Lee's Revised Cardiac Risk Index for risk of cardiac death after noncardiac surgery) or specialty-specific (e.g. the American Society of Anaesthesiologists (ASA) grading system to the complex American College of Surgeons National Surgical Quality Improvement Program risk calculator (NSQIP risk)). Most of these scoring systems are better at predicting mortality rather than outcomes relevant to the very old such as morbidity and functional outcomes. Hence methods of risk assessment for the very old also need to consider geriatric syndromes like frailty, malnutrition, sarcopenia and delir-

Table 9.1 Age-related changes and their impact on the management

System	Changes	Impact on management
CNS	Reduced brain mass, neurotransmitters and receptors. Reduced autonomic responsiveness. Higher sensitivity to anaesthetics	Decreased doses of volatile agents, titration of drugs to effect than using standard doses
Cardiovascular	Systolic hypertension, diastolic dysfunction, labile blood pressure, sensitivity to anaesthetics	Titrate fluid therapy to monitored indices of filling to avoid excess, higher need for infusions of vasopressors to maintain blood pressure
Respiratory	Decreased lung and chest wall elasticity, weaker muscles. Increased VQ mismatching, higher risk of hypoxaemia and aspiration	Preoxygenation, minimising sedative drug doses, monitoring to ensure adequate reversal of muscle relaxants. Early mobilisation and chest physiotherapy postoperatively
Liver	Reduced liver mass and blood flow. Lower albumin levels	Reduce dosing interval of hepatically cleared drugs and highly albumin-bound drugs
Kidney	Reduction in renal mass, muscle mass and total body water makes creatinine a poor predictor of renal function. Decreased ability to handle salt and water overload	Reduce repeat doses of renally excreted drugs (e.g. morphine), minimise use of drugs with renal toxicity (e.g. NSAIDs)
Skin, muscle and fat	Frail skin, decreased muscle mass and subcutaneous fat with increased central fat. High risk of hypothermia. Increased volume of distribution of fat-soluble drugs and reduced volume of distribution of hydrophilic drugs	Active warming of fluids and patient, monitoring of core temperature. Allow prolonged elimination time for fat-soluble agents including volatile anaesthetics

Modified from Strom et al. [37]

ium. The comprehensive geriatric assessment followed by patient-centred interventions has been shown to improve outcome (chances of being alive and in their own home at 6 months) in medical inpatients, but work is ongoing to assess its preoperative role in the elderly [40]. The risk factors for surgery include age over 65 years, coexisting illnesses, urgency and type of surgical procedure [41].

Myocardial infarction is the commonest non-surgical cause of death after noncardiac surgery. There are several cardiac risk indices, Goldman risk index, Detsky's cardiac risk index and Eagle's cardiac risk index, amongst others. In noncardiac surgical patients, the Lee index has been considered to be the best currently available cardiac risk prediction index [42]. It is simple and extensively validated and provides a good estimate of the preoperative risk [43]. Lee's Revised Cardiac Risk Index consists of six independent clinical determinants: history of ischaemic heart disease (angina or myocardial infarction), congestive heart failure, stroke/TIA, renal dysfunction, diabetes mellitus and high-risk surgery [42]. Furthermore preoperative and postoperative risks can be evaluated when adapted for surgical procedures. Vascular, intra-abdominal, thoracic, major orthopaedic and any emergency procedures are considered to have a high risk [44]. NICE preoperative testing guidelines grade surgical severity into three classes, for example, breast biopsy is classed as minor, knee arthroscopy as intermediate and total knee replacement as major [45]. High-risk surgical procedures and reduced functional capacity predict a poor perioperative outcome [46]. There is a high prevalence of preoperative medical problems in this group of patients [47] that require medical attention. The extent of the evaluation will depend on the status of the patient and the urgency for intervention. A multidisciplinary approach can reduce complications following surgery [48]. Preoperatively physicians/geriatricians have a crucial role in making medical recommendations [49], to evaluate, correct clinical abnormalities [48] and stabilise the patient before surgery.

Physical fitness or functional capacity can be estimated by the ability to perform basal activities of daily living or measured in metabolic equivalents (METs). Metabolic demand at rest is equivalent to 1 MET, 2 flight of steps to 4 METs and strenuous sports to >10 METs. Less than 4 METs indicates poor functional capacity [50]. Achieving 6–8 METs of activity without significant symptoms of dyspnoea is considered to represent good functional capacity in a 50–60-year-old patient [44]. Functional capacity can be estimated by the ability to perform the activities of daily living. Physical status can be determined by the ASA (American Society of Anaesthesiologists) Physical Status Classification System [51] score. The ASA is an assessment of the patient's overall health status and is based on six grades and is widely used to ascertain the overall risk [52]. ASA grade 1 is a normal healthy person and ASA grade 6 is a declared brain-dead patient. In between are various grades of system disease from mild to severe to moribund patient [51]. The New York Heart Association (NYHA) assigned patients to one of four functional classes depending on the degree of effort needed to elicit symptoms of shortness of breath or chest pain. The severity of the preoperative functional impairment is linked to postoperative mortality, increasing from 4% in NYHA class 1 to 60% in class 4 [52].

Preoperative Evaluation

Preoperative Cardiac Management for Cardiac Surgery/Noncardiac Surgery

Preoperative evaluation and risk assessment are performed firstly to weigh the potential surgical benefit against the risk of an adverse medical or surgical complication and secondly to identify any comorbidity that can be optimised. As the elderly population grows, issues such as frailty, multimorbidity and terminal illness become more prevalent in the preoperative setting and cloud the risk-benefit decision-making processes. To better guide this growing group of complex patients, a value-based approach is also needed that takes into account patient preferences and attitudes to end-of-life care in addition to the traditional disease-centred approach to managing the problem at hand.

Preoperative evaluation of the elderly commences with the history of the surgical problem and, in particular, the surgical approach proposed. The evaluation also considers the patient's medical comorbidities, medication and allergy history and previous anaesthetic history including techniques used and any complications encountered. The physical assessment of the airway aims to identify any difficulties that might be encountered in securing it. A cardiac examination looks for signs of heart failure or valvular conditions such as aortic stenosis and mitral regurgitation. The respiratory exam aims to assess for signs of wheezing, impaired cough or inability to clear secretions and often incorporates the smoking history. The patient's baseline cognitive function and risk of delirium are also important in assessing their suitability to use techniques like patient-controlled analgesia which are common after major surgery utilising either intravenous opiates or epidural local anaesthetic infusions. Renal function is evaluated by measurement of their serum creatinine, accepting that serum creatinine is dependent on muscle mass and patients who are cachectic may have a normal creatinine even with renal impairment. Increasingly frailty as a syndrome is being assessed formally preoperatively, and its recognition has been shown to affect surgical and anaesthetic decision-making [53]. Though blood tests for full blood count, urea and electrolytes, ECG and CXR are very common, the threshold for performing further invasive testing is dependent on the complexity and invasiveness of the surgery as well the pretest probability of finding a correctable problem.

The outcome of the assessment is a postoperative plan which is developed in discussion between the patient, surgeon, anaesthetist and any other clinicians. Increasingly the postoperative plans take into account advanced care plans that may have been devised before an operation was ever considered. Such advanced care plans often require reinterpretation in the perioperative context given the goal of surgery in the elderly is often to allow survival with a better quality of life.

Postoperative Complications in the Elderly

Postoperative complications mainly arise from the surgery, the patient's pre-existing comorbidities or iatrogenesis. It is worth exploring in more detail common general complications relevant to the elderly such as anaemia, immobility, infections and postoperative cognitive dysfunction including their principles of management.

Anaemia is a common complication after laparotomies and hip surgery in the elderly and may present as hypotension or tachycardia unresponsive to fluid challenge, chest pain due to cardiac ischaemia or pallor and lethargy resulting in a poor ability to mobilise. The FOCUS trial [54] explored liberal (aiming Hb 10 g/dL) vs. restrictive (aiming 8 g/dL) transfusion threshold after hip surgery in the elderly (n = 2016 patients with an average age of 82) and included patients with cardiac risk factors. Though there was a slightly higher proportion of patients who had inability to walk unassisted at 60 days in the restrictive group (28.1% vs. 27.6%), the restrictive group received a median of 0 units of blood, had a pre-transfusion Hb of 7.9 g/dL and had a lower 30-day mortality of 4.3% (vs 5.2%). There were no significant differences in clinical outcomes between the groups. Current strategies for management of anaemia include aggressive management of anaemia preoperatively where time allows by supplementation of iron and/or erythropoietin but reserving transfusion for where there is evidence of ongoing bleeding (persistently dropping Hb), hypotension or tachycardia unresponsive to fluids or cardiac decompensation [55].

Postoperative immobility is associated with pneumonia, pressure ulcers and thromboembolism. It contributes to increased risk of delirium and loss of bone density. Immobility can arise from pre-existing conditions, postoperative pain and tethers applied in the hospital (e.g. oxygen tubing, urinary catheters, intravenous infusions, cardiac monitors, etc.) Management of immobility requires a multidisciplinary approach between surgeons, anaesthetists, nursing staff and physiotherapists. Surgeons can minimise tissue injury and operative time and postoperatively remove tethers that hinder mobilisation. Anaesthetists and pain specialists can use drugs which are short acting and devise an appropriate postoperative analgesia strategy minimising sedation and utilising appropriate regional or local anaesthetic techniques. Monitoring for side effects like constipation or urinary retention is also vital. Nursing staff and physiotherapists are indispensable in delivering specific interventions to encourage mobility [56]. Prehabilitation is a topic of research interest in assessing the ability of subjects to be optimised through a programme of interventions (physical activity, nutrition, psychological support) before a planned operation with the aim of improving their recovery from the surgery. Though the concept has merit from a patient perspective, it is expensive and has not been subject to real-world rigorous efficacy studies in the preoperative frail patient population.

Infections may arise at the site of surgery or in unrelated sites such as in the lungs or urinary tract. Postoperative infections result in longer hospital stays, higher 30-day morbidity and mortality and may contribute to further decline in functional status of an already frail patient. Infection risks are also increased sevenfold in patients with blood sugar levels greater than 12.2 mmol/L (220 mg/dL), and even perioperative stress-induced hyperglycaemia in nondiabetics has been implicated as a risk for surgical wound infection. Management strategies to minimise infection include appropriately timed prophylactic antibiotics prior to incision in theatre, removal of indwelling lines and catheters as early as possible, providing chest physiotherapy to ensure clearance of secretions in combination with analgesic techniques that titrate analgesia to needs avoiding oversedation (e.g. using patient-controlled analgesia) and optimal diabetic control using a basal bolus insulin regime with a long-acting insulin rather than just relying on sliding scale short-acting insulin regimen alone.

There is a spectrum of postoperative cognitive disorders which range from postoperative cognitive dysfunction (or POCD representing a variable impairment of memory, concentration, learning and speed of response postoperatively), dementia (impairment of memory) to delirium (consciousness impaired). Whilst dementia and delirium are well-defined conditions, postoperative cognitive dysfunction is the subject of ongoing research. It has been estimated that the prevalence of dementia in those aged 71 and over in the USA is 13.9% whereas cognitive impairment without dementia is about 22.3%. Many studies have shown that preoperative cognitive impairment is related to postoperative delirium which has been reported to have an incidence of 32–42% [57]. Postoperative delirium has also been associated with major complications like death, prolonged length of stay and need for discharge to rehab or long-term care facility. Postoperative cognitive dysfunction occurs more frequently in those who are over 60 and may result in early retirement from work, decreased quality of life and higher mortality. It usually last from weeks to months and the immediate implication for practice is that patients and their families should be counselled about it so that they make cognitively demanding decisions before surgery or have loved ones willing to help with such decisions in the weeks and months after the surgery. Because the condition usually resolves in months, there are very few randomised controlled studies to guide treatment [58].

Clinical Relevance

The very old demonstrate a reduction in physiological reserve and inability of organ systems to respond to illness and surgical stress [8, 9].

Many of the age-related physiological changes in the functions and composition of the body result in many pharmacokinetic changes in the elderly [22].

There are a number of risk assessment systems that have evolved for different types of surgery.

Preoperative evaluation and risk assessment are performed firstly to weigh the potential surgical benefit against the risk of an adverse medical or surgical complication and secondly to identify any comorbidity that can be optimised.

The outcome of the assessment is a postoperative plan which is developed in discussion between the patient, surgeon, anaesthetist and any other clinicians.

It is worth exploring in more detail common general complications relevant to the elderly such as anaemia, immobility, infections and postoperative cognitive dysfunction including their principles of management.

Higher risks for perioperative cardiac complications are associated with diabetes, renal insufficiency and previous or current cardiac disease [45].

Multiple Choice Questions (MCQs)

1. The following regarding altered pharmacokinetics with ageing are true ***Except***:
   A. Decrease in total body water affects volume distribution resulting in water-soluble drugs attaining a higher serum levels.
   B. Increase in body fat with ageing results in fat-soluble drugs having their half-life increased.
   C. Reduction of liver mass and blood flow with ageing results in decreased rate of drug clearance by the liver.
   D. Serum creatinine is an accurate reflection of renal impairment in the elderly.
2. The following regarding altered pharmacokinetics with ageing are true ***Except***:
   A. The elderly are three times more susceptible to ADRs than those younger than 5 years.
   B. The elderly on multiple drugs have decreased adherence to drug regimes.

C. Reduction in renal function affects not only renally excreted drugs but also drugs that undergo extensive metabolism in the liver.
D. Some effects may be increased in the elderly, for example, the heart rate response and a higher antihypertensive response than the young to beta-blockers.

Answers to MCQs

1. D
2. D

References

1. Siegel-Itzkovich T. So it doesn't hurt: 170 years of anaesthesia-business & innovation-Jerusalem post. http://www.jpost.com/Business-and-Innovation/Health-and-Science/So-it-doesn't-hurt-170-years-of-anaethesia-471185. Accessed 8 May 2017.
2. Kavanagh MF. The origin of the word "anesthesia". http://ncbi.nim.nih.gov/pmc/articles/PMC1655772/?pag=1. Accessed 8 May 2017.
3. Miller AH. The origin of the word 'Anaesthesia'. Boston Med Surg J. 1927;197:1218–22.
4. Robinson DH, Toledo AH. Historical development of modern anaesthesia. J Invet Surg. 2012;25(3):141–9.
5. Podwinska E, Josko J, Kucewicz-Czech E, Misiolek H, Szozoda M. Pioneers of anaesthesiology-Arthur Ernest Guedel (1883-1956). Anesteziol Interns Ter. 2008;40(3):192–4.
6. Beroni AG, Handley WG, Massing MW, Bonds DE, Burke GL, Gott DC Jr. Heart failure prevalence incidence and mortality in the elderly with diabetes. Diabetes Care. 2004;27(3):699–703.
7. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. J Am Coll Cardiol. 1993;22(4 Suppl A):6a–13a.
8. Barnett S. Anaesthesia for the older adult. UpToDate https://222.uptodate.com/contents/anaesthesia-for-the-older-adult. Accessed 8 May 2017.
9. Priebe HJ. The aged cardiovascular risk patient. Br J Anaesth. 2000;85:763–78.
10. Cheitlin MD. Cardiovascular physiology-changes with aging. Am J Geriatr Cardiol. 2003;12(1):9–13e.
11. Anversa PT, Sonnenblick FH, Olivetti G, Megs LG, Capasso JM, et al. Myocyte cell loss and myocyte cellular hyperplasia in hypertrophied ageing rat heart. Circ Res. 1990;67:871–85.
12. Lakatta EG. Cardiovascular ageing in health. Clin Geriatr Med. 2000;16:1419–44.
13. Bansal T, Malhotra N, Hooda S. Anaesthetic considerations in elderly. Int J Pharma Bio Sci. 2012;3:141-1–49.
14. Pugh KG, Wei JY. Clinical implications of physiological changes in the ageing heart. Drugs Aging. 2001;18(4):263–76.
15. Kanonidou Z, Karystianou G. Anaesthesia for the elderly. Hip. 2007;11(4):175–7.
16. Nassimiha D, Aronow WS, Ahn C, Goldman ME. Association of coronary risk factors with progression of valvular aortic stenosis in older persons. Am J Cardiol. 2001;87:313–4.
17. Rooke GA. Cardiovascular aging and anaesthetic implications. J Cardiothorac Vasc Anesth. 2003;17:512–23.
18. Aalami OO, Fang TD, Sang HM, Nacamuli RP. Physiological features of aging persons. Arch Surg. 2003;138:1068–76.
19. Ramly E, Kaafarani H, Velmahos G. The effect of aging on pulmonary function – implications for monitoring and Support of the surgical and trauma patient. Surg Clin North Am. 2015;95(1):53–69.
20. Taylor BJ, Johnson BD. The pulmonary circulation and exercise responses in the elderly. Semin-Respir Crit Care Med. 2010;137(3):411–8.
21. Oyarzun GM. Pulmonary function in ageing. Rev Med Chil. 2009;137(3):41–8.
22. Klotz U. Pharmacokinetics and drug metabolism in the elderly. Drug Metab Rev. 2009;41(2):67076.
23. Fulop T Jr, Worum I, Csongor J, et al. Body composition in elderly people. I. Determination of body composition by multi-isotope method and the elimination kinetics of these isotopes in healthy elderly subjects. Gerontology. 1985;31:6–14.
24. Mitenko PA. Drug monitoring in the elderly. Clin Biochem. 1986;19(2):145–9.
25. El Desoky ES. Pharmakinetic and pharmacodynamic crisis in the elderly. Am J Ther. 2007;14:488–98.
26. Turheim K. Drug dosage in the elderly. Is it rational? Drugs Aging. 1998;13(5):357–79.
27. Shi S, Klotz U. Age-related changes in pharmacokinetics. Curr Drug Metab. 2011;12(7):601–10.
28. Turnheim K. When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. Exp Gerontol. 2003;38(8):843–53.
29. Ramsay LE, Tucker GT. Drugs and the elderly. BMJ. 1981;282:125–7.
30. Schmucker DL. Liver function and phase I drug metabolism in the elderly: a paradox. Drugs Aging. 2001;18(11):837–51.
31. Anantharaju A, Feller A, Chedid A. A review. Gerontology. 2002;48:343–53.
32. Schmucker DL. Aging and the liver: an update. Gerontol Biol Sci Med Sci. 1998;53:B315–20.
33. Lamy P. Comparative pharmacokinetic changes and drug therapy in an older population. J Am Geriatr Soc. 1982;30(Suppl):S11–9.
34. Cusack BJ. Pharmacokintics in older persons. Am J Pharm. 2004;2(4):274–302.
35. Crooks J, O'Malley K, Stevenson IH. Pharmacokinetics in the elderly. Clin Pharmacokinet. 1976;1(4):280–96.
36. Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. Br J Clin Pharmacol. 2004;57(1):6–14.
37. Strom C, Rasmussen LS, Steinmetz J. Practical Management of Anaesthesia in the elderly. Drugs Aging. 2016;33:765–77.
38. Bettelli G. Anaesthesia for elderly outpatient: preoperative assessment and evaluation anaesthetic techniques and postoperative pain management. Curr Opin Anaesthesiol. 2010;23:726–31.
39. Chu CC, Weng SF, Chen KT, Chien CC, Shieh JP, Chen JY, Wang JJ. Propensity score-matched comparison of postoperative adverse outcomes between geriatric patients given a general or a Neuraxial Anaesthetic for hip surgery: a population-based study. Anesthesiology. 2015;123(1):136.
40. Partridge JS, Harari D, Martin FC, Dhesi JK. The impact of preoperative comprehensive geriatric assessment on postoperative outcomes in older patients undergoing scheduled surgery: a systematic review. Anaesthesia. 2014;69 Suppl 1:8–16.

41. Owcznk R. Guidelines for general anaesthesia in the elderly of the committee on quality and safety in anaesthesia. Polish Soc Anaesthesiol Intens Ther. 2013;45(2):57–61.
42. Lee TH, Marcantouro ER, Magione CM, Thomas EJ, Polanczykca CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major non-cardiac surgery. Circulation. 1999;100(10):1043–9.
43. Grasso AW, Jaber WA Cardiac risk stratification for non-cardiac surgery. Cleveland Clinic. 2014. http://wwwclevelandclinicmedcom/medicalpubs/diseasemanagement/cardiology/cardiac-risk-stratification-fornon-cardiac surgery/. Accessed 28 May 2017.
44. Leppo JA. Preoperative cardiac risk assessment for non-cardiac surgery. Am J Cardiol. 1995;75(11):42D.
45. NICE Guidelines. https://www.nice.org.uk/guidance/ng45/chapter/Recommendation. Accessed 5 June 2016.
46. Maddox TM. Preoperative cardiovascular evaluation for noncardiac surgery. Mt Sinai J Med. 2005;72(3):185–92.
47. Covert CR, Fox GS. Anaesthesia for hip surgery. Canad J Anaesthesia. 1989;36(3):311–9.
48. Hung WW, Egol KA, Zuckerman JD, Siu AL. Hip fracture management: tailoring care for the older patient. JAMA. 2012;307(20):21.
49. Morrisson RS, Chassin MR, Siu AL. The medical consultant's role in caring for patients with hip fracture. Ann Intern Med. 1998;128(12 Pt 1):1010–20.
50. Polderman D, Bax JJ, Boersma E, de Hart S, Eeckhout E, Fowkws G, et al. Guidelines for preoperative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. Eur J Anaesthesiol. 2010;27:92–137.
51. Fitz-Henry J. The ASA classification and peri-opertive risk. Ann R Coll Surg.Engl.2011;93(3):185–7.
52. Pinaud M. Evaluation of the cardiac risks in non-cardiac surgery in patients with heart failure. Arch Mal Coeur Vaiss. 2002;95 Spec 4(5):21–6.
53. Hall D, Arya S, Schmid K, et al. Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. JAMA Surg. 2017;152(3):233–40.
54. Caison JL, Terrin ML, Noreck H, Sanders DW, Chsitman BR, Rhonds GG, et al. Liberal or restrictive transfusion in high risk patients after hip surgery. NEJM. 2011;365:2453–62.
55. Willett LR, Carson JL. Management of postoperative complications: anaemia. Clin Geriatr Med. 2014;30:279–84.
56. Sanguineti VA, Wild JR, Fain MJ. Management of postoperative complications: general approach. Clin Geriatr Med. 2014;30:261–70.
57. Kim S, Brooks AK. Groban L preoperative assessment of the older surgical patient: honing in on geriatric syndromes. Clin Interv Aging. 2014;10:13–27.
58. Berger M, Nadler JW, Browndyke J, Terrando N, Ponnusamy V, Cohen HJ, Whitson HE, Mathew JP. Postoperative cognitive dysfunction. Minding the Gaps in Our Knowledge of a Common Postoperative Complication in the Elderly Anesthesiol Clin. 2015;33(3):517–50.

Geriatric Diagnostic Imaging

10

Senan Nagaratnam

Historical Perspective

In 1895 the German physicist Wilhelm Conrad Röntgen accidently noticed a glow on a nearby fluorescent screen when testing whether cathode rays could pass through glass. He called this glow X-rays, because of their unknown nature [1, 2]. Weeks later he took an image of his wife's hand. Röntgen was awarded the Nobel Prize in Physics in 1901. Today X-ray technology is widely used. After a lull, a new wave of advanced technology began with the advent of the CT scanner. In 1972 the British engineer Godfrey Hounsfield and South African-born physicist Allan Cormack invented computed tomography (CT) imaging, also known as computed axial tomography (CAT) scanning [3]. Over the next quarter of a century, CT advanced in terms of speed, patient comfort and resolution [3]. In the mid-1980s, the power slip ring was developed which has brought about a new dawn in CT spiral or helical scanning [4].

In 1882, Nikola Tesla in Budapest discovered the rotating magnetic field, a fundamental discovery in physics, and the strength of a magnetic field is now measured in Tesla or Gauss units [5]. In 1937, Isidor I. Rabi observed the quantum phenomenon dubbed nuclear magnetic resonance and received the Nobel Prize [5]. Today imaging has contributed in a number of ways in the study involving all fields of medicine, and currently there are an array of imaging modalities that are available for research and clinical use.

Ageing and Age-Related Changes

Current demographic data predicts an increase in the elderly population worldwide. Life expectancy has increased dramatically, and the 90 years and older age group represent the fastest-growing segment of the population growing at a faster rate than the 85–89-year-olds [6]. In the United States, it contributes to 2% of the US population [7].

Numerous structural and physiological changes occur with ageing [8]. The kidney decreases in size primarily due to loss of cortical mass [9] which is due to glomerular sclerosis [10]. With ageing there is reduction of renal blood flow, impaired autoregulation and reduction in glomerular filtration rate (GFR) [11, 12]. Renal function declines with age, but the independent effects of age, sex and race have not been studied [13], and the decline has been variously attributed to the effects of hypertension, atherosclerosis or other co-morbidities such as cardiovascular disease [14, 15]. The glomerular filtration rate progressively declines at an average rate of 8 ml/min/1.73m^2 per decade [16]. One third of the people over the age of 65 years have an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73m^2 [17, 18].

With ageing a wide variety of changes occur in structure and function of the brain [19]. The brain shrinks in size with age, and the shrinkage is selective [20]. The frontal, prefrontal, basal ganglia, cerebellum, corpus callosum and the ventricles are the areas most susceptible to changes. MRI has revealed changes in the volume of the amygdala hippocampus and temporal horns of healthy individuals which remains relatively stable till the age of 60 years and thereafter undergoes atrophy with age [21]. In a study of the oldest old ageing without dementia characterised by imaging, the investigators found the brains to be smaller and with cerebrovascular lesions as the individuals aged [22]. Brain loss occurred in the hippocampus and its surrounding structures and the other areas involved were the primary sensory cortex and posterior regions [22].

Neuroimaging in the Elderly

Disability increases rapidly with age and in the oldest old [23] with the highest rates of dementia [24]. About half of the oldest old will have dementia [25]. Sarcopenia, lung function, sedentary life style and chronic degenerative conditions such as arthritis and arteriosclerosis contribute to disability in the oldest old [26].

S. Nagaratnam
Alfred Medical Imaging, Sydney, NSW, Australia

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_10

On the other hand, there is a population of very elderly who are living independently in the community who have scored well on scales that measure well-being and quality of life (QoL) [27]. The clinician is often in doubt as to what to do in terms of whether, in this group of patients, additional diagnostic procedures are helpful [28]. This patient population is less prone to the long-term effects of radiation burden or contrast-induced nephropathy [29], and the use of advanced imaging techniques is justifiable. Age alone should not be a determining factor of whether or not to provide procedures to the elderly for diagnostic purposes [30].

Currently, screening for diagnosis and monitoring of disease are largely possible due to the availability of modalities such as CT, MRI, positron emission tomography (PET), combined PET-CT and ultrasound, but they come with a risk [31]. In older patients with obstructive coronary artery disease, the use of dipyridamole-thallium imaging has been shown to be a safe non-invasive procedure and similar to that seen in younger patients [32]. Apart from potential risk of cancer following exposure of patients to ionising radiation, hypersensitivity reactions, risks related to use of IV contrast agents [31] and thyrotoxicosis [33] are other adverse effects. The risk of developing cancer to ionising radiation in the oldest old is insignificant for it takes several years for cancer to occur after radiation exposure. Asthma increases the risk of bronchospasm, and beta-blockers may worsen bronchospasm and have been associated with hypersensitivity [33].

Contrast-induced nephropathy (CIN) is commonly defined as acute renal failure occurring within 48 h of exposure to IV contrast but not to any other causes [34]. There are many risk factors, such as nephrotoxic drugs, advancing age and route of administration, among others, which may contribute to CIN, but the only two confirmed independent risk factors are pre-existing impairment of renal function and renal impairment associated with diabetes mellitus [35]. Patient-dependent risk factors for development of CIN are congestive heart failure, age over 70 years, elevated creatinine levels and nephrotoxic drugs [36]. However a more comprehensive pre-procedural assessment may be justifiable, especially in a high-risk hospital population undergoing interventional radiology procedures [35].

Prevention of CIN

Hydration and avoidance of nephrotoxic drugs are used to decrease the incidence of CIN [35]. Some of the strategies used are shown in Box 10.1.

Box 10.1 Strategies Used to Prevent CIN

Hydrate the patient
- Avoid contrast in high risk patents
- Cease nephrotoxins early
- Look for imaging alternatives
- Use the lowest dose
- Avoid repetitive dosing within one study
- Information sources: [35, 37]

Radiographic contrast agents have been classified as iodinated contrast media and non-iodinated contrast media, and the former is further classified as non-ionic and ionic [33]. The non-ionic agents are selectively used where osmolality may affect the examination quality as in cardiac CT coronary angiography and lower-limb angiography [33]. The non-iodinated contrast agents are generally used in ultrasound and MRI [33]. Nearly 4% of diabetic patients with normal renal function may develop CIN with non-ionic contrast material [37].

Intravenous administration of iodinated contrast media to patients on metformin can result in lactic acidosis [38, 39]. Patients on metformin with an eGFR of less than 60 ml/min should stop taking the metformin at the time of contrast administration [40]. The European Society of Urogenital Radiology recommends that in patients with eGFR less than 45 ml/min, metformin should be stopped 48 h before CT [41]. It has been reported that 8% of the patients with diabetes on metformin and baseline serum creatinine levels <1.5 mg/dl acquire a risk of lactic acidosis with non-ionic contrast [37]. Others have recommended that there is no justification to withhold the metformin before the procedure but to withhold it after the administration of the contrast material for 48 h and if the renal function is normal to restart the metformin [38]. The Royal College of Radiologists advice is that metformin should not be used in the 48 h before and after intravenous contrast medium [39]. According to McCartney et al. [39], it is safe to give IV contrast medium to patients on metformin with normal renal function.

Geriatric Imaging in Clinical Practice and Research

Geriatric chest imaging With ageing changes occur in both the chest wall and lungs with multiple changes in structure and function [42] giving rise to changes in pulmonary mechanics, respiratory muscle strength [43] and ventilation control. It is important to have a clear understanding of the changes in respiratory structure and function associated with ageing as these changes may affect, for instance, in the interpretation of

Table 10.1 Aging-related chest imaging findings and likely misinterpretation as age-related diseases

Anatomical structure	Imaging findings	
I. Thoracic cage		
Intervertebral cartilages, costo-vertebral joints	Calcification	Solitary pulmonary nodules
Parietal muscles	Loss of muscle mass (atrophy)	Increase in pulmonary transparency on X-ray
Intercostal muscles		
Spine-kyphosis, degenerative changes	'barrel-shaped chest'	COPD
II. Diaphragm		
Loss of muscle mass dyskinesis	'hump' (bulging)	Hemi- diaphragm
III. Lung parenchyma		
Enlargement of distal air-spaces,	Hyperinflation on X'ray	Emphysema
Interstitial changes.	Sub-pleural reticular pattern	Interstitial lung disease
Thickening of interloper septa,	Moderate basal fibrosis	Laminar atelectasis
Bronchial thickening and dilatation	Parenchymal changes	Sub-pleural thickening
Reduction in calibre and number of the vessels		
Cardiovascular		
I. Cardiac		
Loss of myocytes and increase in remaining, left ventricular wall thickens,left atrium hypertrophies	Cardiac enlargement	Left ventricular size of dysfunction
Fibrous tissue of skeleton- sclerotic and calcify	Mitral annular and aortic valve calcify	Valve insufficiency
II. Vascular		
Reduction of elastic connective tissue	Enlargement and tortuosity of aorta	widened mediatinum

Information sources: Mereu et al. [45]; Grossman and Nau [46]; Sharma and Goodwin [47]; Hochhegger et al. [44]; Copley [48]; Caskey [49]; Carmeli et al. [50]; Booth et al. [51]

imaging findings. Table 10.1 shows the changes with ageing and age-related imaging changes in relation to the chest. It may be difficult to differentiate normal, age-related X-ray findings and that due to disease and often impossible to distinguish between them on imaging tests alone [44].

Geriatric brain imaging Over one half of the oldest old will have dementia [52, 53], and this group has the highest rate of dementia in the population [23]. The diagnosis of dementia is a clinical one. The diagnosis of dementia in the oldest old can be challenging especially in the early stages of the disease [54]. The main subtypes of dementia include Alzheimer's disease (AD), frontotemporal dementia (FTD), diffuse Lewy body dementia (DLBD) and vascular dementia (VD). AD is the most common neurodegenerative disease characterised by progressive loss of memory and other cognitive functions, by inability to perform basal activities of daily living and in the later stages by behavioural and psychiatric symptoms. The hallmarks of AD are the extracellular accumulation of amyloid beta (Abeta) peptides forming the core of the senile plaques and intracellular neurofibrillary tangles [55] which spreads in stages from the entorhinal cortex to the neocortex [56]. The Abeta deposits involve the neocortex, while the intracellular accumulation mainly affects the hippocampus [57]. Figure 10.1 shows atrophy of the hippocampi and medial temporal lobes. The earliest sites involved affected by atrophy are the medial temporal lobes (Fig. 10.2) [58], followed by atrophy in the medial parietal regions, posterior cingulate and precuneus (Fig. 10.3) and, in the later stages of the disease, the association areas of the frontal and lateral temporal lobes [59] (Fig. 10.4).

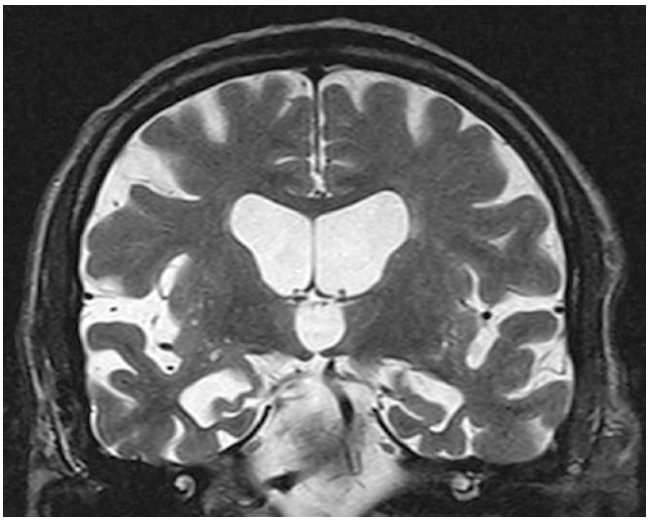

Fig. 10.1 Alzheimer's disease. Coronal T2: Atrophy of the hippocampi and medial temporal lobes. (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

Prominent involvement of the frontal and temporal lobes give rise to frontotemporal dementia (FTD). Frontotemporal lobar degeneration is a syndrome that embraces various pathological substrates including Pick's disease, corticobasal degeneration, FTLD with microtubule-associated protein tau gene mutation and FTLD-U with progranulin gene mutation among others [60]. It has three patterns of presentation, frontal variant with gradual change in behaviour and the temporal

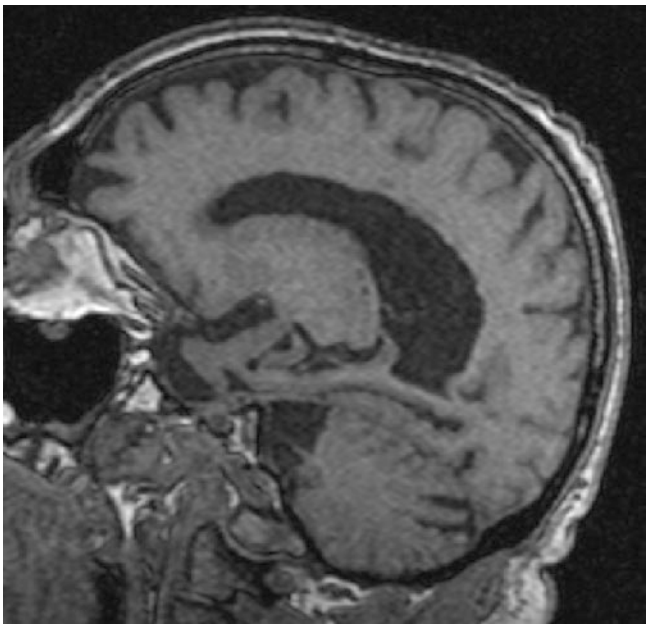

Fig. 10.2 Alzheimer's disease. Sagittal MRI. Atrophy of the medial temporal lobe. (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

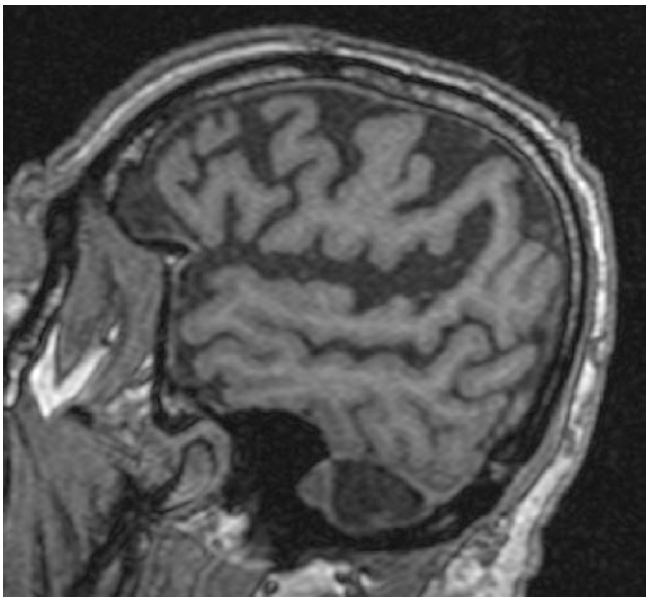

Fig. 10.4 Alzheimer's disease. Sagittal MRI T1. Lateral parietal lobe and posterior temporal lobe (lateral parieto-temporal association cortex) atrophy. (Reproduced, with kind permission, from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

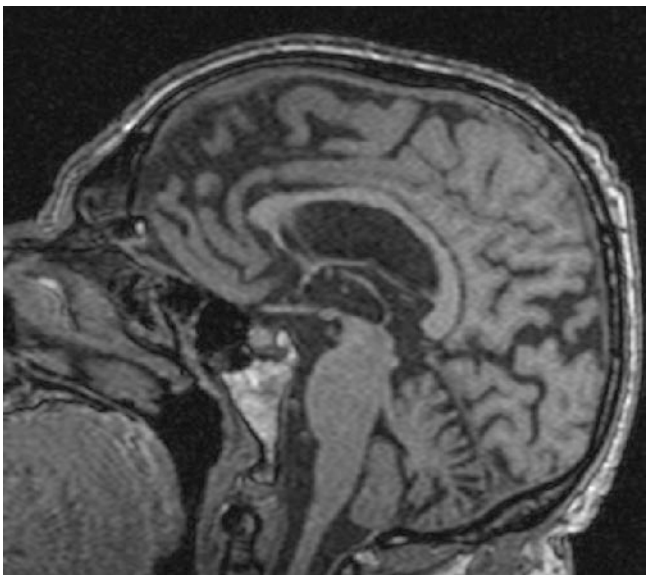

Fig. 10.3 Alzheimer's disease. MRI T1 Sagittal. Showing atrophy of precuneus (and posterior cingulate to a less degree). (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

variant with gradual progressive language dysfunction (semantic dementia and progressive non-fluent aphasia) [59].

Dementia with Lewy bodies also known as cortical Lewy body dementia or diffuse Lewy body dementia is a neurodegenerative disorder associated with abnormal structures (Lewy bodies) which are formed by aggregates of insoluble a-synuclein [59]. It is the second most common form of degenerative dementia [61]. It is characterised by fluctuating cognitive impairment, parkinsonism and recurrent visual hallucinations [61]. It could present like Alzheimer's disease or Parkinson's disease or a combination of the two [62]. There are three phases of dementia in Parkinson's disease, namely, that of Alzheimer's disease, that of cortical Lewy bodies and cell loss in the nucleus basalis and remaining cells showing tangles [62].

Vascular dementia (VaD) now termed vascular cognitive impairment includes a wide spectrum of cognitive decline ranging from mild deficits in one or more cognitive domains referred to as vascular mild cognitive impairment (vaMCI) to a broad dementia-like syndrome [63]. It includes vascular cognitive impairment with no dementia and mixed Alzheimer's disease and cerebrovascular disease [64].

The detection of pre-dementia Alzheimer's disease (AD) is crucial, to begin early and improved management [65] for symptoms which appear long after the onset of degeneration. About half of the demented oldest old do not appear to have significant pathology to account for their cognitive loss, while a similar proportion of non-demented oldest old have high degree of AD and other pathologies while preserving their cognition [66]. Kawas and Corrado [66] hypothesised that AD, vascular and other pathologies represent preclinical disease in non-demented oldest old (i.e. significant pathology but without actual dementia). Thus there seem to be notable differences in this group, and better appreciation of the pathology is crucial. Although clinical-based testing is helpful, rarely does it allow the clinician to make a firm diagnosis [65] and in distinguishing between the subtypes.

Therapeutic regimens vary depending on the type of dementia, and hence accurate diagnosis is vital [54].

Imaging biomarkers are emerging as valuable tools [54] for clinical and preclinical studies, to interpret their pathophysiology [65] and their usefulness in subtype management [67]. The brains of the very elderly usually have mixed pathologies associated with dementia, the commonest being Alzheimer's disease, and other pathologies include Lewy bodies, hippocampal sclerosis, white matter disease and infarction [68]. Neuroimaging techniques are increasingly used as additional markers to detect AD onset and predict conversion of mild cognitive impairment (MCI) to AD [69, 70], and a variety of neuroimaging biomarkers have been put forward to identify the patterns of the pathology in AD and MCI [69]. Magnetic resonance imaging and positron emission tomography (Figs. 10.5, 10.6, 10.7, 10.8 and 10.9) play an important role in the diagnosis of primary neurodegenerative disorders [71] and have been used to demonstrate structural, functional and metabolic changes and have been shown to provide useful disease markers [70]. Basically structural and molecular imaging in patients with dementia have a supportive role rather than diagnostic [72]. Functional connectivity MRI, diffusion tensor imaging and magnetic resonance spectroscopy and molecular imaging techniques such as 18F-fluoro-deoxy-glucose positron emission tomography (PET), amyloid PET and tau PET are now available for clinical use [72]. Measurement of the regional cerebral glucose metabolism (rCMR glc) using PE7 and 18F-fluoro-deoxy-glucose (FDG) has become the accepted technique for dementia research [73]. FDG-PET provides diagnostic specificity [74] and has been used to categorise the dementia subtypes such as Alzheimer's diseases; frontotemporal, diffuse Lewy body, vascular dementias [75]; and posterior cortical atrophy [76].

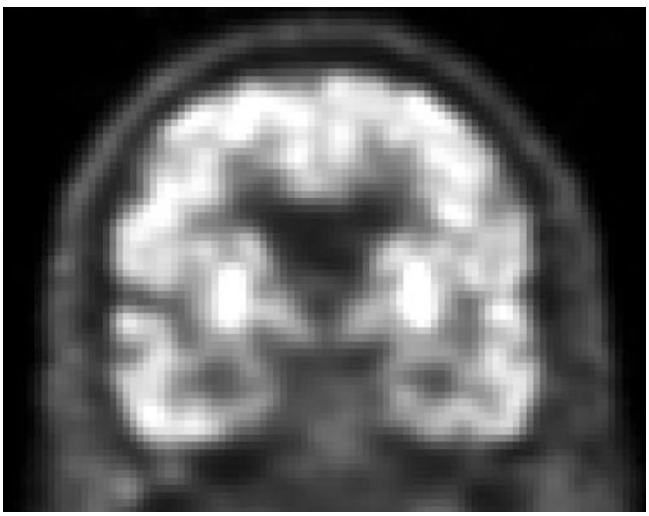

Fig. 10.5 Alzheimer's disease. Coronal PET: Hypometabolism in the hippocampi and medial temporal lobes. (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

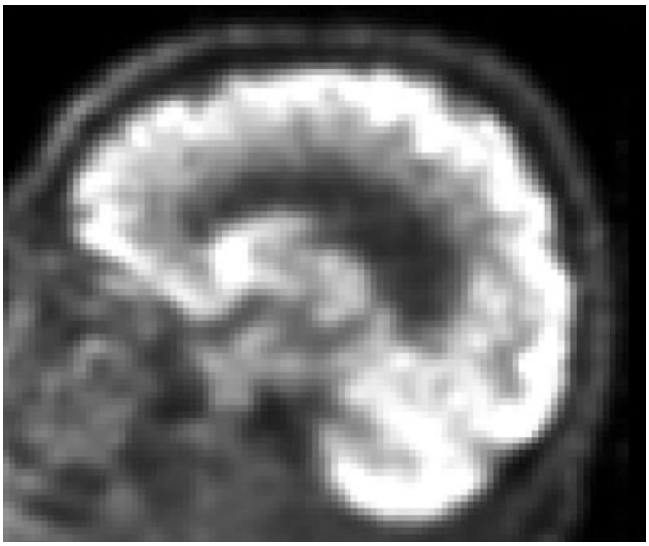

Fig. 10.6 Alzheimer's disease. Sagittal PET. Hypometabolism in medial temporal lobe. (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

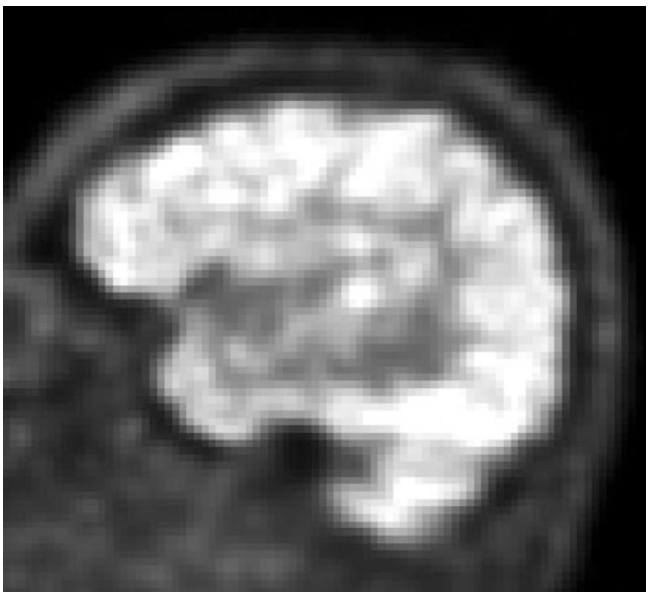

Fig. 10.7 Alzheimer's disease. Sagittal PET. Hypometabolism in lateral parietal lobe and posterior temporal lobe (lateral parieto-temporal association cortex). (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

The pathological hallmark of AD is amyloid beta peptide 42 (Aβ42) [70], and amyloid load may identify increased risk of developing AD [77]. Amyloid load determined by florbetapir F18 positron emission tomography in non-demented old correlated with poorer cognition and faster cognitive decline in this group [77], and high amyloid on florbetapir PET can identify oldest old individuals

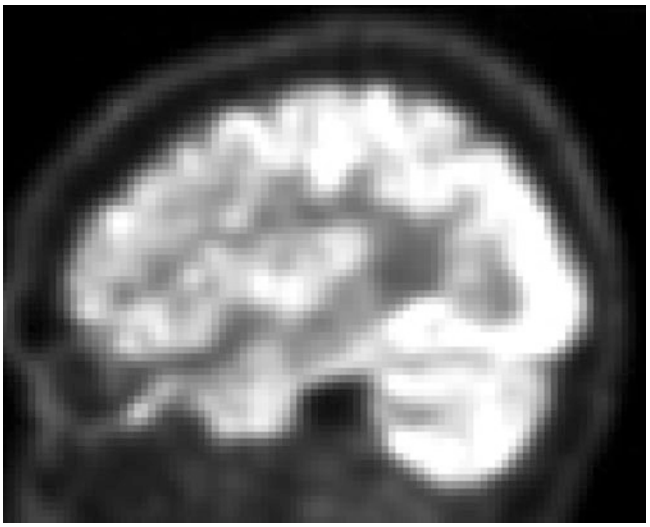

Fig. 10.8 Frontotemporal dementia-sagittal PET. Subtle but definite reduced metabolism in the frontal and anterior temporal lobes 1 year before the MRI show changes. (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

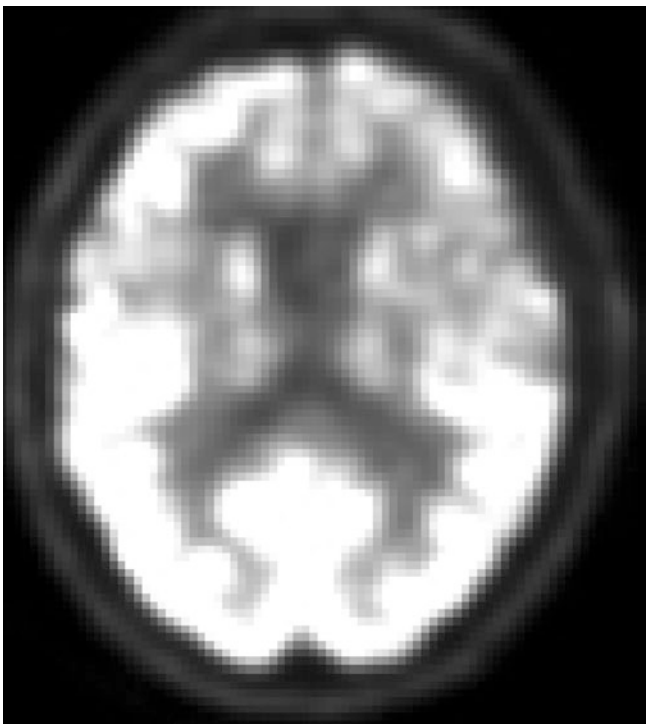

Fig. 10.9 Frontotemporal dementia. Axial PET. Shows subtle but definite reduced metabolism in the frontal and temporal lobes. Changes are more prominent in the left than in the right. The changes of FTD in both PET and MRI are often asymmetrical. (Reproduced with kind permission from Dr. Lisa Tarlinton and courtesy of Nepean Hospital)

at high risk of cognitive decline [78]. MR imaging-derived hippocampal atrophy and white matter hyperintensities are regarded as biomarkers in AD and cerebrovascular disease [79]. Cortical thickness can be quantified allowing early diagnosis and rate of progression from mild cognitive impairment to dementia [80]. Individuals with Lewy body dementia show as array of impaired indicators of dopaminergic function which helps to distinguish them from healthy elderly and those with Alzheimer's disease [81]. Abnormal FP-CIT SPECT [79] and dopamine transporter imaging with iodine-123-b-carbo-methoxy-3-b-(4-iodophenyl tropane) fluoropropyl SPECT support the diagnosis of dementia with Lewy bodies in clinical practice [72]. In healthy individuals, the i-123 ioflupane images show comma-shaped structure bilaterally in the region of the corpus striatum [82] (Fig. 10.10). In Parkinson's disease the usual pattern is the unilateral disappearance of the 'comma' beginning with the tail [82]. Majority of the patients with DLB show a similar pattern, but the change is often symmetrical [82]. Perfusion SPECT [67, 79] and molecular imaging with FDG-PET showing defects in the frontal and/or anterior temporal atrophy are characteristic of frontotemporal dementias (Fig. 10.10). The diffusion tensor magnetic resonance imaging categorises the microstructural soundness of the white matter [83] and could be used to detect white matter changes and is a useful tool to detect early MCI/Alzheimer's disease [84–86].

Procedure Utilisation in the Oldest Old

In a study of utilisation patterns, the oldest old consumed 3.9% of the studies carried out in nuclear medicine although they comprised 1.3% of the state population [87]. The average number of procedures per person during the year was 1.56 in the oldest old compared to 1.57 in younger persons [87]. In a study of oldest old seen in a radiology department over a period of 7 years, the overall activity had increased by 22% over that period, and the activity in the 90 years old age group had increased by 51% with 12.3% more CT in this age group [88]. Digital X-ray fluoroscopy, ultrasound and MRI have made considerable advancement in their ability to image the chest and abdomen. Some of the imaging procedures, such as magnetic resonance imaging, require patient cooperation and tolerance [30]. The oldest old are associated with decreased physical activity and a higher number of chronic diseases such as osteoarthritis, osteoporosis and cardiovascular diseases, including hypertension and stroke [89], and physicians will hesitate to use MRI in the elderly because of the discomfort it may cause [30]. In a study of feasibility and discomfort of MRI procedures in subjects >90 years, Wollman et al. [30] reported that very long sessions of MRI are attainable even in the oldest old and are not associated with any serious discomfort. The key points are summarised in Box 10.2.

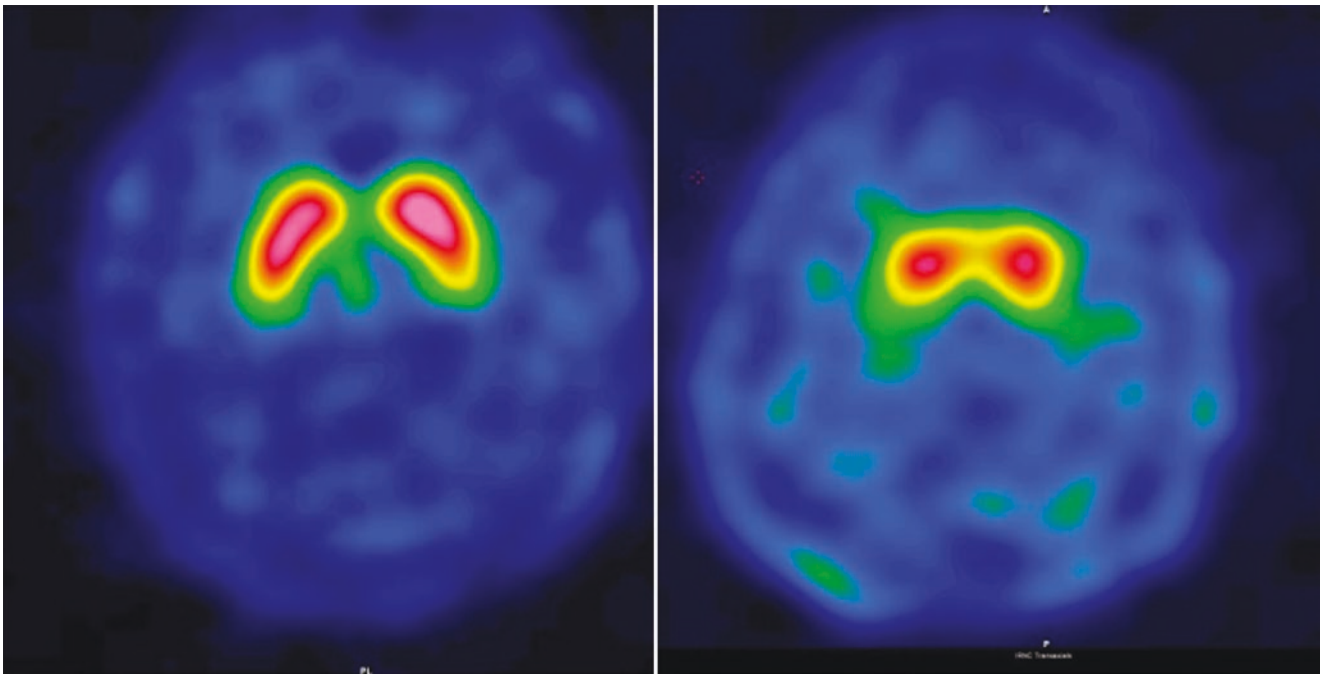

Fig. 10.10 DAT scan showing (i) normal and (ii) abnormal images. (Reproduced with kind permission of Yuliya S Jhanwar, MD. Assistant Professor of Radiology, Chief and Program Director, Nuclear Medicine, Weill Cornell Medicine, New York, NY 10065)

Box 10.2 Key Points: Imaging in the Oldest Old

Disability increases rapidly with age in the oldest old [23] with the highest rates of dementia [24].

Renal function declines with age [13].

There is a population of very elderly who are living independently in the community who have scored well on scales that measure well-being and QoL [27].

Age alone should not be a determining factor whether or not to provide procedures to the elderly for diagnostic purposes [30].

Currently screening for diagnosis and monitoring of disease are largely possible due to the availability of modalities such as CT, MRI, positron emission tomography (PET), combined PET-CT and ultrasound, but they come with a risk [31].

Potential imaging risks include cancer over time following exposure of patients to ionising radiation, hypersensitivity reactions and risks related to use of IV contrast agents [31].

Two confirmed independent risk factors for contrast-induced nephropathy are pre-existing impairment of renal function and renal impairment associated with diabetes mellitus [35].

The European Society of Urogenital Radiology recommends that in patients with eGFR less than 45 ml/min, metformin should be stopped 48 h before CT [41].

Hydration and avoidance of nephrotoxic drugs are used to decrease the incidence of CIN [35].

Neuroimaging is increasingly used to identify the patterns of the pathology in AD with MCI [69].

Tolerance of MRI procedures in subjects >90 years with very long sessions of MRI is attainable even in the oldest old [30].

Acknowledgements I wish to thank Dr. Mark Wilkinson for his comments.

Multiple Choice Questions

1. The following are true of imaging in the oldest old, EXCEPT:
   A. Nearly 4% of diabetic patients with normal renal function may develop CIN with non-ionic contrast material.
   B. Hydration and avoidance of nephrotoxic drugs are used to decrease the incidence of CIN.
   C. Intravenous administration of iodinated contrast media to patients on metformin can result in lactic acidosis.
   D. The older patient population is more prone to the long-term effects of radiation burden or contrast-induced nephropathy.

2. The following are true in relation to neuroimaging in the oldest old, EXCEPT:
   A. The non-iodinated contrast agents are generally not used in ultrasound and MRI.
   B. A variety of neuroimaging biomarkers have been put forward to identify the patterns of the pathology in AD and MCI.
   C. MR imaging-derived hippocampal atrophy and white matter hyperintensities are regarded as biomarkers in AD.
   D. Cortical thickness can be quantified allowing early diagnosis and rate of progression from mild cognitive impairment to dementia.

References

1. Website 1: German scientist discovers X-rays. http://www.history.com/this-day-in-history/german-scientist-discovers-x-rays. Accessed 3 Nov 2016.
2. Website 2: History of the X-ray. Australia's Science Council. http://riaus.org.au/articles/history-of-the-x-rays/. Accessed 3 Nov 2016.
3. Website 3: Brief history of CT. http://www.imaginis.com/ct-scan/brief-history-of-ct. Accessed 3 Nov 20016.
4. Website 4: Spiral CT and helical CT. http://www.imaginis.com/ct-scan/spiral-ct-and-helical-ct-1. Accessed 3 Nov 2016.
5. Website 5: a short history of the magnetic resonance imaging (MRI). http://www.teslasociety.com/mri.htm. Accessed 3 Nov 2016.
6. Bullain SS, Corrado MM. Dementia in the oldest old. Continuum (Minneap Minn). 2013;19(2 Dementia):457–69.
7. US Census Bureau. Annual estimates of population by sex and five-year age groups for the United States: Apri11, 2000 to July1, 2007, 2008. May 2008. http://www.census.gov/popest/mational/arsh/NC-EST2007-sa.html. Accessed 6 Aug 2009.
8. Epstein M. Aging and the kidney. J Am Soc Nephrol. 1996;7(8):1106–22.
9. Dunnill MS, Halley W. Some observations on the quantitative anatomy of the kidney. J Pathol. 1973;11:121.
10. Porush JG, Faubert PF. Renal disease in elderly patients. Rev Clin Gerontol. 1997;7(4):299–307.
11. Lameire N, Hste E, Van Lo A, Dondt A, Bernaert P, Vanholder R, et al. Pathophysiology causes and prognosis of acute renal failure in the elderly. Ren Fail. 1996;8:333–46.
12. Abdel-Kader K, Palevsky P. Acute kidney injury in the elderly. Clin Geriatr Med. 2009;25(3):331–5.
13. Shlipak MG, Katz R, Kestenbaum B, Fried LF, Newman AS, Siscorick S, et al. Rate of kidney function decline in older adults: a comparison using creatinine and cystatin C. Am J Nephrol. 2009;30(3):171–8.
14. Fliser D, Franek E, Joest M, Block S, Mutdschler E, Ritz E. Renal function in the elderly: impact of hypertension and cardiac function. Kidney Int. 1997;5:1196–204.
15. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. J Am Geriatr Soc. 1985;33:278–85.
16. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis. 2003;41:1–12.
17. Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Wilborn TA, Zimmet PZ, et al. Prevalence of kidney damage in Australian adults: the Aus Diab kidney study. J Am Soc Nephrol. 2003;14(7):S131–8.
18. White SL, Polkinghome KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD epidemiology collaboration (CKD-EPI) and modification of diet in renal disease (MDRD) study GFR estimating equations: the Aus Diab (Australian diabetes, obesity and lifestyle study). Am J Kidney Dis. 2010;55:660–70.
19. Convit P, Leon MJ, Hoptman MJ, Tarshish CM, De Santi S, Rusinek H. Age-related changes in the brain, i. Magnetic resonance imaging measures of temporal lobe volumes in normal subjects. Psychiatry Q. 1995;66(4):343–8.
20. Raz N, Rodrique KM. Differential aging of the brain: patterns cognitive correlates and modifiers. Neurosci Biobehav Rev. 2006;30:730–48.
21. Mu Q, Xie J, Wen Z, Shyun Z. Quantitative MR study of the hippocampal formation, the amygdala and the temporal horn of the lateral ventricle in healthy subjects 40-90 years of age. AJNR Am J Neuroradiol. 1999;20:207–11.
22. Yang Z, Sahdev PS. Brain imaging of the oldest old who aged successfully. Alas of Science. https://altlasofscience.org/brain-imaging-of-the-oldest-old-who-aged-successfully/
23. Berlau DJ, Corrado NMM, Peltz CB, Kawas CH. Disability in the oldest old: incidence and risk factors in the 90+ study. Am J Geriatr Psychiatry. 2012;20(2):159–68.
24. Corrada MM, Brookmeyer R, Paganini-Hill A, Berlau D, Kawas CH. Dementia incidence continues to increase with age in the oldest old: the 90+ study. Ann Neurol. 2010;67910:59–168.
25. Kravitz E, Schmeidler J, Been MS. Cognitive decline and dementia I the oldest old. Rambam Maimonides Med J. 2012;3(4):e0026.
26. Nybo H, Petersen HC, Gaist JD, Jeune B, Andersen K, McGue M, et al. Predictors of mortality in 2249 nonagenarians –the Dutch 1905 cohort study. J Am Geriatr Soc. 2013;52:1365–73.
27. Godwin M, Gadag V, Pike A, Pitcher H, Parsons K, McCrate F, et al. The healthy aged. Can Fam Physician. 2015;61(3):e142–7.
28. Nijveldt R, Pflederer T, Achenbach S. Coronary CT angiography in the elderly. Neth Hear J. 2014;22(3):124–5.
29. Laugharne MJ, Paravasthu M, Preston A, Hill KO. CT pulmonary angiography in elderly patients: outcomes in patients aged >85 years. Clin Radiol. 2013;68(5):449–54.
30. Wollman DE1, Beeri MS, Weinberger M, Cheng H, Silverman JM, Prohovnik I. Tolerance of MRI procedures by the oldest old. Magn Reson Imaging. 2004;22(9):1299–304.
31. Scatliff JH, Morris PJ. From Roentgen to magnetic resonance imaging: the history of medical imaging. NC Med J. 2014;75(2):111–3.
32. Lam JY, Chaitman BR, Glaenzer M, Byers S, Fite J, Shah Y, et al. Safety and diagnostic accuracy of dipyridamole-thallium imaging in the elderly. J Am Coll Cardiol. 1988;11(3):585–9.
33. Thomson KP, Varma DK. Safe use of radiographic contrast media. Aust Prescr. 2010;33:35–7.
34. Barrett BJ, Parfrey PS. Prevention of nephrotoxicity induced by radiocontrast agents. NEJM. 1994;331:1449–50.
35. Gleeson TG, Bulugahapitiya S. Contrast-induced nephropathy. Genitourinary imaging. Am J Roentgenol (AJR). 2004;183(6):1673–89.
36. Marcos SK, Thomsen HS, Webb JA, Members of the Contrast Media Safety Committee of the European Society of Urogenital Radiology (EIS). Contrast –media-induced nephrotoxicity: a consensus report. Eur Radiol. 1999;9:1602–13.
37. Parra D, Legreid AM, Beckey NP, Reyes S. Metformin monitoring and change in serum creatinine levels in patients undergoing radiologic procedures involving administration of intravenous contrast media. Pharmacotherapy. 2004;24(8):987–93.
38. Rasuli P, Hammond DI. Metformin and contrast media: where is the conflict? Can Assoc Radiol J. 1998;49(3):161–6.
39. McCartney MM, Gilbert FJ, Murchison LE, Pearson D, McHardy K, Murray AD. Metformin and contrast media-a dangerous combination? Clin Radiol. 1999;54(1):29–33.

40. Benko A, Fraser-Hill M, Magner P, Capusten B, Barrett HB, Myers A, et al. Canadian Association of Radiologists Canadian Association of radiologists : consensus guidelines for the prevention of contrast-induced nephropathy. Can Assoc Radiol J. 2007;58:79–87.
41. Stacul F, van der Molen AJ, Reimer P, Webb JA, Thomsen HS, Morcos SK, Contrast Media Safety Committee of European Society of Radiology (ESUR), et al. Contrast induced nephropathy: updated ESUR contrast media safety committee guidelines [review]. Eur Radiol. 2011;21:2527–41.
42. Oyarzum GM. Pulmonary function in aging. Rev Med Chil. 2009;137(3):411–8.
43. Janssens JP, Pache JC, Nicol NP. Physiological changes in respiratory function associated with aging. Eur Respir J. 1999;13:197–205.
44. Hochhegger B, Meirelles GS, Irion K, Zanetti G, Garcia E, Moreira J, et al. The chest and aging: radiological findings. J Bras de Pneumol. 2012;38:5. https://doi.org/10.1590/S1806-37132012000500016.
45. Mereu M, Verdecchia M, D'Adessandro F, Cerasu B, Patea IL, Giammarini A, et al. Chest imaging I the elderly: what radiologist should know about. https://doi.org/10.1594/esti2014/P-0061.
46. Gossner I, Nau R. Geriatric chest imaging: when and how to image the elderly lung, age-related changes and common pathologies. Radiol Res Pract. 2013;2013:1–9. https://doi.org/10.1155/2013/584793.
47. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. Clin Interv Aging. 2006;1(3):253–60.
48. Copley SJ, Wells AU, Hawtin KE, Gibson DJ, Hodson JM, Jacques AE, et al. Lung morphology in the elderly: comparative CT study of subjects over 75 years old versus those under 55 year old. Radiology. 2009;251(2):566–73.
49. Caskey CI, Zerhouni EA, Fishman EK, Rahmoini AD. Aging of the diaphragm: a CT study. Radiology. 1989;171(2):385–9.
50. Carmeli E, Reznick AZ. The physiology and biochemistry of skeletal muscle atrophy as a function of age. Pro Soc Exp Biol Med. 1994;206(2):103–13.
51. Booth FW, Weeden SH, Tseng BS. Effect of aging on human skeletal muscle and motor function. Med Sci Sports Exerc. 1994;26(5):556–60.
52. Savva GM, Wharton SB, Ince PG, Forster G, Matthews FE, Brayne C. Age neuropathology and dementia. N Engl J Med. 2009;360:2302–9.
53. Poon LW, Woodward JL, Stephen Miller L, Green R, Gearing M, Davey A, et al. Understanding dementia prevalence among centenarians. J Gerontol A Biol Sci Med Sci. 2012;67:358–65.
54. Brown RK, Bohnen NI, Wong KK, Minoshima S, Frey KA. Brain PET in suspected dementia: patterns of altered FDG metabolism. Radiographics. 2014;34(3):684–701.
55. Goedert M, Klug A, Crowther RA. Tau protein ,the paired helical filament and Alzheimer's disease. J Alzheimers Dis. 2006;9(3Suppl):195–207.
56. Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol. 1991;82:239–59.
57. Duyckaerts C, Perruchini C, Lebouvier T, Potiier MC. The lesions of Alzheimer's disease: which therapeutic perspectives? Bull Acad Natl Med. 2008;192(2):303–18.
58. Braak H, Braak E, Bohl J, Bratzke H. Evolution of Alzheimer's disease related to cortical regions. J Neural Transm Suppl. 1998;54:97–106.
59. Bonifacio G, Zamboni G. Brain imaging in dementia. BMJ. 92(1088). http://pmj.bmj.com/content/92/1088/333. Accessed 29 Aug 2017.
60. Yokota O. Frontotemporal lobar degeneration and dementia with Lewy bodies: clinic-pathological issues associated with antemortem diagnosis. Psychogeriatrics. 2009;9(2):91–102.
61. Barber R, Panikkar A, McKeith IG. Dementia with Lewy bodies: diagnosis and management. Int J Geriatr Psychiatry. 2001;16(Suppl 1):S12–8.
62. Gibbs WRG. Dementia and Parkinson's disease. J Psychiatry. 1989;154:596–614.
63. Jellinger KA. Pathology and pathogenesis of vascular cognitive impairment-a critical update. Front Aging Neurosci. 2013;5:17. https://doi.org/10.3389/fnagi.2013.00717.eCol.
64. Black SE. Therapeutic issues in vascular dementia: studies designs and approaches. Can J Neurol Sci. 2007;34(Suppl 1):S125–30.
65. Eisenmenger LB, Huo EJ, Hoffmaan JM, Minoshima S, Matesan MC, Lewis DH, et al. Advances in PET imaging of degenerative cerebrovascular and traumatic causes of dementia. Semin Nucl Med. 2016;46(1):57–87.
66. Kawas CH, Corrado M. Clinical, imaging and pathological studies in the oldest old: the 90+study. http://grantome.com/grant/NIH/R01-AG021055-12. Accessed 3 Apr 2016.
67. O'Brien JT. Role of imaging techniques in the diagnosis of dementia. Br J Radiol. 2007;80(2):S71–7. https://doi.org/10.1259/bjr/33117326.
68. Kawas CH, Kim RL, Sonneen JA, Bullain SS, Trieu T, Corrado MM. Multiple pathologies are common and related to dementia in the oldest old. The 90+ study. Neurology. 2015;85(6):535–42.
69. Liu S, Cai W, Pijol S, Kikinis R, Feng DD. Alzheimer's disease staging. Front Aging Neurosci. 2016;8:23. https://doi.org/10.3389/fnagi.2016.00023.
70. Pauwels EK, Volterrani D, Mariani G. Biomarkers for Alzheimer's disease. Drugs News Perspect. 2009;22(3):151060.
71. Del Sole A, Malaspina S, Magenta Biasina A. Magnetic resonance imaging and positron emission tomography in the diagnosis of neurodegenerative dementias. Funct Neurol. 2016;31(4):205215.
72. Narayanan L, Murray AD. What can imaging tell us about cognitive impairment and dementia? World J Radiol. 2016;8(3):240–54.
73. Herholz K, Carter SF, Jones M. Positron emission tomography imaging in dementia. Br J Radiol. 2007;80(2):S160–7. https://doi.org/10.1259/bjr/97295129.
74. Atri A. Imaging of neurodegenerative cognitive and behavioural disorders: practical considerations for dementia clinical practice. Handb Clin Neurol. 2016;136:971–84.
75. Tripathi M, Tripathi M, Damie N, Kushwaha S, Jaimini A, D'Souza MM, et al. Differential diagnosis of neurodegenerative dementias using metabolic phenotypes on F-18 FDG PET/CT. Neuroradiol J. 2014;27(1):13–21.
76. Spehl TS, Hellwig S, Amtage F, Weiller C, Borman T, Weber WA, et al. Syndrome-specific patterns of regional cerebral glucose metabolism in posterior cortical atrophy in comparison t dementia with Lewy bodies and Alzheimer's disease—a[F-18]-FDG pet study. J Neuroimaging. 2015;25(2):281–8.
77. Kawas CH, Greenia DE, Bullain SS, Clark CM, Pontecorvo MJ, Joshi AD, et al. Amyloid imaging and cognitive decline in non-demented oldest –old: the 90+ study. Alzheimers Dement. 2013;9(2):199–203.
78. Greenia D, Kawas C, Caunca M, Bullain S, Corrada M. PET Amyloid imaging with florbetapir predicts cognitive decline in the oldest old. Neurology. 2014;82(10 suppl P4 011).
79. Murray AD. Imaging approaches for dementia. Am J Neuroradiol (AJNR). 2012. https://doi.org/10.3174/ajnr.A2782.
80. Roman G, Pascual B. Contribution of neuroimaging to the diagnosis of Alzheimer's disease and vascular dementia. Arch Med Res. 2012;43(8):671–6.
81. Tatsch K. Imaging of dopaminergic system in differential diagnosis of dementia. Eur J Nucl Med Mol Imaging. 2008;35(Suppl 1):551–7.
82. McCleery J, Morgan S, Bradley KM, Noel-Storr AH, Ansorge O, Hyde C. Dopamine transporter imaging for the diagnosis of dementia wit Lewy bodies. https://doi.org/10.1002/14651858.CD01633.pub2.
83. Stebbins GT, Murphy CM. Diffusion tensor imaging in Alzheimer's disease and mild cognitive impairment. Behav Neurol. 2009;21(1):39–49.

84. Chua TC, Wen W, Slavin MJ, Sachdev PS. Diffusion tensor imaging in mild cognitive impairment ad Alzheimer's disease: a review. Curr Opin Neurol. 2008;21(1):83–92.
85. Ukmar M, Makuc E, Onor ML, Garbin G, Trevisiol M, Cova MA. Evaluation of white matter damage in patients with Alzheimer's diseases in patients with mild cognitive impairment using diffusion tensor imaging. Radiol Med. 2008;113(6):915–22.
86. Naggara O, Oppenheim C, Rieu D, Raoux N, Rodrigo S, Dalla Barba G, et al. Diffusion tensor imaging in early Alzheimer's disease. Psychiatry Res. 2006;146(3):243–9.
87. Rosenberg RJ, Sziklas JJ, Spencer RP. Nuclear medicine studies of aging-1. Procedure utilization in the oldest old. Int J Rad Appl Instrum B. 1988;15(3):251–3.
88. Fawcett R, McCoubne P. Pitfalls in imaging the frail elderly. Br J Radiology. https://doi.org/10.1259/bjr20140699.
89. Melzer D, Tavakoly B, Winder RE, Mason JAH, Henley WE, Ble A, et al. Much more medicine for the oldest old: trends in UK electronic clinical records. Age Ageing. 2015;44:46–5.

Geriatric Care in General Practice

11

Gowrie Pavan

Historical Perspective

The origins of general practice in England date back to 1617, and the term general practitioner was first formally used in 1844 [1]. It was only in the nineteenth and early twentieth century that general practice as is known today began [2]. In the 1600 and 1700s in England, the general practitioners were the primary care physicians [1], and different divisions of the profession were not differentiated until the sixteenth century. In 1518 the Royal College of Physicians was founded and the Company of Surgeons in 1740 [3]. With the introduction of the National Insurance Act of 1911, general practitioners became responsible for providing a state-funded primary health care for eligible working males, and subsequently in 1948 this was extended to everyone with the introduction of the National Health Service (NHS) [2]. The Royal College of General Practitioners was founded in 1952 and has more than 50,000 members.

With England's original colonisation of the United States, the practice of general practitioners was carried over to the United States [1]. The American Board of General practice, American College of General Medicine and the American Academy of General Physicians have largely contributed to the recent history of general practice in the United States [1].

When the First Fleet arrived in Australia in 1760, the Australian traditional healers were the Aboriginal medicine men [4]. Medical practice began in Australia in 1788 [3]. In 1801 William Redfern, a surgeon was convicted and transported from England and like the others practiced as a physician and surgeon a description used by early GPs [3] and this state continued well into the twentieth century [3]. Before 1900 specialist and specialist teaching positions were mainly recruited from abroad [3]. In 1958 the Australian College of General practitioners was incorporated under the NSW Companies Act [3].

In 1984 the Commonwealth Government introduced a universal health insurance scheme, the Medicare. Medicare provides free treatment as a public patient and in a public hospital to all Australian residents. The GPs provide on a fee-for-service. For older patients after-hour care can pose problems because of the increasing levels of co-morbidities, transport difficulties and reluctance to leave home at night [5]. There are several medical deputising services that provide after-hour home visits by GPs.

Demographic Characteristics of the Elderly

The oldest old are the most rapidly growing segment of the population, and similar trends are seen not only in the industrialised nations but also seen around the world. This demographic trend will continue, and although life expectancy continues to increase, there will be an unparalleled increase in age-related illnesses. The demographic characteristics of the oldest old are unique and different to that in the young old people, for example, in general they are more likely to be widowed, to live alone, to suffer from chronic illnesses and to have more visits to the general practitioner and to the hospital out-patient [6]. There is increased risk of dependency, disability, frailty, hospitalisation, institutionalisation and mortality in the elderly population over the age of 75 [7]. With life expectancy increasing, the workload of the general practitioner involving consultations with older people will increase [8].

About 85% of the Australian population made at least one contact with a general practitioner per year [9], and an increasing proportion of the visits rising significantly from 27% to 30% were from the patients aged 65 and over [10]. The older patients who are the most socioeconomic disadvantaged are the very high and frequent GP attenders [11]. Of the frequent high attenders, 32% were aged 75 and above, and among very high and frequent GP attenders, arthritis and osteoporosis were the two most common long-term conditions [11]. Other common health conditions were heart and circulatory, long-term injury, asthma, diabetes and mental health [11].

G. Pavan
Family Medical Practice, Carlingford, NSW, Australia

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_11

General Practitioner Involvement

People consult the GP for a number of reasons including short-term illnesses, management of long-term conditions and preventive health practices [12]. Nearly one-third of people 85 years and over visited their GP on 12 or more occasions in the previous year compared to 6.0% aged 15–24 [12]. A Dutch study found that the out-of- hours primary health care has moved from practice-based services to GPs, the GPs handling 88% compared to 12% by the accident and emergency department [13]. An interplay of factors such as physical, psychological and social forms the basis for their decision to consult their GP [14]. The very elderly have a lower physical health and functional level than their younger counterparts for they suffer more economic losses and more cognitive impairment and have a lower educational level [15].

Acute Short-Term Illnesses

In general practice life-threatening conditions are uncommon and that due to traumatic injuries have declined [16]. Jones et al. [17] divided acute illnesses into minor and major illness. They drew attention to the undifferentiated nature of the problems presented to the GPs and recorded that the content of general practice was strikingly alike across the Western care systems including Australia, New Zealand and the United States. The acute major illness may present as acute serious illness, as acute exacerbation of an existing condition or as a new chronic illness [17].

Long-Term Conditions

Chronic Medical Conditions

In Australia 90% of all deaths in 2011 were due to chronic diseases [18]. The 2007–2008 National Health Survey indicated that one-third of the population had at least one of the following chronic conditions: asthma, type 2 diabetes, coronary heart disease, cerebrovascular disease (largely stroke), arthritis, osteoporosis, COPD, depression or hypertension; and the proportion increased with age [19]. Most of the chronic diseases reported by GPs were hypertension, diabetes, depression, arthritis and lipid disorders [20]. Older persons have a higher burden of chronic diseases and are heavy users of health care both ambulatory and in institutions such as hospitals and nursing care facilities [21].

Arthritis

The two common types are rheumatoid arthritis and osteoarthritis. Rheumatoid arthritis (RA) is a systemic disease, and the pathogenesis involves genetics [22], environmental factors [23] and autoimmunity [24, 25]. Osteoarthritis was thought to be a noninflammatory condition, but now it is evident that this is not so [26], and there is evidence linking local inflammation with pain measured as synovitis/effusion [27]. RA is a severe disabling illness with deleterious effects [28] and affects every aspect of daily life, impacts health, threatens independence and has large economic and health costs [29]. Similarly osteoarthritis can have an equally negative impact on daily living due to severe chronic pain. Management of the pain can be a challenge because of the side effects of many of the pain medications with respect to the elderly.

Role of the General Practitioner

Early diagnosis and aggressive treatment [30] can be beneficial in treating synovial inflammation of RA [31]. The aim of treatment is to minimise or prevent joint damage, preserve function and induce clinical remission [32, 33]. Early recognition of symptoms and prompt referral by the GP to a rheumatologist for accurate diagnosis and to prescribe the course of medication [34]. The GP should provide the patient with information about their arthritis, to ensure access a support network and develop a patient-centred care plan [34].

Diabetes

Diabetes in the elderly poses special problems, a high degree of co-morbidities and age-related risk of developing or worsening of many geriatric syndromes such as cognitive impairment, chronic pain, falls, polypharmacy, urinary incontinence and depression [35, 36]. The macrovascular and microvascular complications are well recognised.

Role of the General Practitioner

The GP should have the knowledge to recognise the symptoms and the risk factors (Box 11.1).

Box 11.1 Management Guidelines of Diabetes

1. Test for micro-albumin.
   Subsequent examination performed annually
2. Lifestyle changes.
3. Glycaemic control.
4. Blood pressure control.
5. Drug therapy – ACE inhibitors and ARBs can reduce micro-albuminuria and may retard progression to overt diabetic nephropathy.
6. Eye checks.
7. Neuropathic screening and podiatry.

Information sources: ADA 2004 [37]

Dementia

Dementia is a common disease, and most general practices will care for a significant number of demented patients. It can pose problems in diagnosis more so in the mild end of the spectrum. Several studies have shown that the GPs identify only a segment of the cases [38–42]. Some of the reasons for failure to diagnose or underdiagnose dementia in a fair proportion of patients by the general practitioners could be attributed to a fear of committing to a diagnosis, lack of confidence on their diagnostic ability, lack or inadequate knowledge, referral routines and lack of awareness of current practice requirements; the diagnosis of dementia is time consuming [41–43]. Few general practitioners perform routine assessments of cognitive function [42, 44]. However if there has been a long-term relationship with the patient, the GP may be the best person to note early changes in the behaviour of the patient.

Role of the General Practitioner

GPs must have the knowledge and the diagnostic ability to perform standardised cognitive assessments, take a proactive role in screening all patients for suspected dementia, be aware of the symptoms and risk factors for dementia and make appropriate referral to specialised units and have shared care arrangements with specialist arrangements services [34].

Depression

Primary care physicians may have difficulty in detecting and treating depression unless they have a high index of suspicion and additional mental health training [45]. Once the diagnosis is arrived at, the next important task in general practice is the assessment of risk. The patient should undergo thorough psychiatric and medical assessment including a suicide assessment. The elderly before making serious suicide attempts frequently contact family and doctor [46]. Several studies have revealed that 70% of the elderly suicide victims saw their primary care physician within a month of death. Late-onset dementia is associated with a greater incidence of completed suicide and poorer outcome [47].

General Practitioner's Role

GPs have to recognise that dealing with depression is an essential part of their role and have the self-reliance doing this [34].

Preventive Health Practices

Cardiovascular diseases, cancer, COPD and diabetes account for 75% of all chronic disease deaths, and the common behavioural risk factors are smoking, physical inactivity, poor nutrition and alcohol abuse [20]. Illnesses and death due to chronic diseases are increasing in all developed countries and becoming common in developing countries due to the falling food prices and increasing urbanisation leading to changes in diet, overweight and decrease in physical activity [48].

Preventive interventions such as healthy diet, increased physical activity and cessation of smoking have shown that an estimated 80% of premature heart disease and type 2 diabetes and 40% of cancer could be prevented [49]. The general practitioner is best placed to deliver such care for he/she is often the first person of contact; the long-term prolonged care to many patients and the prolonged association with the patients can lead to mutual respect and trust [50].

The forms of preventive care that doctors provide are immunisation, screening and early identification of chronic conditions such as hypertension, diabetes, cardiovascular and mental health, providing preventative advice, counselling and improving health literacy [50]. An estimated half the number of patients with chronic disease do not receive optimal treatment [51, 52]. The Australian Government Department of Health and Aging in 2009/2010 introduced several initiatives to provide preventive care to the over 75-year-olds. The Enhanced Primary Care (EPC) programme is a comprehensive annual assessment of an older patient's physical, psychological and social health status [53]. The

assessment can be carried out in the GP's surgery or in the patient's home. GPs should make certain their prevention strategies are carried out on recommended guidelines. Practice Incentive Programme [54] and the service incentive payments [55] are available for chronic diseases such as diabetes, arthritis and mental disorder. Earlier evaluations have shown a variability in the uptake of these initiatives [56] depending on the outcomes studied [57, 58], and there is evidence of underutilisation of case-conferencing items [59].

Other Roles

Palliative Care in General Practice

In the last year of life, 90% of the care of patients occurs at home with the assistance of the GP and community service teams [60]. In the United Kingdom, GPs and generalist hospital doctors provide the majority of palliative and terminal care [61]. GPs have an important role in palliative care, but some feel uncomfortable when faced with dying patients about their ability to deliver palliative care adequately [62].

Self-Care Practices

In the management of long-term conditions, self-care is an essential component [63, 64]. In self-care management, the patients have an active role in the everyday care of their illnesses and treatment together with maintaining good health [65]. For better self-management of their chronic illness, a wide range of interventions have been developed [66–68] which require collaboration between health-care providers and patients [65]. The commitment to self-care has been confirmed by the National Health Service (NHS) plan [69]. After family and friends, it is the general practitioner the people prefer as the main source for self-care information [70]. General practitioners can support self-management in a number of ways such as to identify problems from patient's perspective by structuring patient-physician interactions, providing education individually and through community self-management resources [64]. Studies suggest that although GPs value increased patient involvement and increased self-management, there are significant barriers to attainment of these outcomes [71]. There is a strong belief that even a small shift from self-care to doctor care could lead to increased demands on the general practitioner practice [72]. In Australia it has been reported that 77% of Australians have at least one long-term condition [73] and self-management is provided by health-care and community services [73]. However there has been limited engagement between Australian general practice and other services providing self-management support [74].

Aged Care Facilities

On-site primary care services in residential aged care facilities are provided by GPs. [75]. But according to available estimates, less than 21% of GPs are regularly engaged in residential aged care [76], and the reason for this low participation includes inadequate remuneration [77]. The Royal Australian College of General Practitioners has released a guide to assist the GPs and residential aged care facilities to identify clear roles and obligations in providing high-quality care for residents [78].

End of Life

The general practitioner is the most consulted professional and most helpful in this situation. The general practitioner could assist older patients and their families on decisive issues thereby the elderly may be able to maintain authority, autonomy and dignity as they face death.

Senior Drivers

Older drivers are at higher risk of dying in a crash as well as that of pedestrians and passengers in comparison to that of any other age group. The risk of being killed or injured increases with age. In the United States on average, 16 older adults had been killed and 648 injured in crashes every day in 2014 [79, 80].

For safe driving, a robust visual, cognitive and motor functioning is crucial. With normal ageing there is a decline in these functions. Structural changes occur in the eye with ageing. It is not unusual for older adults to complain of glare while driving at night from headlights of oncoming vehicles [81]. This is due to lens opacities and changes in the vitreous with ageing. Daytime glare with bright light occurs with opacities beneath the posterior lens capsule. With ageing there is difficulty in focussing near objects due to thickened lens. A number of changes occur in the retina resulting in deterioration of vision with age and are due to a combination of factors associated with ageing [82]

Cognition declines with age, and for the elderly to maintain functional independence, for example, to manage finances and to drive safely, cognition is vital [83]. The most affected cognitive function with age are attention and memory, and some form of attention is involved in various cognitive domains [84]. In the elderly attention deficits can have significant effect on the ability to function independently [83].

With ageing there is an age-related atrophy of the corpus callosum and motor cortical regions that may cause a motor decline such as balance and gait defects, coordination deficits and slowing of movement [85] that may affect the ability

of older adults to perform their activities of daily living. Reaction time increases slowly until the 50s and 60s, and thereafter it declines faster as the person gets older [86, 87]. Disability increases with age. Not all medical conditions affect driving performance.

An important role of the GP is to identify and manage at risk drivers [88]. Proper assessment is not only to assist the elderly who drive to maintain their driving ability by driving as long as it is safe but also to help drivers to determine when to stop driving [88]. With the oldest old segment of the population increasing, there will be a large number in this group on the road driving. In New South Wales, those license holders over 75 must prove by annual medical test their competence to drive, and those above the age of 85 by practical driving assessment every second year. This means that as the population increases, the workload of the GPs to write reports about fitness to drive will increase. The ILC-UK policy brief recommends that GPs in order to highlight the impact of ageing should be involved in education schemes for older drivers [89]. The brief highlights that age-related decline does not always display as a specific medical condition and GPs must continue to advise patients where fitness to drive is related to ageing in general rather than to medical conditions [89]. Furthermore on decisions around driving in later life, GPs should have a crucial role in advising patients and patients' families [89].

Clinical Relevance

The demographic characteristics of the oldest old are unique and different to that in the young old people [6].

There is increased risk of dependency, disability, frailty, hospitalisation, institutionalisation and mortality in the elderly population over the age of 75 years [7].

Frequent GP attenders, are those with arthritis and osteoporosis, the two most common long-term conditions [11].

The forms of preventive care that GPs provide are immunisation, screening and early identification of chronic conditions such as hypertension [50], diabetes, cardiovascular and mental health, providing preventative advice, counselling and improving health literacy [50].

General practitioners can support self-management in a number of ways [64].

GPs have an important role in palliative care [62].

GPs then should have a crucial role in advising patients and patients' families on decisions around driving in later life [89].

The general practitioner could assist older patients and their families in making and acting on decisive issues, thereby the elderly may be able to maintain authority, autonomy and dignity as they face death.

Multiple Choice Questions

1. The following are true, EXCEPT:
   A. The demographic characteristics of the oldest old are unique and different to that in the young old people.
   B. Very high and frequent GP attenders are those with arthritis and osteoporosis.
   C. In general practice life-threatening conditions are common.
   D. GPs have an important role in palliative care.
2. The following are true, EXCEPT:
   A. Primary care physicians may have difficulty in detecting and treating depression.
   B. Several studies have revealed that 10% of the elderly suicide victims saw their primary care physician within a month of death.
   C. An important role of the GP is to identify and manage risk drivers.
   D. Some GPs feel uncomfortable when faced with dying patients about their ability to deliver palliative care adequately.

Answers

1. C
2. B

References

1. Origins of the general practice of medicine. www.origins-of-general-pratice.org. Accessed 28 Jan 2017.
2. Royal College of General Practitioners. History of the college http://www.rcgp.org.uk/about-us/history-heritage-and-archive/history-of-the-college.aspz. Accessed 30 Jan 2017.
3. Fisher E. College history. Australian general practice-a celebration. http://www.racgp.org.au/yurracgp/organisation/history/college-history/australan-general-practice. Accessed 30 Jan 2017.
4. General practitioners of Australia. The history of general practice in Australia. http://www.gp.org.au/history.html. Accessed 30 Jan 2017.
5. Foster J, Dale J, Jessopp L. A qualitative study of older people's views of out of hours service. Br J Gen Pract. 2001;51:719–23.
6. Tomassini C. The oldest old in Great Britain: change over the last 20 years. Natl Stat Popul Trends. 2006;123:32–9.
7. Topinkova E. Aging disability and frailty. Ann Nutr Metab. 2008;52(Suppl 1):6–11.
8. Charles J, Britt H, Harrison C. General practice workforce and workload. In: Britt H, Moller GC, editors. General practice in Australia, health promotions and policies 1998 to 2008.General practice series.no.24.Cat. noGEP24. Canberra: Australian Institute of Health and Welfare; 2009.
9. Britt H, Moller GC, Henderson J, Bayram C, Harrison C, Valenti L, et al. General practices activity in Australia 2014–15. General Practice Series no.38. Sydney: Sydney University Press; 2015.
10. Britt H, Moller GC, Henderson J, Charles J, Valenti L, Harrison C, et al. A decade of Australian general practitioner activity, 2003-04

to 2012-13. BEACH (bettering the evaluation and Care of Health). Sydney: Sydney University Press; 2013.
11. National Health Performance Aurhority (NHPA). Health communities: Frequent GP attenders and their uses of health services in 2012–13. 2015. www.myhealthycommunities.gov.au. Accessed 30 Jan 2017.
12. Australian Bureau of Statistics. Patient experiences in Australia: Summary of findings. 2012–13. http:/www.abs.gov.au/ausstats/abs@.nsf/Lookup/4839.Omain+features32012-13
13. van Charante EPM, van Steenwijk-Opdam PCE, Bindels PJE. Out-of –hours demand for GP care and emergency services: patients' choices and referrals by general practitioners and ambulance services. BMC Fam Pract. 2007;8:46. https://doi.org/10.1186/1471-2296-8-46.
14. Campbell SM, Roland MO. Why do people consult the doctor? Family Pract. 1996;3(1). (Oxford University Press; 1996).
15. Haug ML, Folmar ST. Longevity, gender and life quality. J Health Soc Behav. 1986;27:332–5.
16. RACGP. Acute serious illness and trauma. http://curriculum.racgp.org.au/statements/acute-serious-illness-and-trauma/. Accessed 6 Jan 2017.
17. Jones R, White P, Armstrong D, Ashworthy M, Peters M. Managing acute illness. www.kingsfund.org.uk/sites/files/kf/field_document/managing-acute- illnesses-gp-inquiry-research-paper-maii.pdf. Accessed 6 Feb 2017.
18. Australian Institute of Health and Welfare (AIHW). Key indicators of progress for chronic disease and associated determinants data report. Cat no. PHE 142. Canberra: AIHW; 2011.
19. Australian Institute of Health and Welfare (AIHW). Australian health 2012. Australia's health series. no. 13. Cat no. AUS 156. Canberra: AIHW; 2012.
20. Australian Institute of Health and Welfare (AIHW). Australian health 2014. Australia's health series. no. 14. Cat no. AUS 1578. Canberra: AIHW; 2014.
21. Verbrugge LM. Women and men: Mortality and health of older people. In: Riley MW, Hess RB, Bond K, editors. Aging in Society: Selected reviews of recent research. Hillsdale: Lawrence Eribaum Associates.
22. Basisht G, Singh RH, Chandola H. Management of rheumatoid arthritis (Aamavata) using symbiohealth health care system. Ayu. 2012;33(4):466–74.
23. Choy E. Understanding the dynamics: pathways involved I the pathogenesis of rheumatoid arthritis. Rheumatology. 2012;51(suppl 5):v3–v11. https://doi.org/10.1093/rheumatology/kes113.
24. Kurko J, Besenyei T, Laki J, Glant TT, Mihecz K, Szekanecz Z. Genetics of rheumatoid arthritis-a comprehensive review. Clin Rev Allergy Immunol. 2013;45(2):170–9.
25. Kawabata K, Yamamoto K. Recent advances in the pathogenesis of rheumatoid arthritis. Clin Calcium. 2009;19(3):303–9.
26. Jones G. What's new in osteoarthritis pathogenesis? Intern Med J. https://doi.org/10.1111/imj.2763.
27. Jones G. Sources of pain in osteoarthritis: implications for therapy. Int J Clin Rheumatol. 2013;8:335–46.
28. Pollard L, Choy EH, Scott DL. The consequences of rheumatoid arthritis: quality of life measures in the individual patient. Clin Exp Rheumatol. 2005;23(suppl 39):S43–52.
29. Lapsley HM, March LM, Tribe KL, Cross MJ, Courtnay BG. Brooks PM for the arthritis cost and outcome project group. Living with rheumatoid arthritis: expenditures health status and social impact on patients. Ann Rheum Dis. 2002;61:818–21.
30. Tayar JH, Suarez-Almazor M. New understanding and approaches to treatment of rheumatoid arthritis. Br Med Bull. 2010;94(1):201–14.
31. Agarwal SK. Biologic agents in rheumatoid arthritis: an update for managed care professionals. J Manag Care Pharm. 2011;17(Suppl 11B):S14–8.
32. Suresh E. Recent advances in rheumatoid arthritis. Postgrad Med J. 2010;86(1014):243–50.
33. Therapeutic guidelines. 2006.
34. Goodwin N, Curry N, Naylor C, Ross S, Duldig W. Managing people with long term conditions. www.kingsfund.org.uk/files/kf/field/field_document/managing-profile-long-term-conditions-gp-inquiry-research-pper.mariipdf. Accessed 5 Feb 2017.
35. Rockwood K, Await E, Macknight C, MDowell I. Incidence and outcomes of diabetes mellitus in elderly eople. Report from the Canadian Study of Health and Aging. CMAJ. 2000;162(6):769–72.
36. Bloomgarden ZT. Type 2 diabetes in the young. Am Diabetes Assoc Diabetes Care. 2004;27(4):998–1010.
37. American Diabetes Association. Diagnosis and classification of diabetes. Diabetes Care. 2004;27:S5–S10. DA.
38. Williamson J, Stokoe IH, Gray S, Fisher M, Smith A, McGhee A, et al. Old people at home. Their unreported needs. Lancet. 1974;1:1117–20.
39. Parsons PL. Mental health of Swansea's old folk. Br J Psychiatr Soc Med. 1983;19:43–7.
40. Mant A, Eyland EA, Pond CD, Saunders NA, Chancellor AH. Recognition of dementia in general practice. Fam Pract. 1988;5:184–8.
41. Bowers J, Jorm AF, Henderson S, Harris P. General practitioners detection of depression and dementia in elderly patients. Med J Aust. 1990;153:192–6.
42. Nagaratnam N, Lewis-Jones M. Predictive properties of referral communications for mental illness and dementias in a community. Dement Geriatr Cogn Disord. 1998;9:1117–20.
43. Brodaty H, Howarth GC, Mant A, Kurrie SE. General practice and dementia. Med J Aust. 1994;160:10–4.
44. O'Connor DN, Pollitt PA, Hyde JB, Brook CP, Reiss BB, Roth M. Do general practitioners miss dementia in the elderly patients? Br Med J. 1988;297:1107–10.
45. Hickie I, Scott E, Wilhelm K, Brodaty H. Subcortical hyperintensities on magnetic resonance imaging in patients with severe depression-a longitudinal evaluation. Biol Psychiatry. 1997;42:367–74.
46. Stoppe G, Sandholzer H, Huppertz C, Duwe H, Staedt J. Family physician and the risk of suicide in the depressed elderly. J Affect Disord. 1999;50:193–8.
47. Bellini M, Matteucci V. Late onset depression and suicide outcome. Arch Gerontol Geriatr. 2001;33:37–40.
48. Australian Institute of Health and Welfare. Australia's food and nutrition. Cat. No. PHE163. Canberra: AIHW; 2012.
49. Guidelines for preventive activities in general practice. 8th ed. Melbourne: The Royal Australian College of General Practitioners; 2012.
50. Australian Medical Association (AMA). Doctors and preventative care-2010. https://ama.com.au/position-statement/doctors-and-preventative-care-2010. Accessed 5 Feb 2017.
51. Woolcock AJ, Bastiampillai SA, Marks GB, Keena VA. The burden of asthma in Australia. Med J Aust. 2001;175:141–5.
52. Senes S, Britt HA. A general practice view of cardiovascular disease and diabetes in Australia. Canberra: Australian Institute of Health and Welfare and University of Sydney, June 2001; Cardiovascular disease. Series No. 18.
53. Department of Health and Aging (DoHA). Enhanced primary care program: overview. Canberra: DoHA; 2008.
54. Health Insurance Commission. Practice incentives program (PIP). http://www.health.gov.au/providers/incentives:allowances/pip.htm. Accessed 2 Feb 2017.
55. Health Insurance Commission. Service incentives payments (SIP). http://www.health.gov.au/providers/incentives:allowances/opip.scheme/service.Incentives.Htm. Accessed 2 Feb 2017.
56. Blakeman T, Harris MF, Comino E. Implementation of the enhanced primary care items requires ongoing education and evaluation. Aust Fam Physician. 2001;30:75–7.

57. Chan A, Amoros C, Harris M. New 45–49 year health uptake checks: General practitioner uptake of MBS item 717. Aust Fam Physician. 2008;37(9):765–8.
58. Williams I, O'Doherthy L, Mitchell G, Williams K. Identifying unmet needs in older patients: nurse –GP collaboration in general practice. Aust Fam Physician. 2007;36(9):772–6.
59. Mitchell GK, de Jong IC, Del Mar CB, et al. General practitioner attitudes to case conferences: how can we increase participation and effectiveness? Med J Aust. 2002;177:95–7.
60. Hinton J. Can home care maintain a acceptable quality of life for patients with terminal cancer and their relatives? Palliat Med. 1994;8:183–96.
61. Barclay S, Wyatt P, Shore S, Fnlay I, Grande G, Todd C. Caring for the dying: how well are general practitioners? A Questionnaire study in Wales. Palliat Med. 2003;17(1):27–39.
62. Mitchell GK. How well do general practitioners deliver palliative care? A systematic review. Palliat Med. 2002;16(6):457–64.
63. MacKichan F, Paterson C, Henley WE, Britten N. Self-care in people with long term health problems: community based survey. BMC Fam Pract. 2011. https://doi.org/10.1186/1471-2296-12-53.
64. Colman MT, Newton KS. Supporting self-management in patients with chronic illness. Am Fam Physician. 2005;72(8):1503–10.
65. Novak M, Costantini L, Schneider S, Beanlands H. Approaches to self-management in chronic illness. Semin Dial. 2013;26(2):188–94.
66. Newman S, Steed L, Mulligan K. Self-management interventions for chronic illness. Lancet. 2004;364(9444):1523–37.
67. Franek J. Self-management support interventions for persons with chronic disease: an evidence –based analysis. Ont Health Technol Assess Ser. 2013;13(9):1–60.
68. Greaves CJ, Campbell JL. Supporting self-care in general practice. Br J Gen Pract. 2007;57(543):814–21.
69. Department of Health. The NHS plan: a plan for investment and plan for reform. London: Department of Health Publications; 2000.
70. Department of Health. Public attitudes to self-care –baseline survey. London: Department of Health Publications; 2005.
71. Blakeman T, Macdonald N, Bower P, Gately C. A qualitative study of general practitioner's attitudes to self-management of chronic disease. Br J Gen Pract. 2006;5(527):407–44.
72. Morrel DC, Wale CJ. Symptoms perceived and recorded by patients. J R Coll Gen Pract. 1976;26:398–403.
73. Jordan JE, Briggs AM, Brand CA, Osborne RH. Enhancing patient engagement in chronic disease self-management support initiatives in Australia: the need for an integrated approach. Med J Aust. 2008;189(10Suppl):S9–S13.
74. Harris ME, Williams AM, Dennis SM, Zwar NA, Powell Davies G. Chronic disease self-management: implementation with and within Australian general practice. Med J Aust. 2008;189(10 Suppl):S17–20.
75. Reed RL. Models of general practitioner services in residential aged care facilities. http://www.racgp.org.au/afp/2015/april/models-of-general-practitioer-services-in-residetial-age-care-facilites/. Accessed 6 Feb 2017.
76. O'Halloran J, Britt H, Valenti L. General practitioner consultations at residential aged-care facilities. Med J Aust. 2007;187:88–91.
77. Hambleton S. Aged care: three areas in need of support. Financ Rev 2. April 2014.
78. Australian Aged Care Quality Agency. More collaboration between GPs and RACFs. www.aacqa.gov.au. Accessed 5 Feb 2017.
79. Centers for Disease Control and Prevention, National Center for Injury prevention and Control. Web-based injury statistics query and reporting system (WISQARS). Atlanta, GA: CDC;2016 [cited 2016 Dec 21]. https://www.cdc.gov/imjury/wisgars/index.html://cdc.gov/imjury/wisgars/index.html
80. National Highway Traffic Safety Administration, Department of Transportation (US). Traffic safety facts 2014: older population. Washington(DC): NHTSA; 2016.
81. van den Berg TJ, René van Rijn LJ, Kaper-Bongers R, Vonhoff DJ, Volker-Dieben HJ, Grabner G, et al. Disability glare in the aging eye. Assessment and impact on driving. J Optom. 2009;02(03):112–8.
82. Salvi SM, Aktar S, Currie Z. Ageing changes in the elderly. Postgrad Med J. 2006;82:581–7.
83. Murman DL. The impact of age on cognition. Semin Hear. 2015;36(3):111–21.
84. Glisky EL. Chapter1: Changes in cognitive function in human aging. Riddle DR Brain aging: models, methods and mechanisms. Boca Raton :CRC Press/Taylor &Francis; 2007.
85. Seidler RD, Bernard JA, Burutolu TB, Fling BW, Gordon MT, Gwin JT, et al. Motor control and aging: links to age-related brain structural, functional and biochemical effects. Neurosci Biobehav Rev. 2010;34(5):721–33.
86. Jevas S, Yan JH. The effect of ageing on cognitive function: a preliminary quantative review. Res Q Exerc Sport. 2001;72:A-49.
87. Luchies CW, Schiffman J, Richards LG, Thompson MR, Bazuin D, De Young AJ. Effects of age step direction, reaction condition on ability to step quickly. J Gerontol A Biol Sci Med. 2002;57(4):M248–9.
88. O'Dell M, Charlton J, Koppel S. Assessing fitness to drive. Australian doctor.www.australiandoctor.com.au
89. Berry C. Older drivers and behavioural change. An ILC-UK policy brief. Nov. 2011. www.ileuk.org.uk

Geriatric Rehabilitation

12

Gary Cheuk and Nages Nagaratnam

Historical Perspective

Ignatz Leo Nascher invented the word 'geriatrics', and this was the birth of modern geriatrics [1]. In 1914, he published a book, *Geriatrics: The Diseases of Old Age and Their Treatment*, and a number of articles on geriatrics [1]. In 1935, Marjory Warren ('the mother of geriatrics') of Middlesex Hospital was the first to introduce active rehabilitation programmes [2], and Lionel Cosin an orthopaedic surgeon is credited for rehabilitating older persons after surgery for hip fracture [2]. Domiciliary (home) visits for rehabilitation of the elderly were introduced by Eric Brooke at St Helier Hospital in Carshalton [1].

General Considerations

Rehabilitation is the return of patients to their fullest physical, mental and social capacity [3]. Geriatric rehabilitation is one of the essential components of an all-embracing geriatric care [4]. Both fields of geriatric medicine and physical medicine and rehabilitation are directed towards improving functional abilities [5], preserving functional independence and improving quality of life [6]. The key to services for the aged is the diagnosis of the disease, assessment of the disability and treatment and rehabilitation to restore health and independence and keeping older persons in the community. In-patient geriatric rehabilitation has been shown to be effective [7] and to improve outcomes related to physical function, prevent nursing home admissions and improve mobility [7, 8]. There has been an increase in the need for health and long-term care in these groups which are often entangled by countless and complex clinical problems such as cognitive problems, polypharmacy, multiple comorbidities and end-of-life decisions [8] requiring different health-care needs and increasing health-care costs [9]. Hence a comprehensive geriatric assessment of the elderly's problems embracing medical, functional, psychosocial and environmental evaluation together with a treatment plan [10] is imperative.

Pathophysiology

As the elderly age, they have to contend with three major issues, namely, (i) age-related changes [11], (ii) disuse [12] and deconditioning [13] and (iii) disease and disability [14].

Age-Related Physiological Changes

Age-related physiological changes involve number of organ systems and occur by the third or fourth decade of life. They have an impact on functions of several systems [15] such as diminished hearing, vision, dexterity and flexibility. The physiological changes occur at different rates in all body systems, for example, an individual may have impaired hearing or vision, while the function of his heart and lung is fine. Furthermore biological and chronological ages are not the same.

Deconditioning and Disuse

The effect of deconditioning and disuse is brought about by curtailed activity and includes loss of strength and flexibility and metabolic and haemodynamic abnormalities [16]. Deconditioning may result from enforced immobility caused by an acute illness or hospitalization. The measures to address the hazards of prolonged immobility are shown in Box 12.1. With increasing age there is a decline in muscle mass, and the resulting loss of muscle strength is about 1–2%

G. Cheuk (✉)
Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia
e-mail: gcheuk@optusnet.com.au

N. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_12

per year [17]. Loss of muscle mass and strength [18] and quality [19] caused by ageing is known as sarcopenia. The cause of sarcopenia is unclear; there are many likely mechanisms leading to sarcopenia such as intrinsic loss of muscle contractile function, central nervous system decline, change in humoral factors such as loss of gonadal steroids and increase in the catabolic cytokines [18, 20]. Disuse causes reduction in the size of the muscle fibre, whereas ageing results in reduced number of muscle fibres [21].

Deconditioning, sarcopenia and frailty can adversely affect rehabilitation outcomes [22]. The syndrome of frailty lacks a clear definition. Patients with frailty exhibit loss of muscle strength, fatigue easily, are physically inactive and have an unsteady gait [23]. They are more prone to experience impaired cognition and depression and are said to die sooner, and frailty may be complicated by a variety of illnesses [23].

As one's age advances the muscle strength declines, and a greater portion of the muscle strength is required for a precise activity; further decline in muscle strength will result in functional impairment and inability to perform activities of daily living [19]. A brief period of inactivity such as an acute illness can accelerate this decline and cause dependence, for instance, inability to rise from a seated position if the quadriceps are implicated. The threshold for quadriceps contraction for the above mentioned is reached by the age of 80 years in women and a few years later in men [21]. Deconditioning and disuse can adversely affect balance in a number of ways. Disuse atrophy can reduce the functional reserve of muscles. Loss of strength in the muscles, for example, the dorsiflexors of the ankle, has been associated with falls in nursing home residents [21]. An elderly person with imbalance has an increasing risk of falls [24], fear of falling and decreased activity. The prevention of deconditioning in hospitals during an acute illness requires a multifaceted approach. Box 12.1 summarizes the prevention of problems while in bed due to an acute illness in the elderly.

Box 12.1 Prevention of Complications of Illness While in Bed

Exercise – to increase muscle power
Early pressure movements – to prevent venostasis, contractures and bed sores
Relieve pain – to prevent nihilism and depression
Skin care
Postural modification – sequence from bed–chair–standing–walking with two-walking with one;+ aid, walking independently
Reality orientation – emotional support to prevent confusion

Disease and Disability

The incidence and prevalence of chronic diseases increase with age, and in countries of low and middle income, only 23% are burdened with disability compared to 36% in high-income countries [14]. Several diseases virtually involving all organs co-exist in older people, and disease of one organ affects another compounding both and heralding debility and if not corrected may lead to death [25]. As age advances the elderly people have several comorbidities [14], illnesses accumulate and the total burden of medical illness and the number of organ systems affected can have a negative impact on clinical outcome. Because of the high prevalence of comorbid conditions in the older population together with the age-associated physiological changes in a variety of organ systems, there are important age-related differences in the rehabilitation for nearly every condition may have to be treated with rehabilitation [22]. Patients referred for rehabilitation centre seldom suffer from a single disease. Hence a structured routine evaluation of comorbidity ensures a complete overview of each patient [26]. An overall evaluation of the comorbidities ensures a comprehensive assessment, and quantification of physical illness burden can be used as a variable in predicting outcome [27]. There are a number of scales but they have their limitations. The Cumulative Illness Rating Scale (CIRS) is an objective measure of physical illness burden and is a comprehensive evaluation of medical problems by organ system [28]. There have been several studies [27, 29–31], and CIRS was found to be a valid measure of physical illness.

The CIRS embraces 13 items in relation to the different systems, namely, cardiovascular- respiratory, gastrointestinal, genitourinary, neuropsychiatric and general systems. Each system is rated as follows:

(a) 0, None (no impairment to that organ or system)
(b) 1, Mild impairment (normal activity)
(c) 2, Moderate impairment (interferes with normal activity)
(d) 3, Severe impairment (disabling)
(e) 4, Extremely severe impairment (life-threatening) [27]

The comorbidity index (CI) score is based on the count of the organ system with moderate to greater impairment.

Evaluation

The ability to benefit from rehabilitation is the major consideration, and the primary determinants are the severity of the presenting disability and the extent of the pre-existing

disability [32]. Age by itself should not be a factor in considering potential benefits of rehabilitation programme in the elderly. An all embracing person view is important when an elderly person is assessed for rehabilitation.

A comprehensive clinical, functional and psychosocial assessment is mandatory. The underlying medical problems are identified and overall physical fitness together with a cognitive assessment for mental clarity and memory which may manifest as anxiety, depression or lack of motivation in all patients being assessed for rehabilitation. Impairments in vision and hearing or sense of touch and a premorbid functional status should be assessed. Frail elderly should be screened for nutrition and rehabilitation potential [33]. The results of these assessments are then integrated into the identification of goals for rehabilitation and formulation of care plans. Rehabilitation providers are specially trained personnel working in a team usually in a rehabilitation centre or in a hospital, and the approach should be multidisciplinary [7, 33].

In a study of nonagenarians, the three top-ranked diagnoses at the time of hospitalization were musculoskeletal (includes hip fracture) (28%), cardiovascular (23%) and respiratory (20%) [33]. Majority of the participants in general rehabilitation programmes are elderly people with stroke and hip fracture [34]. According to the American Academy of Physical Medicine and Rehabilitation (AAPMR) [35], geriatric rehabilitation covers three areas: (i) normal ageing due to disuse and deconditioning, (ii) cardiovascular problems like vascular disease and stroke and (iii) skeletal problems including osteoporosis and osteoarthritis and conditions such as hip and knee replacements. The conditions selected for review are based on the AAPMR's statement [35].

Rehabilitation

Disuse and Deconditioning

Deconditioning and frailty are highly pertinent to geriatric rehabilitation, and exercise programmes [13] alone or in combination with other treatments such as nutritional support are being used in the treatment. For both the healthy and frail elderly including those above the age of 85, exercise programmes have been shown to be beneficial [36]. Improved lower-limb muscle strength, exercise endurance, speed of walking and overall levels of physical activity have improved with exercise [21]. With ageing there is a decrease in appetite resulting in decreased nutritional intake, weight loss and decreased physical activity which may lead to further inactivity and deconditioning. These patients should receive nutritional supplements [37].

Cardiovascular Problems

Stroke Rehabilitation

For a stroke patient, rehabilitation is in both acute and later stages. The most suitable place for stroke rehabilitation is in a rehabilitation centre or stroke unit. Several studies have demonstrated the benefits of stroke rehabilitation regardless of age and the need for additional therapy in facilitating recovery [38–41]. Elderly patients should not be denied stroke rehabilitation based solely on advanced age [42]. Many patients with stroke have several disabilities such as hemiplegia, hemianopia, dysphasia and dysphagia, as well as neuropsychological disturbances such as speech, mood and gnostic functions together with comorbidities. Severe cognitive deficits, significant neglect or apraxia, poor balance or recurrent medical complications may have a negative impact on the outcome of a rehabilitation programme. Thus the clinical evaluation should include all these areas (Box 12.2).

Our understanding of stroke and its rehabilitation has changed over the years. An earlier concept which is still perpetuated is the cortical map illustrating numerous areas of the brain as having specific and discrete functions and distinct from other areas of the brain [43]. Over the last few decades with a better understanding of the workings of the brain, a more dynamic and holistic picture has evolved [43]. Aims of therapy embrace the retraining of the affected side and strengthening the good side to take over the weak side (functional rehabilitation). Matching specific impairments to different rehabilitation techniques, improvements in arm function were seen with constraint-induced movement therapy (CIMT), electromyographic biofeedback and robotics [44]. Today studies of adult brain plasticity have shown that the negative effects of brain plasticity with ageing can, with appropriately designed behavioural training programmes, be overcome and a considerable improvement can be achieved in function and/or recovery from losses in sensation, cognition and motor control [45]. The elderly show more detailed brain activation in the motor coordination regions than younger controls when performing motor tasks as demonstrated by functional imaging studies, and this marks neuroplasticity at the system level in the ageing brain [46].

Some of the barriers to recovery include poor motivation, depression, dementia, severe motor deficits, perceptual impairment and communication problems. There are a number of comorbid conditions which can impede recovery. The management of complications both medical and neurological plays an important part in in-patient stroke rehabilitation [47]. Immediate stroke complications include spasticity, spasms and spastic dystonia [48], shoulder subluxation, shoulder-hand syndrome [49], post-stroke dystonia, post-stroke depression [50], anxiety and post-stroke fatigue and

pain [51]. Stroke-related depression is associated with poor functional outcome, and its treatment may improve cognitive function post-stroke [52].

Box 12.2 Medical Assessment and Prognosis

(i) Motor deficit (ability to lift the leg from bed, usually has a good prognosis)
(ii) Sensory deficits – vision and proprioception
  – Total loss of proprioception usually associated with poor prognosis
  – Total neglect even with return of power do badly
(iii) Mental deficits – level of consciousness, memory and cognition, emotional, lability and incontinence
(iv) Communication – dysarthria and dysphasia
(v) Postural capability
(vi) Comorbidities

Peripheral Vascular Disease

Peripheral vascular disease is often associated with diabetes mellitus, smoking and hypertension. In the case of intermittent claudication, conservative management is advocated. Patients with intermittent claudication are encouraged to walk and to stop when pain occurs and resume when the pain abates. 80% of patients with intermittent claudication remain stable, 10–12% will require intervention and approximately at 5 years 1–2% will undergo amputation [53]. The annual mortality of patients with the lowest ankle-brachial index is 25% due to critical leg ischaemia [54].

Amputation

Most lower-limb amputations are now done because of vascular insufficiency [55], and about 80% of the patients are above the age of 60 at the time of amputation. Age alone should not be a determinant for prosthetic rehabilitation [56]. The functional outcome of a lower limb amputee in the rehabilitation process will depend on several factors such as age, gender, body mass index, comorbid conditions such as diabetes mellitus and cardiovascular disease, level of amputation and the time lag between surgery and prosthetic fitting [57]. Sufficient time must be available to prepare the patient with arterial ischaemia of the lower limb for amputation if salvage is not possible. Rehabilitation must start immediately and not postoperatively. Furthermore most amputations are planned, allowing time for full medical and social assessments, improvement of general health, control of pain and counselling [58]. Comorbid diseases may affect the functional outcome following amputation. The problems associated with amputation are not only those of achieving independent mobility but also managing these diseases and those associated with advancing years [55].

With regards to prescribing prosthesis, the comorbidities rather than the age per se should be the determinants [56]. In assessing an amputee for prosthesis, the requisites are (i) the amputee's motivation to amputation; (ii) the amputated limb with regard to range of movements of the hip and knee, pain and infection of the condition of the other limb and trunk; (iii) general health and comorbidities; [56] and (iv) domestic situation and social support. Several studies of older amputees with bilateral amputations and amputation with concurrent hemiplegia have shown successful outcome following rehabilitation programmes [59, 60].

Skeletal Problems

Rehabilitation interventions are used to treat arthritic and related musculoskeletal problems. Reviews of exercise for arthritis had shown conflicting results [22]. For osteoarthritis affecting the knee, it is reasonable to believe that excercises that strenthen the muscles and tendon that provide support to the knee joint will improve its biomechanical function [22].

Clinical Relevance

Geriatric rehabilitation is one of the basic constituents of an all-embracing geriatric care [4].

As the elderly age, they have to contend with three major issues, (i) age-related changes, (ii) disuse and deconditioning and (iii) disease and disability [11–14].

Deconditioning and frailty are highly pertinent to geriatric rehabilitation, and exercise programmes [13] alone or in combination with other treatments such as nutritional support are being used in the treatment.

Age by itself should not be a factor in considering potential benefits of rehabilitation programme in the elderly.

Elderly patients should not be denied stroke rehabilitation based solely on advanced age [42].

Patients referred for rehabilitation seldom suffer from a single disease, and hence, comprehensive, clinical, functional and psychosocial assessment is mandatory.

Multiple Choice Questions

1. The following is true in relation to rehabilitation in the elderly, EXCEPT:
   A. As age advances muscle strength declines.
   B. Disuse causes reduction in the number of muscle fibres, whereas ageing results in reduction in the size of the muscle fibres.
   C. Deconditioning, sarcopenia and frailty can adversely affect rehabilitation outcomes.

D. As the elderly age, they have three major issues to contend with, age-related problems, disuse and deconditioning and disease and disability.

Short Answer Questions (SAQs)

1. List four barriers to recovery following stroke.
2. List four hazards of prolonged immobilization.

Answers to MCQs

1. B

1. SAQs

1. Poor motivation, depression, poor pre-stroke health and severe motor deficits
2. Osteoporosis, muscle wasting, dependency and bed sores

References

1. Morley JL. A brief history of geriatrics. J Gerontol A Biol Sci Med Sci. 2004;59(11):1132–52.
2. Barton A, Mulley G. History of the development of geriatric medicine in the UK. Postgrad J Med. 2003;79:229–34.
3. Hewer RL. Rehabilitation after stroke. QJM. 1990;76(279):659–74.
4. Wedgewood J. The place of rehabilitation in geriatric medicine :an overview. Int Rehabil Med. 1985;7(3):107–9.
5. Christian A. Geriatric rehabilitation an issue of clinics in geriatric medicine in clinics in geriatric medicine. Philadelphia: Elsevier-Health Science Division; 2006.
6. Weber DC, Fleming KC, Evans JM. Rehabilitation of geriatric patients. Mayo Clin Proc. 1995;70(12):1198–204.
7. Jonsson A, Gustafson Y, Schroll M, Hansen FR, Saarela M, Nygaard H, et al. Geriatric rehabilitation as an integral part of geriatric medicine in the Nordic countries. Dan Med Bull. 2003;50(4):439–45.
8. Bachmann S, Finger C, Huss A, Egger M, Stuck AE, Clough-Goff KM. Inpatient rehabilitation specifically designed for geriatric patients: systematic review and meta-analysis of randomised controlled trials. BMJ. 2010;340:c1718.
9. Callahan D. Controlling the costs of health care for the elderly: fair means or foul. N Engl J Med. 1996;335:744–6.
10. Stuck AE. Multidimensional geriatric assessment in the acute hospital and ambulatory practice. Schweiz Med Wochenschr. 1997;127(43):1781–8.
11. Boss GR, Seegmiller E. Age-related physiological changes and their clinical significance. West J Med. 1981;135(6):434–40.
12. Timiras PS. Disuse and aging:same problem, different outcomes. J Gravit Physiol. 1994;1(1):P5–7.
13. Vorhies D, Riley BE. Deconditioning. Cln Geriatr Med. 1993;9(4):745–63.
14. Sousa RM, Ferri CP, Acosta D, Albanese E, Guerra M, Huang Y, et al. Contribution of chronic diseases to disability in elderly people in countries with low and middle incomes: a 10/66 Dementia Research Group population-based survey. Lancet. 2009;374(9704):1821–30.
15. Riberio F, Oliveira J. Aging effects on joint proprioception: the role of physical activity in proprioception preservation. Eur Rev Aging Phys Act. 2007;4(2):71–6.
16. Hoenig HM, Rubenstein LZ. Hospital-associated decondirioning and dysfunction. J Am Geriatr Soc. 1991;39:220–2.
17. Novelguide.com. Deconditioning. http://www.novelguide.com/a/discover/eoa_01/eoa_01_00094.html retreived 28 December 2008.
18. Roubenouff R. Sarcopenia and its implications for the elderly. Eur J Clin Nutr. 2000;53(Suppl 3):S40–7.
19. Dutta C. Significance of sarcopenia in the elderly. J Nutr. 1997;127(5):992S–3S.
20. Roubenouff R, Hughes VA. Sarcopenia: current concepts. J Gerontol. 2000;55A:M716–24.
21. O'Keefe S. Deconditioning. Http://www.novelguide.com/a/discover/eoa_01/eoa_1_00094.html. Accessed 12/28/2008.
22. Hoenig H, Siebens HC. Geriatric rehabilitation. New Frontiers for Geriatric Research. http://www.frycomm.com/ags/rasp/chapter.asp?ch=12
23. Vanitlallie TB. Frailty in the elderly: contributions of sarcopenia and visceral protein depletion. Metab Clin Exp. 2003;52:22–6.
24. Wolfson L, Judge J, Whipple R, King M. Strength is a major factor in balance, gait and the occurrence of falls. J Gerontol A Biol Sci Med Sci. 1995;50A:64–7.
25. Solichova D, Melichar B, Blaha V, Klejua M, Vavrova J, Pallicka V, et al. Biochemical profile and survival in nonagenarians. Clin Biochem. 2001;34:563–9.
26. Di Libero F, Fargnoli M, Pittiglio S, Mascio M, Giaquinto S. Comorbidity and rehabilitation. Arch Gerontol Geriatr. 2001;32:15–22.
27. Conwell Y, Forbes NT, Cox C, Caine ED. Validation of a measure of physical illnesses burden at autopsy. The cumulative illnesses rating scale. J Am Geriatr Soc. 1993;41:38–41.
28. Fortin M, Hudon C, Dubois MF, Almirall J, Lapointe L, Soubhl M, et al. Comparative assessment –of three different indices of multimorbidity for studies on health-related quality of life. Health Qual. Life Outcome. 2005;3:74–82.
29. Miller MD, Peradis CF, Honck PR, Mazumdar S, Stack J, Rifal AH, et al. Rating chronic medical illness burden in geropsychiatric practice and research. Application of the cumulative illnesses rating scale. Psychiatry Res. 1999;41:237–41.
30. Iosifescu DV, Nierenberg AA, Alperet JE, Smith M, Bitran S, Dording C, et al. The impact of medical comorbidity on acute treatment in majordepressive disorder. Am J Psychiatry. 2003;60:2122–7.
31. Nagaratnam N, Gayagay G Jr. Validation of Cumulative Illness Rating Scale (CIRS) in hospital nonagenarians. Arch Gerontol Geriatr. 2007;44:29–36.
32. Valderrama-Gama E, Damian J, Guallar E, Rodriguez-Manas L. Previous disability as a prediction of outcome in geriatric rehabilitation unit. J Gerontol A Biol Sci Med Sci. 1998;53:M405–9.
33. Wells JL, Seabrook JA, Stolee P, Borrie MJ, Knoefel F. State of the art in geriatric rehabilitation. Part I: review of frailty and comprehensive geriatric assessment. Arch Phys Med Rehabil. 2003a;84(6):890–7.
34. Cameron ID, Kurrie SE. Rehabilitation and older people. MJA. 2002;177(7):387–91.
35. American Academy of Physical Medicine and Rehabilitation.
36. Hoenig H, Nusbaum N, Brummel-Smith K. Geriatric rehabilitation: state of the art. J Am Geriatr Soc. 1997;45(11):1371–81.
37. Wells JL, Seabrook JA, Stolee P, Borrie MJ, Knoefel F, et al. State of the art in geriatric rehabilitation. Part II. Clinical challenges. Arch Phys Med Rehabil. 2003b;84(6):898–903.
38. Friedman PJ. Stroke rehabilitation in the elderly: a new patient management system. NZ Med J. 1990;103:234–6.
39. Kalra L, Dale P, Crome P. Improving stroke rehabilitation. Br Med J. 2007;334:86–90.
40. Indredavik B, Bakke F, Solberg R, Rokseth R, Haaheim LL, Holme I. Benefit of stroke unit: a randomized controlled trial. Stroke. 1991;22:1026–31.
41. Garraway WM, Ambler AJ, Prescott RJ, Hockey L. Management of acute stroke in the elderly: preliminary results of a controlled trial. Br Med J. 1980;280:1040–3.
42. Bagg S, Pombo AO, Hopman W. Effect of age on functional outcomes after stroke rehabilitation. Stroke. 2002;33:179–85.
43. Ruskin AP. Understanding stroke and its rehabilitation. Current concepts of cerebrovascular disease-stroke. Stroke. 1982;14:438–42.
44. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. Lancet Neurol. 2009;8(8):741–54.

45. Mahncke HW, Bronstne A, Merzenich MM. Brain plasticity and functional losses in the aged: scientific bases for a novel intervention. Prog Brain Res. 2006;157:81–109.
46. Heuninckx S, Wenderoth N, Swinnen SP. Systems neuroplasticity in the aging brain: recruiting additional neural resources for successful motor performance in elderly persons. J Neurosci. 2008;28(1):91–9.
47. Dobkin B. Neuromedical complications in stroke patients transferred for rehabilitation before and after diagnostic related groups. J Neuroeng Rehabil. 1987;1:3–7.
48. Watkins CL, Leathley MJ, Gregson JM, Moore AP, Smith TL, Sharma AK. Prevalence of spasticity post-stroke. Clin Rehabil. 2002;16(5):515–22.
49. Zyluk X, Zyluk B. Shoulder hand syndrome in patients after stroke. Neurol Neurochir Pol. 1999;33(1):131–42.
50. Paolucci S. Epidemiology and treatment of post-stroke depression. Neuropsychiatr Dis Treat. 2008;4(1):145–54.
51. Staub F, Bogousslavsky J. Fatigue after stroke: a major but neglected issue. Cerebrovasc Dis. 2001;12(2):75–8145.
52. Kimura M, Robinson RG, Kosier JT. Treatment of cognitive impairment after poststroke depression: a double-blind treatment trial. Stroke. 2000;31:1482–6.
53. Trans Atlantic Inter-Society Consensus (TASC) on the management of peripheral arterial disease. Eur J Vasc Endovasc Surg. 2000;19(suppl A):S1–S224.
54. Dormandy JA, Heeck L, Vig S. The fate of patients with critical leg ischaemia. Semin Vasc Surg. 1999;12:142–7.
55. Chadwick SJD, Wolfe JHN. ABC of vascular disorders: rehabilitation of the amputee. Br Med J. 1992;304:373–6.
56. Cutson TM, Bongiorni DR. Rehabilitation of the older lower limb amputee: a brief review. J Am Geriatr Soc. 1996;44(11):1388–93.
57. Shinde A. Functional outcome in below knee amputees using prosthesis- a descriptive study. http://hdl.handle.net/123456789/1206
58. Lindsay JA. Rehabilitation of the amputee. Letter to editor. Br Med J. 1992;304:542.
59. O'Connell PG, Guntz S. Hemiplegia and amputation: rehabilitation in the dual disability. Arch Phys Med Rehabil. 1989;70:451–4.
60. Wolf E, Lelling M, Ferber I, Marcus J. Prosthetic rehabilitation of elderly bilateral amputee. Int J Rehabil Res. 1989;12:271–8.

Geriatric Palliative Care

13

Jayasingham Jayamohan, Puma Sundaresan, and Nages Nagaratnam

Historical Perspective

The word hospice comes from the Latin word 'hospitum' meaning guest house, 'hospitality'. In 1879 the Irish Sisters of Charity opened Our Lady's Hospice in Dublin for the dying, and later they founded St Joseph's hospice in London [1]. Dr. Cicely Saunders later Dame Cicely Saunders who focussed on comfort care [2] expressed her views about modern hospice care for dying patients in the late 1950s [3]. She later established the first modern hospice, the St. Christopher's Hospice in a London residential suburb [4]. It was Dr. Balfour Mount, a surgical oncologist in Montreal, Canada, who coined the term palliative care [3]. Hospice and palliative medicine were recognised as a subspeciality by the American Board of Medical Specialities and the Accreditation Council for Graduate Education in 2006 [3].

Hospice care and palliative care are similar, but the only great difference is in the care location, timing and eligibility for services [5]. To be eligible for most hospice care, the patient is considered terminal or has 6 months to live [5]. Hospice focuses attention on comfort care. Palliative care however is not limited to end-of-life care but strives to relieve suffering at all stages of disease [6] and even concurrently with restorative life-prolonging therapy [7]. Thus, where patients may be eligible for palliative care input over the many months of the disease course, typically, to be eligible for most hospice care, the patient would be need to be considered terminal with only up to 6 months of life expectancy [5].

J. Jayamohan (✉) · P. Sundaresan
Crown Princess Mary Cancer Centre, Westmead, NSW, Australia
e-mail: psun.4806@sydney.edu.au

N. Nagaratnam
Sydney Medical School, The University of Sydney,
Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

Introduction

Palliative care is an interdisciplinary medical speciality that aims on preventing and relieving suffering, to achieve the best possible quality of life for patients with serious illness and provide support for their families [7]. According to the World Health Organization [8], the goal of palliative care is to improve the quality of life of patients and their families facing a life-threatening illness through the prevention of suffering by early recognition, meticulous assessment and treatment of other problems, physical, psychosocial and spiritual. The treatments and care delivered to patients in the palliative setting must be aligned with patients' and families' preferences and values [9]. The inclusion of psychological, social and spiritual realms and the last is considered a specific domain of quality within palliative care [10].

Elderly people are particularly vulnerable and require a spectrum of services to address their various needs. Palliative care in this setting must be able to address a range of issues and embrace these multiple needs of patients who may at varying stages along a wide spectrum that spans from the independent patient with limited comorbidity to those with multiple comorbidities and frailty and to those who have a prolonged terminal phase towards death [11]. There is now general acceptance that palliative care needs of the elderly require particular consideration [12–14]. Although palliative care was focussed traditionally on care of people with cancer, in the last 10 years or more, it has been extended to include other life-limiting illnesses including dementia [15]. Geriatric palliative care in these varied disease settings will not only require focus on the previously described multiple domains of quality of life, but it will also additionally require focus on support for functional independence [16]. This often requires multi-interdisciplinary input (varies medical specialities and allied health) and collaboration in care delivery [17].

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_13

Demographic and Patient Characteristics

Worldwide the above 85 years (described as the oldest old) are the rapidly growing section of the population. The proportion of the Australian population consisting of those who are aged 85 years and older has grown exponentially from 0.5% in 1971 to 2% in 2014 [18]. This is the result of increased life expectancy across the board with women living longer than men overall. It remains unclear whether these added years of life are for health and strength or disease and disability. Certainly with advancing years, there is an increased risk of disorders involving virtually all organ systems and resulting in an increase in morbidity [19]. The prevalence of comorbidity increases with age [20, 21], and about third of the oldest old are afflicted [21]. Indeed multimorbidity is highest in the oldest old, in women and among the low socio-economic groups [22, 23]. Multiple comorbidities when combined with increasing age are often tied to functional decline across several domains. Of all individuals aged 80 or over, the subgroup with 2 or more chronic diseases were more likely to be confined to bed or chair (42%) compared to the group as a whole [24]. According to the 2012 Survey of Disability, Ageing and Carers, the severity of disability has increased with increasing age, increasing from 9% for 65–69 years to 67% in the 90+ age group [25]. Further to this, the number and type of comorbid conditions together with the decline of the immune system predispose older adults to infections [26].

Most oldest old people come by serious progressive illnesses [27] which include heart and lung disease, Parkinson's disease, dementia, stroke, neuromuscular degenerative diseases and many cancers [28]. Comorbid psychiatric disorders are also frequent [24]. Several diseases virtually involving all organs coexist in older people, and disease of one organ affects another compounding both and heralding debility [19]. With the increase in the aging population, there has been a rapid increase in these comorbid conditions. As a result, the spectrum groups requiring palliative care for incurable cases have also broadened [29]. Different diseases have different trajectories [27], and the three distinct group illness trajectories have been described (i) a steady progression of disease and decline of wellbeing with a certain terminal phase (e.g. malignancy); (ii) a gradual decline in wellbeing interrupted by acute exacerbations (e.g. respiratory diseases and heart failure) and (iii) (e.g. dementia with associated frailty), frail old people with dementia [30, 31]. Distinguishing between expected trajectories is helpful to direct strategies and more appropriate programs of care prior to death [31].

Common Diseases at End of Life

Advanced Heart Failure

Advanced heart failure is when the standard heart therapies and symptom management strategies are ineffective. Both incidence and prevalence of heart failure increase steeply with age. It is a progressive disorder. In spite of novel therapies for heart failure, the outcome has not changed [32]. This has been attributed to the combined effects of comorbidity and frailty [32]. A significant number of them will progress to advanced heart failure, and many of them are not suitable for cardiac transplantation or mechanical circulatory support [33]. The prevalence of frailty among those with heart failure ranges between 15 and 74% [34, 35] depending on the population studied. Frailty contributes to the high set rates of hospitalization, visits to the emergency departments and mortality and falls in patients with heart failure [34, 35].

Advanced Dementia

Those with advanced Alzheimer's disease require assistance with personal care, as they experience a decline in their physical abilities and become chair- or bed-bound as well as losing their ability to communicate. Three in ten people over the age of 85 and one in ten over 65 have dementia [36]. About half the nursing home residents suffer from dementia, and it is projected that the number of people who will develop dementia will increase from 220,000 currently to 730,000 in 2050 [37]. In a study of 323 nursing home residents with dementia, the 6-month mortality in those who had pneumonia was 46.7%, in those who experience febrile episode 44.5% and those with an eating problem 38.6% [38]. Distressing symptoms and burdensome interventions were common among these patients in the final 3 months of their life with 41% of them undergoing at least one intensive intervention [38]. Only about one-third of those who died during the follow-up period in this study had been referred to palliative and hospice care [38].

Advanced Cancer

Symptom control and improvements of quality of life can be achieved in the setting of incurable malignancies through facilitation of early access to palliative care. Some results have shown that this can also extend survival [39]. Most oncologists recognize the value of palliative care of their

patients with advanced cancer [40], and most are content with end-of-life care provided to their patients [41]. This is reflected in the increased utilisation of primary palliative care and greater number of referrals made to specialist palliative care services [41]. There may be a role for ongoing active cancer treatments for the management of symptoms, prevention of symptom progression and improvement of quality of life. This may include short courses of palliative radiotherapy to manage distressing symptoms such as malignant bone pain, bleeding, impending airway obstruction, compression of neurological structures (spinal cord, nerve roots, cauda equina) or extrinsic compression of major vessels such as the superior vena cava. Even in the setting where active anticancer therapies are being used, a comprehensive approach to managing the patient through involvement of the palliative care service is important in order to address the multitude of other symptoms that may be commonly associated with cancers and which can be distressing. Indeed [42] have shown that patients who had the addition of palliative care early in their disease course had improvements in the quality and quantity of life even though these patients may have had less aggressive care.

Advanced Chronic Obstructive Pulmonary Disease

Several studies have focussed attention on the importance of palliative care in the management of advanced COPD [43, 44]. Patients with advanced stage COPD are likely to have several acute exacerbations which are associated with severe physical disability, poor quality of life, depression, anxiety and isolation [45].

Symptom Burden, Assessment and Management

Patients with advanced stage of illness experience multiple symptoms. Symptoms in the end stage of life vary according to the advanced stage illnesses, but there are some common symptoms experienced in the end of life. In the end-stage heart failure, those in the last 6 months of life experienced breathlessness (86%), pain (75%) and 89% fatigue [46]. The major symptoms in chronic obstructive pulmonary disease are dyspnoea, cough, fatigue, depression and emotional and psychosocial problems [47]. In advanced-stage non-small cell lung cancer, dyspnoea, cough, fatigue, anorexia and pain are the most common symptoms [48]. Psychiatric disorders are more prevalent in cancer patients than in the general population [49, 50]. Depression is often a significant symptom in about a quarter of the patients admitted to a palliative care unit [51]. It is requisite that palliative care in this patient group requires proper recognition of all their symptoms, and the Comprehensive Geriatric Assessment (CGA) would be decidedly useful. CGA was introduced with the belief that a team of health professionals could identify treatable health problems and functional impairment [24]. It should also include the geriatric syndromes such as delirium, incontinence and osteoporosis which represent an endorsement of frailty [52].

Symptom management and advance care planning are high priority for these patients. Management decisions must take into consideration the patient's prognosis in terms of life expectancy, functional reserves, social supports, spiritual beliefs and needs, as well as their personal and family preferences [53]. Several studies reporting general symptoms of nursing home residents at end of life have predominantly focussed on management of pain [54–56]. While there may be variations in the spectrum and magnitude of symptom burden, the most common symptom control need is in the eradication of pain [57]. Opiate analgesia is important for moderate and severe pain for patients with cancer but is unfortunately often under-prescribed [58]. In considering pain it is important to distinguish between background pain (from various causes including visceral, bone and neuropathic pain) and incident pain which is pain related to movement. The latter can be poorly addressed in elderly and palliative care patients [59]. Although end-of-life patients are generally bed-bound, pre-emptive use of as-required medications before they attempt active and passive movements known to bring on pain is important and can offer them meaningful benefit [59]. Although the use of opioids for chronic non-cancer pain is debatable, the American Geriatrics Society however supports its use for older adults who continue to have moderate or severe pain in spite of non-opioid therapy [58].

Ethical Issues and Legal Aspects in Palliative Care

Clinicians often encounter an array of ethical issues relating to palliative care and end-of-life care. These include ethically intricate treatment-related decisions where patients' wishes regarding treatments and their perceptions on impact to their quality of life may not be congruent with the clinicians' perceptions of the benefits of treatments and their side effects, the

difficulties in day-to-day patient management in palliative care such as concern about use of opiate analgesia to relieve pain and stress while recognising the possible respiratory depression that will likely ensue and the value of parenteral nutritional support in those who decline nutritional intake and are nearing end of life [60]. While it is commonly feared that the institution of symptom control measures may hasten the process of death, specialists in palliative care believe that even in patients who may wish for a quick death in order to be relieved of their suffering, access to meticulous assessment, good symptom control and supportive care can often result in improved quality of life to a point that their patient's desire to die may be expelled. Many physicians receive requests from patients asking them to help them end their suffering by means of death. Physician-assisted death (PAD), where legally available, is where physician provides the terminally ill patient an option to end their life, when and where they choose to do so. Even where legally allowable, there are multiple protective measures in place to govern the practice of PAD which should only be considered as a last resort when such treatment has failed [61]. Legalisation of physician-assisted death or euthanasia remains a highly debatable issue.

Clinical Relevance

Hospice care and palliative care are similar, but the only great difference is in the care location, timing and eligibility for services

Palliative care must be able to provide a wide range of services and embrace the needs of patients from independent to those with multiple comorbidities, frailty and drawn-out dying.

It is requisite that palliative care in this patient group requires proper recognition of all their symptoms, and the Comprehensive Geriatric Assessment (CGA) would be decidedly useful.

Symptom management and advance care planning are a high priority for these patients.

The treatment should consider their individual life expectancy, functional reserves, social support and preferences.

Multiple Choice Questions

1. An 88-year-old previously fit man presents with a 1-month history of dysphagia and odynophagia with solids. Endoscopic examination reveals a 4 cm circumferential lesion involving the mid-oesophagus and causing narrowing/obstruction. Biopsy of this lesion confirms squamous cell carcinoma. Staging investigations demonstrate two liver lesions suggestive of metastases. Which of the following interventions are appropriate to consider in this clinical scenario?
   A. Insertion of a stent to relief the obstruction
   B. Referral to dietician
   C. Symptomatic management of pain
   D. Short course of palliative radiotherapy
   E. All of the above
2. The following are true of palliative and hospice care, EXCEPT:
   A. Hospice focuses attention on comfort care.
   B. Palliative care is not limited to end-of-life care but strives to relieve suffering at all stages of disease.
   C. To be eligible for most hospice care, the patient is considered terminal or has 1 year to live.
   D. In the last 10 years or more, palliative care has been extended to include other life-limiting illnesses including dementia.
3. The following are true of patients receiving palliative care, EXCEPT:
   A. There is now general acceptance that palliative care needs of the elderly require particular consideration.
   B. Symptom control and quality of life can be improved by early access to palliative care.
   C. Symptom management and advance care planning are a high priority for these patients.
   D. Distinguishing between expected trajectories is not helpful to direct strategies.
4. The following are true of palliative sedation, EXCEPT:
   A. Palliative sedation is the use of medications when other treatments have failed.
   B. Palliative sedation remains a contentious issue.
   C. It is usually given for refractory pain, agitated delirium, dyspnoea and psychological distress.
   D. Palliative sedation is not aimed at bringing about a state of decreased awareness or absent awareness.

Answers to MCQs

1. E
2. C
3. D
4. D

References

1. Millennium.culmination/The-Revolutin-of-Hospice.pdf. Accessed 23 Dec 2016.
2. Amelia EJ. Geriatrics and palliative care: collaboration for quality of life until death. J Hosp Palliat Nurs. 2003;5(1): http://www.medscape.com/viewarticle/449130
3. Loscalzo MJ. Palliative care: An historical perspective. ASH education program book. https://doi.org/10.1182/asheducation-2008.1.465. Accessed 23 Dec 2016.

4. National Hospice and Palliative Care Organisation. History of hospice care. http://www.nhpco.org/history-hospice-care. Accessed 23 Dec 2016.
5. Hospice vs Palliative Care. http://www.caregiverslibrary.org/caregivers-resources/grp-end-of-life-issues/hsgrp-hopice/hospice-vs-palliative-care-article.aspx. Accessed 23 Dec 2016.
6. Bruera E, Dev R. Overiew of managing common non-pain symptoms in palliative care. UPToDate. http:www.uptodate.com/contents/overview-of-managing-common-non-pain-symptoms-in-palliative-care?source=se_link. Accessed 23 Dec 2016.
7. Bailey FA, Harman SM. Palliative care: the last hours and days of life. www.update.com/contents/14241. Accessed 16 Nov 2017.
8. World Health Organisation. WHO definition of palliative care. http://www.who.int/cancer/palliative/definition/en/. Accessed 23 Dec 2016.
9. National Consensus Project for Quality Palliative Care. Clinical practice guidelines for quality palliative care. Pittsburgh. 2009.
10. Balboni MJ, Balboni TA. Influence of spirituality and religiousness on outcomes in palliative care patient. UpToDate. http://www.uptodate.com/contents/influence-of-spirituality-and-religiousness-on-outcomes-in-palliative-care-patients?source=see_link
11. Kite S. Palliative care for older people. Age Aging. 2006;35(5):459–60.
12. Age Concern. Policy position paper: dying and death. London: Policy Unit, Age Concern England; 2005.
13. Help the Aged. Dying in older age. Reflections and experiences from an older person's perspective. Tom Owen ed. 2005. www.helptheaged.org.uk
14. The National Council for Palliative Care. The palliative care needs of older people. Briefing Bulletin. No.14. www.ncpc.org.uk (January 2005).
15. Murphy E, Frogatt K, Connolly S, O'Shea E, Sampson EL, Casey D, et al. Palliative care interventions in advanced dementia. Cochrane Database Syst Rev. 2016;12:CD011513. https://doi.org/10.1002/14651858.CD011513.pub2.
16. Morrison RS, Meier DE. Clinical practice: palliative care. NEJM. 2004;350(25):2582–90.
17. Gatto M, Zwicker De A. Palliative care. http://consultgeriin.org/topics/palliatiecare/want_to_know_more. Accessed 24 Dec 2016.
18. Australian Institute of Family Studies. Australia's older population: demography and health statistics. https://aifs.gov.au/publications/eldr-abuse/4-australias-oldrr-population-demography-and-health-statistics. Accessed 7 Jan 2017.
19. Solichova D, Melichar B, Blaha V, Klejna M, Vavrova J, Palicka V, et al. Biochemical profile and survival in nonagenarians. Clin Biochem. 2001;34:563–9.
20. Guralnik JM. Assessing the impact of comorbidity in the older population. Ann Epidemiol. 1996;6:376–80.
21. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures and complications of multiple chronic conditions in the elderly. Arch Intern Med. 2002;162:2269–76.
22. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Aging Res Rev. 2011;10(4):430–9.
23. Sousa RM, Clensa CP, Acosta D, Albanese E, Guerrn M, Huang Y, et al. Contribution of chronic diseases to disability in elderly people in countries with low and middle incomes: A 10/66 Dementia Research Group Population-Based Survey. Lancet. 2009;374(97794):1821–30.
24. Blazer DG. Psychiatry and the oldest old. https://doi.org/10.1176/1ppi.ajp.157.12.1915. Accessed 14 Feb 2017.
25. Australian Bureau of Statistics. Disability, aging and carers, Australia. Summary of Findings. 2012. www.abs.gov.au/ausstats/abs@nsf/Lookup/4430.0.ExplanatoryNotes.50002012
26. Kaye KS. Co-morbidities metabolic changes make elderly more susceptible to infection. Infectious disease news. Http://Www.Healio.Com/Infectious-Disease/News/Print/Infectious-Disease-News/%7bao…Ceb%7D/Comorbidities-Metabolic-Changes-Make-Elderly-More-Susceptible-To-Infection. Accessed 7 Jan 2017.
27. Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. BMJ. 2005;330(7498):1007–11.
28. Morrison RS. Research priorities in geriatric palliative care: an introduction to a new series. J Palliat Med. 2013;16(7):726–9.
29. AIHW-Palliative Care. http://www.aihw.gov.au.palliative-care
30. Murtagh FE, Preston M, Higginson I. Patterns of dying: palliative care for non-malignant disease. Clin Med (Lond). 2004;4(1):39–44.
31. Lunney JR, Lynn J, Foley DJ, Lipson S, Guralnik JM. Patterns of functional decline at end of life. JAMA. 2003;289(18):2387–92.
32. Murad K, Kitzman DW. Frailty and multiple comorbidities in the elderly patient with heart failure: implications for management. Heart Fail Rev. 2012;17(90):581–8.
33. Stokes MB, Bergin P, McGriffin D. Role of long-term mechanical circulatory support in patients with advanced heart failure. Intern Med J. 2016;46:530. https://doi.org/10.1111/imj.12817.
34. Uchmanowicz I, Loboz-Rudnicka M, Szelag P, Jankowska-Polariska B, Loboz-Grudzien K. Frailty in heart failure. Curr Heart Fail Rep. 2014;11:268–7.
35. Jha SR, Ha HS, Hickman LD, Hannu M, Davidson PM, Macdonald PS, et al. Frailty in advanced heart failure: a systematic review. Heart Fail Rev. 2015;20(5):553–60.
36. AIHW. www.aihw.gov.au/dementia/
37. Health Times. The future of aged care nursing in Australia. http://healthtimes.com.au/hub/aged-care/2/news/no1/the-future-of-aged-care-nursing-in-australia/495. Accessed 8 Dec 2016.
38. Mitchell SL, Teno JM, Kiely DK, Shaffer ML, Jones RW, Prigerson HG, et al. The clinical course of advanced dementia. NEJM. 2009;361:1529–38.
39. Bruera E, Yennurajalingam S. Palliative care in advanced cancer patients: how and when? Oncologist. 2012;17(2):267–73.
40. Cherry NI, Catane R. European Society of Medical Oncology Taskforce on Palliative and Supportive Care. Attitudes of medical oncologists toward palliative care for patients with advanced and incurable cancer: report on a survey by the European Society of Medical Oncology Taskforce on Palliative and Supportive Care. Cancer. 2003;98(11):2502–10.
41. Hui D, Cerana MR, Park M, Hess K, Bruera E. Impact of oncologists' attitudes toward end-of-life care on patients access to palliative care. Oncologist. 2016;21(9):1149–55.
42. Temet JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small cell lung cancer. NEJM. 2010;363:733–42.
43. O'Donnell D, Aaron S, Bourbeau J, Hernande P, Marciniuk D, Balter M. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease. Can Respir J. 2003;10(SupplA):11A–65A.
44. Lanken P, Terry P, Delisser HM, Fahy B, Hansen-Flaschen J, Heffner JE. An official American Thoracic Society clinical policy statement: palliative care for patients with respiratory diseases and critical illnesses. Am J Respir Crit Care Med. 2008;177:912–27.
45. Yohannes AM. Palliative care provision for patients with obstructive pulmonary disease. Health Qual Life Outcomes. 2007;5:17.
46. Nordgren L, Sorensen S. Symptoms experienced in the last 6 months of life in patients with end stage heart failure. Eur J Cardiovasc Nurs. 2003;2:213–7.
47. Modlinska A, Buss T, Lichodziejewska-Niemierko M. Palliative care in chronic pulmonary disease. Pneumonol Alergol Pol. 2007;75(4):383–8.
48. Tremet JS, Pirl WF, Lynch TJ. Comprehensive symptom management in patients with advanced-stage non-small-cell lung cancer. Clin Lung Cancer. 2006;7(4):241–9.
49. Block S. Assessing and managing depression in the terminally ill patient. Ann Inter Med. 2000;132:209–18.

50. Brietbart W, Bruera E, Chechinov H, Lynch M. M+Neuropsychiatric syndromes and psychological symptoms in patients with advanced cancer. J Pain Symptom Manage. 1995;10:131–41.
51. Barraclough J. Cancer and emotion. Abingdon: Radcliffe Medical; 1994.
52. Balducci L, Beghe C. The application of the principles of geriatrics to the management of the older person with cancer. Crit Rev Oncol Haematol. 2000;35(3):147–54.
53. Terret C, Albrand G, Jeanton M, Courpron P, Droz JP. What's new in geriatric oncology? Bull Cancer. 2006;93(1):119–23.
54. Teno J, Bird C, Mor V. The prevalence treatment of pain in US nursing homes. Providence: The Center for Gerontology and Health Care Research, Brown University; 2002.
55. Bernabei R, Gambassi G, Lapane K, Landi F, Gatsonis C, Dunlop P, et al. Management of pain in elderly patients with cancer. SAGE Study Group. Systematic assessment of geriatric drug use via epidemiology. JAMA. 1998;279:1877–82.
56. Won AB, Lapane KL, Vallow S, Schein J, Morris JN, Lipsitz LA. Persistent non-malignant pain and analgesic prescribing patterns in elderly nursing home residents. J Am Geriatr Soc. 2004;52:867–974.
57. Wijk H, Grimby A. Needs of elderly patients in palliative care. Am J Hosp Palliat Care. 2008;25:106.
58. O'Neill LB, Morrison RS. Palliative care: issues specific to geriatric patients. http://www.uptodate.com/contents/palliative-care-issues-spcific-to-geriatric-patienrs. Accessed 22 Dec 2016.
59. Tai V, Lovell MR. Pain relief and the end of life. Med Today. 2013;14(4):16–24.
60. Kinzbrunner BM. Ethical dilemmas in hospice and palliative care. Support Care Cancer. 1995;3(1):28–36.
61. Quill TE, Sussman B. Physician assisted death. From Bioethics Briefings. http://www.thehastingscenter.org/briefingbook/physician-assisted-death/ Accessed 20 Feb 2017.

The Elderly in Intensive Care

14

Graham Reece and Latesh Poojara

Historical Perspective

The concept of intensive care arose from the devastating Copenhagen polio epidemic of 1952 [1], which resulted in hundreds of victims experiencing respiratory and bulbar failure. Over 300 patients required artificial ventilation for several weeks. By 1953, Bjorn Ibsen, the anaesthetist who had suggested that positive pressure ventilation should be the treatment of choice during the epidemic (replacing the "negative pressure tank ventilators" favoured over the preceding 20 years) had set up the first intensive care unit (ICU) in Europe, gathering together physicians and physiologists to manage sick patients. Many would consider him to be the "father" of modern intensive care. He presented his concept of intensive care in 1957 in a professional meeting in Geneva and then noted rapid dissemination to Canada, France and New Zealand. The Australian experience began with the management of tetanus between 1956 and 1959.

By 1960, numerous publications existed, reporting common themes around specialised units providing invasive, mechanical ventilatory support. The assisted respiratory unit was proposed in 1962 in Vienna under the auspices of the First European Congress of Anaesthesiology. Matt Spence from Auckland and Victor Hercus set the scenes for intensive care in Australia from 1959 to 1961, with pioneering clinical work also occurring in Adelaide, Melbourne and Sydney. Between 1963 and 1972, there were early prototypes developing of intensive care units – some models with accompanying coronary care units, recovery units and outreach intensive care (e.g. medical retrieval services).

G. Reece (✉) · L. Poojara
Intensive Care Unit, Blacktown Mount Druitt Hospitals, Mount Druitt, NSW, Australia
e-mail: Graham.Reece@health.nsw.gov.au

General Considerations

Age-Related Changes

Ageing is the process which is complex, multifactorial, less understood and poorly defined. It is made more complicated by different life expectancies in different parts of the world. Ageing is associated with progressive physiological [2] changes with loss of functional reserve in all organ systems with considerable variation from person to person. The more important structural and functional age-related changes in the major organ systems are shown in Table 14.1.

Intensive Care: Age Demographics

In Australia and New Zealand [3], a review of 120,000 admissions in the ANZICS Adult Patient Database covering 57 ICUs demonstrated that the admission rates for those aged >80 increased by 5.6% per year over the study period from 2001 to 2005. In 2001, this group comprised 11% of admissions, rising to 14% by 2005. By 2020, roughly one in four admissions is predicted to be over the age of 80. Worldwide population predictions, however, demonstrate that the population over the age of 80 will more than double in most regions around the world from 2020 to 2050 [4], significantly intensifying this growing demand for ICU services. By 2040, the oldest old are projected to account for one in four older patients in Europe, North America and Oceania [5] (Fig. 14.1).

Sim [6] retrospectively viewed 16,935 admissions over the decade from January 2003 to a single adult South Korean tertiary 46-bed general ICU. The spectrum of ages of ICU admissions demonstrated the highest admission rate in the seventh decade, 11% of patients aged >80 and only 1% of admissions, in South Korea, aged >90.

Mechanical ventilation has become one of the foremost options for ICU admissions in the elderly [7–10], and this approach is increasing in the ICUs. Tripp [11], reviewing all

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_14

Table 14.1 Structural and functional changes with ageing

Cardiovascular
Ventricular wall stiffening, myocardial dysfunction and increased filling pressures
Increased arteriosclerosis
LVH, decreased conduction fibre density and sinus node cells, conduction disturbances
Vascular wall changes, increased capillary permeability
Changes to autonomic system and decreased response to B-blocker
Less responsive to sympathetic stimulation
Respiratory
Respiratory centre blunted, decreased O2 consumption, decreased CO2 production
Decreased elastic recoil and chest wall stiffness and decreased surfactant production
Decreased total compliance – slower expiratory flow rates
Decreased FVC and FEV1
Increasing A – a gradient with age
Decreased protective reflexes
Central nervous system
Neuronal mass and brain size decreases
Decrease in noradrenalin and dopamine synthesis
Decreased sympathetic and parasympathetic responsiveness
Loss of visual and auditory abilities
Memory impairment
Renal
Decreased renal mass and glomeruli – reduced GFR
Decreased clearance of drugs
Decreased tubular function and hormonal responsiveness leading to hypovolemia, overload and electrolyte disturbances
Decreased creatinine clearance and normal creatinine due to decreased production

admissions to intensive care units in New Zealand who required invasive mechanical ventilation (IMV) for the 11-year period from 1999 to 2010, using a national, linked administrative database, demonstrated some interesting trends in the nature of therapy delivered by NZ ICUs. 58,000 patients received IMV during the selected period. The study demonstrated that patients over 80 were half as ilkely, per head of the general population (28 versus 50.6/10,000 population), compared to those aged 65–79, to receive IMV. Interestingly, this New Zealand group was also able to demonstrate, despite an increased raw number of octagenarians, when compared to the general population, a reduced percentage (−1.1% per year, over the 11 year period) receiving this particular modality of ICU treatment .

Disease Profile

In a study of 372 patients 90 years and over, 248 were admitted to the ICU as an emergency admission of which half underwent unscheduled surgery, 33.3% had elective surgery, 28% had trauma, 12.5% had cardiac disease and 10.5% gastrointestinal disease were the most frequent admissions [12].

Sjoding [13] used the US Medicare beneficiaries dataset from 1996 to 2010 to track trends in the reason for admission of 27.8 million admissions to ICU. Those aged over 85 comprised 15% of the annual cohort in 1996 and 22% in 2010. The trends demonstrate that sepsis and respiratory failure are becoming more prominent. Becker et al. [12] found that 70% of the patients over the age of 90 years were discharged alive

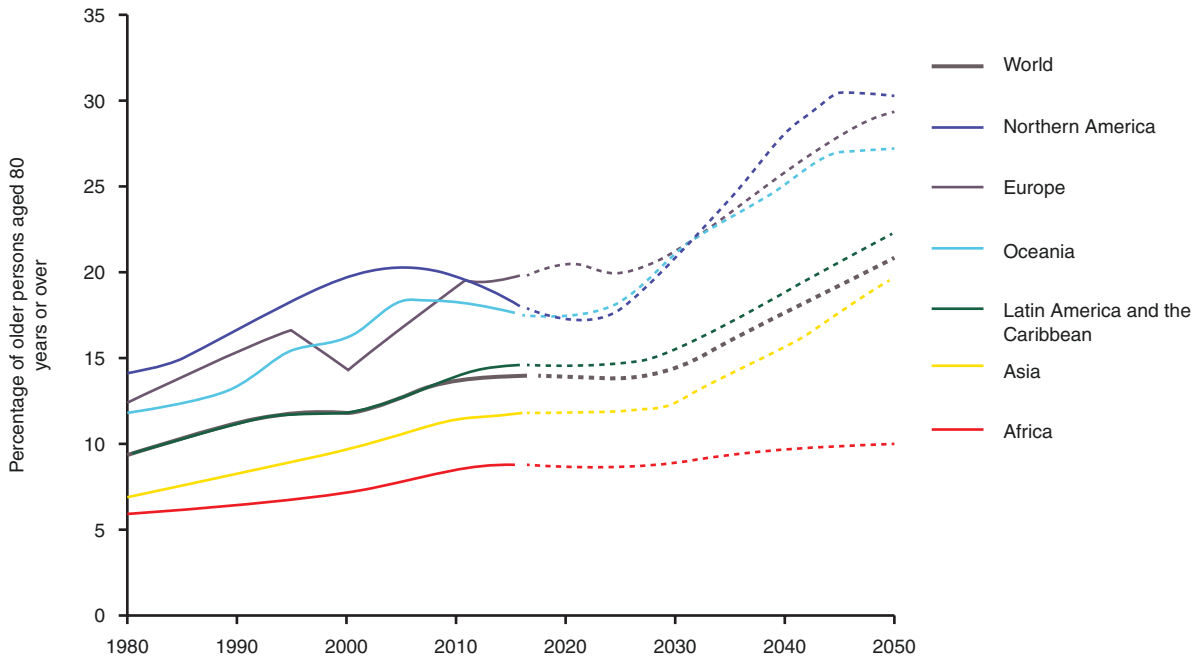

Fig. 14.1 United Nations (2015). World Population Prospects: The 2015 Revision. Percentage of oldest old (aged 80 years or over) amongst the older population (aged 60 years or over) by region, 1980–2050. Department of Economic and Social Affairs Population Division World Population Ageing, 2015, United Nations, New York [5]. (Reprinted with the permission of the United Nations)

after treatment at the ICU and more than one-third were alive 1 year after discharge.

Urgent referrals over the age of 80 to Canberra Hospital tertiary referral (Australia) ICU over a 3.3 year interval from 2011 compromised 443 from a total of 8415 patients – or 6.9% of its admissions. This group had 32% mortality by hospital discharge and 46% 1-year mortality. However, of 583 considered too well for ICU admission, their mortality rate at 12 months was 41%. Adverse prognostic factors at 12 months were cancer, metastatic cancer, heart failure and dialysis dependence, with chemotherapy and radiotherapy being predicative of hospital mortality. Dementia was associated with increased hospital survival, possibly reflecting selection of patients otherwise in good health, as was chronic obstructive airways limitation, again indicative perhaps of a lower acceptance threshold [14].

Rellos [15] reviewed the in-hospital mortality within 30 days of admission for patients over the age of 90, admitted over 4 years to a 30-bed general tertiary ICU in Greece. One percent of the 5505 admissions were aged >90. Sixty percent in this single-centre study received mechanical ventilation, and 30% were for elective surgery – with a mean ICU length of stay of 5 days, an ICU mortality of 20% and an in-hospital mortality of 40% (compared to 9% in the younger cohort). Eighty percent of the 36 survivors were able to be discharged home. Multivariate analysis within this group revealed APACHE 2 was the only prognostic factor.

A South Korean [6] study over a 10-year period demonstrated a 15% ICU overall mortality rate for those aged <90 and a 32% mortality rate for the 1% aged >90 years. Becker [12] reviewed the outcomes of 372 patients aged >90 admitted to a single 132-bed tertiary referral intensive care in Hamburg, Germany, from 2008 to 2013. ICU mortality was 18.3%, hospital mortality 30.9%, and 1-year mortality 63% for the cohort overall and 52% for planned surgical admissions. The group concluded that "1-year survival prognosis of very old ICU patients is not as poor as often perceived and that age per se should not be an exclusion criterion for ICU admission".

Bagshaw [3] reported the outcomes of 15, 640 patients aged >80 from 57 self-selected intensive care units – predominantly tertiary and metropolitan – across Australia and New Zealand, from the binational ICU database, for 6 years from 2000 to 2005. For the subgroup aged in excess of 90 years, the overall ICU mortality was 12%, with a 27% hospital mortality rate.

Heyland [16] reported a multicentre prospective cohort study of all admissions over the age of 80, admitted to ICUs of 24 Canadian hospitals from 2009 to 2013. A total of 1671 aged patients were studied, a mean age of 85.76% were mechanically ventilated and 85% received mechanical ventilation, vasopressors or dialysis. Twenty-two percent died in ICU, 35% died during the hospitalisation, and 46% were discharged home. Of those who died, 50% were still receiving mechanical ventilation, dialysis or inotropes. The 14% however admitted for elective surgery demonstrated an OR for survival against medical or emergency surgical admissions of 4.37 (95% CI 2.24–8.54, $P < 0.0001$).

Reason for ICU Admission

Type of Admission: Acute Medical Versus Acute Surgical Versus Elective Surgical

Andersen [17] published a follow-up of 12 years of ICU survivors over the age of 80, from Norwegian ICUs. His group demonstrated that patients admitted for planned surgery had a significantly superior survival rate than those admitted for emergency surgical or medical reasons. Interestingly, by 3 years, however, the rate of death had become the same, regardless of whether the ICU admission was for emergency surgery, elective surgery or medical diseases. Tripp [11] confirmed in patients requiring IMV. When analysing 11-year cumulative data from all New Zealand ICUs, highest mortality rates were noted in patients admitted for acute medical than acute surgical or elective surgical admissions, respectively. Mortality rates in the ICU at 1 year and at 2 years were respectively close to double in each of these categories for those aged 80. The fact that not all ICU patients receive IMV comparisons between groups remain relevant.

High-Risk Surgery with Prolonged Mechanical Ventilation

Nabozny [18] 2016 examined the outcome following prolonged (>96 h) post-operative mechanical ventilation, using the US Medicaid claims database, between 2005 and 2009. A 5% random sampling of beneficiaries over the age of 66 who underwent 1 of 227 predefined "high-risk" surgeries was analysed. 117, 000 patients underwent these surgeries, with 4% requiring long-term ventilation. The 1-year mortality rate was 64% in this group, compared to the control cohort's 17% mortality (see Fig. 14.1 below). Of the long-term ventilation group who survived 30 days, the 1-year mortality was 47%. Considering the 30-day survivors who did not receive prolonged ventilation, 71% returned home – compared with 10% returning home who did receive prolonged ventilation. Requirement of a tracheostomy, haemodialysis and increasing age from 66 years and comorbidities were all adversely related to prognosis at 12 months. In this particular cohort, severe sepsis very closely approached statistical significance.

Acute Medical Diagnosis

Sepsis

The interaction between septic shock, age and outcome has been studied in a single-centre tertiary ICU in India [19]. Although the mortality rate from sepsis is reducing in most ICUs, its incidence is rising. In a review of 132 patients, the mortality rate for severe sepsis or septic shock increased from 45% in those less than 60–60% in those aged 60–80 to 79% in those above 80 years of age.

Cardiogenic

Aissaoui [20] reviewed outcomes of cardiogenic shock (CS) post-acute myocardial infarction, over a 15-year period in 10,610 French patients. 3,389 patients were aged ≥75 years (the FAST-MI programme). The incidence of CS decreased from 11.6% in 1995 to 6.7% in 2010, $P = 0.02$. Challenging the classical position regarding poor 12-month survivals, however, from 1995 to 2010, mortality decreased from 87% to 59% in CS patients and from 30% to 17% in patients without CS ($P < 0.001$). Hence, although 1-year mortality remained considerable, it decreased by 32% in this period.

Similarly, Bangalore [21] compared the outcomes in cardiogenic shock in a nationwide inpatient sample from 2002 to 2011. 11,004 patients aged >75 were included in this study. The "in-hospital" mortality rate for these elderly reduced from 63% to 44%, with invasive interventions such as cardiac catheterisation, percutaneous coronary intervention or coronary artery bypass graft surgery.

Personal Traits

In a single-centre study of retired Chinese ex-military personnel, Zeng [22] reported the use of a locally derived frailty index (FI) to examine 30- and 90-day post-ICU mortality rates. Fifty-two variables such as acute medical conditions, chronic diseases, symptoms, signs, premorbid function for 1 month prior to admission (from an informant), psychological health, lifestyle attitude and laboratory measures were selected. Each variable needed to be present in between 1 and 80% of the general population, be related to health and adverse outcomes, increase in prevalence with ageing and have <5% missing data. 92% of the subjects were married males, 99% living with their families, with a mean age of 82. FIs ranged from 0 (no deficit) to 1.0 (all deficits), with only <1% actually scoring an FI >0.7. The least frail – the 40% with a FI <0.22 – all survive to 30 days. The most frail, with FI >0.46, had no survivors at 66 days. Even though APACHE 4 was the next best predictive tool, APACHE 4 was not able to discriminate 5 of the 15 with an FI >0.46, who did not survive 6 days. Each 1% increase in FI was associated with an increased relative risk of death at 30 days. FI is compared favourably to Karnofsky Scale, APACHE 2, APACHE 4, GCS and Palliative Performance Scale, in this select population.

ICU Resuscitative Interventions Required

Biston [23] reported the results from 8 Belgium intensive care units of 1679 patients requiring vasopressor agents to treat shock. A 28-day mortality rose according to centile from 25% to 80%, for ages <25 to >90. Mortality differences were distinct for those aged 70–75, 75–85 and >85 by 28 days. By 12 months, 3% of those aged >85 were alive, compared with 16% between the ages of 75 and 85 and 34%, of those aged 70–75.

Chronic Comorbidities

A retrospective cohort study [24] of every ICU admission for the state of Ontario, Canada, from 2002 to 2012 using an administrative linked dataset noted that amongst 500,124 ICU patients, 46% required attendance at the emergency department within 6 months of discharge, and 25% were rehospitalised. Being an administrative database, measures of frailty and muscle strength were not available, although comorbidities were documented and matched. Mortality against non-ICU controls over 10 years was reported. On multivariate analysis, age was an independent and strong predictor of mortality. Hazard ratios are important but less strong predictors such as COPD, congestive cardiac failure, pneumonia/other infections, cancer and percutaneous tracheostomy.

Long-Term Recovery

Andersen [17] retrospectively analysed long-term ICU survivors from a university hospital in Norway, aged over 80 years, from the years 2000 to 2012. Follow-up ranged from 1 to 13 years, with a mean of 3.3 years. Of these 395 patients, 75% survived hospital and 42% survived the first year. Very interestingly, after surviving the first year, the rate of dying was the same as the rate amongst nonhospitalised octogenarians; mean survival, after reaching this 1-year mark, was 5.1 years.

Rate of Recovery

Physical Recovery

The rate of physical recovery of 80-year-old Canadian residents, who had spent over 24 h in intensive care, was separately reported by Heyland [25]. 610 patients from 22 ICUs were thus prospectively studied using the physical function domain of the SF-36, at 3, 6, 9 and 12 months, with potential scores ranging from 0 (least function) to 100 (normal). Only

26% had recovered to within ten points of their initial physical function score, by 12 months. A lower Charlson comorbidity index, lower frailty index and admission for CABG/valve replacement were associated with improve outcomes, whilst conversely, those admitted with strokes were one-ninth as likely to return to normal function.

Psychological Recovery

Pandharipande [26] examined the incidence of long-term cognitive defects in 826 ICU survivors of respiratory failure or shock (2013) as part of the BRAIN-ICU study, conducted at Vanderbilt University Medical Center. Overall, 34% at 12 months had levels of cognitive dysfunction similar to that found in moderate traumatic brain injury, and 24% produced scores similar to those with mild Alzheimer's disease. For the 228 aged over 65 years, the severity of these deficits was more profound.

Iwashyna [27] studied a prospective cohort of 27,000 representative community dwelling individuals aged over 50, as part of the US Health and Retirement Study (HRS), wherein patients were interviewed each 2 years to assess cognitive function. The average age was 77. Of 1520 identified episodes of severe sepsis from 1998 to 2006, 1194 patients responded. Long-term cognitive impairment was evaluable in 516 survivors of severe sepsis. Patients or proxies were interviewed up to three times (over a 3-year period) before sepsis and up to three times afterwards (on average 5-year follow-up).The results, shown below, demonstrate on average a 10% increase in those with moderate to severe cognitive impairment, persisting for at least 3 years.

Function had not returned to baseline by 5 years. The odds of acquiring moderate to severe cognitive impairment were 3.3 times higher following an episode of sepsis. It was estimated that this equated to an additional 40 h per week of informal care required to be provided by families, for these patients.

Functional Recovery

Villa [28], in a single-centre Spanish prospective study, reviewed both the functional status and quality of life, 12 months after ICU discharge for those aged over 75. Of the 176, 62% were discharged alive and 53% were alive at 12 months. Short-term mortality was mainly related to severity of the acute illness, long term to the individual's preadmission status (cognitive function, functional state and comorbidity). Overall, one-third of participants had moderate to severe dependence requiring significant family support on discharge. Of the group with best baseline function (Barthel Index >90), a higher number (40%) were dependent at hospital discharge, with some significant improvement by 3 months, but a plateauing effect for the ensuing 9 months, such that normal function had not been attained by 12 months. Likewise, the group with a premorbid moderate BI (60–90) also had not recovered their premorbid status, by 12 months. Ninety percent of the entire survivor cohorts were included in these two BI stratifications.

Prognostic Models

Heyland [29] observed their dataset of 527 patients over the age of 80 from 22 Canadian ICUs to develop and test a prognostic model for recovery of function at 12 months. Defining recovery as a Palliative Performance Scale score at 12 months of over 60 (0 for death, 100 for full ambulation, normal activity, no evidence of disease, full self-caring and normal nutritional intake), approximately one-quarter (29%) had attained this somewhat arbitrary benchmark. Fifty-four percent were deceased by 12 months (PPS =0), and 17% scored 0–50.

Seventeen variables, including Palliative Performance Scale score and the clinical frailty scale (1 for very fit to 8, severely frail), were then incorporated using logistic regression in to a model to predict recovery at 12 months. Being married and having a primary diagnosis of emergency coronary artery bypass grafting and a higher baseline PPS were independently predictive of having a 12-month PPS exceeding 60, whilst male gender, stroke, higher APACHE 2, clinical frailty scale or Charlson comorbidity scores independently proved adverse prognostically. The c-statistic was 0.81 when applied internally to this dataset of predominantly Caucasian patients [30].

Following multivariate analysis of 10 years of ICU admissions to a single ICU in South Korea, Sim [6] developed a clinical mortality index. Five of the risk factors (poor nutrition, chronic renal failure, cancer, pneumonia and admission from wards) were evident on admission, and three (active DNR orders, vasopressors and mechanical ventilation) were treatment related. In patients with pneumonia, previous work had demonstrated that each additional decade of age above the age of 60 had been associated with a 24% increase in ICU mortality. All of the patients in Sim's study presenting without any of the prognostic factors identified survived. On the other hand, none of the patients with five or more of the prognostic factors survived. The higher the number of risk factors, the progressively higher the mortality rate. Clearly this model requires testing in a multicentred, prospective cohort.

Economic Comparisons

Chin-Yee [31] analysed the cost of those over the age of 80–22 Canadian ICUs from 2009 to 2013. The mean cost per ICU admission was $ 31,000, equating to $48,000 per survivor to hospital discharge. In context, Owens [32] and Marseille [33] note that around $50,000–$100,000 per QALY is generally viewed in United States as acceptable, although this figure varies from country to country. By comparison, coronary artery bypass grafting costs $88,000 per life-year gained [22, 26]; 1 year of dialysis for chronic renal failure costs $ 50,000 per QALY; $44,000 for HIV referral, testing and counselling in high-risk groups; $90,000 per QALY for surgical treatment of spinal canal stenosis; and $100,000 per QALY for neurosurgical intervention for a malignant brain tumour. Despite such favourable financial comparisons, the philosophical and scientific validity of reducing the multidimensional societal benefits of a senior's final years to formulated QALYs has been fundamentally challenged.

Cultural Variabilities

Prognosis for many diagnoses – not just in the most elderly patients – is dependent on the level of medical resources that a society, hospital or ICU has at its disposal. Pivotal decisions including thresholds for admitting to intensive care, for example, depend on a combination of cultural expectations, personal philosophies, financial concerns as well as medical factors. For example, regarding end-of-life issues, in a review for the World Federation of Societies of Intensive and Critical Care Medicine, Myburgh [34] note that in Japan withdrawal of life support is considered illegal, in Israel law prohibits ceasing continuous but not intermittent life-prolonging therapies, in Belgium euthanasia is legal but not generally applicable to ICU patients, in South Africa resources are generally limited and in China, there is neither local nor national legislation governing treatment withdrawal, with marked cultural, religious and financial diversities. Cultural factors therefore impact on selection of patients for ICU as well as on their short- and long-term prognosis.

Political as well as legal factors, both locally and internationally, are also relevant in establishing the level of support and limits of care for medical staff in caring for a particular patient. In a recent case [35] at Great Ormond Street Hospital, London, UK – although involving a patient at the other extreme of life – judgements of Britain's highest court (the High Court) and subsequently the European Court of Human Rights have both been publically challenged by the Pope as well as the President of the United States. Respectively, these officials represent 1.2 billion and 321 million people (or 5 times the population of the entire United Kingdom). Recently emerged therapeutic options which confer purported survival benefits being trialled in a different continent have become central in this tenuous debate. The prevalent legal and political milieu in foreign countries, which are in themselves dynamic, therefore may also prove of major relevance.

Not only do variations in applying treatments (and treatment limitations) occur according to country of practice but intensivist and clinicians, as noted in a review of patients also admitted to 1 Canadian 21-bed ICU over a 20-month period in 2013–2014, even within 1 ICU, may have value systems and personal viewpoints disparate from those of their patients. Consensual considerations regarding potential therapeutic options shared goal setting and agreed evaluations of therapeutic trials that may therefore prove at least challenging, in clinical settings where intrinsic fundamental human values and subsequently definitions of therapeutic success are not shared. Such inconsistencies in basic human values could easily catalyse, within the routine day-to-day functioning of most intensive care units, what Cook [36] described as a "major existential crisis for most dying persons and their families".

A prospective French study of 2115 patients aged over the age of 80 admitted in the Paris region observed that in only 13%, the patients' opinion was sought as to whether they would like ICU admission. Despite all included patients having the necessary faculties to be able to express their opinion, marked variation between hospitals was observed, ranging from 1% to 53%. Younger doctors were more likely to solicit patients' viewpoints than older doctors. The opinions of families were also not routinely sought, although surrogate decision-making has demonstrated variable reliability in a number of studies [37].

Rusinova [38] observed the dynamic nature of therapeutics currently offered with increasing regularity to octogenarians, with standard guidelines for the performance of percutaneous coronary intervention in ST elevation myocardial infarction and recombinant tissue plasminogen activator administration for stroke management, recently removing upper age limits of 80. "Minimally invasive" laparoscopic, endoscopic and thoracoscopic interventions – even to the point of open coronary artery regrafting – are performed more frequently on octogenarians, particularly in the absence of "significant comorbidities". Demonstrating the evolution of minimally invasive technology over the last decade, Melbourne's Monash Medical Centre [39] reported 190 transvenous aortic valve implants (TAVIs) with a mean age of 84. Device success rate was 92%; mortality rate was 1% with a 1% stroke rate. Other horizon technologies, according to the 2016 Annual Cleveland Clinic's Medical Innovation Summit and others, include the following [40, 41]:

- Chimeric antigen receptor – T cell (CAR – T) therapies, as less toxic and more targeted immunotherapy for malignancies
- Advanced gene-editing and gene-splicing techniques such as clustered regularly interspaced short palindromic repeats (CRISPR/Cas 9)
- Three-dimensional visualisation during retinal and neurosurgery, including holographic CT and MRI reconstructions
- Prosthetic limbs incorporating neural control and sensory perception
- NHS trials of stem cell-derived blood products
- Point-of-care gene sequencing
- Skin biosensors for glycaemic biocontrol without needles
- Early cancer detection using nanoparticles
- Implantable neurostimulators for Parkinson's disease and memory regeneration
- Health checks, rehabilitation and sterilisation performed by robots
- Leadless cardiac pacemakers to reduce infection risks and
- Mobile stroke treatment units dispatched from hospital emergency departments

Finally, the accuracy of life expectancy prognostications by intensivist and senior ICU staff has recently been reported by Detsky [42]. 340 patients from 5 ICUs in the University of Pennsylvania Health System, who received more than 48 h mechanical ventilation and vasoactive infusions for more than 24 h or both, were enrolled from the third to the sixth day of their ICU stay. Senior staffs were asked to prognosticate on a number of variables, including 6-month survival. Eighty-nine percent of patients consented. Ninety percent of the doctors were more than 10 years postgraduation. Globally, clinicians performed better than chance. For physicians, their highest accuracy was in predicting survival at 6 months, with 63% sensitivity (a positive likelihood ratio of 5.9, negative likelihood ratio 0.4 and C statistic, 0.76). The accuracy of prediction was only meaningfully high when the confidence of the prediction was "high" for both doctors and nurses, but this level of concordance and confidence was attained for approximately one in four (between 22% and 33%) admissions. Cognition and ability to self-toilet at 6 months were least well predicted. Ongoing calibration amongst clinicians was therefore concluded to remain vital in terms of accurately relaying to families realistic assessments of therapeutic outcomes. Hall [43] in an accompanying editorial acknowledged that "even the most accurate of scores do not have a role in prognostication for the individual patient but perform very well across patient populations". Note that even this level of prognostic accuracy was not achieved as a result of a "once-off" review – rather, these predictions resulted from senior intensivist spending days familiarising themselves with each patient.

Patients' attitudes also change with time [34]. Both younger patients and doctors alike often report an attitude reflecting a "struggle against a disease" – such as a large hemispheric stroke. More senior patients however more often reflect a nuanced resolve, opting to "live and cope with a handicap", adopting a more passive and adaptive approach. The definition of what comprises an "acceptable" handicap therefore often demonstrates considerable variance, depending on the perspective, training and personal experiences of the observer.

Conclusion

With each new decade, intensive care has demonstrated its ability to support both the quantity and quality of life of progressively more aged patients, with less attendant morbidities and greater efficacy. The raw number of elderly patients worldwide will continue to climb, even if the percentage of the elderly accepted into intensive care units declines. The number of less invasive but cost-efficient procedures generally available to the senior community shows no signs of anything but escalating. Prognostically predictive indexes, incorporating quantifiable physical dimensions such as "frailty" – as well as psychosocial parameters – will continue to evolve. Temporal and geographical recalibration of such tools, within the resources available to each local health precinct, will however be necessary. Finally dynamic, transparent, honest and respectful dialogue with both the patient where possible and also their closest friends will lead to the maturation of robust shared values, the development of realistic treatment goals and through mutually agreed evaluation processes, optimal achievement of gratifying and holistic outcomes.

Clinical Relevance

- More effective and universal health-care coverage together with the aging of the world population will ensure that the care of the very elderly in intensive care units numerically becomes more common. More than one in four of ICU admissions by 2020 is likely to be aged >80.
- Prognostic markers, such as physical frailty, are becoming more clearly characterised. More expeditiously translated technological innovations, for example, robotic rehabilitation, are being tailored to target specific deficits.
- Evolving prognostic scoring systems will require both currency and external validation and, whilst

useful for cohorts, are presently not reliable for individual patient use. Reason for ICU admission, the nature of comorbidities and physiological reserve each appear more strongly predictive than chronological age, by itself.

- Psychological, physical and functional recovery frequently lags significantly behind hospital discharge. Effective mitigation strategies are available but with variable implementation between and within countries.
- Elderly patient's attitudes to receiving intensive care support are often not garnered in advance.
- Cultural, legal and political environments are inconsistent across the globe and significantly influence health outcomes, particularly amongst the elderly.
- As niche and emerging minimally invasive therapeutics substantially increase the quality of life of survivors, the raw numbers of elderly to whom these treatments are offered in the intensive care setting will escalate.

Multiple Choice Questions

1. The following statements in relation to intensive care in the elderly are true, EXCEPT:
   A. The population over the age of 80 will more than double in most regions significantly intensifying this growing demand for ICU services.
   B. Elderly patient's attitudes to receiving intensive care support are often not garnered in advance.
   C. Short-term mortality was mainly related to severity of the acute illness, long term to the individual's preadmission status.
   D. Cultural factors do impact on selection of patients for ICU as well as on their short- and long-term prognosis.
2. The following statements are true regarding the elderly and intensive care, EXCEPT:
   A. Sepsis and respiratory diagnoses are becoming more frequent indications for admission to intensive care, with cardiac failure and lung cancer being less common.
   B. Recently published data from Norway regarding long-term elderly survivors demonstrated that after 12 months, mortality rates parallel those of aged-matched controls.
   C. Elective surgery has a superior outcome to medical admission, which has a lower mortality rate than emergency surgical patients.
   D. Frailty is unimportant in terms of prognostication, and prognostic indices have been proven to be robust across all societies.

Answers to MCQs

1. D
2. D

References

1. Kelly FE, Fong K, Hirsch N, Nolan JP. Intensive care medicine is 60 year old: the history and future of Intensive care unit. Clin Med. 2014;14(4):376–9.
2. Bagshaw SM, Webb SA, Delaney A, George C, Pilcher D, Hart GK, Bellomo R. Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. Crit Care. 2009;13(2):R45.
3. Bagshaw SM, Webb S, Delaney A, George C, Pilcher D, Hart G. Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. Crit Care. 2009;13(2):1–14.
4. Nguyen Y, Angus DC, Voumendil A, Guidet B. The challenge of admitting the very elderly to intensive care. Ann Intensive Care. 2011;1(29):1–7.
5. Department of Economic and Social Affairs Population Division World Population Ageing, United Nations, New York; 2015.
6. Sim Y, Fuhrmann V, Kluge S, Becker S, Muller J. Mortality and outcomes in very elderly patients 90 years of age or older admitted to ICU. Respir Care. 2014;60(3):341–55.
7. Brochard L. Mechanical ventilation:invasive versus non-invasive. Eur Respir J Suppl. 2003;47:31s–7s.
8. Benhamou D, Muir JF, Melen B. Mechanical ventilation in elderly patients. Monaldi Arch Chest Dis. 1998;53(5):547–51.
9. Lieberman D, Nachshon L, Meloslavasky O, Dvorkin V, Shimini A, Zelinger J, et al. Elderly patients undergoing mechanical ventilation in and out of ICUs: a comparative prospective study of 579 ventilations. Crit Care. 2010;14(2):R48. https://doi.org/10.1186/cc8935.
10. Neto SCGB, Oliviera AK, Amarin FF, Cipriano FB, Vilaca HKC. Impact of mechanical ventilation on outcomes of critical care elderly patients: a cohort study. Eur Respir J. 2015;46:PA2152. https://doi.org/10.1183/13993003.congres.2015.PA2152.
11. Tripp DK, Purdie G, Hicks P. Trends in the incidence of intensive care unit invasive mechanical ventilation and subsequent 2-year survival in very elderly New Zealanders. Intern Med J. 2015;45(1):80–5.
12. Becker S, Muller J, De Heer G, Braune S, Fuhrmann V, Kluge S. Clinical characteristics and outcome of very elderly patients ≥90 years in intensive care: a retrospective observational study. Ann Intensive Care. 2015;5(53):1–8.
13. Sjoding M, Prescot H, Wunsch H, Washyna T, Crooke C. Longitudinal changes in icu admission among elderly patients in the United States. Crit Care Med. 2015;44(7):1353–60.
14. Hoffman KR, Loong B, Haren V, Rellos K. Very Old patients urgently referred to the ICU: long term outcomes for admitted and declined patients. Crit Care Resusc. 2016;18(3):157–64.
15. Rellos K, Leong B, Haren FV. Outcome of critically ill oldest- old patients (aged 90 and older) admitted to the ICU. J Am Geriatr Soc. 2016;54(1):110–4.

16. Heyland DK, Garland A, Bradshaw S, Cook D, Rockwood K, Stelfox H, et al. The very elderly admitted to ICU: a quality finish? Crit Care Med. 2016;43(7):1352–60.
17. Anderson F, Flaatten H, Klepstad P, Romlid U, Kvale R. Long term survival and quality of life after intensive care for patients 80 years of age or older. Ann Intensive Care. 2015;5(13):1–13.
18. Nabozng MJ, Barnato A, Rathouz P, Havlena H, King A, Zhao Q, et al. Trajectories and prognosis of older patients who have prolonged mechanical ventilation after high risk surgery. Crit Care Med. 2016;44(6):1091–7.
19. Nasa P, Singh O, Juneja P. Server Sepsis and its impact on outcomes in elderly and very elderly patients admitted in Intensive care unit. J Intensive Care Med. 2012;27(3):179–83.
20. Aissaoui N, Cattan S, Scheile F, Ferrieries J, Tabassome S, Juillier Y. Cardiogenic shock in elderly patients with acute myocardial infarction. The FAST-MI programme. Arch Cardiovasc Dis Suppl. 2016;8:110–3.
21. Bangalore S, Gupta N, Lala A, Rosewell RO, Hochman JS, Balsam L, et al. Outcomes with invasive vs. conservative management of cardiogenic shock complicating acute myocardial infarction. Am J Med. 2015;128(6):601–8.
22. Zeng A, Dong J, Mitnitski A, Guo Z, Rockwood K. Mortality in relation to frailty in patients admitted to a specialized geriatric intensive care unit. J Gerontal A Biol Sci Med Sci. 2014;70(12):1586–94.
23. Biston P, Aldcoa C, Deveindt J, Madl C, Chochard D, Vincent J, De Backer D. Outcome of elderly patients with circulatory failure. Intensive Care Med. 2014;40(1):50–6.
24. Hill D, Fowler RA, Herridge MS, Cuthberg BH, Scales DC. Long term outcomes and health care utilization following critical illness – a population –based study. Crit Care. 2016;20:76:1–10.
25. Heyland DK, Garland A, Bradshaw S, Cook D, Rockwood K, Stelfox H, Burns K, Fowler R. Recovery after critical illness in patients aged 80 years or older: a multi-centre prospective observationals cohort study. Intensive Care Med. 2015;41(11):1911–20.
26. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, Brummel NE, et al. Long term cognitive impairment after critical illness. N Engl J Med. 2013;369(14):1306–16.
27. Iwashyna T, Wesley W, Smith S, Lang KM. Long term cognitive impairment and functional disability among survivors of severe sepsis. JAMA. 2010;304(16):1787–94.
28. Villa P, Pinado M, Lujan J, Gonzalez N, Trascasa M. Functional status and quality of life in elderly intensive care unit survivors. J Am Geriatr Soc. 2016;64:536–42.
29. Heyland DK, Garland A, Bradshaw S, Cook D, Rockwood K, Stelfox H, et al. Predicting performance status 1 year after critical illness in patients 80 years or older: development of multivariable clinical prediction model. Crit Care Med. 2010;44(9):1718–25.
30. Sligl WI, Eurich DT, Marrie TJ, Majundar SR. Age still matters: prognosticating short and long term mortality for critically ill patients with pneumonia. Crit Care Med. 2010;38(11):2126–32.
31. Chin-Yee N. Cost analysis of the very elderly admitted to intensive care units. Crit Care. 2017;21:109:1–7.
32. Owens D. Interpretation of cost effectiveness analyses. J Gen Intern Med. 1998;13(10):716–7.
33. Marseille E. WHO Thresholds for the cost–effectiveness of interventions alternative approaches. Bull World Health Organ. 2015;93:118–24.
34. Myburgh J, Dobb J, Jacob S, Kleinpell R, Abillama F, Vincent G, et al. End of life care in the Intensive Care Unit: report from the taskforce of World Federation of Societies of Intensive and Critical Care Medicine. J Crit Care. 2016;34:125–30.
35. http://www.seattletimes.com/nation-world/london-hospital-reconsiders-decision-to-turn-off-sick-infants-life-support/. Accessed 9.07.17.
36. Cook D, Rose T, Boyle A, Toledo F, Woods A, Shappard R. Personalising death in the Intensive Care Unit: The 3 wishes project. Ann Intern Med. 2015;163(4):271–80.
37. Le Gruen J. Are elderly patient's opinions sought before admission to an Intensive Care Unit? results of the ICE-CUB study. Age Aging. 2016;45:303–9.
38. Rusinova K, Guedet B. Are you sure its about age ? Intensive Care Med. 2014;40:14–116.
39. Rashid H. Large single-centre outcome of next-generation Tran catheter Aortic Valve Replacement (T.A.V.R) systems in low-intermediate surgical risk patients. Intern Med J. 2017;47. (Supp 3:14.
40. http://www.modernhealthcare.com/article/20161027/NEWS/161029924. Accessed 10.07.17.
41. http://medicalfuturist.com/20-potential-technological-advances-in-the-future-of-medicine-part-ii/. Accessed 10.07.17.
42. Detsky M. Discriminative accuracy of physician and nurse predictions for survival and functional outcomes 6 months after ICU admission. JAMA. 2017;317(21):2187–95.
43. Hall JB. Making sound recommendations for limiting care in the ICU based on sound prognosis. JAMA. 2017;317(21):2170–1.

Part II

Common Diseases in Older Adults

Cardiovascular Diseases in the Very Elderly

15

Logan Kanagaratnam

Introduction

In June 2015, people over the age of 85 were 1.98% of the total Australian population. This age group is expected to be 5–7% of Australia's population by year 2056 [1]. Population estimates in the USA suggest that population older than 85 years are likely to increase to 4.49% of the total population by year 2050 (when compared to 1.96% of population 2015) [2].

Treating cardiac conditions in the extremely elderly patient can be challenging due to multiple co-morbid conditions, frailty and deteriorating social situation. The clinical presentation may not be typical. Many patients will be on multiple medications prone to drug interactions, worsening renal function and poor compliance with drug therapy.

Unfortunately there is no adequate clinical trial data in these very elderly patients. Therefore whether many of the evidence-based therapies used in normal adult population are applicable to this age group is questionable. Recently released document from the American College of Cardiology, American Heart Association and American Geriatric Society acknowledges this issue and recommends clinical trials [3].

In competent patients, management goals need to be set with full discussion with the patient regarding therapeutic options and alternatives. Patients in this age group are more aware of their mortality and are often reluctant to accept invasive measures. However judicious use of invasive procedures like permanent pacemaker insertion and coronary angiography should not be withheld in this age group just because of patient's age. Although it is reasonable not to do invasive procedures in the extremely elderly patients with primary aim of prognostic benefit, it would be prudent to consider procedures that would improve the patient's quality of life. This would include coronary intervention for disabling angina or pacemaker insertion to treat or prevent syncope. Emergence of newer procedures like transcatheter aortic valve implantation (TAVI) may be especially relevant in this age group.

L. Kanagaratnam
Royal North Shore, Ryde, North Shore Private and Macquarie University Hospitals, University of Sydney, St. Leonards, NSW, Australia

Common Cardiovascular Diseases

Hypertension in the Elderly

Prevalence of hypertension increases with age. In males more than 75 years, about 75% have systolic hypertension. About 65% of females in this age group will have systolic hypertension. Diastolic hypertension only affects 10% of the elderly [4]. Hypertension in the elderly is due to multiple factors. Arterial stiffness contributes to reflected pulse wave and late systolic augmentation. Progressive renal dysfunction may contribute to hypertension, and medications including steroids and non-steroidal anti-inflammatory medications (NSAIDs) could also exacerbate blood pressure. Lifestyle factors and sleep apnoea also play a part. Although higher blood pressures in all decades of life increase cardiovascular events, the oldest patients seemed to tolerate higher blood pressures with lower events when compared to younger patients in INVEST study [5] (Fig. 15.1).

Management

Treatment of hypertension and regression of Left Ventricular Hypertrophy (LVH) has been demonstrated to show reduction in heart failure and cardiovascular events [6]. In HYVET trial with a blood pressure target of <150/80, patients older than 80 years treated with diuretics (or with added perindopril) had 21% reduction in mortality at 2 years [7].

The SHEP study which included patients with a mean age of 72, showed antihypertensive therapy which achieved an average systolic BP of 143 had 36% reduction of stroke at a mean follow up of 4.5 years. In this study primary anti hypertensive therapy was a diuretic and if this was not adequate a beta blocker was added [8]. Systolic hypertension and elevated heart rate have been associated with cognitive decline in the elderly [9].

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_15

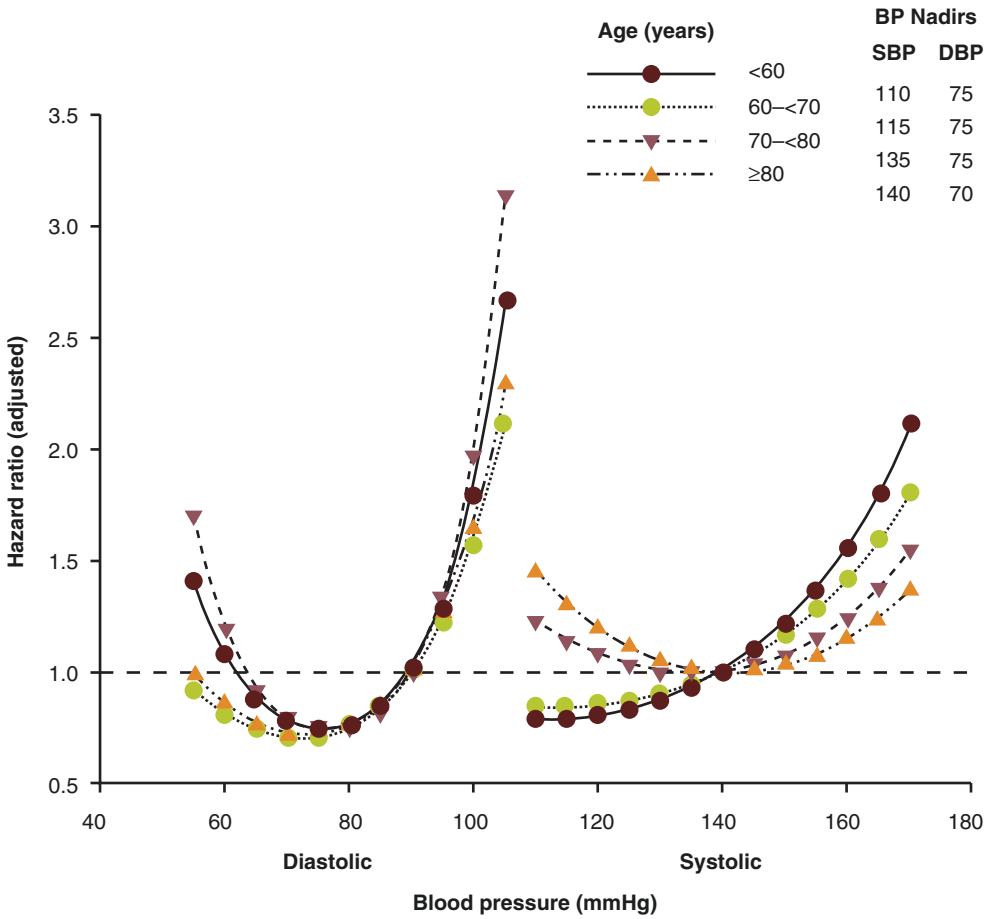

Fig. 15.1 Risk of adverse outcomes by age and blood pressure. BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure. (Reproduced with kind permission, from Figure from [5])

Non-pharmacological management includes salt restriction, regular exercise, weight control, smoking cessation and avoidance of excessive alcohol intake.

In the consensus document by ACCF/AHA, it is suggested that in patients more than 80 years of age, systolic BP of 140–145 (if tolerated) is acceptable. There is no data to support stricter BP control in the very elderly with co-morbidities like diabetes, chronic kidney disease and coronary artery disease [10].

Choice of antihypertensive agent is often dictated by the co-morbidities. Although multiple medications may be required for achieving optimal control, "start low and go slow" approach should be taken. Thiazide and non-thiazide diuretics, angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blocker (ARB), beta blocker, calcium channel blocker and vasodilators (Nitrates and alpha blockers) are commonly used agents.

Patients with heart failure benefit by beta blocker, ACE- I or ARB and diuretics. Patients with angina benefit by beta blocker, calcium channel blocker or nitrates. Patients with kidney disease and proteinuria benefit by treatment with ACE- I or ARB [11].

In the elderly patients it is often necessary to use more than one anti- hypertensive medication to achieve control. Combination therapy has the advantage of reducing the dose of single agent, decreasing the side effect from the higher dose, longer duration of action, higher efficacy and having an additive or potentiating effect of the second agent.

Resistant hypertension is defined as BP above the goal despite adherence to lifestyle measures and with treatment using three medications at maximal tolerated doses where one of these agents is a diuretic [12]. There is no good data to know the prevalence of resistant hypertension in the

Box 15.1 Hypertension in the Elderly

Systolic hypertension is common in the elderly.

Treatment of hypertension with regression of LVH has been shown to reduce cardiovascular events and heart failure.

Combination therapy of hypertension is more effective.

elderly [10]. However the incidence of resistant hypertension increases with age.

Coronary Artery Disease (CAD)

Stable CAD

Diagnosis is often made from typical history of angina. An individualised treatment goal would need to be formulated with the concurrence of the patient and the family.

Main agents used in the medical management of patients are antiplatelet agents, statins, beta blockers, calcium channel blockers, ACE inhibitors, ARBs and nitrates. Some patients would also benefit by agents like ivabradine and nicorandil. It is important to recognise the limitations or potential side effects of number antianginal medications in the extremely elderly. Vasodilators like nitrates may aggravate postural drop in blood pressure and may cause falls or syncope. Beta blockers could impair the heart rate response to exercise and could cause exertional dyspnoea and fatigue. Calcium channel blockers could cause or aggravate leg oedema. When choosing the appropriate medications in this age group, careful consideration should be given to co-morbidities, and start medications at a low dose and gradually build up.

All patients should be on aspirin 75–150 mg daily unless contraindicated as per ACC/AHA (American College of Cardiology, American Heart Association) guidelines [13]. Beta blockers by slowing of the heart rate increase the duration of diastole which increases coronary perfusion [14].

ACE inhibitors and ARBs reduce the myocardial oxygen consumption by reducing the afterload. Studies including HOPE and EUROPA have demonstrated beneficial effect of ACE inhibitor therapy by reducing cardiovascular death, myocardial infarction and cardiac arrest.

Calcium channel blockers and nitrates provide symptom relief but have not shown to have prognostic benefit [14]. The calcium channel blockers with negative inotropic effects (verapamil, diltiazem) should be avoided in patients with heart failure or low ejection fraction.

Ranolazine, an inward sodium channel blocker which increases the intracellular calcium, has been shown to reduce angina in the young and elderly [15, 16].

Patients who have accelerating symptoms or symptoms not controlled with medical therapy may be considered for further investigations including invasive assessment. Depending on the anatomy of the coronary circulation and patient's co-morbidities, decisions could be made whether to continue medical therapy or consider angioplasty and stenting – percutaneous intervention (PCI) or in rare instances coronary artery bypass grafting (CABG).

Studies have shown CABG to be superior to stenting in left main disease and in diabetics with triple vessel disease (SYNTAX, FREEDOM). However in the very elderly, operative risks may be prohibitive, and PCI may be considered for symptom relief [17–20].

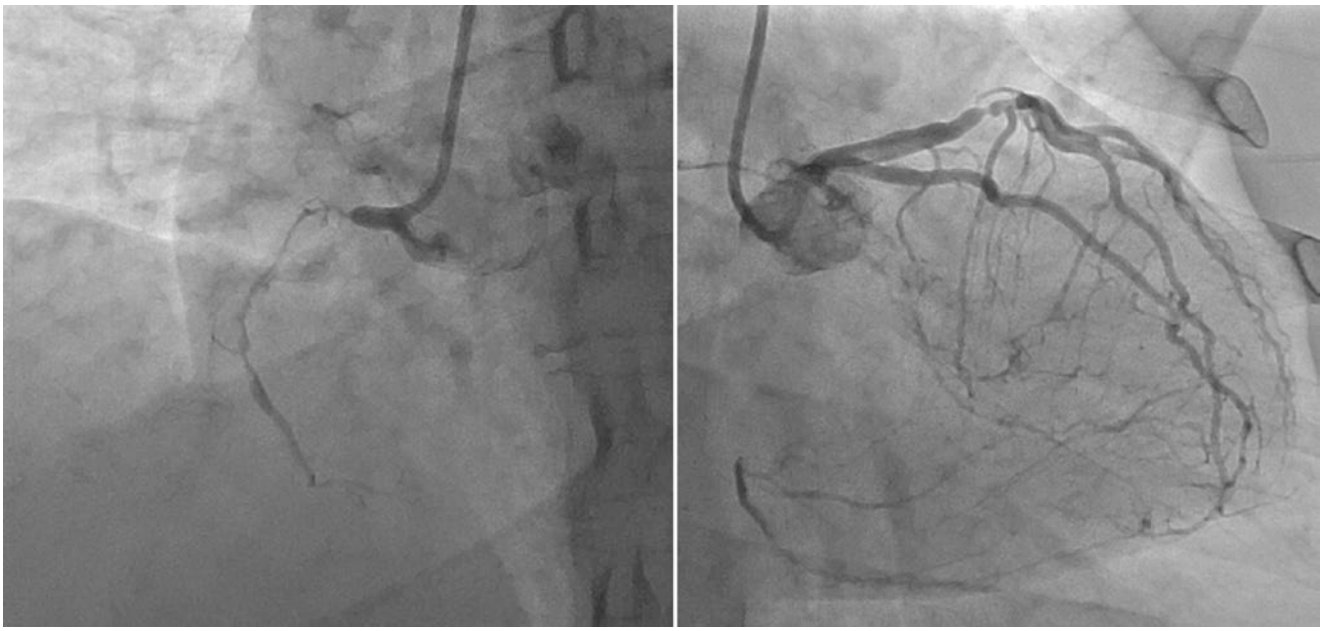

Fig. 15.2 Coronary angiography showing triple vessel disease. Right coronary artery (left panel) and the circumflex coronary artery (right panel) are occluded with some retrograde flow. The left anterior descending coronary artery in the upper part of the left panel shows diffuse disease with tight lesion close to the origin of the diagonal branch

PCI in Elderly

Elderly tend to have more complex coronary disease (Fig. 15.2). Compared to younger patients, the very elderly have more incidence of tortuosity, complex plaques, osteal disease, multivessel disease and triple vessel disease [21, 22]. Although the elderly have higher procedural risk, their outcome is favourable when compared to conservative approach [23]. Second- and third-generation stents are superior to bare metal stents by decreasing myocardial infarction and improving target vessel revascularisation without increasing bleeding risk [24]. In a large multicentre registry, outcome of unprotected left main stenting with drug eluting stent in octogenarians was comparable to surgery at a median of 3-year follow-up [25].

Coronary Artery Bypass Grafting (CABG)

Octogenarians have higher incidence of morbidity and mortality with coronary artery bypass surgery. In NCN database, the CABG mortality in the older than 80-year-olds was 8.1% compared to the 3% in the rest of the population. The very elderly also have a longer duration of hospital stay after the surgery [26, 27]. However follow-up of the patients older than 80 years after bypass surgery demonstrated good functional status with significant improvement in symptoms [28, 29].

Unstable Angina and Non-ST-Elevation Myocardial Infarction (NSTEMI)

The 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes had specific guidelines for the very elderly. It states that management decisions for the very elderly presenting with NSTEMI should be based on patient preferences, goals, co-morbidities, cognitive and functional status and life expectancy [30].

Elderly have higher risk with unstable angina and NSTEMI. Only about 40% of the patients over 85 years present with typical chest pain. The others present with dyspnoea, diaphoresis, nausea and vomiting or syncope [31]. Those presenting with chest pain may present with chest pain at rest or angina type of pain lasting 20 min or increasing angina symptoms in the preceding 1–2 weeks.

Those above age of 85 years have high rates of mortality with NSTEMI. Patients with atypical presentation had worse prognosis. This was possibly due to delay in diagnosis [31].

In the very elderly, a high index of suspicion is warranted. ECG changes involving ST segment and T waves and raised cardiac enzymes (troponin) confirm the diagnosis.

Antiplatelet Therapy

In the absence of high bleeding risk, dual anti-platelet therapy should be considered. One of the anti-platelet agents is aspirin. The second agent is usually clopidogrel. Although newer anti- platelet agents are more potent, they also cause more bleeding in the elderly and need to be used with caution. Prasugrel is relatively contraindicated in patients older than 75 due to high bleeding risk. Although ticagrelor may be used in the elderly, it is more expensive and has to be taken twice daily. It also has higher incidence of breathlessness [32].

Glycoprotein IIb/IIIa inhibitors, which is a class of intravenous anti-platelet agent, have been shown to reduce death and infarction in patients over 65 years. However meta-analysis suggests less benefit in the very elderly [33].

In the absence of bleeding, treatment with low molecular weight heparin or unfractionated heparin should be considered.

Beta blockers and nitrates could be used for control of symptoms. ACE-I and ARB may be used in patients with heart failure and who do not have contraindication. Statins have beneficial effect in elderly with acute coronary syndromes.

ST Segment Elevation Myocardial Infarction (STEMI)

Early reperfusion decreases the morbidity and mortality in the elderly with STEMI (Fig. 15.3). Elderly are often not eligible for thrombolytic therapy. Due to atypical presentation the diagnosis may be delayed and push them outside the window of therapeutic benefit with thrombolysis. They also often have more co-morbidities and contraindications.

In hospitals without PCI facility, thrombolytic therapy may be considered. There are few patients who are more than 75 years of age in thrombolytic trials. Risk of intracranial haemorrhage is higher in the over 85-year-old age group. In one study the incidence of intracranial haemorrhage was 2.9% in this age group [34]. Tenecteplase had slightly higher incidence of intracranial haemorrhage when compared to tissue plasminogen activator [35].

In a study comparing thrombolytic therapy with PCI in acute STEMI in elderly patients, PCI was superior, and the study was terminated prematurely [36]. Similar benefit for PCI has been demonstrated in other trials as well [37]. Pooled analysis of elderly patients showed superiority of PCI over thrombolytic therapy in STEMI patients. In fact patients older than 85 years had more benefit when compared to younger patients [38, 39].

When very elderly patients present with acute ST segment elevation myocardial infarction, PCI should be the preferred form of therapy. Even in patients with cardiogenic shock, PCI has been shown to be beneficial [40]. However if PCI is not available within a reasonable time frame, thrombolytic therapy should be considered [40].

Patients with STEMI will need ongoing therapy with antiplatelet agents and statin and in the absence of contraindica-

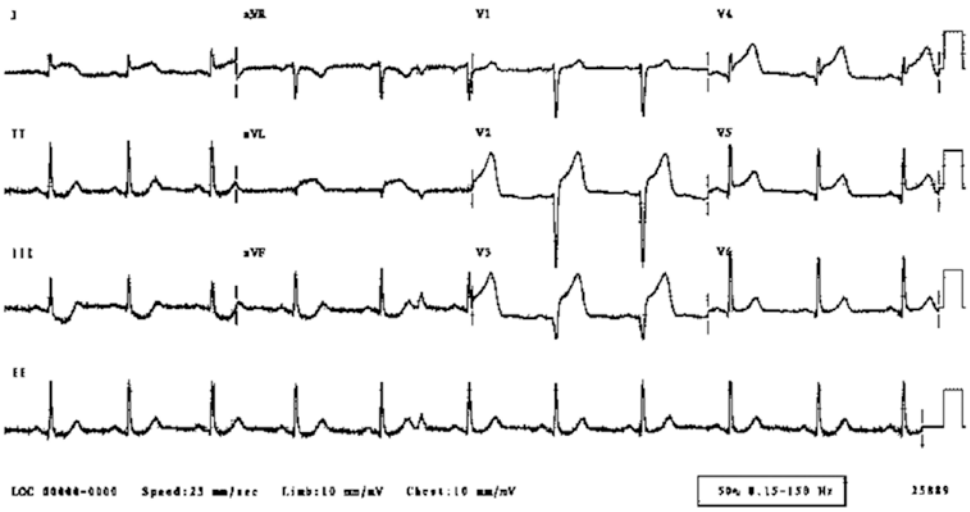

Fig. 15.3 Acute anterior ST segment elevation myocardial infarction

tions, beta blocker and ACE-I or ARB. Although younger patients have shown benefit with eplerenone as an aldosterone antagonist, patients over 75 years have failed to show benefit [39]. Even very elderly will benefit by cardiac rehabilitation programme [41].

Box 15.2 Coronary Artery Disease

In patients with stable angina, routine addition of percutaneous intervention to optimal medical therapy did not have significant impact.

Elderly with acute coronary syndromes have a higher risk of mortality.

Elderly patients with STEMI benefit by percutaneous intervention.

Heart Failure

Introduction

In the community, prevalence of heart failure increases with age. In Framingham study it increased with age. In age groups 60–69, 70–79 and >80 years the prevalence of heart failure was 2.3%, 4.9% and 9.1%, respectively [42]. Heart failure is a common cause of hospital admission in elderly. It can be precipitated by infection, ischaemia, arrhythmia or anaemia. The presentation may be with shortness of breath or leg oedema. At other times, the presentation may be with features of the precipitating factor like infection or arrhythmia. Some of the very elderly may have uncommon symptoms like confusion, weakness, sleep disturbance and cough.

Diagnosis

Heart failure is diagnosed by typical clinical features of fatigue, dyspnoea and leg swelling. However some of these features could be encountered in other clinical conditions as well. ECG can be helpful if there are features of old infarction, evidence of ischaemia or evidence of left ventricular hypertrophy. Chest X-ray may show pulmonary congestion and cardiomegaly. Echocardiography is the main form of investigation. It helps to assess the systolic function (ejection fraction) and diastolic function. Severity of diastolic dysfunction can be assessed especially by studying the mitral inflow Doppler profile. Biochemical markers like BNP can be helpful but not essential.

Systolic Heart Failure

In systolic heart failure, there is reduction in ejection fraction. This could be due to ischaemic or non-ischaemic aetiology.

Management

In all patients salt and fluid restriction should be considered. Neurohormonal blockade with beta blockers, ACE-I, ARB and aldosterone antagonists have been shown to reduce morbidity and mortality in patients with systolic heart failure. ACE inhibitors have proven benefit in systolic heart failure. One study comparing ACE inhibitor with digoxin in the very elderly nursing home patients found ACE inhibitor to have survival advantage [43].

ARBs are recommended for patients who cannot tolerate an ACE inhibitor. In CHARM sub-study, the patients older than 75 years had similar benefit to the younger cohort [44]. When ACE-I or ARB treatment is initiated, it is important to monitor renal function and potassium. In patients with rela-

tive hypotension, it may be necessary to withhold diuretics for 1–2 doses while initiating therapy with ACE-I or ARB.

Beta blockers have proven mortality reduction in patients with heart failure. In SENIORS study, nebivolol was studied in patients older than 70 years presenting with heart failure (regardless of the ejection fraction). There was 4.2% absolute risk reduction for the primary end point of death and hospitalisation at 21 months [45].

Although other beta blockers including carvedilol, long-acting metoprolol and bisoprolol have been shown to be effective in systolic heart failure, there have been very few very elderly patients included in these trials.

Aldosterone antagonists, spironolactone and eplerenone, have been beneficial in patients with systolic dysfunction and older than 65 years of age (without significant renal dysfunction and hyperkalaemia). RALES study evaluated spironolactone [46]. The sub-study of patients older than 65 showed beneficial effect. In EMPHASIS trial patients 65 years and older, eplerenone was found to decrease hospital admission and mortality [47]. However in EPHESUS trial patients over the age of 65 treated with eplerenone failed to show benefit that was demonstrated by the younger patients [48]. Patients treated with aldosterone antagonists should be carefully monitored for hyperkalaemia.

In patients who cannot take an ACE inhibitor, VHEFT trial has shown benefit of hydralazine and nitrate combination. Even though specific trial data is lacking in the very elderly, when the patients have significant renal impairment, it is reasonable to consider this combination [49].

In SHIFT study, ivabradine, a selective IK_f current inhibitor which acts on the sinus node, has been shown to reduce heart failure admission and mortality when used in patients in sinus rhythm with ejection fraction of less than 35%, who despite optimal therapy had resting heart rate of 70 or more. The mean age of this trial population was 60.7 years [50].

Digoxin has been shown to decrease hospital admissions in heart failure in DIG trial. There was no mortality reduction in this trial. Subgroup analysis showed that patients older than 80 years had similar benefit [51, 52].

Older patients with renal impairment and concomitant therapy with amiodarone and calcium channel blockers are at higher risk of digoxin toxicity. It would be important to monitor digoxin level and keep it at lower end of the therapeutic range.

Diuretics help in treating symptoms of heart failure. They help in improving congestion and fluid overload. However they have not been shown to decrease mortality. Diuretic therapy can worsen renal function and could lead to electrolyte abnormalities of Na and K. It is important to understand that the typical extremely elderly patient has multiple co-morbidities and will not have been included in the many published studies.

Device Therapy

Patients with left bundle branch block (Fig. 15.4), wide QRS complex and evidence of dyssynchrony (between the septum and lateral wall in the echocardiogram) may benefit with cardiac re-synchronisation therapy (bi-ventricular pacing). Elderly patients over age of 75 have shown benefit. However

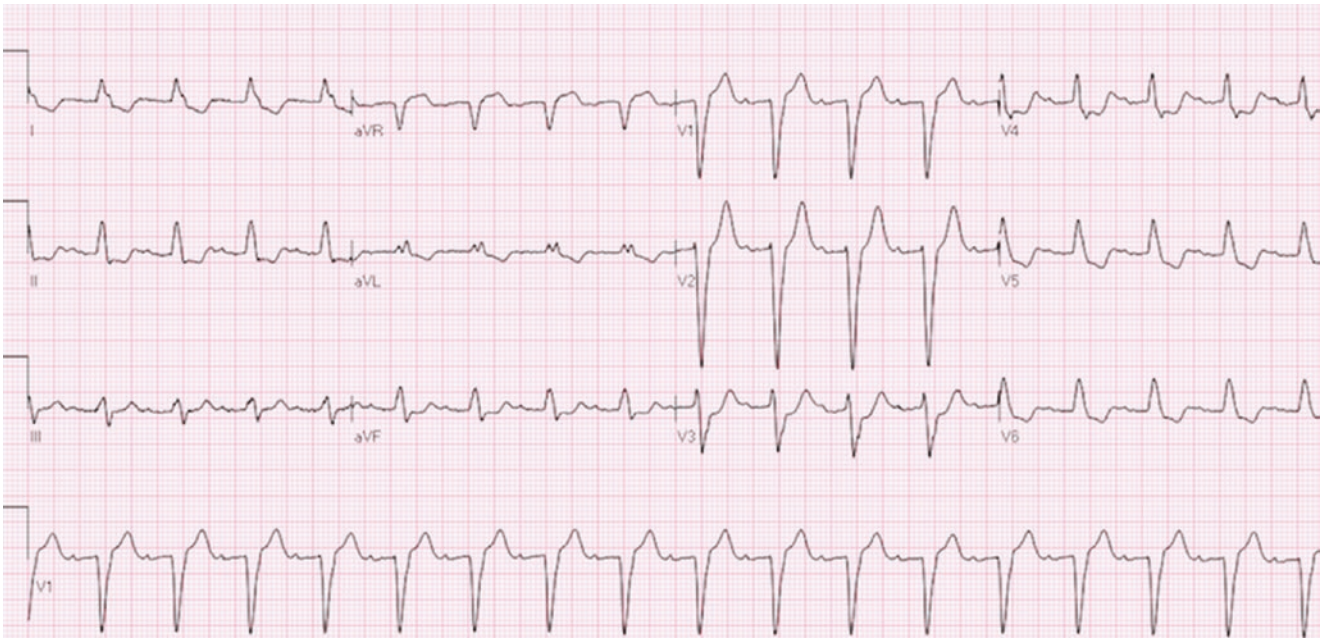

Fig. 15.4 Left bundle branch block

only limited data is available in the extremely elderly [53–56]. Ventricular assist devices have been used in refractory heart failure in younger patients. Age more than 80 is considered a relative contraindication [57].

Diastolic Heart Failure

This also referred to as heart failure with preserved ejection fraction (HFpEF). This is predominantly a disease of the elderly, especially affects females with hypertension, and often observed with obesity, diabetes and coronary artery disease [58, 59]. Among patients more than 65 years of age with congestive heart failure, 55% of all subjects and 67% of women had normal systolic function [60].

Diagnosis and Management

The diagnosis is mainly made by exclusion. Echocardiography findings are helpful to confirm and grade the diastolic dysfunction.

The ACC/AHA heart failure guidelines acknowledge that currently there are no proven therapies for HFpEF. The treatment is therefore empiric with judicious use of diuretic, control of aggravating factors like hypertension, control of atrial fibrillation and treatment of ischaemia. The very elderly should be carefully monitored when treated with diuretics as they are especially vulnerable to hypotension and renal impairment due to renal hypo-perfusion.

In SENIORS study patients with heart failure and normal ejection fraction had benefit with nebivolol therapy. This benefit was seen in all ejection fractions and in the elderly patients [45]. However the magnitude of benefit in the very elderly was small [61]. In CHARM sub-study, candesartan did not show benefit in the elderly with preserved ejection fraction [62] nor did irbesartan [63].

Box 15.3 Heart Failure

Neurohormonal blockade with beta blockers, ACE-I, ARB and aldosterone antagonists have been shown to reduce morbidity and mortality in patients with systolic heart failure.

Diastolic heart failure is especially common in the elderly – especially in females and hypertensives.

Cardiac Arrhythmia

Cardiac arrhythmia is common in the elderly. One study quotes that more than 10% of those more than 80 year age have significant arrhythmia.

Tachyarrhythmias

Atrial Fibrillation

Atrial fibrillation (Fig. 15.5) is the commonest arrhythmia in the elderly and its prevalence increases with age. In ATRIA study the prevalence of atrial fibrillation in patients over the age of 85 was 9.1% in females and 11% in males [64]. Apart from advanced age, other conditions that predispose to atrial fibrillation include hypertension, coronary artery disease, valvular heart disease (especially mitral valve disease), obesity, sleep apnoea, cardiac failure and thyroid dysfunction.

Atrial fibrillation is considered paroxysmal when the episodes last usually less than 48 h (but can be up to 7 days) and spontaneously terminate. When episodes of atrial fibrillation last longer than 7 days or cardioversion is required for termination, it is classified as persistent atrial fibrillation. Long-standing persistent atrial fibrillation is where the atrial fibrillation has been present for more than 1 year [65].

Management

It is important to control risk factors and precipitating factors such as hypertension, ischaemic heart disease and thyroid dysfunction. Infections and heart failure could precipitate an episode of atrial fibrillation. Atrial fibrillation increases the risk of thromboembolic complications, and the rapid ventricular rates could cause symptoms of palpitations and dyspnoea and can cause cardiac failure.

Thromboembolic risk is assessed by CHA_2DS_2-VASc score (see Table 15.1). With increasing score the annual thromboembolic risk rises. This annual risk is likely to be higher for the extremely elderly patients [66]. This risk could be reduced by anticoagulation. Oral anticoagulation should be considered for patients with CHA_2DS_2-VASc score of 2 or more. By virtue of their age, all extremely elderly will have a minimum score of 2. However anticoagulation predisposes the elderly patients to bleeding risk. HAS-BLED score assesses bleeding risk with anticoagulant therapy (Table 15.2). A score of more than 3 would indicate higher bleeding risk.

Traditionally anticoagulation has been done with warfarin. However warfarin therapy is difficult especially in the elderly. It needs frequent monitoring. At time of warfarin initiation, there is higher bleeding risk [67]. Multiple drug interactions also make warfarin therapy difficult. However warfarin has the advantage of longer half -life (therefore

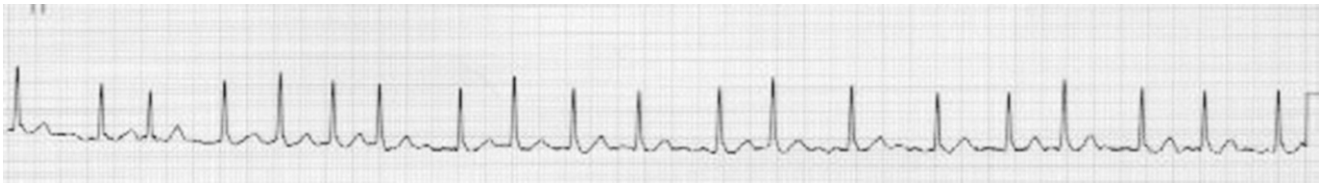

Fig. 15.5 Atrial fibrillation

Table 15.1 CHA_2DS_2 VASC score

Risk Factor	Score
Congestive heart failure or LVEF≤40%	1
Hypertension	1
Age ≥75	2
Diabetes	1
History of stroke or TIA	2
Vascular disease	1
Age 65–74	1
Sex – Female	1

Table 15.2 HAS-BLED score

	Clinical feature	Score
H	**Hypertension** (systolic BP >160)	1
A	**Abnormal liver function** (AST or ALT >3 times upper limit; bilirubin >2 times upper normal or cirrhosis) **or abnormal renal function** (creatinine >200 μmol/L or prior renal transplant) (1 point each)	1 or 2
S	**Stroke**	1
B	**Bleeding**	1
L	**Labile INR**	1
E	**Elderly** (age >65)	1
D	**Drugs** (anti-platelet agents or NSAIDS) or **alcohol abuse** (1 point each)	1 or 2

HAS-BLED score 0–2 indicates low risk

missing a dose is less harmful) and can be used in patients with significant renal impairment and can be readily reversed in the event of catastrophic bleeding.

In the last few years alternatives to warfarin have become available. These agents often classed as DOAC (direct-acting oral anticoagulants) or NOAC (novel oral anticoagulants) act as factor Xa inhibitor (rivaroxaban, apixaban, edoxaban) or as thrombin inhibitor (dabigatran). Table 15.3 gives a summary of the commonly used NOACs. They have the advantage of fixed dose and do not need monitoring. They have been shown non-inferior to warfarin in multiple studies. The mean age of the study group was around 70 years, and about a third of the patients were over 75 years [68–71]. The proportion of patients above 85 years in these studies were not available.

However as they have significant renal excretion, they cannot be used in severe renal impairment. Apixaban has only partial excretion by the kidneys. Therefore it can be used if the creatinine clearance is more than 25. Missing a single dose could expose the patient to thromboembolic risk. Reversal agent for dabigatran is already available, and other NOACs are expected to have reversal agent in the near future.

Patients should also be assessed to see whether they are best managed by a rate control strategy or rhythm control strategy. Rate control is best achieved by beta blockers or non-dihydropyridine calcium channel blockers. However if there is contraindication (especially hypotension), one may need to consider digoxin. Although digoxin controls heart rate at rest, it is often not effective during exertion.

If rate control cannot be achieved with medications (due to intolerance or inefficiency), one option would be implantation of a permanent pacemaker followed by AV nodal ablation. Although average age of all these studies were less than 75 years of age, this approach would be especially suitable for extremely elderly patients with refractory atrial fibrillation and significant symptoms attributable to rapid heart rate.

For rhythm control strategy, the commonly used antiarrhythmics are sotalol, flecainide and amiodarone. The choice of agent would depend on the patient's underlying cardiac pathology, renal and hepatic function and thyroid status. Table 15.4 summarises some relevant points. Antiarrhythmic agents could have pro-arrhythmic effects, and the extremely elderly would be especially vulnerable. Many of the elderly would also have coexisting sinus node dysfunction. Use of antiarrhythmic therapy could aggravate this and may necessitate pacemaker implantation.

Dronedarone is an amiodarone analogue which has less side effects, but it is less effective than amiodarone. Amiodarone is the most effective medication in maintaining sinus rhythm. However it has potential for significant side effects with long-term therapy and hence should be used with caution.

Pro-arrhythmic Effects of Anti-arrhythmic Medications

When sodium channel-blocking agents are used for treatment of atrial fibrillation, they could sometimes organise the rhythm to atrial flutter. Also in atrial flutter they can reduce the flutter rate and sometimes paradoxically increase the ventricular rate (by changing the atrioventricular conduction from 2:1 to 1:1). Therefore these agents like flecainide should be used with an AV nodal slowing agent (beta blocker, calcium channel blocker or digoxin).

Table 15.3 Novel oral anticoagulants (Cr Cl – creatinine clearance)

Medication	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Oral bioavailability	6.5%	80–100%	50%	62%
Renal clearance	85%	66%	27%	50%
Need to take with food	No	Yes	No	No
Time for onset of action	1–2 h	0.5–3 h	3–4 h	1–2 h
Elimination half-life	12–17 h	5–9 h for young 11–13 h for elderly	12 h	9–11 h
Drug interactions	Amiodarone Verapamil	Antifungals, protease inhibitors Dronedarone	Diltiazem	Dronedarone Quinidine
Contraindications	Cr Cl <30 ml/min	Cr Cl <30 ml/min	Cr Cl <25 ml/min	Avoid if Cr Clearance>95 ml/min or less than 15 ml/min
Dose	150 mg bd or 110 mg bd	20 mg daily(if Cr Cl >50 ml/min) If Cr Cl <50 ml/min- 15 mg daily	5 mg bd 2.5 mg bd – when 2 of the 3 following present Age ≥80, weight <60 Kg, creatinine ≥133 μmol/L(1.5 mg/dl)	Wt >60Kg and Cr Cl 50–95 ml/min- 60 mg once daily If weight <60 or Cr Cl 15-50 ml/min- 30 mg once daily

Table 15.4 Antiarrhythmic medications

Medication	Indication	Caution/contraindication	Monitor
Amiodarone After loading dose maintenance dose usually 200 mg/day	Ventricular arrhythmia Atrial fibrillation – not responding to other medications or when other medications are contraindicated	Thyroid dysfunction, bradycardia, abnormal LFT	Heart rate, TFT, LFT, lung function test- DLCO
Sotalol Dose 80–160 mg bd (max 480 mg/day) Lower dose for renal impairment	Atrial fibrillation Supraventricular tachycardia Ventricular arrhythmia	Renal impairment, bradycardia, long QT syndromes	QTc, heart rate, renal function(for dose adjustment)
Flecainide Dose 50–150 mg bd (consider use with AV nodal slowing agent)	Atrial fibrillation Atrial tachycardia Supraventricular tachycardia	Ischaemic heart disease, impaired cardiac function Brugada syndrome Severe renal impairment	Heart rate, QRS duration(avoid prolongation more than 25% of baseline QRS duration)
Quinidine In Australia not available for general use	Atrial fibrillation Uncommon ventricular arrhythmia – e.g. Brugada syndrome	Long QT syndromes	QTc, platelet count
Disopyramide 300–800 mg daily in three doses; if extended release formulation available twice daily; dose reduction for renal impairment	Atrial fibrillation	Long QT syndromes Heart failure Heart block	QTc, urinary retention, constipation, dry mouth
Procainamide (USA) Intravenous available in the USA	Atrial fibrillation Supraventricular tachycardia Resistant ventricular arrhythmia	Heart failure	SLE-like effects
Propafenone (USA) 150–300 mg tds If sustained release available twice daily	Atrial fibrillation	Heart block, heart failure Known Brugada syndrome	Avoid QRS prolongation more than 25% above baseline
Dronedarone(USA) Dose 400 mg bd	Atrial fibrillation	Hepatic dysfunction Class III/IV heart failure	Liver function, Bradycardia
Dofetilide (USA) Dose 500 mcg bd but dose reduced for renal impairment	Atrial fibrillation	Long QT syndromes Renal impairment	QTc interval

Potassium channel-blocking agents like sotalol can prolong QT interval and provoke polymorphic VT (torsade de pointes).

Some patients may require DC cardioversion to achieve sinus rhythm. However cardioversion (chemical or electrical) should only be done after a period of anticoagulation of at least 4 weeks. If the duration of therapeutic anticoagulation has been shorter, trans-oesophageal echocardiogram is necessary to exclude left atrial appendage thrombus prior to cardioversion.

Although curative procedure like pulmonary vein isolation has been done for younger patients, very little information is available about its safety and efficacy in the extremely elderly age group [72].

In rare instances where the patient has high thromboembolic risk but has prohibitive anticoagulation risk, they may be considered for left atrial appendage exclusion procedures – e.g. left atrial appendage occlusion with devices like Watchman or Amplatzer Amulet [73].

Atrial Flutter

Treatment principles of atrial flutter (Fig. 15.6) is similar to atrial fibrillation. However in fit very elderly, if there is difficulty to rate control, cavo-tricuspid isthmus ablation can be considered. This can be done with high success rate and low risk of complications [74].

Patients with supraventricular tachycardia could be treated with medical therapy. Beta blockers and calcium channel blockers may be adequate for a small number of patients. If they are not effective, antiarrhythmic agents like flecainide, sotalol or amiodarone could be used. Those who are not controlled with medications or those who are not tolerating medications could be considered for electrophysiology study and radiofrequency ablation.

Ventricular Arrhythmia

Ventricular tachycardia is classified as sustained when it lasts more than 30 s and non-sustained if it is of shorter duration. On the surface ECG, QRS complexes occur at a rapid but mostly at a regular rate. There could be precordial concordance (where from V1 to V6 all QRS complexes are positive or all are negative). Atrioventricular dissociation may be noted. Ventricular capture beats and fusion beats also help to diagnose ventricular tachycardia.

Although the incidence of ventricular arrhythmia increases with age, there is a decline in sudden cardiac death after the age of 80 due to other competing causes of death [75].

Amiodarone and sotalol are the two common medications used in the treatment for ventricular arrhythmia. Elderly have higher likelihood of bradyarrhythmia when treated with antiarrhythmic medications, and careful monitoring would be needed. Sotalol is excreted by the kidneys and would require dosage reduction in renal impairment. Sotalol therapy would also require monitoring of corrected QT interval.

Small group of extremely elderly who have ventricular tachycardia that is not controlled with medications can be considered for implantable cardioverter defibrillator (ICD). This device is often capable of terminating the ventricular tachycardia by overdrive pacing without resorting to shock (defibrillation).

In extremely small number of the very elderly whose ventricular arrhythmia is not controlled with antiarrhythmic medications and ICD therapies, may be considered for radiofrequency ablation.

Bradyarrhythmias

With ageing there is higher incidence of bradyarrhythmia. This is usually due to degenerative changes in the conduction system. This may also be aggravated by use of agents which have negative chronotropic effects like beta blockers and non-dihydropyridine calcium channel blockers. Antiarrhythmic medications like amiodarone, sotalol and flecainide also can aggravate bradyarrhythmia.

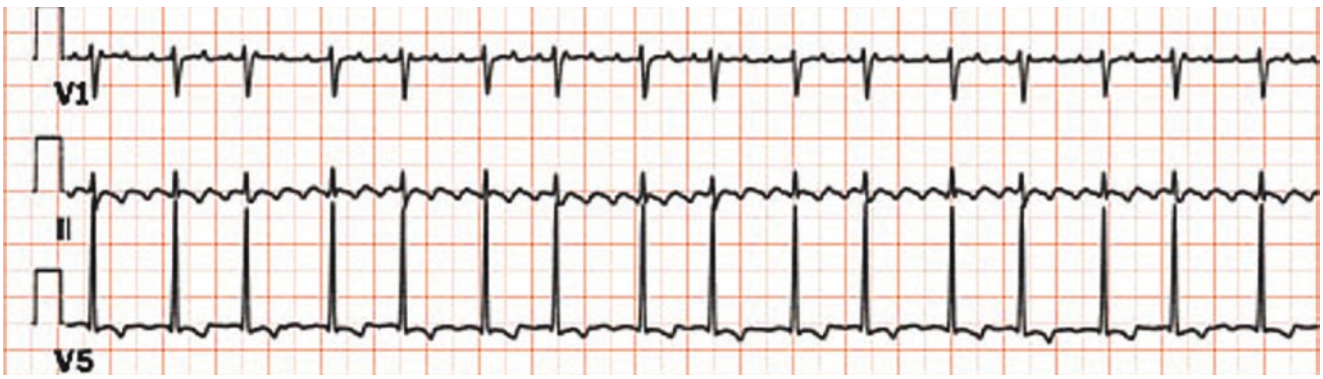

Fig. 15.6 Atrial flutter

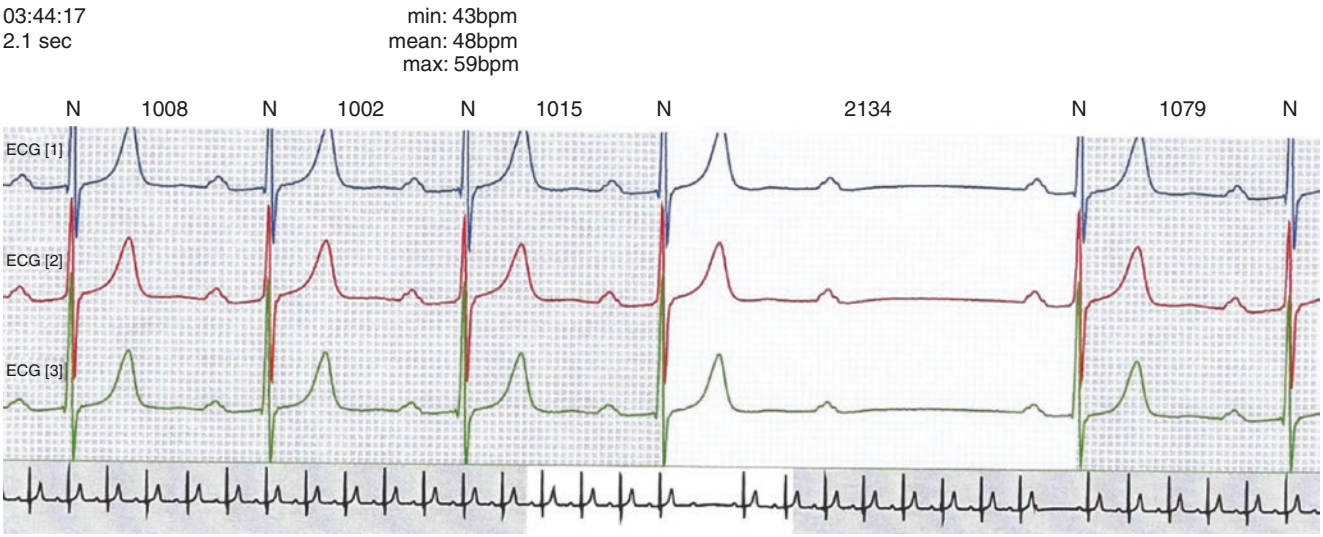

Fig. 15.7 Holter monitor strip of Wenckebach second-degree AV block

In patients with symptomatic sinus node dysfunction or atrioventricular conduction block, initial approach should be to see whether there are any correctable factors like medications. In the absence of correctable factors, those with symptoms should be considered for pacemaker implantation.

Atrioventricular conduction disturbance may present with first-, second- or third-degree heart blocks. In first-degree AV block, there is PR prolongation to more than 0.2 s. This may be due to medications or high vagal tone. When it is noted on an ECG if the patient is asymptomatic, no further measures need to be taken. However if they have symptoms of fatigue, pre-syncope or syncope, further assessment like Holter monitor or exercise testing may be necessary to exclude coexisting higher-degree AV block.

The second-degree heart block is of two types. In Wenckebach block (also called Mobitz type I), there is progressive prolongation of the PR interval until a P wave is not conducted (Fig. 15.7). If this is the only abnormality, it is usually due to high vagal tone and is often not serious. In the benign form, with activity the conduction should improve to 1:1 conduction.

The Mobitz II heart block manifests as intermittently blocked P wave with fixed PR interval at other times. This usually indicates more significant conduction system disease, and the patients would require Holter monitoring and exercise testing to exclude higher-degree heart block.

In complete heart block, there is no conduction from the atria to the ventricles. There is a regular escape rhythm from the AV node or ventricle which is much slower than the atrial rate. Commonest cause of heart block is age-related degenerative changes. Indication for PPM implant is outlined in Table 15.5, and the contraindications are listed below the table.

Box 15.4 Cardiac Arrhythmias

Oral anticoagulation should be considered for patients with atrial fibrillation and CHA_2DS_2-VASc score of 2 or more.. However their bleeding risk should also be factored in this decision-making process.

When treating patients with antiarrhythmic medications, they need to be monitored for bradycardia and drug-induced pro-arrhythmia.

Valvular Heart Disease

Aortic stenosis and mitral regurgitation are the commonest valvular dysfunctions encountered in the very elderly in the western world.

Aortic Stenosis

The commonest cause of aortic stenosis in the very elderly is calcific degeneration of the aortic valve. Prevalence of aortic stenosis increases with age. The development of aortic stenosis is a slow process over many years. Rarely presentation is with angina, syncope or heart failure. Clinical symptoms and signs of aortic stenosis are less sensitive and less specific in the elderly when compared to younger patients [76]. Disease progression could also happen more rapidly in the older patients [77]. Echocardiography confirms the diagnosis and helps to assess severity.

Table 15.5 Pacemaker indications above and contraindications listed below

	Class I indication	Class II indication
Sinus node dysfunction	Sinus bradycardia with symptoms due to bradycardia (HR <40 or frequent or long sinus pauses) Symptomatic chronotropic incompetence (unable to get heart rate up to 85% of predicted maximum) Symptomatic bradycardia due to medications but with the need to continue medications	Sinus bradycardia HR <40 with symptoms suggestive of bradycardia Sinus node dysfunction (at electrophysiology study) in a patient with unexplained syncope Chronic heart rates <40 beats per minute while awake in a minimally symptomatic patient
Heart block	Complete (third-degree) AV block with or without symptoms Advanced second-degree AV block Symptomatic second-degree AV block, Mobitz type II Symptomatic second-degree AV block, Mobitz type I (Wenckebach) Second degree AV block, Mobitz type II with a widened QRS or chronic bifascicular block, with or without symptoms Exercise-induced second- or third-degree AV block (in the absence of myocardial ischaemia)	Asymptomatic Mobitz II second-degree AV block with a narrow QRS interval First-degree AV block when there is hemodynamic compromise because of effective AV dissociation secondary to a very long PR interval. Bifascicular or trifascicular block or Left bundle branch block associated with syncope that can be attributed to transient complete heart block

Pacemaker is not indicated when
- Sinus bradycardia without significant symptoms
- Sino-atrial block or sinus arrest without significant symptoms
- Asymptomatic pauses during atrial fibrillation
- Asymptomatic bradycardia during sleep
- Asymptomatic second-degree Wenckebach AV block
- Bifascicular block without syncope or other symptoms of intermittent AV block
- Reversible AV block – e.g. due to electrolyte abnormalities, Lyme disease, sleep apnoea, enhanced vagal tone, atrioventricular block associated with drugs such as beta blockers, calcium channel blockers(when these medications are not essential)

Management

Surgical mortality of aortic valve surgery also increases with age. Perioperative mortality of aortic valve surgery is about 1.3% in those younger than 70 years of age. It increases to 5% in 80–85-year-olds and to 10% in those older than 90 [78, 79]. TAVI has been an alternative procedure to open surgery and has been available in the last few years. It is especially an option for the very elderly with co-morbidities that increase surgical risk.

TAVI usually involves delivering the valve mounted on a large stent via the femoral artery. Rarely delivery using alternative arterial access and trans-apical implantation has been carried out on those who do not have suitable vascular access to the large-calibre delivery system from the femoral route. TAVI procedure avoids sternotomy and thereby reduces morbidity of open surgery. However it has the potential for vascular injury, stroke and impingement on conduction system requiring permanent pacemaker and acute kidney injury due to contrast use. Incidence of vascular injury increases with age [80]. Currently TAVI is indicated in elderly patients who have predicted perioperative mortality of more than 20% with the EuroSCORE or >10% with the STS score, as long as life expectancy is a year or more [81].

Aortic Regurgitation

The commonest cause of isolated aortic regurgitation in the very elderly would be secondary to aortic annular dilatation. Echocardiography confirms the diagnosis. It also helps in assessing severity of regurgitation and to assess for potential causes and left ventricular function.

Management

Medical management would include vasodilator therapy and diuretics if needed. Surgical treatment is considered when severe aortic regurgitation is present with impaired left ventricular systolic function or when patients have severe aortic regurgitation with symptoms attributable to it. However in the very elderly, the co-morbidities may preclude surgical option. In a very small group of patients with suitable anatomy, TAVI may be an option [82].

Mitral Regurgitation

Mitral regurgitation of more than mild intensity is present in 2–3% of population.

Mitral regurgitation (MR) is usually symptomatic when severe, and it may take many years to develop symptoms. Patients may present with dyspnoea and fatigue. There may be features of left ventricular failure. Sometimes patients may present with atrial fibrillation.

Diagnosis

CXR may show cardiomegaly and pulmonary congestion; there may be straightening of the left heart border due to left atrial enlargement. Echocardiogram is the most useful diagnostic tool. It helps to assess severity of MR and to evaluate the mitral apparatus.

Management

In patients with functional and ischaemic mitral regurgitation, preload reduction may be beneficial [83]. Patients with systolic dysfunction would benefit by standard heart failure therapies. Patients with severe mitral regurgitation and symptoms or with ejection fraction less than 60% or left ventricular end-systolic dimension of more than 40 mm may be considered for intervention. The surgery may involve mitral valve repair, especially in those with mitral valve prolapse or mitral valve replacement.

However in very elderly due to co-morbidities, surgical option may not be appropriate. Recently catheter-based endovascular therapeutic options have been used in the very elderly with high surgical risk. A clip which helps apposition valve leaflet edges (MitraClip – Abbot Vascular) has been used in number of studies and has shown promising results [84, 85].

Mitral Stenosis

Mitral stenosis in the vey elderly is usually a consequence of rheumatic heart disease. Less commonly it could be due to severe mitral annular calcification.

Diagnosis and Management

Chest X-ray may show left atrial enlargement and pulmonary congestion. Echocardiography confirms the diagnosis and helps to assess the severity by measurement of pressure gradient across the valve and by calculated valve area. Echo also helps to assess the valve anatomy and suitability for valvuloplasty or need for surgery. Patients with severe mitral stenosis and symptoms and those with pulmonary hypertension with pressures more than 50 mm Hg are considered for intervention.

Infective Endocarditis

Introduction

Due to increased number of elderly having pacemakers and prosthetic valves, the potential pool for endocarditis has been increasing. Central venous catheters and other intravascular devices would also contribute to this. This has been noted in multiple studies. In a 1-year study in France, the peak incidence of endocarditis was in the 70–80-year age group, and there were also a substantial number of patients in their 80s and 90s [86].

In a prospective international collaboration, the elderly frequently reported a hospitalisation or a procedure prior to IE. Diabetes and gastroenterological and genitourinary cancers were main predisposing factors. *S. aureus* was the commonest organism in the elderly. *S. bovis* and enterococci were also more prevalent. The elderly had lower rates of embolism and immune-mediated phenomena. The elderly had fewer vegetations (Fig. 15.8) on the echocardiogram, but they had higher incidence of abscesses. Fewer elderly underwent cardiac surgery, and the in-hospital mortality in the over 65-year-olds was twice that of younger patients (24.9% vs. 12.8%). However in this study there was no breakdown of the age of the elderly to get further information about the extremely elderly [87].

Prevention of Infective Endocarditis

The ACC/AHA guidelines were revised in 2007. The current guideline recommends antibacterial prophylaxis for patients with prosthetic heart valves, prior valve repair, prior history of endocarditis, cyanotic congenital heart disease and repaired and unrepaired congenital heart disease. It may also be reasonable to consider prophylaxis in cardiac transplantation recipients who develop cardiac valvulopathy. Antibiotic regimen would depend on the type of surgical or invasive procedure. Table 15.6 gives recommendation for dental procedures.

For urinary tract procedures, amoxicillin and ampicillin are the preferred agents for enterococcal prophylaxis. Vancomycin can be considered if the patients are unable to tolerate ampicillin. If infection is caused by a known or suspected strain of resistant enterococcus, consultation with an infectious diseases expert is recommended. Skin and subcutaneous surgery should be covered with anti-staphylococcal penicillin or a cephalosporin. Vancomycin or clindamycin may be administered to patients unable to take penicillin or who are known or suspected to have an infection caused by a methicillin-resistant strain of staphylococcus.

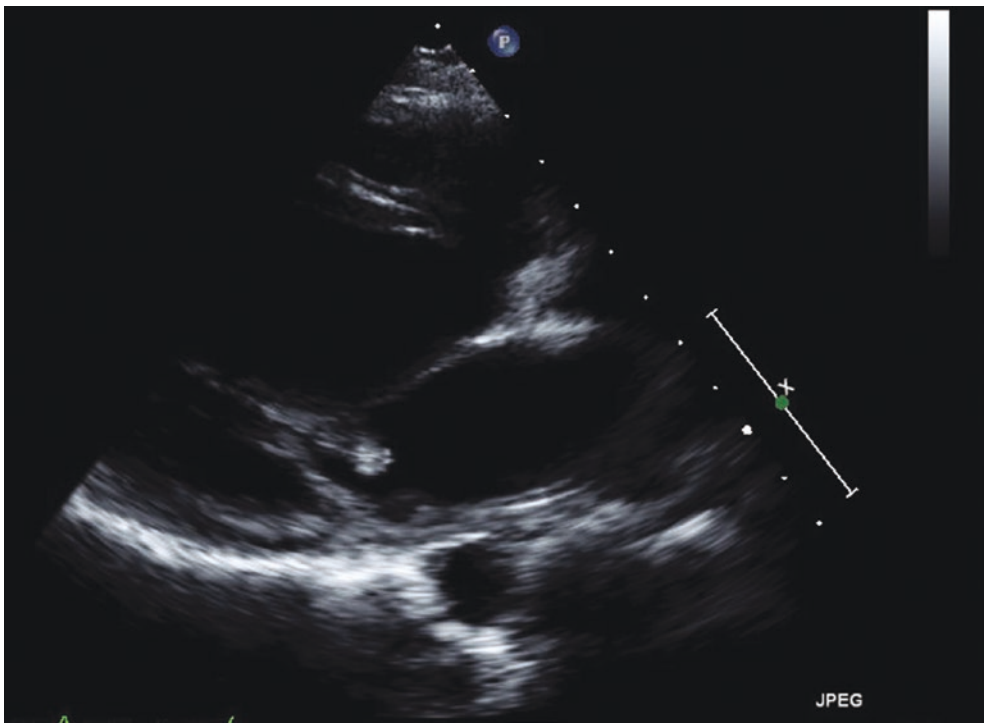

Fig. 15.8 Echocardiogram parasternal long-axis view showing a vegetation on the atrial aspect of the anterior mitral leaflet

Table 15.6 Antibiotic prophylaxis for dental procedures

	Agent	Dose (to be taken 30–60 min before the procedure)
Oral If cannot take oral	Amoxil Cephalexin Ampicillin Cefazolin or ceftriaxone	2 g 2 g 2 g IV or IM 1 g IV or IM
For those with penicillin allergy If cannot take oral	Clindamycin Azithromycin Clindamycin	600 mg 500 mg 600 mg IV or IM

Diagnosis

Patients at risk of endocarditis presenting with unexplained fever for more than 48 h should have two sets of blood cultures. Diagnosis is often made when positive blood cultures are obtained in a susceptible patient. Transthoracic and transoesophageal echocardiography help to visualise the valve. Modified Duke criteria is used for diagnosis [88]. Endocarditis is diagnosed when 1 major criterion and 1 minor criterion or 3 minor criteria are present.

Management

Antibiotic therapy is guided by the valve involved, whether it is a native valve or prosthetic valve and the type of organism. An infectious disease specialist advice should be sought.

Once the blood cultures are obtained if streptococcal infection is suspected, therapy is started with intravenous penicillin (or ampicillin) and aminoglycoside (gentamicin). If staphylococcal infection is suspected, therapy is commenced with flucloxacillin or vancomycin (in patients allergic to penicillin or with MRSA infection) and gentamicin. Once the pathogen is identified, therapy may be refined. Usual duration of intravenous therapy is 4–6 weeks. Careful monitoring of renal function and clinical progress is essential. When aminoglycosides and vancomycin are used, serum levels need monitoring.

Small group of elderly patients may have culture-negative endocarditis. This may be due to fastidious organisms like HACEK organisms (*Haemophilus aphrophilus*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella kingae*) or fungal infection. More commonly it may be due to previous antibiotic therapy or inadequate blood culture. Serological testing and PCR on blood sample may help with diagnosis of fastidious organisms. If IE is strongly suspected, empiric antibiotic therapy with careful clinical monitoring is necessary.

Surgery is considered in the following situations.

Native valve endocarditis – evidence of severe valve dysfunction causing heart failure, abscess formation or heart block, embolic manifestations, infection with fungal or other highly resistant organisms, valve malfunction, paravalvular leak, abscess formation, persistent bacteraemia and resistant organism are some of the indications for surgical intervention [89].

Prognosis

Elderly often have worse prognosis. This is partly due to delay in diagnosis due to atypical presentation [90]. Patients with *Staphylococcus aureus* or fungal infection and those with neurological manifestations have worse prognosis.

Box 15.5 Infective endocarditis
Infective endocarditis in the elderly may have atypical presentation with features of anaemia, weight loss, heart failure or fatigue.
Modified Duke criteria is used for diagnosis of infective endocarditis.

Multiple Choice Questions

1. Which of the following statements regarding hypertension is true?
   A. In the very elderly patients the target systolic blood pressure should be 130 mm Hg or less.
   B. Resistant hypertension is when maximal doses of two medications are not adequate to control the blood pressure.
   C. Systolic hypertension in the elderly has been associated with cognitive decline.
   D. Combination therapy should be avoided in the elderly.
2. Which of the following statements regarding ischaemic heart disease is false?
   A. Compared to younger patients, elderly have more complex coronary artery disease.
   B. Elderly patients presenting with NSTEMI may be treated with percutaneous intervention or with thrombolytic therapy.
   C. In octogenarians left main stent implantation has worse outcome when compared to bypass surgery.
   D. Prasugrel is best avoided in patients older than 75 years.
3. With regard to heart failure, which of the following is false?
   A. Elderly patients with heart failure may present with confusion or weakness.
   B. Beta blockers have been shown to reduce mortality.
   C. Hydralazine and nitrates may be alternative to patients who cannot take and ACE inhibitor or ARB.
   D. Digoxin therapy has been shown to reduce mortality in heart failure.
4. With regard to atrial fibrillation/flutter, which of the following is false?
   A. Elderly should not be treated with novel oral anticoagulants (NOACs).
   B. Medical therapy of atrial flutter is similar to that of atrial fibrillation.
   C. Flecainide should be combined with an AV nodal blocking agent.
   D. Sotalol dosage will be influenced by the patient's renal function.

Answers
1. C
2. C
3. D
4. A

References

1. http://www.abs.gov.au/AUSSTATS.
2. http://www.census.gov/population/projections/.
3. Rich MW, Chyun DA, Skolnick AH, Alexander KP, Forman DE, Kitzman DW, et al. Knowledge gaps in cardiovascular care of the older adult population: a scientific statement from the American Heart Association, American College of Cardiology, and American Geriatrics Society. J Am Coll Cardiol. 2016;67:2419.
4. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart Association statistics committee and stroke statistics subcommittee. Circulation. 2009;119:e21–181.
5. Denardo SJ, Gong Y, Nichols WW, Messerli FH, Bavry AA, Cooper-Dehoff RM, et al. Blood pressure and outcomes in very old hypertensive coronary artery disease patients: an INVEST substudy. Am J Med. 2010;123:719–26.
6. Mathew J, Sleight P, Lonn E, Johnstone D, Pogue J, Yi Q, et al. Reduction of cardiovascular risk by regression of electrocardiographic markers of left ventricular hypertrophy by the angiotensin-converting enzyme inhibitor ramipril. Circulation. 2001;104:1615–21.
7. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. N Engl J Med. 2008;358:1887–98.
8. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). JAMA. 1991;265:3255–64.
9. Bohm M, Schumacher H, Leong D, Mancia G, Unger T, Schmieder R, et al. Systolic blood pressure variation and mean heart rate is associated with cognitive dysfunction in patients with high cardiovascular risk. Hypertension. 2015;65:651–61.
10. Aronow WS, Fleg JL, Pepine CJ, Artinian NT, Bakris G, Brown AS, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. J Am Coll Cardiol. 2011;57:2037–114.
11. Jafar TH, Schmid CH, Landa M, Giatras I, Toto R, Remuzzi G, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data. Ann Intern Med. 2001;135:73–87.

12. Sarafidis PA, Bakris GL. State of hypertension management in the United States: confluence of risk factors and the prevalence of resistant hypertension. J Clin Hypertens (Greenwich). 2008;10:130–9.
13. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2012;60:e44–e164.
14. Kones R. Recent advances in the management of chronic stable angina II. Anti-ischemic therapy, options for refractory angina, risk factor reduction, and revascularization. Vasc Health Risk Manag. 2010;6:749–74.
15. Stone PH, Gratsiansky NA, Blokhin A, Huang IZ, Meng L. Antianginal efficacy of ranolazine when added to treatment with amlodipine: the ERICA (efficacy of Ranolazine in chronic angina) trial. J Am Coll Cardiol. 2006;48:566–75.
16. Rich MW, Crager M, McKay CR. Safety and efficacy of extended-release ranolazine in patients aged 70 years or older with chronic stable angina pectoris. Am J Geriatr Cardiol. 2007;16:216–21.
17. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2014;130:1749–67.
18. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360:961–72.
19. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Stahle E, Colombo A, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the synergy between percutaneous coronary intervention with TAXUS and cardiac surgery (SYNTAX) trial. Circulation. 2010;121:2645–53.
20. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, et al. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med. 2012;367:2375–84.
21. Ronak Rajani ML, Dixon G, Khawaja MZ, Hildick-Smith D, Holmberg S, de Belder A. Evolving trends in percutaneous coronary intervention. Br J Cardiol. 2011;18:73–6.
22. Shanmugam VB, Harper R, Meredith I, Malaiapan Y, Psaltis PJ. An overview of PCI in the very elderly. J Geriatr Cardiol. 2015;12:174–84.
23. Vlaar PJ, Lennon RJ, Rihal CS, Singh M, Ting HH, Bresnahan JF, et al. Drug-eluting stents in octogenarians: early and intermediate outcome. Am Heart J. 2008;155:680–6.
24. de Belder A, de la Torre Hernandez JM, Lopez-Palop R, O'Kane P, Hernandez Hernandez F, Strange J, et al. A prospective randomized trial of everolimus-eluting stents versus bare-metal stents in octogenarians: the XIMA trial (Xience or vision stents for the Management of Angina in the elderly). J Am Coll Cardiol. 2014;63:1371–5.
25. Conrotto F, Scacciatella P, D'Ascenzo F, Chieffo A, Latib A, Park SJ, et al. Long-term outcomes of percutaneous coronary interventions or coronary artery bypass grafting for left main coronary artery disease in octogenarians (from a drug-eluting stent for LefT main artery registry substudy). Am J Cardiol. 2014;113:2007–12.
26. Ghanta RK, Shekar PS, McGurk S, Rosborough DM, Aranki SF. Nonelective cardiac surgery in the elderly: is it justified? J Thoracic Cardiovasc Surg. 2010;140:103–9, 9.e1.
27. Bardakci H, Cheema FH, Topkara VK, Dang NC, Martens TP, Mercando ML, et al. Discharge to home rates are significantly lower for octogenarians undergoing coronary artery bypass graft surgery. Ann Thorac Surg. 2007;83:483.
28. Conaway DG, House J, Bandt K, Hayden L, Borkon AM, Spertus JA. The elderly: health status benefits and recovery of function one year after coronary artery bypass surgery. J Am Coll Cardiol. 2003;42:1421–6.
29. Huber CH, Goeber V, Berdat P, Carrel T, Eckstein F. Benefits of cardiac surgery in octogenarians--a postoperative quality of life assessment. Eur J Cardiothorac Surg. 2007;31:1099–105.
30. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol. 2014;64:e139–228.
31. Brieger D, Eagle KA, Goodman SG, Steg PG, Budaj A, White K, et al. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. Chest. 2004;126:461–9.
32. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2007;357:2001–15.
33. Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet. 2002;359:189–98.
34. White HD, Barbash GI, Califf RM, Simes RJ, Granger CB, Weaver WD, et al. Age and outcome with contemporary thrombolytic therapy. Results from the GUSTO-I trial. Global Utilization of Streptokinase and TPA for Occluded coronary arteries trial. Circulation. 1996;94:1826–33.
35. Van de Werf F, Barron HV, Armstrong PW, Granger CB, Berioli S, Barbash G, et al. Incidence and predictors of bleeding events after fibrinolytic therapy with fibrin-specific agents: a comparison of TNK-tPA and rt-PA. Eur Heart J. 2001;22:2253–61.
36. de Boer MJ, Ottervanger JP, van 't Hof AW, Hoorntje JC, Suryapranata H, Zijlstra F. Reperfusion therapy in elderly patients with acute myocardial infarction: a randomized comparison of primary angioplasty and thrombolytic therapy. J Am Coll Cardiol. 2002;39:1723–8.
37. Bueno H, Betriu A, Heras M, Alonso JJ, Cequier A, Garcia EJ, et al. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) randomized trial and pooled analysis with previous studies. Eur Heart J. 2011;32:51–60.
38. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J. 2006;27:779–88.
39. Alexander KP, Newby LK, Armstrong PW, Cannon CP, Gibler WB, Rich MW, et al. Acute coronary care in the elderly, part II: ST-segment-elevation myocardial infarction: a scientific statement for healthcare professionals from the American Heart Association Council on clinical cardiology: in collaboration with the Society of Geriatric Cardiology. Circulation. 2007;115:2570–89.
40. Dzavik V, Sleeper LA, Cocke TP, Moscucci M, Saucedo J, Hosat S, et al. Early revascularization is associated with improved survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock: a report from the SHOCK trial registry. Eur Heart J. 2003;24:828–37.

41. Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. Am Heart J. 2001;142:748–55.
42. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. J Am Coll Cardiol. 1993;22:6a–13a.
43. Gambassi G, Lapane KL, Sgadari A, Carbonin P, Gatsonis C, Lipsitz LA, et al. Effects of angiotensin-converting enzyme inhibitors and digoxin on health outcomes of very old patients with heart failure. SAGE Study Group. Systematic assessment of geriatric drug use via epidemiology. Arch Intern Med. 2000;160:53–60.
44. Pfeffer MA, Swedberg K, Granger CB, Held P, McMurray JJ, Michelson EL, et al. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-overall programme. Lancet. 2003;362:759–66.
45. Flather MD, Shibata MC, Coats AJ, Van Veldhuisen DJ, Parkhomenko A, Borbola J, et al. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). Eur Heart J. 2005;26:215–25.
46. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone evaluation study investigators. N Engl J Med. 1999;341:709–17.
47. Zannad F, McMurray JJ, Krum H, van Veldhuisen DJ, Swedberg K, Shi H, et al. Eplerenone in patients with systolic heart failure and mild symptoms. N Engl J Med. 2011;364:11–21.
48. Pitt B, Remme W, Zannad F, Neaton J, Martinez F, Roniker B, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med. 2003;348:1309–21.
49. Cohn JN, Archibald DG, Ziesche S, Franciosa JA, Harston WE, Tristani FE, et al. Effect of vasodilator therapy on mortality in chronic congestive heart failure. Results of a veterans administration cooperative study. N Engl J Med. 1986;314:1547–52.
50. Bohm M, Robertson M, Ford I, Borer JS, Komajda M, Kindermann I, et al. Influence of cardiovascular and noncardiovascular co-morbidities on outcomes and treatment effect of heart rate reduction with Ivabradine in stable heart failure (from the SHIFT trial). Am J Cardiol. 2015;116:1890–7.
51. Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. N Eng J Med. 1997;336:525–33.
52. Rich MW, McSherry F, Williford WO, Yusuf S. Effect of age on mortality, hospitalizations and response to digoxin in patients with heart failure: the DIG study. J Am Coll Cardiol. 2001;38:806.
53. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346:1845–53.
54. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140–50.
55. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005;352:1539–49.
56. Kron J, Aranda JM Jr, Miles WM, Burkart TA, Woo GW, Saxonhouse SJ, et al. Benefit of cardiac resynchronization in elderly patients: results from the multicenter InSync randomized clinical evaluation (MIRACLE) and multicenter InSync ICD randomized clinical evaluation (MIRACLE-ICD) trials. J Interv Card Electrophysiol. 2009;25:91–6.
57. Peura JL, Colvin-Adams M, Francis GS, Grady KL, Hoffman TM, Jessup M, et al. Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. Circulation. 2012;126:2648–67.
58. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2013;62:e147–239.
59. Paulus WJ, Tschope C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. J Am Coll Cardiol. 2013;62:263–71.
60. Burlew BS. Diastolic dysfunction in the elderly--the interstitial issue. Am J Geriatr Cardiol. 2004;13:29–38.
61. Kitzman DW, Daniel KR. Diastolic heart failure in the elderly. Heart Fail Clin. 2007;3:437–53.
62. Yusuf S, Pfeffer MA, Swedberg K, Granger CB, Held P, McMurray JJ, et al. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-preserved trial. Lancet. 2003;362:777–81.
63. Massie BM, Carson PE, McMurray JJ, Komajda M, McKelvie R, Zile MR, et al. Irbesartan in patients with heart failure and preserved ejection fraction. N Engl J Med. 2008;359:2456–67.
64. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and risk factors in atrial fibrillation (ATRIA) study. JAMA. 2001;285:2370–5.
65. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010;31:2369–429.
66. Marinigh R, Lip GY, Fiotti N, Giansante C, Lane DA. Age as a risk factor for stroke in atrial fibrillation patients: implications for thromboprophylaxis. J Am Coll Cardiol. 2010;56:827–37.
67. Hylek EM, Evans-Molina C, Shea C, Henault LE, Regan S. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation. 2007;115:2689–96.
68. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139–51.
69. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883–91.
70. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981–92.
71. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, et al. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2013;369:2093–104.
72. Yamada T, Kay GN. Catheter ablation of atrial fibrillation in the elderly. Pacing Clin Electrophysiol. 2009;32:1085–91.
73. Gafoor S, Franke J, Bertog S, Boehm P, Heuer L, Gonzaga M, et al. Left atrial appendage occlusion in octogenarians: short-term and 1-year follow-up. Catheter Cardiovasc Interv. 2014;83:805–10.
74. Zado ES, Callans DJ, Gottlieb CD, Kutalek SP, Wilbur SL, Samuels FL, et al. Efficacy and safety of catheter ablation in octogenarians. J Am Coll Cardiol. 2000;35:458–62.
75. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol. 2006;48:e247–346.

76. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2014;63:2438–88.
77. Munt B, Legget ME, Kraft CD, Miyake-Hull CY, Fujioka M, Otto CM. Physical examination in valvular aortic stenosis: correlation with stenosis severity and prediction of clinical outcome. Am Heart J. 1999;137:298–306.
78. Sawaya F, Stewart J, Babaliaros V. Aortic stenosis: who should undergo surgery, transcatheter valve replacement? Cleve Clin J Med. 2012;79:487–97.
79. Assmann A, Minol JP, Mehdiani A, Akhyari P, Boeken U, Lichtenberg A. Cardiac surgery in nonagenarians: not only feasible, but also reasonable? Interact Cardiovasc Thorac Surg. 2013;17:340–3. discussion 3
80. Yamamoto M, Meguro K, Mouillet G, Bergoend E, Monin JL, Lim P, et al. Comparison of effectiveness and safety of transcatheter aortic valve implantation in patients aged >/=90 years versus <90 years. Am J Cardiol. 2012;110:1156–63.
81. Vahanian A, Alfieri O, Al-Attar N, Antunes M, Bax J, Cormier B, et al. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European association of cardio-thoracic surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J. 2008;4:193–9.
82. Roy DA, Schaefer U, Guetta V, Hildick-Smith D, Mollmann H, Dumonteil N, et al. Transcatheter aortic valve implantation for pure severe native aortic valve regurgitation. J Am Coll Cardiol. 2013;61:1577–84.
83. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RW, Sonnenblick EH. Mechanism of reduction of mitral regurgitation with vasodilator therapy. Am J Cardiol. 1979;43:773–7.
84. Fam NP, Ross HJ, Verma S. Mitral clip - looking back and moving forward. Curr Opin Cardiol. 2016;31:169–75.
85. Downs EA, Lim DS, Saji M, Ailawadi G. Current state of transcatheter mitral valve repair with the MitraClip. Ann Cardiothorac Surg. 2015;4:335–40.
86. Hoen B, Alla F, Selton-Suty C, Beguinot I, Bouvet A, Briancon S, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. JAMA. 2002;288:75–81.
87. Durante-Mangoni E, Bradley S, Selton-Suty C, Tripodi MF, Barsic B, Bouza E, et al. Current features of infective endocarditis in elderly patients: results of the international collaboration on endocarditis prospective cohort study. Arch Intern Med. 2008;168:2095–103.
88. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000;30:633–8.
89. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2006;48:e1–148.
90. Dhawan VK. Infective endocarditis in elderly patients. Curr Infect Dis Rep. 2003;5:285–92.

Kidney Diseases in the Elderly

16

Sarah So, Jessica Stevenson, and Vincent Lee

General Considerations

The Ageing Kidney

Renal ageing is associated with structural and physiological changes, with a decline in glomerular filtration rate, the number of functional nephrons and ability to maintain usual function in response to changes [1]. These age-related changes, termed organ senescence, are thought to be mediated by ischaemic injury to nephrons from arteriolosclerosis of the small arteries, but not thought to represent true organ pathology [2].

'Nephrosclerosis' describes the constellation of microscopic ageing-related changes. Characteristic findings include glomerulosclerosis (focal and global, but not segmental), tubular atrophy with interstitial fibrosis (infiltrating interstitial cells consisting of myofibroblasts and macrophages) and vascular sclerosis (fibrointimal thickening) [3, 4] (Table 16.1).

Renal ageing is also associated with altered vasculature structure, responsiveness and autoregulation. Arterioles have smaller cross-sectional areas, and an older kidney has a higher number of aglomerular arterioles, afferent and efferent arterioles that communicate directly with each other resulting in a sclerotic glomerulus [7]. Dysregulated blood flow, with impaired vasodilatation and increased sensitivity to vasoconstrictor stimuli, has also been noted [3, 5, 6, 8–11].

Table 16.1 Histologic changes in the ageing kidney

Glomerulus	Glomerulosclerosis Thickening of the basement membrane Increase in mesangial matrix
Tubulointerstitium	Tubulointerstitial fibrosis Decrease in tubular number Decrease in tubular volume and length
Vascular	Arteriolosclerosis Hyaline deposition Higher numbers of aglomerular arterioles

Information sources: Glassock and Rule [5], Hill et al. [6], Karam and Tuazon [3], Zhou et al. [4]

Furthermore, the renal tubules become less efficient at electrolyte and fluid handling. The ability of the kidney to concentrate the urine diminishes with age, due to changes such as reduced expression of channels instrumental for water and sodium chloride reabsorption and reduced hypertonicity of the medulla relative to younger individuals [12–14]. This accounts for increased susceptibility to volume depletion. Potassium handling is also altered, with decreased transtubular potassium gradients resulting in a failure to increase distal tubular potassium excretion in response to hyperkalaemia [15].

Acute Kidney Injury

Elderly patients are at high risk for development of acute kidney injury (AKI), also a risk factor for progression of CKD. AKI is associated with a very high rate of mortality and morbidity. The outcomes of elderly patients who develop AKI requiring dialysis are uniformly poor, with reported mortality rates ranging from 31% to 80% [16, 17]. The most important risk factor for the development of AKI is the presence of comorbidities, particularly CKD. Hypertension, diabetes mellitus, atherosclerosis and heart failure are all conditions more commonly encountered amongst older individuals that can directly or indirectly increase

S. So
Renal Department, Westmead Hospital, University of Sydney, Westmead, NSW, Australia

Sydney Medical School, Westmead, The University of Sydney, Westmead, NSW, Australia

J. Stevenson
Westmead Hospital, Westmead, NSW, Australia

V. Lee (✉)
Renal Department, Westmead Hospital, University of Sydney, Westmead, NSW, Australia

Sydney Medical School, The University of Sydney, Westmead, NSW, Australia

Westmead Hospital, Westmead, NSW, Australia

Norwest Private Hospital, Bella Vista, NSW, Australia
e-mail: vincent.lee@sydney.edu.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_16

the risk for AKI [18, 19]. For example, atherosclerosis and hypertension impair the autoregulatory capacity of the kidney to maintain perfusion in the setting of hypotension [19]. Causes of AKI in the elderly are multifactorial. Conditions seen more commonly in the elderly such as prostatic hypertrophy or congestive cardiac failure can induce AKI through obstructive or prerenal mechanisms. The elderly are also predisposed to dehydration, which may be due to physiological age-related changes or due to decreased thirst sensation or a reduced ability to access fluids [19, 20]. Furthermore, the effects of polypharmacy and drug toxicity exacerbate susceptibility to AKI. Nephrotoxic drugs including nonsteroid anti-inflammatories are commonly co-prescribed in older adults for comorbidities including arthritis [21] (Table 16.2). Age-related changes in renal function and pharmacokinetics increase exposure to small molecules and the risk for toxicities, and ageing-related structural changes preclude compensation for acute decreases in GFR [22]. Contrast-induced nephropathy may develop after contrast-enhanced imaging or angiographic procedures and represents one of the most common forms of iatrogenic AKI [21]. Age older than 65 is also a risk factor for non-recovery from AKI and even progression to CKD [21, 23]. Regenerative potential after AKI decreases with age through mechanisms such as increased oxidative stress and decreased cellular proliferation rates [20, 24, 25].

Table 16.2 Common nephrotoxic drugs in the elderly

Drug	Mechanism of renal injury
Analgesia	
Nonsteroidal anti-inflammatory drugs	Acute or chronic interstitial nephritis Altered intraglomerular haemodynamics (inhibition of prostaglandins resulting in lack of vasodilatation of afferent arterioles) Glomerulonephritis (minimal change disease)
Antimicrobials	
Beta-lactams (penicillins and cephalosporins)	Acute interstitial nephritis
Aminoglycosides	Tubular cell toxicity
Cardiovascular agents	
Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers	Altered intraglomerular haemodynamics (inhibits vasoconstriction of efferent arterioles)
Statins	Rhabdomyolysis
Contrast dye	Tubular cell toxicity
Diuretics	
Loop diuretics, thiazide diuretics	Prerenal (intravascular depletion)
Reflux treatments	
Proton pump inhibitors	Acute interstitial nephritis
Osteoporosis treatment	
Pamidronate	Glomerulonephritis (minimal change) and interstitial nephritis
Zoledronate	Tubular cell toxicity

Information sources: Geevasinga et al. [28], Graham et al. 2004 [29], Naughton [30], Markowitz and Perazella [31], Palmer [32], Perazella [33]

The diagnostic workup for AKI in the elderly begins with a thorough history and physical examination to investigate for possible prerenal, renal or postrenal causes. This would include a review of medications, recent procedures and contrast exposures, urine output and signs and symptoms of systemic disease and a fluid status examination. Helpful investigations include renal ultrasonography, bladder scans, urinalysis and urine microscopy and examination for casts. Granular casts may indicate tubular injury and acute tubular necrosis, whereas a potential diagnosis of glomerulonephritis may be facilitated by dysmorphic red blood cells or red blood cell casts. Urinary eosinophilia may suggest interstitial nephritis [19].

The management of AKI is largely supportive, by reversing the cause of AKI, maintaining adequate renal blood flow and avoiding further injury and renal replacement if necessary. The key elements therefore involve avoidance of hypovolaemia, particularly in the context of sepsis which may be masked in an elderly patient, and avoidance of nephrotoxins, including contrast media [20]. Initial fluid resuscitation is often necessary in treating AKI. However, care must be taken to prevent fluid overload in elderly who may have impaired cardiac function, as fluid accumulation is associated with increased mortality risk and tissue oedema and may contribute to decompensated cardiac failure, which can in turn lead to further AKI [26]. Low or iso-osmolar contrast agents, intravenous isotonic fluids and avoidance of concomitant nephrotoxins such as NSAIDs can be effective in reducing risk of contrast nephropathy [21]. Renal injury should be identified promptly to ensure that contributing causes are addressed and to prevent additional renal insults. Unfortunately, serum creatinine is an unreliable marker of acute renal dysfunction in most patients as it often lags behind changes in GFR by several days [27]. In addition, serum creatinine may not correlate reliably with GFR in the elderly, as discussed further below. Unfortunately, other markers of kidney injury such as cystatin C are even less useful in diagnosing AKI in routine practice. Early detection of AKI relies on a high index of clinical suspicion in high-risk situations, e.g. after major surgery or in patients with sepsis or organ failure.

Chronic Kidney Disease in the Elderly

Chronic kidney disease (CKD) is currently defined as a glomerular filtration rate (GFR) of <60 mL/min/1.73m^2 or by the presence of markers of kidney damage (such as albuminuria or urinary sediment abnormalities) for 3 or more months [34]. CKD is classified based on cause, degree of GFR impairment and albuminuria (Table 16.3).

Table 16.3 Prognosis of CKD progression by GFR and albuminuria categories

				Persistent albuminuria categories		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g in 24 h	30–300 mg/g in 24 h	>300 mg/g in 24 h
				<3 mg/mmol	3–30 mg/mmol	>30 mg/mmol
GFR categories (mL/min/1.73m^2) Description and range	G1	Normal or high	≥90	Low risk	Moderately increased risk	High risk
	G2	Mildly decreased	60–89	Low risk	Moderately increased risk	High risk
	G3a	Mildly to moderately decreased	45–59	Moderately increased risk	High risk	Very high risk
	G3b	Moderately to severely decreased	30–44	Very high risk	Very high risk	Very high risk
	G4	Severely decreased	15–29	Very high risk	Very high risk	Very high risk
	G5	Kidney failure	<15	Very high risk	Very high risk	Very high risk

Reproduced with permission from KDIGO [34]

Worldwide prevalence of CKD in the general population is approximately 8–16% [35]. However, as an unintended consequence of these guidelines, many older adults with ageing-related decline in renal function are now being classed as having CKD. Some studies cite the prevalence of CKD in patients over the age of 80 as >50% [36, 37]. Age is a risk factor in developing CKD [38].

CKD is traditionally described as a disease associated with progressive reduction in kidney function. However, over 90% of older adults identified to have CKD do not progress to end-stage renal disease (ESRD) [39–41]. It is unclear whether the decreased rate of decline in GFR is a true finding or reflects a survival bias in that those with rapidly progressive CKD have higher mortality. In patients over the age of 75, the risk of death was higher than the risk of progression to ESRD [40]. This data has led some to question whether a moderate reduction in GFR with no other signs of kidney damage in the elderly should be designated as a disease and consequently how much intervention is required.

Causes of Chronic Kidney Disease

Amongst the elderly, many cases of CKD manifest without a readily apparent cause [22]. Nevertheless, epidemiological evidence suggests that vascular disease may be the predominant cause in this population, with hypertension listed as the top cause of ESRD amongst patients 85 years or older in Australia, accounting for 35% of prevalent patients and 40% of incident patients [42]. Numerous cardiovascular risk factors, including diabetes and hypertension, become more prevalent in older populations [22], and in Australia, over 50% of patients 85 years or over commenced on renal replacement therapy in 2015 had a history of coronary artery disease [42].

Glomerular Filtration Estimating Equations

A notable consideration is the validity of GFR-estimating equations in older populations. The most commonly used include the Modification of Diet in Renal Disease (MDRD) equation and the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation. The original creatinine clearance equation was the Cockcroft-Gault (C-G) equation, published in 1976. Few older adults were included in the development of these equations [37, 43, 44], although data suggests that the performance of CKD-EPI and MDRD was similar in older patients (median age of 80) compared to younger people [45].

Australian laboratories largely use CKD-EPI for estimating GFR. However, some studies of populations aged over 70 have found that CKD-EPI tends to underestimate GFR compared to MDRD [46, 47]. A similar effect was found in the oldest old. In patients aged 90 or above, CKD-EPI can underestimate renal function and increase CKD prevalence estimates [48]. Choice of equation affects reported prevalence of CKD. In one cohort of over 2000 patients with a mean age of over 80 years, the prevalence of CKD, defined as eGFR <60 mL/min/1.73m^2, was reported as 37.9% using CKD-EPI, 37.1% using MDRD and 55.9% using C-G [49].

These equations are all based on creatinine, which is dependent on muscle mass, nutritional status and protein intake. As creatinine production and urinary creatinine output decline due to the age-related decrease in muscle mass and body weight, creatinine clearance may not be an accurate measure of the GFR in the elderly. Plasma creatinine does not increase with increasing age, despite the ageing-related reduction in creatinine clearance [4]. At present, there is insufficient evidence to prefer one GFR-estimating equation since all perform equally and misclassification can occur with any of these equations when used in older patients with differing body composition [50].

Other Associations with 'Chronic Kidney Disease' in the Older Population

In adults over 80, CKD is associated with metabolic complications such as anaemia, acidosis, hyperphosphataemia, hyperparathyroidism and hypertension [36, 51]. Patients with an eGFR <45 mL/min/1.73m^2 have nearly twice the prevalence of these complications [36]. The association between CKD and cardiovascular disease has been well-described in the general population [41, 52] but is not as clear-cut in older patients [53]. Although there is a higher prevalence of coronary artery disease, peripheral vascular disease and cardiovascular risk factors amongst elderly individuals with reduced kidney function [40, 53], it is unclear whether cardiovascular risk factors are causative of CKD or whether CKD additionally predisposes to coronary artery disease. Similarly, although a relationship between CKD and cognitive impairment has been described, small vessel disease may be causing both the decline in renal function and cognition [54]. There is conflicting evidence regarding the elevated risk of mortality in patients over 75 with reduced eGFR [40, 55, 56], likely due to the issue of competing risk of death versus decline in kidney function in older individuals.

Management Aspects of Chronic Kidney Disease in the Elderly

CKD management in the older population ideally should be individualised and maintain a geriatric perspective, which may prioritise quality of life over prolonging life. Strategies for managing CKD in the oldest old are similar to those in younger patients, aimed at preventing progression through blood pressure and metabolic control and minimising sequelae from complications of CKD such as anaemia and renal bone disease. However, treatment and objectives may need to be adjusted if initial therapy causes adverse effects or significantly reduces quality of life.

Hypertension

Blood pressure control significantly reduces the risk for strokes, major cardiovascular events and heart failure even in patients older than 80 years [57, 58]. A Cochrane review sub-analysis specifically including patients 80 years or older demonstrated no reduction in total mortality with blood pressure treatment [59]. Conversely, in the HYVET trial, antihypertensive treatment for patients aged 80 or older with a sustained blood pressure of >160 mmHg (aiming a target systolic BP of <150 mmHg and target diastolic BP of <80 mmHg) reduced all-cause mortality and stroke [58]. However, elevated serum creatinine was an exclusion criterion. In patients over 75 without CKD, intensive blood pressure control aiming systolic BP <120 mmHg compared with standard blood pressure control aiming systolic BP <140 mmHg was found to adversely affect renal function (defined in the study as 30% decrease in eGFR to an eGFR of <60 mL/min/1.73m^2) [60]. Mortality risk in patients 80 years or older has been shown to increase when systolic BP reduces below 140 mmHg or diastolic BP below 70 mmHg [61]. Due to insufficient evidence for the oldest old with CKD, blood pressure targets are therefore individualised taking into account factors such as frailty, comorbidities and albuminuria [62]. Antihypertensives should be introduced gradually as the elderly with CKD often have reduced tolerance to medication and aggressive treatment may lead to orthostatic hypotension with subsequent complications including falls. The elderly are also more at risk of 'normotensive acute renal failure', an acute GFR deterioration when their blood pressure is reduced to the 'normal' range. This is attributed to reduced kidney perfusion secondary to vascular autonomic dysregulation accompanying ageing [63].

Renin-angiotensin system (RAAS) blocking agents reduce albuminuria and retard the progression of CKD [64, 65]. Nephron loss, which occurs with ageing, leads to hyperfiltration and glomerular hypertension [66]. RAAS blockade reduces glomerular hyper-filtration [67]. However, use of these agents must be carefully balanced with the risk of orthostatic hypotension or an unacceptable rise in serum potassium or creatinine over 25%. Serum biochemistry should be rechecked 1–2 weeks after initiation of treatment [68].

Even though salt restriction is often prescribed for blood pressure control, the elderly have less capability for sodium reabsorption [14]. Consequently, restricting salt too stringently may result in hyponatraemia and excessive volume depletion. Salt restriction in the elderly should be followed by monitoring blood pressure and serum sodium level, and if adverse consequences are detected, a normal sodium diet would be a better prescription [69].

Diabetes Control

In large controlled trials, tighter glucose control was associated with less frequent development or progression of albuminuria, but not a lesser decline in GFR. However, groups with tighter glycaemic control had more frequent episodes of hypoglycaemia, which increases risk of mortality [70–74]. A haemoglobin A1C target (HbA1C) of <8% is recommended for elderly patients [75]. Metformin is often considered first-line therapy in type 2 diabetes. Its low risk of hypoglycaemia may be beneficial in older adults, but gastrointestinal intolerance and weight loss may be

detrimental in frail patients. In addition, the dose requires adjustment if eGFR is 30–60 mL/min and cannot be used if eGFR <30 mL/min [75]. Sulfonylureas are an alternative; however their risk of hypoglycaemia may be problematic in older patients [76]. To reduce the risk of hypoglycaemia with insulin therapy, an insulin dosage reduction of 25% has been recommended in renal patients with eGFR 10–50 mL/min. If a long-acting insulin is used, a starting dose should be 50% of the usual initial dosage of 0.1 units/kg with gradual titration until target fasting blood glucose concentrations are reached [76].

Lipid Control

A statin study in older adults (aged between 70 and 82 years) found a 15% reduction in coronary artery disease events with pravastatin [77]. However, data in patients 85 years and older is scarce [75].

Bone Disease

Renal bone disease is a heterogeneous disorder comprising multiple entities, including high turnover bone disease, adynamic bone disease or a low turnover state. Elderly individuals with CKD are likely to have even higher fracture rates than the general population, due to the age-related traditional risk factors for fracture [78]. Assessment of fracture risk is important. Low BMD should be treated [79]. There is evidence that bisphosphonates and denosumab are effective and safe in CKD stages 1–4 but only anecdotal reports for their use in CKD stage 5 [78]. In general, treatment will have to be individualised, and exclusion of a bone turnover state would be required before considering anti-resorptive therapy.

Frailty

The 'frailty phenotype' is characterised by a reduction in strength and endurance, culminating in vulnerability to age- or disease-associated stressors [80, 81]. CKD is an independent risk factor for functional impairment and frailty [82]. In older CKD patients with frailty, mortality risk at 1 year is three times higher compared to those without frailty [83]. Older patients with advanced CKD (eGFR <45 mL/min) should be screened regularly for functional impairment and malnutrition [50]. Therapeutic strategies to address this include low intensity and aerobic physical exercises, adequate nutrition and protein intake and appropriate vitamin D supplementation [69]. Anaemia should also be addressed. Iron deficiency is common in CKD, and supplementation with oral or intravenous iron is required [84].

Relevant Discussions in Chronic Kidney Disease

Progression of chronic kidney disease is variable and can follow any number of trajectories. Median survival of elderly patients with advanced chronic kidney disease managed via a non-dialysis pathway ranges from 16 to 21 months, with a 1-year survival of 50–65% [85–89]. Acutely unwell patients, when faced with the option of dialysis, are unable to deliberate about treatment. These patients often did not consider the decision to be their own [90], a situation that may be avoided with earlier prognostic discussions. Qualitative studies suggest that patients on haemodialysis often believe that they were not given sufficient information on dialysis and management alternatives [91, 92]. Explaining the option of conservative care and establishing goals of care, including quality of life considerations such as the fact that hospital-free survival may be similar in dialysis and non-dialysis treated groups [93, 94], can improve the end-of-life phase for patients with multiple comorbidities and with a poor overall prognosis.

End-Stage Renal Disease

Current practice includes three potential pathways for patients with end-stage renal disease (ESRD): dialysis, transplantation and a (non-dialysis) supportive (conservative) care pathway. However, management decisions depend also on complex factors such as comorbidities, frailty and patient wishes.

Renal Replacement Therapy

Dialysis as a Treatment Option in the Elderly

The number of patients aged 85 and over ('old elderly') on dialysis is increasing. In Australia, less than 200 'old elderly' patients in 2005 were managed with renal replacement therapy (either dialysis or transplant). This has grown to over 600 as of 2015 [42]. Similarly, the United States has seen a 57% increase in the rate of starting dialysis in patients aged 80 and over [95].

'Shared decision-making' is paramount to discussions of ESRD in the elderly. This includes informed consent leading to the initiation of dialysis, including an explanation of quality of life and prognostic considerations and raising the conservative or 'not for dialysis' pathway so that patients do not feel it is compulsory that they receive dialysis [96]. In patients over 80 with CKD stages 3 and 4, the risk of death exceeded the risk of ESRD. Even in patients with ESRD, the risk of death exceeded their need for haemodialysis [40, 97],

as some will die from other comorbidities before commencing dialysis. Delaying dialysis may preserve quality of life and avoid hospitalisations, infections and cardiovascular mortality [86, 94, 98, 99]. Many older patients regard quality rather than length of life as more important and may feel that dialysis is a burden they would rather not face at the end of their lives [95].

Haemodialysis is often the default dialysis modality for the older patient [100]. In Australia, 87% of patients 85 years or older in 2015 with ESRD were being managed with haemodialysis [42]. However, there are unique challenges in vascular access. The elderly are more likely to have long-term haemodialysis catheters [100, 101], despite these being associated with higher mortality [102]. Preference is generally for arteriovenous (AV) fistulae, but fistulae require more time to mature, and increased age is associated with non-maturation and worse primary cumulative fistulae survival [101, 103], as the elderly are more likely to have poor quality veins because of prior medical interventions, atheroma or medial calcifications [104].

Special considerations accompany the initiation of dialysis in elderly patients. The benefits of correcting uraemia may be outweighed by physical risks and the psychosocial burden associated with dialysis. Old age is accompanied by deterioration in cognitive and physical function, vision and hearing and a higher prevalence of chronic disease, depression and malnutrition. All of these impact on physical, mental and social tolerance of dialysis, but are often overlooked [105].

Box 16.1 Special Considerations in Initiation of Dialysis in the Elderly

- Frailty and higher prevalence of comorbidities impacting on physical tolerance of dialysis.
- Reduction in time available for social activities and meals impacting on mental tolerance of dialysis.
- Difficulties in creation of vascular access resulting in greater dependence on central venous access devices.
- Similar numbers of hospital-free days between elderly patients managed conservatively or managed with dialysis.
- Survival advantage with dialysis in the elderly is lost with frailty or two or more comorbidities.

In one Australian study, patients with CKD reported that they would be less likely to choose dialysis over conservative care if the number of hospital visits increased or if there were more restrictions in their ability to travel. Patients were willing to sacrifice 7 months of life expectancy to reduce the number of hospital visits or sacrifice 15 months to increase their ability to travel [106]. Improved life expectancy may be outweighed by the fact that the majority of the time spent is in hospital, either for dialysis sessions or admissions for complications such as infection [86, 107]. Median survival for patients managed conservatively (mean age 77 years) was 13 months shorter than that of patients on haemodialysis (mean age 60.6 years); however 10 of those months represented dialysis days [108].

The survival advantage seen with dialysis may be partly accentuated due to selection bias, as patients commencing on dialysis often have less comorbidities [109]. However, frailty or significant comorbidity appears to offset the survival advantage of dialysis [105]. In patients over 75 years of age, there is no statistically significant survival difference between renal replacement therapy and conservative care if the patient had two or more comorbidities or a poor performance status [85, 86, 88, 110–112]. Patients residing in long-term care facilities at time of initiation have an especially poor outcome, with elevated mortality, deteriorating functional status and poor quality of life [105, 113]. Clinical judgement coupled with geriatric assessment and prognostic tools to assess frailty and functional status may help determine which patients are suitable for dialysis [114, 115].

Peritoneal Dialysis

Despite concerns of deteriorating vision and cognition, elderly patients are capable of learning to perform PD. Technique survival is not inferior in elderly patients [116, 117]. In Australia, 1-year technique survival in patients 75 years or older is 75%, comparing favourably with 80% in patients younger than 75 years [118]. Assisted automated peritoneal dialysis, with the support of family or staff to set up the cycler, is an option for patients with reduced physical dexterity or vision [117], with similar technique survival and peritonitis-free periods compared with self-administered PD [116].

Peritoneal dialysis is usually carried out at home, and so permits an independent lifestyle. It can be a good option for elderly with cardiovascular comorbidities as it avoids the haemodynamic shifts associated with the intermittent nature of haemodialysis [119, 120]. In patients over 70, patients on peritoneal dialysis had significantly less perception of illness intrusion, lower illness and modality-related stress and fewer mood disturbances compared with haemodialysis [119, 121, 122]. There is no mortality difference between haemodialysis and peritoneal dialysis in elderly patients [100, 119, 123].

Dialysis Withdrawal

In patients who are approaching the end of their lives, withdrawal from dialysis may be appropriate if it is no longer

helping patients to achieve an adequate quality of life. However, initiating these discussions is difficult. Doctors must be certain that there are no treatable, reversible causes of the patient's deterioration and that depression is not impacting on the patient's capacity before considering withdrawal. If clinical assessment suggests dementia, a frank discussion should be carried out with the patient and family about whether dialysis is continuing to provide a net benefit in their lives [124]. In some cases, where cognitively impaired patients are unable to sit still during dialysis and pull at lines, they endanger both themselves and dialysis staff, and the risk-benefit ratio of continuing dialysis is low. Patients should be reassured that it is ethically and medically acceptable to choose to stop dialysis if no longer achieves an acceptable quality of life or in line with their goals of care [114]. Patients are often unaware of other options, with one study reporting that over 80% of an elderly cohort with CKD did not know what palliative care was [91].

Survival after withdrawal varies from 3 to 17 days, with a mean of 8–10 days [124]. Patients and families need to be prepared for what to expect if dialysis is withdrawn. Reassurance can be offered that for most patients, progressive drowsiness from uraemia results in a peaceful death with little suffering.

Ethical and Legal Considerations

Conflict may arise in situations in which dialysis is being requested to support a controversial end, such as maintaining a patient in a severely compromised physical and/or mental state. Legally and ethically, doctors are not obligated to provide treatment that they believe is of no benefit to the patient, including dialysis [96]. Beneficence and non-maleficence mandate that health professionals provide only treatments that offer a reasonable expectation of benefit without unacceptable harm. Practice of dialysing frail elderly patients often violates non-maleficence and beneficence, as beneficence is often narrowly interpreted to focus on life extension and fails to consider other priorities in patient's lives [92]. Such demands for treatment will need to be dealt with through open communication that addresses the patient's values, balancing these with adequate knowledge of the prognosis. This will often require negotiation, cultural sensitivity and use of conflict resolution techniques [113].

Transplantation

Kidney transplantation can improve quality and length of life for elderly patients [125–127]. In patients over 70, receiving a kidney transplant reduced mortality, with a reduced risk of death by up to 41%, compared to wait-listed patients remaining on dialysis [126, 128]. However, the survival advantage benefit diminishes with age [125], with only a 1-year increase in lifespan in patients aged 70–74, compared to 4.3 years in patients aged 60–64. There is also an increased mortality risk post-transplant up until 106–125 days post-operatively [125–127], compared to similar patients who remained waitlisted.

Despite this, the majority of elderly patients on renal replacement therapy will have too many comorbidities to be eligible or develop complications rendering them ineligible while waitlisted. In Australia, only 11 new transplants were performed in patients aged 75 or older in 2014 [129].

Conservative Care

Conservative care, also known as renal supportive care, shifts the goals of care from prolonging life to relief of suffering, preservation of functional status and maximising quality of life through symptom control. Active medical management without dialysis can control uraemic symptoms and biochemical makers of uraemia such as bicarbonate, and potassium (Table 16.4).

Symptom Control

Patients with advanced CKD have identified symptom burden as a high priority [132, 134]; therefore palliative care input is vital within a renal supportive care team. The WHO definition of palliative care is that of 'an approach which improves the quality of life of patients and their families facing life threatening illness, through

Table 16.4 Aspects of renal supportive care

Medical management	Control biochemical markers of uraemia such as bicarbonate with replacement Prevent complications of ESRD such as hypercalcaemia (may involve medical or dietary management) Minimise fluid overload with diuretics and dietary management Optimise anaemia using erythropoietin and iron supplementation Minimise progression with use of angiotensin-converting enzyme inhibitors [130]
Maintaining quality of life	Addressing common symptoms such as pain, fatigue and dyspnoea Multidisciplinary intervention including dietary management to minimise protein-calorie malnutrition
Psychosocial support	Education for both patient and family/carers Addressing co-existing depression or anxiety End-of-life and advanced care planning [131]

Information sources: Berzoff et al. [131], Steinhauser et al. [132], Raghavan and Holley 2016 [133]

Table 16.5 Symptoms in ESRD and strategies for management

Symptom	Causes	Management
Pain	Primary cause of kidney failure such as a ruptured cyst in polycystic kidney disease Metabolic derangements may lead to bone disease or calciphylaxis Comorbidities such as osteoarthritis or diabetes resulting in peripheral neuropathy Restless legs syndrome	Attempt to address underlying cause Long-acting scheduled medications with as-needed breakthrough short-acting medications Stepwise escalation of pain medication doses as per WHO analgesic ladder [133] Adjuvant agents such as gabapentin for neuropathic pain Monitor for side effects May require dose adjustment [133] Alternatives such as fentanyl that are less likely to accumulate in renal failure [137] Neuropathic agents can be used for restless legs syndrome [133]
Fatigue	Insomnia Malnutrition Anaemia Medication side effects Depression	Evaluate for and treat sleep disorders – may require sleep hygiene techniques. Neuropathic agents can be used for restless legs syndrome [133] Evaluate for and treat anaemia Dietary management of malnutrition Modification of medication regimens Treatment with antidepressants
Pruritis [138]	Hyperphosphataemia Anaemia Hyperparathyroidism Dry skin	Medical and dietary management of calcium-phosphate imbalance Evaluate for and treat anaemia Emollients Oral antihistamines
Nausea and vomiting	Uraemia Medication side effects	Anti-emetics Review protein intake Modification of medication regimens
Dyspnoea	Fluid overload Response to metabolic acidosis Comorbidities such as cardiac failure or lung disease	Diuretic management Dietary management – sodium restriction and fluid intake control Symptomatic management with opioids Management of metabolic acidosis with bicarbonate supplementation Non-medical interventions such as fans, careful positioning, breathing and relaxation techniques
Anorexia	Uraemia Malnutrition	Avoid any unnecessary dietary restrictions Food fortification strategies Consider higher energy, lower protein nutritional supplements
Dysgeusia	Uraemia Oral candidiasis Medication side effects	Review protein intake Interventions to alter saliva composition Oral sodium bicarbonate mouthwashes Treatment of oral candidiasis Review medications
Constipation	Malnutrition Overly strict fluid restriction	Encourage oral fluids (within limits) Encourage higher fibre diet (aim for 30 g/day) Encourage physical activity

Information sources: Raghavan and Holley [133]; Barokzoy and Moss [137]

the prevention and relief of suffering…and treatment of pain and other problems, physical, psychosocial and spiritual' [93]. Dispelling the misconception that 'palliative care' is adopted only very close to the time of death allows formal engagement of palliative care expertise earlier to stabilise or improve the majority of patients' symptoms [85]. In one Australian study, the majority of patients managed through renal supportive care experienced improvement in their symptoms, and studies have shown no difference in symptom control management between patients on the supportive care pathway and dialysis [85, 135].

The causes of these symptoms are often multifactorial. Routine symptom assessment is paramount to assessing effectiveness of quality end-stage renal disease care. Three global symptom screening tools have been validated in kidney disease: the modified Edmonton Symptom Assessment System, the Patient Outcomes Scale Renal Symptom module and the Dialysis Symptom Index [136] (Table 16.5).

Dietary Management in Conservatively Managed End-Stage Renal Disease

Dietary management should consider patients' goals and prioritise strategies that improve quality of life and reduce symptom burden. Flexibility with traditional renal dietary

Table 16.6 Nutrition guidelines for patients on a conservative, non-dialysis pathway

Energy (/kg IBW/day)	Individualised based on nutritional status, comorbidities, physical function and activity levels
Protein	0.75–1.0 g /kg IBW/day[a]
Potassium	If serum potassium elevated, discuss strategies (e.g. food substitutions)
Sodium (mg/day)	Individualised based on symptoms and patient goals[b]
Phosphate	Individualised. Consider restriction in pruritus[c]
Fluid (ml/day)	Individually assessed by the medical team

Information sources: Stevenson et al. 2017 [139], Carerro 2011 [140]
IBW Ideal Body Weight
[a]Given the lack of evidence in this area, it is suggested to adapt recommendations from pre-dialysis and general population guidelines
[b]Restriction may be warranted to help manage fluid overload and minimise associated symptoms. Conversely, sodium intake may be unrestricted in times of malnutrition or inadequate oral intake
[c] If serum phosphate elevated and patient experiencing pruritus, consider sources of dietary phosphate

prescription is warranted, with dietary control for minimising malnutrition, addressing acute complications (e.g. hypercalcaemia and fluid overload) and reduction of nutrition impact symptoms, taking precedence over long-term complications (e.g. renal bone disease).

Timely nutrition education and support may delay symptom onset and minimise symptoms when present. Nutrition-related symptoms such as anorexia [141, 142], nausea (including dry retching [85]), taste changes [143] and constipation are common and may contribute to inadequate nutritional intake and the development of malnutrition [140]. Regular review with a dietitian is recommended to help minimise nutrition-related complications (Table 16.6).

End-of-Life Discussions

Delay in end-of-life discussions occurs for many reasons. Health providers may delay this for fear that patients will lose hope [144, 145]. However, patients report that the sense of loss of control and uncertainty are distressing. Advanced care planning with psychosocial interventions can help to reduce this sense of loss of control and caregiver anxiety [109, 146]. Many patients with ESRD value early discussion and open communication regarding the course of their disease, treatments and realistic explanations of each treatment pathway and early discussion of advanced care planning [91, 98], with emphasis on pain and symptom management and available home support towards the end of life [91, 109].

It is important to tactfully navigate cultural barriers in providing conservative care. For example, advanced care planning is not common practice for most people of Aboriginal or Torres Strait Islander descent [93]. Family/kinship rules may mean that certain family members have stronger cultural responsibilities to a particular individual and it is imperative to identify early in planning who is the culturally appropriate person. Family meetings, preferably in the presence of a cultural healthcare worker to explain treatment pathways and care issues, can inform choices in care [93].

Clinical Relevance

AKI in the elderly is often multifactorial. Supportive management of AKI would involve identifying and cessation of nephrotoxins, which include some common medications, minimising postrenal contributors to AKI and careful fluid management.

The elderly that are most at risk of AKI include those with pre-existing CKD, those of older age and those with cardiovascular risk factors or comorbidities. Identifying these patients and pre-emptively minimising nephrotoxins may prevent the development of AKI.

Prevalence of CKD in the elderly increases with age. However, one must be aware that the creatinine-based glomerular filtration rate estimating equations may not be entirely accurate in the elderly.

CKD may be associated with metabolic complications such as anaemia, acidosis and hyperphosphataemia and hypertension, which may require treatment in order to optimise quality of life and delay further progression of CKD.

CKD management decisions are highly individualised in the elderly, depending on factors such as comorbidities, frailty and, above all, impact of potential therapy on quality of life.

The elderly with ESRD have a high prevalence of frailty and thus are more vulnerable to stressors associated with both their comorbidities and dialysis itself. Dialysis initiation may be accompanied by higher medical risks and psychosocial burden.

In elderly patients with ESRD, the risk of death exceeds the risk of needing haemodialysis. Therefore, management of ESRD-related symptoms and early discussion with patients regarding their priorities, wishes and prognosis is paramount to optimising care.

Multiple Choice Questions

1. Which of the following statements are **UNTRUE** regarding the use of creatinine-based equations for estimating glomerular filtration rate and prevalence of chronic kidney disease in the elderly?

A. Creatinine is related to muscle mass.
B. Creatinine is the ideal biomarker for calculating estimated glomerular filtration rate.
C. Use of different creatinine-based equations to estimate glomerular filtration rate may give varying prevalences of chronic kidney disease in an elderly population.
D. The cohort used to develop the CKD-EPI and MDRD equations did not include many elderly patients.

2. Which of the following is **NOT** true regarding management of end-stage renal failure in the elderly?
A. Technique survival and patient mortality with peritoneal dialysis in the elderly is not significantly different compared to younger patients.
B. Elderly patients on haemodialysis are more likely to have long-term haemodialysis catheters as vascular access.
C. Withdrawal from dialysis may be reasonable if dialysis is no longer providing a good quality of life for the patient.
D. In a patient over 75 with CKD stage 5 with diabetes and ischaemic heart disease, dialysis will prolong lifespan compared to conservative management.

3. Which of the following is **TRUE** regarding renal supportive care?
A. Referral to renal supportive care is only appropriate when the patient is very close to the end of their life.
B. Advanced care planning discussions should be delayed for as long as possible because they may cause patients to lose hope.
C. Causes of symptoms in end-stage renal failure are often multifactorial and may require a multifaceted approach.
D. Doctors are always obligated to provide dialysis if the patient or family wishes it, even if they believe that the risks of dialysis are greater than the benefits.

MCQs Answers

1. B
2. D
3. C

References

1. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. J Am Geriatr Soc. 1985;33(4):278–85.
2. Denic A, Glassock RJ, Rule AD. Structural and Functional Changes With the Aging Kidney. Adv Chronic Kidney Dis. 2016;23(1):19–28.
3. Karam Z, Tuazon J. Anatomic and physiologic changes of the aging kidney. Clin Geriatr Med. 2013;29(3):555–64.
4. Zhou XJ, Rakheja D, Yu X, Saxena R, Vaziri ND, Silva FG. The aging kidney. Kidney Int. 2008;74(6):710–20.
5. Glassock RJ, Rule AD. The implications of anatomical and functional changes of the aging kidney: with an emphasis on the glomeruli. Kidney Int. 2012;82(3):270–7.
6. Hill GS, Heudes D, Bariety J. Morphometric study of arterioles and glomeruli in the aging kidney suggests focal loss of autoregulation. Kidney Int. 2003;63(3):1027–36.
7. Takazakura E, Sawabu N, Handa A, Takada A, Shinoda A, Takeuchi J. Intrarenal vascular changes with age and disease. Kidney Int. 1972;2(4):224–30.
8. Brenner BM. Hemodynamically mediated glomerular injury and the progressive nature of kidney disease. Kidney Int. 1983;23(4):647–55.
9. Hollenberg NK, Adams DF, Solomon HS, Rashid A, Abrams HL, Merrill JP. Senescence and the renal vasculature in normal man. Circ Res. 1974;34(3):309–16.
10. Esposito C, Plati A, Mazzullo T, Fasoli G, De Mauri A, Grosjean F, et al. Renal function and functional reserve in healthy elderly individuals. J Nephrol. 2007;20(5):617–25.
11. Fuiano G, Sund S, Mazza G, Rosa M, Caglioti A, Gallo G, et al. Renal hemodynamic response to maximal vasodilating stimulus in healthy older subjects. Kidney Int. 2001;59(3):1052–8.
12. Rowe JW, Shock NW, DeFronzo RA. The influence of age on the renal response to water deprivation in man. Nephron. 1976;17(4):270–8.
13. Musso CG, Oreopoulos DG. Aging and physiological changes of the kidneys including changes in glomerular filtration rate. Nephron Physiol. 2011;119(Suppl 1):p1–5.
14. Sands JM. Urine concentrating and diluting ability during aging. J Gerontol A Biol Sci Med Sci. 2012;67(12):1352–7.
15. O'Sullivan ED, Hughes J, Ferenbach DA. Renal aging: causes and consequences. J Am Soc Nephrol. 2017;28(2):407–20.
16. Kayatas K, Sahin G, Tepe M, Kaya ZE, Apaydin S, Demirtunc R. Acute kidney injury in the elderly hospitalized patients. Ren Fail. 2014;36(8):1273–7.
17. Chronopoulos A, Rosner MH, Cruz DN, Ronco C. Acute kidney injury in elderly intensive care patients: a review. Intensive Care Med. 2010;36(9):1454–64.
18. Coca SG. Acute Kidney Injury in Elderly Persons. Am J Kidney Dis. 2010;56(1):122–31.
19. Rosner MH. Acute kidney injury in the elderly. Clin Geriatr Med. 2013;29(3):565–78.
20. Chronopoulos A, Cruz DN, Ronco C. Hospital-acquired acute kidney injury in the elderly. Nat Rev Nephrol. 2010;6(3):141–9.
21. Anderson S, Eldadah B, Halter JB, Hazzard WR, Himmelfarb J, Horne FM, et al. Acute kidney injury in older adults. J Am Soc Nephrol. 2011;22(1):28–38.
22. Stevens LA, Viswanathan G, Weiner DE. Chronic kidney disease and end-stage renal disease in the elderly population: current prevalence, future projections, and clinical significance. Adv Chronic Kidney Dis. 2010;17(4):293–301.
23. Schmitt R, Coca S, Kanbay M, Tinetti ME, Cantley LG, Parikh CR. Recovery of kidney function after acute kidney injury in the elderly: a systematic review and meta-analysis. Am J Kidney Dis. 2008;52(2):262–71.
24. Sturmlechner I, Durik M, Sieben CJ, Baker DJ, van Deursen JM. Cellular senescence in renal ageing and disease. Nat Rev Nephrol. 2017;13(2):77–89.
25. Yang HC, Fogo AB. Fibrosis and renal aging. Kidney Int. Suppl (2011). 2014;4(1):75–8.
26. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol. 2010;6(2):107–15.

27. Lameire N, Hoste E. Reflections on the definition, classification, and diagnostic evaluation of acute renal failure. Curr Opin Crit Care. 2004;10(6):468–75.
28. Geevasinga N, Coleman PL, Webster AC, Roger SD. Proton pump inhibitors and acute interstitial nephritis. Clin Gastroenterol Hepatol. 2006;4(5):597–604.
29. Graham DJ, Staffa JA, Shatin D, Andrade SE, Schech SD, La Grenade L, et al. Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs. JAMA. 2004;292(21):2585–90.
30. Naughton CA. Drug-induced nephrotoxicity. Am Fam Physician. 2008;78(6):743–50.
31. Markowitz GS, Perazella MA. Drug-induced renal failure: a focus on tubulointerstitial disease. Clin Chim Acta. 2005;351(1–2):31–47.
32. Palmer BF. Renal Dysfunction Complicating the Treatment of Hypertension. NEJM. 2002;347(16):1256–61.
33. Perazella MA. Drug-induced nephropathy: an update. Expert Opin Drug Saf. 2005;4(4):689–706.
34. KDIGO. Chapter 1: Definition and classification of CKD. Kidney Int Suppl. 2013;3(1):63–72.
35. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(9888):260–72.
36. Bowling CB, Inker LA, Gutierrez OM, Allman RM, Warnock DG, McClellan W, et al. Age-specific associations of reduced estimated glomerular filtration rate with concurrent chronic kidney disease complications. Clin J Am Soc Nephrol. 2011;6(12):2822–8.
37. Shastri S, Tighiouart H, Katz R, Rifkin DE, Fried LF, Shlipak MG, et al. Chronic kidney disease in octogenarians. Clin J Am Soc Nephrol. 2011;6(6):1410–7.
38. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D. Predictors of new-onset kidney disease in a community-based population. JAMA. 2004;291(7):844–50.
39. Dalrymple LS, Katz R, Kestenbaum B, Shlipak MG, Sarnak MJ, Stehman-Breen C, et al. Chronic kidney disease and the risk of end-stage renal disease versus death. J Gen intern Med. 2011;26(4):379–85.
40. O'Hare AM, Choi AI, Bertenthal D, Bacchetti P, Garg AX, Kaufman JS, et al. Age affects outcomes in chronic kidney disease. J Am Soc Nephrol. 2007;18(10):2758–65.
41. Hemmelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, et al. Relation between kidney function, proteinuria, and adverse outcomes. JAMA. 2010;303(5):423–9.
42. Registry A. 2017.
43. Fung E, Kurella TM. Epidemiology and public health concerns of CKD in older adults. Adv Chronic Kidney Dis. 2016;23(1):8–11.
44. Delanaye P, Mariat C. The applicability of eGFR equations to different populations. Nat Rev Nephrol. 2013;9(9):513–22.
45. Kilbride HS, Stevens PE, Eaglestone G, Knight S, Carter JL, Delaney MP, et al. Accuracy of the MDRD (Modification of Diet in Renal Disease) study and CKD-EPI (CKD Epidemiology Collaboration) equations for estimation of GFR in the elderly. Am J Kidney Dis. 2013;61(1):57–66.
46. Murata K, Baumann NA, Saenger AK, Larson TS, Rule AD, Lieske JC. Relative performance of the MDRD and CKD-EPI equations for estimating glomerular filtration rate among patients with varied clinical presentations. Clin J Am Soc Nephrol. 2011;6(8):1963–72.
47. Willems JM, Vlasveld T, den Elzen WP, Westendorp RG, Rabelink TJ, de Craen AJ, et al. Performance of Cockcroft-Gault, MDRD, and CKD-EPI in estimating prevalence of renal function and predicting survival in the oldest old. BMC Geriatr. 2013;13:113.
48. Carter JL, Stevens PE, Irving JE, Lamb EJ. Estimating glomerular filtration rate: comparison of the CKD-EPI and MDRD equations in a large UK cohort with particular emphasis on the effect of age. QJM. 2011;104(10):839–47.
49. Ebert N, Jakob O, Gaedeke J, van der Giet M, Kuhlmann MK, Martus P, et al. Prevalence of reduced kidney function and albuminuria in older adults: the Berlin Initiative Study. Nephrol Dial Tansplant. 2017;32(6):997–1005.
50. Farrington K, Covic A, Nistor I, Aucella F, Clyne N, De Vos L, et al. Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR<45 mL/min/1.73 m2): a summary document from the European Renal Best Practice Group. Nephrol Dial Transplant. 2017;32(1):9–16.
51. Drawz PE, Babineau DC, Rahman M. Metabolic complications in elderly adults with chronic kidney disease. J Am Geriatr Soc. 2012;60(2):310–5.
52. van der Velde M, Bakker SJ, de Jong PE, Gansevoort RT. Influence of age and measure of eGFR on the association between renal function and cardiovascular events. Clin J Am Soc Nephrol. 2010;5(11):2053–9.
53. Manjunath G, Tighiouart H, Coresh J, Macleod B, Salem DN, Griffith JL, et al. Level of kidney function as a risk factor for cardiovascular outcomes in the elderly. Kidney Int. 2003;63(3):1121–9.
54. Seliger SL, Siscovick DS, Stehman-Breen CO, Gillen DL, Fitzpatrick A, Bleyer A, et al. Moderate renal impairment and risk of dementia among older adults: the Cardiovascular Health Cognition Study. J Am Soc Nephrol. 2004;15(7):1904–11.
55. Raymond NT, Zehnder D, Smith SC, Stinson JA, Lehnert H, Higgins RM. Elevated relative mortality risk with mild-to-moderate chronic kidney disease decreases with age. Nephrol Dial Transplant. 2007;22(11):3214–20.
56. Muntner P, Bowling CB, Gao L, Rizk D, Judd S, Tanner RM, et al. Age-specific association of reduced estimated glomerular filtration rate and albuminuria with all-cause mortality. Clin J Am Soc Nephrol. 2011;6(9):2200–7.
57. Gueyffier F, Bulpitt C, Boissel JP, Schron E, Ekbom T, Fagard R, et al. Antihypertensive drugs in very old people: a subgroup meta-analysis of randomised controlled trials. INDANA Group. Lancet. 1999;353(9155):793–6.
58. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. NEJM. 2008;358(18):1887–98.
59. Musini VM, Tejani AM, Bassett K, Wright JM. Pharmacotherapy for hypertension in the elderly. Cochrane Database Syst Rev. 2009;(4):Cd000028.
60. Williamson JD, Supiano MA, Applegate WB, Berlowitz DR, Campbell RC, Chertow GM, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–82.
61. Oates DJ, Berlowitz DR, Glickman ME, Silliman RA, Borzecki AM. Blood pressure and survival in the oldest old. J Am Geriatr Soc. 2007;55(3):383–8.
62. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507–20.
63. Abuelo JG. Normotensive ischemic acute renal failure. NEJM. 2007;357(8):797–805.
64. Casas JP, Chua W, Loukogeorgakis S, Vallance P, Smeeth L, Hingorani AD, et al. Effect of inhibitors of the renin-angiotensin system and other antihypertensive drugs on renal outcomes: systematic review and meta-analysis. Lancet. 2005;366(9502):2026–33.
65. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al. Renoprotective effect of the angiotensin-receptor antagonist

irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001;345(12):851–60.
66. Hill GS. Hypertensive nephrosclerosis. Current Opinion Nephrol Hypertens. 2008;17(3):266–70.
67. Somma C, Trillini M, Kasa M, Gentile G. Managing end-stage renal disease in the elderly: state-of-the-art, challenges and opportunities. Aging Health. 2013;9:539–52.
68. Phoon RK. Chronic kidney disease in the elderly - assessment and management. Aust Fam Physician. 2012;41(12):940–4.
69. Musso CG, Vilas M, Onuigbo M. Nephroprevention in the oldest old with chronic kidney disease: Special considerations. World J Nephrol. 2015;4(1):1–5.
70. Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. NEJM. 2008;358(24):2560–72.
71. Duckworth W, Abraira C, Moritz T, Reda D, Emanuele N, Reaven PD, et al. Glucose control and vascular complications in veterans with type 2 diabetes. NEJM. 2009;360(2):129–39.
72. Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in Type 2 diabetes. NEJM. 2008;358(24): 2545–59.
73. Moen MF, Zhan M, Hsu VD, Walker LD, Einhorn LM, Seliger SL, et al. Frequency of hypoglycemia and its significance in chronic kidney disease. Clin J Am Soc Nephrol. 2009;4(6):1121–7.
74. Zoungas S, Patel A, Chalmers J, de Galan BE, Li Q, Billot L, et al. Severe hypoglycemia and risks of vascular events and death. NEJM. 2010;363(15):1410–8.
75. Kirkman MS, Briscoe VJ, Clark N, Florez H, Haas LB, Halter JB, et al. Diabetes in older adults. Diabetes Care. 2012;35(12):2650–64.
76. Abaterusso C, Lupo A, Ortalda V, De Biase V, Pani A, Muggeo M, et al. Treating elderly people with diabetes and stages 3 and 4 chronic kidney disease. Clin J Am Soc Nephrol. 2008;3(4):1185–94.
77. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet. 2002;360(9346):1623–30.
78. Ng BL, Anpalahan M. Management of chronic kidney disease in the elderly. Intern Med J. 2011;41(11):761–8.
79. Maw TT, Fried L. Chronic kidney disease in the elderly. Clin Geriatr Med. 2013;29(3):611–24.
80. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146–56.
81. Shlipak MG, Stehman-Breen C, Fried LF, Song X, Siscovick D, Fried LP, et al. The presence of frailty in elderly persons with chronic renal insufficiency. Am J Kidney Dis. 2004;43(5): 861–7.
82. Painter P, Roshanravan B. The association of physical activity and physical function with clinical outcomes in adults with chronic kidney disease. Curr Opin Nephrol Hypertens. 2013;22(6):615–23.
83. Johansen KL, Chertow GM, Jin C, Kutner NG. Significance of frailty among dialysis patients. J Am Soc Nephrol. 2007;18(11):2960–7.
84. Gotloib L, Silverberg D, Fudin R, Shostak A. Iron deficiency is a common cause of anemia in chronic kidney disease and can often be corrected with intravenous iron. J Nephrol. 2006;19(2):161–7.
85. Brown MA, Collett GK, Josland EA, Foote C, Li Q, Brennan FP. CKD in elderly patients managed without dialysis: survival, symptoms, and quality of life. Clin J Am Soc Nephrol. 2015;10(2):260–8.
86. Hussain JA, Mooney A, Russon L. Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. Palliat Med. 2013;27(9):829–39.
87. O'Connor NR, Kumar P. Conservative management of end-stage renal disease without dialysis: a systematic review. J Palliat Med. 2012;15(2):228–35.
88. Murtagh FE, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE. Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. Nephrol Dial Transplant. 2007;22(7):1955–62.
89. Wong CF, McCarthy M, Howse ML, Williams PS. Factors affecting survival in advanced chronic kidney disease patients who choose not to receive dialysis. Ren Fail. 2007;29(6):653–9.
90. Hussain JA, Flemming K, Murtagh FE, Johnson MJ. Patient and health care professional decision-making to commence and withdraw from renal dialysis: a systematic review of qualitative research. Clin J Am Soc Nephrol. 2015;10(7):1201–15.
91. Davison SN. End-of-life care preferences and needs: perceptions of patients with chronic kidney disease. Clin J Am Soc Nephrol. 2010;5(2):195–204.
92. Thorsteinsdottir B, Swetz KM, Albright RC. The Ethics of Chronic Dialysis for the Older Patient: Time to Reevaluate the Norms. Clin J Am Soc Nephrol. 2015;10(11):2094–9.
93. Crail S, Walker R, Brown M. Renal supportive and palliative care: position statement. Nephrology (Carlton). 2013;18(6):393–400.
94. Carson RC, Juszczak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? Clin J Am Soc Nephrol. 2009;4(10):1611–9.
95. Brown EA. Can quality of life be improved for the increasing numbers of older patients with end-stage kidney disease? Expert Rev Pharmacoecon Outcomes Res. 2010;10(6):661–6.
96. Brennan F, Stewart C, Burgess H, Davison SN, Moss AH, Murtagh FEM, et al. Time to improve informed consent for dialysis: an international perspective. Clin J Am Soc Nephrol. 2017;12(6):1001–9.
97. Demoulin N, Beguin C, Labriola L, Jadoul M. Preparing renal replacement therapy in stage 4 CKD patients referred to nephrologists: a difficult balance between futility and insufficiency. A cohort study of 386 patients followed in Brussels. Nephrol Dial Transplant. 2011;26(1):220–6.
98. Combs SA, Davison SN. Palliative and end-of-life care issues in chronic kidney disease. Curr Opin Support Palliat Care. 2015;9(1):14–9.
99. Crews DC, Scialla JJ, Liu J, Guo H, Bandeen-Roche K, Ephraim PL, et al. Predialysis health, dialysis timing, and outcomes among older United States adults. J Am Soc Nephrol. 2014;25(2):370–9.
100. Letourneau I, Ouimet D, Dumont M, Pichette V, Leblanc M. Renal replacement in end-stage renal disease patients over 75 years old. Am J Nephrol. 2003;23(2):71–7.
101. Moist LM, Lok CE, Vachharajani TJ, Xi W, AlJaishi A, Polkinghorne KR, et al. Optimal hemodialysis vascular access in the elderly patient. Semin Dial. 2012;25(6):640–8.
102. Vachharajani TJ, Moist LM, Glickman MH, Vazquez MA, Polkinghorne KR, Lok CE, et al. Elderly patients with CKD--dilemmas in dialysis therapy and vascular access. Nat Rev Nephrol. 2014;10(2):116–22.
103. Berger JR, Jaikaransingh V, Hedayati SS. End-stage kidney disease in the elderly: approach to dialysis initiation, choosing modality, and predicting outcomes. Adv Chronic Kidney Dis. 2016;23(1):36–43.
104. Roake J. Dialysis in the elderly. N Z Med J. 2004;117(1195):U904.
105. Kurella Tamura M, Covinsky KE, Chertow GM, Yaffe K, Landefeld CS, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. NEJM. 2009;361(16):1539–47.

106. Morton RL, Snelling P, Webster AC, Rose J, Masterson R, Johnson DW, et al. Factors influencing patient choice of dialysis versus conservative care to treat end-stage kidney disease. CMAJ. 2012;184(5):E277–83.
107. Davison R, Sheerin NS. Prognosis and management of chronic kidney disease (CKD) at the end of life. Postgrad Med J. 2014;90(1060):98–105.
108. Da Silva-Gane M, Wellsted D, Greenshields H, Norton S, Chandna SM, Farrington K. Quality of Life and Survival in Patients with Advanced Kidney Failure Managed Conservatively or by Dialysis. Clin J Am Soc Nephrol. 2012;7(12):2002–9.
109. Murtagh FE, Cohen LM, Germain MJ. The "no dialysis" option. Adv Chronic Kidney Dis. 2011;18(6):443–9.
110. Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. Nephrol Dial Transplant. 2011;26(5):1608–14.
111. Shum CK, Tam KF, Chak WL, Chan TC, Mak YF, Chau KF. Outcomes in older adults with stage 5 chronic kidney disease: comparison of peritoneal dialysis and conservative management. J Gerontol A Biol Sci Med Sci. 2014;69(3):308–14.
112. Verberne WR, Geers AB, Jellema WT, Vincent HH, van Delden JJ, Bos WJ. Comparative Survival among Older Adults with Advanced Kidney Disease Managed Conservatively Versus with Dialysis. Clin J Am Soc Nephrol. 2016;11(4):633–40.
113. Germain MJ, Davison SN, Moss AH. When enough is enough: the nephrologist's responsibility in ordering dialysis treatments. Am J Kidney Dis. 2011;58(1):135–43.
114. Beben T, Rifkin DE. The Elderly are Different: Initiating Dialysis in Frail Geriatric Patients. Semin Dial. 2015;28(3):221–3.
115. Couchoud CG, Beuscart JB, Aldigier JC, Brunet PJ, Moranne OP. Development of a risk stratification algorithm to improve patient-centered care and decision making for incident elderly patients with end-stage renal disease. Kidney Int. 2015;88(5):1178–86.
116. Li PK, Law MC, Chow KM, Leung CB, Kwan BC, Chung KY, et al. Good patient and technique survival in elderly patients on continuous ambulatory peritoneal dialysis. Perit Dial Int. 2007;27(Suppl 2):S196–201.
117. Dimkovic N, Oreopoulos DG. Chronic peritoneal dialysis in the elderly: a review. Peri Dial Int J Internat Soc Perit Dial. 2000;20(3):276–83.
118. Registry A. 38th Report, Chapter 5: Peritoneal Dialysis. 2016. Adelaide, Australia. Available from: http://www.anzdata.org.au.
119. Brown EA, Johansson L, Farrington K, Gallagher H, Sensky T, Gordon F, et al. Broadening Options for Long-term Dialysis in the Elderly (BOLDE): differences in quality of life on peritoneal dialysis compared to haemodialysis for older patients. Nephrol Dial Transplant. 2010;25(11):3755–63.
120. Baek MY, Kwon TH, Kim YL, Cho DK. CAPD, an acceptable form of therapy in elderly ESRD patients: a comparative study. Adv Perit Dial. 1997;13:158–61.
121. Nissenson AR. Quality of life elderly and diabetic patients on peritoneal dialysis. Perit Dial Int J Internat Soc Perit Dial. 1996;16(Suppl 1):S406–9.
122. Cameron JI, Whiteside C, Katz J, Devins GM. Differences in quality of life across renal replacement therapies: a meta-analytic comparison. Am J Kidney Dis. 2000;35(4):629–37.
123. Lamping DL, Constantinovici N, Roderick P, Normand C, Henderson L, Harris S, et al. Clinical outcomes, quality of life, and costs in the North Thames Dialysis Study of elderly people on dialysis: a prospective cohort study. Lancet. 2000;356(9241):1543–50.
124. Quill TE. Perspectives on care at the close of life. Initiating end-of-life discussions with seriously ill patients: addressing the "elephant in the room". JAMA. 2000;284(19):2502–7.
125. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. NEJM. 1999;341(23):1725–30.
126. Rao PS, Merion RM, Ashby VB, Port FK, Wolfe RA, Kayler LK. Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. Transplantation. 2007;83(8):1069–74.
127. Huang E, Poommipanit N, Sampaio MS, Kuo HT, Reddy P, Gritsch HA, et al. Intermediate-term outcomes associated with kidney transplantation in recipients 80 years and older: an analysis of the OPTN/UNOS database. Transplantation. 2010;90(9):974–9.
128. Knoll GA. Kidney transplantation in the older adult. Am J Kidney Dis. 2013;61(5):790–7.
129. Registry A. 38th Report, Chapter 8: Transplantation. 2016. Adelaide, Australia. Available from: http://www.anzdata.org.au.
130. Kent DM, Jafar TH, Hayward RA, Tighiouart H, Landa M, de Jong P, et al. Progression risk, urinary protein excretion, and treatment effects of angiotensin-converting enzyme inhibitors in nondiabetic kidney disease. J Am Soc Nephrol. 2007;18(6):1959–65.
131. Berzoff J, Swantkowski J, Cohen LM. Developing a renal supportive care team from the voices of patients, families, and palliative care staff. Palliat Support Care. 2008;6(2):133–9.
132. Steinhauser KE, Christakis NA, Clipp EC, McNeilly M, McIntyre L, Tulsky JA. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA. 2000;284(19):2476–82.
133. Raghavan D, Holley JL. Conservative Care of the Elderly CKD Patient: A Practical Guide. Adv Chronic Kidney Dis. 2016;23(1):51–6.
134. Singer PA, Martin DK, Kelner M. Quality end-of-life care: patients' perspectives. JAMA. 1999;281(2):163–8.
135. De Biase V, Tobaldini O, Boaretti C, Abaterusso C, Pertica N, Loschiavo C, et al. Prolonged conservative treatment for frail elderly patients with end-stage renal disease: the Verona experience. Nephrol Dial Transplant. 2008;23(4):1313–7.
136. Davison SN. The ethics of end-of-life care for patients with ESRD. Clin J Am Soc Nephrol. 2012;7(12):2049–57.
137. Barakzoy AS, Moss AH. Efficacy of the world health organization analgesic ladder to treat pain in end-stage renal disease. J Am Soc Nephrol. 2006;17(11):3198–203.
138. Zucker I, Yosipovitch G, David M, Gafter U, Boner G. Prevalence and characterization of uremic pruritus in patients undergoing hemodialysis: uremic pruritus is still a major problem for patients with end-stage renal disease. J Am Acad Dermatol. 2003;49(5):842–6.
139. Stevenson J, Meade A, Randall AM, Manley K, Notaras S, Heaney S, et al. Nutrition in Renal Supportive Care: Patient-driven and flexible. Nephrology (Carlton). 2017;22:739.
140. Carrero JJ. Mechanisms of altered regulation of food intake in chronic kidney disease. J Ren Nutr. 2011;21(1):7–11.
141. Bossola M, Luciani G, Rosa F, Tazza L. Appetite and gastrointestinal symptoms in chronic hemodialysis patients. J Ren Nutr. 2011;21(6):448–54.
142. Murphy EL, Murtagh FE, Carey I, Sheerin NS. Understanding symptoms in patients with advanced chronic kidney disease managed without dialysis: use of a short patient-completed assessment tool. Nephron Clin Pract. 2009;111(1):c74–80.
143. Fernstrom A, Hylander B, Rossner S. Taste acuity in patients with chronic renal failure. Clin Nephrol. 1996;45(3):169–74.

144. Davison SN. Facilitating advance care planning for patients with end-stage renal disease: the patient perspective. Clin J Am Soc Nephrol. 2006;1(5):1023–8.
145. Davison SN, Simpson C. Hope and advance care planning in patients with end stage renal disease: qualitative interview study. BMJ. 2006;333(7574):886.
146. Chan KY, Yip T, Yap DY, Sham MK, Wong YC, Lau VW, et al. Enhanced psychosocial support for caregiver burden for patients with chronic kidney failure choosing not to be treated by dialysis or transplantation: a pilot randomized controlled trial. Am J Kidney Dis. 2016;67(4):585–92.

Mental Illness in the Oldest-Old

17

Paul Cullen

Introduction

There is comparatively limited data on psychiatric illness in the elderly and even less so in the oldest-old. Whilst there are broad similarities in clinical presentation and management between the oldest-old and their younger counterparts, some qualitative differences between these groups highlight the need for clinicians to modify their diagnostic and management approaches.

Psychiatry differs from most other branches of medicine in that it is based largely on the description and treatment of syndromes. Whilst research is gradually closing in on many of the biological substrates associated with psychiatric conditions, for now at least there are no definitive investigative markers with which to confirm the presence of a specific mental illness. A diagnosis of major depression or schizophrenia is based on clinical assessment, not a blood test or cerebral scan. Given the great potential for symptomatic overlap between different conditions, this can make for challenging diagnostic waters and underscores the particular importance of performing a careful history and mental state examination as part of a methodical diagnostic and management approach in this group.

Historically, distinction was made between psychological conditions that were *secondary* to "organic" disease (i.e. demonstrated physical conditions) and those that were *primary*, due to "functional or non-organic" disease (i.e. occurring in the absence of demonstrable physical illness and so assumed to have some other aetiology). This is obviously a limiting and artificial categorisation, particularly in the oldest-old where multiple physical comorbidities and polypharmacy are largely the norm and any distinction between "primary or non-organic" and "secondary or organic" becomes increasingly blurred. Nevertheless, a broad appreciation of the interplay between the "psychological" and the "physical" can still assist in diagnostic formulation and therefore in directing best initial management. This relationship could be considered as follows:

A physical problem (or its treatment) causes psychological symptoms.
A psychological problem (or its treatment) causes physical symptoms.
A separate condition causes both psychological and physical symptoms.

Common Psychiatric Presentations

The major neuropsychiatric syndromes encountered in the oldest-old include the *mood disorders* (depression and mania), *anxiety disorders*, *psychotic disorders*, and *cognitive disorders* (covered elsewhere in this text). On encountering these symptoms in the elderly patient, the clinician should consider whether they are:

1. Due to an acute, potentially reversible medical issue
2. Due to an acute, reversible, or transient stress
3. Part of a more sustained, pervasive disorder

Psychological Disturbance Due to an Acute, Potentially Reversible Medical Issue

The elderly present with underlying vulnerability in the form of age-related systemic changes, multiple medical comorbidities, and frequent polypharmacy. Even relatively minor homeostatic disturbances can result in significant psychological and behavioural symptoms. Potentially treatable causes of psychological symptoms are shown in Table 17.1.

Psychological Disturbance Due to an Acute, Reversible, or Transient Stress

Distinguishing these conditions from other psychiatric disorders is important, as symptom course, impact on function, and level of associated risk are different. It will also

P. Cullen (✉)
Berkeley Vale Private Hospital, Berkeley Vale, NSW, Australia
e-mail: porlsim@iinet.net.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_17

Table 17.1 Potentially treatable causes of psychological symptoms

Delirium
Depression, mania, anxiety, psychosis [1]
Neurological conditions
Pain (of any kind)
Epilepsy (especially complex partial seizures): mood disorders, psychosis, cognitive changes
Normal pressure hydrocephalus: apathy, inertia, cognitive changes [2]
Endocrine disease [3]
Hypothyroidism: depression, cognitive changes, psychosis
Hyperthyroidism: anxiety, mania/mixed affective states, psychosis
Cushing's syndrome: fatigue, depression, cognitive changes
Addison's disease: apathy, depression
Metabolic or nutritional problems [3]
B12/folate deficiency: can contribute to depression
Anaemia: fatigue, can contribute to depression
Hypercalcaemia: depression, cognitive changes
Hypoglycaemia: anxiety, irritability, cognitive changes
Respiratory
Obstructive sleep apnoea: can present with amotivation, lethargy, dysphoria
Cancer (direct and indirect effects): mood changes, psychosis
Prescribed medication
Opiates/benzodiazepines: depression, anxiety, cognitive changes
Antihypertensives: depression, anxiety (beta-blockers, calcium blockers)
Corticosteroids: depression, anxiety, cognitive changes, or mania/psychosis (esp. higher doses)
Anti-Parkinsonian medication (dopaminergic): psychosis, anxiety/depression (during "off" cycles), pathological gambling
Anti-epileptic medications: depression, cognitive changes
Substance use
Caffeine: anxiety, insomnia
Nicotine: anxiety
Alcohol: depression, anxiety, cognitive changes

Information sources: American Psychiatric Association [1]; Lovestone [2]; Harrison & Kopelman [3]

affect management; identifying these conditions does not mean no intervention is required, only that a different range of treatment approaches may be more appropriate. Common time-limited psychological reactions to intermittent stress include grief and loss, other "adjustment disorders", to specific life stresses, and transient demoralisation, anxiety, or misperceptions in cognitive impairment and dementia [4].

Psychological Disturbance Due to a More Sustained, Pervasive Disorder

Sometimes depression, mania, anxiety, and psychosis presenting in the elderly are part of a more pervasive, entrenched constellation of symptoms that may not respond to simple general measures and require a more elaborate treatment approach. In the elderly, these may be either:

1. A relapse of a pre-existing condition (with its onset earlier in life)
2. A new condition of late onset

Pathogenesis involves a combination of underlying predisposing vulnerability factors interacting over time with any number of accumulating stresses, eventually manifesting clinically as disease. These include genetic, medical, psychological, social, and cultural influences. The extent and manner in which they combine in a particular individual can influence the way symptoms manifest.

Studies of mood and psychotic disorders in the elderly that have had their first onset earlier in life consistently show stronger associations with a positive family history. In contrast, disorders presenting for the very first time in old age have fewer genetic links. Late-onset conditions have weaker direct association with stressful psychosocial triggers and instead are more commonly associated with underlying neurological signs and medical problems, particularly cerebrovascular disease [5–16] Table 17.2.

Late-onset mental illness is more commonly associated with cognitive deficits. Neurocognitive assessment has demonstrated varying degrees of impaired executive function, processing speed, and attention, memory, and language function, reflecting predominantly frontosubcortical changes [23–32]. Imaging studies have shown reductions in caudate or hippocampal neuronal volume in depression and in bipolar disorder. The pathological basis remains unclear. Theories include a

Table 17.2 Other medical conditions associated with late-onset psychological symptoms

Cerebrovascular disease
Generalised (in the form of accumulating small vessel disease or silent lacunar infarcts) or localised (ischaemic or haemorrhagic stroke), often on a background of vascular risk factors
Other neurological conditions
Parkinson's disease: depression, anxiety, cognitive changes, psychosis [16–18]
Dementia
(behavioural and psychological symptoms of dementia – BPSD)
Given the widespread, progressive neurochemical and structural impacts on the brain, any array of psychopathology is possible and occurs in as many as 90% of cases. Depression, anxiety, or psychosis (often with persecutory beliefs or hallucinations) are common. Mania and excitability are reported. Agitation and aggression or withdrawal and apathy can occur [19, 20]. Whilst these psychiatric features can occur in any type of dementia, some symptom patterns may more commonly accompany specific dementia types. Lewy body disease commonly presents with vivid visual hallucinations. Frontal dementias (of any cause) may have significant cross-sectional symptomatic overlap with either depression (apathy, diminished communication, and indifference) or mania (social disinhibition, impulsivity, and hyperactivity) [21, 22]

Information sources: Nilsson et al. [16]; Zhang et al. [17]; Schneider et al. [18]; Brodaty et al. [19]; van der Linde et al. [20]; Pose et al. [21]; Wylie et al. [22]

process of CNS neuroinflammation (associated with elevated inflammatory markers including white cells, cytokines, and CRP), reduced neurogenesis (associated with decreased brain-derived neurotrophin factor), and cumulative damage caused by repetitive stress-induced high-cortisol states [33–39]. Other studies emphasise the role of cerebrovascular disease in the pathogenesis of both mental illness and cognitive impairment. Certainly, cognitive changes are far more likely in the presence of underlying cerebrovascular disease, which is also associated with poorer treatment response [10–12, 15, 36, 40, 41]. Regardless of underlying aetiological factors, several pervasive psychiatric syndromes are commonly encountered in the elderly and are discussed below.

Major Depression

In the oldest-old, the prevalence of significant depression has been reported as ranging from around 5–32% [42–44]. Perhaps not surprisingly, there is a higher risk in those living alone or isolated from loved ones, those with poor physical health or impaired IADLs, and those with cognitive impairment [43, 45–47]. In general, depression in the very old presents in a similar fashion to other age groups. However the depressed elderly may present with less typical clinical features including higher rates of sub-threshold depressive features and "depression without sadness", somatic preoccupation or unexplained physical symptoms, and apathy. This may affect diagnostic accuracy, particularly when using narrower definitions or excluding high-risk subpopulations (those with cognitive impairment or dwelling in residential facilities) [47–52].

Numerous attempts have been made to classify depressive subtypes. One hierarchical model proposes three broad subgroups: non-melancholic depression (where anxiety is common, and mood disturbance is more closely linked to the underlying temperament and personality), melancholic depression (with more distinctive mood, sleep, and psychomotor changes), and psychotic depression (melancholia along with distortions in beliefs and perception that often have a mood-congruent quality) [53]. All require treatment.

Hypomania and Mania

Bipolar disorder in the elderly is uncommon, estimated at 0.1–0.5% prevalence in over 65-year-olds (compared with 1.4% in young adults) although rates are much higher in inpatient populations [54, 55]. Many cases may represent relapse of an early-onset illness, either of a previously established bipolar disorder or through a recurrent depression that has switched to mania for the first time in late life, often after a latency of some decades. New-onset cases of mood elevation have associations with the various medical, cerebrovascular, and cognitive factors described earlier. Whilst the clinical features are broadly similar at any age, mania in the elderly is arguably less intense and more likely associated with longer duration of symptoms [54]. In mania, symptoms last at least a week, cause significant functional impairment, and can be so severe that psychosis (including grandiose or paranoid delusions and marked thought disorder) occurs. At least one lifetime episode of mania enables a diagnosis of bipolar I disorder. In hypomania symptoms can be briefer (4 days) and are generally less severe (so overall function remains mostly intact). Hypomania can occur in bipolar I disorder (if mania has previously occurred) but otherwise if associated with a history of previous major depression would enable a diagnosis of bipolar II disorder [4].

Anxiety Disorders

Anxiety disorders are prevalent in the elderly at 15%, with even higher rates of less specific anxiety symptoms [56, 57]. Almost all begin earlier in life, following a relapsing-remitting course across the lifespan with a tendency to flare-up in response to life stresses (psychosocial and physical), often recurring in the elderly at the very time when long-established coping structures are starting to fail. Risk factors include female gender, being single, multiple medical comorbidities (including vascular disease), and certain temperamental traits (neuroticism and perfectionism) [58–60]. Only a minority will have new-onset anxiety in late life. This could be in the context of an adjustment disorder or in the setting of cognitive decline or medical illness. More prominent agitation and dysphoria would raise suspicion of anxiety secondary to a major depression, although depression and anxiety often co-exist independently in the oldest-old [61]. Common anxiety disorders include generalised anxiety disorders (GADs), phobias, panic disorder, obsessive compulsive disorder (OCD), and post-traumatic stress disorder (PTSD) [4].

In the elderly, GAD is the most common form, is highly comorbid with other psychiatric illnesses (especially depression), and is possibly more common in some medical illnesses (such as stroke or Parkinson's disease) [61–63]. Phobias are also common. Specific phobias in the elderly more often involve fears around the natural environment (lightning, heights) than younger adults. They also have high rates (around 60% in some samples) of fear of falling, a multifactorial condition more frequent in the setting of balance problems or after a previous fall, which can be associated with generalised anxiety and depression [64–68]. Agoraphobia can be the product of fear of falling, fear of social embarrassment (e.g. in incontinence), or of having a panic attack in public. It can result in social isolation, physi-

cal deconditioning (and worsening mobility), and reduced quality of life.

Panic disorder, OCD, and PTSD are much less common and often associated with physical illness or cognitive impairment [69]. Some studies suggest more frequent obsessions around sin, more compulsive hand-washing, and more severe hoarding in older people with OCD compared to their younger counterparts [70, 71]. New traumas in late life (such as falls, cancer scares, traumatic bereavements, and frightening delirium experiences) can present with PTSD-like anxiety features, whilst physical, cognitive, and psychosocial stresses in old age can also reignite PTSD from earlier-life traumas (including childhood and military experiences).

Psychotic Disorders

Psychotic disorders are characterised by varying patterns of "positive symptoms": distortion in beliefs (delusions), perception (illusions, hallucinations), and thought form. Delusions are strongly held convictions outside of social or cultural norms, either entirely false or unrealistic, and largely impervious to reason. There are many different forms, including persecutory, grandiose, somatic, nihilistic, and referential. Perceptual distortions in the absence (hallucinations) or presence (illusions) of an external trigger may occur in any sensory modality. Formal thought disorder, inferred through the expression of language, may be subtle (such as the divergent loss of goal in tangentiality) or prominent (such as loosening of the associated connectedness between different ideas or topics or the more dramatic loss of grammatical cohesion in "word salad"). "Negative symptoms" (flattening of affective expression, avolition, alogia, ambivalence, and reduced attention) can occur in some forms of psychosis.

Psychosis is common in old age. This is usually a secondary psychosis (as discussed earlier), although primary psychotic disorders also occur. Secondary psychotic syndromes in the elderly include delirium, dementia, and mood disorders. The primary psychotic syndromes include delusional disorder, schizophrenia, and schizoaffective disorder [4]. Whilst there is much symptomatic overlap irrespective of the underlying cause of psychosis, some patterns are often evident and hint at likely aetiology.

Primary psychotic illnesses with their onset early in life follow a variable course and can persist into old age. Depending on the severity of the illness and the efficacy of previous treatment, one may expect to see the psychosocial impacts of many decades of a chronic or relapsing-remitting illness. The toll of many years of antipsychotic dopaminergic blockade or mood stabiliser use will also often be evident in the form of extrapyramidal side effects, tardive syndromes, metabolic disease, or renal and electrolyte abnormality.

Primary psychotic conditions can also have their onset in late life. There is a clear female preponderance. Higher rates have been reported in populations who experience marginalisation, discrimination, or communication difficulties such as migrants and the hearing or vision impaired. Clinically they may meet traditional criteria for schizophrenia or delusional disorder, or fall somewhere in between. They have been variously referred to as late paraphrenia, late-onset (after age 40) schizophrenia, and very late-onset (after age 60) schizophrenia-like psychosis, reflecting the lack of clarity in definition, classification, and phenomenology in the literature, in what is likely a very heterogeneous group of patients [72, 73]. Persecutory beliefs occur in the majority, often in the form of "partition delusions" (the belief of being monitored or affected by someone through the walls, floor or ceiling, either directly or with gas, radiation, or electricity). Auditory hallucinations are common. Disorder of thought form is rare and affect is usually preserved. Mild cognitive deficit may be evident [32, 74–76].

Suicide in the Elderly

Suicide is significantly more common in males, with two peaks across the lifespan: one in middle age and a second in the oldest-old. Australian rates in 2015 were 31.5/100,000 men aged 45–49 and 39.3/100,000 men over 85 [77]. Depression is a prominent risk factor, especially when anxiety is comorbid, yet in a concerning majority of cases, it will remain undetected prior to the attempt [78–81]. Higher rates are reported in the presence of physical illness (especially cancer and cardiovascular disease) or disability, in social isolation, and in temperaments characterised by introversion, anxious, and obsessional features [78, 79, 82–84]. A disrupted sense of self following traumatic loss, loneliness, intolerable anxiety, loss of control or autonomy, and hopelessness have been described as common underlying themes [84–86].

Key Elements of the Psychiatric Assessment in the Elderly

History and Examination

1. Obtain collateral information (from family, friends, caregivers) especially in the presence of cognitive impairment, where recollection and articulation of symptoms can become limited. In addition to aiding diagnosis, this provides valuable information regarding premorbid personality style, baseline function, and extent of existing social and supportive structures.

2. Explore risk in all its forms:
   - Risk to self (through deliberate self-harm, misadventure, self-neglect)
   - Risk to reputation or financial security
   - Risk from others (through neglect or deliberate abuse)
   - Risk to others (through aggression or negligence)

   The nature and extent of risk will strongly influence choice of treatment setting.
3. Clarify whether this is the first presentation of psychological illness or relapse of a longstanding recurrent illness. Look for underlying triggers and risk factors (including family history, underlying cerebrovascular risk factors, a history of relevant medical conditions, or use of medications commonly associated with mental disturbance).
4. Be mindful of the high prevalence of sub-syndromal or somatic presentations of depression and anxiety in this age group.
5. Always ask about substance use. Misuse or abuse of alcohol or prescription medications (especially benzodiazepines and opiates) or excessive caffeine intake is easily overlooked.
6. Always perform a bedside cognitive assessment.

Medical Investigation

Whilst there is no standardised approach to selection of investigations, a reasonable initial "aged care psychiatry screen" would include (Table 17.3).

The use of reliable, valid rating scales is no substitute for careful clinical assessment but may add weight to diagnostic impressions. The Geriatric Depression Scale is a commonly used self-rating 30-item questionnaire that is quick and simple to administer; a shorter 15-item version may be preferable in the presence of fatigue or mild cognitive impairment. In dementia, the Cornell Scale for Depression in Dementia, which combines patient and carer interviews, is preferred and also has validity in patients without dementia [91–93].

Table 17.3 Initial investigative screen

Investigation	Details
Electrolytes Renal and liver function Calcium, magnesium Fasting blood sugar Fasting lipids	Derangement can be associated with psychological disturbance Renal or hepatic impairment can impact on pharmacokinetics Lithium is eliminated by the kidneys and can cause renal impairment Antidepressants and mood stabilisers commonly cause hyponatraemia in the elderly Metabolic syndromes can result from atypical antipsychotics
Thyroid function	Derangement can be associated with psychological disturbance Lithium can affect thyroid function
Full blood count	Anaemia can impact on energy and mood Some psychotropic medications can cause neutropenia
Iron studies	Deficiency can cause anaemia and has associations in neuroleptic malignant syndrome [88]
Vit B12 and folate	Deficiency has been associated with depression, reduced antidepressant response, and cognitive impairment [89, 90]
Vit D	Deficiency associated with depression
Urine microscopy/ culture	Infections are common and can cause dramatic psychological disturbances
Cerebral imaging CT or MRI	Quantify extent and location of any vascular disease or atrophy Exclude other pathology
Electrocardiogram	As part of the general vascular risk work up Many psychotropics are associated with QTc prolongation

Information source: Dodd et al. [87]; Rosebush & Mazurek [88]; Robinson et al. [89]; Nahas &Sheikh [90]

Treatment

The burden of untreated mental illness, at any age, is readily apparent. The anguish of "psychological pain" is as profound as physical pain. It impacts on self-confidence, identity, relationships, and function; active mental illness impairs our ability to maintain meaningful connections with who we are, what we do, and who we do it with.

There are also hidden risks of untreated illness. Depression is an established independent risk factor for coronary heart disease, impacts on recovery and increases adverse outcomes following heart attack. It has been shown to increase risk of stroke. Similar evidence is growing for anxiety disorders. Mental illness generally carries increased mortality risk via medical illness and suicide [78, 94–96]. Therapy aims to reduce suffering and disability, improve quality of life, and where possible reduce morbidity and mortality.

General Treatment Approaches

Treatment of any acute medical issues identified during the initial physical assessment should occur, along with rationalisation of any polypharmacy (and where possible tapering of agents detrimental to mental state). Given the interaction between psychological distress, psychosocial risk factors, and physical problems in the oldest-old, there are several initial broad management approaches that have relevance regardless of the presenting flavour of mental disturbance and can be promoted by any clinician Box 17.1.

Box 17.1 General Treatment Measures

Supportive contact

Facilitating access to practical supports such as transport and assistance around the home, and supportive interaction with an empathic clinician.

Regular exercise

Aerobic exercise has shown benefits in both prevention and treatment of depression. It has positive effects in anxiety and can help improve sleep [97–99]. Both aerobic and anabolic exercise have been shown to increase cortical volume and improve memory and executive function in mild cognitive impairment [100–102].

Sunlight and sleep hygiene

Dysregulation of circadian rhythms can have significant impacts on sleep and mental well-being. A dose of direct morning sunlight soon after waking can be beneficial, along with broader healthy sleep hygiene habits [97, 103].

Manage substance use

The negative impacts (psychologically and physically) of alcohol and benzodiazepines should be addressed. Nicotine and caffeine can aggravate anxiety and impair quality of sleep.

Healthy diet

Encouraging good hydration and a healthy balanced diet is important in brain health. Regular intake of omega-3 fatty acids can be beneficial in cerebrovascular health and in depression. Folate has shown benefits in augmentation of antidepressants [90, 104, 105].

Socialisation and diversional activity

Encourage regular engagement in pleasurable diversional activities across the week, alone and in company, in and out of the home.

Education and "self-help" resources

Psychoeducation helps empower individuals, is a fundamental element of informed consent, and facilitates collaborative management.

Information sources: Nagas et al. [90]; Malhi et al. [97]; Ensai et al. [98]; Schuch et al. [99];Suo et al. [100]; Fiatarone et al. [101]; Colcombe et al. [102]; Wirz-Justice et al. [103]; Lin et al. [104]; Opie et al. [105].

Focused Approaches: Psychological/ Behavioural Therapies

In combination with general treatment approaches, non-pharmacological strategies may be all that is required for some types of disorder. They can be delivered individually or in a group setting. One of the more rigorously studied interventions is cognitive behavioural therapy (CBT), which comprises a wide array of psychological and behavioural strategies delivered in a systematic and structured manner, aiming to modify unhelpful patterns of thinking or action that may be contributing to ongoing symptoms or distress, with a focus on "here and now" issues. There is a considerable body of evidence for efficacy of CBT in insomnia, chronic pain, substance use, depression, delusions, and hallucinations in some psychoses, and it is particularly effective in anxiety disorders (often as stand-alone treatment), although limited data exists for the oldest-old [106, 107]. Success in therapy requires a degree of motivation and commitment to the process.

Focused Approaches: Biological Therapies

Biological treatment options include medication and neurostimulation and are generally similar to other age groups. Despite the inherent risks of adverse effects, rates of antidepressant, antipsychotic, and sedative prescription are significantly higher in the oldest-old than any other group, particularly in aged care residential settings [108]. As always, obtaining informed consent should be the first step.

Depression

Antidepressants are indicated in moderate-severe depression, when they are often combined with CBT. Generally, different antidepressant classes have shown comparable efficacy (around 50–60%) in most studies, and choice of agent will be influenced more by tolerability, although some studies have suggested superior efficacy for venlafaxine or tricyclic antidepressants over SSRIs. Some studies suggest less benefit for late-onset depression in the setting of vascular disease and in dementia [23, 97, 109, 110].

SSRIs (selective serotonin reuptake inhibitors) are a reasonable first-line choice. Early side effects usually settle within 1–2 weeks. Alternatives would include SNRIs (serotonin and noradrenaline reuptake inhibitors, particularly if depression is more severe or if there is comorbid neuropathic pain), NaSSA (noradrenaline and specific serotonin antidepressant), agomelatine, or NARI (noradrenaline reuptake inhibitor) (Tables 17.4 and 17.5).

Whilst early benefits may be seen within a few weeks, onset can be considerably delayed (10–12 weeks) in the elderly; it is important to resist the temptation to change treatment too early and instead allow an adequate therapeutic trial. If intolerable or ineffective, options would include changing dose or changing antidepressant class. Thereafter, options would include a switch in class to a second- or third-line antidepressant or augmentation with a different agent (lithium, atypical antipsychotics, thyroxine) [97] [Table 17.6].

In major depression with psychosis, an antipsychotic will often be added to the antidepressant early in treatment. In bipolar depression, antidepressants can induce a mood swing into mania or rapid mood cycling. Initial monother-

apy with a mood stabiliser (lithium, valproate, lamotrigine) or second-generation antipsychotic may suffice; alternatively an antidepressant may be used in combination with a mood stabiliser [97].

All antidepressants (but especially SSRI/SNRI) can cause hyponatraemia. Serotonergic antidepressants have the potential to cause serotonin syndrome, especially if combined with other serotonergic agents.

Neurostimulation therapy is an ever-developing field. Electroconvulsive therapy is a well-established antidepressant treatment superior to medication, with remission rates of around 60–90% [113–115]. Whilst often used in cases of medication intolerance or inadequacy, it can be used as first line for its more rapid onset of effect if there are acute risks (active suicidality or poor oral intake) or in melancholic and psychotic subtypes where it is particularly effective. It also has demonstrated benefits in the treatment of mania, schizophrenia, and several neurological conditions (catatonia, Parkinson's disease, neuroleptic malignant syndrome). As long as the patient can tolerate a general anaesthetic and the cardiovascular effects of treatment (rapid changes in heart rate and blood pressure) and has no relative contraindications (very recent MI or CVA, raised intracranial pressure or space-occupying lesion, retinal detachment), the treatment can be used safely in the oldest-old, where response rates are similar but relapse rates high [115, 116]. Side effects are usually minor (headache, nausea); however, the main concern is the potential for cognitive problems (acute confusion, anterograde and retrograde memory problems, executive dysfunction); in the vast majority these are time-limited and resolve once clear of the treatment course; however, some will experience persisting deficits into the longer term. Whilst ECT remains unsurpassed in terms of efficacy in depression, other emerging promising neurostimulation modalities include transcranial magnetic stimulation (TMS), which has the advantage of no anaesthetic or cognitive impacts.

Mania

Medications used to treat mania comprise a diverse collection of agents from different pharmacological groups (Table 17.7).

In mania, any medication that could be contributing to mood elevation should be weaned and an anti-manic agent commenced. If ineffective, options include a switch in agent, trial of second-line treatments (such as carbamazepine), or use of combinations. ECT can also be effective and should be used early if symptoms are severe [97].

Table 17.4 SSRIs

Name	Advantages/disadvantages	Adverse effects
Sertraline Citalopram Escitalopram	Minimal CYP isoenzyme activity (so less drug interactions)	GIT symptoms (nausea, diarrhoea, constipation, cramps) Headache Sexual dysfunction Agitation, sweating, insomnia QTc prolongation (citalopram) Hyponatraemia common in the elderly Osteoporosis and falls Bleeding risk (platelet dysfunction) Extrapyramidal side effects (less common)
Paroxetine	Higher propensity for anticholinergic side effects. Can be difficult to wean (due to short half-life and often marked rebound anxiety)	
Fluoxetine	Very long half-life	
Fluvoxamine	Potentially less sexual side effects Can be sedating	

Information sources: Katona & Livingston [110]; Taylor et al. [111]; Draper & Berman [112]

Table 17.5 Other first-line antidepressant options

Class/name	Advantages/disadvantages	Adverse effects
SNRI Venlafaxine Desvenlafaxine Duloxetine	May be more effective in severe depression or melancholia May be more effective in pain	Similar to SSRIs Hypertension at higher doses
NaSSA Mirtazapine Mianserin	Can be beneficial for insomnia and anorexia Sexual dysfunction uncommon	Sedation (at low dose) Increased appetite/weight (Mirtazapine) Oedema, restless legs Neutropaenia
Melatonergic agonist Agomelatine	Can be beneficial for insomnia Sexual dysfunction uncommon	Can cause hepatic problems
NARI Reboxetine	Can be activating	Sweating, tachycardia, dry mouth Insomnia Nausea, constipation Urinary hesitancy

Information sources: Malhi et al. [97]; Katona & Livingston [110]; Taylor et al. [111]

Table 17.6 Second-line antidepressants

Name	Advantages/disadvantages	Adverse effects
Tricyclic antidepressants (TCA) Nortriptyline Dothiepin Doxepin Amitriptyline Clomipramine	Can be more effective in melancholic depression Nortriptyline has less anticholinergic/hypotensive effects (so preferable in elderly)	Sedation, weight gain Anticholinergic side effects (confusion, dry mouth, constipation, urinary hesitancy, risks in glaucoma) Cardiovascular effects (hypotension, tachycardia, QTc prolongation, increased morbidity in IHD) Seizures in high doses Risk in overdose
Monoamine oxidase inhibitors Phenelzine Tranylcypromine	Risk of tyramine reaction (hypertensive crisis) with some medication, foods, and alcohol. Dietary restriction required	Dizziness, sedation Hypotension Constipation, urinary retention Hepatotoxicity

Information sources: Malhi et al. [97]; Katona & Livingston [110]; Taylor et al. [111]

Table 17.7 First-line anti-manic medications

Name	Advantages/disadvantages	Adverse effects
Lithium	Efficacy for both antidepressant augmentation and anti-manic effects Can reduce suicidality Higher risk of toxicity in the elderly due to reduced renal function and fluid balance and can occur within traditional therapeutic serum ranges Regular monitoring of serum trough levels, renal and thyroid function, calcium is required	Diarrhoea, vomiting Neurotoxicity Fine tremor, Parkinsonism Polyuria, polydipsia (nephrogenic diabetes insipidus) Weight gain Psoriasis Renal impairment Hypothyroidism, Hyperparathyroidism Cardiac effects (sick sinus syndrome, T wave flattening)
Valproate	Monitoring of serum trough levels to avoid toxicity	Nausea, vomiting, headache Weight gain Sedation Neutropaenia, thrombocytopaenia Hyponatraemia Tremor, Parkinsonism
Second-generation antipsychotics Olanzapine Quetiapine Risperidone Aripiprazole	Can be used as anti-manic monotherapy, or for sedative/antipsychotic augmentation (of lithium or valproate)	Sedation Cardiovascular effects (hypotension, QTc prolongation) Metabolic effects (less with aripiprazole) Anticholinergic effects (less with risperidone) Extrapyramidal effects (least with quetiapine) Neutropaenia

Information sources: Malhi et al. [97]; Katona & Livingston [110]; Taylor et al. [111]

Anxiety

Antidepressants have efficacy in anxiety disorders. SSRIs or SNRIs may be used as first line and often augment psychological approaches [58]. Anxious patients are often somatically hypervigilant and can misattribute symptoms of anxiety to medication side effects; careful explanation can often prevent premature abandonment of treatment or unnecessary multiple trials. In some cases, addition of other anxiolytics in low dose (including atypical antipsychotics and pregabalin) early in the course of treatment may help control some symptoms of arousal until the antidepressant agent has achieved response [117, 118]. Benzodiazepines should be avoided if possible or used in low doses for brief periods only.

Psychosis

In the elderly, antipsychotics carry a considerable risk of side effect burden. As always, this risk needs to be weighed against the risk of untreated symptoms and the likelihood the antipsychotic will improve things. In dementia, non-pharmacological options should always be the primary therapeutic focus, with antipsychotic medication reserved for

Table 17.8 Side effects of antipsychotic medications

Extrapyramidal (EPSE) (especially in Lewy body/Parkinson's disease) Dystonia, Parkinsonism Akathisia Tardive dyskinesia	*Neuroleptic malignant syndrome* (in <2%) Autonomic and thermoregulatory instability Tachycardia Hypertension Hyperthermia Diaphoresis, tachypnoea Neurological changes Muscle rigidity Tremor Confusion, stupor, coma Investigations Raised creatine kinase Leucocytosis Renal/electrolyte/ hepatic abnormality
Metabolic and endocrine Weight gain, dyslipidaemia Impaired glucose tolerance, diabetes Hyperprolactinaemia (and increased risk of osteoporosis and breast cancer) Hyponatraemia	
Anticholinergic Dry mouth, blurred vision Constipation, urinary retention Confusion	
Cardiovascular Hypotension QTc prolongation	
Other Sedation Gastrointestinal (nausea, diarrhoea, constipation, raised liver enzymes) Sexual dysfunction	

Information sources: Katona & Livingston [110]; Taylor et al. [111]; Galletly et al. [121]; Musselman et al. [122]

more persistent psychotic symptoms associated with distress, problematic behaviours, or elevated risk. Late-onset schizophrenia tends to respond to much smaller antipsychotic doses than early-onset forms [73, 119, 120].

Atypical (second-generation) antipsychotics are generally preferred for their more tolerable side effect profile. Nevertheless, they also carry risk of adverse effects (Table 17.8). Furthermore studies have shown in some populations (dementia) an increased risk of mortality (especially through pneumonia and cardiac problems) and morbidity (including cerebrovascular disease) [119]. Apart from clozapine (rarely used in the elderly), quetiapine has the least potential for EPSE. Aripiprazole has fewer metabolic side effects, and risperidone has fewer anticholinergic side effects (Table 17.8). Whilst oral preparations are preferable, in cases of poor compliance, injectable depot administration may be utilised.

Clinical Relevance

- Mental illness in the elderly can be due to relapse of early-onset disease or a new late-onset process.
- Medical causes of psychological disease in the oldest-old are very common. Identification and treatment is always the first priority.
- Depression in the elderly commonly presents with somatic or sub-syndromal features.
- Whilst treatment approaches are similar to younger populations, medication should be introduced slowly in low doses.
- Antidepressants and antipsychotics carry a significant side effect burden, and their potential benefit must outweigh this risk.
- Electroconvulsive therapy is most effective for melancholic or psychotic depression subtypes and can be safely used in the elderly.
- In dementia, non-pharmacological strategies for behavioural and psychological symptoms are first line.
- Elderly males have the highest suicide rates. Exploring suicide and other risks is an essential part of the basic assessment.

Multiple Choice Questions

1. In the treatment of depression, a reasonable first-line antidepressant agent would be:
   A. Lithium
   B. An SSRI
   C. A tricyclic antidepressant
   D. Oxazepam
   E. All of the above
2. A patient you are treating for late-onset psychosis presents with abrupt onset of confusion, fever, muscle stiffness, and new hypertension. A reasonable initial approach would include:
   A. Supportive nursing measures
   B. Withholding of their regular antipsychotic
   C. Medical work up including full blood count, renal and liver function, creatine kinase
   D. Obtaining additional information from family or friends
   E. All of the above
3. ECT would be considered early in the setting of:
   A. Acute paranoid psychosis
   B. Recurrent disabling panic attacks
   C. Parkinson's disease
   D. Melancholic depression
   E. All of the above
4. Which of the following form part of the basic assessment of any elderly patient?
   A. Cognitive screen
   B. Physical examination and investigation
   C. Careful assessment of risk including suicidality
   D. Obtaining a corroborative history
   E. All of the above

Answers to MCQs

1. B
2. E
3. D
4. E

References

1. American Psychiatric Association. Practice guideline for the treatment of patients with delirium. Am J Psychiatry. 1999;156(5 Supp):1–20.
2. Lovestone S. Other disorders of the nervous system. In: David AS, Fleminger S, Kopelman MD, Lovestone S, Mellers JDC, editors. Lishman's organic psychiatry. A textbook of neuropsychiatry. 4th ed. West Sussex: Wiley-Blackwell; 2009. Chap 14.
3. Harrison NA, Kopelman MD. Endocrine diseases and metabolic disorders. In: David AS, Fleminger S, Kopelman MD, Lovestone S, Mellers JDC, editors. Lishman's organic psychiatry. A textbook of neuropsychiatry. 4th ed. West Sussex: Wiley-Blackwell; 2009. Chap 10.
4. American Psychiatric Association: diagnostic and statistical manual of mental disorders, 5th ed. Arlington: American Psychiatric Association; 2013.
5. Gallagher D, Mhaolain AN, Greene E, Walsh C, Denihan A, Bruce I, et al. Late life depression: a comparison of risk factors and symptoms according to age of onset in community dwelling older adults. Int J Geriatr Psychiatry. 2010;25:981–7.
6. Hayes JC, Krishnan KRR, George LK, Blazer DG. Age of first onset of bipolar disorder: demographic, family history, and psychosocial correlates. Depress Anxiety. 1998;7:76–82.
7. Almeida OP, Howard RJ, Levy R, David AS. Psychotic states arising in late life (late paraphrenia). The role of risk factors. Br J Psychiatry. 1995;166(2):215–28.
8. Grace J, O'Brien JT. Association of life events and psychosocial factors with early but not late onset depression in the elderly: implications for possible differences in aetiology. Int J Geriatr Psychiatry. 2003;18:473–8.
9. Hickie I, Simons L, Naismith S, Simons J, McCallum J, Pearson K. Vascular risk to late-life depression: evidence from a longitudinal community study. ANZ J Psychiatry. 2003;37: 62–5.
10. Subramaniam H, Dennis M, Byrne E. The role of vascular risk factors in late onset bipolar disorder. Int J Geriatr Psychiatry. 2007;22:733–7.
11. Wijeratne C, Malhi GS. Vascular mania: an old concept in danger of sclerosing? A clinical overview. Acta Psychiatr Scand. 2007;116(Suppl.434):35–40.
12. Tamashiro JH, Zung S, Zanetti MV, de Castro CC, Vallada H, Busatto GF, et al. Increased rates of white matter hyperintensities in late-onset bipolar disorder. Bipolar Disord. 2008;10: 765–75.
13. Taylor WD, MacFall JR, Steffens DC, Payne ME, Provenzale JM, Krishnan KR. Localization of age-associated white matter hyperintensities in late-life depression. Prog Neuro-Psychopharmacol Biol Psychiatry. 2003;27(3):539–44.
14. Flint AJ, Rifat SL, Eastwood MR. Late-onset paranoia: distinct from paraphrenia? Int J Geriatr Psychiatry. 1991;6(2):103–9.
15. Sachdev P, Brodaty H. Quantitative study of signal hyperintensities on T2-weighted magnetic resonance imaging in late-onset schizophrenia. Am J Psychiatry. 1999;156(12):1958–67.
16. Nilsson FM, Kessing LV, Sørensen TM, Andersen PK, Bolwig TG. Affective disorders in neurological diseases: a case register-based study. Acta Psychiatr Scand. 2003;108:41–50.
17. Zhang N, Liu W, Ye M, Cohen AD, Zhang Y. The heterogeneity of non-motor symptoms of Parkinson's disease. Neurol Sci. 2015;36:577–84.
18. Schneider F, Althaus A, Backes V, Dodel R. Psychiatric symptoms in Parkinson's disease. Eur Arch Psychiatry Clin Neurosci. 2008;258(Supp5):55–9.
19. Brodaty H, Draper B, Saab D, Low L, Richards V, Paton H, Lie D. Psychosis, depression and behavioural disturbances in Sydney nursing home residents: prevalence and predictors. Int J Geriatr Psychiatry. 2001;16:504–12.
20. van der Linde RM, Dening T, Matthews FE, Brayne C. Grouping of behavioural and psychological symptoms of dementia. Int J Geriatr Psychiatry. 2014;29:562–8.
21. Pose M, Cetkovich M, Gleichgerrcht E, Ibanez A, Torralva T, Manes F. The overlap of symptomatic dimensions between frontotemporal dementia and several psychiatric disorders that appear in late adulthood. Int Rev Psychiatry. 2013;25(2):159–67.
22. Wylie MA, Shnall A, Onyike CU, Huey ED. Management of frontotemporal dementia in mental health and multidisciplinary settings. Int Rev Psychiatry. 2013;25(2):230–6.
23. Alexopoulos G, Kelly R. Research advances in geriatric depression. World Psychiatry. 2009;8:140–9.
24. Bagulho F. Depression in older people. Curr Opin Psychiatry. 2002;15:417–22.
25. Rock PL, Roiser JP, Riedel WJ, Blackwall MD. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol Med. 2014;44(10):2029–40.
26. Thomas AJ, O'Brien JT. Depression and cognition in older adults. Curr Opin Psychiatry.; Jan. 2008;21(1):8–13.
27. Gildengers AG, Mulsant BH, Al Jurdi RK, Beyer JL, Greenberg RL, Gyulai L, Moberg PJ, Sajatovic M, Ten Have T, Young RC, The GERIBD Study Group. The relationship of bipolar disorder lifetime duration and vascular burden to cognition in older adults. Bipolar Disord. 2010;12:851–8.
28. Porter RJ, Robinson LJ, Malhi GS, Gallagher P. The neurocognitive profile of mood disorders – review of the evidence and methodological issues. Bipolar Disord. 2015;17(Suppl. 2):21–40.
29. Schouws SN, Comijs HC, Stek ML, Dekker J, Oostervink F, Naarding P, et al. Cognitive impairment in early and late bipolar disorder. Am J Geriatr Psychiatry. 2009;17(6):508–15.
30. Chowdhury R, Ferrier IN, Thompson JM. Cognitive dysfunction in bipolar disorder. Curr Opin Psychiatry. 2003;16:7–12.
31. Almeida OP, Howard RJ, Levy R, David AS, Morris RG, Sahakian BJ. Cognitive features of psychotic states arising in late life (late paraphrenia). Psychol Med. 1995;25(4):685–98.
32. Hassett A. A descriptive study of first presentation psychosis in old age. ANZ J Psychiatry. 1999;33:814–24.
33. Zhou H, Li R, Ma Z, Rossi S, ZU X, Li J. Smaller gray matter volume of hippocampus/parahippocampus in elderly people with subthreshold depression: a cross-sectional study. BMC Psychiatry. 2016;16:219.
34. Hickie I, Naismith S, Ward PB, Turner K, Scott E, Mitchell P, et al. Reduced hippocampal volumes and memory loss in patients with early- and late-onset depression. Br J Psychiatry. 2005;186:197–202.
35. Sawyer K, Corsentino E, Sachs-Ericsson N, Steffens D. Depression, hippocampal volume changes, and cognitive decline in a clinical sample of older depressed outpatients and non-depressed controls. Aging and Ment Health. 2012;16(6):753–62.
36. Kohler S, Thomas A, Lloyd A, Barber R, Almeida O, O'Brien JT. White matter hyperintensities, cortisol levels, brain atrophy and continuing cognitive deficits in late-life depression. Br J Psychiatry. 2010;196:143–9.
37. Beyer JL, Kuchibhatla M, Payne M, Moo-Young M, Cassidy F, MacFall J, et al. Caudate volume measurement in older adults with bipolar disorder. Int J Geriatr Psychiatry. 2004;19:109–14.

38. Alexopoulos G, Morimoto SS. The inflammation hypothesis in geriatric depression. Int J Geriatr Psychiatry. 2011;26:1109–18.
39. Hurley LL, Tizabi Y. Neuroinflammation, neurodegeneration, and depression. Neurotox Res. 2013;23:131–44.
40. Aizenstein HJ, Baskys A, Boldrini M, Butters MA, Diniz BS, Jaiswal MJ, et al. Vascular depression consensus report – a critical update. BMC Med. 2016;14:161.
41. Breitner JC, Husain MM, Figiel GS, Krishnan KR, Boyko OB. Cerebral white matter disease in late-onset paranoid psychosis. Biol Psychiatry. 1990;28(3):266–74.
42. Paivarinta A, Verkkoniemi A, Niinisto L, Kivela SL, Sulkava R. The prevalence and associates of depressive disorders in the oldest-old Finns. Soc Psychiatry Psychiatr Epidemiol. 1999;34:352–9.
43. Stek ML, Gussekloo J, Beekman AT, van Tilburg W, Westendorp RG. Prevalence, correlates and recognition of depression in the oldest old: the Leiden 85-plus study. J Affect Disord. 2004;78(3):193–200.
44. Petersson S, Mathillas J, Wallin K, Olofsson B, Allard P, Gustsfson Y. Risk factors for depressive disorders in very old age: a population-based cohort study with a 5-year follow-up. Soc Psychiatry Psychaitr Epidemiol. 2014;49:831–9.
45. Jopp DS, Park MS, Lehrfeld J, Paggi M. Physical, cognitive, social and mental health in near-centenarians and centenarians living in New York City: findings from the Fordham Centenarian Study. BMC Geriatr. 2016;16:1.
46. Wilson K, Mottram P, Sixsmith A. Depressive symptoms in the very old living alone: prevalence, incidence and risk factors. Int J Geriatr Psychiatry. 2007;22:361–6.
47. Hybels CF, Landerman LR, Blazer DG. Age differences in symptom expression in patients with major depression. Int J Geriatr Psychiatry. 2012;27:601–11.
48. Snowden J. Is depression more prevalent in old age? ANZ J Psychiatry. 2001;35(6):782–7.
49. Zarit SH, Femia EE, Gatz M, Johansson B. Prevalence, incidence and correlates of depression in the oldest old: the OCTO study. Aging Ment Health. 1999;3(2):119–28.
50. O'Connor DW. Do older Australians truly have low rates of anxiety and depression? A critique of the 1997 National Survey of mental health and wellbeing. ANZ J Psychiatry. 2006;40:623–31.
51. Brodaty H, Luscombe G, Parker G, Wilhelm K, Hickie I, Austin MP, et al. Increased rate of psychosis and psychomotor change in depression with age. Psychol Med. 1997;27(5):1205–13.
52. Brodaty H, Cullen B, Thompson C, Mitchell P, Parker G, Wilhelm K, et al. Age and gender in the phenomenology of depression. Am J Geriatr Psychiatry. 2005;13(7):589–96.
53. Parker G. Classifying depression: should paradigms lost be regained? Am J Psychiatry. 2000;157(8):1195–203.
54. Depp CA, Jeste DV. Bipolar disorder in older adults: a critical review. Bipolar Disord. 2004;6:343–67.
55. Dols A, Kupka RW, van Lammeren A, Beekman AT, Sajatovic M, Stek ML. The prevalence of late-life mania: a review. Bipolar Disord. 2014;16:113–8.
56. Bryant C, Jackson H, Ames D. The prevalence of anxiety in older adults: methodological issues and a review of the literature. J Affect Disord. 2008;109(3):233–5.
57. Golden J, Conroy RM, Bruce I, Denihan A, Greene E, Kirby M, Lawlor BA. The spectrum of worry in the community-dwelling elderly. Aging Ment Health. 2011;15(8):985–94.
58. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske MG. Anxiety disorders in older adults: a comprehensive review. Depress Anxiety. 2010;27:190–211.
59. Chang WH, Chen WT, Lee IH, Chen PS, Yang YK, Chen KC. Coexisting anxiety disorders alter associations with physical disorders in the elderly: a Taiwan cross-sectional nationwide study. Psych Clin Neurosci. 2016;70:211–7.
60. Handley AK, Egan SJ, Kane RT, Rees CS. The relationships between perfectionism, pathological worry and generalised anxiety disorder. BMC Psychiatry. 2014;14:98.
61. Van der Weele GM, Gussekloo J, MWM DW, AJM DC, Van der Mast RC. Co-occurrence of depression and anxiety in elderly subjects aged 90 years and its relationship with functional status, quality of life and mortality. Int J Geriatr Psychiatry. 2009;24:595–601.
62. Flint AJ. Epidemiology and comorbidity of anxiety disorders in the elderly. Am J Psychiatry. 1994;151(5):640–9.
63. Flint AJ. Generalised anxiety disorder in elderly patients. Epidemiology, diagnosis and treatment options. Drugs Aging. 2005;22(2):101–14.
64. Fredrikson M, Annas P, Fischer H, Wik G. Gender and age differences in the prevalence of specific fears and phobias. Behav Res Ther. 1996;34(1):33–9.
65. Arfken CL, Lach HW, Birge SJ, Miller JP. The prevalence and correlates of fear of falling in elderly persons living in the community. Am J Public Health. 1994;84(4):565–70.
66. Ribeiro O, Santos AR. Psychological correlates of fear of falling in the elderly. Educ Gerontol. 2015;41:69–78.
67. Payette MC, Bélanger C, Benyebdri F, Filiatrault J, Bherer L, Bertrand JA, et al. The association between generalized anxiety disorder, subthreshold anxiety symptoms and fear of falling among older adults: preliminary results from a pilot study. Clin Gerontol. 2017;40(3):197–206.
68. Visschedijk JHM, Caljouw MAA, Bakkers E, van Balen R, Achterberg W. Longitudinal follow-up study on fear of falling during and after rehabilitation in skilled nursing facilities. BMC Geriatr. 2015;15:161.
69. Koychev I, Ebmeier KP. Anxiety in older adults often goes undiagnosed. Practitioner. 2016;260(1789):17–20.
70. Kohn R, Westlake RJ, Rasmussen SA, et al. Clinical features of obsessive-compulsive disorder in elderly patients. Am J Geriatr Psychiatry. 1997;5:211–5.
71. Ayers CR, Saxena S, Golshan S, Loebach Wetherall J. Age at onset and clinical features of late life compulsive hoarding. Int J Geriatr Psychiatry. 2010;25:142–9.
72. Roth M, Kay DWK. Late paraphrenia: a variant of schizophrenia manifest in late life or an organic clinical syndrome? A review of recent evidence. Int J Geriatr Psychiatry. 1998;13:775–84.
73. Howard R, Rabins PV, Seeman MV, Jeste DV, The International Late-Onset Schizophrenia Group. Late-onset schizophrenia and very-late-onset schizophrenia-like psychosis: an international consensus. Am J Psychiatry. 2000;157:172–8.
74. Howard R, Castle D, O'Brien J, Almeida O, Levy R. Permeable walls, floors, ceilings and doors. Partition delusions in late paraphrenia. Int J Geriatr Psychiatry. 1992;7:719–24.
75. Sato T, Bottlender R, Schröter A, Möller HJ. Psychopathology of early-onset versus late-onset schizophrenia revisited: an observation of 473 neuroleptic-naive patients before and after first-admission treatments. Schizophr Res. 2004;67(2–3):175–83.
76. Almeida OP, Howard RJ, Levy R, David AS. Psychotic states arising in late life (late paraphrenia) psychopathology and nosology. Br J Psychiatry. 1995;166(2):205–14.
77. Australian Bureau of Statistics. Age-specific death rates for intentional self-harm, by sex, 2015. Cat no. 3303.0; 2016.
78. Snowden J, Baume P. A study of suicides of older people in Sydney. Int J Geriatr Psychitry. 2002;17:261–9.
79. Harwood D, Hawton K, Hope T, Jacoby R. Psychiatric disorder and personality factors associated with suicides in older people: a descriptive and case-control study. Int J Geriatr Psychiatry. 2001;16:155–65.
80. Oude Voshaar RC, van der Veen DC, Hunt I, Kapur N. Suicide in late-life depression with and without comorbid anxiety disorders. Int J Geriatr Psychiatry. 2016;31:146–52.

81. Suominen K, Isometsä E, Lönnqvist J. Elderly suicide attempters with depression are often diagnosed only after the attempt. Int J Geriatr Psychiatry. 2004;19(1):35–40.
82. Harris EC, Barraclough BM. Suicide as an outcome for medical disorders. Medicine. 1994;73(6):281–96.
83. Shelef A, Hiss J, Cherkashin G, Berger U, Aizenberg D, Baruch Y, Barak Y. Psychosocial and medical aspects of older suicide completers in Israel: a 10-year survey. Int J Geriatr Psychiatry. 2014;29:846–51.
84. Chan J, Draper B, Banerjee S. Deliberate self-harm in older adults: a review of the literature from 1995 to 2004. Int J Geriatr Psychiatry. 2007;22:720–32.
85. Bonnewyn A, Shah A, Bruffarts R, Schoevaerts K, Rober P, Van Parys H, Demyttenaere K. Reflections of older adults on the process preceding their suicide attempt: a qualitative approach. Death Stud. 2014;38:612–8. https://doi.org/10.1080/07481187.2013.835753.
86. Westefeld JS, Casper D, Galligan P, Gibbons S, Lustgarten S, Rice A, et al. Suicide and older adults: risk factors and recommendations. J Loss Trauma. 2015;20:491–508. https://doi.org/10.1080/15325024.2014.949154.
87. Dodd S, Malhi G, Tiller J, Schweitzer I, Hickie I, Khoo JP, et al. A consensus statement for safety monitoring guidelines of treatments for major depressive disorder. ANZ J Psychiatry. 2011;45(9):712–25.
88. Rosebush PI, Mazurek MF. Serum iron and neuroleptic malignant syndrome. Lancet. 1991;338(8760):149–51.
89. Robinson DJ, O'Luanaigh C, Tehee E, O'Connell H, Hamilton F, Chin AV, et al. Associations between holotranscobalamin, vitamin B12, homocysteine and depressive symptoms in community-dwelling elders. Int J Geriatr Psychiatry. 2011;26:307–13.
90. Nahas R, Sheikh O. Complementary and alternative medicine for the treatment of major depressive disorder. Can Fam Physician. 2011;57:659–63.
91. Sharp L, Lipsky M. Screening for depression across the lifespan: a review of measures for use in primary care settings. Am Fam Physician. 2002;66(6):1001–8.
92. Debruyne H, Van Buggenhout M, Le Bastard N, Aries M, Audenaert K, De Deyn PP, et al. Is the geriatric depression scale a reliable screening tool for depressive symptoms in elderly patients with cognitive impairment? Int J Geriatr Psychiatry. 2009;24:556–62.
93. Alexopoulos GS, Abrams RC, Young RC, Shanoian CA. Cornell scale for depression in dementia. Biol Psychiatry. 1988;23:271–84.
94. Cohen BE, Edmondson D, Kronish IM. State of the art review: depression, stress, anxiety, and cardiovascular disease. Am J Hypertens. 2015;28(11):1295–302.
95. Liebetrau M, Steen B, Skoog I. Depression as a risk factor for the incidence of first-ever stroke in 85-year-olds. Stroke. 2008;39(7):1960–5.
96. Scott KM. Depression, anxiety and incident cardiometabolic diseases. Curr Opin Psychiatry. 2014;27(4):289–93.
97. Malhi G, Bassett D, Boyce P, Bryant R, Fitzgerald P, Fritz K, et al. Royal Australian and New Zealand college of psychiatrists clinical practice guidelines for mood disorders. ANZ J Psychiatry. 2015;49(12):1–185.
98. Ensari I, Greenlee TA, Motl RW, Petruzzello SJ. Meta-analysis of acute exercise effects on state anxiety: an update of randomised controlled trials over the past 25 years. Depress Anxiety. 2015;32(8):624–34.
99. Schuch FB, Deslandes AC, Stubbs B, Gosmann NP, Silva CT, Fleck MP. Neurobiological effects of exercise on major depressive disorder: a systemic review. Neurosci Biobehav Rev. 2016;61:1–11.
100. Suo C, Singh MF, Gates N, Wen W, Sachdev P, Brodaty H, et al. Therapeutically relevant structural and functional mechanisms triggered by physical and cognitive exercise. Mol Psychiatry. 2016;21(11):1633–42.
101. Fiatarone Singh MA, Gates N, Saigal N, Wilson GC, Meiklejohn J, Brodty H, et al. The study of mental and resistance training (SMART) study-resistance training and/or cognitive training in mild cognitive impairment: a randomised, double-blind, double-sham controlled trial. JAMA. 2014;15:873–80.
102. Colcombe SJ, Erickson KI, Scalf PE, Kim JS, Prakash R, McAuley E, et al. Aerobic exercise training increases brain volume in aging humans. J Gerontol A Biol Sci Med Sci. 2006;61(11):1166–7.
103. Wirz-Justice A, Benedetti F, Berger M, Lam RW, Martiny K, Terman M, et al. Chronotherapeutics (light and wake therapy) in affective disorders. Psychol Med. 2005;35(7):939–44.
104. Lin PY, Mischoulon D, Freeman MP, Matsuoka Y, Hibbeln J, Belmaker RH, et al. Are omega-3 fatty acids antidepressants or just mood-improving agents? The effect depends upon diagnosis, supplement preparation, and severity of depression. Mol Psychiatry. 2012;7:1161–3.
105. Opie RS, Itsiopoulos C, Parletta N, Sanchez-Villegas A, Akbaraly TN, Ruusunen A, et al. Dietary recommendations for the prevention of depression. Nutr Neurosci. 2017;20(3):161.
106. Hofman SG, Asaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of cognitive behavioural therapy: a review of meta-analyses. Cogn Ther Res. 2012;36:427–40.
107. Hendriks GJ, Oude Voshaar RC, Keijsers GPJ, Hoogduin CAL, Van Balkom AJLM. Cognitive-behavioural therapy for late-life anxiety disorders: a systematic review and meta-analysis. Act Psychiatr Scand. 2008;117:403–11.
108. Hollingworth SA, Lie DC, Siskind DJ, Byrne GJ, Hall WD, Whiteford HA. Psychiatric drug prescribing in elderly Australians: time for action. ANZ J Psychiatry. 2001;45:705–8.
109. Banerjee S, Hellier J, Romeo R, Dewey M, Knapp M, Ballard C, et al. Study of the use of antidepressants for depression in dementia: the HTA-SADD trial--a multicentre, randomised, double-blind, placebo-controlled trial of the clinical effectiveness and cost-effectiveness of sertraline and mirtazapine. Health Technol Assess. 2013;17(7):1–166.
110. Katona C, Livingston G. Drug treatment in old age psychiatry. London: Martin Dunitz; 2003.
111. Taylor D, Paton C, Kapur S. The Maudsley prescribing guidelines. 10th ed. London: Informa Healthcare; 2009.
112. Draper B, Berman K. Tolerability of selective serotonin reuptake inhibitors. Issues relevant to the elderly. Drugs Aging. 2008;25(6):501–19.
113. NSW Government Health. Electroconvulsive therapy: ECT minimum standards of practice in NSW, 2016 Jan. Document Number PD2011_003.
114. Van der Wurff FB, Stek ML, Hoogendijk WJG, Beekman ATF. The efficacy and safety of ECT in depressed older adults, a literature review. Int J Geriatr Psychiatry. 2003;18:894–904.
115. Burke D, Shannon J, Beveridge A. Electroconvulsive therapy use in a 97-year-old woman. Aust Psychiatry. 2007;15(5):427–30.
116. Flint AJ, Gagnon N. Effective use of electroconvulsive therapy in late-life depression. Can J Psychiatr. 2002;47(8):734–41.
117. Albert U, Carmassi C, Cosci F, De Cori D, Di Nicola M, Ferrari S, et al. Role and clinical implications of atypical antipsychotics in anxiety disorders, obsessive-compulsive disorder, trauma-related, and somatic symptom disorders: a systematized review. Int Clin Psychopharmacol. 2016;31(5):249–58.
118. Frampton J. Pregabalin: a review of its use in adults with generalized anxiety disorder. CNS Drugs. 2014;28:835–54.
119. Royal Australian and New Zealand College of Psychiatrists, Faculty of Psychiatry of Old Age and Committee for Therapeutic Interventions and Evidence-based Practice. Antipsychotic medi-

cations as a treatment of behavioural and psychological symptoms of dementia. 2016, Aug. PPG10.
120. Palmer BW, McClure FS, Jeste DV. Schizophrenia in late life: findings challenge traditional concepts. Harvard Rev Psychiatry. 2001;9:51–8.
121. Galletly C, Castle D, Dark F, Humberstone V, Jablensky A, Killackey E, et al. Royal Australian and New Zealand college of psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. ANZ J Psychiatry. 2016;50(5):1–117.
122. Musselman ME, Saely S. Diagnosis and treatment of drug-induced hyperthermia. Am J Health-Syst Pharm. 2013;70: 34–42.

Eye Problems in the Oldest Old

18

Weng Onn Chan and Jagjit S. Gilhotra

Introduction

The world's population is rapidly ageing. The National Institute of Aging (WHO) has estimated that the people over 65 in 2050 will be a staggering 1.5 billion; it will represent 16% of the world's population. In fact, the over 65s will be the fastest-growing segment in society for many countries [1]. In contrast, the current number of over 65 only represents 8% of the world's population [2]. Most these people will be from the developed world, reflecting the ever improvements in life expectancy. This statistics is sobering considering the major causes of blindness in the developed world are intricately more prevalent in elderly patients; prevalence of sight-threatening disease drastically increases after 75 years of age [1]. Uncorrected refractive error, cataract, macular degeneration, glaucoma and diabetes are leading causes of visual impairment and blindness in both developing and developed world [3]. Of note, rapidly developing countries like India and China will have disproportionally higher number of new 50+ years old, and unless health policies matches the influx of elderly populations, the number of patients with both avoidable visual impairment and blindness will balloon [3].

The Ageing Eye

The eye is an amazing sense organ when one considers the anatomical requirement that results in sight. Light needs to pass through its structures starting from the tear film, the cornea, the aqueous, the lens, the vitreous and the retina finally to the photoreceptors. Here light is finally converted into electrical signal that is sent to visual cortex via the optic nerve which translates this into sight. While this is an overly simplistic overview of the eye, it serves to highlight that if any of the structures are compromised, visual impairment follows. The effect of age on the eye is cruel, and inherently the eye does not age well. From the gradual attrition of fixed number of corneal endothelial cells that are responsible for maintaining corneal clarity to the weakening lens zonules that lead to the loss of accommodation or presbyopia, the compaction of lens fibres is from the moment that we are born to the eventual opacification of the cataract, the wear and tear of the photoreceptors manifesting as age-related macular degeneration and finally the gradual loss of optic nerve's ganglion cells which can be accelerated in the setting of high intraocular pressure. While normal attrition and degeneration is beyond our current therapeutic intervention (exciting new developments in the field of neurodegeneration, stem cells and gene therapy may mean that reversing some of these changes may be possible in the near future) in the following sections, we will attempt to highlight the current trends in managing these age-related conditions in the elderly population.

The Impact of a Poorly Seeing Ageing Eye

The worldwide economic impact of visual loss by the year 2020 has been estimated to be around 3.6 trillion, 2.8 trillion are direct medical cost (e.g. cost of glasses prescription, cost of cataract surgery, cost of intravitreal injections), and around 800 billons are attributed to indirect medical cost (e.g. due to productivity loss, cost of care and loss of independence) [1, 4]. Rein in a recent analysis of the cost of visual impairment noted that indirect medical cost may be greater and cumulatively may exceed the direct burden of visual impairment [4].

In the following subsections for each disease, we will attempt to highlight the global and personal impact of the individual disease.

W. O. Chan
Southern Australian Institute of Ophthalmology, University of Adelaide, Adelaide, SA, Australia

J. S. Gilhotra (✉)
University of Adelaide and The Queen Elizabeth Hospital, Adelaide, SA, Australia

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_18

Cataract

Clinically significant cataract is one of the major reversible causes of visual impairment in the oldest old. It accounts for up to 33% and 51% of the worlds rates of visual impairment and blindness [3]. While a very prevalent problem, cataract surgery is also one of the most successful surgeries in the world. Modern cataract surgery has relatively low complication rates and consistently ranks highest in terms of patient satisfaction and quality-of-life improvement following surgery. While a highly effective treatment, delay in the delivery of cataract surgery to the needed population is often the rate-limiting step in both the developing and developed world. The impact of waiting for cataract surgery is significant. Hodge et al. found in a systemic review that while waiting for cataract surgery, patient's vision and quality of life continue to deteriorate and the risk of fall increases [5]. Cataract can increase the risk of falls in the oldest old by affecting postural balance, stability and hazard detection [6].

Randomized controlled studies have shown that falls risk is 67% less following expedited (within 4 weeks) first eye surgery when compared to normal waiting time for cataract surgery, but this effect was not observed in second eye surgery [7, 8]. Regardless on the rates of falls, the randomized controlled trials all showed the positive effect of cataract surgery on both objective and subjective parameters, patients' activity and confidence increase, and anxiety, depression and handicap levels are lowered compared to the control group [7, 8]. A recent prospective study has shown that in a US population of over 65, the odds of hip fracture within 1 year after cataract surgery were 16% less compared with patients who had not undergone cataract surgery [9]. The odds are further reduced by 23% if the presenting level of cataract was severe [9]. While age related is a bilateral condition, cataract surgery is usually performed one eye at a time. Meuleners et al. have shown in a population-based study that during this time, patients are at an increased risk of falls compared to prior to having the first eye and after having both eyes done [6]. This may be accounted by the uncorrected refractive error, the loss of stereopsis and possible increased level of activity following first eye surgery [6]. The implication is clear, patient will need to be warned about the increased risk of falls while awaiting second eye surgery, and all efforts are to minimize refractive difference during this critical period.

Elderly patient undergoing cataract surgery often has significant systemic and ocular implications. Cataract surgery is increasingly being done under topical anaesthesia which makes systemic co-morbidities less important in the preoperative considerations for patients having cataract surgery. It is important to note that ocular co-morbidities are common in this age group. Pham et al. have shown that the commonest causes of ocular co-morbidities are age-related macular degeneration, diabetic retinopathy and glaucoma [10]. These need to be considered fully and are vital to the preoperative counselling for patients. Patients will need to have their expectations adjusted to avoid disappointment. Refractive goal should also be discussed fully. In the oldest old, patients are often content with having different single-vision glasses for distant vision and near vision. This avoids the risk of falls that are associated with bifocal lenses and progressive addition lens. This may happen with image jump associated with bifocal lens and blurring distance objects in the lower visual field (e.g. stairs) with all lens type. In a randomized controlled trial, Haran et al. found that provision of single-lens distance glasses to older wearers of multifocal glasses reduces falls by 8%. But in patients with low level of outdoor activity, this significantly increased the risk of fall [11].

Monovision is a state where one eye is rendered emmetropic and other myopic; the end effect is patient will be glasses-free for both distance and reading vision. This however reduces the stereoacuity for patient. There is paucity of data on the effect of monovision on elderly patients. However, indirectly, reduction in stereoacuity is a known risk factor for falls; as such clinician should err on the side of caution when discussing this option with elderly patients. Another recent addition to the optical correction armamentarium following cataract surgery is multifocal intraocular lenses. As their name implies, these lenses allow the user to see clear at various focal points. User of earlier reiterations of the lenses was troubled with significant ghosting, glare and haloes that may necessitate reoperation to explant intraocular lens. These symptoms may be particularly prominent in mesopic conditions. Again, there is paucity of research in the impact of these newer intraocular lenses on the elderly population and on falls risk. Further prospective studies investigating the effect of these "premium" lenses are required to determine their impact on the oldest old.

Finally, with the advent of femtosecond laser-assisted cataract surgery, patients are finally justified when they ask if their cataract surgery will be done by laser. Patient is often misinformed about traditional cataract surgery that is performed with ultrasound probe in most of the developed world or still manually in the developing world. Femtosecond laser is increasingly being used in ophthalmology, and in cataract surgery, it is used to create corneal wounds, create a capsulorhexis and fragment the cataract. However, the cataract fragments are still removed using a traditional ultrasound probe. At its current state, laser-assisted cataract surgery perhaps is a more apt description of the procedure. Proponents argue that laser-assisted cataract surgery is better for complicated cases and better at preserving corneal endothelium. However, a recent Cochrane review could not determine the equivalence or superiority of laser-assisted cataract surgery compared to standard manual phacoemulsification [12]. They found similar complication rates, surgical times and

very similar visual outcomes between the two groups [12]. More importantly, at its current cost, laser-assisted cataract surgery is not cost-effective when compared to traditional cataract surgery [13].

Patients are increasingly being bombarded with "choices" when it comes to cataract surgery: choice of refractive outcome, choice of intraocular lens and choice of surgery. When approaching an elderly patient, it appears that "simple, traditional cataract extraction with monofocal lens implant" is still the most evidence backed and probably the most appropriate.

Glaucoma

Glaucoma is one of the main causes of irreversible visual loss in the world [3]. It is when the optic nerve is damaged (Fig. 18.1) invariably due to elevated intraocular pressures and presents with typical glaucomatous field defects. Mechanistically, glaucoma can be divided into open-angle and closed-angle glaucoma. The elderly is more at risk of both forms of glaucoma [14]; open-angle glaucoma is where the drainage pathway is anatomically patent but defective which leads to gradual rise in the intraocular pressure. Closed-angle glaucoma typically presents acutely when the drainage pathway is obstructed which leads to sudden rise in intraocular pressure. Both forms of glaucoma represent 2% of global cause of visual impairment and 8% of blindness in the world population [3]. Additionally, glaucoma also presents a significant health burden to the population due to its chronic nature and lifelong treatment requirement. In the USA alone, the annual direct cost of glaucoma treatment is estimated to be 5.8 billion USD in 2013 [1]. This does not account for the indirect cost including loss of productivity, cost borne by carers and family members. The cost of glaucoma also increases with increasing severity [14].

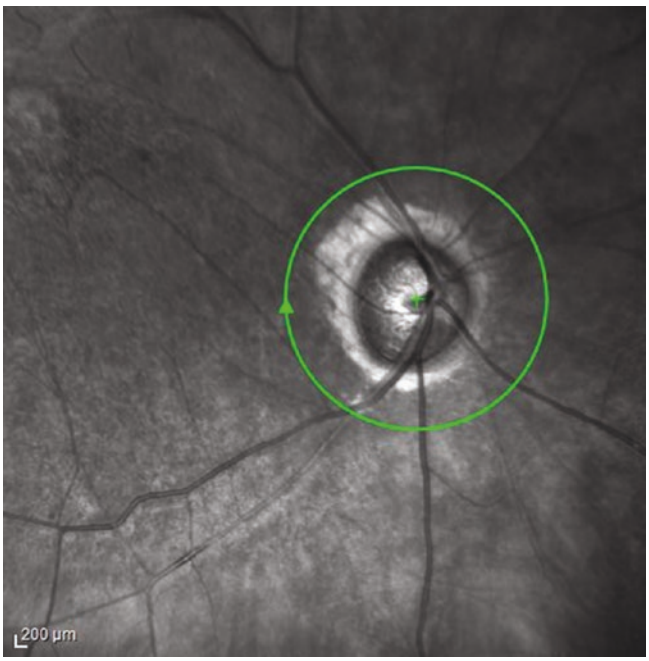

Fig. 18.1 A red-free fundus image of a glaucomatous disc. There is increase cup to disc ratio with thinning of the neural retinal rim which is characteristic of glaucomatous optic neuropathy

The burden to individuals is also substantial. Visual loss from glaucoma can negatively affect health-related quality of life even in patients who are unaware they have glaucoma. There is a linear relationship between the severity of visual loss with the amount of loss in health-related quality of life [14]. Compared to aged-matched individuals, patients with glaucoma are also three times more likely to have falls and six times more likely to be involved in motor vehicle accidents and more likely to be at fault in the collision in the preceding year [15].

Regardless of mechanism, there is only one effectively known treatment which is lowering of intraocular pressure. As the change with glaucoma is often insidious, compliance to medication can be a major issue. Gurwitz et al. have previously shown that in the elderly population, there can be up to 23% non-compliance following initiation of therapy, and patients can go without therapy for up to 112 days during the first year of treatment. They also found that medications requiring more than twice daily use and presence of concurrent medications are risk factors for non-compliance [16]. Simple once a night dosing of prostaglandin analogue has been shown to result in better compliance for adherence [17]. While we know that lowering intraocular pressures slows progression of glaucoma progression, the effect of non-compliance on glaucoma progression is less well defined. In a meta-analysis of the literature, Waterman et al. found that education and personalized interventions can lead to better adherence in ocular hypotensive therapy, but the effect on intraocular pressures and visual field progression is unclear. They also found weak evidence that simplifying drug regime also improves treatment adherence [18].

When compared to recent advancement in cataract surgery, treatment for diabetes and age-related macular degeneration and the treatment for glaucoma remain relatively similar. The traditional stepwise algorithm of medical, laser and drainage surgery still holds for glaucoma. More recently, the use of minimally invasive glaucoma surgery is increasing. The main impetus is to provide a glaucoma treatment that is minimally invasive and effective, has high safety profile and provides rapid recovery [19]. The role of this surgery is to provide an intermediate management for patient that requires "something more" before committing them to full glaucoma surgery that can be associated with significant morbidities. In a recent meta-analysis, Lavia et al. concluded that while before and after studies showed that MIGS are

effective in lowering intra ocular pressures and number of glaucoma medications, these results were derived from non-comparative studies. However, there were limited evidence found when looking at trials that directly compare MIGS to medical therapy [20].

Age-Related Macular Degeneration

The oldest old is especially susceptible to age-related macular degeneration; while only 2% of under 50s will be affected by ARMD, this rises to over 35% for over 85s [1]. ARMD is multifactorial, and both environmental and genetics factors have been elucidated recent. Of particular importance is the genome-wide association studies that were identified to be involved in the complement pathway being associated with increased risk of developing wet macular degeneration.

While the majority of patients suffering from macular degeneration have the "dry" or non-exudative form (Fig. 18.2) which are characterized by slow and gradual loss of vision, 10–20% of patients can progress into the exudative or "wet" ARMD that leads to sudden and often severe loss of central vision if left untreated (Figs. 18.3 and 18.4) [21]. Since the landmark study of ANCHOR [22] and MARINA [23], the use of anti-vascular endothelial growth factors has taken off. What was once considered an irreversible loss of vision from wet ARMD is now treatable; ophthalmologists are now able to regain vision loss by regular injections of anti-VEGF agent. This was a dramatic shift in treatment paradigm when considering prior to anti-VEGF; the dictum of exchanging a large scotoma with a smaller scotoma was the standard of care with thermal laser and photodynamic therapy. All the initial trials on anti-VEGF showed that with intensive treatment, visual gain of more than two Snellen lines can be achieved in ~30–40% of patients and upwards of 90% of patients will maintain their pretreatment visual acuity, and less than 5% will be resistant or not responsive to initial treatment [22, 23].

However, with longer-term real-world data of unselected group of patients in routine clinical practice, we now know that if patients are commenced on treat-and-extend protocols, the number of injections and clinic visits is significantly less when compared to original trial protocols of monthly injections while achieving similar success rates. Even with the reduced treatment visits, the average number of injections during the first 2 years is around 13 injections. Fortunately, patients can be reassured that eventually more

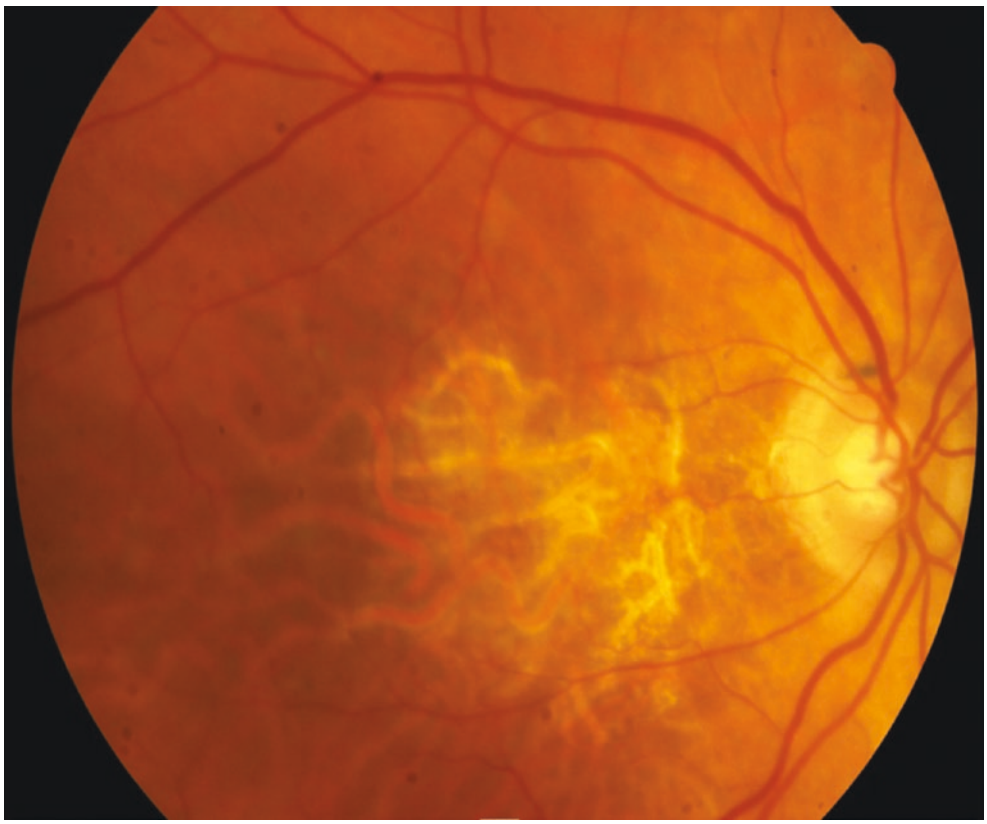

Fig. 18.2 End-stage "dry" or non-exudative macular degeneration. The macula is atrophic and subjectively the patient would have very poor central vision but preserved peripheral vision

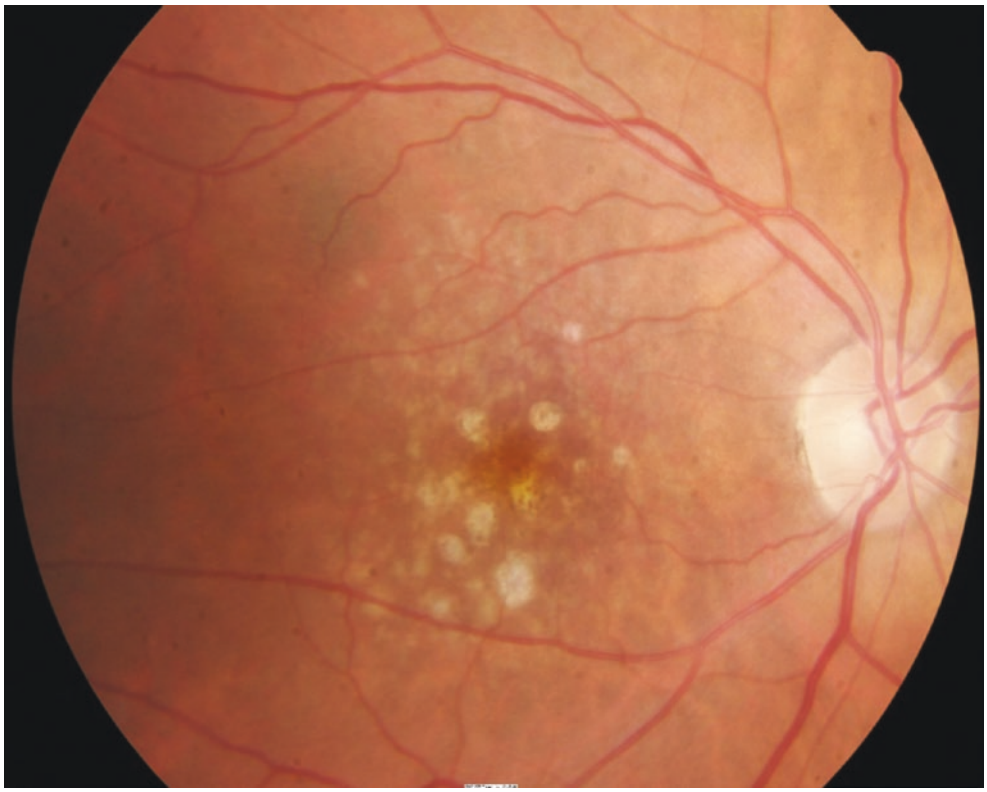

Fig. 18.3 Colour fundus image of right wet age-related macular degeneration. Pigmentary changes and drusens are hallmarks of age-related macular degeneration

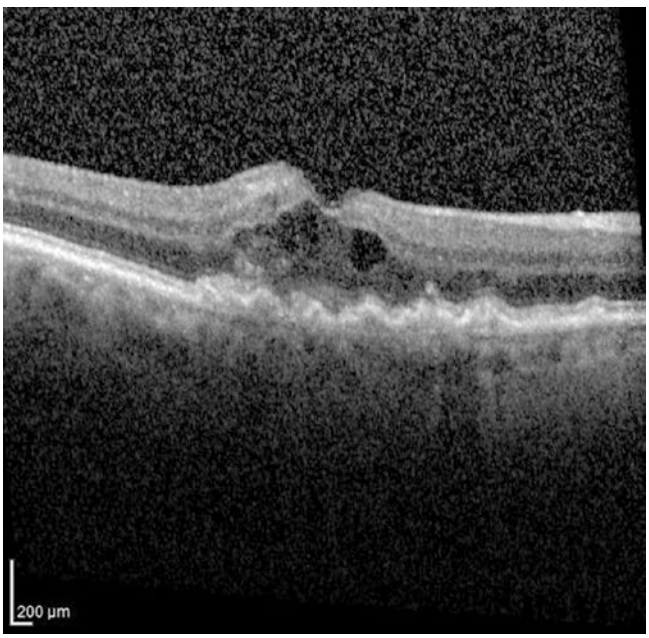

Fig. 18.4 Corresponding optical coherence tomography showing cross section of the macula. The hyporeflective cystic spaces are exudative changes from wet age-related macular degeneration. The rippled layers under the cystic spaces are drusens. Anti-VEGF treatment has revolutionized the management of this condition

than 50% of patients can stay in disease remission with 8 weekly or less injections [24].

While these data are impressive, the treatment burden on patients and clinicians to maintain trial-like conditions is enormous. Both direct cost to the patient and indirect cost for caregiver services for ARMD are substantial and proportional to the disease progression [25]. It is estimated that in UK, the annual cost for treating wet ARMD is 860 million, and in India, the annual cost for anti-VEGF drug alone is 1.2 billion [26]. This cost is prohibitively expensive for developing countries and will only continue to rise as the world ages and maintenance anti-VEGF therapy tends to be life-long. Not only the economic cost to patients and society, overall quality of life and independence are affected in parallel with worsening visual loss [25]. Having to relinquish valued activities due to worsening visual acuity from macular degeneration has been associated with increased risk of cognitive decline [27]. Time commitment for staff and patient is also significant, with ARMD patients accounting for up to 20% of healthcare staff's time per week and up to 90 h of patient and caregivers time per visit [25].

In the elderly patients, frank communication about the treatment frequency and duration of treatment is vital. Unless clearly communicated, most patients do not understand that

anti-VEGF treatment is life-long and cessation of treatment can lead to reactivation of wet CNVM [24]. Equally important is for clinicians to stress compliance on measures to detecting and reducing risk of wet CNVM in the other eye with Amsler grid monitoring, AREDS2 formulation and stop smoking. AREDS formulation for ARMD is the only shown preventative measures that reduce the risk of ARMD progression by 25–30% by 5 years [28]. Importantly, compliance of these lifestyle modifications is often poor, and often repeated multidisciplinary reminders are required given that ARMD is bilateral in up to 40% of patients [21].

While the vogue over the last 15 years has been on wet ARMD, there are increasing foci on dry macular degeneration. GA accounts for 85–95% of ARMD patients up to 20% of blindness due to macular degeneration [29]. While there is currently effective treatment for wet ARMD, the only evidence-based intervention in dry ARMD is AREDS supplementation [28]. Currently trials are underway to evaluate the role of anti-inflammatory, anti-oxidative, lipofuscin and visual cycle inhibitors, choroidal blood flow modulators and stem cell therapy on drusen load and geographic atrophy [30]. Surgically, implantable telescopes seem to be effective in improving vision but at its current state are complicated with significant rates of persistent inflammation and explantation [30].

It is not infrequent that patients with end-stage macular degeneration will enquire about the role of bionic eye in the treatment of ARMD. While there are no published results, retinal implants have been implanted in patients with macular degeneration with promising reported outcomes. In a series of five patients, Stanga et al. reported that patients reported no confusion between normal peripheral vision and the artificial phosphene vision; more importantly patient reported improved visual acuity up to BCVA of 1/40 and ability to recognize facial features [31].

Currently, we have a respectable armamentarium of treatment options for patients suffering from ARMD, and new research in this field is promising. However, at its current state, ARMD remains one of the major causes for visual impairment in the elderly and treatment while effective, exacts a significant treatment burden to patient and society.

Visual Aids and Practical Tips for the Elderly

Practical Advices

When dealing with visual loss in the oldest old, the clinicians play an extremely important role as the primary health advocate for the patients. Often patients and family members are unaware of services available to help make visual loss more manageable. Unfortunately, even conditions such as ARMD are often misunderstood and often receive with similar dread to a "blind" sentence. A simple reassurance to the patients that they will never go "lights-out" blind but will always retain navigational vision but with a "blurry central blob" is enough to help them through the initial shock of dealing such diagnosis. Similarly, aligning patient's expectation and helping them understand treatment goal in glaucoma help significantly with compliance. Often patients may lapse in compliance as the "drops are not helping me see any better" or "I don't notice any difference", explaining that "no change is good news" and drops should never be stopped is essential in ensuring treatment continuation. From a multidisciplinary viewpoint, ensuring patient has not lapsed in follow-up for chronic conditions such as glaucoma and diabetic retinopathy is equally important.

Friendly Services

Even ophthalmology clinics are often ill equipped from time and equipment perspectives when dealing with patients with severe visual loss. Developing a working relationship with allied health services such as local low vision society and occupational therapist can ensure a smooth transition of care for patients. Low vision centre plays a critical role in coordinating various services for such patients, from introducing appropriate visual aids or adaptive technologies to implementing home modifications, providing print alternative, coordinating social services and improving lighting conditions for patients. The importance of these cannot be overstated in helping patients with low vision maintain independence. Adaptive technology has improved dramatically in the age of smart phones and tablets. Electronic magnification is easily achieved and apps specially designed for low visions are abound to help with magnification, contrast and voice command for the low vision user. Optical character recognition has improved significantly and allows patients with severe visual loss to again enjoy reading materials through audio. The low vision centres are invaluable in assessing which of these options are suitable for the individual and helping the patients get accustom to the new technologies. While these technologies are comparatively cheaper than before, the initial investment into such technologies can be prohibitively expensive for pensioners. Low-vision centres often provide short-term loan or trial units coupled with training for patients before they commit to certain products. Finally, from a practical viewpoint, often there is a misconception and even reluctance from a patient's perspective in being referred to low-vision centres. Attending such services is often viewed as resignation to giving in to low vision. The clinician plays an important role in encouraging patients in attending such services as building up an early therapeutic alliance and implementing some of the aforementioned services when patient still has relatively good vision which can help patients adapt better to them.

Evidence for Visual Aids

A recent Cochrane analysis found that there were insufficient evidence to support the use of specific type of reading aid for low vision users [32]. Several small studies of moderate or low quality were inconclusive but suggested patients can achieve faster reading speed with stand-based or hand-held electronic devices when compared to stand-mounted or hand-held optical magnifiers [32]. Optical magnifiers also seem to perform better than head-mounted electronic devices [32]. However the authors also contended that the technology of electronic devices may have significantly improved since the studies have been conducted [32].

Clinical Relevance

- In the developed world, the major blinding conditions disproportionately affect the oldest old.
- The worldwide economic impact of visual loss by the year 2020 has been estimated to be around 3.6 trillion.
- The burden of these care for these diseases is substantial on both a community level and personal level.
- Exciting and promising treatments are becoming more common place for multiple age-related eye disease.
- Advancements in cataract surgery may present elderly patients with too many choices; cataract extraction with monofocal implants may be the most appropriate for this age group.
- Age-related macular degeneration treatment has been revolutionized by intravitreal injection of anti-vascular endothelial growth factors.
- Compliance to glaucoma therapy has been shown to be poor in the elderly population, and simplified regime may improve compliance.
- Multidisciplinary approach between clinicians and ophthalmologist in co-managing elderly patients with visual loss is vital ensuring that their needs are met.

Multiple Choice Questions

1. The following are true of cataract, EXCEPT:
   A. Cataract surgery is also one of the most successful surgeries in the world.
   B. Elderly patient undergoing cataract surgery often has significant systemic and ocular implications.
   C. Monovision is a state where one eye is rendered emmetropic and other myopic, and this increases the stereoacuity for the patient.
   D. Reduction in stereoacuity is a known risk factor for falls.
2. The following are true of age-related macular degeneration (ARMD), EXCEPT:
   A. Majority of patients suffering from macular degeneration have the "dry" or non-exudative form.
   B. Wet ARMD is now treatable; ophthalmologists are now able to regain vision loss by regular injections of anti-VEGF agent.
   C. The average number of injections during the first 2 years is around six injections.
   D. Anti-VEGF treatment is life-long, and cessation of treatment can lead to reactivation of wet CNVM.
3. The following are true of glaucoma, EXCEPT:
   A. Regardless of mechanism, there is only one known effective treatment which is lowering of intraocular pressure.
   B. Glaucoma represents 2% of global cause of visual impairment and 8% of blindness in the world population.
   C. More recently, the use of minimally invasive glaucoma surgery is increasing.
   D. The traditional stepwise algorithm of medical, laser and drainage surgery no longer holds for glaucoma.

Answers to MCQs

1. C
2. C
3. D

References

1. Chader GJ, Taylor A. Preface: the aging eye: normal changes, age-related diseases, and sight-saving approaches. Invest Ophthalmol Vis Sci. 2013;54(14):ORSF1–4.
2. WHO. Global health and aging: world health organization.
3. Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. Br J Ophthalmol. 2012;96(5):614–8.
4. Rein DB. Vision problems are a leading source of modifiable health Expenditures Leading source of modifiable health expenditures. Invest Ophthalmol Vis Sci. 2013;54(14):ORSF18-ORSF22.
5. Hodge W, Horsley T, Albiani D, Baryla J, Belliveau M, Buhrmann R, et al. The consequences of waiting for cataract surgery: a systematic review. CMAJ. 2007;176(9):1285–90.
6. Meuleners LB, Fraser ML, Ng J, Morlet N. The impact of first- and second-eye cataract surgery on injurious falls that require hospitalisation: a whole-population study. Age Ageing. 2014;43(3):341–6.
7. Foss AJ, Harwood RH, Osborn F, Gregson RM, Zaman A, Masud T. Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial. Age Ageing. 2006;35(1):66–71.
8. Harwood RH, Foss AJ, Osborn F, Gregson RM, Zaman A, Masud T. Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial. Br J Ophthalmol. 2005;89(1):53–9.
9. Tseng VL, Yu F, Lum F, Coleman AL. Risk of fractures following cataract surgery in Medicare beneficiaries. JAMA. 2012;308(5):493–501.

10. Pham TQ, Wang JJ, Rochtchina E, Maloof A, Mitchell P. Systemic and ocular comorbidity of cataract surgical patients in a western Sydney public hospital. Clin Exp Ophthalmol. 2004;32(4):383–7.
11. Haran MJ, Cameron ID, Ivers RQ, Simpson JM, Lee BB, Tanzer M, et al. Effect on falls of providing single lens distance vision glasses to multifocal glasses wearers: VISIBLE randomised controlled trial. BMJ. 2010;340:c2265.
12. Day AC, Gore DM, Bunce C, Evans JR. Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery. Cochrane Database Syst Rev. 2016;7:CD010735.
13. Abell RG, Vote BJ. Cost-effectiveness of femtosecond laser-assisted cataract surgery versus phacoemulsification cataract surgery. Ophthalmology. 2014;121(1):10–6.
14. Varma R, Lee PP, Goldberg I, Kotak S. An assessment of the health and economic burdens of Glaucoma. Am J Ophthalmol. 2011;152(4):515–22.
15. Haymes SA, Leblanc RP, Nicolela MT, Chiasson LA, Chauhan BC. Risk of falls and motor vehicle collisions in glaucoma. Invest Ophthalmol Vis Sci. 2007;48(3):1149–55.
16. Gurwitz JH, Glynn RJ, Monane M, Everitt DE, Gilden D, Smith N, et al. Treatment for glaucoma: adherence by the elderly. Am J Pub Health. 1993;83(5):711–6.
17. Joseph A, Pasquale LR. Attributes associated with adherence to Glaucoma medical therapy and its effects on Glaucoma outcomes: an evidence-based review and potential strategies to improve adherence. Semin Ophthalmol. 2017;32(1):86–90.
18. Waterman H, Evans JR, Gray TA, Henson D, Harper R. Interventions for improving adherence to ocular hypotensive therapy. Cochrane Database Syst Rev. 2013;(4):CD006132.
19. Saheb H, Ahmed II. Micro-invasive glaucoma surgery: current perspectives and future directions. Curr Opin Ophthalmol. 2012;23(2):96–104.
20. Lavia C, Dallorto L, Maule M, Ceccarelli M, Fea AM. Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: a systematic review and meta-analysis. PLoS One. 2017;12(8):e0183142.
21. Ehrlich R, Harris A, Kheradiya NS, Winston DM, Ciulla TA, Wirostko B. Age-related macular degeneration and the aging eye. Clin Interv Aging. 2008;3(3):473–82.
22. Brown DM, Kaiser PK, Michels M, Soubrane G, Heier JS, Kim RY, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med. 2006;355(14):1432–44.
23. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, et al. Ranibizumab for Neovascular age-related macular degeneration. N Engl J Med. 2006;355(14):1419–31.
24. Kim LN, Mehta H, Barthelmes D, Nguyen V, Gillies MC. Meta-analysis of real world outcomes of intravitreal ranibizumab for the treatment of neovascular age-related macular degeneration. Retina. 2016;36(8):1418–31.
25. Prenner JL, Halperin LS, Rycroft C, Hogue S, Williams Liu Z, Seibert R. Disease burden in the treatment of age-related macular degeneration: findings from a time-and-motion study. Am J Ophthalmol. 2015;160(4):725–31. e1
26. Azad R, Chandra P, Gupta R. The economic implications of the use of anti-vascular endothelial growth factor drugs in age-related macular degeneration. Ind J Ophthalmol. 2007;55(6):441–3.
27. Rovner BW, Casten RJ, Leiby BE, Tasman WS. Activity loss is associated with cognitive decline in age-related macular degeneration. Alzheimers Dement. 2009;5(1):12–7.
28. Chew EY, Clemons T, SanGiovanni JP, Danis R, Domalpally A, McBee W, et al. The age-related eye disease study 2 (AREDS2): study design and baseline characteristics (AREDS2 report number 1). Ophthalmology. 2012;119(11):2282–9.
29. Hanus J, Zhao F, Wang S. Current therapeutic development for atrophic age-related macular degeneration. Br J Ophthalmol. 2016;100(1):122–7.
30. Taskintuna I, Elsayed MEAA, Schatz P. Update on clinical trials in dry age-related macular degeneration. Middle East Afr J Ophthalmol. 2016;23(1):13–26.
31. P. Stanga (2016 September), First report on use of electronic retinal prosthesis in 5 AMD patients with 6 months to over one year follow up. Paper presented at the meeting of the European Society of Retina Specialists, Copenhagen.
32. Virgili G, Acosta R, Grover LL, Bentley SA, Giacomelli G. Reading aids for adults with low vision. Cochrane Database Syst Rev. 2013;10:CD003303-CD.

Dental and Oral Conditions in the Very Elderly

19

Arumugam Punnia-Moorthy

Introduction

There has been a dramatic increase in the number of old people in world population during the last century, and this is set to accelerate in the coming decades. Such a change in the population has led to many economic and social changes throughout the world causing challenges to the provision of services including healthcare. Older people suffer from a range of medical and dental conditions which are distinct to this group, and management of these conditions will pose special challenges depending on factors such as patient's age, nature of disabilities, the type of medical conditions they suffer from and whether they are living independently or institutionalised. This paper will highlight and discuss the dental and oral conditions which are of relevance in the very elderly.

For population measurement purposes, 'older person' is defined as people aged 65 and over. 1n 2010, an estimated 8% of the world's population (524 million) were aged 65 and over and by 2050, this number is expected to nearly triple to 16% (1.5 billion) [1]. This remarkable change in ageing of world population is a consequence of longer life expectancy and a decline in fertility. It is projected that very soon the number of people aged 65 and over will outnumber children under the age of 5 [1]. Although this change is seen particularly in developed countries of Europe, North America and Japan, a dramatic increase in the number of older population is expected by 2050 in less developed countries of Latin America, China and India [1]. It is expected that between 2010 and 2050, the number of older people in less developed countries will increase to more than 250%, compared with a 71% increase in developed countries [1]. It is projected that there will be a dramatic increase in older population in the world's two most populous countries: China and India. China's population of age 65 and over will likely to increase to 330 million by 2050 from 110 million today, and that of India's current older population of 60 million is projected to exceed 227 million by 2050 [1].

As expected, the trend in demographic changes to Australian population is like that of global population in that older Australians are accounting for an increasing percentage of the country's population. It was reported that in 2013, 14% of the population (3.3 million) were aged 65 and over and 1.9% were aged 85 and over (439,000). It is predicted that by 2053, based on Australian Bureau of Statistics medium-level growth assumptions, 21% of the population will be aged 65 and over (8.3 million) and 4.2% aged 85 and over (1.6 million) [2].

Structural and Physiological Changes in the Mouth with Ageing

It is estimated that more than 66% of elderly people now retain a varying number of their natural teeth unlike the previous generations [3]. Retention of teeth in older age group often lead to accumulation of plaque, calculus and debris due to the inability to maintain good oral hygiene causing an increase in the incidence of caries and periodontal disease. It is essential to understand the mechanisms underlying the deterioration of the oral environment that occurs with ageing and its consequences. It is difficult sometimes to ascertain that the changes that occur in teeth with ageing are due to advancing age or a consequence of pathological conditions which can occur early in life and become more aggravated with age.

Changes in the colouration, form or shape of the teeth will occur due to wear and tear with advancing age. The biting surfaces of teeth show signs of attrition. The cementum covering the roots becomes gradually thickened with age, and in some cases, the roots become very bulbous due to excessive deposition of cementum, a condition called hypercementosis. Extraction of such teeth will prove to be difficult. The pulp of vital teeth become less vascular with decrease in

A. Punnia-Moorthy (✉)
Formerly Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, The University of Sydney, Sydney, NSW, Australia
e-mail: apunniam@optusnet.com.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_19

number of cells and increase in the amount of fibrous tissue. The pulp chamber becomes reduced in size due to secondary dentine deposits. All these age-related changes will compromise a tooth's capacity to recover from physical trauma and caries [4].

Similarly, in relation to the periodontal ligament, cells can lose their ability to proliferate and produce protein as they age. These changes in combination with periodontal disease which is more prevalent in the elderly can result in the retraction of the periodontal attachment causing loss of bone support around teeth [5]. The changes observed in the oral mucosa with ageing include loss of elasticity and reduction of tactile sensitivity around the mouth [6–8]. It has also been observed that the sensation of taste diminishes with ageing [9].

The curved articulating surfaces of the temporomandibular joint flatten slightly with age [10]. Studies relating to osteopenia and osteoporosis of the craniofacial skeleton reveal a naturally occurring age-related loss of alveolar bone which occurs independent of loss of teeth and periodontal disease [11]. The loss of teeth remains an important factor in the extent and location of osteoporosis of the jaws. After the loss of teeth, there is a phase of accelerated resorption of the residual alveolar bone which lasts for several months followed by a slower rate of localised osteoporosis which may continue for many years despite of wearing dentures [12]. Although it is difficult to directly compare age-related changes in jaw muscles with changes observed elsewhere in the body, loss of muscle mass and loss in muscle strength occur with the jaw musculature with advancing age in a curvilinear fashion [13, 14].

Reduction in salivary flow rate was claimed as a normal feature of ageing by many earlier studies. However, the validity of these findings has been questioned based on possible errors with these study designs. Recent cross-sectional and longitudinal studies comparing the salivary flow between healthy young individuals and older, debilitated individuals found no age-dependent significant changes in salivary flow rates [15]. The current understanding is that the salivary gland dysfunction is not a normal process of ageing, but is due to a combination of other factors such as systemic diseases, immunological disorders and drug treatments.

Common Dental Conditions

The main conditions in the elderly regarding their dentition requiring attention are:

- Edentulism and tooth loss
- Dental caries
- Periodontal disease

Edentulism and Tooth Loss

Edentulism is the state where all the natural teeth have been lost, and transition to this state occurs with incremental loss of teeth throughout adult life. The decision to become edentulous is often made on social and clinical grounds. It is generally regarded by clinicians as an undesirable outcome and a reflection of failure of self-care and the dental care system. Edentulism have been shown to cause difficulties with chewing and eating by having no teeth or wearing ill-fitting dentures leading to social and nutritional disadvantages [16].

However, in some cases, loss of decayed and diseased teeth heralds the end of long-standing misery and eating problems and fewer oro-dental complications when institutionalised later in life. Edentulism has been reported in 21.9% of over 74-year-olds in the United States [17] and in 39.6% of over 74-year-olds in New Zealand [18].

Tooth loss occurs because of dental caries and periodontal disease. Nowadays, incremental loss of teeth is more common than edentulism among adults of all ages, and it is an ongoing problem in those aged 65 and over. Such tooth loss is less predictable and can pose challenges with the provision of prostheses. The other consequences are drifting and over-eruption of teeth causing more problems with maintenance of oral hygiene and with the construction of prostheses.

Dental Caries

Caries remains a major oral health problem in the elderly for several reasons, namely, exposure of the root surface due to gingival recession, poor diet, poor oral hygiene, dry mouth and preservation of teeth with complex restorations. In a study conducted in South Australia, the annual dental caries increment among older people residing in nursing homes and those with dementia was more than double to that observed among their community-dwelling counterparts [19]. The current emphasis with treatment of caries in the elderly is to remove the least possible amount of decayed tooth and to focus on remineralising the affected tooth with fluoride applications in the form of mouth rinses, toothpastes, gels and varnishes.

Periodontal Disease

This is a chronic infectious disease that affects tooth supporting tissues including the gingiva and the alveolar bone. It is an inflammatory condition causing gingivitis which may spread to involve the periodontium and eventually result in loss of periodontal attachment, loss of alveolar bone and formation of deep periodontal pockets. In the end stage of the disease, the tooth becomes mobile affecting mastication and

even tooth loss. A recent critical review of studies from 37 countries revealed that the incidence of severe periodontitis was higher with increasing age but was low and generally constant among the elderly [20]. However, with more people surviving into old age with natural teeth, there could be an increase in the prevalence of periodontitis among this population. Several epidemiological studies during the past two decades have evaluated the association between oral infections particularly periodontitis and systemic diseases including coronary heart disease. Although there is some scientific evidence to support this proposition, outcome of these studies has not been conclusive [21].

Dry Mouth (Xerostomia) in the Elderly

Xerostomia and salivary gland hypofunction have been found to be more common among the elderly population. Salivary gland hypofunction is a condition in which both unstimulated and stimulated salivary flow is reduced and there can be alterations of the chemical composition of the saliva as well. Whereas xerostomia is defined as the subjective perception of dry mouth. Both conditions can exist independently, but the perception of dry mouth is often associated with a reduction in salivary flow [22]. Dry mouth is associated with several systemic diseases, medications and head and neck radiotherapy. The most common systemic disease that causes dry mouth in the elderly is Sjögren's syndrome which is a chronic, autoimmune disease characterised by symptoms of oral and ocular dryness. Other systemic causes of dry mouth include rheumatoid arthritis and diabetes. Another common cause of dry mouth in the elderly is prescription and non-prescription medications which have anticholinergic and antiadrenergic effects such as antihypertensives, antidepressants and antipsychotics. Chemotherapeutic agents such as radioactive iodine used for thyroid cancer will cause salivary hypofunction. Radiotherapy which is a common therapeutic modality for the treatment of head and neck cancer causes severe and permanent dry mouth.

Symptoms of dry mouth include halitosis, soreness and burning of mouth and difficulty with swallowing, speech and altered taste. There is also an increased risk of caries, periodontal disease, oral candidal infections and poor retention of dentures. The oral health-related quality of life is relatively poorer in people suffering from dry mouth.

Treatment modalities for dry mouth include the use of artificial saliva and saliva- stimulating drugs (pilocarpine), treatment of the underlying systemic diseases (drugs, diabetes, etc.) and palliative or symptomatic treatment such as avoidance of dry foods, alcohol, smoking, use of frequent sips of water and lip balm. Importantly, people suffering from dry mouth require preventive treatment against the development of caries, periodontal disease and candidiasis.

Common Oral Mucosal Conditions in the Elderly

Oral mucosal lesions are common in the elderly and particularly among full denture wearers. It was reported that the prevalence of mucosal lesions was 51% among elderly wearing full dentures, while the prevalence was 31% among those with some natural teeth present [23]. The common mucosal conditions in the elderly are:

- Candidosis (candidiasis)
- Denture stomatitis
- Angular cheilitis
- Denture irritation hyperplasia
- Candidal leukoplakia
- Lichen planus
- Burning mouth syndrome
- Leukoplakia
- Erythroplakia
- Oral cancer

Candidosis

Candidosis or yeast infections are common in the elderly, and this may be due to several factors such as disturbance of oral microflora by antibiotics, long-term use of corticosteroids, xerostomia, immune defects, immunosuppression, leukaemias, lymphomas and diabetes. The common types of candidosis are pseudomembranous (thrush) (Fig. 19.1) which presents as white or creamy plaques that can be wiped off to leave an erythematous mucosal surface and erythematous that may cause a sore red mouth and often seen in

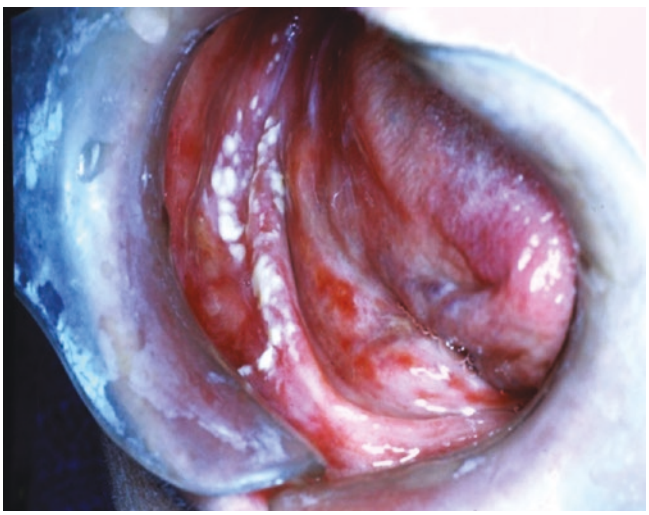

Fig. 19.1 Pseudomembranous candidosis on lower alveolar ridge, floor of mouth and lateral tongue

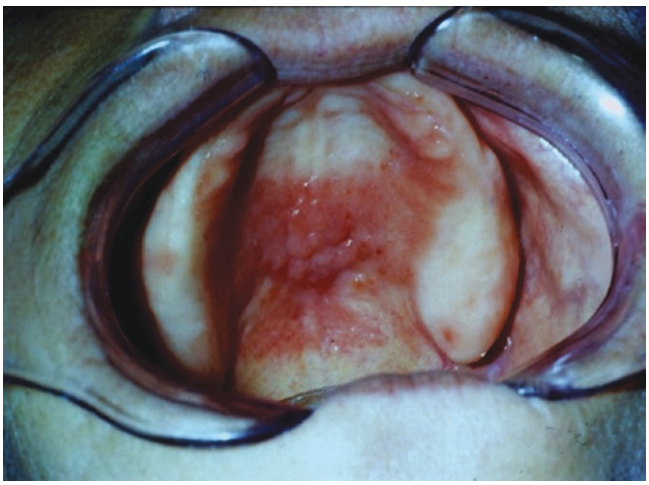

Fig. 19.2 Denture stomatitis on the palate and associated papillary hyperplasia

patients on broad-spectrum antimicrobials. Diagnosis is usually clinical, but Gram stain smear may help.

Management includes treatment of the predisposing causes and with antifungals in the form of oral suspension (nystatin), lozenges (amphotericin) gels or tablets (miconazole; fluconazole).

Denture Stomatitis

Denture sore mouth or denture stomatitis is a condition seen mainly in elderly people as diffuse erythema confined to denture bearing area and is associated with ill-fitting complete or partial dentures (Fig. 19.2). The main predisposing factor is constant denture wearing, but other factors may include poor oral hygiene, high-carbohydrate diet and HIV infection. Management includes attention to dentures, antifungals and soaking dentures out at night in antifungal solutions (e.g. hypochlorite, chlorhexidine).

Angular Cheilitis

Angular cheilitis is commonly seen in elderly edentulous patients who wear an upper denture and presents as symmetrical erythematous fissures on the skin of oral commissures (Fig. 19.3). It is usually caused by *Candida albicans*, but *Staphylococcus aureus* and/or streptococci may be cultured from the lesions. Management is by eliminating any underlying systemic causes, correcting vertical dimension of dentures, improving oral and dental hygiene and treating with topical antifungals such as miconazole.

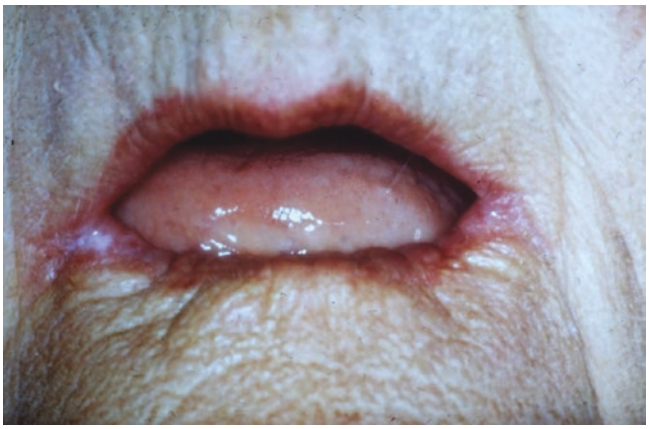

Fig. 19.3 Angular cheilitis in an elderly, edentulous patient

Denture Irritation Hyperplasia

This condition is common among elderly complete denture wearers and is usually seen in the buccal sulcus as a painless lump with a smooth mucosal surface, parallel to the alveolar ridge. It is often seen in relation to lower complete denture, particularly in the anterior region, and may be grooved by the denture margins. It is caused by pressure from the ill-fitting, overextended denture flange resulting in chronic irritation and hyperplastic reaction. Diagnosis is straightforward on clinical grounds, but ulcerated lesion may mimic carcinoma. Management includes surgical removal of the hyperplastic tissue and adjustment of the denture flange to prevent recurrence.

Candidal Leukoplakia

Candidal leukoplakia appears as white plaques, may be speckled in appearance and is seen in older people, many of whom are heavy smokers. It is typically seen on the cheek mucosa just within the commissures of the mouth (Fig. 19.4) but may be seen on the dorsum or the edges of the tongue. Biopsy is necessary to differentiate from other white lesions and to detect any premalignant or malignant transformations. Management strategies include antifungals, cessation of smoking and removal (surgery, laser or cryosurgery).

Lichen Planus

This is a mucocutaneous disorder, common among elderly females, which manifests frequently in the mouth as white striations and papules, often found on the buccal mucosae

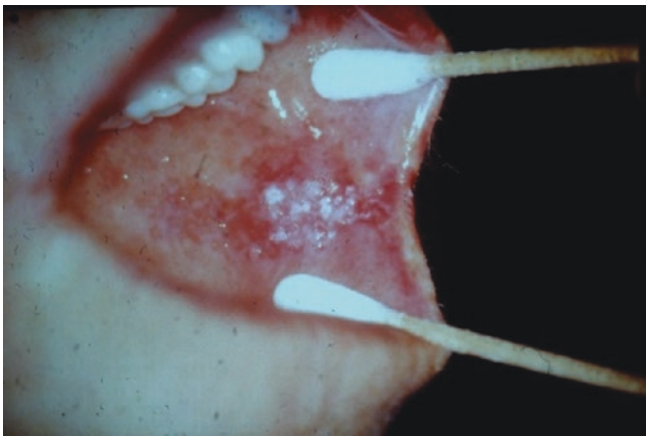

Fig. 19.4 Candidal leukoplakia (speckled) on the left cheek and the commissure

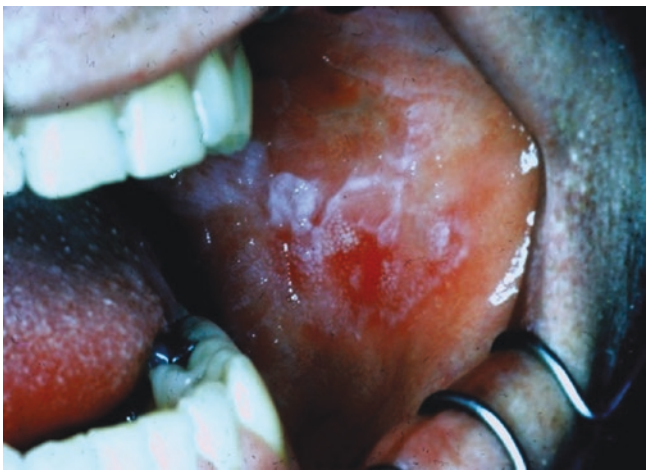

Fig. 19.5 Erosive lichen planus on the left cheek

(Fig. 19.5) and occasionally on the tongue (Fig. 19.6). Sometimes the lesions are atrophic with erosions which are irregular, persistent and painful, with a yellowish slough, and often associated with white lesions. Lichen planus can also cause 'desquamative gingivitis'. Concurrently, skin and genital lesions may appear. The condition has been recognised as a T-lymphocyte-mediated disorder, but in most cases no aetiological factor is identifiable. Minority of cases are due to drugs (NSAIDs, antimalarials, ACE inhibitors, beta-blockers), called lichenoid reactions, and rarely due to amalgam and gold. Diagnosis is based on drug history and biopsy.

No treatment is necessary for asymptomatic cases, and symptomatic cases are commonly managed with topical corticosteroids and rarely with a combination of topical and systemic corticosteroids. Lichen planus has been found to have premalignant potential of about 1% over a 10-year period [24].

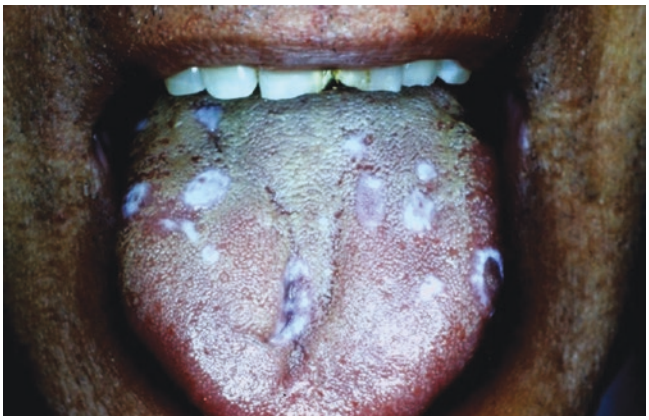

Fig. 19.6 Non-erosive lichen planus on the dorsum of tongue

Burning Mouth Syndrome (Dysaesthesia)

Burning mouth syndrome is common among older people, especially females, and presents as a persistent burning sensation in the tongue, occasionally involving the palate or lip with no evidence of organic disease. Similar symptoms may be caused by deficiency states, erythema migrans, lichen planus, candidosis and diabetes mellitus. The condition is commonly associated with psychogenic causes, in the absence of detectable organic conditions. Management includes treatment of any organic cause, otherwise psychotherapy or antidepressants may be useful.

Leukoplakia

Leukoplakia is defined as a white lesion of the oral mucosa that cannot be characterised as any other lesion on clinical and histological basis. It is the most common premalignant lesion of the oral mucosa. There are three main types of leukoplakia: most are smooth plaques (homogeneous leukoplakia), some are warty (verrucous leukoplakia) (Figs. 19.7 and 19.8) and others are mixed white and red lesions (speckled leukoplakia). In general, homogenous leukoplakias are benign, while the premalignant potential is higher in verrucous leukoplakia and highest in speckled leukoplakia.

Erythroplakia

Erythroplakia or erythroplasia presents as a red velvety patch and the soft palate and the floor of the mouth are the common sites. It is much less common compared to leukoplakia and is mainly seen in elderly males. Unlike leukoplakia, this condi-

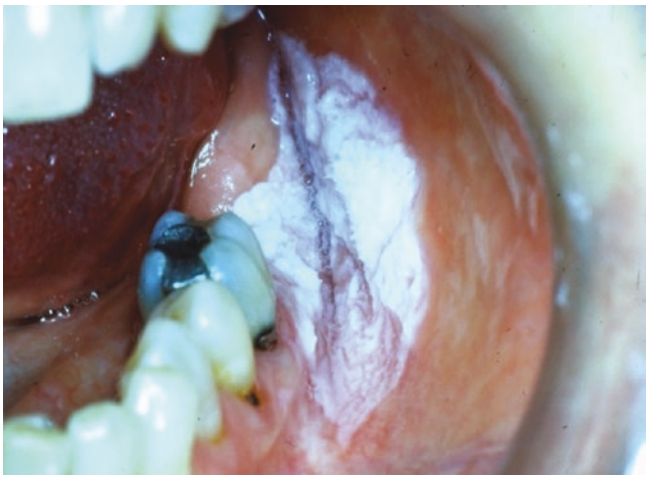

Fig. 19.7 Leukoplakia involving the gingiva and left cheek (verrucous type)

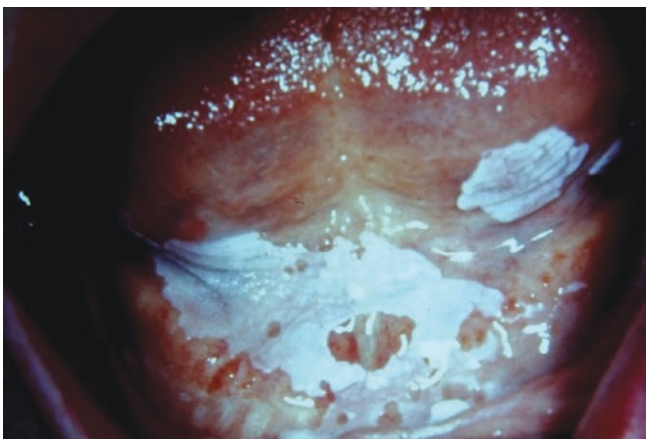

Fig. 19.8 Leukoplakia on the floor of mouth (sublingual keratosis)

tion is far more likely to be dysplastic or malignant. The predisposing factors are like that of oral carcinoma. Oral inflammatory and atrophic conditions such as deficiency anaemias, geographic tongue and lichen planus may mimic this condition.

Oral Cancer

Oral cancer, a potentially fatal disease, is the eleventh most prevalent cancer in the world [25] and over 90% of oral cancers present as squamous cell carcinomas [26]. It is common in the elderly and the incidence is about two-thirds higher among men than women. The primary risk factors are tobacco and excessive consumption of alcohol. The chewing of tobacco is a major cause of oral cancer in several countries including India. Other predisposing factors include human papillomavirus, extensive exposure to sun (lip cancer), immunosuppression and malnutrition.

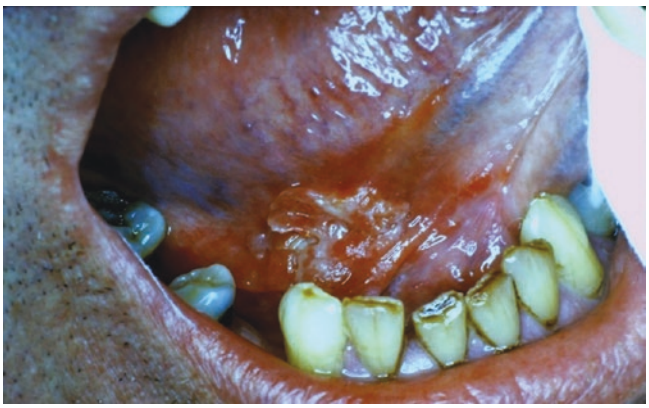

Fig. 19.9 Squamous cell carcinoma on the floor of the mouth

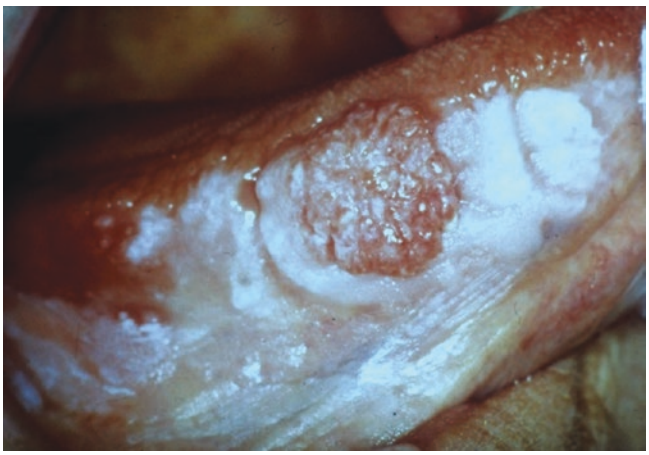

Fig. 19.10 Squamous cell carcinoma of lateral aspect of the tongue and extensive leukoplakia

Common sites in the mouth include the floor of mouth (Fig. 19.9), ventral and lateral borders of tongue (Fig. 19.10), retromolar trigone and the soft palate/tonsillar region. Early lesions can be asymptomatic with superficial changes to mucosal colour and texture. It can present as a red, white or speckled lesions with areas of induration and ulceration. It may also resemble or coexist with conditions such as candidosis or lichen planus. In later stages, the presentation is one of an indurated, non-healing ulcer with elevated margins and may also exhibit prominent exophytic and endophytic growth features with the involvement of regional lymph nodes.

The main treatment modalities are surgery or radiotherapy or a combination of the two, depending on the staging of the tumour which is based on the size of the tumour and the presence or absence of regional and distant metastases. Mortality of oral cancer is particularly high despite being relatively easy to diagnose in the early stages. It is because the disease is frequently asymptomatic and is often diagnosed at a later stage when the cancer has already metastasised.

Medical Problems in the Elderly of Importance for the Provision of Oral Health Care

The prevalence of chronic medical conditions is more common in the elderly population and is higher in the frailer population in nursing homes compared to the noninstitutionalised elderly population. About 75% of this population are likely to suffer from more than one medical condition and 30% of this group are likely to suffer from more than three chronic medical conditions [27].

Cardiovascular Disorders

Of importance to the elderly are those with artificial heart valves, history of previous endocarditis, recent myocardial infarction (MI), recent coronary artery bypass graft (CABG), angina, coronary stents, congestive heart failure (CHF) and arrhythmias. Patients with a previous history of endocarditis, prosthetic heart valves, heart transplant patients with valve damage and those patients who had surgery for congenital heart disease with patches and conduits will require antibiotic prophylaxis for the prevention of endocarditis for dental procedures with a high incidence of bacteraemia such as tooth extraction, periodontal surgical procedures and other oral surgical procedures. The current recommended oral regimen for prophylaxis in adults is amoxicillin 2 g 1 h before procedure, and for those patients hypersensitive to penicillins, clindamycin 600 mg orally, 1 h before procedure is recommended [28].

For patients who have had (MI) recently, it is advisable to postpone elective dental care for a period of 6 months. However, emergency dental treatment such as a single tooth extraction for relief of acute pain should be carried out in consultation with the treating physician. Care should be taken with the use of local anaesthesia with adrenaline, consider employing sedation such as nitrous oxide and provide adequate postoperative pain control.

For patients who have had CABG recently, it is prudent to consult the physician prior to undertaking any invasive dental procedures, and it is advisable to wait for about 6 weeks before providing elective dental care.

When managing angina patients, particularly when angina is unstable, keep the appointments short, consider giving oral sedation or nitrous oxide and have nitroglycerin medication readily available.

Coronary stents have become common in the treatment of coronary heart disease in the elderly, and the main issue for dental treatment is anticoagulation usually with aspirin or antiplatelet drug such as clopidogrel or both for at least 6–12 months after stent placement. Currently, there is no need to interfere with these medications for dental treatment including tooth extractions as any excessive bleeding can be controlled with the use of haemostatic agents, suturing and tranexamic acid mouthwash or tablets.

In the case of patients with pacemakers, the use of electronic dental devices such as ultrasonic scalers, electric pulp testers and electrocautery should be avoided because of possible interference with pacemaker.

Patients with congestive heart failure may suffer from orthopnoea and should be treated in the upright position in the dental chair as they may not tolerate supine position. Some may suffer from orthostatic hypotension due to medications, and they must be raised to sitting position slowly over several minutes.

Management of patients with cardiac arrhythmias in the dental practice include consideration for increased bleeding in those who are anticoagulated and care with the use of local anaesthetic containing adrenaline.

Other Medical Issues of Importance in the Elderly

Diabetes Mellitus

The main consideration for dental management of diabetic patients is the prevention of hypoglycaemia during treatment and the possibility of poor response to treatment of dental and periodontal infections. To avoid hypoglycaemia, morning appointments are more suitable ensuring that the patient has eaten a normal breakfast and received the normal insulin dose. If the patient is unable to eat after the procedure, the insulin dose needs to be reduced. Poorly controlled diabetics may require hospitalisation for extensive dental or surgical treatment and managed in conjunction with the physician.

Radiotherapy

External beam radiotherapy used in the treatment of head and neck cancers inevitably damages surrounding normal tissues such as the oral mucosa, salivary glands and the bone causing complications which include mucositis, xerostomia, radiation caries, trismus and osteoradionecrosis of the jaws. The incidence of complications is much reduced with precise dosimetry, careful shielding of healthy tissues and thorough dental evaluation and strict application of preventative measures. Prior to radiotherapy, teeth which are affected by advanced caries and periodontal disease and are unsalvageable should be extracted, and thorough oral prophylaxis of cleaning the remaining teeth, application of fluoride and meticulous oral hygiene instruction should be instituted.

Chemotherapy

A wide range of cancers are treated with cytotoxic drugs. Myelosuppression during chemotherapy causes mucositis, gingival bleeding and mucosal infections. As with radiotherapy, preventive measures such as extractions of teeth with poor prognosis, oral prophylaxis and oral hygiene measures should be carried out to prevent or minimise oral complications following chemotherapy. Oral antifungal prophylaxis may be appropriate when the neutrophil count is significantly depressed. Fluoride rinses or fluoride gel will help to prevent caries.

Osteonecrosis

Osteoporosis is common in the elderly, and many of these patients are treated with bisphosphonate medications to slow the process of bone loss. Bisphosphonates and denosumab are anti-resorptive drugs used in the management of osteoporosis and metastatic bone disease. Avascular necrosis or bisphosphonate-related osteonecrosis of the jaws (BRONJ) has been confirmed as an adverse effect of this group of medications and is caused by suppression of normal bone turnover. The current term for this condition is 'medication-related osteonecrosis of the jaw' (MRONJ) which was introduced by the American Association of Oral and Maxillofacial Surgeons[29] to include all drug-induced forms of osteonecrosis of the jaw [29]. The diagnosis of MRONJ is based on three criteria, namely, presence of exposed bone in the maxillofacial region over a period of 8 weeks, current or previous treatment with anti-resorptive or anti-angiogenic agents and no history of radiation therapy to the jaw or obvious metastatic disease to the jaw [30].

The incidence of MRONJ is up to 15% for patients with malignant disease receiving bisphosphonates and denosumab compared with 0.01% in patients with osteoporosis. Clinical presentation ranges from asymptomatic exposure of bone (94%) to severe cases of mandibular fractures (4.5%). MRONJ commonly follows tooth extraction, denture trauma, invasive dental procedures and dental infections. It is important to employ preventive strategies such as elimination of potential risk factors which could lead to invasive dental procedures and maintenance of good oral hygiene before commencing treatment with bisphosphonates [30].

Oral Health-Related Quality of Life

Oral conditions that commonly affect the elderly, such as missing teeth, dry mouth and limitations with chewing food, have been found to correlate with worse quality of life when the influences of other associated factors such as general health, income and marital status were controlled [31]. There is some evidence in the literature to support the view that poor oral health in the elderly impairs their self-esteem and social interactions [32]. Poor oral health and hygiene will have an adverse effect on social interactions among the elderly and can cause an increase in self-consciousness, disturbed body image and personal relationships. Elderly often feel embarrassed by teeth that they see as unsightly, bad breath, ill-fitting dentures that move visibly when eating and dentures that are uncomfortable to chew or inefficient.

Preventive Oral Health Care for the Elderly

The best way to control dental caries and periodontal disease in the elderly is to employ strategies to reduce the accumulation of plaque on the teeth, gums and dental prostheses. This is generally achieved by mechanical cleaning with a manual toothbrush, but electric toothbrush with an oscillation-rotation action has been found to be more effective in reducing plaque and improving gingival health [33]. Combining mechanical cleaning with plaque control with antimicrobial agents such as chlorhexidine mouthwash will further decrease the number of bacteria in the mouth. The use of fluorides in toothpaste or mouthwash would help to prevent dental decay particularly root caries.

Candidal infections increase with age and are associated with removable dental prostheses. Mechanical cleaning of dentures after every meal is necessary to reduce candida count, and the most effective way to clean dentures is to soak them overnight in an antimicrobial solution or 1% sodium hypochlorite solution. Ill-fittings dentures irritate the oral mucosa causing mucosal ulcers and overgrowths. Therefore, frequent check-ups are necessary to carry out adjustments to dentures. Prevention and management of oral mucositis in patients undergoing radiotherapy or chemotherapy should be undertaken by dentists in conjunction with the physicians. Those elderly patients with chronic mucosal conditions and premalignant oral conditions require close and frequent follow-up to detect early malignant transformation.

Xerostomia can be controlled by avoidance if possible of drugs with anticholinergic effect, effective management of diseases which are associated with hyposalivation such as rheumatic diseases and diabetes and shielding of salivary glands during radiotherapy.

Measures such as reduction in the use of tobacco and alcohol, management of ill-fitting prostheses, maintenance of good oral hygiene and prevention of papillomavirus and HIV infections can be undertaken to reduce the incidence of oral cancer in the elderly. Frequent follow-up of patients who have had treatment for any malignancy is essential.

Prevention of alveolar bone loss is necessary for good retention of dentures. Measures like keeping one's natural

dentition, control of caries and periodontal disease, control of osteoporosis, avoidance of long-term corticosteroid therapy and hormone replacement therapy in postmenopausal women will help significantly to reduce bone loss.

Clinical Relevance

The retention of natural teeth is becoming more common in the elderly, but the inability to maintain good oral hygiene is causing an increase in the incidence of caries and periodontal disease.

Presently, incremental tooth loss is more common than edentulism in the elderly, and this poses ongoing problems with extractions of teeth and the provision of complex prostheses.

Dental caries remains a major oral health problem in the dentate elderly and preservation of teeth requires regular dental visits, treatment and preventive oral health care.

There is an increase in the prevalence of periodontal disease with advancing age due to poor oral hygiene and when left untreated will lead to abscess formation and eventually tooth loss.

Dry mouth is more common in the elderly and it affects the quality of life. Treatment is aimed at dealing with the causative factors and preventive measures against the development of caries, periodontal disease and candidosis.

Candidosis is common in the elderly, particularly those wearing dentures and those who are immunocompromised. Management include treatment of predisposing conditions and with antifungals.

Oral cancer is a fatal disease, common in the elderly males. Prognosis is good with early diagnosis and treatment.

Medication-related osteonecrosis of the jaw (MRONJ) is an adverse condition affecting patients receiving bisphosphonates. Preventive measures should be undertaken before commencement of treatment to avoid future invasive dental procedures that can trigger this often-intractable condition.

Multiple Choice Questions

1. Which of the following is not true about dental caries in the elderly:
   A. Root caries is common.
   B. Xerostomia is a causative factor for caries.
   C. Osteoporosis is a causative factor for caries.
   D. Poor oral hygiene is a cause for caries.
2. The following about oral lichen planus is true EXCEPT:
   A. A mucocutaneous disorder
   B. Manifests as white lesions
   C. Has premalignant potential
   D. Causes periodontal disease
3. The diagnosis of medication-related osteonecrosis of the jaw (MRONJ) is based on the following EXCEPT:
   A. Presence of exposed bone in the maxillofacial region over a period of 8 weeks
   B. Current or previous treatment with anti-resorptive agents
   C. Current or previous treatment with anti-angiogenic agents
   D. History of radiation therapy to the jaw

Answers to MCQs

1. C
2. D
3. D

References

1. United Nations. World population prospects: the 2010 revision. Available at: http://esa.un.org/unpd/wpp.
2. Australian Institute of Health and Welfare 2014 Australia's health 2014. Australia's health series no.14. Cat. No. AUS 178. Canberra: AIHW.
3. Olshansky SJ. Demography – impact of an expanding elderly population. Textbook of geriatric dentistry. 3rd. Wiley-Blackwell; 2015. p. 1–5.
4. Mandojana JM, Martin-de las Heras S, Valenzuela A, Valenzuela M, JD L. Differences in morphological age-related dental changes depending on post-mortem interval. J Forensic Sci. 2001;46:889–92.
5. Papapanou PN, Wennström JL, Gröndahl K. A 10-year retrospective study of periodontal disease progression. J Clin Periodontol. 1989;16:403–11.
6. Landt H, Fransson B. Oral ability to recognise forms and oral muscular coordination ability in dentulous young and elderly adults. J Oral Rehabil. 1975;2:125–38.
7. Nedelman C, Bernick S. Age changes in mucosa and bone. J Prosthet Dent. 1978;39:494–501.
8. Wolff A, Ship JA, Tylenda CA, Fox PC, Baum BJ. Oral mucosal appearance is unchanged in healthy different-aged persons. Oral Surg Oral Med Oral Pathol. 1991;71:569–72.
9. Easterby-Smith V, Besford J, Heath RM. The effect of age on the recognition thresholds of three sweeteners: sucrose, saccharin and aspartame. Gerodontology. 1994;11:39–45.
10. Magnusson C, Ernberg M, Magnusson T. A description of a contemporary human skull material in respect of age, gender, temporomandibular joint changes, and some dental variables. Swed Dent J. 2008;32:69–81.
11. Wactawski-Wende J, Hausmann E, Hovey K, Trevisan M, Grossi S, Genco RJ. The association between osteoporosis and alveolar crestal height in postmenopausal women. J Periodontol. 2005;76(suppl 11):2116–24.
12. Bodic F, Hamel l LE, Baslē MF, Chappard D. Bone loss and teeth. Joint Bone Spine. 2005;72:215–21.

13. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18 – 88 yr. J Appl Physiol. 2000;89:81–8.
14. Newton JP, Yemm R, Abel RW, Menhinick S. Changes in jaw muscles with age and dental state. Gerodontology. 1993;10:16–22.
15. Baum BJ. Evaluation of stimulated parotid saliva flow rate in different age groups. J Dent Res. 1981;60(7):1292–6.
16. Slade GD, Spencer AJ. Social impact of oral conditions among older adults. Aust Dent J. 1994;39:358–64.
17. Dye BA, Li X, Thorton-Evans G. Oral health disparities as determined by selected healthy people 2020 oral health objectives for the United States, 2009-2010. NCHS Data Brief. 2012;104:1–8.
18. Ministry of health. Our oral health; Key findings of the 2009 New Zealand Oral Health Survey. Wellington: Ministry of Health; 2010.
19. Chalmers JM, Carter KD, Spencer AJ. Caries incidence and increments in Adelaide nursing home residents. Spec Care Dentist. 2005;25:96–105.
20. Kassebaum NJ, Bernabė E, Dahiya M, Bhandari B, Murray CJ, Marcenes W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. J Dent Res. 2014;93(11):1045–53.
21. Tavares M, Lindefjeld Calabi KA, San Martin L. Systemic diseases and oral health. Dent Clin N Am. 2014;58(4):797–814.
22. Fox PC, Busch KA, Baum BJ. Subjective reports of xerostomia and objective measures of salivary gland performance. J Am Dent Assoc. 1987;115:581–4.
23. Espinoza I, Rojas R, Aranda W, Gamonal J. Prevalence of oral mucosal lesions in elderly people in Santiago, Chile. J Oral Pathol Med. 2003;32:571–5.
24. Gandolfo S, Richiardi L, Carrozzo M, Broccoletti R, Carbone M, Pagano M, et al. Risk of oral squamous cell carcinoma in 402 patients with oral lichen planus: a follow-up study in an Italian population. Oral Oncol. 2004;4:77–83.
25. World Health Organisation (WHO) Global data on incidence of oral cancer. WHO/NMH/CHP/HPR/ORH. 2005.
26. Neville BW, Day TA. Oral cancer and precancerous lesions. CA Cancer J Clin. 2002;52:195–215.
27. Scully C. Medical problems in dentistry. 6th ed. Chap. 25. Churchill Livingstone; 2010. p. 573.
28. Therapeutic guidelines: Antibiotic, version 15; 2014.
29. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw-2014 update. J Oral Maxillofac Surg. 2014;72(10):1938–56.
30. Möcke TM, Krestan CR, Mitchell DM, Kirschke JS, Wutzl A. Bisphosphonate and medication-related osteonecrosis of the jaw: A review. Semin Musculoskelet Radiol. 2016;20:305–14.
31. Locker D, Matear D, Stephens M, Jokovic A. Oral health-related quality of life of a population of medically compromised elderly people. Community Dent Health. 2002;19(2):90–7.
32. Kandelman D, Petersen PE, Ueda H. Oral health, general health and quality of life in older people. Spec Care Dentist. 2008;28(6):224–36.
33. Davies RM. The rational use of oral care products in the elderly. Clin Oral Investig. 2004;8:2–5.

Cancer in the Very Elderly and Management

20

Niluja Thiruthaneeswaran, Lucinda Morris, and Jayasingham Jayamohan

Introduction

As the worldwide population ages and the life expectancy improves, increasing numbers of older patients will be diagnosed with cancer and represent a rising majority of patients seen in cancer clinics [1, 2]. Cancer incidence is the highest in the age group 65–85 years and seems to decline in the oldest-old with extremely low rates when >100 years of age [3, 4]. The decline in incidence is partly due to the widespread adoption of cancer screening of breast, prostate and colorectal moving the incident age on average a decade forward [5]. It is estimated that of 8% all cancer incidence is accounted for by those aged 85 years and older and this is expected to increase to 17% by 2050 [3]. The epidemiology data available in this cohort of patients comes mainly from the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) database which aggregates cancer incidence for the 85+-year-olds which is limiting to study trends in the oldest-old [3]. A number of studies have listed the most common cancers in ≥85-year-olds to be breast, colorectal, prostate and lung [2, 6]. In centenarians breast cancer has the highest prevalence; however this is likely related to the higher female-to-male ratio in this group. Cancer-specific mortality rates are affected by the stage at diagnosis which has a significant impact in the ≥85 years likely due to diagnosis bias and absence of treatment. Study reports on cancer-specific mortality are limited, but generally, they have reported a decrease after 100+ years, and this is supported by autopsy series. However, cancer was only accurately diagnosed in 30% of centenarians compared to 70% in patients aged between 70 and 90 years [7].

N. Thiruthaneeswaran (✉)
The University of Sydney, Sydney, NSW, Australia

University of Manchester, Manchester, UK

L. Morris · J. Jayamohan
Crown Princess Mary Cancer Center, Westmead, NSW, Australia

Biology of Cancer and Ageing

The pattern of exponential increase in solid tumour incidence with age following sexual maturity is often explained by exposure to endogenous and exogenous carcinogens over time. Along with epidemiological data, there is emerging evidence that there is a difference in the cellular response to damage in elderly subjects [8]. The pathogenesis of ageing and the pathogenesis of tumorigenesis do have overlapping features, but it is less clear to what extent they promote or inhibit cancer development. Age-related physiological changes which are marked in ≥85-year-olds such as cellular metabolism and cell proliferation can account for the decrease of cancer incidence as these factors also affect tumour ability to grow, invade and metastasise. *In vitro* studies have shown links between DNA damage response and genomic instability with ageing and cancer [9]. These changes have been shown to increase with age and hence the corresponding increase in cancer incidence. On the other hand, endocrine changes with advancing age such as decreased exposure to sex hormones, growth hormone and insulin growth-factor 1 (IGF1) may serve as protection from carcinogenesis [9]. The complex interplay of competing pathways may account for the exponential rise in cancer incidence from adolescence to 80–85 years followed by a period of decline.

Treatment Modalities

Surgery

Surgery remains the primary treatment for solid tumours. The complex decision-making process for a surgeon centres on determining the benefits of surgery versus the risks regardless of the patient's chronological age. Currently, there is no robust scientific method to predict adverse surgical outcomes. The PACE (preoperative assessment of cancer in the elderly) method of assessing patients which is a combination of surgical risk assessment tools with geriatric assessment tools has been validated prospectively in 460 patients ≥70 years of age.

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_20

This study found that 44% had at least one major complication with wound infection being the most frequent [10, 11]. Postsurgical complications were the lowest for breast surgery (18.9%) compared to gastrointestinal (59.9%) and genitourinary (52.1%) surgery. No significant relationship between age and complications was reported [10]. Other tools and risk assessment strategies often employed in surgery but not specific to oncological surgery include the American Society of Anaesthesia (ASA) scoring system, the Goldman Cardiac Risk Index (GCRI) and the Acute Physiological and Chronic Health Evaluation (APACHE) [12–14].

Radiotherapy

Radiotherapy (RT) is a fundamental and effective method of treating cancer that contributes to 40% of cancer cure rates worldwide [15]. It can be delivered as external beam radiation therapy (EBRT) as daily treatment with the number of fractions determined by disease status or brachytherapy (i.e. placement of radioactive sources close to or within a tumour). There is a paucity of level I evidence to guide practice in the older population. Early trial protocols have often excluded patients >70 years of age, and despite recent randomised controlled trials being open to all ages, the elderly are generally underrepresented [16, 17]. This may be due to lack of clinician equipoise in the treatment of the elderly and/or limitations to adequately assess fitness for treatment. Figure 20.1 highlights the key randomised controlled trials that have informed and shaped current best practice in radiation oncology showing the median age and age range of the trial participants. With the exception of a small number of phase III trials that were tailored specifically for patients >65 years of age [18, 19], clinical trials across all cancer types have a median age for recruits of <70 years.

Systemic Therapy

Evidence for the use of systemic therapy in the oldest-old is lacking across all solid tumours both in the curative and metastatic setting. Systemic therapy includes chemotherapy (i.e. taxanes, anthracyclines, alkylators, antimetabolites) and targeted agents (i.e. VEGF-I, EGFR-I, TKI). The lack of prospective data combined with a limited understanding of pharmacodynamics and pharmacokinetics of systemic therapy with ageing makes treatment decisions in this population extremely challenging. There are a number of studies that have reported on increasing mortality and toxicity with age including randomised trials [20]. A retrospective cohort of nonagenarians reported a 50% dose reduction at the first cycle, but despite this grade 3 and 4 toxicity were reported in 66% [21]. A larger retrospective series of 318 patients ≥80 years reported similar outcomes with 41% receiving upfront dose reduction, therapy discontinuation and hospitalisation in 32% [22]. In this study capecitabine monotherapy was the most commonly prescribed regimen. These studies highlight that despite clinicians making dose adjust-

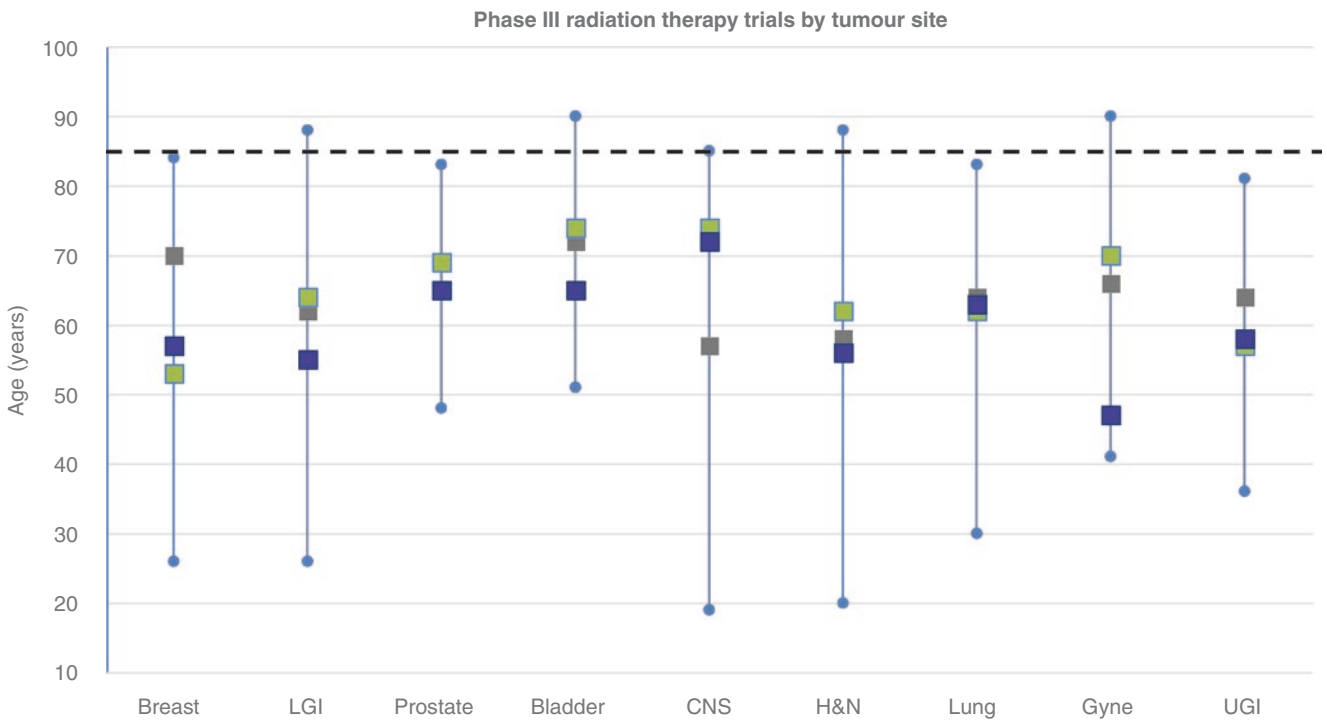

Fig. 20.1 The average age and age range of patients enrolled in modern randomised controlled trials in radiation oncology. *LGI* lower gastrointestinal, *UGI* upper gastrointestinal, *H&N* head and neck, *CNS* central nervous system

ment and regimen modification to mitigate risks in the elderly without guidance from evidence, high toxicity and mortality rates are observed. No general recommendations can be made regarding systemic therapy in the very elderly. Two predictive models for chemotherapy toxicity may aid clinicians in deciding on the risk of treatment. The cancer and ageing research group (CARG) toxicity score is a predicative model for chemotherapy toxicity in patients ≥65 years [23, 24]. It was developed using geriatric assessments, laboratory tests and clinical and pathological factors. It estimates the risk of toxicity from 25% (low toxicity) to 90% (high toxicity). Validation studies using the CARG score are ongoing. The chemotherapy risk assessment scale for high-age patients (CRASH) toxicity tool is another method for assessing toxicity. The total risk score ranges from 50% to 80% for grade 3 or higher toxicity [25]. Both the tools along with the information gained from the CGA may help identify patients that are at high risk of treatment-related toxicity.

Role of Geriatric Assessment

CGA and geriatrician input is strongly recommended in the very elderly to determine overall health, life expectancy and appropriate treatment [26–28]. Chronological age alone should not be the sole determinant of treatment choice in this population. There is strong evidence that CGA detects problems missed by regular assessment, improves functional status, reduces hospitalisation and potentially improves survival in elderly cancer patients with cancer [27–29]. CGA can aid in identifying fit elderly patients who could receive active treatment and those frail elderly patients who should be offered appropriate best supportive care [26–28]. In practice screening tools such as G8 and mini-COG can stratify patients that are fit and suitable for standard treatment and those that require further evaluation [30]. The use of geriatric screening tools in clinical decision-making is based on consensus statements, and prospective studies to validate the screening tools in the very elderly patients are needed. A recent study of oncology trainees found that they were unaware of geriatric assessment tools available, their applicability to elderly cancer patients and the role of the geriatrician in cancer management [31].

Common Cancers and Management

Breast Cancer

Women aged over 85 years are less likely to receive standard management for breast cancer [32–34]. Primary surgery and/or adjuvant RT are omitted, while primary endocrine therapy alone is often utilised [32]. Evidence suggests relative survival in the elderly population is poorer compared to the younger population [32, 35, 36]. This is despite studies showing the prevalence of low-risk indolent tumours is higher in the elderly population [37].

Role of Surgery

Large randomised trials support the use of breast conservation treatment (lumpectomy or partial mastectomy followed by RT) for the treatment of early-stage breast cancer [38, 39]. Although women ≥85 years were not included in these trials, data from smaller studies show breast conservation results in less disability and better quality of life [40, 41] Extrapolating from this data, patients over 85 deemed medically fit could be offered breast conservation treatment. Mastectomy is indicated in T4 or multifocal tumours not technically amenable to breast conservation or in the case of patient preference for mastectomy.

If medically fit, patients of advanced age should be offered surgical lymph node clearance [27]. Axillary sampling using sentinel lymph node biopsy is now widely accepted in patients of all ages with clinically node-negative tumours in order to accurately predict axillary status and the need for potential adjuvant treatment [42]. However omission of sentinel lymph node biopsy may be carefully considered by a multidisciplinary team and caregivers in very elderly women with T1 oestrogen receptor-positive, clinically node-negative tumours with the intention of adjuvant endocrine therapy. This approach is based on the outcomes of several trials showing the avoidance of axillary surgery does not adversely impact on outcomes in elderly women (including those aged over 85) and avoids the postoperative morbidity associated with axillary surgery [43–45].

Role of Radiotherapy

Several large trials have demonstrated the addition of adjuvant RT to conservation surgery achieves equivalent local control and survival rates compared to mastectomy alone while resulting in superior cosmesis and fewer complications [46, 47]. Although these trials often excluded patients aged over 70, other trials exploring the benefit in older patients still demonstrate a reduction in the relative rate of local recurrence, albeit lower as compared to younger women [48–50]. Adjuvant RT is well tolerated in older patients [51]. Evidence supports the use of hypofractionated RT delivered over 15 or 16 fractions, and these shortened courses have clear advantages in terms of convenience for very elderly populations [52–54]. Recent phase III non-inferiority trials that have looked at alternate shorter schedules with partial breast radiotherapy or brachytherapy in early breast cancer may be an attractive option in elderly patients [55, 56].

Studies exploring the omission of adjuvant RT in low-risk older patients often in favour of adjuvant tamoxifen alone have not identified a patient population in which RT does not provide a local control benefit [18, 57, 58]. However the absolute benefit particularly in those aged over 85 may be small, and trials assessing the omission of RT in low-risk elderly patients are ongoing. Thus in patients over 85 with low-risk tumours, the omission of RT may be considered on balance of patient preference, life expectancy and comorbidities and risk of local recurrence [27].

Extrapolating from data of studies of patients aged <70, post-mastectomy RT may be offered to very elderly patients in the presence of involved lymph nodes, positive resection margins or T3/T4 tumours [59]. However, in those aged over 85, it may be argued that given the survival advantage only became apparent after 5 years, the use of adjuvant RT should be based on consideration of life expectancy and the risk of locoregional control alone [27].

Primary RT alone may be considered to gain local control in very elderly patients who refuse or are not fit for surgery, are refractory to hormone therapy or are in locally advanced inoperable breast cancer [60–62]. In such scenarios or in the case of recurrent disease, RT can also provide excellent palliation from local symptoms including ulceration, bleeding, upper limb oedema or brachial plexopathy [63, 64].

Role of Endocrine Therapy

Adjuvant endocrine therapy following breast conservation treatment should be offered to elderly patients with ER-positive breast cancer [27] based on the results of the EBCTCG meta-analysis showing that adjuvant tamoxifen reduces breast cancer death independent of age [65]. It is important to note that when considering endocrine therapy for women aged over 85, few women older than 70 years of age, and very few older than 80, were randomised into the trials included in this overview. In low-risk disease, endocrine therapy may not be deemed necessary on consideration of life expectancy and low likelihood of relapse within the first 10 years [27]. Aromatase inhibitors are slightly more effective in this age group. However, tamoxifen may be used as an alternative if there is concern regarding bone mineral density or the specific toxicities related to aromatase inhibitors [66].

Several trials have investigated the use of primary endocrine therapy alone instead of surgery in elderly patients with hormone receptor-positive disease [67–69]. A Cochrane meta-analysis showed that in medically fit older women, surgery improved local control and progression-free survival but had no impact on overall survival [70]. Although age-related subgroup analysis was not possible on the basis of published data, in frail patients with limited life expectancy or those who refuse surgery, endocrine therapy alone is considered a reasonable treatment option [27, 71, 72].

Role of Chemotherapy

The trials demonstrating benefit of adjuvant chemotherapy in early breast cancer include very few, if any in women aged over 85 [73]. Furthermore, treatment-related toxicity and mortality are of significant concern in elderly breast cancer patients and in principle should be avoided in the very elderly [23, 74–76].

Prostate Cancer

Prostate cancer is the second most common cancer in men worldwide. Globally it is the fifth leading cause of cancer death and it typically ranks second leading cause of death in men in more developed countries [77]. The prognosis for localised disease is good with 80% of patient disease-free at 10 years with recurrence rate for high-risk localised disease at 30% at 3 years and mortality rates approximately 40% at 10 years [78, 79]. As life expectancy increases, the diagnosis and management of prostate cancer in men >75 will represent an increasing challenge and even more so in the older age group of >85 years. No real benefit has been convincingly demonstrated with population-based mass screening, and an individual approach should be considered.

The majority of men with prostate cancer are asymptomatic and patients that are symptomatic usually present with urinary dysfunction or metastatic bone pain. Risk stratification of prostate cancer is based on clinico-pathological features outlined in Table 20.1 [80].

Management

Multiple aspects of the management of localised prostate cancer are controversial, ranging from screening to treatment. In contrast to many other cancers, prostate cancer has a long natural history spanning many years and may not need any treatment, particularly in men >85 years of age. In this population "watchful waiting" and expectant treatment options are often employed. Prospective studies that have shaped current practice in prostate cancer have not included men greater than 80 years of age and rarely above 75 years. Generally, treatment for prostate cancer is based on risk stratification (Table 20.1), and the aim of treatment in the elderly is not to overtreat low- and intermediate-risk disease and undertreat high-risk disease. For localised prostate cancer, options range from surveillance to active treatment. The two main treatment options for localised disease are surgical or RT-based approaches.

Table 20.1 Prostate cancer risk stratification

	Low risk	Intermediate risk	High risk	
Definition	PSA < 10 ng/mL and GS ≤ 6 and cT1-2a	PSA 10–20 ng/mL or GS 7 or cT2b	PSA > 20 ng/mL or GS > 7 or cT2c	Any PSA any GS cT3–4 or cN+
	Localised			Locally advanced

GS Gleason score, *PSA* prostate specific antigen

Role of Surgery

Due to increasing mortality and morbidity rates with age, radical prostatectomy (RP) is not generally considered an appropriate treatment option in the management of localised prostate cancer in the very elderly. Although practice varies and consensus guidelines do not place limits based on age, the majority of surgeons would not consider RP in patients above 70 years. Although age itself should not be a barrier, it is usually considered along with life expectancy, treatment-related morbidity, quality of life and options of alternative radical treatment in the way of RT. There are a few retrospective studies that have reviewed outcomes of RP in octogenarians compared to younger men and found that outcomes were similar between the groups if the older patients were well-selected [81, 82]. It is difficult to conclude treatment-related complications in the elderly due to limitations of published data, but small studies have reported greater complication from RP in men >70 years [83, 84]. In particular increased incontinence rates can have a significant impact on quality of life.

Role of Radiotherapy

RT is an established modality of treatment for localised prostate cancer with no treatment-associated mortality rates and often the treatment of choice for elderly men. It can be delivered daily over a period of weeks as EBRT or brachytherapy over a couple of days which can be given alone or in combination with EBRT. Depending on fitness and life expectancy, active treatment should be offered for patients with high risk and locally advanced disease and considered for unfavourable intermediate-risk disease. Advances in radiation technology with intensity-modulated radiation therapy/image-guided radiation therapy (IMRT/IGRT), stereotactic body radiation therapy (SBRT) and stereotactic radiosurgery (SRS) are extremely promising, and emerging data demonstrate improved efficacy and reduced toxicity and represent appropriate and effective curative options for very elderly patients. Trials are ongoing with shorter courses of RT using SBRT in prostate cancer which will result in significant reduction in the number of daily treatment. SBRT is a highly precise RT technique in which very high doses of RT are used to treat the tumour over a shorter number of fractions than conventional RT, usually ranging from 3 to 8 fractions [85]. Increased efforts are needed to conduct trials specifically evaluating these technologies in older cancer patients.

Recent trials examining hypofractionated RT given daily for 20 days compared to the standard treatment 37 days showed equivalent survival and improved biochemical control in >69 years subgroup without significant increase in toxicity [86, 87].

Role of Endocrine Therapy

Androgen deprivation therapy (ADT), typically LHRH agonist, is a first-line treatment for metastatic prostate cancer and for locally advanced disease when receiving RT. It has been used in the past as monotherapy in elderly men with localised disease, but this practice is declining. Significant side effects with ADT include loss of bone mass leading to osteoporosis, insulin resistance and cardiovascular morbidity and are a concern in the oldest-old. Care should be taken when prescribing ADT for the elderly patients particularly in the setting if there is a history of myocardial infarction, cardiac failure or stroke. Patients on ADT should be placed on supplements for bone health with the option of bisphosphonate or denosumab for prevention of osteoporotic skeletal event.

Active Surveillance or Watchful Waiting

Patients with low-risk disease options of either active surveillance or watchful waiting are appropriate. In patients >85 years, watchful waiting rather than active surveillance may be more appropriate as it avoids the repeated schedule of investigations and avoidance of treatment. Watchful waiting in this age group is also an option for intermediate- and high-risk disease.

Metastatic Prostate Cancer

Until very recently the standard of care for hormone naïve metastatic prostate cancer was ADT. Current trials have addressed the question of the addition of chemotherapy and novel anti-androgen therapy (i.e. abiraterone) with improved survival outcomes [79, 88]. More research is needed on chemohormonal therapy in the oldest-old as the median age of these trials has been ≤67 years. The optimal sequencing of these therapies is subject to ongoing research.

In the setting of castrate-resistant metastatic prostate cancer, options include docetaxel chemotherapy, enzalutamide or abiraterone as first-line therapy with cabazitaxel used as second-line chemotherapy. Increased toxicities and dose reduction have been reported in men ≥75 years [30].

RT is the primary treatment modality for palliation of painful bone metastases, and effective palliation can be achieved with a single fraction of RT [89, 90]. Another option is radium 223 (Ra-223) which has been shown to decrease incidence of skeletal-related events and improve survival in patients with widespread bone disease [91].

Lung Cancer

The incidence of lung cancer increases linearly with age and peaks in the 70–80-year-old age group in both men and women [92, 93]. A high proportion of cases (14%) occur in

octogenarians and currently the numbers of very elderly patients with lung cancer diagnoses are increasing [94]. Non-small cell lung cancer (NSCLC) accounts for approximately 90% of >80 years group with the remainder primary small cell lung cancer (SCLC) [94]. In general, patients aged over 75 years are more likely to present with early-stage disease, presumably as they are more likely to present for medical assessment than younger counterparts [95].

Evidence suggests that a significant proportion of very elderly patients are less likely to receive standard treatment than younger patients [95, 96]. Survival outcomes are poorer for patients aged over 80 for all stages of disease even accounting for demographic subgroups and differences in expected longevity at different ages [94]. However outcomes for elderly patients (including those over 80) who undergo standard therapy such as surgery, RT or chemotherapy were comparable to younger cohorts [94, 96–98]. Evidence indicates elderly patients may be denied potentially beneficial therapy based solely on chronological age and clinician bias or unproven assumptions about the toxicity of various treatment modalities [97, 99, 100]. On an individual patient level, the treatment for lung cancer in the very elderly should depend on a thorough multidisciplinary assessment of all patient and tumour characteristics, molecular subtype, stage of disease, performance status and cardiopulmonary function. International expert consensus guidelines also recommend that this should be combined with the use of CGA-based approach as CGA can add valuable clinical information to guide management, such as estimation of life expectancy and undetected health problems [28, 101, 102].

Stereotactic Radiation Therapy

For elderly patients with early-stage NSCLC, surgical resection with lobectomy remains the standard of care and provides the best chance of long-term survival and cure [102–104]. However many patients, particularly those aged over 85, do not undergo surgery as they are deemed medically inoperable due to comorbidities and/or poor pulmonary function or as a result of patient refusal [102, 105]. Conventional RT is an alternative to surgery and offers a modest magnitude of benefit in terms of overall survival as compared to no treatment. However long-term outcomes with conventional treatment in the elderly remain poor and the majority of patients ultimately die of metastatic disease rather than due to comorbid conditions [106–108].

SBRT has emerged as an alternative curative treatment option for elderly patients with early-stage disease who are not appropriate for surgery [102]. SBRT has dramatically increased the proportion of elderly patients with early-stage NSCLC who can be treated with curative intent [109–111]. Local control rates with SBRT are approximately 90% as opposed to <50% with conventional RT [85]. Severe pneumonitis rates are low at 3% as compared to 13–37% for conventional RT [112, 113]. The only randomised phase III trials comparing SABR with surgery in medically operable patients with stage I NSCLC (STARS and ROSEL) closed early due to slow accrual. Pooled analysis of the data from both of these trials suggested a statistically superior survival rate for those treated with SBRT [114]. However in light of the small sample size and short follow-up and the reduced risk of treatment-related death in those treated with SBRT, this interpretation remains controversial [114]. A retrospective analysis of outcomes of SBRT in a series of 20 patients aged over 85 years with stage I NSCLC compared with patients younger than 85 years found overall SBRT was well tolerated and feasible in the older group and efficacy was comparable to that of the younger cohort although increased radiation pneumonitis rates were reported in the older group [115]. A small mono-institutional study on SBRT in 19 nonagenarians reported no grade 3 or higher toxicity and 2 years overall survival of 47.8% [116].

A large population-based study of treatment patterns and survival for early-stage lung cancer in the elderly in the Netherlands demonstrated the median survival of all 4605 patients increased by 8 months, and survival improvements were seen in patients undergoing both RT (EBRT or SBRT) and surgery [111]. Thus international expert guidelines also recommend that elderly patients with early-stage lung cancer and good functional status should not be denied surgery on the basis of chronological age and should also be referred to a radiation oncologist for evaluation of SBRT as an alternative treatment option [102].

Targeted Drug Therapies in Non-small Cell Lung Cancer

Several trials have demonstrated that single- or double-agent cytotoxic chemotherapy may provide improved clinical outcomes for older patients with NSCLC [117–120]. However, in patients aged 85 and over, data is limited, and the potential safety and toxicity concerns are significant in this population, even in those with a robust functional status.

In the last decade, rapid advances in the characterisation of the molecular pathogenesis of NSCLC have revealed several driver mutations that have yielded new treatment options [102, 121]. Of particular interest in the elderly are epidermal growth factor receptor (EGFR)-targeted drug therapies, which have emerged as attractive alternatives to standard cytotoxic chemotherapy. EGFR mutation-positive NSCLC comprise 10–15% of NSCLC and typically occur in a subset of patients with no history of smoking and more common in females and/or of Asian ethnicity. Positive testing for this characteristics mutation confers a better prognosis and high response rate to EGFR tyrosine kinase inhibitors as initial therapy (such as erlotinib and gefitinib) [122]. Evidence from several key phase II trials suggests these drugs are well tolerated in the elderly and offer significant improvements in

clinical outcomes in patients with the mutation [123–125]. None of the aforementioned trials included patients over 85 years old, and similarly of the 19 trials meeting inclusion criteria of a recent Cochrane review of randomised trials of erlotinib versus vinorelbine, only two included patients over 70 and up to the age of 90 [126]. Nevertheless, in carefully selected very elderly patients with EGFR mutations, it is reasonable to consider EGFR-targeted therapy as first-line treatment [102].

Colorectal Cancer

The median age of colorectal cancer (CRC) is increasing and currently stands at 71 years with 8% being diagnosed in patients >85 years old [127]. The principals of management in the elderly are the same as younger patients with the only curative option of treating localised disease being surgical resection. Surgical methods for colon cancer can be laparoscopic or open and is dependent on the experience of the surgeon and appropriate patient selection. Careful consideration of factors in the very elderly of not only co-morbidities and functional status but the ability to adequately manage a stoma and social supports need to be factored before embarking on primary surgery.

Locally advanced rectal cancer is managed with multimodality therapy which includes surgery and chemoradiotherapy. Low-lying tumours undergo abdominoperineal resection resulting in permanent colostomy. Treatment-related complications and mortality increase with age with reported mortality rates as high as 29% in patients >85 years, and this can occur up to 6 months following the surgical procedure and hence may not be adequately captured in outcome reporting [128]. The impact of neoadjuvant treatment on mortality is unclear. If following comprehensive assessment, an elderly patient is deemed unfit for surgical management, then a number of palliative surgical and RT approaches are available which include stenting to prevent obstruction and short-course EBRT alone or in combination with single line source intraluminal HDR brachytherapy. Combination of HDR-brachytherapy with external beam have reported higher response rates with minimal toxicity and decreased treatment time [129, 130]. Early T1 rectal cancer can be managed with transanal endoscopic microsurgery which is associated with lower morbidity or following a short course of RT to downstage; however it is unlikely that very elderly patients would present with early-stage disease [131].

Role of Chemotherapy

Adjuvant chemotherapy is an integral component of management in high-risk CRC with the greatest benefit demonstrated in patients with nodal disease (stage III). The risk of recurrence is highest in the first 3 years following surgery. Therefore, adjuvant treatment should be considered for anyone with a life expectancy that exceeds that time frame, typically at least ≥5 years. There are a number of chemotherapy regimens in the adjuvant setting that have shown to improve overall survival in phase III trials. The main randomised trials have excluded patients >75 years with one trial with the maximum age of 83 years [132, 133]. The most commonly used protocols are XELOX (capecitabine and oxaliplatin) and modified FOLFOX (leucovorin, fluorouracil, oxaliplatin) chemotherapy. There is controversy over the use of oxaliplatin in patients >70 years, and a reasonable alternative is capecitabine monotherapy or fluorouracil-based (FU/LV) chemotherapy [134, 135]. The safety and efficacy of these regimens in the very elderly is poorly understood with no studies in patients ≥85 years. Results of chemotherapy outcomes in older patients have often pooled analysis into ≥70 years and therefore difficult to determine benefit in ≥85 years [136–138]. Similar issues are encountered when addressing toxicity in the elderly.

Metastatic Colorectal Cancer

There are a number of meta-analysis in metastatic CRC that have shown similar efficacy in elderly patients compared to younger patients. Age-based pooled analysis of randomised trials that compared fluorouracil-based to observation showed no difference in response to chemotherapy based on age [136]. In the pooled results by age, <2% of patients were >80 years of age so the true benefit in very elderly remains unanswered. The most common site of metastases in CRC is the liver, and elderly patients are increasingly receiving treatment strategies that were once only considered in younger patients. A large international cohort study of patients with CRC liver metastases and >70 years of age who received surgical management of the liver disease were compared to a younger cohort. The 3-year overall survival was similar across all age groups including >80 years of age with acceptable morbidity rates [139].

Summary

The burden of cancer in the ageing population has increased considerably and will continue to rise dramatically in the future posing a unique global healthcare challenge. The oldest-old pose a particular challenge as very little high-level evidence exists to guide management. There is also an increasing need for an evidence-based personalised approach as chronological age is no longer accepted as a surrogate for functional status and should not be the sole

determinant of cancer management. Instead, a more detailed process of evaluating individual patients' fitness for treatment is required. In particular the use of a CGA-based approach with multidisciplinary input from geriatricians and allied health professionals will be key to ensuring very elderly cancer patients receive high-quality appropriate care.

References

1. Yancik R. Population aging and cancer: a cross-national concern. Cancer J. 2005;11(6):437–41.
2. Nolen SC, Evans MA, Fischer A, Corrada MM, Kawas CH, Bota DA. Cancer-incidence, prevalence and mortality in the oldest-old. A comprehensive review. Mech Ageing Dev. 2017;164:113–26.
3. Hanson HA, Smith KR, Stroup AM, Harrell CJ. An age-period-cohort analysis of cancer incidence among the oldest old, Utah 1973-2002. Popul Stud (Camb). 2015;69(1):7–22.
4. Harding C, Pompei F, Wilson R. Peak and decline in cancer incidence, mortality, and prevalence at old ages. Cancer. 2012;118(5):1371–86.
5. Linebarger JH, Landercasper J, Ellis RL, Gundrum JD, Marcou KA, De Maiffe BM, et al. Core needle biopsy rate for new cancer diagnosis in an interdisciplinary breast center: evaluation of quality of care 2007-2008. Ann Surg. 2012;255(1):38–43.
6. Andersen SL, Terry DF, Wilcox MA, Babineau T, Malek K, Perls TT. Cancer in the oldest old. Mech Ageing Dev. 2005;126(2):263–7.
7. Stanta G, Campagner L, Cavallieri F, Giarelli L. Cancer of the oldest old. What we have learned from autopsy studies. Clin Geriatr Med. 1997;13(1):55–68.
8. van Heemst D. Biology of cancer and ageing. Eur J Cancer. 2009;45(Suppl 1):414–5.
9. de Magalhaes JP. How ageing processes influence cancer. Nat Rev Cancer. 2013;13(5):357–65.
10. Participants P, Audisio RA, Pope D, Ramesh HS, Gennari R, van Leeuwen BL, et al. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help. A SIOG surgical task force prospective study. Crit Rev Oncol Hematol. 2008;65(2):156–63.
11. Ramesh HS, Boase T, Audisio RA. Risk assessment for cancer surgery in elderly patients. Clin Interv Aging. 2006;1(3):221–7.
12. Leung JM, Dzankic S. Relative importance of preoperative health status versus intraoperative factors in predicting postoperative adverse outcomes in geriatric surgical patients. J Am Geriatr Soc. 2001;49(8):1080–5.
13. Goldman L, Caldera DL, Nussbaum SR, Southwick FS, Krogstad D, Murray B, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med. 1977;297(16):845–50.
14. Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. Crit Care Med. 1981;9(8):591–7.
15. Barton MB, Jacob S, Shafiq J, Wong K, Thompson SR, Hanna TP, et al. Estimating the demand for radiotherapy from the evidence: a review of changes from 2003 to 2012. Radiother Oncol. 2014;112(1):140–4.
16. Kimmick GG, Peterson BL, Kornblith AB, Mandelblatt J, Johnson JL, Wheeler J, et al. Improving accrual of older persons to cancer treatment trials: a randomized trial comparing an educational intervention with standard information: CALGB 360001. J Clin Oncol. 2005;23(10):2201–7.
17. Siu LL. Clinical trials in the elderly–a concept comes of age. N Engl J Med. 2007;356(15):1575–6.
18. Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM, Investigators PI. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol. 2015;16(3):266–73.
19. Roa W, Brasher PM, Bauman G, Anthes M, Bruera E, Chan A, et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: a prospective randomized clinical trial. J Clin Oncol. 2004;22(9):1583–8.
20. Lichtman SM, Wildiers H, Chatelut E, Steer C, Budman D, Morrison VA, et al. International Society of Geriatric Oncology Chemotherapy Taskforce: evaluation of chemotherapy in older patients–an analysis of the medical literature. J Clin Oncol. 2007;25(14):1832–43.
21. Rivoirard R, Chargari C, Kullab S, Trone JC, Langrand-Escure J, Moriceau G, et al. Chemotherapy regimen in nonagenarian cancer patients: a bi-institutional experience. Chemotherapy. 2016;61(2):65–71.
22. Sud S, Lai P, Zhang T, Clemons M, Wheatley-Price P. Chemotherapy in the oldest old: the feasibility of delivering cytotoxic therapy to patients 80 years old and older. J Geriatr Oncol. 2015;6(5):395–400.
23. Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol. 2011;29(25):3457–65.
24. Kim J, Hurria A. Determining chemotherapy tolerance in older patients with cancer. J Natl Compr Cancer Netw. 2013;11(12):1494–502.
25. Extermann M, Boler I, Reich RR, Lyman GH, Brown RH, DeFelice J, et al. Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. Cancer. 2012;118(13):3377–86.
26. Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol. 2014;32(24):2595–603.
27. Wildiers H, Kunkler I, Biganzoli L, Fracheboud J, Vlastos G, Bernard-Marty C, et al. Management of breast cancer in elderly individuals: recommendations of the International Society of Geriatric Oncology. Lancet Oncol. 2007;8(12):1101–15.
28. Extermann M, Aapro M, Bernabei R, Cohen HJ, Droz JP, Lichtman S, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol. 2005;55(3):241–52.
29. Kenis C, Bron D, Libert Y, Decoster L, Van Puyvelde K, Scalliet P, et al. Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicentric study. Ann Oncol. 2013;24(5):1306–12.
30. Droz JP, Albrand G, Gillessen S, Hughes S, Mottet N, Oudard S, et al. Management of prostate cancer in elderly patients: recommendations of a task force of the International Society of Geriatric Oncology. Eur Urol. 2017;72:521.
31. Morris L, Thiruthaneeswaran N, Lehman M, Hasselburg G, Turner S. Are future radiation oncologists equipped with the knowledge to manage elderly patients with cancer? Int J Radiat Oncol Biol Phys. 2017;98(4):743–7.
32. Bastiaannet E, Liefers GJ, de Craen AJ, Kuppen PJ, van de Water W, Portielje JE, et al. Breast cancer in elderly compared to younger patients in the Netherlands: stage at diagnosis, treatment and survival in 127,805 unselected patients. Breast Cancer Res Treat. 2010;124(3):801–7.

33. Lavelle K, Sowerbutts AM, Bundred N, Pilling M, Degner L, Stockton C, et al. Is lack of surgery for older breast cancer patients in the UK explained by patient choice or poor health? A prospective cohort study. Br J Cancer. 2014;110(3):573–83.
34. Lavelle K, Todd C, Moran A, Howell A, Bundred N, Campbell M. Non-standard management of breast cancer increases with age in the UK: a population based cohort of women > or =65 years. Br J Cancer. 2007;96(8):1197–203.
35. Singh R, Hellman S, Heimann R. The natural history of breast carcinoma in the elderly: implications for screening and treatment. Cancer. 2004;100(9):1807–13.
36. Bouchardy C, Rapiti E, Fioretta G, Laissue P, Neyroud-Caspar I, Schafer P, et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. J Clin Oncol. 2003;21(19):3580–7.
37. Gennari R, Curigliano G, Rotmensz N, Robertson C, Colleoni M, Zurrida S, et al. Breast carcinoma in elderly women: features of disease presentation, choice of local and systemic treatments compared with younger postmenopasual patients. Cancer. 2004;101(6):1302–10.
38. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med. 2002;347(16):1227–32.
39. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002;347(16):1233–41.
40. Sweeney C, Schmitz KH, Lazovich D, Virnig BA, Wallace RB, Folsom AR. Functional limitations in elderly female cancer survivors. J Natl Cancer Inst. 2006;98(8):521–9.
41. de Haes JC, Curran D, Aaronson NK, Fentiman IS. Quality of life in breast cancer patients aged over 70 years, participating in the EORTC 10850 randomised clinical trial. Eur J Cancer. 2003;39(7):945–51.
42. Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol. 2005;23(30):7703–20.
43. Hughes KS, Schnaper LA, Berry D, Cirrincione C, McCormick B, Shank B, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. N Engl J Med. 2004;351(10):971–7.
44. International Breast Cancer Study G, Rudenstam CM, Zahrieh D, Forbes JF, Crivellari D, Holmberg SB, et al. Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol. 2006;24(3):337–44.
45. Chagpar AB, McMasters KM, Edwards MJ, North American Fareston Tamoxifen Adjuvant T. Can sentinel node biopsy be avoided in some elderly breast cancer patients? Ann Surg. 2009;249(3):455–60.
46. Early Breast Cancer Trialists' Collaborative G, Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet. 2011;378(9804):1707–16.
47. Ebctcg, McGale P, Taylor C, Correa C, Cutter D, Duane F, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. 2014;383(9935):2127–35.
48. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans V, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005;366(9503):2087–106.
49. Smith BD, Gross CP, Smith GL, Galusha DH, Bekelman JE, Haffty BG. Effectiveness of radiation therapy for older women with early breast cancer. J Natl Cancer Inst. 2006;98(10):681–90.
50. Veronesi U, Luini A, Del Vecchio M, Greco M, Galimberti V, Merson M, et al. Radiotherapy after breast-preserving surgery in women with localized cancer of the breast. N Engl J Med. 1993;328(22):1587–91.
51. Deutsch M. Radiotherapy after lumpectomy for breast cancer in very old women. Am J Clin Oncol. 2002;25(1):48–9.
52. Whelan TJ, Pignol JP, Levine MN, Julian JA, MacKenzie R, Parpia S, et al. Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med. 2010;362(6):513–20.
53. Group ST, Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, et al. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet. 2008;371(9618):1098–107.
54. Group ST, Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, et al. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet Oncol. 2008;9(4):331–41.
55. Coles CE, Griffin CL, Kirby AM, Titley J, Agrawal RK, Alhasso A, et al. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. Lancet. 2017;390(10099):1048–60.
56. Strnad V, Ott OJ, Hildebrandt G, Kauer-Dorner D, Knauerhase H, Major T, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet. 2016;387(10015):229–38.
57. Hughes KS, Schnaper LA, Bellon JR, Cirrincione CT, Berry DA, McCormick B, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol. 2013;31(19):2382–7.
58. Blamey RW, Bates T, Chetty U, Duffy SW, Ellis IO, George D, et al. Radiotherapy or tamoxifen after conserving surgery for breast cancers of excellent prognosis: British Association of Surgical Oncology (BASO) II trial. Eur J Cancer. 2013;49(10):2294–302.
59. Overgaard M, Jensen MB, Overgaard J, Hansen PS, Rose C, Andersson M, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. Lancet. 1999;353(9165):1641–8.
60. Weissberg JB, Prosnitz LR. Treatment of early breast cancer with primary radiation therapy: rationale, results, and techniques. Bull N Y Acad Med. 1982;58(2):203–13.
61. Price A, Kerr GR, Rodger A. Primary radiotherapy for T4 breast cancer. Clin Oncol (R Coll Radiol). 1992;4(4):217–21.
62. Bedwinek J, Rao DV, Perez C, Lee J, Fineberg B. Stage III and localized stage IV breast cancer: irradiation alone vs irradiation plus surgery. Int J Radiat Oncol Biol Phys. 1982;8(1):31–6.
63. Bedwinek J. Radiation therapy of isolated local-regional recurrence of breast cancer: decisions regarding dose, field size, and elective irradiation of uninvolved sites. Int J Radiat Oncol Biol Phys. 1990;19(4):1093–5.
64. Lutz ST, Jones J, Chow E. Role of radiation therapy in palliative care of the patient with cancer. J Clin Oncol. 2014;32(26):2913–9.
65. Early Breast Cancer Trialists' Collaborative G, Davies C, Godwin J, Gray R, Clarke M, Cutter D, et al. Relevance of breast

cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet. 2011;378(9793):771–84.
66. Dowsett M, Cuzick J, Ingle J, Coates A, Forbes J, Bliss J, et al. Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. J Clin Oncol. 2010;28(3):509–18.
67. Fentiman IS, Christiaens MR, Paridaens R, Van Geel A, Rutgers E, Berner J, et al. Treatment of operable breast cancer in the elderly: a randomised clinical trial EORTC 10851 comparing tamoxifen alone with modified radical mastectomy. Eur J Cancer. 2003;39(3):309–16.
68. Mustacchi G, Scanni A, Capasso I, Farris A, Pluchinotta A, Isola G. Update of the phase III trial 'GRETA' of surgery and tamoxifen versus tamoxifen alone for early breast cancer in elderly women. Future Oncol. 2015;11(6):933–41.
69. Fennessy M, Bates T, MacRae K, Riley D, Houghton J, Baum M. Late follow-up of a randomized trial of surgery plus tamoxifen versus tamoxifen alone in women aged over 70 years with operable breast cancer. Br J Surg. 2004;91(6):699–704.
70. Hind D, Wyld L, Reed MW. Surgery, with or without tamoxifen, vs tamoxifen alone for older women with operable breast cancer: cochrane review. Br J Cancer. 2007;96(7):1025–9.
71. Balakrishnan A, Ravichandran D. Early operable breast cancer in elderly women treated with an aromatase inhibitor letrozole as sole therapy. Br J Cancer. 2011;105(12):1825–9.
72. Rai S, Stotter A. Management of elderly patients with breast cancer: the time for surgery. ANZ J Surg. 2005;75(10):863–5.
73. Early Breast Cancer Trialists' Collaborative G. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005;365(9472):1687–717.
74. Du XL, Xia R, Burau K, Liu CC. Cardiac risk associated with the receipt of anthracycline and trastuzumab in a large nationwide cohort of older women with breast cancer, 1998-2005. Med Oncol. 2011;28(Suppl 1):S80–90.
75. Du XL, Osborne C, Goodwin JS. Population-based assessment of hospitalizations for toxicity from chemotherapy in older women with breast cancer. J Clin Oncol. 2002;20(24):4636–42.
76. Klepin HD, Pitcher BN, Ballman KV, Kornblith AB, Hurria A, Winer EP, et al. Comorbidity, chemotherapy toxicity, and outcomes among older women receiving adjuvant chemotherapy for breast cancer on a clinical trial: CALGB 49907 and CALGB 361004 (alliance). J Oncol Pract. 2014;10(5):e285–92.
77. WHO. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide 2012. World Health Organisation; 2012. Available from: http://globocan.iarc.fr/Default.aspx.
78. CRUK. Prostate cancer statistics: Cancer Research UK; 2014. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer.
79. James ND, de Bono JS, Spears MR, Clarke NW, Mason MD, Dearnaley DP, et al. Abiraterone for prostate cancer not previously treated with hormone therapy. N Engl J Med. 2017;377(4):338–51.
80. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol. 2017;71(4):618–29.
81. Thompson RH, Slezak JM, Webster WS, Lieber MM. Radical prostatectomy for octogenarians: how old is too old? Urology. 2006;68(5):1042–5.
82. Jeldres C, Suardi N, Walz J, Saad F, Hutterer GC, Bhojani N, et al. Poor overall survival in septa- and octogenarian patients after radical prostatectomy and radiotherapy for prostate cancer: a population-based study of 6183 men. Eur Urol. 2008;54(1):107–16.
83. Kundu SD, Roehl KA, Eggener SE, Antenor JA, Han M, Catalona WJ. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. J Urol. 2004;172(6 Pt 1):2227–31.
84. Loeb S, Roehl KA, Helfand BT, Catalona WJ. Complications of open radical retropubic prostatectomy in potential candidates for active monitoring. Urology. 2008;72(4):887–91.
85. Palma D, Senan S. Stereotactic radiation therapy: changing treatment paradigms for stage I nonsmall cell lung cancer. Curr Opin Oncol. 2011;23(2):133–9.
86. Dearnaley D, Syndikus I, Sumo G, Bidmead M, Bloomfield D, Clark C, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: preliminary safety results from the CHHiP randomised controlled trial. Lancet Oncol. 2012;13(1):43–54.
87. Catton CN, Lukka H, Gu CS, Martin JM, Supiot S, Chung PWM, et al. Randomized trial of a hypofractionated radiation regimen for the treatment of localized prostate cancer. J Clin Oncol. 2017;35(17):1884–90.
88. Sweeney CJ, Chen YH, Carducci M, Liu G, Jarrard DF, Eisenberger M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med. 2015;373(8):737–46.
89. Hoskin P, Misra V, Hopkins K, Holt T, Brown G, Arnott S, et al. SCORAD III: randomized noninferiority phase III trial of single-dose radiotherapy (RT) compared to multifraction RT in patients (pts) with metastatic spinal canal compression (SCC). J Clin Oncol. 2017;35(15_suppl):LBA10004.
90. Chow R, Hoskin P, Hollenberg D, Lam M, Dennis K, Lutz S, et al. Efficacy of single fraction conventional radiation therapy for painful uncomplicated bone metastases: a systematic review and meta-analysis. Ann Palliat Med. 2017;6(2):125–42.
91. Parker C, Nilsson S, Heinrich D, Helle SI, O'Sullivan JM, Fossa SD, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. N Engl J Med. 2013;369(3):213–23.
92. Pass HI, Mitchell JB, Johnson DH, Turrisi AT, Minna JD. Lung cancer: principles and practice Lippincott. Philadelphia: Williams & Wilkins; 2000. p. 367–88.
93. Brambilla E, TWLcIWCR, Stewart BW, Wild CP, editors. World cancer report 2014. Lyon: World Health Organization; 2014.
94. Owonikoko TK, Ragin CC, Belani CP, Oton AB, Gooding WE, Taioli E, et al. Lung cancer in elderly patients: an analysis of the surveillance, epidemiology, and end results database. J Clin Oncol. 2007;25(35):5570–7.
95. Mery CM, Pappas AN, Bueno R, Colson YL, Linden P, Sugarbaker DJ, et al. Similar long-term survival of elderly patients with nonsmall cell lung cancer treated with lobectomy or wedge resection within the surveillance, epidemiology, and end results database. Chest. 2005;128(1):237–45.
96. Cassidy RJ, Zhang X, Patel PR, Shelton JW, Tian S, Steuer CE, et al. Health care disparities among octogenarians and nonagenarians with stage III lung cancer. J Clin Oncol. 2017;35(15_suppl):e18075.
97. Sawada S, Komori E, Nogami N, Bessho A, Segawa Y, Shinkai T, et al. Advanced age is not correlated with either short-term or long-term postoperative results in lung cancer patients in good clinical condition. Chest. 2005;128(3):1557–63.
98. Firat S, Pleister A, Byhardt RW, Gore E. Age is independent of comorbidity influencing patient selection for combined modality therapy for treatment of stage III nonsmall cell lung cancer (NSCLC). Am J Clin Oncol. 2006;29(3):252–7.
99. Port JL, Kent M, Korst RJ, Lee PC, Levin MA, Flieder D, et al. Surgical resection for lung cancer in the octogenarian. Chest. 2004;126(3):733–8.
100. Matsuoka H, Okada M, Sakamoto T, Tsubota N. Complications and outcomes after pulmonary resection for cancer in patients 80 to 89 years of age. Eur J Cardiothorac Surg. 2005;28(3):380–3.

101. Pallis AG, Gridelli C, van Meerbeeck JP, Greillier L, Wedding U, Lacombe D, et al. EORTC Elderly Task Force and Lung Cancer Group and International Society for Geriatric Oncology (SIOG) experts' opinion for the treatment of non-small-cell lung cancer in an elderly population. Ann Oncol. 2010;21(4):692–706.
102. Pallis AG, Gridelli C, Wedding U, Faivre-Finn C, Veronesi G, Jaklitsch M, et al. Management of elderly patients with NSCLC; updated expert's opinion paper: EORTC Elderly Task Force, Lung Cancer Group and International Society for Geriatric Oncology. Ann Oncol. 2014;25(7):1270–83.
103. Rivera C, Dahan M, Bernard A, Falcoz PE, Thomas P. Surgical treatment of lung cancer in the octogenarians: results of a nationwide audit. Eur J Cardiothorac Surg. 2011;39(6):981–6.
104. Fanucchi O, Ambrogi MC, Dini P, Lucchi M, Melfi F, Davini F, et al. Surgical treatment of non-small cell lung cancer in octogenarians. Interact Cardiovasc Thorac Surg. 2011;12(5):749–53.
105. Wang S, Wong ML, Hamilton N, Davoren JB, Jahan TM, Walter LC. Impact of age and comorbidity on non-small-cell lung cancer treatment in older veterans. J Clin Oncol. 2012;30(13):1447–55.
106. Wisnivesky JP, Halm E, Bonomi M, Powell C, Bagiella E. Effectiveness of radiation therapy for elderly patients with unresected stage I and II non-small cell lung cancer. Am J Respir Crit Care Med. 2010;181(3):264–9.
107. Jeremic B, Zimmermann FB, Nieder C, Molls MM. Radiation therapy alone as an alternative to surgery in patients with early stage non-small-cell lung cancer having cardiovascular (and other) comorbidity. Eur J Cardiothorac Surg. 2004;25(2):297.
108. Zimmermann FB, Bamberg M, Molls M, Jeremic B. Radiation therapy alone in early stage non-small cell lung cancer. Semin Surg Oncol. 2003;21(2):91–7.
109. Palma D, Visser O, Lagerwaard FJ, Belderbos J, Slotman BJ, Senan S. Impact of introducing stereotactic lung radiotherapy for elderly patients with stage I non-small-cell lung cancer: a population-based time-trend analysis. J Clin Oncol. 2010;28(35):5153–9.
110. Louie AV, Rodrigues GB, Palma DA, Senan S. Measuring the population impact of introducing stereotactic ablative radiotherapy for stage I non-small cell lung cancer in Canada. Oncologist. 2014;19(8):880–5.
111. Haasbeek CJ, Palma D, Visser O, Lagerwaard FJ, Slotman B, Senan S. Early-stage lung cancer in elderly patients: a population-based study of changes in treatment patterns and survival in the Netherlands. Ann Oncol. 2012;23(10):2743–7.
112. Kang KH, Okoye CC, Patel RB, Siva S, Biswas T, Ellis RJ, et al. Complications from stereotactic body radiotherapy for lung cancer. Cancers (Basel). 2015;7(2):981–1004.
113. Ricardi U, Badellino S, Filippi AR. Stereotactic radiotherapy for early stage non-small cell lung cancer. Radiat Oncol J. 2015;33(2):57–65.
114. Chang JY, Senan S, Paul MA, Mehran RJ, Louie AV, Balter P, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. Lancet Oncol. 2015;16(6):630–7.
115. Hayashi S, Tanaka H, Kajiura Y, Ohno Y, Hoshi H. Stereotactic body radiotherapy for very elderly patients (age, greater than or equal to 85 years) with stage I non-small cell lung cancer. Radiat Oncol. 2014;9:138.
116. Videtic GM, Woody NM, Reddy CA, Stephans KL. "Never too old": a single-institution experience of stereotactic body radiotherapy for patients 90 years and older with early stage lung cancer. Pract Radiat Oncol. 2017;7(6):e543–9.
117. The Elderly Lung Cancer Vinorelbine Italian Study Group. Effects of vinorelbine on quality of life and survival of elderly patients with advanced non-small-cell lung cancer. J Natl Cancer Inst. 1999;91(1):66–72.
118. Kawaguchi T, Tamiya A, Tamura A, Arao M, Saito R, Matsumura A, et al. Chemotherapy is beneficial for elderly patients with advanced non-small-cell lung cancer: analysis of patients aged 70-74, 75-79, and 80 or older in Japan. Clin Lung Cancer. 2012;13(6):442–7.
119. Davidoff AJ, Tang M, Seal B, Edelman MJ. Chemotherapy and survival benefit in elderly patients with advanced non-small-cell lung cancer. J Clin Oncol. 2010;28(13):2191–7.
120. Brown TPG, Boland A, Oyee J, Tudur-Smith C. Clinical effectiveness of first-line chemoradiation for adult patients with locally advanced non-small cell lung cancer: a systematic review. Health Technol Assess. 2013;17(6):1–99.
121. Langer CJ. The "lazarus response" in treatment-naive, poor performance status patients with non-small-cell lung cancer and epidermal growth factor receptor mutation. J Clin Oncol. 2009;27(9):1350–4.
122. D'Angelo SP, Janjigian YY, Ahye N, Riely GJ, Chaft JE, Sima CS, et al. Distinct clinical course of EGFR-mutant resected lung cancers: results of testing of 1118 surgical specimens and effects of adjuvant gefitinib and erlotinib. J Thorac Oncol. 2012;7(12):1815–22.
123. Maemondo M, Minegishi Y, Inoue A, Kobayashi K, Harada M, Okinaga S, et al. First-line gefitinib in patients aged 75 or older with advanced non-small cell lung cancer harboring epidermal growth factor receptor mutations: NEJ 003 study. J Thorac Oncol. 2012;7(9):1417–22.
124. Asami K, Koizumi T, Hirai K, Ameshima S, Tsukadaira A, Morozumi N, et al. Gefitinib as first-line treatment in elderly epidermal growth factor receptor-mutated patients with advanced lung adenocarcinoma: results of a Nagano Lung Cancer Research Group study. Clin Lung Cancer. 2011;12(6):387–92.
125. Inoue A, Kobayashi K, Usui K, Maemondo M, Okinaga S, Mikami I, et al. First-line gefitinib for patients with advanced non-small-cell lung cancer harboring epidermal growth factor receptor mutations without indication for chemotherapy. J Clin Oncol. 2009;27(9):1394–400.
126. Greenhalgh J, Dwan K, Boland A, Bates V, Vecchio F, Dundar Y, et al. First-line treatment of advanced epidermal growth factor receptor (EGFR) mutation positive non-squamous non-small cell lung cancer. Cochrane Database Syst Rev. 2016;5:CD010383.
127. Census Bureau U. National population projections tables: US Census Bureau; 2014. Available from: https://www.census.gov/data/tables/2014/demo/popproj/2014-summary-tables.html.
128. Rutten HJ, den Dulk M, Lemmens VE, van de Velde CJ, Marijnen CA. Controversies of total mesorectal excision for rectal cancer in elderly patients. Lancet Oncol. 2008;9(5):494–501.
129. Rijkmans EC, Cats A, Nout RA, van den Bongard D, Ketelaars M, Buijsen J, et al. Endorectal brachytherapy boost after external beam radiation therapy in elderly or medically inoperable patients with rectal cancer: primary outcomes of the phase 1 HERBERT study. Int J Radiat Oncol Biol Phys. 2017;98(4):908–17.
130. Corner C, Bryant L, Chapman C, Glynne-Jones R, Hoskin PJ. High-dose-rate afterloading intraluminal brachytherapy for advanced inoperable rectal carcinoma. Brachytherapy. 2010;9(1):66–70.
131. Bokkerink GM, de Graaf EJ, Punt CJ, Nagtegaal ID, Rutten H, Nuyttens JJ, et al. The CARTS study: chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery. BMC Surg. 2011;11:34.
132. Andre T, Boni C, Navarro M, Tabernero J, Hickish T, Topham C, et al. Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial. J Clin Oncol. 2009;27(19):3109–16.
133. Twelves C, Wong A, Nowacki MP, Abt M, Burris HI, Carrato A, et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Engl J Med. 2005;352(26):2696–704.

134. Meyers BM, Cosby R, Quereshy F, Jonker D. Adjuvant chemotherapy for stage II and III colon cancer following complete resection: a cancer care Ontario systematic review. Clin Oncol (R Coll Radiol). 2017;29(7):459–65.
135. Haller DG, O'Connell MJ, Cartwright TH, Twelves CJ, McKenna EF, Sun W, et al. Impact of age and medical comorbidity on adjuvant treatment outcomes for stage III colon cancer: a pooled analysis of individual patient data from four randomized, controlled trials. Ann Oncol. 2015;26(4):715–24.
136. Sargent DJ, Goldberg RM, Jacobson SD, Macdonald JS, Labianca R, Haller DG, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Engl J Med. 2001;345(15):1091–7.
137. Sundararajan V, Mitra N, Jacobson JS, Grann VR, Heitjan DF, Neugut AI. Survival associated with 5-fluorouracil-based adjuvant chemotherapy among elderly patients with node-positive colon cancer. Ann Intern Med. 2002;136(5):349–57.
138. Popescu RA, Norman A, Ross PJ, Parikh B, Cunningham D. Adjuvant or palliative chemotherapy for colorectal cancer in patients 70 years or older. J Clin Oncol. 1999;17(8):2412–8.
139. Adam R, Frilling A, Elias D, Laurent C, Ramos E, Capussotti L, et al. Liver resection of colorectal metastases in elderly patients. Br J Surg. 2010;97(3):366–76.

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Derek Davies

Introduction

The oldest old (>85 years) are the fastest-growing segment of the world's population. Skin disorders have a high impact on the elderly and these include pruritus, ulceration, bacterial infections and fungal disease among others. Chronic itch is a common problem in older patients and is associated with significant morbidity. Seborrhoeic dermatitis occurs with greater frequency in the elderly population [1]. Xerosis refers to dry rough skin and is seen in more than 50% of elderly patients [2]. Bullous pemphigoid mainly affects older people, with onset usually in the 70s. Incidence rises substantially to 150–330 per one million people per year in those older than 80 years [3]. Bacterial, viral and fungal infections may occur commonly in the aged population.

The incidence of skin cancer increases significantly with age. Eighty per cent of non-melanoma skin cancers (NMSCs) occur in people aged 60 years and older [4], and this appears to be mostly related to cumulative exposure to ultraviolet radiation. The incidence of melanoma in patients older than 65 years is up to 10 times higher than in patients younger than 40 years, reaching 100 cases per 100,000 in high-incidence regions of Australia [4, 5].

Selected Skin Conditions

Pathophysiology

Skin ages through both intrinsic and extrinsic factors. The intrinsic functional decline of skin progresses at a genetically determined pace [6] and is compounded by chronic extrinsic insults predominantly ultraviolet radiation (photoageing). Accumulation of reactive oxygen species leads to cellular damage, induction of metalloproteinases, reduced expression of procollagen-1 and increased levels of degraded collagen [7]. There is a reduction in the number of melanocytes, Langerhans cells [8] and Merkel cells in the epidermis. In the dermis there is reduction in fibroblasts [9], nerve receptors, vasculature and appendageal structures [8]. The cumulative effects of these changes result in an elderly skin that is thinned with a diminished blood supply, reduction in elasticity, impaired barrier function, reduced immune function and reduced wound healing [10]. This combination results in increased susceptibility to multiple dermatoses and skin neoplasms.

Pruritus

Pruritus may result in poor sleep patterns, impaired concentration, agitation and depression [11–14]. In severe cases pruritus causes as much discomfort as chronic pain [2]. Pruritus may present with or without rash. Pruritus without rash may be caused by xerosis or be due to systemic conditions [15] (Box. 21.1).

Box. 21.1 Systemic Conditions Associated with Chronic Pruritus

Chronic kidney disease (uremic pruritus), hepatobiliary disease (cholestatic pruritus), iron deficiency, hypothyroidism, diabetes mellitus (causing neuropathic itch), neoplastic disease, particularly lymphoma and other haematologic malignancies and less commonly solid organ malignancies such as renal or lung cancer.

Evaluation

The workup for elderly patients presenting with pruritus without rash should include a thorough medical history, full

D. Davies (✉)
Orange Dermatology, Orange, NSW, Australia
e-mail: Derek@orangedms.com.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_21

blood count with film, creatinine level, liver function tests, bile salts, thyroid function tests, fasting blood sugar levels, HIV serology and thorough examination for adenopathy. Further specialised tests and imaging can be conducted if a cause is not found. In the aging population, polypharmacy is also a risk factor for drug-related itch; however in these cases, itch is usually associated with generalized rash. The most common aetiological agents are calcium channel blockers, thiazides and codeine [8]. Drug eruptions usually occur within weeks of commencing a drug but may occur after the patient has been on the medication for months. Drug-induced itch may persist for several weeks or even months following cessation of the suspect medication. Those patients presenting with pruritus and a rash may have an identifiable dermatologic cause such as xerosis with asteatotic dermatitis, seborrhoeic dermatitis, contact dermatitis, discoid eczema, scabies or bullous pemphigoid. Xerosis is the most common cause of pruritus in the elderly population [10, 16].

Treatment

Treatment of pruritus should be aimed at the underlying condition whether there is specific dermatologic cause or systemic cause. Most patients will benefit from general measures including topical moisturisers applied liberally three times daily. Moisturisers containing 10% urea are particularly effective as urea helps bind moisture to the skin. Patients should avoid all soap products and use a soap substitute when bathing. Bathing should be limited to one short shower or bath daily using tepid water, and a moisturiser should be applied directly after bathing prior to gently towel drying. Topical antipruritic agents such as 0.5% menthol, 0.5% phenol and 0.5% camphor can be added to moisturisers such as sorbolene to provide a cooling effect and can be helpful in some cases. Second-line treatment usually consists of a moderately potent topical steroid in an ointment base applied daily after bathing and after the application of a moisturiser. Topical steroid can be used daily for 2–4 weeks; however prolonged use will result in steroid effects such as atrophy and purpura particularly in the elderly skin [17]. Once the pruritus is controlled, weekend application of topical steroid with ongoing use of moisturisers may be required to maintain remission [18]. Systemic treatments including sedating antihistamines are helpful for patients experiencing nocturnal itch. Low doses are required in the elderly to avoid excessive drowsiness. The selective norepinephrine reuptake inhibitor, mirtazapine, has been shown to be effective in patients with chronic pruritus, as have tricyclic antidepressants; however drowsiness and anticholinergic side effects may be problematic with elderly patients. Other agents have been trialled with varying success including naltrexone, gabapentin and aprepitant [19, 20]. Phototherapy, particularly narrowband UVB, can be a very effective treatment; however access to this treatment may be limited.

Xerosis and Asteatotic Dermatitis

Intrinsic changes in barrier and lipid content, use of soaps and detergents, prolonged or frequent bathing in hot water and overuse of heaters and air conditioners contribute to xerosis [21]. Xerosis may or may not be associated with pruritus but is a common cause of pruritus. Asteatotic eczema is the dermatitis that is caused by xerosis and presents as erythematous diffuse plaques with fine scale, frequently on the legs (Fig. 21.1). It is the most common eczematous condition of the elderly [22]. Generalised and refractory xerosis in the elderly can occur as a paraneoplastic syndrome, and these patients should be investigated for lymphoma [23].

Treatment

Treatment of xerosis and asteatotic dermatitis are the same and include the liberal use of moisturisers applied three times a day, soap avoidance and tepid bathing [24]. Less greasy moisturisers such as 10% urea in sorbolene cream may be preferred during the day, and a thicker paraffin-based emollient ointment can be used at night. Medium potency topical steroids may also be needed initially. Xerosis and asteatotic eczema are also aggravated by low ambient humidity and are more common during winter.

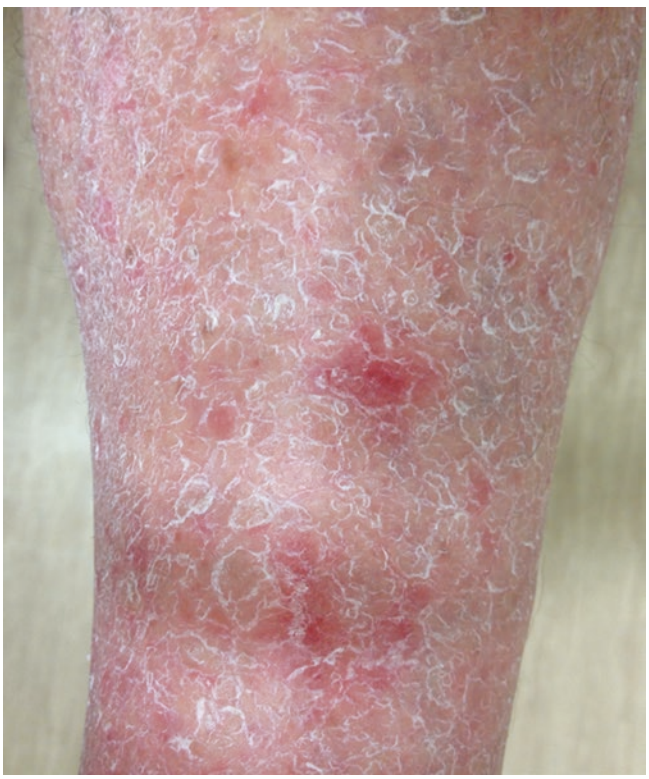

Fig. 21.1 Xerosis and mild asteatotic dermatitis on the lower leg

Seborrhoeic Dermatitis

Seborrhoeic dermatitis is thought to be due to an aberrant host response to *Malassezia* yeasts. It presents as scaly flakes on an erythematous base in the scalp, forehead, eyebrows, along the nasolabial folds and melolabial folds as well as the central chest and groin. It can cause localised pruritus and may be associated with anxiety [25]. It may be seen with increasing frequency in Parkinson's disease [26] and after stroke. Loss of independence in activities of daily living is also a risk factor for seborrheic dermatitis [1].

Treatment

Treatment consists of topical antifungal agents such as antifungal shampoos for the scalp and topical azole containing creams for the skin. Topical calcineurin inhibitors such as topical tacrolimus can also be useful as they may significantly improve the pruritus which may be associated with seborrhoeic dermatitis. Urea-containing moisturisers are also beneficial.

Venous Dermatitis and Venous Ulcers

Venous eczema is part of a spectrum of disease caused by venous incompetence that affects around 20% of people over 70 years of age [27]. Early signs of venous insufficiency include lower leg oedema, hyperpigmentation (due to haemosiderin deposition) and venous eczema. Initial symptoms of venous insufficiency include aching, discomfort and pruritus. Venous eczema, also known as stasis dermatitis or hypostatic eczema, presents as an erythematous, scaling rash on the lower legs which may develop crusting, oozing and erosions caused by scratching [28]. Later signs of venous insufficiency include lipodermatosclerosis and venous ulcers. Lipodermatosclerosis describes the fibrotic skin changes of the lower leg eventually resulting in an inverted champagne bottle appearance (Fig. 21.2). Venous ulcers occur below the knee and commonly on the medial ankle and medial lower leg. Worsening eczema of the lower legs and venous ulceration are subject to secondary bacterial infection.

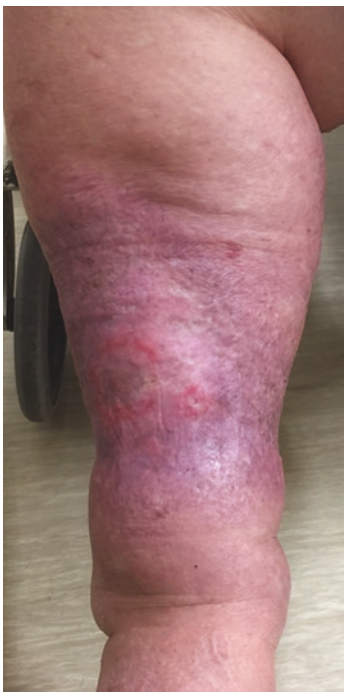

Fig. 21.2 Lipodermatosclerosis of the lower leg. (Reproduced with permission from Orange Dermatology)

Treatment

Venous eczema is treated initially with soap avoidance, use of moisturisers and moderately potent topical steroids often in combination with wet dressings until the eczema settles. Preventative measures are then used comprising of compression stockings worn during waking hours and moisturiser applied at night. Higher compression results in improved venous return; however lighter (Class I) compression may be more practical for some patients.

Venous ulcers are often treated with multilayered compression bandaging systems [29] consisting of a non-stick wound contact layer, a padded bandage, a compression bandage and a flexible cohesive bandage to hold the compression in place. The bandages are changed weekly or more frequently if there is significant exudate. Compression should not be used if there is concomitant significant arterial insufficiency. If intensive compression such as multilayered compression bandage systems is not effective, more definitive treatment of venous insufficiency can be done by ultrasound-guided sclerotherapy and other ambulatory techniques such as endovenous ablation. These minimally invasive procedures have the advantage in the elderly of not requiring a general anaesthetic.

Problems Caused by Skin Fragility

In elderly patients skin fragility is a progressive problem due to declining cutaneous mechanical protection, reduced barrier function, reduced wound healing, decreased production of natural moisturising factors and diminishing cell replacement [10]. This leads to skin that is weaker and more subject to the effects of mechanical trauma and chemical irritation. This results in susceptibility to skin tears due to shearing forces, decubitus ulcers due to pressure and immobility and irritant contact dermatitis (particularly incontinence-associated dermatitis) due to barrier impairment.

Dryness of the skin exacerbates the effects of friction. Eighty per cent of skin tears are seen on the arms and the

dorsum of the hands [10]. Lower legs are another common location. Skin tears can be painful, can be a portal for infection and can become chronic ulcers. Reduction of friction and trauma are the keys to prevention of skin tears and traumatic ulceration.

Treatment

Xerosis should be addressed to reduce friction. Use of moisturisers containing humectants is effective in reducing dry skin and enhancing skin barrier function [10]. Emollients such as petrolatum are also effective at reducing the effects of friction and have the added benefit of providing a barrier function to reduce the risk of irritant dermatitis. Other measures to prevent skin tears include using padded coverings on bed rails, wheelchair arms and legs supports and education of patients and carers on the risk of skin tear prevention [30]. It is important that staff comply with appropriate lift and transfer techniques.

If skin tears occur, treatment consists of cleansing with saline, re-approximation of the skin over the wound and use of a silicone dressing or dressings such as Vaseline impregnated gauze. Sticking plasters should not be applied directly to the skin as this can exacerbate skin tears. Dressings can be held in place with bandages that do not adhere to the skin such as flexible cohesive bandage or a tubular bandage.

Poorer vascular supply of the skin and immobility of aged patients leads to increased susceptibility to decubitus ulcers. Moisturisers will help by reducing friction, and barrier creams assist by reducing the effects of irritants; however appropriate pressure relief is the main preventative measure for pressure ulcers.

Irritant contact dermatitis, particularly incontinence-associated dermatitis, is exacerbated by reduced mobility and reduced skin barrier function. Although the incidence of allergic contact dermatitis does not increase with age, irritant contact dermatitis is more common in the elderly. Dry skin, which is characterized by a decreased lipid content and a delayed reconstitution of the epidermal barrier after skin irritation, is a significant problem in the aged population contributing to the development of irritant contact dermatitis [31]. Treatment involves avoidance of topical irritants, gentle cleansing of affected areas and a mild topical steroid to reduce inflammation combined with a topical antifungal agent to treat superimposed candidiasis. Prevention involves the regular use of barrier creams such as those containing zinc oxide and dimethicone.

Bullous Pemphigoid

It is an autoimmune bullous disease induced by the binding of IgG autoantibodies to target antigens of the basement membrane. Bullous pemphigoid may present with an eczematous eruption 12 months before developing bullae. Alternatively, bullae may develop as the initial presentation. Bullae are tense and may become generalised. Mucous membranes are not commonly involved [16]. The disease can be diagnosed on punch biopsy through the edge of the blister and biopsy of perilesional skin for immunofluorescence.

Treatment

Treatment consists of topical steroids, oral steroids and often immunosuppressive agents such as methotrexate or mycophenolate mofetil. Old age, widespread disease and high doses of oral corticosteroids are risk factors associated with poor prognosis [3].

Infections

Abnormalities with skin barrier function and predisposition to skin tears and ulceration lead to an increased risk infection with *Staphylococcus* and *Streptococcus*. An increase in viral infection is predominantly due to reactivation of varicella zoster virus commonly called shingles. The main morbidity associated with shingles in elderly patients is postherpetic neuralgia which can be severe.

Treatment

Prompt diagnosis and commencement of valacyclovir or famciclovir help to reduce postherpetic neuralgia, and the introduction of regular paracetamol, nonsteroid anti-inflammatory drugs and if needed pregabalin will assist with the pain associated with the active shingles and postherpetic neuralgia. Use of the zoster vaccine is a preventative strategy to reduce morbidity associated with shingles [32]. Reactivation of herpes simplex virus (HSV) can be common in the elderly and is responsive to acyclovir and similar medications.

Fungal Infections

Onychomycosis (fungal infection of the nails) is commonly seen in the geriatric population and is often seen with tinea pedis. This is caused by dermatophytes. A fungal scraping of the material under the toenail allows for microscopy and culture of the organisms.

Treatment

Treatment is not essential; however if it is associated with chronic paronychia, then agents such as fluconazole, itraconazole and terbinafine can be used.

Candidiasis

Candidiasis is another common problem particularly associated with incontinence-associated dermatitis. Candidiasis more commonly presents in intertriginous skin where warmth and moisture promote the growth of candida.

Treatment

Topical antifungal azole creams in combination with mild topical steroids are useful followed by the use of barrier creams such as Bepanthen to help prevent recurrence; however recurrences are common [16].

Neoplasms

Benign Lesions

Benign lesions such as seborrhoeic keratoses, skin tags (fibroepitheliomas), cherry angiomas (Campbell de Morgan spots) and benign lentiginous proliferations are all more common in the elderly population.

Seborrhoeic keratoses are also referred to as seborrhoeic warts. They are variable in colour and size. They present as light tan to dark brown papules and plaques. Numbers increase with age. They do not develop into cancer. Seborrhoeic keratoses are the most common benign lesions in the elderly [16]. On the lower legs, they may present as white well-circumscribed small papules with a stuck on appearance referred to as stucco keratosis (Fig. 21.3). Individual seborrhoeic keratoses which change significantly may require biopsy to exclude a collision lesion where an unrelated malignant tumour arises within or beside a seborrhoeic keratosis.

Treatment

There is usually no need to treat seborrhoeic keratoses; however at times they may cause pruritus in which case regular use of moisturisers and a moderately potent topical steroid can be helpful. Cryotherapy or curettage is helpful for persistently pruritic lesions.

Skin tags (fibroepitheliomas) are common in the elderly population. They occur around skin folds particularly the neck, axillae and sub-mammary region. They can become painful and tender if chafed on clothing and can be removed by snip excision under local anaesthetic.

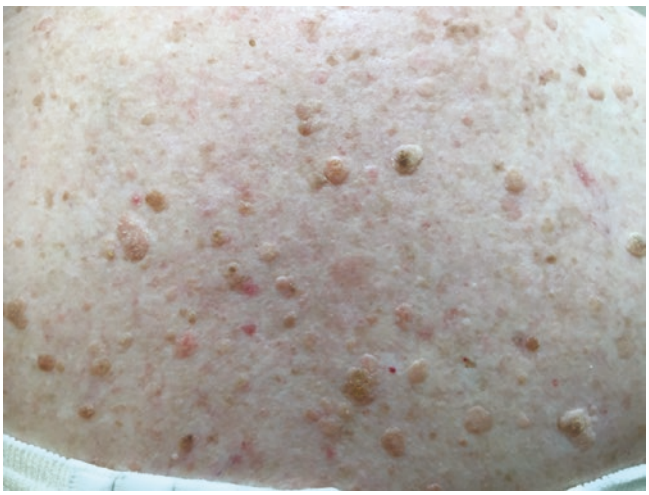

Fig. 21.3 Seborrhoeic keratoses on the back

Campbell de Morgan spots are small cherry angiomas which are seen as bright red or purple papules and are of cosmetic concern only.

Benign lentigines which may present as irregular macular pigmentation in sun-exposed areas are also more common in the elderly population and may be confused with lentigo maligna melanomas.

As the number of lentigines increase with age, the number of benign melanocytic nevi decrease after the fourth decade of life, and elderly patients usually present with few, mainly banal intradermal nevi [4].

Malignant Neoplasia

The most common skin cancers in the elderly are basal cell carcinomas (BCC), squamous cell carcinoma (SCC) and actinic keratoses (AK) which are a precursor to SCC. Malignant melanoma accounts for the greatest number of skin cancer-related deaths in the elderly. Rarer tumours such as Merkel cell carcinoma and angiosarcoma also have increased incidence in the elderly population.

Basal cell carcinoma is the most common type of skin cancer. BCCs are usually located on sun-exposed areas. BCCs are not painful or tender, but bleeding is reported by elderly patients in up to 37% of cases [33]. BCCs tend to ulcerate centrally as they enlarge. Basal cell carcinomas are classified as superficial, nodular, morphoeic/infiltrative and basosquamous. Superficial BCC tumours are limited to the superficial dermis and present as an erythematous patch with a faint pearly edge when the skin is stretched. Nodular BCCs present as a pink or skin-coloured, dome-shaped papule or nodule with a pearly appearance (Fig. 21.4). Morphoeic and infiltrative BCCs can have a sclerotic or scar-like appearance and are poorly defined clinically. Basosquamous tumours have features of both basal and squamous cell carcinomas. BCCs rarely metastasize [34] although basosquamous BCCs have greater propensity to do so [35].

Squamous cell carcinoma is the second most common kind of skin cancer [4]. Although curable when treated early, it has the potential to metastasize. A precursor to squamous cell carcinoma is the actinic keratosis. Histologically AKs show partial-thickness epidermal dysplasia. It is estimated that the risk of progression of actinic keratoses to invasive squamous cell carcinoma is approximately 8% taken as an average among multiple studies; however this range varies considerably [36] and may be lower in practice. Actinic keratoses are common and appear as scaly pink or erythematous papules, most commonly, on the face, ears, neck and dorsum of the hands and forearms (Fig. 21.5).

Squamous cell carcinoma in situ, also known as Bowen's disease, is defined by full-thickness epidermal dysplasia

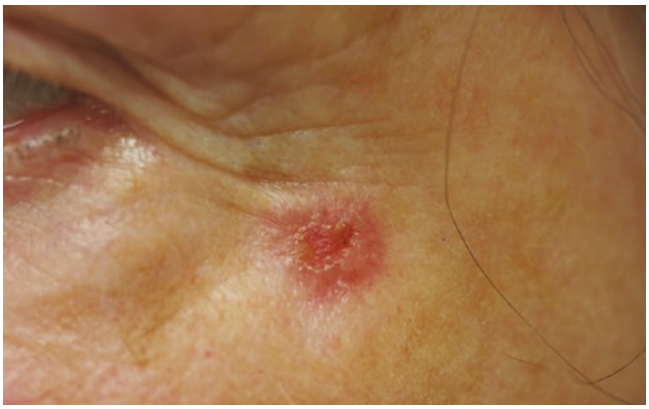

Fig. 21.4 Nodular BCC

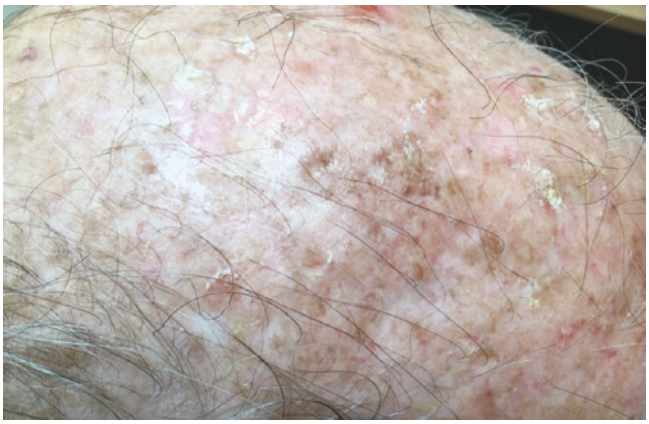

Fig. 21.5 Actinic keratoses on the scalp

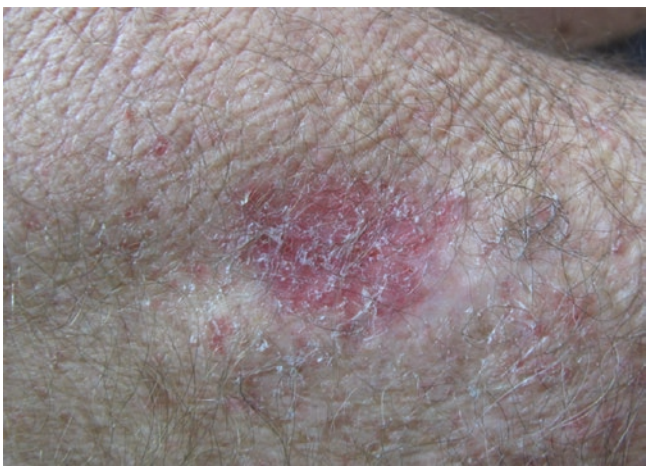

Fig. 21.6 SCC in situ on the arm (Reproduced with permission from Orange Dermatology)

(Fig. 21.6). It is common on the lower legs of the elderly. Risk of invasive transformation is approximately 5% [37].

Invasive squamous cell carcinoma clinically appears as a non-healing keratotic or wart-like growth. More aggressive tumours are classically thicker and larger in diameter, have perineural invasion, are less well differentiated and more likely to metastasize (Fig. 21.7). Tenderness is more commonly reported with SCC (40%) [4].

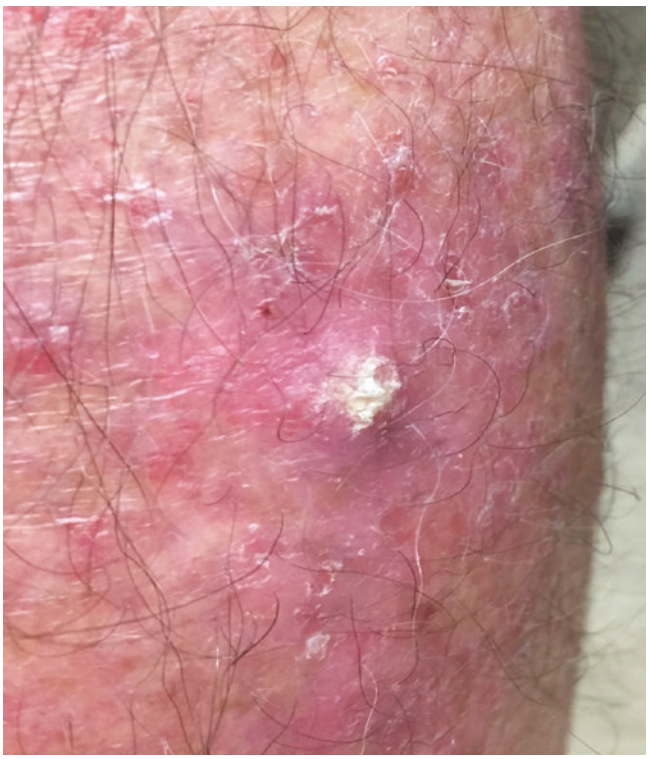

Fig. 21.7 SCC on the leg

Treatment

Treatment of NMSC depends on subtype. AKs, SCC in situ and superficial BCCs can be treated with a variety of non-surgical methods [38] including fluorouracil cream, imiquimod cream, cryotherapy, photodynamic therapy and curettage. Invasive SCCs and larger BCCs are effectively treated by standard excision. When these tumours are located on the face, scalp and ears or if they are large or recurrent, Mohs micrographic excision may be preferred. Mohs surgery allows for the preservation of normal tissue and complete resection of the tumour. The Mohs procedure is typically performed under local anaesthesia which is more suitable for elderly patients who may not tolerate greater sedation [39]. Radiotherapy is an another treatment option which does not require a general anaesthetic or sedation. Radiotherapy regimes can be specifically modified to suit the needs of elderly patients [40, 41].

Melanoma is an aggressive disease and accounts for the greatest skin cancer-related mortality in the elderly [39]. Current understanding of melanoma characterises the disease on the molecular level according to specific mutations such as BRAF, NRAS and KIT [42]. Oncogenic BRAF mutations are present in approximately 40–50% of patients with metastatic melanoma [43]. NRAS mutations occur in approximately

15% of cutaneous melanomas and have been associated with worse patient outcomes [44]. Melanomas with NRAS mutations tend to be thicker and have a higher mitotic rate [45]. These findings allow for more specific classification and have led to the development of targeted therapies showing significantly better outcomes compared to traditional chemotherapy. For example, the combination of BRAF and MEK inhibitors achieves response rates of 70%, with progression-free survival of approximately 10 months [46]. Another new approach is immunotherapy in the form of immune checkpoint inhibition of CTLA-4 and PD-1 which provide other treatment options for patients with metastatic melanoma [47].

The common clinical subtypes of melanoma are lentigo maligna (Hutchinson's melanotic freckle), superficial spreading melanoma and nodular melanoma. Prognostic indicators of melanoma include Breslow thickness, mitotic rate and ulceration. The American Joint Committee on Cancer TNM staging guidelines are then applied to further determine prognosis depending on nodal or distant metastases.

The lentigo maligna (LM) subtype is confined to the epidermis and is a form of in situ melanoma. Lentigo maligna is referred to as lentigo maligna melanoma (LMM) when it penetrates the basement membrane and invades the dermis (Fig. 21.8). This change may be heralded by induration or nodularity developing within a LM. Lentigo maligna and LMM are particularly more common in the elderly population. They are most common after the seventh decade. LMM represents between 4% and 15% of all malignant melanomas [48]. They occur in chronically sun-exposed areas and present as flat, slowly enlarging irregularly shaped tan to black macules. LM often have significant subclinical spread.

The differential diagnoses of lentigo maligna include solar lentigo, flat seborrheic keratosis, lichen planus-like keratosis and pigmented actinic keratosis [49]. The rate of transformation of LM to LMM is not definitively determined [50], but the lifetime risk of conversion has been reported to be as low as 5% and as high as 50% [51].

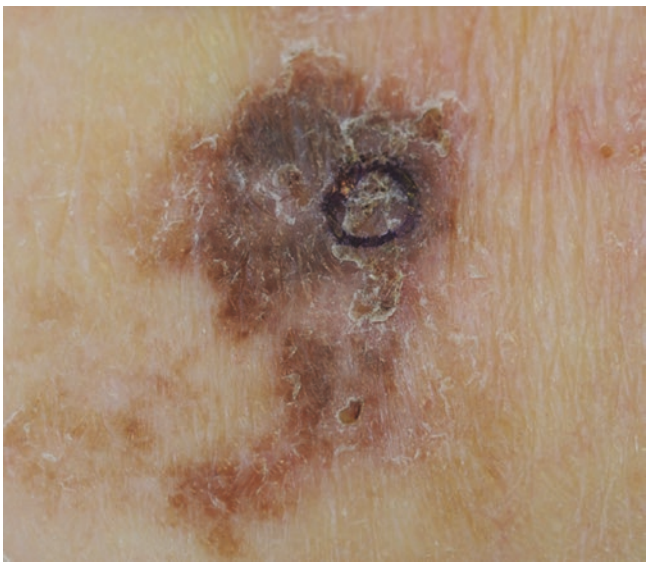

Fig. 21.8 Lentigo maligna melanoma (Reproduced with permission from Orange Dermatology)

Treatment

Although the risk of invasive melanoma developing within LM is not well defined and progression to invasive disease may be slow, treatment is usually recommended because LMM is potentially lethal, whereas LM is curable if removed while still in situ. LM frequently involves the face near critical anatomical structures and clinical management can be challenging [52]. Complete surgical excision is the recommended treatment for LM; however due to the location, size and advanced age of patients, surgery is not always advisable. As a result, less invasive treatment modalities can be considered. Radiotherapy has demonstrated recurrence rates of up to 31% and a mean recurrence rate of 11.5% with follow-up durations of 1–96 months [50]. Multiple authors have concluded radiotherapy to be a safe, well-tolerated and effective treatment for LM [50, 52]. Topical imiquimod recurrence rates are up to 50% (mean 24.5%), with follow-up durations of 2–49 months [50], and treatment regimens can be modified to suit the patient.

Studies report a lower survival rate among elderly versus younger persons with melanoma. Reasons affecting the poor outcome of melanoma in the elderly involve decreased patient awareness and reduced access to skin cancer screening; therefore opportunistic skin cancer screening should be fostered in this age group [4].

Clinical Relevance

Chronic environmental factors, particularly ultraviolet radiation, lead to increased numbers of skin cancers. Deterioration of mechanical strength of the skin results in significant trauma with minimal insult.

Reduction in barrier function, impaired circulation and immunosenescence contribute to xerosis, pruritus, irritant dermatitis, infection and bullous pemphigoid. Xerosis is the most common cause of pruritus in the elderly population. Polypharmacy leads to more drug rashes.

Basal cell carcinoma is the most common type of skin cancer.

The lentigo maligna subtype of melanoma is particularly more common in the elderly population. They occur in chronically sun-exposed areas and present as flat, slowly enlarging irregularly shaped tan to black macules. Studies report a lower survival rate among elderly versus younger persons with melanoma.

Reduced patient awareness in the elderly may delay presentation which in turn affects morbidity and mortality rates in this population subgroup.

Multiple Choice Questions

1. The following are true of pruritus, *except*:
   A. Pruritus without rash is not caused by xerosis.
   B. Drug-induced itch may persist for several weeks or even months following cessation of the suspect medication.
   C. The most common aetiological agents causing pruritus are calcium channel blockers, thiazides and codeine.
   D. Systemic treatments including sedating antihistamines are helpful for patients experiencing nocturnal itch.
2. The following are true of malignant lentigo maligna, *except*:
   A. Lentigo maligna are most common after the seventh decade.
   B. They occur in chronically sun-exposed areas.
   C. Radiotherapy is a safe, well-tolerated and effective treatment modality.
   D. Topical imiquimod is the gold standard for treatment.
3. The following are true of non-melanoma skin cancer, *except*:
   A. Merkel cell carcinomas are common in the elderly.
   B. Basal cell carcinomas rarely metastasize.
   C. Actinic keratoses are a precursor to squamous cell carcinoma.
   D. Morphoeic BCCs have a sclerotic or scar-like appearance.
4. The following are true of pruritus, *except*:
   A. Xerosis is the most common cause of itch in elderly patients.
   B. Pruritus may occur as a paraneoplastic phenomenon.
   C. Severe pruritus causes as much discomfort as chronic pain.
   D. Drug-induced itch is usually not associated with rash.

Answers to MCQs

1. A
2. D
3. A
4. D

References

1. Mastrolonardo M, Diaferio A, Vendemiale G, Lopalco P. Seborrhoeic dermatitis in the elderly: inferences on the possible role of disability and loss of self-sufficiency. Acta Derm Venereol. 2004;84(4):285–7.
2. Berger T, Shive M, Harper MG. Pruritis in the older patient: a clinical review. JAMA. 2013;310(22):2443–50.
3. Schmidt E, Zillikens D. Pemphigoid diseases. [Review]. Lancet. 2013;381(9863):320–32.
4. Zalaudek I, Lallas A, Longo C, Moscarella E, Tiodorovic-Zivkovic D, Ricci C, Albertini G, Argenziano G. Problematic lesions in the elderly. Dermatol Clin. 2013;31(4):549–64.
5. Lasithiotakis KG, Petrakis IE, Garbe C. Cutaneous melanoma in the elderly: epidemiology, prognosis and treatment. Melanoma Res. 2010;20(3):163–70.
6. Farage MA, Miller KW, Elsner P, Maibach HI. Characteristics of aging skin. Adv Wound Care. 2013;2(1):5–10.
7. Kohl E, Steinbauer J, Landthaler M, Szeimies R-M. Skin ageing. J Euro Acad Dermatol Venereol. 2011;25(8):873–84.
8. Montagna W, Carlisle L. Structural changes in aging skin. Br J Dermatol. 1990;122(Suppl 35):61–70.
9. Nagaratnam N, Nagaratnam K, Cheuk G. Skin disorders in the elderly. In: Diseases in the elderly. Age –related changes and pathophysiology. New York: Springer; 2016. p. 215–26.
10. Kottner J, Lichterfeld A, Blume-Peytavi U. Maintaining skin integrity in the aged: a systemic review. Br J Dermatol. 2013;169(3):528–42.
11. Konda D, Chandrashekar L, Rajappa M, Kattimani S, Thappa DM, Ananthanarayanan PH. Serotonin and interleukin-6: association with pruritus severity, sleep quality and depression severity in Prurigo Nodularis. Asian J Psychiatr. 2015;17:24–8.
12. Valdes-Rodriguez R, Stull C, Yosipovitch G. Chronic pruritis in the elderly: pathophysiology, diagnosis and management. Drugs Aging. 2015;32:201–15.
13. Pereira MP, Stander S. Assessment of severity and burden of pruritis. Allergol Int. 2017;66(1):3–7.
14. Weisshaar E, Apfelbacher C, Jager G, Zimmermann E, Bruckner T, Diepgen TL, Gollnick H. Pruritus as a leading symptom: clinical characteristics and quality of life in German and Ugandan patients. Br J Dermatol. 2006;155(5):957–64.
15. Pereira MP, Kremer AE, Mettang T, Stander S. Chronic pruritis in the absence of skin disease: pathophysiology, diagnosis and treatment. Am J Clin Dermatol. 2016;17(4):337–48.
16. Jafferany M, Huynh TV, Silverman MA, Zaidi Z. Geriatric dermatoses: a clinical review of skin diseases in an aging population. Int J Dermatol. 2012;51(5):509–22.
17. Abraham A, Roga G. Topical steroid-damaged skin. Indian J Dermatol. 2014;59(5):456–9.
18. Rathi SK, D'Souza P. Rational and ethical use of topical corticosteroids based on safety and efficacy. Indian J Dermatol. 2012;57(4):251–9.
19. Siemens W, Xander C, Meerpohl JJ, Buroh S, Antes G, Schwarzer G, Becker G. Pharmacological interventions for pruritis in adult palliative care patients. Cochrane Database Syst Rev. 2016;11:CD008320.
20. Stull C, Lavery M, Yosipovitch G. Advances in the therapeutic strategies for the treatment of pruritis. Expert Opin Pharmacother. 2016;17(5):671–87.
21. White-Chu EF, Reddy M. Dry skin in the elderly: complexities of a common problem. Clin Dermatol. 2011;29(1):37–42.
22. Li LF, Lan YZ. Bathing and generalized asteatotic eczema: a case-control study. Br J Dermatol. 2008;159(1):243–5.
23. Sparsa A, Liozon E, Boulinguez S, Bordessoule D, Vidal E, Bonnetblanc JM, Bedane C. Generalized eczema craquele as a presenting feature of systemic lymphoma: report or seven cases. Acta Derm Venereol. 2005;85(4):333–6.
24. Norman RA. Xerosis and pruritis in the elderly: recognition and management. Dermatol Ther. 2003;16(3):254–9.
25. Comert A, Akbas B, Kilic EZ, Akin O, Gokce E, Goktuna Z, Taskapan O. Psychiatric comorbidities and alexithymia in patients with seborrheic dermatitis: a questionnaire study in Turkey. Am J Clin Dermatol. 2013;14(4):335–42.
26. Arsic Arsenijevic VS, Milobratovic D, Barac AM, Vekic B, Marinkovic J, Kostic VS. A laboratory-based study on patients with Parkinson's disease and seborrheic dermatitis: the presence and density of Malassezia yeasts, their different species and enzymes production. BMC Dermatol. 2014;14:5.

27. Nazarko L. Diagnosis and treatment of venous eczema. Br J Community Nurs. 2009;14(5):188–94.
28. Goldsmith LA, Katz SL, Gilchrest BA, Paller AS, Leffell DJ, Fitzpatrick's WK. Dermatology in general medicine. 8th ed: NewYork, USA: McGraw-Hill; 2012. p. 2112–3.
29. Ukat A, Konig M, Vanscheidt W, Munter KC. Short-stretch versus multilayer compression for venous leg ulcers: a comparison of healing rates. J Wound Care. 2003;12(4):139–43.
30. Beechey R, Priest L, Peters M, Moloney C. An evidence-based approach to the prevention and initial management of skin tears within the aged community setting: a best practice implementation project. JBI Database System Rev Implement Rep. 2015;13(5):421–43.
31. Seyfarth F, Schliemann S, Antonov D, Elsner P. Dry skin, barrier function, and irritant contact dermatitis in the elderly. Clin Dermatol. 2011;29(1):31–6.
32. Mick G. Vaccination: a new option to reduce the burden of herpes zoster. Expert Rev Vaccines. 2010;9(3 Suppl):31–5.
33. Askari SK, Schram SE, Wenner RA, Bowers S, Liu A, Bangerter AK, Warshaw EM. Evaluation of prospectively collected presenting signs/symptoms of biopsy-proven melanoma, basal cell carcinoma, squamous cell carcinoma, and seborrheic keratosis in an elderly male population. J Am Acad Dermatol. 2007;56(5):739–47.
34. Shumack SP. Non-surgical tratments for skin cancer. Aust Prescr. 2011;34:6–7.
35. Bowman PH, Ratz JL, Knoepp TG, Barnes CJ, Finley EM. Basosquamous carcinoma. Dermatol Surg. 2003;29:830–3.
36. Glogau RG. The risk of progression to invasive disease. J Am Acad Dermatol. 2000;42(1 Pt 2):23–4.
37. Lee MM, Wick MM. Bowens disease. CA Cancer J Clin. 1990;40(4):237–42.
38. Amini S1, Viera MH, Valins W, Berman B. Nonsurgical innovations in the treatment of nonmelanoma skin cancer. J Clin Aesthet Dermatol. 2010;3(6):20–34.
39. Laurin Council M. Common skin cancers in older patients: approach to diagnosis and management. Clin Geriatr Med. 2013;29(2):361–72.
40. L M, Ramasamy S, Robert F. Weekly radiotherapy for basal cell carcinoma in the frail and elderly. Br J Dermatol. 2014;171(5):1237–9.
41. Pelissero A, Elvio GR, Melano A, Fillini C, Vigna-Taglianti R, Settineri N, et al. Facial basal cell carcinomas treated with hypofractionated radiotherapy: a retrospective analysis in 117 elderly patients. J Am Acad Dermatol. 2015;73(1):166–8.
42. Goldringer SM, Murer C, Sieger P, Dummer R. Targeted therapy in melanoma – the role of BRAF, RAS, and KIT mutations. Eur J Cancer Suppl. 2013;11(2):92–6.
43. Awad MM, Sullivan RJ. Dabrafenib in combination with trametinib for the treatment of metastatic melanoma. Expert Rev Clin Pharmacol. 2015;8(1):25–33.
44. Atkins M. Immunotherapy combinations with checkpoint inhibitors in metastatic melanoma: current approaches and future directions. Semin Oncol. 2015;42(Suppl 3):S12–9.
45. Keller FC, McAarthur GA. Targeting NRAS in melanoma. Cancer J. 2012;18(2):132–6.
46. Dummer R, Goldinger SM, Paulitschke V, Levesque MP. Curing advanced melanoma by 2025. Curr Opin Oncol. 2015;27(2):125–7.
47. Robert C, Ribas A, Wolchok JD, et al. Anti-programmed death receptor 1 treatment with pembrolizumab in ipilumumab refractory advanced melanoma: a randomised dose comparison cohort of a phase 1 trial. Lancet. 2014;384:1109–17.
48. Smalberger GJ, Siegel DM, Khachemoune A. Lentigo maligna. Dermatol Ther. 2008;21(6):439–46.
49. Kallini JR, Jain SK, Khachemoune A. Lentigo maligna: review of salient characteristics and management. Am J Clin Dermatol. 2013;14(6):473–80.
50. Read T, Noonan C, David M, Wagels M, Foote M, Schaider H, Soyer HP, Smithers BM. A systematic review of non-surgical treatments for lentigo maligna. J Euro Acad Dermatol Venereol. 2016;30(5):748–53.
51. Weinstock MA, Sober AJ. The risk of progression of lentigo maligna to lentigo maligna melanoma. Br J Dermatol. 1987;116:303–10.
52. Fogarty GB, Hong A, Scolyer RA, Lin E, Haydu L, Guitera P, Thompson J. Radiotherapy for lentigo maligna: a literature review and recommendations for treatment. [Review]. Br J Dermatol. 2014;170(1):52–8.

Joints and Musculoskeletal Disorders

22

Nages Nagaratnam and Kujan Nagaratnam

Introduction

With the increase in the life expectancy and ageing population, the prevalence of arthritis will increase. In the United States, over half the older adults report joint pain [1]. The prevalence of musculoskeletal chronic conditions is high among the elderly, and it has been reported that 37 million Americans suffer from some form of arthritis [2]. With the rapid growth of the elderly population, the number of elderly with arthritis is expected to double to 41 million in the United States [1]. Estimates of arthritis in the 85+ group range from 24% to 57% [3, 4]. In a study of 1029 unselected individuals aged 85+, the investigators found that bilateral hip, hand, and knee arthritis were common, followed by spondylosis [5]. Knee osteoarthritis and cervical spondylosis were the most common diagnosis [5].

Joints

Osteoarthritis

In 2005, 27 million adults, more than 10% of the US population, had osteoarthritis [6]. In a study of 105 community-dwelling elderly aged 85 and over, 57% had musculoskeletal pain, 18% osteoarthritis and 1% rheumatoid arthritis [7]. The incidence may vary depending on the criteria used, clinical or radiological. In another study the prevalence of radiological osteoarthritis increased with age; the highest was for cervical spine for both men and women, followed by lumber spine and distal interphalangeal joints [8]. Prevalence increases to 10% of men and 20% of women between ages 45 and 60 years and to more than 50% in women over the age of 85 years [9]. About 15% of Australians have self-reported arthritis (about three million), and OA accounts for most of them [10, 11].

Pathophysiology

OA was considered to be a non-inflammatory condition, but now it is evident that this is not so [12], and there is evidence linking local inflammation with pain measured as synovitis/effusion [12]. The histological changes in the synovium in OA are suggestive of an 'inflammatory' synovitis, and the synovial reaction can result in formation and release of cytokines and chemokines [13] causing joint damage through alarmins [14]. Distinct risk factors such as age, obesity and joint injury associated with definite subsets of OA operated through specific pathogenic pathways are being considered by researchers [14]. One of the few modifiable risk factors for osteoarthritis is obesity [15].

Pathogenesis

Currently there is increasing realization that OA affects not only the cartilage but all the joint tissues [13]. These include the synovium [13, 14], meniscal pathology [12], bone marrow lesions [16] and subchondral bone. MRI-based studies have significantly improved our understanding of the pathogenesis of OA. In the pathogenesis of OA, there has been considerable interest in the role of bone [17] and bone marrow lesions (BML), and they are an important source of OA symptoms and implicated in the causation and pathogenesis of the disease [18–20]. Several bone tissue abnormalities such as bone marrow necrosis and fibrosis together with necrotic and remodelled trabeculae are included with BMLs [9] and histologically microfracture or bone damage [21]. Furthermore bone mineral density (BMD) is significantly increased with BML locations [15]. BMLs are associated with pain [18, 22, 23, 24], malalignment [25] and compartment-specific joint space degeneration [15, 25, 26] predic-

N. Nagaratnam (✉) · K. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_22

tive of cartilage loss [19, 27] and predicting progression on radiographs [25, 28]. On T2-weighted fat-suppressed images, they are detected as high-intensity regions [22]. Individuals with a very high risk for compartment-specific OA progression can be identified using BML lesions on MRI [29].

Clinical Manifestations

In a study of OA in the elderly, although there was correlation between clinical and radiological evidence, often clinical signs were present without radiological evidence. On the other hand, moderate to severe radiological changes were present without clinical signs [30]. In the early stages, OA is asymptomatic. The nodal form presents as Heberden's and Bouchard's nodes in the distal and proximal interphalangeal joints. The first carpometacarpal phalangeal and first metatarsal phalangeal joints are primarily involved. A subset of primary osteoarthritis is erosive inflammatory OA characterized by rapid destructive OA of the shoulders and less often knees in the elderly. It is painful and is associated with osteoporosis of the hands and erosions.

Involvement of the carpometacarpal joint of the thumb gives rise to restricted joint movement with compensatory hyper-extensibility of the metacarpophalangeal joint. There is also a subluxation at the carpometacarpal joint causing the metacarpal bone to protrude outwards. With disease progression the abductors of the thumb atrophy resulting in adduction contracture. In a study of 1041 subjects aged 71–100 years, 30% of whom were men, the prevalence of symptomatic hand OA was higher in women (26.2%) than in men (3.4%). Symptomatic hand OA is common among the elders and impairs hand function [31]. There is no correlation between pain and radiological or pathological evidence of disease [32]. The other joints predominantly involved are the weight-bearing joints, the hips and knees. Patients mostly have stiffness and pain, releived by rest and may 'lock' or 'give way' as in internal damage to the cartilage.

Treatment

Although there is no cure for osteoarthritis (OA), symptoms can be controlled by life style changes, physical activity, medication and surgery. Obesity is an important risk factor, and it has been shown that with a 10% weight reduction, there has been a 50% improvement in symptoms [33]. Individualized exercise programme to target muscle strengthening (stretching, a flexibility exercise) is recommended. Pain in osteoarthritis may be helped with medications such as non-steroidal anti-inflammatory drugs (NSAIDS) and paracetamol. NSAIDS are considered to be the first- line drug of choice for osteoarthritis, but because of its adverse effects, paracetamol is preferred for mild and moderate pain in OA. The use of topical preparations such as diclofenac sodium gel reduces the gastrointestinal adverse effects. Topical capsaicin is another topical agent. Duloxetine an antidepressant has been used to treat chronic pain including pain due to OA. Studies on glucosamine and chondroitin sulphate in osteoarthritis have shown mixed results. According to some, they may provide modest relief in some patients with OA. Others have shown that there is no clinical evidence that it is effective in the treatment of mild knee pain from OA [34]. More recently, therapies of chondroitin sulphate plus glucosamine sulphate or chondroitin sulphate plus glucosamine hydrochloride in experimental OA did not improve structural damage or ameliorate inflammation of joint tissues [35]. The American College of Rheumatology in their 2012 guidelines has not recommended the use of chondroitin sulphate and glucosamine for the initial treatment of OA [36]. Corticosteroid injection and injection of hyaluronic acid into the joint may provide pain relief. In patients with severe disease with inadequate response to conservative treatment, surgery should be considered which includes osteotomy and joint replacement (arthropathy).

Cervical Spine

Cervical Spondylosis

Introduction

Cervical spondylosis is a chronic degenerative condition of the cervical spine with changes in the intervertebral discs, annulus fibrosis, formation of bony osteophytes and narrowing of the spinal canal, neural foraminal stenosis [37] or lateral recess, resulting in progressive spinal cord and/or nerve root compression. It increases with age and affects both men and women. 90–95% of the men over 50 years and 70–90% of women over 60–65 years have radiological evidence of degenerative changes in the cervical spine [38–40]. At the age of 60 years, half the men and one-third of women have significant disease [41].

Pathophysiology

The discs with natural processes of ageing lose its elasticity giving rise to radial fissuring of the annulus fibrosis. The annulus normally bulges diffusely beyond the vertebral margins into the vertebral canal. Osteophyte formation occurs in the margins of the vertebral bodies as a result of degenerative changes in the discs together with remodelling of the apophyseal joints [42]. The degeneration of the facet joints together with bony hypertrophy and thickening [43, 44], folding [45] of the ligamentum flavum and the bulging annulus encroaches on the central canal leading to narrowing of the canal (central canal stenosis). The lateral recesses in which the nerve roots

lie are associated with compression of the nerve root [46]. Thickening of the posterior longitudinal ligament decreases the cross-sectional area of the canal [47]. Herniation may occur when the inner nucleus pulposus bulges through the annulus fibrosis. The facet hypertrophy compromises the dorsolateral aspect of the foramen, and the overriding uncinate encroaches on the ventrolateral portion at the intervertebral foramen causing 'pinching' of the spinal nerve (radiculopathy).

Clinical Manifestations

Cervical spondylotic myelopathy results from narrowing of the central canal resulting from degeneration of the facets, bony hypertrophy and disc degeneration with bulging and buckling of the ligament flavum [43, 44] thereby compressing the cord [48, 49]. Cervical spondylotic myelopathy manifests as pain and stiffness more often in the lower cervical region and in certain positions of the neck. The pain radiates to the base of neck, shoulders and back. The symptoms include clumsiness and weakness of the hands, leg stiffness with weakness and an unsteady gait [50, 51]. Lower limb weakness is commonly seen with involvement of the iliopsoas followed by the quadriceps muscles. The gait is stiff and spastic.

Cervical radiculopathy Encroachment of the lateral recess and the neuroforamina by hypertrophy of the superior articular facet and disc fragments is the commonest cause of chronic nerve root impingement. Acute herniated disc can cause cervical radiculopathy. C6 root is most commonly affected and the next is C5 and C7 [52]. It manifests as pain in the neck radiating into either arm, forearm or hand and often accompanied by numbness.

Regional pain syndromes include chronic occipital headache or cervicogenic headache due to upper cervical C2 nerve root lesion or facet joint dysfunction [53, 54]. A chronic suboccipital headache is seen with cervical spondylosis, and it seems likely that occipitoatlantal and atlantoaxial degeneration could cause the pain in those areas [55].

Other manifestations include dysphagia due to large spurs compressing the oesophagus [56–58], vertebra-basilar insufficiency and vertigo.

Imaging Studies

Computed tomography and magnetic resonance imaging are used to assess spinal and foraminal stenosis in cervical spondylosis. High signal intensity lesions can be seen on MRI of spinal cord compression and may indicate myelomalacia and permanent damage [44], and this indicates a poor prognosis [38]. Electrodiagnostic studies may be helpful in assessing continuity of the somatosensory pathways.

Treatment

The only effective treatment for myelopathy is surgical decompression of the cord. The large majority of patients with cervical spondylosis are treated conservatively and surgery reserved for moderate to severe myelopathy or failed medical treatment [43, 49]. In the mild and slowly progressive, immobilization with soft collars or more rigid orthosis like the Philadelphia collar or Minerva body jacket can considerably immobilize the cervical spine. The use of cervical exercises has also been advocated [58]. If progressive, cervical decompression may be required. Reduction of the cord cross-sectional area by 50–60% is associated with poor operative outcome in cervical spondylitic myelopathy with or without operative intervention [59].

Lumbosacral Spine

Introduction

The prevalence of low back pain in the elderly is reported to range between 13% and 49% [60] and in another review ranged from 18% to 57% [61].The aetiology of back pain may be different in older people [62].The most common are lumbar strain and sprain followed by degenerative processes of discs and facets, herniated discs among others. Other causes include spinal conditions (about 1%) such as neoplasia, infection and inflammatory arthritis and visceral disease which includes disease of the pelvic organs, renal disease, aortic aneurysm and gastrointestinal disease [63–65]. As the patients get older, the diagnostic probabilities as to their prevalence change, malignancy/neoplasia, compression fractures, spinal stenosis and aortic aneurysms. Spinal stenosis due to hypertrophic degenerative processes and degenerative spondylolisthesis is more common in older people [63].

Clinical Manifestations

Lumbar strain occurs after an episode of twisting, lifting or bending with pain and tenderness in the lower lumbar area and often felt in the buttock and upper thigh. In piriformis syndrome, the pain in the buttocks is worse on sitting, on climbing stairs and on squatting. In the supine position and relaxed, the ipsilateral foot is rotated externally, and this is taken as a positive sign of the syndrome [66, 67]. The diagnosis is made on the basis of symptoms and physical examination. It can mimic lumbar radiculopathy, intervertebral discitis, sacroiliitis and sciatica, among others [68]. Treatment consists of exercises, TENS and trigger point injections.

Intervertebral discs a. Degenerative disc disease (DDD). Patients with DDD complain of back pain and may complain of leg pain and numbness. b. Herniated disc. Surprisingly patients with herniated disc may complain only of leg pain with minimal low back pain. Sciatica is the hallmark of nerve root irritation, and in almost all of the cases, there is disc protrusion. Depending on the nerve root involved, sciatica is characterized by pain radiating down the posterior or lateral aspect of the leg to the ankle or foot. Weakness may also occur in the areas supplied by that nerve. Pain is often accompanied by numbness or tingling and pain may be worsened by coughing or sneezing. Treatment may include manipulation, physiotherapy, exercise, pelvic/spinal stabilization training, group classes, epidural injections, nerve root blocks and surgery. c. Discogenic disease. Following injury, infection and tear, the patient usually presents with localized back pain. Rurrent episodes of exacerbations are possible even with treatment, similar to herniated disc problems. In patients with lumbar spinal stenosis or multilevel disc abnormalities, 3D MR myelography may be useful to recognize the site most likely the cause for the pathology [69]. Infectious discitis is a primary infection of the intervertebral disc and adjoining vertebrae. There seems to be any difference in the treatment and outcome between discitis and other spinal infections [70].

Spinal stenosis Spinal stenosis is the encroachment of bony or soft tissue structures in the spine on one or more of the neural elements giving rise to symptoms. Patients with spinal stenosis usually present with back pain, initiated by walking [71], bilateral sciatica, neurogenic claudication, pain with hyperextension and with standing and relief with bending forwards at the waist or sitting [70] and by lying down. Extension of the spine causes increase in pain [72, 73]. Central canal stenosis can cause a variety of symptoms depending on its location, and typically it causes neurogenic claudication [46]. Unlike vascular claudication pain is relieved with lumbar flexion [38]. The differential diagnosis in the elderly includes aortic aneurysms, compression fractures and cancer [63]. Treatment includes flexion-based exercises, muscle strengthening, stabilization, epidural injections and surgery.

Osteoporotic compression fractures Patients could present with acute pain following severe flexion compression force. Spontaneous vertebrae collapse is seen in elderly people with osteoporosis or on long-term glucocorticoids.

Osteoporotic sacral insufficiency fractures Sacral insufficiency fractures are said to be uncommon, but this may due in part to lack of awareness resulting in under-diagnosis [74] and under-reporting [75]. It is often overlooked in elderly patients with pelvic pain with minimal trauma [76, 77].There are two groups of sacral fractures, fatigue and insufficiency. The former occurs in bone of normal elasticity exposed to repetitive and abnormal stresses, and the other occurs in weakened bone under normal stress [75]. Insufficiency fractures usually occur in osteoporotic elderly females [74], whereas fatigue fractures occur in the young active individuals [78]. Apart from osteoporosis, other risk factors include osteomalacia; hyperparathyroidism, following radiation therapy; rheumatoid arthritis [75]; and long-term corticosteroid therapy [79].

The patients usually present with low back or pelvic pain (buttock and groin) of acute onset. There is no history of trauma. Mobility is markedly restricted. Physical examination reveals sacral tenderness on lateral compression. There are several passive screening tools available to evaluate the pathologies of the sacroiliac joint, namely, the (Patrick's) Faber test, squish test and Gaenslen's test. The Faber test is a screening test for patients with sacroiliac, hip and lumbar pathologies [80]. It is performed with the leg flexed and the thigh abducted and externally rotated, and the test is positive when these movements cause pain. In the Gaenslen's test, the hip joint is flexed maximally on side and the other hip joint extended stressing both sacroiliac joints simultaneously.

Plain X-ray in general is normal, and computed tomography is useful to make a diagnosis and exclude such conditions as metastatic bone disease, spinal stenosis and sacroiliac joint infection [74, 76]. Bone scintography in the detection of sacral fractures is well accepted [75, 81]. Most frequently there is increased uptake in the body of the sacrum and both sacral alae giving rise to an H- or butterfly-shaped appearance, but this sign is often not seen [75] (Fig. 22.1). To establish the diagnosis, CT and MRI scans are preferred examinations [75].

Neoplasia The pain is worse on lying supine and by activity. With spinal metastases, pain precedes weakness or sensory symptoms by an average of 3 months. About 30% of the vertebral lesions are asymptomatic [82] . Since early diagnosis and treatment determine the functional result, middle aged or older patients with persistent pain for more than a month should have an imaging study of the spine, preferably an MRI. This is mandatory if there is known systemic cancer.

Spondylolisthesis is the forward subluxation of a vertebral body. The low back pain is caused by strain on the ligaments and intervertebral joints. Management is dependent on the severity and progression of the listhesis and may include non-surgical-physical therapy, medications and steroid injections and surgery who do not respond after a trial of medical treatment [83] .

Facet syndrome is a type of arthritis of the facet joints. Studies of low back pain have shown that the prevalence of facet joint involvement is approximately 15–45% and the age-related prevalence of facet neck pain is similar among all age groups [84]. Regardless of clinical severity, more than 90% demonstrate degenerative disc and facet pathology in older adults [85]. There is pain on hyperextension with relief

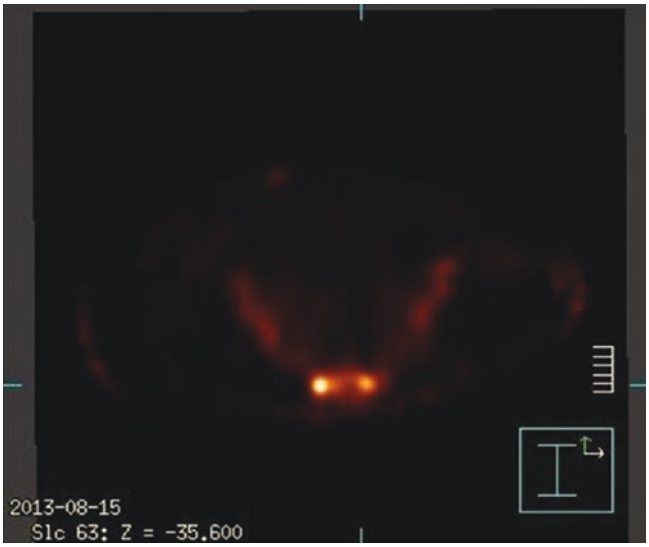

Fig. 22.1 SPECT/CT showing symmetric sacral uptake without the horizontal strut in sacral insufficiency fractures. (Reproduced with permission from Dr. Leo Ha)

on lumbar flexion, decrease in range of movement and local facet tenderness [86, 87]. There is degeneration of the facet joints with 'jamming' causing pinching of the sensitive meniscoid tabs within the joint. It may also cause pinching of the spinal nerves as they exit. It often presents with pain, numbness and tingling, and most of these symptoms may be attributed to pain of discogenic origin [87]. Pain severity among those with chronic low back pain was not associated with radiographic severity of disc and facet disease [85].

Clinical Relevance

OA was considered to be a non-inflammatory condition, but now it is evident that this is not so [12].

In a study of OA in the elderly, although there was correlation between clinical and radiological evidence, often clinical signs were present without radiological evidence.

On the other hand, moderate to severe radiological changes were present without clinical signs [30].

Obesity is an important risk factor, and it has been shown that with a 10% weight reduction, there has been a 50% improvement in symptoms [33] .

90–95% of the men over 50 years and 70–90% of women over 60–65 years have radiological evidence of degenerative changes in the cervical spine [38–40].

The large majority of patients with cervical spondylosis are treated conservatively, and surgery is reserved for moderate to severe myelopathy or failed medical treatment [43, 49].

As the patients get older, the diagnostic probabilities of low back pain as to their prevalence change, malignancy/neoplasia, compression fractures, spinal stenosis and aortic aneurysms. With spinal metastases, pain precedes weakness or sensory symptoms by an average of 3 months.

Pain severity among those with chronic low back pain was not associated with radiographic severity of disc and facet disease [85].

Sacral insufficiency fractures should be excluded in osteoporotic elderly.

Case Study

An 85-year-old widow was brought by the ambulance to emergency department with excruciating low back pain of sudden onset. She was seated when she developed pain and on standing the pain became unbearable and she could not walk. The pain however lessened on lying down in the supine position. There was no history of trauma nor could she recall any incidents that could have led to the pain. She had had cancer of the breast 8 years ago with partial mastectomy and radiation therapy. Two years ago she had pain in the back of her chest, and this led to an X-ray which showed mild kyphosis and rarefaction of the thoracic vertebrae. There were no evidence of fractures. This was followed by measurement of bone mineral density (BMD). The T score on the lumbar spine was −2.5 and left femur −2.0. She was on calcium and vitamin D. Physical examination revealed mild kyphosis and sacral tenderness. Haematological and biochemical tests were within the normal range. The serum alkaline phosphatase was mildly elevated. Plain X-ray was normal. Bone scan showed the classical 'Honda sign'.

Comment

Sacral insufficiency fracture is an important consideration in patients with low back pain and risk of bone metastases.

Polymyalgia Rheumatica and Giant Cell Arteritis

Introduction

Polymyalgia rheumatica (PMR) is a relatively common clinical syndrome, and its frequency varies by country, with highest rates in Northern Europe [88, 89] and a lower incidence in the southern regions [90]. In the United Kingdom, the annual incidence is 100 per 100,000 persons aged 50 years and over [89]. Women are affected 2–3 times more

often than men [91] and this is most common in Caucasians [92]. Polymyalgia rheumatica and giant cell arteritis (GCA) are closely related [93] and often occur concurrently [1]. Lawrence et al. [94] estimated the prevalence and number of individuals with PMR in the United States in 2005 to be 711,000 and giant cell arteritis 228,000. The incidence of PMR and GCA in the 50 years and over, are 50 and 18 per 100,000 per year, respectively [95] and in the Mediterranean populations was 12.7 and 6.9 per 100,000 per year, respectively [90]. About 16–21% of the patients with PMR develop giant cell arteritis (GCA), and about half the patients with GCA have associated PMR [96].

Pathophysiology

The pathophysiology of PMR and GCA is not completely understood. There is an association between GCA with HLA-DR4 and HLA-DRB1 suggesting a genetic predisposition [97]. The frequencies of HLA antigens were determined in patients with PMR and/or GCA in an Italian population. DR4 was found in 24% of the patients and in 36% of patients with GCA, and both instances were not significantly associated [90]. High levels of interleukin-6 (IL-6) which correlated with increased disease activity were seen in patients with PMR [98, 99]. Immunohistochemical studies on muscle biopsy of PMR specimens found major histocompatibility complex (MHC) class 2 products were decidedly seen on intramuscular vessels and combined deposits of IgG and Clq in perimysial arteries in 38% of PMR [100]. An increase in the incidence of PMR was seen following epidemics of chlamydia pneumonia, mycoplasma pneumonia and parvovirus B19 [89] suggesting an infective factor in genetically disposed individuals.

The focus for GCA appears to localize in elastin-containing arteries and can also cause myalgias [101]. Patients diagnosed as GCA and/or PMR are found to have small vessel vasculitis, and it is considered a diagnostic criterion for PMR [102]. Giant cell arteritis (GCA) involves the medium- and large-sized arteries of the extracranial branches of the carotid artery. The aortic arch can be involved. It is a panarteritis predominantly infiltrated with lymphocytes, histiocytes and multinucleated giant cells bordering the internal elastic lamina followed by proliferation of the intima and reduction or occlusion of the lumen. There is immune-mediated damage to the vessel wall. The immune response is initiated by dendritic cells and regulated by CD4-T cells which differentiate into vasculitic T cells [103, 104]. The Notch ligand pathway has a vital role in the initiation and maintenance of large vessel vasculitis, and inhibition of Notch signalling results in curbing cellular responses and diminishes CD4-T cell activation markers and T-cell proliferation [104]. The inflammatory process is patchy.

Clinical Manifestations

PMR usually affects persons over the age of 60 years and the average age is 72 years [92]. Severe pain and stiffness in at least two or three areas, namely, the shoulders, neck or hip are the most commonly affected [95]. It may unilateral but usually becomes bilateral in few weeks. Morning stiffness is the most frequent symptom and is exacerbated by movement and involves the shoulder and pelvic girdles and the neck [88, 95]. Low-grade fever, loss of weight accompanied by fatigue, malaise [105] and depression are often seen. Swelling of the extremities is uncommon. In about 12% of patients with PMR [106], swelling of the distal extremities with pitting oedema over the dorsum of the hands has been described [107]. It has been suggested that PMR and remitting seronegative symmetrical synovitis with pitting oedema (RSPE) syndrome are part of the same clinical syndrome [108]. PMR-like syndrome is also known to occur with elderly-onset spondyloarthritis [109].

GCA is a chronic illness and may last for years and affects persons over the age of 50 years [88, 95, 103] with a mean age of 70 years. The onset may be gradual or abrupt. Malaise, weight loss, fever with the classic symptoms of jaw claudication, headache, scalp tenderness and visual impairment may occur at the beginning of the illness [95, 103, 110] or symptoms of PMR [88]. The headache can be severe and is localized over the temporal or occipital areas [95]. GCA can present as fever of unknown origin [88]. The temporal artery may be tender or pulseless or both in about half the number of patients. In about 40–60% of the patients, it is associated with PMR [99] which is characterized by pain in both shoulders and hips together with stiffness [95, 103, 110]. The thoracic and abdominal aorta can be involved infrequently leading to aortic dilatation or aneurysm. GCA can cause sudden blindness in one or both eyes. There is a persistent risk of permanent visual loss if treatment is delayed [111], and early diagnosis is therefore crucial [112], and it has medicolegal implications. Permanent visual loss has been reported in 15–20% of the patients with GCA [113].

Diagnosis

The diagnosis of PMR is based on clinical manifestations [114] and elevated levels of inflammatory markers [110, 115]. Recently the European League Against Rheumatism and the American College of Rheumatology (EULAR/ACR) [96, 116] developed a criteria, and it has been shown that patients with new-onset PMR are able to distinguish PMR from RA and other inflammatory articular diseases better [117]. The sedimentation rate is frequently elevated and usually is greater than 50 mm/h, but in some patients, it is only mildly elevated or normal [88]. The C-reactive

protein levels are usually elevated and are more sensitive than ESR [89]. A normocytic normochromic anaemia may be present. The liver function tests are normal but the alkaline phosphatase may be mildly increased. In a minority of patients (about 10%) with polymyalgic symptoms, due to similarities in the presentation, the correct diagnosis of late-onset rheumatoid arthritis (LORA), PMR and GCA can be delayed [115]. A persistent raised plasma viscosity, a positive rheumatoid factor and the presence of HLA-DRB1*04 may suggest RA and GCA [28], and in older people, RA and spondyloarthritis can mimic PMR [107]. In the EULAR/ACR criteria, ultrasound has been included in the scoring algorithm [96]. Bilateral subacromial-subdeltoid bursitis is deemed to be a feature of PMR [118].

The erythrocyte sedimentation rate is usually markedly elevated in CGA but rarely it may be normal [88]. Often there is mild anaemia and serum alkaline phosphatase may be elevated. In a few patients with CGA, biopsy may not show changes for CGA as it does not affect every part of the artery. In which case, biopsy on the other side may be fruitful. Histopathologically it is a panarteritis with mainly lymphohistiocytic cell infiltrate [95]. 18-fluorodeoxyglucose-positron emission tomography has been shown to be useful in detecting large-vessel involvement in GCA [93]. Sensitivity of temporal artery duplex ultrasound was 87% and specificity 92% in a large meta-analysis by Karassa et al. [119].

Treatment

Corticosteroids are the cornerstone of the therapy in PMR and CGA [93]; PMR shows prompt and good response to corticosteroids [88, 99] and is initiated at 10–15 mg/day prednisone for 2–4 weeks. When patient becomes asymptomatic, the dose can be lowered by 1–2.5 mg/q 2–4 weeks to find the minimum dose needed to remain symptom-free regardless of the ESR. Once 10 mg is reached, taper by 1 mg/day decrements q 4 weeks. Some may be able to discontinue in a year but mostly within 2 years. Relapses are common and varied from 46% [120] to 68.3% [121] especially where prednisolone is tapered off prematurely. Long-term steroids at the lowest possible dose are sometimes necessary in a small minority of patients due to repeated relapses [91]. There are some who do not respond to the initial doses of steroids and require high doses.

CGA is treated with oral prednisolone 40–60 mg/daily [88]. Other factors that require large doses of corticosteroid are coexisting polymyalgia and giant cell arteritis [122] and those with highly elevated inflammatory markers [123]. A prolonged course of corticosteroid is necessary in both CGA and PMR, the dose gradually tapered and guided by regular clinical evaluation and ESR/CRP measurement [88]. Combination therapy with prednisolone and methotrexate with newly diagnosed PMR reduced the incidence of flare-ups and the amount of prednisolone required to maintain remission [124]. There was however no reduction of steroid-related side effects [123]. In PMR and CGA patients who are refractory to corticosteroids, anti-interleukin-6 receptor therapy appears to be useful [93]. In one trial etanercept, a TNF-alpha inhibitor, showed improvement of symptoms in PMR, but modest [125].

Clinical Relevance

Polymyalgia rheumatica and giant cell arteritis (GCA) are closely related [93] and often occur concurrently [88].

Patients diagnosed as GCA and or PMR are found to have small vessel vasculitis, and it is considered a diagnostic criterion for PMR10 [102].

PMR usually affects persons over the age of 60 years and the average age is 72 years [92].

Severe pain and stiffness in at least two or three areas, namely, the shoulders, neck or hip and are the most commonly affected [95].

GCA is a chronic illness and may last for years and affects persons over the age of 50 years [88, 95, 103] with a mean age of 70 years.

Malaise, weight loss, fever with the classic symptoms of jaw claudication, headache, scalp tenderness and visual impairment may occur at the beginning of the illness [95, 103, 110].

GCA can cause sudden blindness in one or both eyes.

There is a persistent risk of permanent visual loss if treatment is delayed [111], and early diagnosis is therefore crucial [112], and it has medicolegal implications.

The diagnosis of PMR is based on clinical manifestations [104] and elevated levels of inflammatory markers [110, 115].

The erythrocyte sedimentation rate is usually markedly elevated in CGA but rarely it may be normal [88].

Corticosteroids are the cornerstone of the therapy in PMR and CGA [93].

Multiple Choice Questions

1. The following are true of osteoarthritis, *except*:
   A. The first carpometacarpal phalangeal and first metatarsal phalangeal joints are primarily involved.
   B. The histological changes in the synovium in OA are suggestive of an ‘inflammatory synovitis’.

C. Patients mostly feel stiffness and pain and which is not relieved by rest but may 'lock' or 'give way' as of internal damage to the cartilage.
D. There is no correlation between pain and radiological or pathological evidence of disease.

2. The following are true in the treatment of osteoarthritis, *except*:
   A. There is no cure for osteoarthritis (OA).
   B. NSAIDS are considered to be the first-line drug of choice for osteoarthritis.
   C. The American College of Rheumatology guidelines have recommended the use of chondroitin sulphate and glucosamine for the initial treatment of OA.
   D. Injection of hyaluronic acid into the joint may provide pain relief.
3. The following are true of low back pain, *except*:
   A. Spinal stenosis due to hypertrophic degenerative processes and degenerative spondylolisthesis is not common in older people.
   B. As the patients get older, the diagnostic probabilities as to their prevalence change to malignancy/neoplasia, compression fractures, spinal stenosis and aortic aneurysms.
   C. Patients with osteoporosis could present with acute pain following severe flexion compression force.
   D. Regardless of clinical severity, more than 90% of older adults demonstrate degenerative disc and facet pathology.
4. The following are true of polymyalgia rheumatica (PMR) and giant cell arteritis (CGA) *except*:
   A. Polymyalgia rheumatica and giant cell arteritis (GCA) are closely related.
   B. Patients diagnosed as GCA and or PMR are found to have small vessel vasculitis.
   C. Corticosteroids are the cornerstone of the therapy in PMR and CGA.
   D. The mean age of PMR is 50 years and CGR is 70 years.
5. The following are true of giant cell arteritis (CGA), *except*:
   A. GCA is a chronic illness and may last for years.
   B. CGA biopsy always shows changes for CGA.
   C. There is a persistent risk of permanent visual loss if treatment is delayed.
   D. Coexisting polymyalgia and giant cell arteritis require high doses of corticosteroid.

MCQs Answers

1. D
2. C
3. A
4. D
5. B

References

1. Leveille SG. Musculoskeletal aging. Curr Opin Rheumatol. 2004;16(2):114–8.
2. Abyad A, Boyer JT. Arthritis and aging. Curr Opin Rheumatol. 1992;4(2):153–9.
3. Dunlop DD, Manheim LM, Song J, Chang RW. Arthritis prevalence and activity limitations older adults. Arthritis Rheum. 2001;44:212–21.
4. Lawrence RC, Helmick CG, Arnett FC, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum. 1998;41:778–99.
5. Duncan R, Francis RM, Collerton J, Davies K, Jagger C, Kingston A, et al. Prevalence of arthritis and joint pain I the oldest old: finding from the Newcastle 85+ study. Age Aging. 2011;40(6):752–5.
6. Murphy L, Helmick CG. The impact of osteoarthritis in the United States: a population-health perspective. Am J Nurs. 2012;112(3 Suppl 1):S 13–9.
7. van Schaardenburg D, Van den Brande KJ, Lighart GJ, Breedveld FC, Hazes JM. Musculoskeletal disorders and disability in persons aged 85 and over: a community survey. Ann Rheum Dis. 1994;53(12):807–11.
8. van Saase JL, van Romunde LK, Cats A, Vandenbroucke JP, Valkenburg HA. Epidemiology of osteoarthritis: Zoetermeer survey. Comparison of radiological osteoarthritis in Dutch population with that in 10 other populations. Ann Rheum Dis. 1989;48(4):271–80.
9. March LM, Bagga H. Epidemiology of osteoarthritis in Australia. Med J Aust. 2004;180(5 Suppl):S6–S10.
10. Arthritis Foundation of Australia: Access Economics Report 2001. quoted by March and Bagga, 2004.
11. National health survey. Canberra 1995: Australian Bureau of Statistics, 1996.
12. Jones G. What's new in osteoarthritis pathogenesis? Int Med J. https://doi.org/10.1111/imj.2763.
13. Scanzello CR, Goldring SR. The role of synovitis in osteoarthritis pathogenesis. Bone. 2012;51(2):249–57.
14. Malfait AM. Osteoarthritis year in review 2015: biology. Osteoarthr Cartil. 2016;24(1):21–6.
15. Suri P, Morgenroth DC, Hunter DJ. Epidemiology of osteoarthritis and associated comorbidities. PM R. 2012;4(5 Suppl):S10–9.
16. Zanetti E, Bruder E, Romero J, Hodler J. Bone marrow oedema pattern in osteoarthritic knees: correlation between MR imaging and histologic findings. Radiology. 2000;215:835–40.
17. Wang Y, Teichtahl AJ, Cicuttini FM. Osteoarthritis year in review 2015:imaging. Ostreoarthritis Cartilage. 2016;24(1):49–57.
18. Felson DT, Chaisson CE, Hill CL, Totteman SMS, Gale ME, Skinner KM, et al. The association of bone marrow lesions with pain in knee osteoarthritis. Ann Intern Med. 2001;3(7):541–9.
19. Hunter D, Zhang Y, Niu J, Gogns J, Amin S, LaVlley M, et al. Increase in bone marrow lesions is associated with cartilage loss: longitudinal MRI study in knee osteoarthritis. Arthritis Reum. 2006;54:1529–35.
20. Lo GH, Hunter DJ, Zhang Y, McLennan CE, LaVally MP, Kil DP, McLean RR, et al. Bone marrow lesions in the knee are associated with increase local bone density. Arthritis Rheum. 2005;52:2811–21.
21. Taljanovic MS, Graham AR, Bjamin JB, Gmitro AF, Krupinski EA, Schwartz SA, et al. Bone marrow odema pattern in advanced hip osteoarthritis: quantitative assessment with magnetic resonance imaging and correlation with clinical examination, radiographic findings and histopathology. Skelet Radiol. 2008;37(5):423–31.
22. Lowitz T, Museyko O, Bousson V, Laouisset L, Kalender WA, Laredo J-D, et al. Bone marrow lesions identified by MRI in knee osteoarthritis are associated with locally increased bone mineral density measured by QCT. Osteoarthr Cartil. 2013;21(7):957–64.

23. Zhang Y, Nevitt M, Niu J, Lewis C, Torner J, Guermazi A, et al. Fluctuation of knee pain and changes in bone marrow lesions, effusions and synovitis on magnetic resonance imaging. Arthritis Rheum. 2011;63(3):691–9.
24. Yusuf E, Kortekaas MC, Watt I, Huizinga TW, Kloppenburg M. Do knee abnormalities visualise on MRI explain knee pain in knee osteoarthritis? A systematic review. Ann Rheum Dis. 2011;70(1):60–7.
25. Felson DT, McLaughlin S, Goggins J, LaValley MP, Gale ME, Totterman S, et al. Bone marrow oedema and its relation to progression of knee osteoarthritis. Ann Intern Med. 2003;139(5Part1):330–6.
26. Baranyay FJ, Wang Y, Wiuka AE, Engish DR, Giles GG, Sullivan RO, et al. Association of bone marrow lesions with knee structures and risk factors for bone marrow lesions in the knees of clinically healthy community –based adults. Semin Arthritis Rheum. 2007;37:112–8.
27. Hunter DJ, Bowes MA, Eaton CB, Holmes AP, Mann H, Kwoh CK, et al. Can cartilage loss be detected in knee osteoarthritis (OA) patients with 3-6 months observation using advanced image analysis of 3T MRI ? Osteoarthr Cartil. 2010;18(5):677–83.
28. Felson DT, Parkes MJ, Marjanoic M, Callighan A, Gat T, Cootes M, et al. Bone marrow lesions in knee osteoarthritis changes in 6-12weeks. Osteoarthr Cartil. 2012;20(12):1514–151.
29. Hunter DJ, Gersteinfeld L, Bishop G, Davis AD, Mason ZD, Einhorn TA, et al. Bone marrow lesions from osteoarthritis of knees are characterised by sclerotic bone that is less well mineralized. Arthritis Res Ther. 2009;11:R11. https://doi.org/10.1186/ar2601.
30. Bagge E, Bjelli A, Edin S, Svanborg A. Osteoarthritis in the elderly: clinical and radiological findings in 78 and 85 years old. Am Rheum Dis. 1991;50:535–9.
31. Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliaba LP, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly. The Framingham study. Am J Epidemiol. 2002;156:1021–7.
32. Manek NJ, Lane NE. Osteoarthritis: current concepts in diagnosis and management. Am Fam Physician. 2001;61:1795–804.
33. Messier SP, Mihalko SL, Legaut C, Miller GD, Nicklas BJ, DeVita P. Effects of intensive diet and exercise on knee joint loads, inflammation and clinical outcomes among overweight and obese adult with knee osteoarthritis: the IDEA randomized clinical trial. JAMA. 2013;310:1263–73.
34. Distler J, Angueouch A. Evidence-base practice: review of clinical evidence on the efficacy of glucosamine and chondroitin in the treatment of osteoarthritis. J Am Acad Nurse Pract. 2006;18(10):487–93.
35. Roman-Blas JA, Mediero A, Tardio L, Portal-Ninez S, Gratal P, Herrero-Beaumont G, et al. The combined therapy with chondroitin sulphate plus glucosamine sulphate or chondroitin sulphate plus glucosamine hydrochloride does not improve joint damage I a experimental model of knee osteoarthritis in rabbits. Eur J Pharmacol. 2017;794:8–14.
36. Hochberg KT, Altman RD, April KT, Benkhad MI, Guya HG, McGowan MI, et al. American College of Rheumatology 2012. Recommendations for use of non-pharmacological and pharmacological therapies in osteoarthritis of the hand, hip and knee. Arthritis Care Res. 2012;64(4):465–74.
37. Ross J, Bram-Sawadzki M, Moore I, et al. Diagnostic neuroimaging. Spine Amursys. 2005;11(2):64–8.
38. Al-Shatoury HAH, Galhom AA, Wagner FC. Cervical spondylosis 2007.e medicine. http://www.emedicine.com/PMR/topic27.htm.
39. Gore DR, Sepic SB, Gardner GM. Roentgenographic findings of the cervical spondylotic asymptomatic people. Spine. 1986;11:521–5.
40. Garfin SR. Cervical degenerative disorders: etiology, presentation and imaging studies. Instr Course Lect. 2000;40:335–8.
41. Holts S, Yates PO. Cervical spondylosis and nerve root lesions: incidence at routine autopsy. J Bone Joint Surg Br. 1961;48(3):407–23.
42. Vernon-Roberts B, Pirie CJ. Degenerative changes in the intervertebral discs of the lumbar spine and their sequelae. Rheumatol Rehabil. 1977;16(1):13–21.
43. McCormack BM, Weinstein PR. Cervical spondylosis. An update. West J Med. 1996;165(1):43–51.
44. Young WT. Cervical spondylotic myelopathy: a common cause of spinal cord dysfunction in older persons. Am Fam Physician. 2000;62(5):1064–70.
45. Hirpara KM, Butler JS, Dolan RT, O'Byrne JM, Poynton AR. Nonoperative modalities to treat symptomatic cervical spondylosis. Adv Orthop. 2012;2012:294857 5pages. https://doi.org/10.1155/20122/294857.
46. Truumees E. Spinal stenosis: pathophysiology, clinical and radiologic classification. Instr Course Lect. 2005;54:287–302.
47. Emery WF. Cervical spondylotic myelopathy. Diagnosis and treatment. J Am Acad Orthop Surg. 2001;9(6):376–88.
48. Young WF, Weaver M, Mishra B. Surgical outcome in patients with co-existing multiple sclerosis and spondylosis. Acta Neurol Scand. 1999;100(2):84–7.
49. Fehlings MG, Skat G. A review of the pathophysiology of cervical spondylotic myelopathy with insights for potential novel mechanisms drawn from traumatic spinal cord injury. Spine (Phila Pa 1976). 1998;23(24):2730–7.
50. Adams RD, Victor M. Disease of the spinal cord, peripheral nerve and muscle. In: Adams RD, Victor M, editors. Principles of neurology. 5th ed. New York: McGraw-Hill, Health Professionals Division; 1993. p. 1100.
51. Brain NR, Northfield D, Wilkison M. The neurological manifestations of cervical spondylosis. Brain. 1952;75:187–225.
52. Voorhies RM. Cervical spondylosis: recognition differential diagnosis and management. Ochsner J. 2001;3(2):78–84.
53. Kawabori M, Hida Y, Yano S, Iwasaki Y. Cervicogenic headache caused by lower cervical spondylosis. No Shinkeu Gika. 2001;37(5):491–5.
54. Pollmann W, Keidel M, Pfaffenrath V. Headache and the cervical spine: a critical review. Cephalagia. 1997;17(8):801–16.
55. Rana SS. Diagnosis and management of cervical spondylosis. Clinical presentation. http://emedicine.medscape.com/article/1144952-clinical. Accessed 26 Sept 2015.
56. Umerah BC, Mukherjee BK, Ibekwe O. Cervical spondylosis and dysphagia. J Laryngol Otol. 1981;95(11):1179–83.
57. Kanbay M, Seleuk H, Yilmaz U. Dysphagia-caused by cervical osteophytes: a rare case. J Am Geriatr Soc. 2006;54(3):1147–8.
58. Sobol SM, Reginald R. Anterolateral extrapharyngeal approach for cervical osteophyte-induced dysphagia. Literature review. Ann Oral Rhinol Laryngol. 1984;93(5Pt 1):498–504.
59. Fukushima T, Takaski I, Taoka Y, Takta S. MRI study of spinal plasticity in patients with cervical compression myelopathy. Spine. 1991;16:534–8.
60. Bressler HB, Keye WJ, Rochon PA, Badley E. The prevalence of low back pain in the elderly: a systematic review of the literature. Spine. 1999;24(17):1813–9.
61. Thomas E, Silman AL, Croft PR, Macfarlane C. Predicting who develops chronic low back pain in primary care: a prospective study. Br Med J. 1999;318:1662–7.
62. Docking RE, Fleming J, Brayne C, Zhao J, Macfarlane GJ, Jones GT, On behalf of the Cambridge City ovr-75s Cohort Study collaboration. Epidemiology of back pain in older adults: prevalence and risk factors for back pin onset. Rheumatology. 2011; https://doi.org/10.1093/rheumatology/ker175.
63. Deyo RA, Weinstein JN. Low back pain. N Engl J Med. 2001;344(5):363–6369.
64. Hart LG, Deyo RA, Cherkin DR. Physician office visits for low back pain, frequency, clinical evaluation and treatment patterns. US national survey. Spine. 1995;20:31–9.
65. Deyo RA, Rainville J, Kent DL. What can the history and physical examination tell us about low back pain? JAMA. 1992;268:760–5.

66. Te Poorten BA. The piriformis muscle. J Am Osteopath Assoc. 1969;69:150–60.
67. Foster MR. Piriformis syndrome. Orthopedics. 2002;25:821–5.
68. Boyajean-O'Neill LA, McClain RL, Coleman MK, Thomas PP. Diagnosis and management of piriformis syndrome. An Osteopathic approach. J Am Osteopath Assoc. 2008;108(11):657–64.
69. Erdem LO, Erdem CZ, Gundogdu S, CAgavi F, Katayci M, Aclkgoz B. The role of three dimensional MR myelography in lumbar discogenic disease. Tani Girisim Radyol. 2004;10(3):189–95.
70. Hutchinson C, Hanger C, Wilkinson T, Sainsbury R, Pithie A. Spontaneous spinal infections in older people. Intern Med J. 2009;39:845–8.
71. Akutota V, Lento P, Sowa G. Pathogenesis of lumber spine stenosis pain: why do an asymptomatic stenotic patient flare? Phys Med Rehabil Clin N Am. 2003;4:17–28.
72. Katz JN, Dalgas M, Struki G, Katz NP, Bayley J, Fossela H, et al. Degenerative lumber spinal stenosis: diagnostic value of the history and physical examination. Arthritis Rheum. 1995;38:1236–41.
73. Hilibrand AS, Rand N. Degenerative lumbar stenosis: diagnosis and management. J Am Acad Orthop Surg. 1999;7:239–49.
74. Blake SP, Connors AM. Sacral insufficiency fracture. Br J Radiol. 2004;77(922):891–6.
75. Longhino V, Bonora C, Sansone V. The management of sacral stress fractures: current concepts. Clin Cases Miner Bone Metab. 2011;8(3):19–23.
76. Tsidiris E, Upadhyay N, Giannoudis PV. Sacral insufficiency fractures: current concepts of management. Osteoporos Int. 2006;17(12):1716–25.
77. Lee YJ, Bong HJ, Kim JT, Chung DS. Sacral insufficiency fractures: usually overlooked cause of lumbosacral pain. J Korean Neurosurg Soc. 2008;44(3):166–9.
78. Zaman FM, Frey M, Slipman CW. Sacral stress fractures. Curr Sports Med Rep. 2006;5(1):37–43.
79. Yoder K, Bartsokas J, Averell K, McBride E, Long C, Cook C. Risk factors associate with sacral stress fractures: a systematic review. J Man Manip Ther. 2015;23(2):84–92.
80. Dutton M. Orthopaedic: examination, evaluation and intervention. 2nd ed. New York: The McGraw-Hill Companies Inc; 2008.
81. Schneider R, Yacovone J, Ghelman B. Unsuspected sacral fractures: detection by radionuclide bone scanning. AJR Am J Roentgenol. 1985;144:37–41.
82. Schaberg J, Gainor BJ. A profile of metastatic carcinoma of the spine. Spine. 1985;10(1):19–20.
83. Orthoinfo. Acute spondylolisthesis in the low back. http://orthoinfo.aaos.org/topic.cfm?topic=A00588. Retrieved 6 Mar 2015.
84. Manchikanti L, Manchikanti KN, Cash KA, Singh V, Giordano J. Age-related prevalence of facet-joint involvement in chronic neck and low back pain. Pain Physician. 2008;11(1):67–75.
85. Hicks GE, Morone N, Weiner DK. Degenerative lumbar disc and facet disease in older adults: prevalence and clinical correlates. Spine (Phila Pa 1976). 2009;34(12):1301–6.
86. Jackson RP. The facet syndrome, myth or reality? Clin Orthop. 1992;279:110–21.
87. Lippitt AB. The facet joint and its role in some pain management with facet joint injections. Spine. 1984;9:746–75.

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88. Schmidt J, Warrington KJ. Polymyalgia rheumatica and giant cell arteritis in older patients: diagnosis and pharmacological treatment. Drugs Aging. 2001;28(8):651–66.
89. Mitchet CJ, Matteson EL. Polymyalgia rheumatic. BMJ. 2008;336:765–9.
90. Salvarani C, Macchioni P, Zizzi F, Mantovani W, Rossi F, Castri C, et al. Epidemiologic and immunogenetic aspects of polymyalgia rheumatica and giant cell arteritis in Northern Italy. Arthritis Rheum. 1991;34(3):351–6.
91. Poole K, Shah N. Polymyalgia rheumatica in the older patient. https://wwwgmjournal.co.uk/polymyalgia_rheumatica_in_the_older_patient_57698181.aspx. Accessed 11 June 2017.
92. Ghosh P, Borg FA, Dasguota B. Current understanding and management of giant cell arteritis and polymyalgia rheumatica. Expert Rev Clin Immunol. 2010;6(6):913–28.
93. Gonzalez-Gay MA, Pina T. Giant cell arteritis and polymyalgia rheumatica: an update. Curr Rheumatoid Rep. 2015;17(2):6. https://doi.org/10.1007/s11926-014-0480-1.
94. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Arthritis Rheum. 2008;58(1):26–35.
95. Vos PA, Bijlsma JW, Derksen RH. Polymyalgia rheumatica and temporal arteritis. Ned Tijdschr Geneeskd. 2005;149(35):1932–7.
96. Dasgupta B, Cimmino MA, Kremers HM, Schmidt WA, Schirmer M, Salvarani C, et al. Provisional classification criteria for polymyalgia rheumatic: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Arthritis Rheum. 2012;64:943–54.
97. Hunder GG, Birch DA, Michel BA. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum. 1990;33(8):1122–8.
98. Martinez-Taboada VM, Alvarez L, RulzSoto M, Martin-Vidalled MJ, Lopez-Hoyos V. Giant cell arteritis and polymyalgia rheumatica: role of cytokines in the pathogenesis and implications for treatment. Cytokine. 2008;44(2):207–20.
99. Salvarani C, Cantini F, Hunder GG. Polymyalgia rheumatica and giant cell arteritis. Lancet. 2008;372:234–45.
100. Kojima S, Takagi A, Ida M, Shiozawa R. Muscle pathology in polymyalgia rheumatica: histochemical and immunohistochemical study. Jpn J Med. 1991;30(6):516–23.
101. Wilske KR, Healey LA. Polymyalgia rheumatic and giant call arteritis. The dilemma of therapy. Postgrad Med. 1985;77(8):243–8.
102. Chatelain D, Duhant P, Loire R, Bosshard S, Peket H, Piette TC, et al. Small vessel vasculitis surrounding inflamed temporal artery; a new diagnostic criterion for polymyalgia rheumatic. Arthritis Rheum. 2008;58(8):2565–73.
103. Weyand CM, Goromzy JJ. Immune mechanism in medium and large vessel vasculitis. Nat Rev Rheumatol. 2013;9:731–40.
104. Piggott KS. Mechanisms regulating dysfunctional T cell responses in large vessel vasculitis. https://etdlibrary.emoryview/record/pid/emory:7v6zl. Accessed 18 Feb 2016.
105. Uwin B, Williams CM, Gilliland W. Polymyalgia rheumatic and giant cell arteritis. Am Fam Physician. 2006;74(9):1547–54.
106. Yurdakul FG, Bodur H, Sivas F, Baskan B, Eser F, Yilmaz O. Clinical features treatment and monitoring in patients with polymyalgia rheumatic. Arch Rheumatol. 2015;30:028–33.
107. Salvarani C, Gabriel S, Hunder GG. Distal extremity swelling with pitting oedema in polymyalgia rheumatica. Report on nineteen cases. Arthritis Rheum. 1996;39:73–80.
108. Olivieri N, Pipitone N, D'Angelo S, Padula A, Salvarani C. Late-onset rheumatoid arthritis and late-onset spondyloarthritis. Clin Exp Rheumatol. 2009;27(Suppl55):S139–45.
109. Olivieri I, Garcia-Porrua C, Padula A, Cantini F, Salvarani C, Gonzalez-Gay MA. Late onset undifferentiated spondyloarthritis presenting with polymyalgia rheumatica features: description of seven cases. Rheumatol Int. 2007;27:927–33.
110. Salvarani C, Pipiton N, Versari A, Hunder GG. Clinical features of polymyalgia and giant cell arteritis. Nat Rev Rheumatol. 2012;8(9):509–21.
111. Chacko JG, Chacko JA, Sulki MW. Review of giant cell arteritis. Saudi J Ophthalmol. 2015;29(1):48–52.

112. Aiello PD, Trautman JC, McPhee TJ. Visual prognosis in giant cell arteritis. Ophthalmology. 1993;100:530–55.
113. Evans JM, Hunder GG. Polymyalgia rheumatica and giant cell arteritis. Rheum Dis Clin North Am. 2000;26:493–515.
114. Charlton R. Optimal management of giant cell arteritis and polymyalgia rheumatic. Ther Clin Risk Manag. 2012;8:173–9.
115. Pease CT, Haugeberg G, Morgan AW, Montgue B, Hensor EM, Bhakta BB. Diagnosing late onset rheumatoid arthritis, polymyalgia rheumatic and temporal arteritis in patients presenting with polymyalgic symptoms. A prospective long term evaluation. J Rheumatol. 2005;32(6):1043–6.
116. Kermani TA, Warrington KJ. Advances and challenges in the diagnosis and treatment of polymyalgia rheumatic. Ther Adv Musculoskelt Dis. 2014;6(1):8–19.
117. Macchioni P, Boiardi L, Catanoso M, Pazzola G, Salvarani C. Performance of the new 2012 EULAR/ACR classification criteria for polymyalgia rheumatica: comparison with previous criteria in a single-centre study. Ann Rheum Dis. 2014;73(6):1190–3.
118. Camellino D, Cimmino MA. Imaging of polymyalgia rheumatica: indications in its pathogenesis diagnosis and prognosis. Rheumatology (Oxford). 2012;51:77–86.
119. Karassa F, Matsugas M, Schmidt W, Ioannids J. Meta-analysis: test performance of ultrasound for giant cell arteritis. Ann Intern Med. 2005;142:359–69.
120. Lee J, Choi ST, Kim YS, Yoon BY, Kwok SK, Kim H, et al. Clinical characteristics and prognostic factors for relapse with polymyalgia rheumatic (PMR). Rheumatol Int. 2013;33:78–86.
121. Kim HA, Lee J, Ha YJ, Kin SH, Lu CH, Choi HY, et al. Induction of remission is difficult due to frequent relapse during tapering steroids in Korean patients with polymyalgia rheumatica. J Korean Med Sci. 2012;27:224–6.
122. Lundberg I, Hedfors E. Restricted dose and duration of corticosteroid treated patients with polymyalgia rheumatica and temporal arteritis. J Rheumatol. 1990;17:1340–5.
123. Salvarani C, Macchioni PL, Tartoni PL, Rossi F, Baricchi R, Castr C, et al. Polymyalgia rheumatica and giant cell arteritis : a 5-year epidemiologic and clinical study in Reggio Emilia, Italy. Clin Exp Rheumatol. 1987;5:205–15.
124. Cimmino MA, Salvarani C, Macchioni L, Gerli R, Delle Monache F, Montecucco C, et al. Long term follow up of polymyalgia rheumatica patients treated with steroid with methotrexate and steroids. Rheumatology. 2005;44(suppl 3):iii14. https://doi.org/10.1093/rheumatology/keh755.
125. Kreiner F, Galbo H. Effect of etanercept in polymyalgia rheumatica: a randomized controlled trial. Arthritis Res Ther. 2010;12(5):R176.

Respiratory Disorders in the Oldest of the Old

23

Jimmy Chien

Introduction

Physiological changes occur with ageing which result in declining respiratory function with age. Changes occur in the chest wall, respiratory muscles, and lung parenchyma, reducing lung compliance. Airway obstruction or "senile emphysema" is an often quoted term describing this phenomenon. Additionally, the very elderly represent a population with a very high prevalence of past or current smoking. Hence there are associated increases in respiratory disorders such as COPD which may bring about further respiratory function deterioration with ageing. Airway obstruction as determined by spirometry without any significant bronchodilator response is a hallmark of COPD. Exacerbations of COPD may be infective or non-infective, and complications may include hypoxemic respiratory failure with or without hypercapnia. Oxygen therapy, prescribed to aim for a set oximetry range, is essential in the management of hypoxemia. Elderly patients may require non-invasive ventilatory support, and this therapy may be a ceiling of therapy for those who are not candidates for intubation and mechanical ventilation. Stereotactic radiotherapy may be an alternative for management of lung cancer in the very elderly, particularly in those whose degree of frailty may preclude surgical therapy or chemotherapy. In the very elderly population of patients who become critically unwell with respiratory disease, clarification and discussion with patient and family regarding ceiling of therapy and end of life care are essential.

J. Chien
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia

Department of Respiratory Sleep Medicine, Westmead Hospital, Westmead, NSW, Australia
e-mail: jimmy.chien@sydney.edu.au

Effects of Ageing on the Respiratory System

Ageing affects the respiratory system in similar ways to other organs in that maximum function gradually declines. The respiratory system comprises the thoracic cage, lungs, diaphragm, and the associated ventilatory control mechanisms. The distensibility or compliance of the lungs is the change in volume in relation to change in pressure, which may change with ageing.

With ageing, structural changes occur in the thoracic cage leading to a reduction in chest wall compliance, i.e. a greater change in pressure is required for a given change in volume. This change in respiratory mechanics occurs due to stiffening of the chest cage from a variety of factors, including age-related osteoporosis reducing thoracic vertebral height, kyphosis leading to thoracic cage restriction, and stiffening and calcification of the rib cage resulting in limited ability for expansion. The stiffer chest wall may also lead to a higher residual volume and incomplete emptying of the lungs [1].

Respiratory muscle strength and efficiency is also affected by ageing. Respiratory muscle strength may be measured by maximum inspiratory pressure and maximum voluntary ventilation. A decline in respiratory muscle strength, the extreme example of which can be seen in disorders such as motor neuron disease, increases the risk of impaired airway secretion clearance and impaired ventilation. Maximum inspiratory pressures are observed to reduce with age [2], while maximum voluntary ventilation and VO_2 max are also reduced, possibly due to reductions in compliance and an increased elastic load on the respiratory muscles from breathing at higher lung volumes (from higher residual volume) and increased load from a stiffer chest wall [3].

The lung parenchyma undergoes changes with ageing, with degeneration of elastic fibres which support alveolar structures. A poorly defined entity in the medical literature termed "senile emphysema" is often quoted. Starting at approximately 50 years of age, there is a homogenous degeneration of elastic fibres supporting alveolar ducts leading to dilatation of airspaces [4]. This loss of supporting elastic

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_23

tissue may lead to premature airway collapse, with subsequent gas trapping and hyperinflation.

Spirometric measures of lung function decline with age. The FEV1 (forced expiratory volume over 1 s) declines from the age of 35–40 years at a rate of 25–30 ml per year [5]. Total lung capacity (TLC) essentially remains unchanged for life, although there are increases in the functional residual capacity (FRC) and residual volume (RV) with age as described above, with a reduced vital capacity (VC). There is a reduction in the diffusion capacity across the alveolar/capillary membrane with age [6], the precise mechanism of which remains unclear.

COPD in the Elderly

Epidemiology

COPD is a leading cause of morbidity and mortality. The prevalence of COPD increases with age, particularly over the age of 45 years. In Australia, the overall prevalence of COPD is 7.5% for people aged over 40 years and 30% for people aged 75 and over [7]. COPD requiring medical attention usually occurs later in life and is expected to be the third leading cause of death and disability worldwide by 2020 [8].

Pathophysiology

Elderly patients with COPD tend to have other co-morbidities, including cardiovascular co-morbid conditions. The pathophysiology is complex and involves airway inflammation, small airway remodelling, parenchymal lung damage, and systemic inflammation, in addition to the superimposed pathophysiological effects of the ageing lung as described above. A dysregulated immune system with ageing may also have an additive effect. A history of cigarette exposure may accelerate this process with advancing age [9].

Presentation and Investigation

Dyspnoea on exertion or at rest, chronic cough, wheeze, limitation of daily activities, and a history of smoking may all be described on presentation. These symptoms may also be present with concomitant cardiac disease; hence, a thorough history and examination is essential. Airways obstruction should be identified on spirometric testing.

International guidelines from the American Thoracic Society and European Respiratory Society (ATS/ERS) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) have been established to provide objective spirometric measures for determining the presence of airway obstruction in diagnosing COPD. An FEV1/FVC ratio of <70% determines the presence of airway obstruction. The FEV1 as a percentage of predicted values adjusted for age, gender, height, and race determines the severity of airways obstruction, i.e. FEV1/FVC ratio <70%, FEV1 ≥80% mild obstruction, 50% ≤ FEV1 <80% moderate obstruction, 30% ≤ FEV1 <50% severe obstruction, and FEV1 <30% very severe airways obstruction. Lung volume measurements can determine the total lung capacity (TLC) in addition to any gas trapping (increased residual volume – RV) and/or any hyperinflation (increased functional residual capacity – FRC) which may be present in COPD. Additionally, the gas transfer capacity (DLCO) may be reduced subsequent to parenchymal lung damage secondary to smoking.

Radiological investigation may include chest X-Ray and/or a high-resolution CT scan of the chest to determine the presence of emphysematous changes, bullae, or other lung parenchymal changes.

Management of Acute Exacerbations in the Elderly

Elderly patients with severe COPD may present frequently with acute exacerbations, characterised by dyspnoea, productive cough with mucopurulent sputum, wheezing, and hypoxemia. Exacerbations may be triggered by viral or bacterial respiratory exacerbations, environmental or climate factors such as extremes of temperature, and bushfires/pollution/smog.

Patients with severe COPD may present for admission multiple times per year with acute exacerbations, increasing hospital and health-care utilisation, and is associated with a reduction in quality of life and increased risk of mortality as well as increased morbidity from inpatient hospital interventions and polypharmacy.

Management Considerations

Pharmacotherapy

The majority of elderly patients with severe COPD are admitted with either an infective or non-infective exacerbation. However, airway inflammation and obstruction is universally present, and this is often the target of pharmacotherapy. Current available pharmacotherapy can improve quality of life, reduce exacerbation rates, and reduce morbidity and mortality. For patients with mild COPD with FEV1 >80 predicted, a short-acting bronchodilator may be used as needed. For moderate COPD with an FEV1 50–80%, one or more long-acting bronchodilator agents (e.g. a long-acting beta-agonist and long-acting anticholinergic) together with pulmonary rehabilitation may offer improvement in symptoms, quality of life, and exacerbation rates. For severe COPD with an

FEV <50%, the addition of inhaled corticosteroids may reduce exacerbation rates, and if there is significant hypoxemia at rest, then supplemental oxygen therapy may be indicated.

In the setting of an acute exacerbation requiring hospital admission, an escalation of therapy is usually required. An increase in bronchodilator therapy, a course of antibiotics, and corticosteroids are often required to treat the acute exacerbation. There is evidence that a course of oral corticosteroids at a dose of 40 mg daily for 5 days may be an adequate course [10], although prednisolone dosing usually ranges from 25 to 50 mg for 5 days to 2 weeks. Increased frequency of a beta-agonist (e.g. salbutamol) or an anticholinergic (e.g. ipratropium) may be used, either nebulised or via metered dose inhaler via a Volumatic device. Antibiotics with a course for 5–10 days may be used if there are clinical signs of increased sputum production and purulence in addition to increased dyspnoea. Initial choice of antibiotic agents may include a beta-lactam such as penicillin, amoxicillin, cephalosporin, macrolides, and doxycycline.

In an acute exacerbation, elderly patients may present in acute hypoxemic respiratory failure with or without hypercapnia. The lower limit of oxygen saturation in the elderly is 93% for men and 92% for women [11]. Hypoxemia may be present in the setting of acute illness and respiratory disease. Pulse oximetry to determine oxygen saturation is necessary to ascertain degree of hypoxemia and guide treatment to target oxygen saturation ranges. For those who are normocapnic on arterial blood gas testing, or without any risk of hypercapnia, a target oxygen saturation of 92–96% [12] should be attained with supplemental oxygen therapy. Arterial blood gas testing should be performed on patients admitted with severe COPD to assess metabolic parameters such as acid-base status, degree of hypoxemia, and presence of any hypercapnia.

For elderly patients with severe COPD, many have had frequent admissions for exacerbations and may be at risk of hypercapnia. For these patients, supplemental oxygen therapy should be titrated to a target oxygen saturation of 88–92% [13]. Some of those admitted with an exacerbation may develop hypercapnic hypoxic respiratory failure. For severe COPD patients who present with respiratory acidosis, with a pH <7.35 and a $PaCO_2$ >45 mmHg, non-invasive bilevel is often used in the management of hypercapnic respiratory failure to reduce work of breathing, improve alveolar ventilation, and prevent deterioration requiring intubation and mechanical ventilation. Acute respiratory failure in the elderly will be covered in more detail later in the chapter.

Pneumonia in the Elderly

The elderly are more susceptible to increased rates of pneumonia, and its occurrence in the elderly is associated with higher morbidity and mortality. Risk factors for pneumonia include COPD, asthma, nutritional status, alcoholism, institutionalisation, heart disease, and immunosuppression [13].

The most common causative bacterial organism is *Streptococcus pneumoniae*. Mortality rates from pneumococcal pneumonia are higher compared to young adults. Other causative bacterial organisms include *Klebsiella*, *Mycoplasma*, *Legionella*, *Haemophilus*, and *Pseudomonas*. Influenza A is associated with higher mortality rate, both from the acute infective illness and from secondary bacterial infection. Patients admitted for pneumonia may develop complications from sepsis, respiratory failure, renal failure, and acute respiratory distress syndrome (ARDS) [14].

The clinical features of pneumonia may be more subtle in the elderly than in the younger population. Fever, productive cough, and chest pains may occur less frequently, and diagnosis should be confirmed on chest X-Ray and with leucocytosis on blood counts. Prognostic indicators include the presence of renal dysfunction, elevated respiratory rate >30 bpm, blood urea level >19 mg/dL, systolic blood pressure <90 mmHg systolic or <60 mmHg diastolic, confusion, and age 65 or older (CURB-65 score). The risk of death at 30 days increases as the score increases, with a score of 0 having a 0.6% mortality rate, 1 = 2.7%, 2 = 6.8%, 3 = 14%, 4 and 5 = 28% [15].

The treatment of pneumonia is based on the causative infective organism. Since the most common organisms include the ones listed above, the most common antibiotic regimens include agents with a broad spectrum of cover such as beta-lactam, a second-generation cephalosporin, and a macrolide antibiotic which may be adequate for pneumonia in patients not requiring hospital admission. For those with penicillin allergies, a fluoroquinolone antibiotic may be used.

Patients with severe pneumonia who require admission have significant co-morbidities, and often the source of sepsis may be difficult to determine on initial presentation. Intravenous antibiotic therapy is recommended with antibiotic choices being a broad-spectrum antibiotic, such as a beta-lactam combination agent (piperacillin/tazobactam), a third-generation cephalosporin, or, in the setting of penicillin allergy, a fluoroquinolone. A macrolide antibiotic may be added for atypical organisms, particularly *Legionella*. Microbiological cultures should be obtained from sputum cultures to determine the causative agent [16].

Supportive care may be required for patients who develop complications of sepsis including septic shock, ARDS, and multiorgan dysfunction or failure. Patients may require nursing in a monitored environment and possibly supportive care in a high dependency unit or intensive care unit. The overall outcome in older patients admitted with pneumonia may be more dependent on level of function, disability, comorbid disease, and nutritional basis rather than the individual's age alone.

The Very Elderly and ICU

Those patients requiring admission in an intensive care unit may potentially have unnecessary prolongation of life, and quality of end of life care becomes an increasingly important issue. Admission to ICU should be consistent with patient wishes, while goals of care and ceiling of therapy should be classified to avoid unnecessary treatments which may be futile or which may reduce quality of end of life. Ideally, any advanced care directive should be enacted prior to ICU admission, and discussions regarding end of life care in the setting of severe illness should occur with the patient and family prior to significant deterioration requiring ICU [17].

Lung Cancer

With increased age, and potential smoking history, there may be an increased associated risk of lung cancers. Symptoms do not usually occur until late, and cancers are often found incidentally on screening radiology, e.g. on CXR performed for respiratory symptoms or on CT coronary angiogram for cardiac screening.

Many elderly patients are not appropriate for aggressive therapy, and due to co-morbidities, surgery or chemotherapy may not be appropriate, particularly in those with poor functional status. In the oldest of the old, particularly over the age of 80, the negative impact of chemotherapy and its adverse effects on quality of life may outweigh the potential benefits of therapy. Referral to symptomatic and palliative care may be more appropriate in managing symptoms as they arise.

In recent years, stereotactic body radiation therapy (SBRT) has emerged as an option for management of lung cancer in patients whose co-morbidities make them a high operative risk for surgical resection or chemotherapy. For early stage, medically inoperable lung cancer, it may be an attractive option particularly to an octogenarian or nonagenarian who may be too frail for chemotherapy or surgical resection. SBRT can be utilised with curative intent in early stage lung cancer, with no significant toxicities or increased morbidity [18, 19].

Acute Respiratory Failure in the Elderly

Acute hypoxemia can result from a number of illnesses which can disturb normal respiratory physiology. The pathophysiological mechanisms include ventilation/perfusion inequality (e.g. pneumonia, acute exacerbation of COPD, or asthma), increased shunt (e.g. acute respiratory distress syndrome), alveolar hypoventilation (e.g. severe COPD exacerbation with hypercapnic respiratory failure), and diffusion impairment (e.g. interstitial lung disease).

The disease conditions which may result in respiratory failure include (but are not limited to) severe exacerbations of COPD/asthma/bronchiectasis, acute pneumonia, CCF with pulmonary oedema, neuromuscular disease (such as motor neurone disease and muscular dystrophy), opiate medication, neurological disease resulting in respiratory muscle weakness or reduction in level of consciousness, restrictive chest wall disease, acute pulmonary embolism, pleural effusions, pneumothorax, and haemoptysis [20].

The main causes of respiratory failure in the oldest patients include cardiac failure, pneumonia, COPD, and pulmonary embolism [21]. Treatment is usually targeted at the aetiology; however, supportive care includes supplemental oxygen therapy to address hypoxemia. For those patients not at risk of CO_2 retention, a target oxygen saturation range of 92–96% is suggested.

Delivery devices for supplemental oxygen include a simple face mask, nasal cannulae, venturi masks, and partial and non-rebreather reservoir oxygen masks. Humidified high-flow nasal cannulae oxygen therapy has been available recently and provides a new method of not only oxygen delivery but also a humidified air/oxygen mix with variable flow rates depending upon the patient's ventilatory requirements.

CPAP therapy may be considered for patients presenting in acute respiratory failure due to congestive heart failure and acute pulmonary if standard medical management with diuretics, opiates, and glyceryl trinitrate fails to reverse the severe hypoxemia. CPAP works to permit a higher inspired partial pressure of oxygen, recruit under ventilated alveolar units, and reduce work of breathing. A CPAP pressure of 8–10 cm of water is often adequate to manage acute pulmonary oedema and may prevent intubation and admission to intensive care [22].

In the elderly population with a history of chronic respiratory disease, patients presenting with respiratory failure may be at risk of hypercapnia, particularly those with a history of chronic severe COPD, bronchiectasis, neuromuscular or chest wall disease, cystic fibrosis, obstructive sleep apnoea, and obesity hypoventilation syndrome. The target oxygen saturation range should be 88–92% for all patients at risk of or with a history of hypercapnia [13].

Due to the high risk of mortality and impairment of quality at the end of life, for critically ill elderly patients in acute hypercapnic hypoxic respiratory failure, intubation and mechanical ventilation may not be an option for patients or their relatives. Non-invasive positive pressure ventilation or non-invasive ventilation (NIV) may be utilised as a ceiling of therapy. NIV is an effective treatment for patients in hypercapnic respiratory failure, particularly in COPD, neuromuscular, or chest wall diseases. NIV results in improvements in alveolar ventilation and unloads respiratory muscles to reduce work of breathing. In elderly patients with these

underlying respiratory disorders, NIV may effectively reduce the need for intubation, mechanical ventilation, and admission to ICU. NIV is usually delivered via either a full face mask or nasal mask with chinstrap. Bilevel non-invasive ventilators deliver an expiratory positive airway pressure (EPAP) and inspiratory airway pressure (IPAP) with the difference between the two pressures being the pressure support (PS). The ventilators can also deliver a backup respiratory rate in addition to EPAP and IPAP to maintain adequate alveolar ventilation. NIV is often used as the ceiling of therapy in the elderly and frail. In the event of deterioration despite maximal medical therapy and NIV, it may be used in the palliation of symptoms of breathlessness, in conjunction with opiate medication.

Clinical Relevance

The oldest of the old have progressive age-related physiological changes including decreasing chest wall compliance and increases in residual volume and functional residual capacity with airway closure at small volumes from loss of supporting tissues around alveolar and bronchial structures resulting in senile emphysema.

There is also a reduction in respiratory muscle strength and muscle mass with age, while there are possible impairments to the ageing immune system linked to dentition, swallowing dysfunction, nutritional status, and decreased T-cell function.

Respiratory failure is the eventual outcome of the common respiratory conditions that affect the oldest of the old, with the most common being COPD, pneumonia, and PE in order or frequency.

Goals of therapy are important to establish with the patient and their families, since cardio-pulmonary resuscitation, intubation, mechanical ventilation, and intensive care admission may lessen the quality of end of life.

Multiple-Choice Questions

1. The following are true of pneumonia in the elderly, *except*:
   A. The most common causative bacterial organism is *Streptococcus pneumoniae*.
   B. Fever, productive cough, and chest pains occur frequently.
   C. Patients with severe pneumonia who require admission have significant co-morbidities.
   D. For those with penicillin allergies, a fluoroquinolone antibiotic may be used.
2. The following are true of acute respiratory failure, *except*:
   A. The main causes of respiratory failure in the oldest patients include cardiac failure, pneumonia, COPD, and pulmonary embolism.
   B. For critically ill elderly patients in acute hypercapnic hypoxic respiratory failure, intubation and mechanical ventilation is an option for patients or their relatives.
   C. The target oxygen saturation range should be 88–92 for all patients at risk of or with a history of hypercapnia.
   D. In the elderly population with a history of chronic respiratory disease, patients presenting with respiratory failure may be at risk of hypercapnia.

Answers

1. B
2. B

References

1. Poche R, Mittmann O, Kneller O. Remarks on the etiology of bronchial carcinoma. Arztl Forsch. 1965;19(8):417–21.
2. Enright PL, Kronmal RA, Manolio TA, Schenker MB, Hyatt RE. Respiratory muscle strength in the elderly. Correlates and reference values. Cardiovascular Health Study Research Group. Am J Respir Crit Care Med. 1994;149(Pt 1):430–8.
3. McClaran SR, Babcock MA, Pegelow DF, Reddan WG, Dempsey JA. Longitudinal effects of aging on lung function at rest and exercise in healthy active fit elderly adults. J Appl Physiol. 1985;78(5):1957–68.
4. Gillooly M, Lamb D. Microscopic emphysema in relation to age and smoking habit. Thorax. 1993;48(5):491–5.
5. Ware JH, Dockery DW, Louis TA, Xu XP, Ferris BG Jr, Speizer FE. Longitudinal and cross-sectional estimates of pulmonary function decline in never-smoking adults. Am J Epidemiol. 1990;132(4):685–700.
6. Stam H, Hrachovina V, Stijnen T, Versprille A. Diffusing capacity dependent on lung volume and age in normal subjects. J Appl Physiol. 1994;76(6):2356–63.
7. Toelle BG, Xuan W, Bird TE, Abramson MJ, Atkinson D, Burton DL, et al. Respiratory symptoms and illness in older Australians: the Burden of Obstructive Lung Disease (BOLD) study. Med J Aust. 2013;198(3):144–8.
8. World Health Organization. Statistical dataset. Geneva: World Health Organization; 2000. 3-1-2009.
9. Barnes PJ. Future treatments for chronic obstructive pulmonary disease and its comorbidities. Proc Am Thorac Soc. 2008;5(8):857–64. https://doi.org/10.1513/pats.200807-069TH.
10. Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Drescher T, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. JAMA. 2013;309(21):2223–31. https://doi.org/10.1001/jama.2013.5023.
11. Hardie JA, Vollmer WM, Buist AS, Ellingsen I, Morkve O. Reference values for arterial blood gases in the elderly. Chest. 2004;125(6):2053–60.
12. Beasley R, Chien J, Douglas J, Eastlake L, Farah C, King G, et al. Target oxygen saturation range: 92-96% versus 94-98. Respirology. 2017;22(1):200–2. https://doi.org/10.1111/resp.12879.

13. Beasley R, Chien J, Douglas J, Eastlake L, Farah C, King G, et al. Thoracic Society of Australia and New Zealand oxygen guidelines for acute oxygen use in adults: 'Swimming between the flags'. Respirology. 2015;20(8):1182–91. https://doi.org/10.1111/resp.12620.
14. Plouffe JF, Breiman RF, Facklam RR. Bacteremia with Streptococcus pneumoniae. Implications for therapy and prevention. Franklin County Pneumonia Study Group. JAMA. 1996;275(3):194–8.
15. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town G, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003;58(5):377–82.
16. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44(Suppl 2):S27–72.
17. Heyland D, Cook D, Bagshaw SM, Garland A, Stelfox HT, et al. Canadian researchers at the end of life. The very elderly admitted to ICU: a quality finish? Crit Care Med. 2015;43(7):1352–60. https://doi.org/10.1097/CCM.0000000000001024.
18. Merrell KW, Mou B, Hallemeier CL, Owen DA, Nelson K, Garces YI, et al. P1.18: long-term clinical outcomes and safety profile for central lung SBRT for NSCLC: track: early stage NSCLC (stage I – III). J Thorac Oncol. 2016;11(10S):S192. https://doi.org/10.1016/j.jtho.2016.08.040.
19. Owen D, Olivier KR, Mayo CS, Miller RC, Nelson K, Bauer H, et al. Outcomes of stereotactic body radiotherapy (SBRT) treatment of multiple synchronous and recurrent lung nodules. Radiat Oncol. 2015;10:43. https://doi.org/10.1186/s13014-015-0340-9.
20. Aminzadeh F, Dalziel WB. Older adults in the emergency department: a systematic review of patterns of use, adverse outcomes, and effectiveness of interventions. Ann Emerg Med. 2002;39(3):238–47.
21. Ray P, Birolleau S, Lefort Y, Becquemin MH, Beigelman C, Isnard R, et al. Acute respiratory failure in the elderly: etiology, emergency diagnosis and prognosis. Crit Care. 2006;10(3):R82. https://doi.org/10.1186/cc4926.
22. L'Her E, Duquesne F, Girou E, de Rosiere XD, Le Conte P, Renault S, et al. Noninvasive continuous positive airway pressure in elderly cardiogenic pulmonary edema patients. Intensive Care Med. 2004;30(5):882–8. https://doi.org/10.1007/s00134-004-2183-y.

Managing Osteoporosis in Oldest of Old

24

Vasi Naganathan and Kujan Nagaratnam

Introduction

Older people are more likely to have fractures because as people get older they are more likely to fall. Fractures are more likely after a fall because with age there is reduction in bone density and disruption in the microarchitecture leading to increased bone fragility [1]. The main clinical questions when thinking about osteoporosis in older people are: (i) what is the risk of future fracture, particularly hip fracture? (ii) are there any reversible factors responsible for osteoporosis? and (iii) should medication be prescribed with the goal of decreasing the risk of future fractures? In frail older people, especially if they have cognitive impairment and/or multiple comorbidities, there is the added challenge of keeping the deleterious effects of osteoporosis treatment to a minimum.

Osteoporotic fractures commonly occur at the vertebrae, forearm and hip in older people. But minimal trauma fractures occur at other sites as well including the pelvis, ribs, humerus and clavicle. Hip fractures in particular are associated with increased morbidity, dependency and mortality as well as increased health costs due to the fact that treatment requires hospitalization and surgery for fixation of the fracture. Hence, they are significant short-term and medium-term economic costs to the community. Following a hip fracture, approximately 20% of patients do not survive the next year, and 50% do not regain their previous level of independence [2]. Vertebral fractures, which don't always occur after falling, are also associated with adverse outcomes, including height loss, back pain, kyphosis, functional impairment and hospitalization.

V. Naganathan (✉)
Centre for Education and Research on Ageing, Faculty of Medicine and Health, The University of Sydney and Ageing and Alzhiemer's Institute, Concord Hospital, Sydney, NSW, Australia
e-mail: vasi.naganathan@sydney.edu.au

K. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia

Clinical Evaluation and Investigations

Since bone strength decreases in everyone as they get older, "bone health" and fracture risk should be assessed in all older people. History and investigations should be aimed at identifying risk factors for osteoporosis as well as conditions and medications that can reduce bone mass and strength – often referred to as secondary osteoporosis (Boxes 24.1 and 24.2). Patients should also be assessed for risk factors for falls (see Chap. 5). A comprehensive geriatric assessment would help identify these risk factors and determine factors that impact positively and negatively on the management and treatment of osteoporosis. An evaluation of nutritional status should be done as poor nutritional status is a risk factor for osteoporosis and contributes to frailty which in turn increases the risk of falls. Falls prevention is equally as important as osteoporosis management in decreasing risk of fracture especially in older frail people. Therefore, a detailed assessment for falls risk and a management plan to prevent falls go hand in hand with any osteoporosis management plan. Patients should be assessed for gait instability and cognitive function. Kyphoscoliosis, spinal tenderness and pain could be due to vertebral fractures and can have an impact on posture, gait and balance that should be looked for.

Box 24.1 Risk Factors for Osteoporosis

Age
Female
Low body mass index
Smoking
Heavy alcohol intake
Family history of hip fracture
Lack of physical activity
Low dietary calcium intake
Early menopause
Surgically induced oestrogen deficiency
History of minimal trauma fracture
Information sources: Idqbal [3]

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_24

Box 24.2 Causes for Reduced Bone Density and Strength

Endocrine and metabolic diseases
Glucocorticoid excess
Vitamin D deficiency
Hyperthyroidism
Hyperparathyroidism
Hypogonadism
Diabetes mellitus
Other diseases
Chronic renal failure
Liver disease
Rheumatoid arthritis
Multiple myeloma
Malabsorption syndromes
Chronic obstructive pulmonary disease
Medications
Glucocorticoids
Anticonvulsants
Heparin (long-term)
Loop diuretics
Thyroid hormones

Bone mineral density (BMD) that is determined by dual energy X-ray absorptiometry (DEXA) is the most commonly used method to assess bone mass. A BMD lower than −2.5 standard deviations below the mean of a young normal is said to be in the osteoporotic range. A BMD between −1.5 and − 2.5 standard deviation below the young normal is in the osteopenic range. Rather than think about BMD as a way to formally diagnose osteoporosis, it is clinically more useful to think of BMD as useful information to have in assessing the risk of future fracture [4]. In older frail people, it may be reasonable not to assess BMD with DEXA if knowing BMD will not change decisions on osteoporosis treatment. In addition, in older frail people, it isn't clear if assessing change of BMD by DEXA is of any clinical value.

To help clinicians accurately predict patient's absolute risk of future fractures, two validated tools can be used: the fracture risk assessment tool and the Garvan fracture risk calculator. The FRAX tool gives the 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture) [5]. The FRAX models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia. Information on the following clinical risk factors for fracture are used: age, sex, weight, height, previous fracture, history of parent having a hip fracture, current smoking, glucocorticoid use, rheumatoid arthritis, secondary osteoporosis and alcohol intake. The Garvan fracture risk calculator was originally developed and validated using an Australian cohort study database [6]. This tool requires information on a smaller number of risk factors but does include information about falls. Blood tests are aimed at identifying risk factors of osteoporosis and causes for secondary osteoporosis such as thyroid function abnormalities and low vitamin D.

Treatment of Osteoporosis

The reasoning that guides the treatment of osteoporosis in older people is that even in older frail people, bone density has been shown to be predictive of future fracture. The aim of osteoporosis treatment therefore is to improve bone density or at least slow down bone loss. This in turn will improve bone strength resulting in a decreased risk of future fracture. Most clinical trials of osteoporosis treatment have been conducted on postmenopausal women; thus there is the question of whether this evidence applies to older frail people. The main medical treatment options to treat osteoporosis are discussed below. There are no good-quality head-to-head comparisons between the drugs discussed below, so choice of therapy should be based on availability, cost, convenience and patient-related factors. While life-style measures such as exercise are often discussed in guidelines on the treatment of osteoporosis, exercise has a more important role to play in falls prevention and therefore should be "prescribed" with that goal in mind.

Calcium and Vitamin D

Many older people are not able to meet the recommended daily intake of calcium with their usual diet. In addition, vitamin D deficiency is common in older people, especially among people in residential care [7]. Calcium supplementation and vitamin D replacement therapy has therefore been traditionally the commonest and cheapest treatment form of osteoporosis treatment. Fracture prevention studies have shown calcium 1000/day and 500 IU /day are beneficial in the elderly [8]. The evidence however that calcium and vitamin D supplementation are effective in preventing fractures in older people is conflicting. At the time of writing this chapter, the most recent high-quality meta-analysis of randomized clinical trials found that the use of supplements that included calcium, vitamin D or both compared with placebo or no treatment was not associated with a lower incidence of hip, non-vertebral, vertebral, or total fractures among community-dwelling older adults [9]. These results appeared consistent regardless of the dose of calcium or vitamin D, sex, fracture history, calcium intake and baseline serum 25-hydroxyvitamin D concentration. The authors concluded that these findings do not support the routine use of these

supplements in community-dwelling older people. This contrasts with earlier meta-analysis that concluded that calcium supplementation did prevent fractures [10]. Prior meta-analyses also concluded that that vitamin D supplementation was effective in preventing fractures and suggested that this dose of vitamin D needed to be ≥800 IU daily [11–13]. Zhao et al. [9] in a recent analysis pointed out that these results may be influenced by the inclusion of data from trials conducted in residential care and there are a few recent trials not included in these earlier meta-analyses that found that high-dose vitamin D increased fracture risk.

On the basis of the conflicting evidence, there is variation in clinical practice in terms of routinely screening for vitamin D deficiency in older community dwellers and prescribing of calcium and vitamin D supplementation to this group. In older people who have had an osteoporotic fracture, vitamin D levels are usually checked, vitamin D deficiency corrected and calcium supplementation prescribed on the basis that all pivotal trials of anti-osteoporotic agents (anti-resorptive, anabolic or dual-action agents) included supplementation with calcium and vitamin D. In older people living in residential care, vitamin D supplementation is often given because it is commonly found, and on the basis of an older landmark, clinical trial found that calcium and vitamin D supplements lowered the risk of fractures in older women living in nursing homes [14].

Bisphosphonates

Most of the randomized controlled trials (RCTs), for anti-osteoporotic agents in reducing fragility fractures, were conducted on women up to the age of 80 years, but there is evidence from a few studies and subgroup analyses of trials that provide evidence that anti-resorptive agents do reduce the risk of fractures in older people. Anti-resorptive agents prevent bone loss by slowing bone turnover that results in a decrease in bone resorption which enhances bone density. The evidence is strongest for the bisphosphonates. A post hoc analysis of the Hip Intervention Program (HIP) study found that risedronate reduced the risk of hip fractures in women aged over 70 with established osteoporosis (baseline femoral neck T score ≤ −2.5 and ≥1 prior vertebral fracture) [15]. After 3 years, hip fracture had occurred in 3.8% of risedronate-treated patients and 7.4% of placebo-treated patients (relative risk 0.54; 95% confidence interval 0.32–0.91). The most direct evidence that bisphosphonates can reduce the risk of fractures specifically in frail older people comes from the HORIZON Recurrent Fracture Trial [16]. This was a secondary prevention trial looking at the efficacy of yearly intravenous zoledronic acid in patients of both sexes who had a hip fracture and subsequent surgical fixation. In this trial more than 50% of those recruited were over the age of 75 years (age range 50–85 years). The rates of any new non-vertebral fracture were 7.6% in the zoledronic acid group and 10.7% in the placebo group (RR 0.73; 95% confidence interval 0.55–0.98).

Oral bisphosphonates are poorly absorbed, are difficult to take orally and are not well tolerated, so long-term compliance with these medications is a challenge. Having said that there is no reason to believe that they will not be effective in older people on the basis of large body of evidence that they reduce the risk of non-vertebral fractures in postmenopausal women including the HIP study mentioned above. Osteonecrosis of the jaw (ONJ) is a rare adverse effect of bisphosphonates and when seen usually occurs in the setting of cancer [17].

Denosumab

Denosumab is a human monoclonal antibody that targets and binds with high affinity and specificity to the receptor activator of nuclear factor-kappa B ligand (RANKL) [18, 19] preventing the activation of the RANK receptor [20] which is found on osteoclast precursors and osteoclasts. This leads to a decrease in bone resorption and an increase in bone density. The Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM) trial for 36 months investigated the efficacy of denosumab on the incidence of new fractures [20]. Postmenopausal women aged 60–90 years with osteoporosis were recruited, of whom almost a third were over the age of 75 years. Denosumab reduced the risk of hip fracture, with a cumulative incidence of 0.7% in the denosumab group versus 1.2% in the placebo group (hazard ratio, 0.60; 95% CI, 0.37 to 0.97), and also reduced the risk of non-vertebral fracture, with a cumulative incidence of 6.5% in the denosumab group versus 8.0% in the placebo group (hazard ratio, 0.80; 95% CI, 0.67 to 0.95). Some people find it more convenient to have a twice a year subcutaneous injection [21, 22] compared to oral treatment or yearly intravenous infusion. Denosumab is good alternative treatment for osteoporosis in people with severe renal impairment in whom zoledronic acid is contraindicated. Currently bisphosphonates and denosumab are the mainstay of oestrogen therapy [23].

Parathyroid Hormone (PTH)/ PTH Analogues

Parathyroid hormone (PTH) or its analogues, given by subcutaneous injection once daily, are anabolic agents that directly stimulate osteoblastic bone formation, resulting in substantial increases in trabecular bone density and connectivity. This mechanism of action is very different from that of the anti-resorptive agents mentioned previously, which reduce bone resorption. Two PTH-related analogues are currently in common use: teriparatide (PTH 1–34) and recombinant human

PTH (1–84). For teriparatide, the pivotal trial showed that daily subcutaneous injection of teriparatide decreased the risk of vertebral and non-vertebral fractures in postmenopausal women [24]. The study did not have the power to look at the effect of teriparatide on hip fractures. For PTH (1–84) the pivotal trial found that it reduced the risk for new or worsened vertebral fracture in postmenopausal women with low bone density [25].

In clinical practice, because of the costs, the daily subcutaneous injections, the lack of evidence in older people specifically and the long-term safety concerns, teriparatide and PTH (1–84) are generally not used as first-line therapy. They are used sometimes in people who have severe osteoporosis, who continue to have fractures on other osteoporosis treatment or who cannot tolerate or have contraindications to bisphosphonates.

Other Treatments

There is evidence that strontium ranelate has efficacy for fracture prevention in older people but is no longer used for osteoporosis treatment in most countries because of safety concerns. Hormone replacement therapy and selective oestrogen receptor modulators (SERMs) are also not used much in older people. Neither of these treatments have high-level evidence that they prevent hip fractures which is the main outcome concern in older people. In addition, for hormone replacement therapy, there are concerns about risk of breast cancer and venous thromboembolism. SERMs also increase the risk of venous thromboembolism [26] but decrease breast cancer risk.

Clinical Relevance

The risk of osteoporotic fractures increases as people get older.

Only a few RCTs investigating anti-osteoporotic agents with fracture endpoints have included participants over the age of 80 years.

The strongest evidence for fracture prevention in older people is for bisphosphonates.

Falls prevention strategies are just as important as osteoporosis management in preventing fractures in older people.

Case Study

An 83-year-old lady is seen in clinic 1 month after an admission to hospital for management of a hip fracture that occurred after a fall at home. She is medically stable and now walking well with a walking stick. She has hypertension and osteoarthritis but is otherwise well. Her cognition is good. Her BMI is 24 kg/m^2. Investigations while she was in hospital found no medical reasons for why she might have osteoporosis apart from low vitamin D which has now been corrected with vitamin D supplementation.

Given her reasonably good life expectancy, she should be considered for osteoporosis treatment on the basis that she has had a previous minimal trauma fracture. In this situation there are different opinions on whether bone density should be measured. The argument for doing the test is that if her bone density was in the normal range, then perhaps the clinician would not recommend osteoporosis treatment and some people use bone density to monitor treatment. The argument against doing a bone density is that she has osteoporosis on the basis of having had a minimal trauma fracture and most clinicians do not monitor bone density to assess response to treatment in older people. Her risk of future fracture could be assessed with a tool such as the FRAX, but this is not necessary in this situation. For interest, based on the FRAX tool (without bone density results), her 10-year probability of major osteoporotic fracture is 27% and of hip fracture 7.6% using Australian cohort data and 17% and 7.6% using Indian cohort data (risk of fractures varies by country).

On the basis of the pivotal HORIZON-recurrent fracture trial, the recommendation would be for her to have intravenous zoledronic acid annually on the basis that this has been shown to decrease the risk of future osteoporotic fractures in older people who have had a hip fracture. If zoledronic acid is not available or cannot be given, denosumab subcutaneously every 6 months is a reasonable alternative. Oral bisphosphonates could also be considered but are often not well tolerated.

In terms of falls prevention, she should be assessed for whether an assessment of her home by occupational therapist should occur with the aim of making the home environment safer. She should also see a physiotherapist for advice on strength and balance exercises that she could do which have been shown to be effective in preventing falls.

Multiple Choice Questions

1. Which of the following is the most important fracture to prevent in older people because it associated with the greatest long-term adverse effect on function?
   A. Hip
   B. Wrist
   C. Humerus
   D. Vertebral
   E. Clavicle

2. Which of the following diseases is the most common contributor to low bone density?
   A. Hyperthyroidism
   B. Vitamin D deficiency
   C. Hyperparathyroidism
   D. Multiple myeloma
   E. Celiac disease
3. Which of the following medications that are used in osteoporosis treatment has the strongest evidence in terms of hip fracture prevention in older people?
   A. Vitamin D
   B. Calcium supplementation
   C. Hormone replacement therapy
   D. Bisphosphonates
   E. Raloxifene

MCQ Answers

1. A
2. B
3. D

References

1. Heaney RP. Pathophysiology of osteoporosis. Endocrinol Metab Clin N Am. 1998;27(2):255–65.
2. Crischilles EA, Butler CD, Davis CS, Wallace RB. A model of lifetime osteoporosis impact. Arch Intern Med. 1991;151:2026–32.
3. Iqbal MM. Osteoporosis: epidemiology, diagnosis and treatment. Medscape. http://www.medscape.com/viewarticle/410461_3. Retrieved 24 Feb 2015.
4. Davison KS, Kendler DL, Ammann P, Bauer DC, Dempster DW, Dian L, et al. Assessing fracture risk and effects of osteoporosis drugs: bone mineral density and beyond. Am J Med. 2009;122(11):992–7.
5. Kanis JA, Oden A, Johansson H, Borgstrom F, Strom O, McCloskey E. FRAX and its applications to clinical practice. Bone. 2009;44(5):734–43. http://www.sheffield.ac.uk/FRAX/.
6. Nguyen ND, Frost SA, Center JR, Eisman JA, Nguyen TV. Development of prognostic nomograms for individualizing 5-year and 10-year fracture risks. Osteoporos Int. 2008;19(10):1431–44. https://www.garvan.org.au/promotions/bone-fracture-risk/calculator/.
7. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev. 2001;22(4):477–501.
8. Trived DP, Doll R, Kahm KT. Effect of four months oral vitamin D3 (cholecalciferol) supplement in fractures and mobility in men and women living in the community: randomized double-blind controlled trial. BMJ. 2003;326:468.
9. Zhao JG, Zeng XT, Wang J, Liu L. Association between calcium or vitamin D supplementation and fracture incidence in community-dwelling older adults: a systematic review and meta-analysis. JAMA. 2017;318(24):2466–82.
10. Tang BM, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. Lancet. 2007;370(9588):657–66.
11. Bischoff-Ferrari HA, Willett WC, Wong JB, Stuck AE, Staehelin HB, Orav EJ, et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med. 2009;169(6):551–61.
12. Group D. Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe. BMJ. 2010;340:b5463.
13. Bergman GJ, Fan T, McFetridge JT, Sen SS. Efficacy of vitamin D3 supplementation in preventing fractures in elderly women: a meta-analysis. Curr Med Res Opin. 2010;26(5):1193–201.
14. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, et al. Vitamin D3 and calcium to prevent hip fractures in elderly women. N Engl J Med. 1992;327(23):1637–42.
15. Masud T, McClung M, Geusens P. Reducing hip fracture risk with risedronate in elderly women with established osteoporosis. Clin Interv Aging. 2009;4:445–9.
16. Lyles KW, Colon-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, et al. Zoledronic acid and clinical fractures and mortality after hip fracture. N Engl J Med. 2007;357(18):1799–809.
17. Arrain Y, Masud T. A current update on osteonecrosis of the jaw and bisphosphonates. Dental Update. 2011;38(10):672–6.
18. McClung MR, Lewiecki EM, Cohen SB, Bolognese MA, Woodson GL, Moffet AH, et al. Denosumab in postmenopausal women with low bone mineral density. NEJM. 2006;354:81–91.
19. Burkiewicz JS, Scarpace SL, Bruce ST. Denosumab in osteoporosis and oncology. Ann Pharmacother. 2009;43(9):1445–55. doi: https://doi.org/10.1345/aph.1M102. Epub 2009 Jul 21.
20. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med. 2009;361(8):756–65.
21. Ebeling PR. Strategies for the treatment of osteoporosis. Aust Prescr. 2011;34:176–81.
22. Gambacciani M, Levancini M. Management of postmenopausal osteoporosis and prevention of fractures. Panminerva Med. 2014;56(2):115–31.
23. Reid IR. Editorial. Controversies in osteoporosis management. Intern Med J. 2016;47(7):767–70.
24. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med. 2001;344(19):1434–41.
25. Greenspan SL, Bone HG, Ettinger MP, Hanley DA, Lindsay R, Zanchetta JR, et al. Effect of recombinant human parathyroid hormone (1-84) on vertebral fracture and bone mineral density in postmenopausal women with osteoporosis: a randomized trial. Ann Intern Med. 2007;146(5):326–39.
26. Raloxifene Hydrochloride. Australian Prescriber. 1999;22:95.

Part III

Geriatric Syndromes and Related Problems

Malnutrition and Malabsorption in the Elderly

25

Nages Nagaratnam

Introduction

Malnutrition occurs with inadequate intake and/or increased requirements, defective absorption and changes in the transport and in nutrient utilization [1]. Malabsorption can be due to either inadequate absorption and uptake of nutrients or to defective digestion. Malnutrition is not uncommon in the elderly and is a problem of immense concern. About 15% of the community-dwelling ambulatory elderly, 5–44% of homebound persons [2–4], 12–50% of hospitalized patients and 23–60% of among institutionalized elderly patients [5, 6] are malnourished. Several studies have shown a marked variation in the prevalence rates [7–10], and these could be due to variation in the diagnostic criteria and screening tools used which make comparison difficult. Using the Subjective Global Assessment (SGA) screening tool, it was found that 59% of a general hospital population on admission were malnourished [11]. In Australia similar studies have shown the prevalence rates between 17% and 26% [12, 13].

Malabsorption is present in the elderly more often than is realized, and symptoms resulting from malabsorption tend to be muted in the elderly [14]. In a study of 490 patients admitted to an acute geriatric ward, 55 were found to be malnourished, and in 24 previously unrecognized, malabsorption was detected [15].

Causes of Malnutrition

With ageing there is decreased food intake often referred to as *anorexia of ageing* and is related to several factors. Sense of smell and taste is depressed [16]. The decrease in the food intake is also due to decrease in the fat intake. There is a decline in gastric emptying of large meals associated with satiation [17]. Factors such as physical disabilities, malabsorption, faddish diets, lack of appetite, depression, loneliness and social isolation can result in malnutrition. The major risk factors of malnutrition in the elderly are isolation and multi-morbidity [18]. Community dwellers who are poor and homebound [2–4] and have lack of access to medical care are particularly at risk, and these factors should create a higher degree of awareness among primary care physicians (Fig. 25.1).

Numerous medical conditions, medications and increased susceptibility to infection could give rise to anorexia and weight loss in older people especially those in nursing homes. The medical conditions are caused by a variety of disorders, namely, problems of dentition, swallowing difficulty and malabsorption of nutrients among others. Chronic illnesses could affect food intake. In the elderly eating disorders are alarming because of chronic diseases or disorders that may have already compromised their health [16]. Weight loss could also be attributed to increased metabolism associated with diseases such as hyperthyroidism, Parkinson's disease and pheochromocytoma or could be due to pancreatic insufficiency through malabsorption [19]. Loss of appetite, altered taste and nausea could be related to medications resulting in reduced food intake, so do therapeutic diets and modified fluid which are often unpalatable and poorly tolerated [20].

Unrecognized depression is a well-known cause of anorexia, and weight loss is common in the elderly [21]. Dementia patients often refuse to eat or forget to eat, and feeding becomes time-consuming [19], and many dementia patients develop apraxia of swallowing and have to be constantly reminded to swallow. Late-life paranoia, late-life mania and anorexia nervosa [22] could also lead to malnutrition in the elderly.

N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney,
Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_25

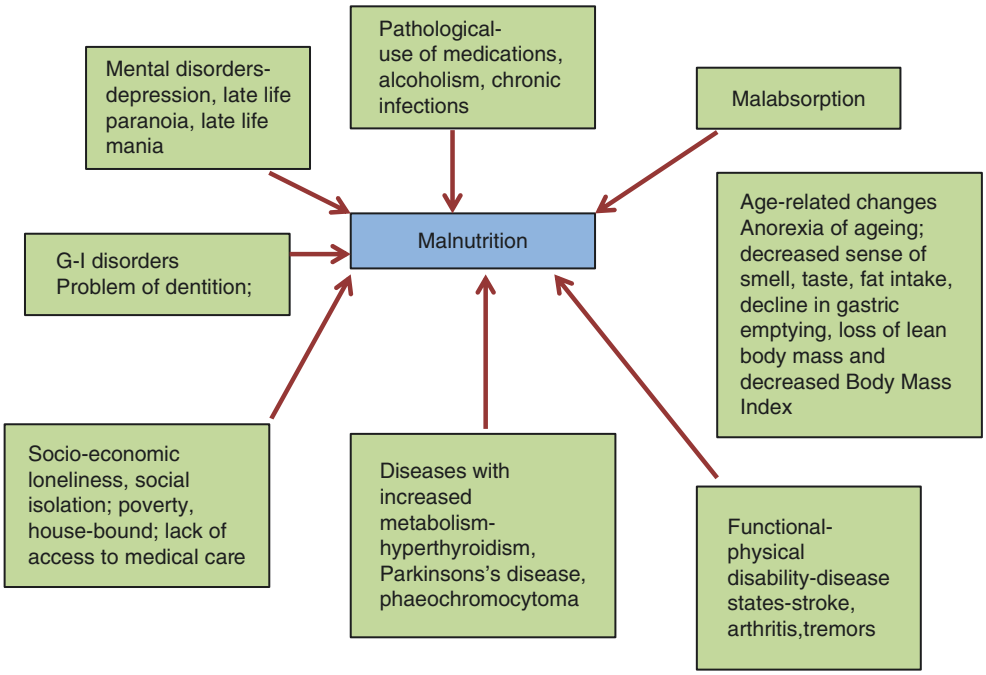


Fig. 25.1 Causes of malnutrition. (Information sources: Dudrik [16], Hajjar [19], Coulson et al. [20], and Nagaratnam and Ghougassion [22])

Screening Tools

There is no lack of screening tools to assess malnutrition, but each has its limitations. Combinations of diverse measurements have received considerable attention to increase sensitivity and specificity [23] because of the poor performance of single assessment methods. Some screening assessments use laboratory data or rely heavily on functional capacity. Others are self-administered or heavily dependent on the screening clinician for accuracy. Determination of prealbumin and albumin is no longer used to identify malnutrition for they are measures of illness and inflammation rather than measures of nutritional status [1].

I. The Mini-Nutritional Assessment (MNA) [24] is a simple, rapid and reliable tool for assessing nutrition in the elderly in the community or in hospital [25] and is widely used by geriatricians. The MNA is a two-step procedure, screening with the MNA-SF followed by assessment and if needed by the full MNA [26]. It has been shown to be 95% accurate when compared with a comprehensive nutritional assessment [27]. It is useful in hospitals and aged care facility centres (Appendix 1). It is comprised of 18 items (6 screenings and 12 assessments) that require a professional to administer and takes about 10–15 min. In the screening section (MNA-SF), five questions are asked and the body mass index calculated. The five questions relate to the severity of loss of appetite, weight loss, mobility and presence of psychological stress or acute disease and neuropsychological illness such as dementia or depression. A score based on the six items at this stage indicates whether malnutrition is possible. The screening part could easily be administered by the primary care physician. Those at risk require full assessment. The assessment section includes ten questions and two anthropometric measurements (triceps skinfold and mid-arm circumference).

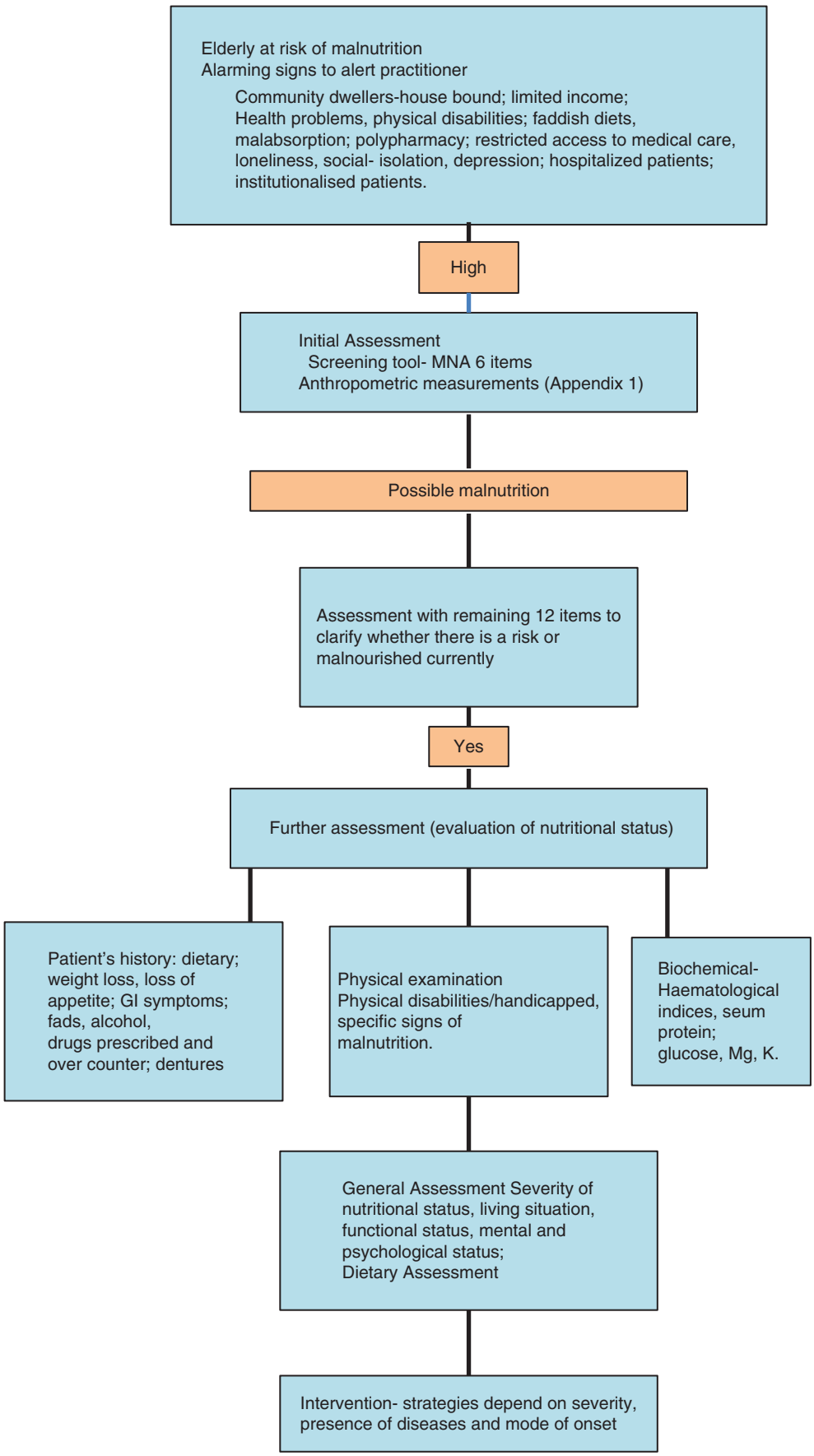
II. The Subjective Global Assessment (SGA) [19] relies on functional capacity and physical signs of malnutrition. It combines patient's history (such as dietary intake, functional status and weight loss), physical examination (such as muscle and fat distribution, oedema) and clinician's judgement. Studies have revealed the SGA is only reliable in the hands of well-trained clinicians [19].

III. The Instant Nutritional Assessment (INA) is the most practical nutritional screening tool and is relatively simple and is widely used. It uses the lymphocyte count, albumin and weight change. The items singly have a low predictive value and when combined however have a higher degree of accuracy in identifying individuals at risk for malnutrition [28].

Anthropometric Measurements

Anthropometric measurements and SGA are the most readily available tools. Anthropometry is easily performed, and as a measure of malnutrition in hospitalized patients, anthropometric measurements were found to be more sensitive than per cent ideal body weight [29]. Decrease in fat is reflected as a decrease in skinfold thickness and is measured with skin calipers. Another measurement is the mid-arm circumference [18]. Serial measurements should be taken by the same operator to avoid interoperator error. The body mass index (BMI) should be ascertained (Algorithm 25.1).

Algorithm 25.1 A practical approach to assessment and management of patients with malnutrition. (Information sources: Sullivan [2], Cederholm et al. [3], Hart [4], Wallace [5], Ennis et al. [6], Seiler and Stahelin [18], Guigoz et al. [26], and Evans [30])



Assessment of Patient

The medical history documents dietary intake, weight, gastrointestinal symptoms and changes in functional status. The physical examination includes evidence of loss of subcutaneous fat, muscle wasting, physical disabilities and specific signs of malnutrition. Depending on the history and physical findings, a selected number of nutritional parameters are determined, and these include the following measurements of serum proteins, vitamins (B12, folic acid, B1, B2, B6, C and D), minerals and trace elements (iron, calcium, magnesium and zinc) and lymphocyte count [18]. In a study of hospitalized frail elderly, the total lymphocyte count was below normal (<1500 cells mm) in 53%, and in 24% it was severely depressed <800 cells/mm^3 [4, 29]. The Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition (ASPEN) characterized malnutrition into three categories, namely, starvation-related malnutrition (chronic starvation, anorexia nervosa), chronic disease-related malnutrition (organ failure, cancer, rheumatoid arthritis among others) and thirdly acute disease or injury-related malnutrition (major infection, burns among others), and they in turn were subdivided into non-severe and severe [1].

Clinical Relevance in Malnutrition

Malnutrition is not uncommon in the elderly.

With ageing there is decreased food intake referred to as anorexia of ageing and is related to several factors.

Numerous medical conditions and medications in the elderly can give rise to anorexia and weight loss.

Depression in the elderly is a well-known cause of malnutrition and often unrecognized [21].

The family physician should ensure that residents of nursing care facilities with eating problems are independently assessed by the dietician.

The cornerstone in the treatment of malnutrition in the elderly is early diagnosis and assessment of the nutritional status.

The Mini-Nutritional Assessment (MNA) is a simple, rapid and reliable tool for assessing nutrition in the elderly in the community or in hospital [25].

The missing nutrients should be replaced and nutrient-rich foods and supplements for specific deficiencies made available.

Management

The cornerstone in the treatment of malnutrition in the elderly is early diagnosis and assessment of the nutritional status. There may be several and potentially reversible or preventable conditions. Older people have one or more medical conditions that may affect the nutritional status. Institutionalized old people contribute to persistently low nutrition intake. About 16% of the elderly population eat less than 1000 kcal/day, and the daily recommended daily intake is 25–35 kcal/d [31]. This may be due to a number of reasons, and simple interventions will go a long way to improve the nutrient intake. The missing nutrients should be replaced and nutrient-rich foods and supplements for specific deficiencies made available. Supplements can be nutritionally complete and are useful, for example, in patients with poor appetite or need specific nutritional requirements [32]. The causes of malnutrition in the elderly are multifactorial. Socio-economic status, functional ability and advanced age limit some patient's capability to purchase and prepare food. Issues such as social, psychological, education and functional may be causing or exacerbating the malnutrition such as access to nutritious food [33].

Causes of Malabsorption

Malabsorption may result from problem arising from improper mixing or with the digestive mediators (e.g. post-gastrectomy), mucosal and mural causes (e.g. gluten-sensitive enteropathy) and microbial causes (bacterial overgrowth) [34].

Coeliac Disease

Coeliac disease, a chronic malabsorption disease, is characterized by intolerance to gluten found in wheat, rye and barley. It is a chronic inflammatory disorder giving rise to villous atrophy with intraepithelial lymphocytes and crypt hyperplasia most marked in the proximal small bowel. Predisposing causes are genetic susceptibility and immune-mediated injury. Coeliac disease can be associated with small intestinal bacterial overgrowth and giardiasis in relation to IgA deficiency coeliac disease [35].

There are three peaks in its presentation, in infancy, in the third decade and in the fifth or sixth decade. About 1/3 of new patients diagnosed are above the age of 65 years [36]. In the latter it usually presents as a specific nutrient deficiency

such as iron, folic acid or calcium. Apart from the symptoms described above, the patients may have a papulovesicular rash of dermatitis herpetiformis on the extensor surfaces, peripheral neuropathy, psychiatric disturbances and fractures from vitamin D deficiency. In the elderly the diagnosis is not often considered until serological tests which includes endomysial antibodies or tissue transglutaminase [37] are carried out and small intestinal biopsy performed for confirmation [14]. Gliadin antibodies are not helpful for the diagnosis as they have poor specificity and sensitivity [35]. Treatment is an adherence to a lifelong gluten-free diet [38].

Bacterial Overgrowth

Small intestine bacterial overgrowth (SIBO) defined as the existence of $>10^5$ bacteria /mm in small bowel fluid culture [34, 39] can result in malabsorption of carbohydrates, fats and micronutrients. Normally there are only a small number of aerobic Gram-positive organisms in the small intestine. In SIBO these are replaced by anaerobic but not exclusively [35] facultative Gram-negative organisms that typically colonize the colon. The bacteria compete for essential nutrients, deconjugate luminal bile salts and damage the surface enterocytes. It frequently occurs in conditions where the motility is affected and when there is lack of gastric acid secretion and alterations in intestinal anatomy [40]. Other predisposing causes are conditions with decreased gastric acid production, any condition that impairs peristalsis, following surgery. Symptoms include abdominal pain and bloating [40, 41]. The 14C–xylose test showed high specificity (89%) and low sensitivity (30%) compared to duodenal culture and is the best predictor of high bacterial counts [41]. Treatment is with non-absorbable antibiotics like rifaximin [42] or broad-spectrum antibiotics such as tetracycline, penicillin or cephalosporin [43].

Disaccharidase Deficiency

Disaccharidase enzyme is an apical membrane enzyme of the surface absorptive cells which cleaves lactose. The surface of the small intestine is made up of tiny finger-like structure, villi, with additional extensions called microvilli forming the apical brush border [44]. With the enzyme deficiency, the lactose remains in the lumen and exerts an osmotic pull and leads to diarrhoea and malabsorption [45]. Bloating, cramps and diarrhoea occur after intake of milk products. Weight loss and steatorrhoea are mild. Diagnosis is by trial of abstinence, abnormal lactose tolerance test and hydrogen breath test.

Pancreatic Insufficiency Following Chronic Pancreatitis

Chronic pancreatic insufficiency and intestinal bacterial overgrowth are syndromes specific to the elderly [14]. In a study of 70 patients over the age of 65 years, 14 had pancreatic insufficiency, and most of them had no history of pain, alcoholism or gallstones [46]. It is only after several years in the natural history of chronic pancreatitis does diarrhoea, steatorrhoea and diabetes occur. Chronic pancreatitis is characterized as asymptomatic or recurrent attacks of pain at varying intervals. The stools become bulky, frothy and greasy, and excessive diarrhoea can be life-threatening. Serum trypsin levels are reduced. In moderate to severe disease, the faecal elastase−1 test is reliable and is widely used [47] and alternatively the 13C mixed triglyceride breath test [48].

Symptomatology of Malabsorption

The clinical presentation in malabsorption is diarrhoea, steatorrhoea and weight loss. Other manifestations include abdominal discomfort, bloating, distension [36], borborygmi, anorexia or hyperphagia, nausea and vomiting with muscle wasting [49]. Cramp-like lower abdominal pain precedes bowel movement. Associated symptoms are that of the severity of the caloric and vitamin deficiencies. About 60–80% of the elderly with coeliac disease may have anaemia [50, 51].

Approach to Patient with Malabsorption

A careful history and physical examination will help to determine the remaining evaluations and direct towards specific laboratory, imaging and invasive studies. The history should include the current complaint, the history of the complaint as to mode of onset and duration of symptoms, bowel habits and recent history of travel abroad. A general system enquiry about loss of weight or skin rash. A full enquiry is about past illnesses such as pancreatitis, liver disease, diabetes mellitus, gastrointestinal symptoms, abdominal surgery and the respiratory system. A family history may be relevant as in coeliac disease where there be evidence of family clustering and in abetalipoproteinaemia which exhibits familial, autosomal recessive inheritance [25]. Details of social history include dietary history, medication and drinking habits.

Physical examination should include assessment of the patients' current weight and body mass index (BMI) together

Table 25.1 Laboratory studies in the diagnosis of malabsorption syndromes

Studies	Coeliac disease	Small intestine bacterial overgrowth	Chronic pancreatic insufficiency
Full blood count	Microcytic/ iron, deficiency, macrocytic/folic acid or dimorphic	Macrocytic, anaemia	To evaluate anaemia
Vitamin B12	Frequently low	Low or normal	Low
Red cell folate	Normal	High or normal	–
Serum calcium	Low	–	Low
Serum magnesium	Low	–	–
Serum amylase, lipase	–	–	Elevated
Circulating antibodies-gliadin	Poor sensitivity and specificity	–	–
Endomysial	Increased		
Tissue transglutaminase	Increased		
Pancreatic function tests	–	–	After IV secretin-cholecystokinin-lipase bicarbonate, proteolytic enzymes reduced
Breath tests			
C-13-xylose	High sensitivity and Specificity	–	–
C-14-xylose			
Hydrogen using glucose or lactulose	–	Useful	
13C mixed triglyceride	–		Useful
Faecal fat estimation faecal fat excretion	>7 g/day after 3 day ingesting at least 100 g fat daily	Useful	>6 g faecal fat /24 h after ingesting at least 100 g of fat per day faecal elastase-1 test

Information sources: Tivet et al. [52], Simren et al. [53], and Dominque-Munoz [54]

with general inspection of oral cavity, especially the dentition and ability to swallow, for pallor, rash, easy bruising, oedema and evidence of signs of specific deficiencies. A full examination of the respiratory, cardiovascular, abdominal and neurological systems is indicated.

Pertinent laboratory for diagnosing patients with common malabsorption syndromes is shown in Table 25.1. Breath tests are noninvasive and assist in diagnosis of a variety of gastrointestinal problems. For coeliac patients C-13-xylose and C-14-xylose tests are useful and have an 84–98% sensitivity and 87–94% specificity [52]. Hydrogen breath tests usually with glucose or lactulose for SIBO [53] and 13-C-triglyceride breath test [54] for pancreatic exocrine insufficiency are helpful in their diagnosis.

Clinical Relevance in Malabsorption

Malabsorption is present in the elderly more often than is realized, and symptoms resulting from malabsorption tend to be muted in the elderly [14].

The clinical presentation in malabsorption is diarrhoea, steatorrhoea and weight loss. Other manifestations include abdominal discomfort, bloating, distension, borborygmi, anorexia or hyperphagia, nausea and vomiting with muscle wasting [36].

Coeliac disease, a chronic malabsorption disease, is characterized by intolerance to gluten found in wheat, rye and barley.

Small intestine bacterial overgrowth (SIBO) can result in malabsorption of carbohydrates, fats and micronutrients.

Disaccharidase enzyme is an apical membrane enzyme of the surface absorptive cells which cleaves lactose; the lactose remains in the lumen and exerts an osmotic pull and leads to diarrhoea and malabsorption [45].

In chronic pancreatitis there is weight loss and the stools become bulky, frothy and greasy, and excessive diarrhoea can be life-threatening.

Multiple Choice Questions

1. The following in relation to malnutrition in the elderly dementia patients are true. EXCEPT:
   A. With ageing there is decreased food intake referred to as *anorexia of ageing.*
   B. There is a high prevalence of malnutrition among hospitalized and institutionalized patients.

C. Therapeutic diets are often palatable and well tolerated.
D. Many dementia patients develop apraxia of swallowing and have to be constantly reminded to swallow.

Short Answer Questions (SAQs)

1. List four factors associated with ageing which may contribute to nutritional inadequacy in the elderly.

SAQ Depressed

1. smell
2. taste
3. gastric emptying
4. food intake

2. Extended Matching Questions (EMQs)
   1. Vitamin D deficiency
   2. Vitamin A deficiency
   3. Niacin deficiency
   4. Thiamine deficiency
   5. Vitamin K deficiency
   6. Vitamin B12 deficiency
   7. Iodine deficiency
   8. Iron deficiency

EMQs

1. A = 5
2. B = 2
3. C = 6
4. D = 3
5. E = 4

2. Match the specific deficiencies with the most characteristic signs and symptoms listed below. Use each answer only once.
   A. Easy bruising, bleeding
   B. Night blindness, impaired dark adaptation
   C. Loss of memory, depression, anaemia and neurological deficits
   D. Cutaneous mucous membrane lesions – stomatitis, glossitis, diarrhoea
   E. Polyneuritis, Wernicke's encephalopathy, Korsakoff's syndrome
3. The following are true in relation to absorption and digestion EXCEPT:
   A. Luminal availability of B12 is not affected by bacterial overgrowth.
   B. The fats are broken down to triglycerides and fatty acids in assumable forms.
   C. Deficiency of lactase in the brush border of the small intestine impairs breakdown of the unabsorbable disaccharides.
   D. After absorption the nutrients enter the systemic circulation via the portal vein and via the thoracic duct.
4. The following causes of malabsorption are true EXCEPT:
   A. Coeliac disease presents in three peaks in infancy, in the third decade and in the fifth or sixth decade.
   B. Small intestine bacterial overgrowth can result in malabsorption of carbohydrates, fats and micronutrients.
   C. Within a few weeks in the natural history of chronic pancreatitis diarrhoea, steatorrhoea and diabetes occur.
   D. Disaccharidase enzyme is an apical membrane enzyme of the surface absorption cells that cleaves to lactose.

MCQs Answers

1. C
3. A
4. C

Appendix 1: Mini-Nutritional Assessment

Mini Nutritional Assessment
MNA®

Nestlé Nutrition Institute

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

Complete the screen by filling in the boxes with the appropriate numbers. Total the numbers for the final screening score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F1 Body Mass Index (BMI) (weight in kg) / (height in m)²
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

IF BMI IS NOT AVAILABLE, REPLACE QUESTION F1 WITH QUESTION F2.
DO NOT ANSWER QUESTION F2 IF QUESTION F1 IS ALREADY COMPLETED.

F2 Calf circumference (CC) in cm
0 = CC less than 31
3 = CC 31 or greater ☐

Screening score (max. 14 points)

12 - 14 points: Normal nutritional status
8 - 11 points: At risk of malnutrition
0 - 7 points: Malnourished ☐☐

References
1. Vellas B, Villars H, Abellan G, *et al.* Overview of the MNA® - Its History and Challenges. *J Nutr Health Aging.* 2006; **10**:456-465.
2. Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: Developing the Short-Form Mini Nutritional Assessment (MNA-SF). *J. Geront.* 2001; **56A**: M366-377
3. Guigoz Y. The Mini-Nutritional Assessment (MNA®) Review of the Literature - What does it tell us? *J Nutr Health Aging.* 2006; **10**:466-487.
4. Kaiser MJ, Bauer JM, Ramsch C, *et al.* Validation of the Mini Nutritional Assessment Short-Form (MNA®-SF): A practical tool for identification of nutritional status. *J Nutr Health Aging.* 2009; **13**:782-788.

For more information: www.mna-elderly.com

References

1. White JV, Guenter P, Jensen G, Malone A, Schofield M, the Academy Malnutrition Work Group, et al. Consensus statement: Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). J Parenter Enteral Nutr. 2012;36(3):275–83.
2. Sullivan DH. Undernutrition in older adults. Ann Long Term Care. 2000;8:41–6.
3. Cederholm C, Hellerstrom K. Nutritional status in recently hospitalized and free-living elderly subjects. Gerontology. 1992;38:105–10.
4. Hart PD. Research Associates Inc. Nutrition screening initiative: telephone survey of 750 doctors, nurses and health care administrators. 1–8 Apr 1993.
5. Wallace JI. Malnutrition and enteral/parenteral alimentation. In: Hazzard WR, Blass JP, Ettinger WH, Halter JB, Ouslander JG, editors. Principles of geriatric medicine and gerontology. 4th ed. New York: McGraw-Hill; 1999. p. 1455–69.
6. Ennis BW, Saffel-Shrier S, Verson H. Diagnosing malnutrition in the elderly. Nurse Pract. 2001;26(3):52–6, 61-2,65.

7. Pablo AMR, Izaja MA, Aldey LA. Assessment of nutritional status on hospital admission: nutritional cores. Eur J Clin Nutr. 2003;57:824–31.
8. Silver AJ, Morley JE, Strome LS. Nutritional status in an academic nursing home. J Am Geriatr Soc. 1988;36:487–91.
9. Shaver HJ, Loper JA, Lutes RA. Nutritional status of nursing home patients. J Parenter Enter Nutr. 1980;4:367–70.
10. Muncie HJ, Carbonetto C. Prevalence of protein-calorie malnutrition in an extended care family. J Fam Pract. 1982;14:1061–4.
11. Braunschwerg C, Gomez S, Sheean PM. Impact of declines in nutritional status on outcomes in adult patients hospitalized for more than 7 days. J Am Diet Assoc. 2000;100:1316–22.
12. Middleton MH, Nazarenko O, Nivison-Smith J, Smerdely P. Prevalence of malnutrition of malnutrition and 12 month incidence of mortality in two Sydney teaching hospitals. Intern Med J. 2001;1:455–61.
13. Ferguson M, Bauer J, Binks M, Capra S. Coding for malnutrition enhances re-imbursement under case-mix-based finding. Aust J Nutr Diet. 1997;54:102–8.
14. Holt PR. Diarrhoea and malabsorption in the elderly. Gastroenterol Clin N Am. 2009;30:427–44.
15. McEvoy A, Dutton J, James OF. Bacterial contamination of the small intestine is an important cause of occult malabsorption in the elderly. BMJ. 1983;27:789.
16. Dudrik SJ. Eating disorders' prevalence increases. Todays Geriatr Med. 2013;6(4):18.
17. Morley JE, Keimar VB, Mattammal MB. Inhibition of feeding by nitric oxide synthase inhibitor effect of aging. Eur Pharmacol. 1996;15:311–5.
18. Seiler WO, Stahelin HB. Special aspects of malnutrition in geriatrics. Schweiz Med Wochenschr. 1995;125(5):149–58.
19. Hajjar RR, Kamel HK, Denson K. Malnutrition in aging. Internat J Geriatr Gerontol. 2004;191:1–5.
20. Coulston AM, Mendelbaum D, Reaven GM. Dietary management of nursing home residents with non-insulin dependent diabetes mellitus. Am J Clin Nutr. 1990;51:67–71.
21. Rosen N. Anorexia nervosa in the elderly. Eat Disord Rev. Website. http://www.eatingdisordersreview.com/nl/nl.edt 3html. 2010.
22. Nagaratnam N, Ghougassion D. Anorexia nervosa in a 70-year old man. Br Med J. 1988;29:1443–4. N. X0.
23. Schneider SM, Hebutenne X. Use of nutritional scores to predict clinical outcomes in chronic disease. Nutr Rev. 2000;1:31–8.
24. Guigoz V, Vellas B, Garry PJ. Mini-nutritional assessment: a practical assessment tool for grading the nutritional status of elderly patients. Facts Res Gerontol. 1994;4(Suppl 2):15.
25. Vellas BJ, Guigoz Y, Garry PJ, Nourshemi F, Bennahum D, Lauque E, et al. The mini-nutritional assessment (MNA) and its use in grading the nutritional state of elderly people. Nutrition. 1998;14:116–22.
26. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The mini nutritional assessment. Clin Geriatr Med. 2001;18(4):737–57.
27. Detsky AS, Baker JP, Mandelson RA. Evaluation of the accuracy of nutritional assessment techniques applied in hospitalized patients and comparisons. JPEN. 1984;8:153.
28. Seltzer MA, Bastidas JA, Cooper DM. Instant nutritional assessment. J PEN J Parenter Enteral Nutr. 1979;3:157.
29. Lansey S, Waslien C, Mulvihill M, Filit H. The role of anthropometry in the assessment of malnutrition in the hospitalized frail elderly. Gerontology. 1993;39(6):346–53.
30. Evans C. Malnutrition in the elderly: a multifactorial failure to thrive. http://xnet.kp.org/permanente/sum05/elderly.html. 2008
31. Muche JA. Geriatric rehabilitation. Malnutrition. Medscape. http://emedicine.medscape.com/article/38521-overview#a5. Accessed 26 Jan 2017.
32. Hodgson RS. Malnutrition: why should we care? Editorial. Intern Med J. 2013;43:473–5.
33. Labtest Online-Malnutrition website: http://www.labtestonline.org.au/understanding/conditions/malnutrition-3.html. Retrieved 16 Apr 2008.
34. Owens SR, Greenson JK. The pathology of malabsorption: current concepts. Histopathology. 2007;50:64–82.
35. Murray JA, Rupio-Tapia A. Diarrhoea due to small bowel diseases. Best Pract Res Clin Gastrenterol. 2012;26(5):581–600.
36. Rashtak S, Murray JA. Coeliac disease in the elderly. Gastroenterol Clin N Am. 2009;38(3):433–46.
37. Leffler DA, Schuppan D. Update in serologic testing in coeliac disease. Am J Gastroenterol. 2010;105(12):2520–4.
38. See J, Murray JA. Gluten free diet: the medical nutritional management of coeliac disease. Nutr Clin Pract. 2006;21(1):1–15.
39. Quigley EM, Quera R. Small intestinal overgrowth, roles of antibiotics, prebiotics and probiotics. Gastroenterology. 2000;130(2suppl1):S78–90.
40. Saltzman JR, Russel RM. Nutritional consequences of intestinal bacterial overgrowth. Compr Ther. 1994;20(0):523–30.
41. Donald IP, Kitchingmam G, Donald F, Kupfer RM. The diagnosis of small bowel bacterial overgrowth in elderly patients. J Am Geriatr Soc. 1992;40(7):692–6.
42. Lauritano EG, Gabrelli M, Lupascu AS, Antoliquido A, Nucera G, Scarpellini E, et al. Rifaximin dose-finding study in the treatment of small intestinal bacterial overgrowth. Aliment Pharmacol Ther. 2005;22(1):3105.
43. Singh VV, Toskes PP. Small intestinal bacterial overgrowth ; presentation diagnosis and treatment. Curr Treat Options Gastroenterol. 2004;7(11):19–28.
44. Ingram CJE, Swallow DM. Lactose malabsorption. In: Advanced dairy chemistry: New York: Springer; 2009. p. 203–29.
45. Robbins S, Cotran RS, Kumar V. Pocket companion to Robbins pathologic basis of disease. 5th ed. Philadelphia: WN Saunders Company; 1995.
46. Montgomery RD, Haboubi NY, Mike NH, Chesner M, Asquith P. Causes of malabsorption in the elderly. Age Aging. 1986;15(4):235–40.
47. Lankisch PG, Schmidt I, Konig H, Lehnick D, Knollmann R, Lohr M, et al. Faecal elastase −1 not helpful in diagnosing chronic pancreatic associated with mild to moderate exocrine insufficiency. Gut. 1988;42:511–54.
48. Dominguez Munoz JE, Igelesa-Garcia J. Velarino –I nM. 13-C mixed triglyceride breath test to assess oral enzyme substitution therapy in patients with chronic pancreatitis. Clin Gasteroenterol Hepatol. 2007;5:484–8.
49. Kerr M. Malabsorption syndrome. Health Line. http://www.healthline.ca/health/malabsorption#overview. Retrieved 10 Feb 2015.
50. Freeman H. Clinical spectrum of biopsy-defined coeliac disease in the elderly. Can J Gastroenterol. 1995;9(1):42–61.
51. Hankey GL, Holmes GK. Coeliac disease in the elderly. Gut. 1994;35(1):65–7.
52. Tvelto K, Brunborg C, Sandvik L, Loberg EM, Shar V. C-13-xylose and C-14-xylose breath tets for coeliac disease. Scand J Gasroenterol. 2008;43:166–73.
53. Simren M, Stotzer P-O. Use and abuse of hydrogen breath tests. Gut. 2006;55(3) https://doi.org/10.1136/gut.2005/075627.
54. Dominquez-Munoz JE. Pancreatic exocrine insufficiency: diagnosis and treatment. J Gastroenterol Hepatol. 2011;26(suppl 2):12–6.

Constipation, Faecal and Urinary Incontinence

26

Gary Cheuk and Nages Nagaratnam

Constipation

Introduction

The prevalence of constipation increases with age [1], and it is a common condition in the elderly over the age of 65 years [2]. The estimated prevalence of constipation is highly variable from 2% [3] to 28% [4]. Older men and women are equally affected and are often related to multiple age-related problems which may account for the increased prevalence in older people. About three-quarters of the elderly hospitalised patients and nursing home residents use laxatives for bowel regulation [5]. Constipation occurs in about half the number in nursing homes and 15–20% of the community dwelling elderly [6]. Chronic constipation is often a cause of great discomfort and often affects quality of life negatively [7]. It may be a sign of a more serious underlying problem such as mass lesions or colonic dysmotility [8].

Slow colon transit, irritable bowel syndrome and pelvic floor dysfunction are three distinct pathophysiologies causing constipation [9]. Normal defaecation begins with the passage of faecal bolus into the rectum. The rectum distends and there is transient relaxation of the internal anal sphincter. Continence is preserved by the contraction of the external anal sphincter. If the individual complies and adopts a squatting position, the anorectal angle becomes straightened. A Valsalva manoeuvre increases the intra-abdominal pressure and overcomes the resistance of the external anal sphincter. The pelvic floor descends, and pressure on the faecal mass increases the intrarectal pressure. The internal anal sphincter, the external anal sphincter and the puborectal muscle relax synchronously, and the faecal mass is discharged. The sympathetic pathway to the IAS emerges from the 5th lumbar segment. The IAS is also supplied by the preganglionic parasympathetic fibres that emerge from the second, third and fourth sacral segments. The EAS is supplied by the inferior rectal nerves and by the perianal branch of the 4th sacral nerve, and the reflex has its afferent and efferent pathway in the pudendal nerve. The fibres in the pelvic splanchnic nerves reach the intestines by way of plexuses.

Many age-related problems such as multiple medical conditions, increased use of medications, decreased mobility and dietary changes, such as reduced fibre intake, due to poor chewing, contribute to constipation. Frailty and bedriddeness and weak straining ability also contribute to the increased prevalence of constipation in this group [10]. Drug-induced constipation is the use of medications that affect the central nervous system, nerve conduction and smooth muscle fibres. Drugs that are associated with constipation are the anticholinergics, narcotics and dopaminergics [10]. Other causes of secondary constipation are the neurological diseases, endocrine and metabolic dis-

G. Cheuk (✉)
Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia
e-mail: gcheuk@optusnet.com.au

N. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_26

eases, psychological conditions and structural abnormalities (Box 26.1).

Box 26.1 Causes of Constipation

A. Functional
- Functional activity
- Psychological
- Life-style changes
  - Insufficient water intake
  - Low fibre diet
  - Changes in routine
  - General immobility

B. Organic/secondary
- I. Neurological-cerebrovascular disease, autonomic neuropathy, multiple sclerosis, Parkinson's disease, spinal cord injury, diabetic neuropathy
- II. Endocrine/metabolic – hypothyroidism, hyperparathyroidism; hypercalcaemia, uraemia, diabetes mellitus
- III. Psychiatric – depression, anxiety
- IV. Structural lesions – obstructive lesions (mass lesions), rectal prolapse, rectocele, haemorrhoids, anal fissure, inflammatory disease of the bowel
- V. Organic intestinal lesions: obstruction; cancer, diverticulitis, faecal impaction and anorectal abnormalities
- VI. Drugs – especially those affecting the central nervous system, nerve conduction and smooth muscle function – NSAIDs, opioids, anticholinergics, analgesics and diuretics, among others.

Information sources: De Giorgio et al. [11]; Choung et al. [12]; Schaeffer et al. [8]; Rao and Go [13].

Evaluation of Patient with Constipation

Evaluation of a patient is based on (i) history of the symptoms, (ii) physical examination with focus on the underlying cause and (iii) investigations.

1. History should include a past medical history, for instance, dementia, diabetes mellitus, drug history, weight loss, pain, change in bowel habits, change in dietary habits, hydration, physical activity and psychological factors.
2. Physical examination includes a general examination – signs of systemic illness, abdominal mass, local haemorrhoids, fissures, digital rectal examination and sphincter tone.
3. Investigation – stool screened for occult blood, plain X-ray of the abdomen, bowel obstruction, volvulus, mass lesions, extent of faecal retention and megacolon and flexible sigmoidoscopy in patients without any obvious cause. In those with change in bowel habits, further diagnostic evaluation-include colonoscopy and if the constipation is refractory referral to specialist -anorectal manometry, colonic transit time, defaecography or a balloon expulsion test.

Management

If there is no secondary cause to be found, non-pharmacological measures will be the first step to improve bowel regularity, and this will include increased fluid intake, high fibre intake and regular physical exercise [6]. If this not successful, then proceed to the use of laxatives. The first-line agents recommended are the bulk-forming and osmotic laxatives. The former increases stool mass and softness by absorbing water from the intestinal lumen, thereby increasing the stool bulk. Some may cause bloating and gas formation [8]. Patients with functional normal transit constipation benefit most, but the need to maintain good hydration is a limitation in the use of bulk-forming laxatives especially in frail elderly patients [6]. The osmotic laxatives cause secretion of water into the intestinal lumen by osmotic activity. It has been shown to relieve faecal impaction in frail patients with neurological disease, but a serious limitation is the patients are at high risk of aspiration [6]. If the patients do not respond to the above two, stimulant laxatives are used as intermittent treatment. The prokinetic agents act by increasing intestinal motility. Tegaserod maleate, a 5HT4 presynaptic receptor agent which enhances peristaltic reflex and increases colonic motility, has been suspended in the United Kingdom and Canada due to concerns regarding serious cardiovascular events [14].

Faecal Impaction

Faecal impaction is a common problem in the elderly and closely associated with chronic or severe constipation, structural anorectal abnormalities and neurological or functional gastrointestinal disorders [15]. The hospitalised and institutionalised patients are at high risk [16] and are associated with increased morbidity and mortality [15]. Complications attributed to faecal impaction include bowel obstruction

Table 26.1 Medications for chronic constipation

Agent	Formula/strength	Adult dose
Bulk laxatives		
Methylcellulose (Citrucel)	Tab 500 mg	Two tabs up to six times a day
Psyllium (Metamucil)	Powder 3.4 g/tsp. with 8 oz. liquid	One to three times daily
Osmotic laxatives		
Magnesium hydroxide (milk of magnesia)	400 g/5 ml	30–60 ml/once daily
Sorbitol liquid	4.80 ml	30–150 ml/day
Stimulant laxatives		
Bisacodyl (Dulcolax)	Tab 5 mg	5–15 mg daily
Senna (Senokot)	Tab 8.6 mg	Two or four tablets daily
Cascara sagrada	Tab3 and 5	One tab daily
Stool softeners		
Docusate (calcium sulphate)	Capsule 240 mg	Once daily
Docusate sodium	Cap. 50 or 100 mg	50–300 mg daily
Prokinetic agents		
[a]Tegaseroid (zelnorm)	2 mg, 6 mg	Two times daily

Information Sources: Gartlehener et al. [14]
[a]Suspended due increased risk of cardiovascular events. (Gartlehener et al. [14])

leading to stercoral ulcer, perforation, peritonitis or cardiopulmonary collapse [15], faecal incontinence and urinary tract obstruction and can prove fatal [17].

Impacted faeces are removed by manual extraction, proximal and distal washout enema and a short-term use of laxatives. If this is not successful, polyethylene glycol is recommended [13]. The extent of the impaction may be determined using water-soluble contrast media such as Gastrografin [15]. Recurrence is common; hence a bowel regimen should be implemented [15]. Table 26.1 shows the medications used in constipation.

Clinical Relevance

Chronic constipation is a cause of great discomfort and affects quality of life [7].

Attributed to many age-related problems, multiple medical conditions, increased use of medications, decreased mobility and dietary changes, frailty and bedriddeness

First step in the management is, to non-pharmacologically improve bowel regularity, for example, increase fluid intake, high fibre diet and regular physical exercises [6].

Faecal Incontinence

Introduction

Faecal incontinence is defined as an inability to control voluntarily the internal anal sphincter with passage of faeces and flatus. There are three types of faecal incontinence: (i) urge incontinence, there is an urge but inability to make it to the toilet in time; (ii) passive incontinence, there is an involuntary loss of gas or stool without awareness; and (iii) faecal seepage, there is leakage after normal evacuation with soiling of undergarments [18]. Faecal incontinence in the elderly can be further categorised as (i) overflow incontinence, (ii) reservoir incontinence and (iii) recto-sphincteric incontinence [19, 20]. Factors involved in conserving continence are shown in Box 26.2.

Box 26.2 Conserving Continence

Sphincter integrity
Pelvic floor and mucosal seal
Bowel motility
Sensory function and co-ordination
Life-style factors
Psychological factors
Stool consistency

The true prevalence of faecal incontinence is not known but could be as high as 2.2% in the general population [21]. It is high in nursing home residents [22] and in hospitalised patients. In institutionalised patients, the prevalence had been estimated between 30% and 60% [23]. Almost 1 in 10 residents in 30 residential homes for the elderly had faecal incontinence at least once weekly [24]. In 73% of the patients, faecal incontinence had been present for over a year, and yet only 4% had been referred to the general practitioner [24]. Estimates of the prevalence of incontinence in the older adult population vary widely, but clearly it is significantly more common in older adults [25]. The number of old people is expected to increase in the future, and as the prevalence of faecal incontinence increases with increasing age, there will be more elderly with incontinence.

An understanding of the physiology of the defaecation mechanism is necessary to control the problem [26]. The rectum acts as a storage reservoir until the contents can be disposed. The pelvic floor muscles including the puborectalis muscle and the anal sphincters are essential for defaecation and to maintain continence [21]. Altered stool consistency and delivery of contents to the rectum, abnormal rectal capacity and compliance, decreased anorectal sensation and pelvic floor or anal sphincter dysfunction may result in incontinence [27].

In the elderly faecal incontinence is more often related to multiple medical diagnoses, medications, general impairment of health and social circumstances than among younger persons. The commonest cause of faecal incontinence in the female is structural damage to the anal sphincter during vaginal delivery often accompanied by injury to the pudendal nerve [28]. Vaginal delivery and chronic straining are risk factors for double incontinence, and involvement of the pudendal nerve may result in worsening of continence [29]. It has been postulated that since vaginal delivery may be more likely to cause pudendal nerve injury, Caesarian section should be protective, but a Cochrane systemic review did not confirm such hypothesis [30]. Postsurgical sphincter damage is the second commonest cause [31]. Other conditions associated with faecal incontinence are faecal impaction which is an important factor in the elderly, diarrhoeal states, connective tissue disorders, neurological impairment related to stroke, diabetes and multiple sclerosis [23]. In the elderly vision, speech and gait impairments from any cause can have an impetus on the control of continence [32].

Evaluation of a Patient with Faecal Incontinence

Faecal incontinence is of great discomfort with loss of confidence which often affects the quality of life and is socially and psychologically devastating to the patients and their families [21]. Many old people do not seek help for the problem believing that it is part of aging. This is largely due to lack of knowledge of the condition, oblivious to the treatment available and a general acceptance of the symptoms. Patients are embarrassed and reluctant to tell anyone, and both physician and patient are hesitant to talk about it [21].

A detailed clinical history and physical examination including a neurological examination are essential. Attention should be paid to the sphincters and faecal impaction. Digital rectal examination is crucial. It is important to remember the causes of loose stool such as inflammatory bowel disease, overuse of laxatives and overflow from faecal impaction can present as incontinence with a normal functioning anal sphincter [33]. Diminished sensation and lack of anal contraction ('winking') indicate an underlying neurological condition [34]. Generally patients with faecal incontinence have poor anal sphincter tone on digital examination and low anal canal pressures on manometric assessment. Diagnostic tests should be directed towards evaluation of the anorectal continence mechanisms. Anorectal manometry, pudendal nerve latency studies [35] and electromyography are part of the standard primary evaluation [27]. Radiological tests such as defaecography and anal endosonography can provide additional information [35]. Patients with double incontinence should further be evaluated by a multidisciplinary group of specialists [29]. Most patients however do not have a serious physical disorder requiring intensive investigation [34].

Management

Faecal incontinence varies in severity from minor faecal soiling to frank incontinence of solid stool. Basically faecal incontinence is either symptomatic or due to structural and sphincter damage. Choice of proper therapy will depend on the cause and severity of the incontinence. Contributory factors such as faecal impaction, overuse of laxatives and inflammatory bowel disease may present as faecal incontinence and must be corrected. If the cause for the diarrhoea is not evident, dietary measures may be helpful and in some instances antidiarrhoeals such loperamide, given after a stooling episode. Loperamide does not cross the blood-brain barrier and acts locally in the intestine and possibly on the anal sphincter [36].

Mild cases usually respond to simple medical therapy, reassurance and dietary advice. Certain foods such as excessive fruit juice can aggravate the incontinence. If the patient is incontinent with liquid or soft stool, measures to make the stool firm and to keep the rectum empty. Some will benefit by insertion of a glycerine suppository immediately after defaecation on retention for about 20 min as this will help in further evacuation of the rectum [34]. Stool-bulking agents and biofeedback are other methods employed. Biofeedback is effective in the short term in majority of the patients with faecal incontinence but is most useful in those with passive leakage and urge incontinence and, in patients with structural anal damage, can lead to some symptom improvement or cure [37]. For the biofeedback therapy to be successful, the patient has to be motivated and understand the requirements [32].

In more severe cases, a variety of therapeutic interventions, dietary, behavioural, pharmacological and surgical, are employed on the basis of the results of diagnostic testing [19]. Surgery for faecal incontinence is indicated after failure of nonoperative measures [32]. New surgical techniques include (i) dynamic graciloplasty, the gracilis muscle is wrapped around the anal canal and battery stimulation produces muscle contraction increasing the pressure [33], (ii) in patients with intact or repaired anal sphincter sacral nerve stimulation [38]. by means of percutaneous electrode in a sacral foramen and if successful a permanent pulse generator is implanted [34]. iii. An artificial sphincter is a circular cuff implanted around the anal canal and inflated to maintain sphincter closure [39].

Clinical Relevance

Faecal incontinence is common and a treatable condition.

It causes great discomfort and reduces quality of life.

Many old people do not see medical help believing the problem is part of ageing or feel embarrassed.

When faecal incontinence becomes distressful, patients seek help usually from the primary care physician.

Faecal incontinence is amenable to treatment that can be delivered in primary care [34].

Urinary Incontinence

Introduction

Urinary incontinence is one of the biggest challenges facing the elderly population. It increases with age and was found in 17% of men and 48% of women over 70 years of age, and women had eight times higher odds of having urinary incontinence than men when all ages 70–97 were pooled [40]. In another study 55% of women and 34% of men older than 65 years had urinary incontinence [41]. At least 15% of community-dwelling elderly and 50% of institutionalised elderly have significant incontinence [42]. Double incontinence (urinary and faecal) is common in community-residing elderly in Japan [43] and in the Netherlands [44] and increases with age.

Three important components that play a major role in the maintenance of continence are the detrusor muscle, internal sphincter and the external sphincter. The S2, S3 and S4 spinal segments at the lateral horns cells from which emanates the pelvic nerves. The preganglionic parasympathetic fibres travel with the pelvic nerves through the inferior hypogastric plexus to synapse with the postganglionic neurons in the adventitia of the detrusor and internal sphincter. The presacral nerves or sympathetic originate from the lower lumbar regions (L1–L2) to travel to the superior hypogastric plexus from which arises the hypogastric nerve. The hypogastric nerve consists of two distinct sympathetic receptors, the alpha-adrenergic receptors to the trigone and proximal urethra (increases tone) and the beta-receptor to the body of the urinary bladder (reduces tone causing relaxation). The pudendal nerve from the primary rami of S2–S4 supplies the external sphincter (Fig. 26.1).

Risk Factors

In the elderly the risk factors are multifactorial among them being age-related changes, comorbidity, polypharmacy and functional impairments [45]. Urinary incontinence is often attributable to medical problems or disease and general impairment of health [46, 47], many of which are more common among older adults and could disrupt the mechanisms of continence. Medications, impaired mobility and comorbidity such as depression, stroke, transient ischaemic attacks, dementia and heart failure are risk factors for urinary incontinence in older people [48]. Damage to the bladder efferent nerves in the pelvis, as in infiltrative cancer, produces a flaccid bladder and sphincter, with constant dribbling. In men stress incontinence is uncommon and is usually due to neurological disease, tumour or prior surgery to the prostate. Radical prostatectomy is complicated by urinary incontinence in a range of 5–34% [49] and following transurethral resection in less than 1% of patients [50]. In a study of a large cohort of 64,396 women, Mathews et al. [51] found that dual incontinence was primarily associated with advanced age, decompensating medical conditions, depression and multiparity. Men mostly tend to have urge incontinence, but women suffer from both urge and stress incontinence. Men do not have stress incontinence for the anatomical reason in that their urethra is long and tortuous with the sphincter and prostate helping to prevent urine loss [52]. In women the short and straight urethra and the less effective sphincter together with pregnancies are reasons for the stress incontinence [53]. In frail elderly detrusor hyperactivity with impaired contractility (DHIC) leads to increased post-void residual urine [54]. Several researchers have found a correlation between urinary incontinence and frailty [55, 56]. It has been suggested that urinary incontinence is a marker of frailty also in nonagenarians and it can also be considered as a precursor of frailty [55].

Clinical Considerations

Detrusor hyperreflexia may also contribute to urgency [57] due to increased afferent signalling, and urge incontinence is the most common form in older men and increases with age [58]. In stress incontinence the loss of urine is caused by activities such as exercise, coughing, laughing and sneezing and associated with increased intra-abdominal pressure and decreases with age [56, 58, 59]. In older women parity hardly contributes to stress incontinence compared to the younger and middle-aged [58]. Overflow incontinence is the involuntary loss of small amounts of urine or a constant leak from a full bladder. This results from inability of the bladder to empty completely due to

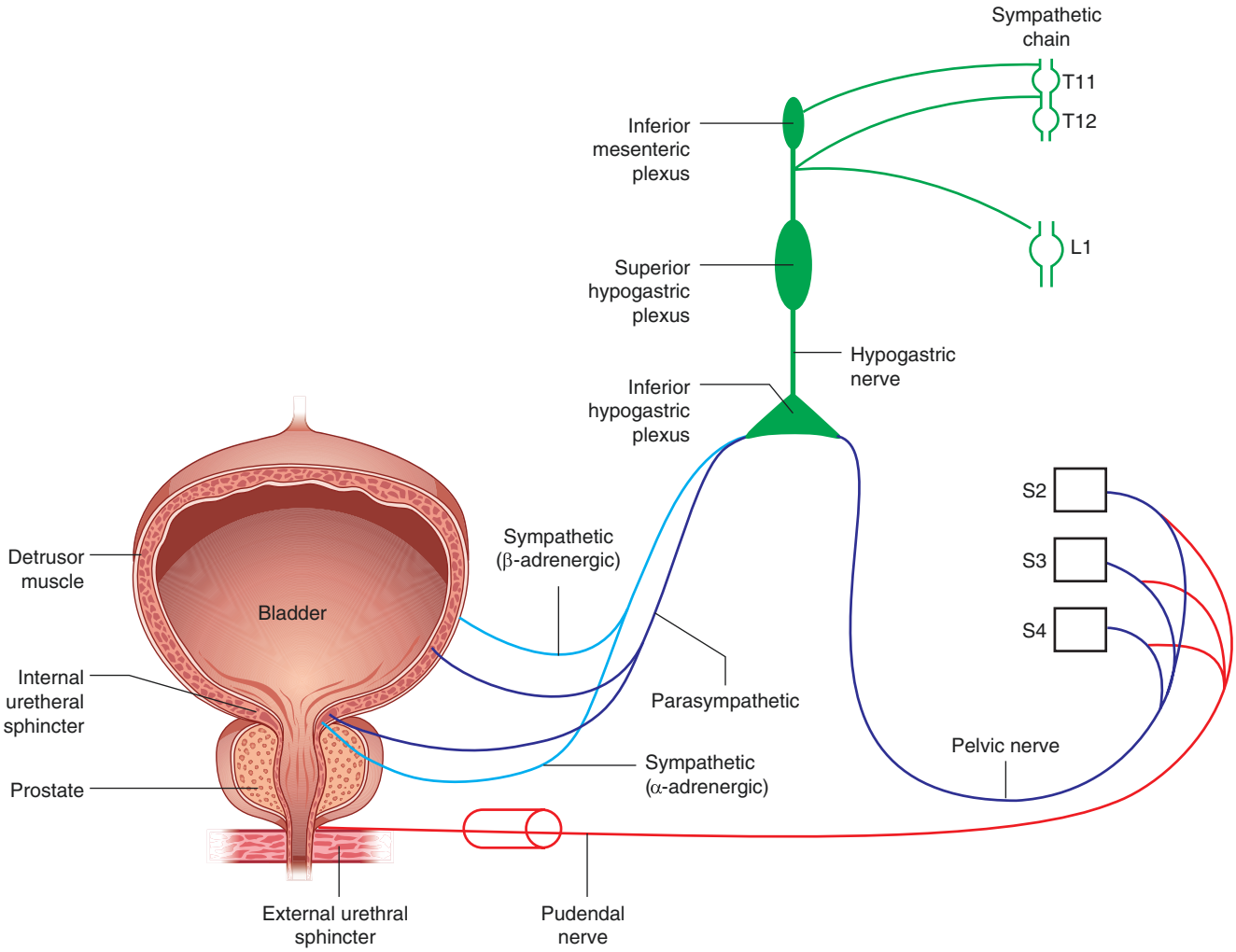


Fig. 26.1 Neuroanatomy and physiology of normal micturition

contractile dysfunction or when the flow of urine is blocked [59]. The causes include benign hypertrophy of the prostate; medications such as sedatives, antidepressants, antipsychotics and anticholinergics; neurological causes such as spinal cord injuries; and medical conditions such as diabetes and multiple sclerosis. They have frequent or constant dribbling of urine. Another type of incontinence is functional incontinence. Persons with physical disability or a medical condition may have difficulty in reaching the toilet [56]. In the elderly common voiding problem is urgency with urge incontinence, and bladder overactivity is a common underlying factor [60].

It is useful to categorise the problem into acute and chronic forms. The acute form is often remediable, for example, the post-stroke UI patient is prone to delirium, recurrent urinary tract infections, faecal impaction, constipation, restricted mobility and numerous medications which can contribute to the UI [57, 59]. The chronic forms are classified as urge, stress, mixed, overflow and functional.

UI is physically and emotionally disruptive [61] and in general has a negative impact on the quality of life through multiple effects on daily activities or interpersonal relationships [62]. Urinary incontinence is associated medically with sepsis, recurrent urinary tract infections, decubitus ulcers, decreased mobility, increased mortality [63], restriction of social and sexual activities, dependency and depression [64]. It affects the physical well-being of the patient and has a negative effect on the patient's quality of life. The dissatisfaction with the quality of life has been attributed to social and psychological problems [62]. These include loss of independence, inability to work, diminished self-esteem and depression [64]. The patients with urinary incontinence do not tell anyone because they are embarrassed and ashamed [65]. Apart from social and psychological consequences, it results in high rates of institutionalisation. Furthermore, it not only has direct consequences for the patients and their relatives but also has an economic impact on the health system. The annual cost of urinary incontinence has been estab-

lished to account for 2% of the total health costs in the United States and Sweden [66, 67].

Assessment and Management

In most patients with the history, physical examination, urine analysis, urine culture and measurement of post-void residual urine (PVR), a diagnosis can be made. The history should include the onset of urinary incontinence, frequency, volume, timing, associated events and medications [58]. Physical examination should include cognitive and functional assessments, rectal and vaginal examinations, a meticulous neurological examination and a cystoscopy only for haematuria or unexplained pelvic pain [58]. A clinical stress test in patients with stress UI may be helpful [58]. In a study of asymptomatic perimenopausal and postmenopausal women, the investigators [68] found the PVR urine volume to be less than 50 ml in most of the women. According to the AHCPR clinical guidelines for urinary incontinence in adults [69], a PVR of less than 50 ml is indicative of satisfactory bladder emptying and a PVR of more than 200 ml unsatisfactory emptying. However, there are no recommendations as to the implication of PVR between 50 and 200 ml [69].

Treatment of UI includes behavioural and pharmacological interventions. Correction of reversible and contributing factors is all-important [58]. For example, if confusion can be reduced and mobility restored, continence too will often return [70]. Patients who recognise their incontinence, attention-focused training is an effective measure in re-establishing bladder control [71]. The avoidance of caffeinated beverages and alcohol and minimising evening fluid intake and cessation of smoking may be helpful especially in patients with stress incontinence [58]. In those with overflow bladder, life-style changes such as reduction in weight and in caffeine intake may help.

Behavioural techniques include Kegel's exercises, bladder training and bladder drill, prompted voiding, urge suppression and timed voiding [62]. Pelvic muscle exercises are effective for urge, stress and mixed UI [57, 59]. When they do not respond to behavioural techniques, anticholinergics and bladder training are options. Drugs with anticholinergic [59] and smooth muscle relaxant properties (oxybutynin, solifenacin, darifenacin, trospium and tolterodine) are effective for urge incontinence and overactive bladder and have similar efficacy [58]. The side effects include dry mouth, constipation, confusion and blurred vision. Alpha-adrenergic drugs are used in stress incontinence and can be combined with oestrogen therapy in women, and surgical treatment can be highly effective in properly selected women [61]. Imipramine can be used for both stress and urge incontinence. On the other hand cholinergics (bethanechol) and alpha-adrenergic blocker (prazosin) which stimulates bladder contractions and relax the sphincter are used in overflow UI (Fig. 26.2).

Clinical Relevance

Urinary incontinence increases with age and was found to be 17% in men and 48% in women aged 70 years of age [40].

It affects the physical well-being of the patient and has a negative effect on the patient's quality of life [62].

It results in high rates of institutionalisation.

In both men and women, the ability to postpone voiding bladder capacity and urinary flow rate declines with age.

Urinary incontinence should not be considered a part of ageing.

It is useful to categorise the problem into urge, stress, mixed and overflow incontinence.

Most men tend to have urge incontinence, but women suffer from both urge and stress incontinence.

Treatment of UI includes behavioural and pharmacological interventions.

Case Study

An 86-year-old presented with voiding problems. Six months earlier she has had a stroke which left her with weakness of the left side of her body, the arm more than the leg. She could now walk independently but slowly. She had developed urinary incontinence during her stay in hospital and has had an indwelling catheter for several weeks following the stroke and which was removed a day before she was discharged from hospital. She has been incontinent since then. On returning home she has a compelling desire to void and has had several episodes of wetting herself between the bed and the toilet. On many occasions while in the garden watering with a hose, she has had the urge to void and was incontinent. She restricts fluid intake whenever she has to go out. She continues with Kegel's exercises which were started when she was in hospital.

In all probability she has urge incontinence related to the stroke, an overactive bladder and functional incontinence due to being confined to the bed and decreased mobility. She has hypertension for which she is on hydrochlorothiazide 12.5 mg daily and SR 240 mg verapamil daily. She was diagnosed with mild dementia prior to the stroke and has been on donepezil for several months. She continues on the donepezil for according to her it has done some good although it can increase bladder contractions. Even though anticholinergics should be avoided in patients with dementia more so when

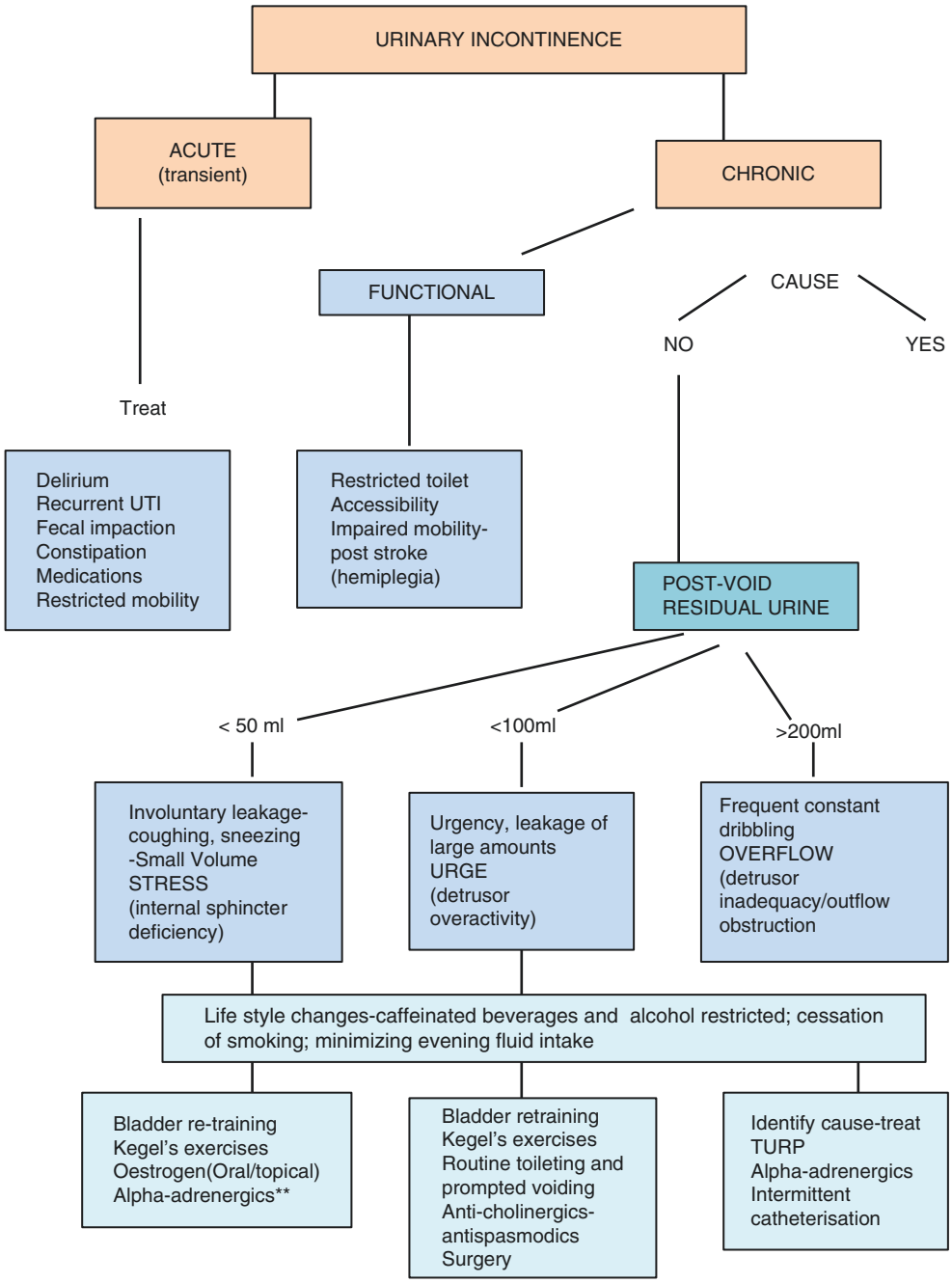


Fig. 26.2 Evaluation and management of urinary incontinence. (Information sources:Frank & Szlanta [57]; Merkel [59]; Ouslander [61]; AHCPR [69] ** with caution in elderly women Anticholinergics: Oxybuytrin (ditropin); Solifnacin (Vesicare); Trospium (Trosec); Darienacin (Enablex; Toterodine (Detrol). Alpha-adrenergic terazosin (Hytrin);tamsulasin (Flomax))

they are on a cholinesterase inhibitor, she was commenced on oxybutynin 2.5 mg at bed time, and this was increased to 5 mg daily. The hydrochlorothiazide was ceased. She remains on the verapamil, a non-dihydropyridine calcium channel blocker which reduces bladder contractions and may be useful in the treatment of detrusor hyperactivity.

Multiple Choice Questions

Answers at the end of References

1. The following in relation to constipation are true EXCEPT:
   A. Constipation in the elderly may be a sign of a more serious underlying problem such as a mass lesion.
   B. Constipation is three bowel movements per fortnight.
   C. Frailty and bedridden contributes to increased prevalence.
   D. Increased use of medications with side-effect profile is an important cause of constipation in the elderly.
2. In the management of chronic constipation in the elderly, the following are true EXCEPT:

A. First step is to improve bowel regularity – increased fluid intake, high fibre diet and physical exercise.
B. Bulk-forming laxatives increase stool mass softness by absorbing water from the intestinal lumen.
C. Impacted faeces are removed by enema, stool softeners and long-term use of laxatives.
D. Osmotic laxatives cause secretion of water into the lumen by osmotic activity.

3. The following are true of faecal incontinence, EXCEPT:
A. Faecal impaction is associated with faecal incontinence.
B. In the elderly faecal incontinence is more often related to multiple medical diagnoses.
C. Postsurgical sphincter damage is the commonest cause.
D. Diminished sensation and lack of anal contraction 'winking' indicate an underlying neurological condition.
4. The following are true of urinary incontinence, EXCEPT:
A. In men stress incontinence is uncommon.
B. In the elderly common voiding problem is urgency with urge incontinence, and bladder overactivity is a common underlying factor.
C. In frail elderly detrusor hyperactivity with impaired contractility (DHIC) leads to decreased post-void residual urine (PVR).
D. A PVR of less than 50 ml is indicative of satisfactory bladder emptying.

MCQ Answers

1. A
2. B
3. C
4. C

References

1. Gallagher P, O'Mahony D. Constipation in old age. Best Pract Res Clin Gastroenterol. 2009;23(6):875–87. https://doi.org/10.1016/j.bpg.2009.09.001.
2. Brandt LJ, Prather CH, Quigley EM, Schiller LC, Schoenfeld P, Talley NJ. Systematic review on the management of chronic constipation in North America. Am J Gastroenterol. 2005;100(Suppl 1):S5–S21.
3. Sonnenberg A, Koch T. Epidemiology of constipation in United States. Dis Colon Rectum. 1989;32:1–8.
4. Stewart WF, Liberman JN, Sandler RS, Woods MS, Stemhaagen A, Chee E, et al. Epidemiology of constipation (EPOC) in the United States: relation of clinical subtypes to socio-demographic features. Am Gastroenterol. 1999;94:530–40.
5. Primrose WL,Caperwell HE, Simpson GK, Smith RG. Prescribed patterns observed in registered nursing homes and long stay geriatric wards. Age and Aging 1987;16:28–8.
6. Bosshard W, Dreher R, Schnegg J-F, Bula CJ. The treatment of chronic constipation in elderly people: an update. Drugs Aging. 2004;21:911–30.
7. Talley NJ, O'Keefe EA, Zinsmeister AR, Melton LJ 3rd. Prevalence of gastrointestinal symptoms in the elderly: a population based study. Gastrenterology. 1992;102:895–901.
8. Scheffer DC, Cheskin LJ. Constipation in the elderly. Am Fam Physician. 1998;58(4):907–14.
9. Mertz H, Naliboff B, Mager E. Physiology of refractory chronic constipation. Am J Gastroenterol. 1998;94(3):608–15.
10. Miller-Lissner S. General geriatrics and gastroenterology: constipation and faecal incontinence. Best Prac Res Clin Gastroenterol. 16:115–33.
11. De Giorgio R, Ruggeri E, Stanghellini V, Eusebi LH, Bazzoli F, Chiarioni G. Chronic constipation in the elderly: a primer for the gastroenterologist. BMC Gastroenterol. 2015;15:130. https://doi.org/10.1186/s12876-015-0366-3.
12. Choung RS, Rey E, Richard Locke G 3rd, Schleck CD, Baum C, Zinsmeister AR, et al. Chronic constipation and co-morbidities: a prospective population-based nested case-control study. United Eur Gastroenterol J. 2010;4(1):142–51.
13. SSc R, Go JT. Update on the management of constipation in the elderly: new treatment options. Clin Interv Aging. 2010;5:163–71.
14. Gartlehner G, Jonas DE, Morgan LC, Ringel Y, Hanen RA, Byrant CM, et al. Drug class review: constipation drugs: final report [Internet]. Portland (OR): Oregon Health & Science University. 2007. https://www.ncbi.nim.nih.gov/books/NBK10506/table/A7report=objectonly. Accessed 22 June 2017.
15. Hussain ZH, Whitehead DA, Lacy BE. Fecal impaction. Curr Gastroenterol Rep. 2014;16(9):404. https://doi.org/10.1007/s11894-014-0404-2.
16. Falcon S, Lopez BM, Munoz M, Sanchez A, Rey E. Faecal impaction A systematic review of its medical complications. BMC Geriatr. 2016;16:4. https://doi.org/10.1186/s12877-015-0162-5.
17. Tracey J. Fecal impaction: not always a benign condition. J Clin Gastroenterol. 2000;30(3):228–9.

Faecal Incontinence

18. Rao SS. Diagnosis and management of faecal incontinence. Ameican Journal Gastroenterology Parameters Committee Am J Gateroenterol. 2004;99:1585–604.
19. Wald A. Faecal incontinence in the elderly: epidemiology and management. Drugs Aging. 2005;22:132–9.
20. Gordon PH, Nivatrongs S. Principles and practice of surgery for the colon, rectum and anus. 3rd ed. New York: Information Health Care; 2007.
21. Cooper ZR, Rose S. Faecal incontinence: a clinical approach. Mt Sinai J Med. 2000;67:96–105.
22. Norton C, Whitehead WE, Bliss DLZ, Harari D, Lang J. Management of fecal incontinence in adults: report from the 4th international consultation on incontinence. Neurourol Urodyn. 2010;29(1):199–206.
23. Roberts RO, Jacobson SJ, Reilly WT, Pemberton JH, Lieber MM, Talley NJ. Prevalence of combined faecal and urinary incontinence: a community-based study. J Am Cleveland Soc. 1999;47:837–41.
24. Tobin GW, Brocklehurst JC. Faecal incontinence in residential homes for the elderly: prevalence, aetiology and management. Age Aging. 1988;15:41–6.
25. Johnson JF, Lafforty J. Epidemiology of faecal incontinence: the silent affliction. J Gastroenterol. 1996;91:33–6.
26. Dodge J, Bachman C, Silverman H. Fecal incontinence in elderly patients. Postgrad Med. 1988;83(8):258–60.

27. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum. 1993;36(1):77–97.
28. Snooks SJ, Swash M, Setchell M. Injury to innervation of pelvic floor sphincter musculature in child birth. Lancet. 1984;2:546.
29. Lacima G, Pera M. Combined fecal and urinary incontinence: an update. Curr Opin Obstet Gynecol. 2003;15(5):405–10.
30. Nelson RL, Furner SE, Westercamp M, Farquhar C. Cesarean delivery for the prevention of anal incontinence. Cochrane Database Syst Rev. 2010;(2):CD006756. https://doi.org/10.1002/14651858.CD006756pub2.
31. Kalantar JS, Howell S, Tallet NJ. Prevalence of faecal incontinence and associated risk factors: an underdiagnosed problem in the Australian community. Med J Aus. 2001;176:54–7.
32. Shah BJ, Chokhavatia S, Rose S. Fecal incontinence in the elderly. Am J Gasreroenterol. 2012;107:1635. https://doi.org/10.1038/ajg.2012.284.
33. Madoff RD, Rosen HR, Baeten GG, La Fontaine LJ, Cavine E, Devesa M, et al. Safety and efficacy of dynamic muscle plasty for anal incontinence: lessons from a prospective multicenter trial. Gastroenterology. 1999;116:549–56.
34. BMJ. Managing faecal incontinence. Editorial BMJ. 2005;330:207–8.
35. Rao SS. Manometric evaluation of defecation disorders: Part II. Faecal incontinence Gastrenterologist. 1997;5(2):99–111.
36. Read M, Read NW, Barber DC, Duthie H. Effects of loperamide on anal sphincter function in patients complaining of chronic diarrhoea with faecal incontinence and urgency. Dig Dis Sci. 1982;27:807–14.
37. Norton C. Outcome of biofeedback for faecal incontinence. Br J Surg. 1999;86:1159–6321.
38. Matzell KE, Stadmalier U, Hohenfeliner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of fecal incontinence. Lancet 1995;346:1124-.
39. Vaizey CJ, Kamm MA, Gold DM, Bartram C, Halligan S, Nicholls RJ. Clinical physiological and radiological study of a new purpose-designed artificial bowel sphincter. Lancet. 1998;352:105–9.

Urinary Incontinence

40. Mollander U, Sundh V, Stein G. Urinary incontinence and related symptoms in older men and women studied longitudinally between 70 and 97 years of age. A population study. Arch Geriatr Geront. 2002;35:237–44.
41. Couture JA, Valiquette L. Urinary incontinence. Ann Pharmacother. 2000;34(5):646–55.
42. Mayo Foundation for Medical Education and Research Geriatric Medicine. Urinary Incontinence (Internet) USA Mayo Clinic c2010. http://www.mayo.edu/. Retrieved 4 Aug 2013.
43. Nakanishi N, Tatara K, Naramura H, Fujiwara H, Tahashima Y, Fukoda H. Urinary and faecal incontinence in a community residing older people in Japan. J Am Geriatr Soc. 1997;4592:215–9.
44. Teunissen TA, van denBosch WJ, van den Hoogen HJ, Largo-Jansson AL. Prevalence of urinary and faecal incontinence among community dwelling elderly patients in Nijmegen, The Netherlands. Ned Tidschr Geneeskf. 2006;150(44):2430–4.
45. Inouye SK, Studenski S, Tinett ME, Kuchel GA. Geriatric syndromes: clinical research and policy implications of a core geriatric concept. J Am Geriatr Soc. 2007;55:780–91.
46. Yu L, Thomas JR, Kaltreider L, Hu TW, Igou JF, Dennis PJ. Profile of urinary incontinent elderly in long term care institutions. J Am Geriatr Soc. 1990;38:433–9.
47. Vehkalalahti I, Kivela S-L. Urinary incontinence: and its correlates in very old age. Gerontology. 1985;31:391–5.
48. Du Beau CE. Beyond the bladder management of urinary incontinence in older women. Clin Obstet Gynecol. 2007;50:720–34.
49. Bocon-Gitod L. Urinary incontinence after radical prostatectomy. Eur Urol Update Series. 1997;6:112–6.
50. McConnell JD, Barry MS, Bruskewitz RC. Prostatic hyperplasia, diagnosis, treatment. Clinical practice guide-line. No.8. US Dept health and human services public health service aging for health care policy and research. Rockville.
51. Mathews CA, Whitehind WE, Townsend HK, Grodstein F. Risk factors for urinary and faecal incontinence on nurses' health study. Obstet Gynecol. 2013;122(3):539–48.
52. Schulman C, Claesin H, Matthijs J. Urinary incontinence in Belgium: a population based survey. Eur Urol. 1997;32:315–20.
53. Milson I, Ekelund P, Molander U, Arvidsson L, Aresking B. The influence of age, parity, oral contraception, hysterectomy and the menopause in the prevalence of urinary infection in women. J Urol. 1997;149:1459–62.
54. Resnick NM, Yalla SV, Laurino E. The pathophysiology of urinary incontinence among institutionalized elderly persons. NEJM. 1989;320:1–7.
55. Berardelli M, De Rango F, Morelli M, Corsonello A, Mazzei B, Mari V, et al. Urinary incontinence in the elderly and in the oldest old: correlation with frailty and mortality. Rejuvenation Res. 2013;16(3):206–11.
56. Gibson W, Wagg A. Urinary incontinence in the frail elderly: what do we still need to learn. Clin Pract. 2014;11(4):431–40.
57. Frank C, Szlanta A. Office management of urinary incontinence among older patients. Canad Fam Physician. 2010;56:1115–9.
58. Kuchel GA, DuBeau CE. Chapter 30: Urinary incontinence in the elderly. Geriatric Nephrology Curriculum Am Soc Nephrol. 2009;1–4.
59. Merkel JI. Urinary incontinence in the elderly. Southern Med J. 2001;94(10):952–7.
60. O'Donnell PD. Special considerations in elderly individuals with urinary incontinence. Urology 1998;51(2A suppl):20–23.
61. Ouslander JG. Geriatric urinary incontinence. Dis Mon. 1992;38(2):65–149.
62. Charalambous S, Trantapylidis Y. Impact of urinary incontinence on quality of life. pelvicperineology.org/june_2009/pdf/impact_of_urinary_incontinence_on_quality_of_life
63. Weiss BD. Diagnostic evaluation of urinary incontinence in geriatric patients. Am Fam Physician. 1998;57(11):2675–84.
64. Wyman JF, Harkins SW, Fanti JA. Psychological impact of urinary incontinence in the community dwelling population. J Am Geriatr Soc. 1990;38:282–8.
65. Malmsten UGH, Milsom I, Molander U, Norlen LJ. Urinary incontinence and lower urinary tract symptoms: an epidemiological study of men aged 45-99 years. J Urol. 1997;158:1733–7.
66. Ekelund P, Grimby A, Milson I. Urinary incontinence and functional costs high. Br Med J. 1993;306:1344.
67. Wagner TH, Hu TW. Economic costs of urinary in 1955. Urology. 1998;51:355–61.
68. Gehrich A, Stany MP, Fischer JR, Buller J, Zahn CA. Establishing a mean post void residual volume in asymptomatic premenopausal and postmenopausal women. Obstet Gynecol. 2007;110(4):827–32.
69. United States Department of Health and Human Services agency for Health Care Policy and Research (AHCPR). Clinical practice guidelines. Urinary incontinence in adults. Washington DD: United States Department of Health and Human Service Manual, 1992 as quoted by Gehrich et al,2007.
70. Currie CT. Urinary incontinence after stroke. Brit Med J. 1986;293(6558):1322–3.
71. Pettersen R, Saxby BK, Wylller TB. Poststroke urinary incontinence: one year outcome and relationship with measures of attentiveness. J Am Geriatr Soc. 2007;55(10):15.

Gait Disorders in the Elderly

27

Nages Nagaratnam and Kujan Nagaratnam

Introduction

Gait disorders in the elderly may arise from a single or a combination of neurological and musculoskeletal factors. They may interact with physiological-related changes which increase with age and are part of normal ageing. Ageing however is not necessarily accompanied by disordered gait for some elderly maintain a normal gait into their 90s [1].

From 8% to 10% of non-institutionalised older adults and 60% of nursing home residents reported having difficulty in walking and required assistance of another person or special equipment to walk [2–4]. Abnormal gait is seen in 35% of people over the age of 70 years [5], and gait changes are seen in the majority of people over the age of 85 years [6].

Physiology

The normal gait consists of a repetitive gait cycle (Fig. 27.1). The gait cycle is the time interval occurring from heel strike to heel strike of the same foot [7, 8]. The gait cycle has two phases, a stance phase which takes up to 60% of the gait cycle and the swing phase which takes up to 40% of the cycle [7]. The stance phase is divided into the heel strike (the initial contact of foot on the ground), the mid-stance (when the full foot is on the ground) and the toe off (the point when the stance phase ends [8]. The toe off phase is also known as the propulsive period [8, 9]. At average walking about 10% of the entire gait cycle is represented by double-leg stance, that is, both feet are on the ground, and this decreases with increase in the walking speed and is eliminated on running [8]. About 40% of the gait cycle comprises the single-leg stance in a normal walk [7]. From the toe off phase to the heel strike phase is the swing phase. There are two extra phases in the swing phase – acceleration and deceleration phase [10]. In the former, the swing leg makes an accelerated forward movement resulting in propelling the body weight forward [9]. The velocity of the forward movement is braked by deceleration in order to place the foot on the ground with control [9]. Between these two phases is the mid-swing phase, when heels of both feet are next to each other [11] (Fig. 27.1).

Pathophysiology

With ageing there are decreased muscle bulk, flexibility and strength together with loss of vision and hearing. The major changes in gait are in the reduction in the overall step/stride length and velocity. There are also decreased rotation and more flat-footed landing and less vigorous push off [12–14]. Other workers however have found no differences with step length, stride length and velocity [15]. When healthy young women were compared with elderly women, the stride length, step length, velocity and range of ankle motion had lower values in the elderly [16]. Similar studies between healthy young men and older men showed no significant differences between them but for stride length [15]. When gender was compared, the free-speed cadence was faster for women than for both young and older men. According to Hageman [17], the gait characteristics of older healthy adults are an adaptation towards safe walking rather than an abnormality or disability. Thus there is no accepted standard of normal gait in the elderly [18].

What has been described as ‘senile gait disorder’ [19] is characterised as a gait pattern with broad base small steps, diminished arm swing, stooped posture, flexion at the hip and knees, uncertainty, stiffness in turning and occasional difficulty in initiating steps and to perform tandem gait and a tendency to fall. Many of the older adults labelled senile gait disorder have cognitive impairment [20], and others are mildly demented [21]. It is likely that senile gait disorder is

N. Nagaratnam · K. Nagaratnam (✉)
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net; kujan@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_27

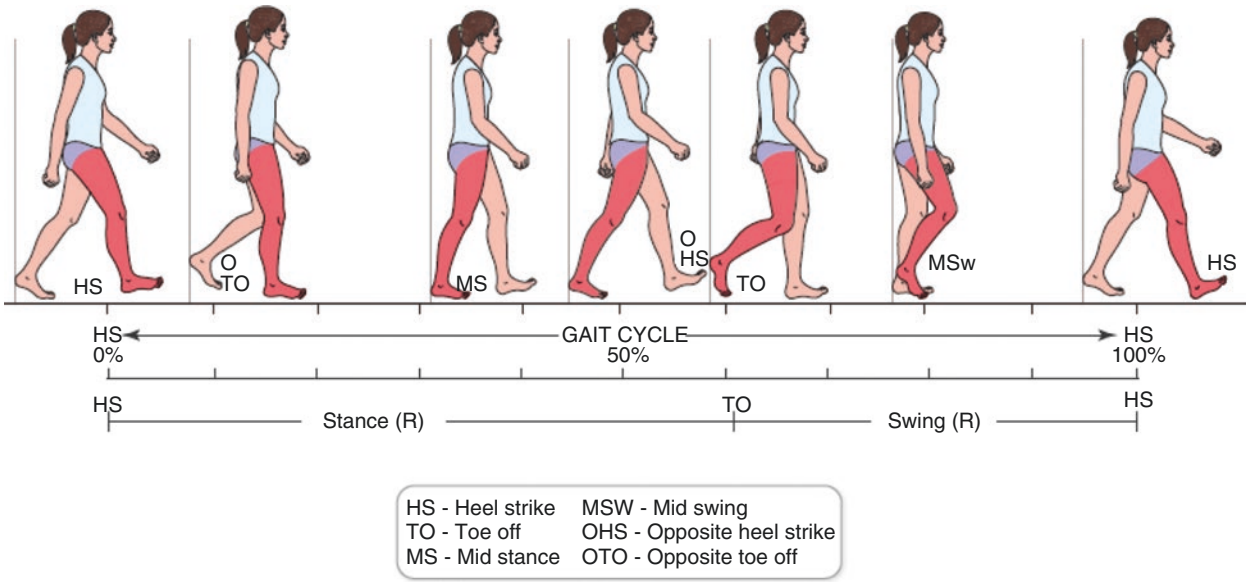


Fig. 27.1 The gait cycle. (Information sources: Malanga and De Lisa [7, 8], De Krester et al. [9])

of multifactorial aetiology, and it is now believed that these changes are early manifestations of subclinical disease [22].

Neurological and musculoskeletal factors together with physiological changes with ageing contribute to gait changes in the elderly (Fig. 27.2). Age-related changes include sensory impairment and visual, auditory and tactile sense. Postural stability or balance is maintained by continued adjustments to sensory, visual, vestibular and somatosensory outputs [23] which tend to decline with age. Loss of visual acuity, peripheral vision, depth perception and contrast sensitivity occur with ageing [24]. Proprioceptive loss includes the threshold to movement and impaired sense of vibration in the legs, leading to increased postural sway [25]. The vestibular system is also affected by ageing.

Nutt et al. [26] drew attention to gait disorders termed higher-level gait disorder that are not explained by basic sensorimotor deficits in comparison to lower-level and middle-level disorders. Basically the abnormal gait is motor programming failure [27]. Five types have been described, namely, frontal gait disorder, frontal disequilibrium, subcortical disequilibrium, isolated gait ignition failure and cautious gait [26]. The middle level are largely from basal ganglia disorders (Parkinson's disease), cerebrovascular disease (hemiparesis, paraparesis associated with UMN signs) and spinal cord lesions leading to spastic paraparesis with sensory and cerebellar levels [6]. The lower level includes weakness of muscles involving the motor neurones (LMN spinal muscular atrophy; UMN + LMN amyotrophic lateral sclerosis, UMN primary lateral sclerosis), the peripheral nerves (peripheral neuropathy, radiculopathy, plexopathy), the neuromuscular junction, (myasthenia) and the primary muscle disorders (dystrophies, myopathies) [6].

Types of Gait

Neurological

Spastic Gait

Spastic gait is a disorder of the upper motor neurone and the cortico-spinal tract. In spastic paraparesis the gait is stiff-legged, with slight flexion at the hips with tendency to circumduct and in extreme instances the legs cross (scissoring) and poor toe clearance. This occurs with cord compression, bilateral strokes, motor neurone disease, amyotrophic lateral sclerosis, multiple sclerosis, myelopathy and subacute combined degeneration of the cord (due to vitamin B12 deficiency). It is important to exclude cord compression because of the urgency for surgical intervention. Myelopathy is sometimes due to a structural lesion, for example, tumour or A-V malformation. Myelopathy from cervical spondylosis is a common cause of gait disorder in the elderly and accounts for 18% in a combined series [28]. With cerebral spasticity, involvement of the upper extremities with flexed posture is often observed as in multiple sclerosis and strokes. In hemiparetic gait, there are circumduction, stiffness and foot drop with abducted arm and internally rotated shoulder with pronation of the forearm and flexion of the wrist and fingers.

Cerebellar Ataxia

The gait is wide based with unsteadiness and irregularity of steps [29], and if the lesion is unilateral, the staggering may be to one side with a lurching quality. The individual may walk in a zigzag course mimicking a drunken sailor with swaying of the head and trunk. Cerebellar ataxia includes paraneoplastic cerebellar degeneration, toxins such as alco-

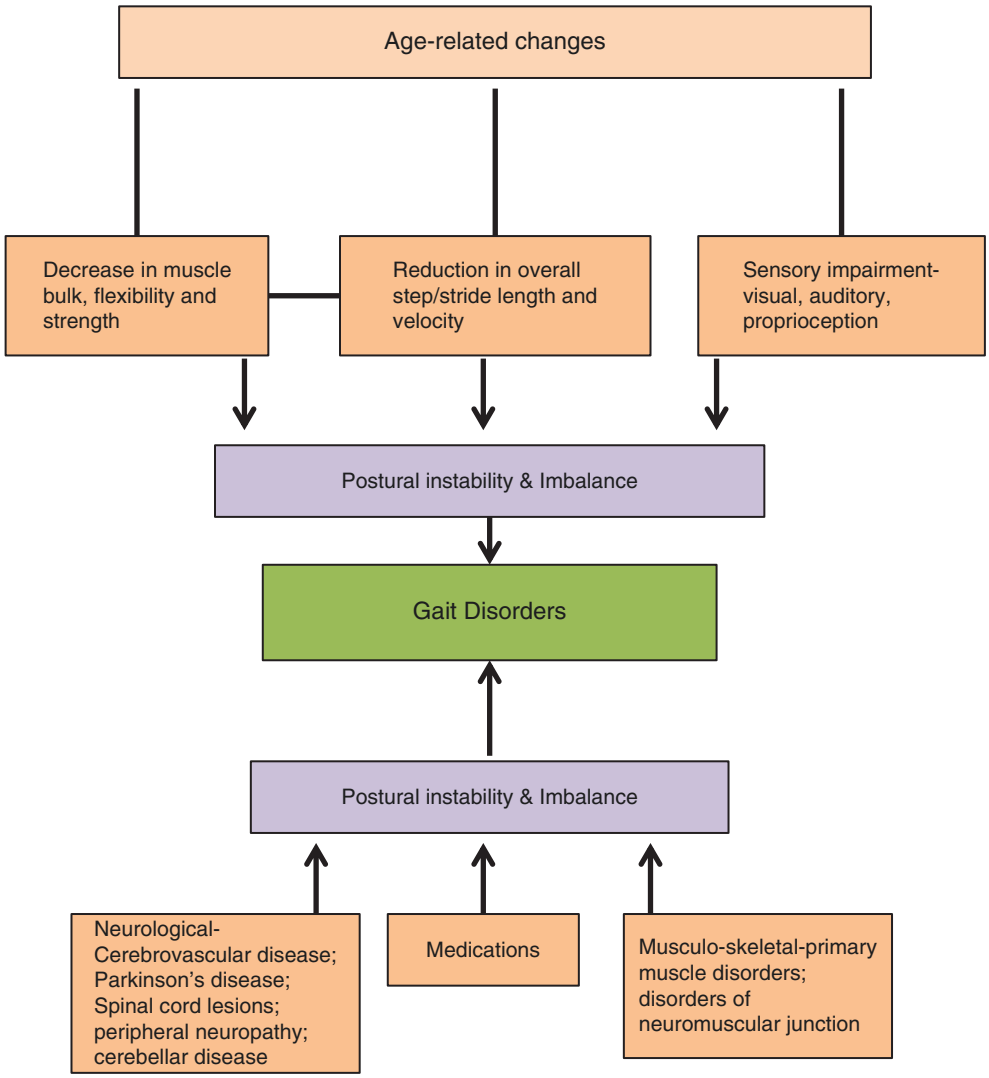


Fig. 27.2 Pathophysiology of gait disorders. (Information sources: Lee and Lishman [23], Spirduso [24], Brockelhurst et al. [25])

hol, possibly phenytoin, strokes, hypothyroidism and tumours. Chronic alcoholics with anterior vermis atrophy may experience primary truncal ataxia [30].

Sensory Ataxia

The gait is described as 'high steppage'; the feet may be raised too high and brought down too hard more so when the patient is walking in the dark.

Extrapyramidal Gait

The gait is shuffling and narrow based with difficulty in starting and turning (turning en bloc), no arm swinging, hesitation, festination, propulsion and retropulsion.

Frontal Gait Disorder

Frontal lobe damage often shows abnormalities of gait characterised by short steps but without festination or an inability to lift the feet from the floor ('magnetic feet'), loss of balance with difficulty initiating gait and start hesitation (freezing of gait), difficulty with turns and inability to walk even though simple leg movements may be possible seated or lying down (gait apraxia) [31]. Gait apraxia has often been seen in normal pressure hydrocephalus which is in effect a frontal lobe syndrome manifesting the clinical triad of gait disorder, cognitive impairment and incontinence. The characteristic shuffling, small-stepped gait is related to interruptions of the thalamo-cortical and cortico-spinal connections. Liston et al. [27] described patients with cerebral multi-infarcts in the absence of cognitive impairment and neurological signs and hypothesised three main types, ignition apraxia, equilibrium apraxia and mixed gait apraxia. They suggested that ignition apraxia could be due to lesions in the supplementary motor area and its connections. Binswanger's disease (subcortical arteriosclerotic encephalopathy) is characterised by mental change which may be variable in degree, dysarthria, pseudobulbar palsy, hyperre-

flexia and a gait disorder [32, 33]. The gait pattern somewhat resembles that seen with hydrocephalus and frontal lobe lesions [34]. The gait disturbance is similar to cerebellar ataxia suggesting common mechanisms [27, 35]. Impairment of balance and ambulation has been noted following therapeutic thalamotomy [36]. Patients with thalamic infarction [33, 37] and thalamic tumour [38] are unable to stand in the absence of weakness or marked sensory loss and referred to as thalamic astasia [39]. This spectrum of gait disturbance in frontal gait disorders could be due to involvement of the frontal cortex and its subcortical connections including the basal ganglia, cerebellum and brain stem [31].

Musculoskeletal

Musculoskeletal causes often include joint alignment and bone abnormalities and may be due to hip, knee, foot and ankle pathology and leg length discrepancy [9].

Antalgic Gait

To avoid pain on the weight-bearing structures such as knee, hip and ankle injuries, the patient adopts a limp characterised by a very short stance phase on the affected side.

Trendelenburg Gait

There is a weight shift on the affected side, for example, with a painful hip or hip abductor weakness. The Trendelenburg sign is where the pelvis drops towards the side of the raised limb and indicates that the abductor muscles on the standing limb are weak.

Gait disorders have been classified as neurological, musculoskeletal and mixed [40].

Clinical Evaluation

The initial evaluation includes characterisation of the gait, determination of the cause, defining factors pertaining to its aetiology, identifying risks and debility and management (Box 27.1) Majority of the gait disorders appear in connection with underlying disorders. The history and the mode of presentation are important and may provide indications as to the diagnosis. In one study in the age group 65–81 years, it was identified that pain was the most frequent cause of walking difficulty followed by stiffness, dizziness, numbness, weakness and a sensation of abnormal movement [18]. Often the presenting symptom is one of generalised weakness which is often due to a systemic disease and only rarely has a specific cause. When it is not a generalised weakness, the pattern of disability could be of immense diagnostic value. The gait pattern together with the history and physical examination would be helpful in elucidating the cause and determining the treatment plan.

I. History

The history should include the mode of presentation, drugs and medications (psychotropic), anticonvulsants and salicylates (in chronic intoxication) and symptoms relating the cardiovascular system.

II. Physical examination

A thorough neurological examination should include the motor, sensory (including proprioception) and cerebellar functions. Impaired motor functions would result in muscle weakness and joint instability. The initiation and co-ordination of movements are the result of integrated frontal cortex, basal ganglia and cerebellar function. Postural stability depends on the integration of visual, vestibular and proprioceptive information.

Examination of the musculoskeletal system – neck, spine, extremities and feet – for deformities, limitation in range of movement and pain
Examination of the other systems with emphasis on the cardiovascular system
Determining visual acuity
Determining mental status

III. Assessment of patient's
  (a) Balance for postural control
    (i) Tandem gait
    (ii) One-legged stance ('stalk' stance), Berg's balance test [41]
    (iii) Romberg test
    (iv) Sternal nudge – the ability to withstand displacement (the examiner pushes with slight even pressure over the sternum with the patient standing with feet as close as possible)
    (v) To evaluate vestibular function
    Dix-Hallpike manoeuvre
    Fukuda-Unterberger test (the patient marches on the same spot with eyes closed. If the patient deviates to one side, the test is positive and this generally towards the side with lower vestibular activity.)
  (b) Walking ability
    The following components should be looked at: initiation of gait, step height, step length, step symmetry, step continuity, path deviation, trunk stability, walk stance and turning [42]. Useful information as to the level of dysfunction can be obtained by quantifiable performance

tests such as Timed 'Up and Go' test [43]. The gate velocity will be an easy test to perform, and the pathological gait velocity is <0.8 m/sec and correlates with a pathological performance of Get up and Go test and with the incapacity to perform the one-leg balance test [44]. Dual-task-related gait changes are ways to assess age-associated change in gait control, comparing walking performance alone to walking performance while performing an attention-demanding task at the same time [45]. Dual-task-related changes may provide information between gait disorders and cognitive decline [45]. Unravelling the association between early gait disturbance and early cognitive changes may be useful in recognising elderly at risk of declining mobility and progression to dementia [46].

IV. Other investigations

Choice of other investigations and imaging will depend on the history and physical examination findings to use the most accurate and discriminatory tests (Box 27.1).

The algorithm addresses the problem of diagnosis in a patient presenting with a gait disorder based on the history and neurological findings (Algorithm. 27.1).

Box 27.1 Minimum Evaluation

History and physical examination to define

- Pattern of gait
- Determining the cause
- Defining factors pertaining to its aetiology
- Ascertaining risks and extent of disability
- Management

Assessment of patient's

- Balance
- Walking ability

Management

Gait disorder in the elderly reduces mobility and leads to increased morbidity through falls and impairs quality of life. It is an important cause of disability through decrease in mobility and psychomotor misadaptation which is characterised by loss of independence, loss of self-confidence and restrictions in mobility and activity due to fear of falling, social withdrawal and risk of institutionalisation [47].

In a study of 50 patients with a mean age of 71.5 years with gait disorders, effective therapy was available in only 24% of the disorders. Fifty-six percent is said to have had a single causal diagnosis. 16% had myelopathy of the cervical spine, 10% had multiple sensory disorder, and in 8% a diagnosis of idiopathic senile disorder was made because of the failure to establish other causes [37]. More often than not, the gait disorders are only partially treatable even if the causal condition is found and regaining premorbid status is unachievable [48]. However it is meaningful to identify amenable factors associated with gait disorders and to treat the remediable pathology, for example, in gait disorders, associated with conditions such as hypothyroidism, vitamin B12 deficiency, inflammatory arthritis and Parkinson's disease, among others.

In the elderly, there is an increasing frequency of disorders involving virtually all organ systems resulting in increasing morbidity, and this will influence treatment outcome. If a single cause is not identifiable but many potential processes are found, management should be directed towards correcting these factors. The medications should be reviewed.

Physiotherapy can improve mobility. Combined aerobic, strength and function-based group exercises had increased gait speed in about 5% of patients with osteoarthritis [49]. In those with vestibular deficits, vestibular rehabilitation can be beneficial.

Surgical treatment for lumbar stenosis, cervical myelopathy and normal pressure hydrocephalus (NPH) had shown modest improvement. Ventriculo-peritoneal or ventriculo-atrial shunting in some patients with NPH had resulted in clinical improvement. Brief improvement after serial removal of about 50 ml of cerebrospinal fluid has shown to be a good predictor of likely response to shunting. In a series of 127 patients, 36% showed improvement (only 21% showed marked improvement) after shunt surgery, and 28% suffered complications with death and disability in 7% [50].

Clinical Relevance

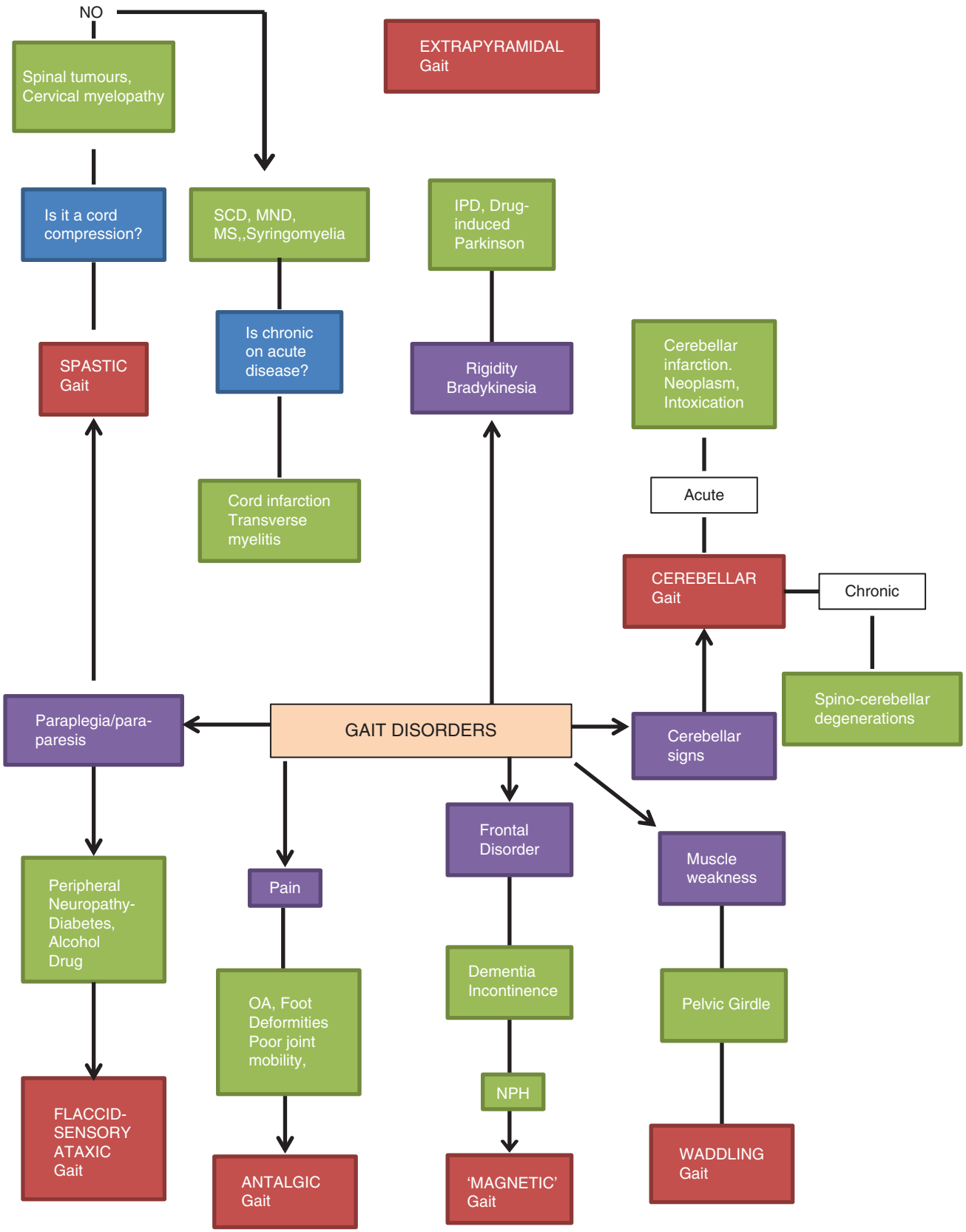
Ageing is not necessarily accompanied by disordered gait for some elderly maintain normal gait into their 90s [1].

With ageing there is decreased muscle bulk, flexibility and strength together with loss of vision and hearing.

The major changes in gait are in the reduction of overall step/stride length and velocity.

Types of gait disorder

I. Frontal gait disorder – short steps, loss of balance, freezing but with a wider base and upright posture unlike in parkinsonism



Algorithm 27.1 An approach to evaluation of patient with gait disorders (Information sources: De Krester et al. [9], Thompson [28], Sudarsky and Ronthal [37], Adams et al. [39], Lim et al. [40])

II. Spastic gait – short, shuffling, stiff-legged with slight flexion at the hips and, in extreme form, scissoring
III. Cerebellar ataxia – wide based and staggering
IV. Sensory ataxia – high steppage and imbalance
V. Extrapyramidal gait – shuffling, narrow based, difficulty in starting and turning
VI. Antalgic gait – adopts a limp with very short stance phase
VII. Trendelenburg gait – weight shift on the affected side

It is meaningful to identify amenable factors associated with gait disorders and to treat the remediable pathology.

If a single cause is not identifiable but many potential processes are found, management should be directed towards correcting these factors.

Multiple Choice Questions

In relation to gait disorders in the elderly, the following are true, EXCEPT:

A. The major changes in gait in the elderly are the reduction of overall step/stride and velocity.
B. Frontal gait disorder is characterised by short steps, loss of balance, freezing and stooping posture.
C. Myelopathy from cervical spondylosis is a common cause of gait disorder in the elderly.
D. In normal pressure hydrocephalus, the clinical triad consists of gait disorder, incontinence and cognitive impairment

MCQ Answers
1. B

Extended Matching Questions

1.

A. Scissor gait
B. Drunken gait
C. Steppage gait
D. Hemiparetic gait
E. Antalgic gait
F. Frontal gait disorder
G. Waddling gait
H. *Marche a petit pas*
I. Trendelenburg gait
J. Spastic gait

The following have in common a gait disorder. Choose the most likely type of gait from the list above. Each option can be used only once.

1. A 60-year-old man developed sudden pain in his low back while trying to lift a heavy object. The pain radiated down the back of the left leg. He adopted a limp with very short stance phase on walking.
2. A 65-year-old man with known cancer complained of difficulty in walking over a week. There was weakness with increase in tone in both lower limbs right more than left. The deep reflexes and plantar extensor were brisk, with diminution in sensation with sensory level at the level of the umbilicus. He was stiff-legged with slight flexion at the hips.
3. A 70-year-old man has been slowing down over the past 6 months or more. He had a rest tremor in the right hand with rigidity and bradykinesia. He had difficulty in turning and starting, and gait was narrow based.
4. A 72-year-old woman in a nursing care facility had difficulty in rising from the chair and walking. She had weakness of the pelvic girdle muscles; her serum calcium was low and the alkaline phosphatase raised.
5. A 70-year-old man was seen with difficulty in walking. On examination his left arm was flexed at the elbow and at the wrist. The flexors were weak in the leg and extended with slight crossover.

EMQ Answers
1. E
2. J
3. H
4. G
5. D

References

1. Bloem BR, Gussekloo J, Lagaay AM Remarque EJ, Haan J, Westendorp RG. Investigation of gait in elderly subjects over 88 years of age. J Geriatr Psychiatry Neurol. 1992;5:78–84.
2. Dawson D, Hendershot G, Fulton J. Aging in the eighties: functional limitations of individuals age 65 and over. National Center for Health Statistics. ADVANCE DATA. 1987;(133):1–12.
3. Leon J, Lair T. Functional status of the non institutionalised elderly: estimates of ADL and IADL difficulties (DHHS Publication No.(OPHS) 90–3462. National Medical Expenditure survey Research Findings Agency for Health Care Policy and Research. Rockville: Public Health Service; 1990 (as quoted by Alexander, 2007).
4. Lair T, Lefkowitz D. Mental health and functional status of residents of nursing and personal care homes. (DHHS publication No. (PHS) 90-3470). National Medical Expenditure Survey Research

Findings, Agency for Health Care Policy and Research, Rockville: Public Health Service; 1990 (as quoted by Alexander, 2007).
5. Verghese J, LeValley A, Hall CB, Katz MJ, Ambrose AF, Lipton RG, et al. Epidemiology of gait disorders in community –residing older adults. J Am Geriatr Soc. 2006;54(2):255–61.
6. Camiciolli R, Rosano C. Understanding gait in aging: Finding the way forward: Part I. Website Edition April/May 2012: The Movement Disorder Society MDS. http://www.movement disorders.org/monthly_edition/2012/04/understanding_gait_in. Retrieved 18 July 2013.
7. Malanga G, De Lisa JA. Clinical observation. Section One. In: De Lisa JA, editor. Gait analysis in the science of rehabilitation. Baltimore: Diane Publishers; 1998. p. 1–10.
8. The gait cycle. Definition and description of the gait cycle. http://www.gla.ac.uk/ibis/US/tab/tutorial/anatomy/hfgait.html. Accessed 8 Feb 2017.
9. De Krester K, O'Reilly N, Jackson D, Buxton S, Thomas E. Gait. http://www.physio-pedia.com/Gait#Gait_Analysis. Accessed 7 Feb 2017.
10. Demos. Gait analysis. http://www.ncbi.nlm.nih.gov/books/NBK27235/,2004.
11. Berger W, Deitz V, Quintern J. Corrective reactions to stumbling in man: neuronal co-ordination of bilateral leg activity during gait. J Physiol. 1984;357:109–25.
12. Murray MP, Kory RC, Clarkson BH. Walking patterns in healthy old men. J Gerontol. 1969;24(2):169–78.
13. Winter DA, Patla AE, Frank JS, Walt SE. Biomechanical walking changes in the fit and healthy elders. Phys Ther. 1980;70:740–7.
14. Judge JO, Ounuu S, Davis RB. Effects of age in the biomechanics and physiology of gait. Clinics Geriatr Med. 1996;12(4):659–78.
15. Blanke DJ, Hageman PA. Comparison of gait of young men and elderly men. Phys Ther. 1989;69:2.
16. Hageman PA, Blanke DJ. Comparison of gait of young women and elderly women. Phys Ther. 1986;66(9):1382.
17. Hageman PA. Gait characteristics in healthy elderly: a literature review. Section of geriatrics. Am Physiol Therapy Assn. 1995;18(2):2–5.
18. Alexander NB. Gait disorders in older adults. Clin Geriatr. http://www.clinicalgeriatrics.com/article/1231.
19. Koller WC, Wilson RS, Glatt SC, Huckman MS, Fox JH. Senile gait. Correlation with computed tomographic scans. Ann Neurol. 1983;13:343–4.
20. Hogan DB, Berman P, Fox RA, Huble-Kozey CL, Turnbull G, Wall J. Idiopathic gait disorders in the elderly. Clin Rehab. 1987;1:17–22.
21. Eible RJ, Hughes L, Higgins C. The syndrome of senile gait. J Neurol. 1992;239:71–5.
22. Bloem BR, Gussekloo J, Lagaay AM, Remarque EJ, Haan J, Westerkorp RG. Idiopathic gait disorders are signs of subclinical disease. J Am Geriatr Soc. 2000;48(99):1098–101.
23. Lee D, Lishman R. Vision in movement and balance. New Sci. 1975;9:59–61.
24. Spirduso WW. Physical dimensions of aging. Human kinetics. Champaign, IL, USA 995.
25. Brockelhurst JC, Robertson D, James-Groin P. Clinical correlates of sway in old age-sensory modalities. Age Aging. 1982;11:1–10.
26. Nutt JG, Marsden CD, Thompson PD. Human walking and higher –level gait disorders, particularly in the elderly. Neurology. 1993;43(2):268–79.
27. Liston R, Mickelboruogh J, Bene J, Tallis R. A new classification of higher level gait disorders in patients with cerebral multi-infarct states. Age Ageing. 2003;32:252–8.
28. Sudarsky L, Ronthal M. Gait disorders among elderly patients: a survey study of 50 patients. Arch Neurol. 1983;40:740–3.
29. Adams RD, Victor M, Ropper AH. Disorders of stance and gait. New York: McGraw –Hill; 1009.
30. Victor M, Adams FD, Mancall EL. A restricted form of cerebellar cortical degeneration occurring in alcoholic patients. Arch Neurol. 1959;1:579–688.4.
31. Thompson PD. Frontal lobe ataxia. Handb Clin Neurol. 2012;103:619–22.
32. Babikian V, Ropper AH. Binswanger's disease: a review. Stroke. 1990;93:961–5.
33. Nagaratnam N, Nagaratnam K. Psychiatric and behavioural aspects of dementia of the Binswanger type. Am J Alz Dis. 1998;13:173–8.
34. Thompson PD, Marsden CD. Gait disorder of subcortical arteriosclerotic encephalopathy: Binswanger's disease. Mov Disor. 1987;2(1):1–8.
35. Ebersbach G, Sojer M, Valldeoriola F, Wissel J, Mullr J, Tolosa E, et al. Comparative analysis of gait in Parkinson's disease, cerebellar ataxia and subcortical arteriosclerotic encephalopathy. Brain. 1999;122(Pt 7):1349–55.
36. Zoll JG. Transient anosognosia associated with thalamotomy. Is it caused by proprioceptive loss? Consin Neurol. 1969;31:48–55.
37. Nagaratnam N, Leung H, Bou-Hader P. Lacunar thalamic stroke proclivity for falls. Int J Clin Pract. 2004;58:83–5.
38. Nagaratnam N, Ting R, Jolley D. Thalamic tumour presenting as frontal lobe dysfunction. Int J Clin Pract. 2001;55:492–3.
39. Marsden JC, Gordick PB. Thalamic astasia: inability to stand after unilateral thalamic lesions. Ann Neurol. 1988;223:596–693.
40. Lim MR, Huang RC, Wu A, Girardi FP, Cammisa FP Jr. Evaluation of the elderly patient with an abnormal gait. J Am Acad Orthop Surg. 2007;15:107–17.
41. Berg KO, Maki BG, Williams JI, Holliday PJ, Wood-Dauphinee SL. Clinical and laboratory measures of postural balance in the elderly population. Arch Phys Med Rehabil. 1992;73(4):1073–80.
42. Tinetti M. Performance-oriented assessment of mobility problems in elderly patients. J Am Geriatr Soc. 1986;34:119–26.
43. Podsiaddio D, Richardson S. The timed "Up and Go" a test of basic functional mobility in frail elderly patients. J Am Geriatr Soc. 1991;39:142–8.
44. Montaro-Odesso M, Schapira M, Varila C. Gait velocity in senior people: an easy test for detecting mobility impairment in community elderly. J Nutr Health Aging. 2004;8:340–3.
45. Beauchet O, Berrut G. Gait and dual task: definition, interest and perspectives in the elderly. Psychol Neuropsychiatr Vieil. 2006;4(3):215–25.
46. Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM. Gait and cognition: a complementary approach to the understanding their function and risk of falls. J Am Geriatr Soc. 2012;20(11):2127–36.
47. Pfitzenmyer P, Mourey F, Tavernier B, et al. Psychomotor misadaptation syndrome. Arch Gerontol Geriatr. 1999;28:217–28.
48. Alexander NB. Gait disorders in elder adults. J Am Geriatr Soc. 1996;44:430–51.
49. Fransen M, Cresbie J, Edmonds J. Physical therapy is effective in patients with osteoarthritis of the knee: a randomized controlled clinical trial. J Rheumatol. 2001;20:156–64.
50. Vanneste J, Augustijin P, Dirven C, Tan WF, Goedhart ZD. Shunting normal pressure hydrocephalus. Do benefits outweigh the risks. Neurology. 1992;42:54.

Cognitive Decline and Dementia in Some Chronic Disorders

28

Nages Nagaratnam and Gary Cheuk

Introduction

The oldest old represent a rapidly growing age group worldwide. About 5.5% of the combined population from the more developed regions – Europe, North America, Australia New Zealand and Japan – will be aged >85 years by the middle of this century [1]. It is predicted to increase by 291% in the more developed countries and by 1065% in the less developed countries [2]. With the increase in the ageing population, there is a widespread prevalence of chronic diseases including dementia [3].

Hearing Loss and Cognitive Decline

Introduction

Hearing loss is the third most prevalent chronic condition affecting older adults [4]. Nearly 50% to 63% of Americans over the age of 70–75 years have hearing loss [3]. In Europe 30% males and 25% of females have hearing loss at 70 years or more and 55% of males and 45% of females at the age of 80 years [3]. It is prevalent in almost two-thirds of adults at 70 years and remains undertreated [5]. A Norwegian study demonstrated that 60% of the population aged 60–79 years and 90% of the people aged >80 years have acquired hearing loss [6]. The incidence of hearing loss increases with age [6, 7, 8]. The prevalence (per cent in the population) of hearing impairment increases from about 2% per cent age at 20–24 years of age to 85% at 74–85 years [9]. More than 350 million people suffer from severe hearing loss, and it increases especially after the age of 65 years [7].

Neuropathology

The basic pathology of age-related hearing loss (ARHL) includes loss of hair cells of the organ of Corti, stria vascularis atrophy, loss of spiral ganglion neurons and changes in the central auditory pathways [10, 11]. ARHL is a complex disease with multifactorial aetiology [12] in which cochlear ageing, environmental, genetic predisposition and health co-morbidities are important risk factors in its causation [10, 13].

Decline in the peripheral auditory system can have profound effects on the central auditory system and function [14]. Neuroanatomical changes due mild to moderate hearing loss have been observed in the auditory cortex with reduction in the grey matter volume and changes in the extra-temporal grey and white matter in middle-aged and older adults [15]. Not only does the auditory cortex suffer from atrophy [16]; magnetic resonance spectroscopy shows their changes in the content of the metabolites in the aged brain [17]. Hearing impairment is associated with reduction in whole brain volume [18] and regional volumes confined to the right temporal lobe [19].

At the molecular level intracellular signalling is regulated by reactive oxygen species (ROS) under normal physical conditions [20]. Ageing is associated with accumulation of mitochondrial DNA (mtDNA) mutations [20] and decreased antioxidant function [11] resulting in further overproduction of ROS [20]. ROS and specific mitochondrial DNA (mtDNA) deletions occur with increasing frequency with age, and when enough mtDNA accumulates, the cell becomes bioenergetically defective [19, 21]. It has been suggested that ROS and mtDNA play an important role in the pathophysiology of ARHL [10]. The mitochondrial dysfunction-derived ROS production axis forms a vicious cycle, and this is the basis of the mitochondrial free radical theory of ageing [20].

N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

G. Cheuk
Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia
e-mail: gcheuk@optusnet.com.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_28

Association Between ARHL and Dementia

Longitudinal studies have shown that hearing loss in older adults is associated with accelerated cognitive decline and incident dementia [19, 22, 23]. According to Lin et al. [22], individuals with mild hearing loss are twice as likely to develop dementia compared to those with normal hearing. In community-dwelling older adults, it is independently associated with accelerated cognitive decline and incident cognitive impairment [24] and incident dementia and falls [12, 25]. Whether hearing loss is a marker for early-stage dementia or is a modifiable risk factor of cognitive decline merits further study [7, 26]. Deficits in both peripheral auditory system and central auditory system can contribute to ARHL, and both have been linked with accelerated cognitive decline, incident cognitive impairment and AD [27]. It has been suggested that in older adults hearing loss may be associated with dementia by decreasing stimulatory input and impeding social interaction [23, 28].

Management

Of the older adults who could benefit from treatment, only a small ratio seek help [29]. The remaining suffer from social isolation, a negative impact on health and poor quality of life. The National Council of Aging in 1999 conducted a survey of about 400 adults with hearing loss and found that those who were not wearing hearing aids had higher rates of anxiety, depression and psychosocial disorders [30]. The effects of hearing loss on long-term health and quality of life can be improved by early assessment and treatment [31].

Vitamin B12 and Folic Acid and the Risk of Cognitive Decline

Introduction

Folic acid is an important nutrient and together with vitamin B12 plays an important role in contributing to both nerve and brain function [32] and physical well-being [33]. Inadequate intake of folic acid in the elderly may relate to hyperhomocysteinaemia which is a risk factor for cognitive impairment [34], cardiovascular diseases and procarcinogenic effects [35]. Folic acid is essential for functioning of the nervous system at all ages, and fortification of bread and grains with folic acid is used to prevent neural tube defects [36]. Deficiency of both vitamins is associated with declining neurocognitive function and atherosclerotic lesions [33].

In elderly persons B12 and folic acid deficiencies are common. An Australian study showed low serum B12 levels in 22.9% of the older participants, serum folate in 2.3% and an elevated homocysteine in 51% among those with low B12 and folate [37]. In another study 3–60% of the elderly were classified as B12 deficient and 29% as folate deficient [33]. In later stage of life, B12 deficiency affects 10% of people over the age of 60 years [38–40]. In the Leiden 85+ study, there was high prevalence of both deficiencies in the elderly aged more than 75 years [41]. The prevalence of low red blood cell folate was higher in the centenarians than in octogenarians (6.5%vs 103%), and the risk was greater in association with vitamin B12 in African Americans and nursing facility residents [42].

Pathophysiology

In the elderly low B12 is rarely due to low dietary intake and differed from folic acid intake by the elderly which is far below the required dietary requirements [33]. The elderly have a higher prevalence of vitamin B12 deficiency as a result of absorption problems [36]. In the elderly the low B12 has been attributed to the increased occurrence of atrophic gastritis type B which occurs with a frequency rate of 20–50% [33]. Low RBC folate however was higher in centenarians than in octogenarians but was not affected by the presence of atrophic gastritis [42].

Both Vitamin B12 and folate are required [43] for the methylation of homocysteine into methionine. Hence decreased availabity of methyl groups in the brain due to B12 and folate deficiency [44] results in impaired formation of myelin, membrane phospholipids and *S*-adenosylmethionine and synthesis of neurotransmitters [45] such as catecholamines and serotonin [46–48]. Folic acid is not needed in the metabolism of methylmalonic acid (MMA) [32], and clearance of MMA and homocysteine is weakened by reduced kidney function [49]. Homocysteine can be elevated in other conditions such as renal insufficiency, hypothyroidism and vitamin B6 and folate deficiencies and hence is not an absolute marker for vitamin B12 deficiency [50].

Risk of Cognitive Impairment

Cognitive decline and some forms of dementia including Alzheimer's dementia (AD) are associated with low folate levels [51–53]. RBC folate levels are directly related to cognitive function scores and inversely to dementia [53]. Elevated concentration of homocysteine has been associated with increased prevalence of poor cognitive function and increased risk of developing dementia and AD, for elevated homocysteine is a risk factor for vascular disease, and hence it may be pertinent to AD [54]. Elevated homocysteine [34, 55], decreased folate and low B12 have been associated with poor cognitive function, cognitive decline and dementia

[56, 57], but controlled trials have not shown any clear evidence of supplementing B12 or folate improves dementia or slows cognitive decline [56]. Divergent results were seen in studies; some studies have shown direct association between B12 and cognitive function scores [57], but other studies have found no such relationship [44]. Deficits in constructional ability and processing speed have been associated with elevated homocysteine in exceptionally functioning elderly Chinese population [58]. The reasons are varied and manifold. The measurement of total vitamin B12 has limitations [50] for it has been shown the individuals with neurological and vascular abnormalities may present with normal range of B12 [59]. It has been suggested B12 status is better indicated by MMA and is better predictor of cognitive function in older adults than total B12 or holotranscobalamin (holoTC) but has restricted benefit as a screening test for B12 deficiency [50]. According to Miller [50], to categorise B12 deficiency, there must be at least more than two of the analyses, holoTC, MMA or homocysteine and total B12.

Specific cognitive abilities may have differential outcomes with homocysteine and folate [53, 60, 61]. In a healthy elderly Chinese population, elevated homocysteine levels were associated with cognitive deficits such as constructional ability and processing speed and folate with episodic memory and language [58]. A decline in recall memory was seen with and high concentrations of homocysteine and with low vitamin B12 predicts cognitive decline [34].

Treatment

Randomised controlled trials have not provided any clear evidence that supplementation of folic acid or vitamin B12 had any efficacy in slowing cognitive decline or improving cognitive function though it may normalise homocysteine levels [56]. Other trials have shown no discernible effectiveness in improving cognitive function [62, 63].

Some Aspects of Thyroid Dysfunction in the Elderly

Introduction

Thyroid diseases are common in the elderly and take the form of clinical and subclinical hypothyroidism and hyperthyroidism, thyroid nodules, toxic and nontoxic multinodular goitre and thyroid cancer [64, 75]. Abnormal thyroid tests are common in the elderly, and the prevalence of thyroid dysfunction is reported to be very high [66]. Thyroid diseases increase as age advances [67] and its incidence [67] and with the prevalence increasing and reaching its highest rates in the elderly [65]. Studies of the aetiology in dementia revealed only 1 case of reversible dementia out of 2781 cases analysed [68]. Subclinical thyroid disorders are common in the elderly [69]. In women older than 60 years, the prevalence of subclinical hypothyroidism may vary in different populations and is about 4 to 8.5% but may be as high as 20% [70]. Subclinical hyperthyroidism is found in about 2% in the population and is increased in aged subjects of both sexes [71], affecting up to 7–8% in iodine deficient areas [72]. Subclinical hypothyroidism increases with age, and in individuals aged 60 years and older, it ranges between 3 and 16% [73]. In a prospective longitudinal study of men and women aged 72–82 years, subclinical hyperthyroidism and subclinical hypothyroidism were found in 65 and 161 participants, respectively [74].

Pathophysiology

As the age advances thyroid function changes, but their significance in the very old remains unclear. There is an increased prevalence of serum thyroid antibodies [71]. The most common cause of hypothyroidism in the elderly is autoimmune thyroiditis. In a study of 764 patients 85 years old, using the TSH reference range as 0.3–4.7 mU/L, Mitchell et al. [75] found 90% to be euthyroid, 7.8% subclinical hypothyroid and 1.3% subclinical hyperthyroid and overt hyperthyroidism and overt hypothyroidism in 0.2% and 0.7%, respectively. 13.7% who were disease-free had thyroid peroxidase (TPO) antibodies, and the TSH levels gradually rose in many of the elderly [75]. Thyroid concentrations change with age [76]. After the ninth decade, the T_3 and TSH show a decline and rT_3 an increase [77]. In euthyroid individuals, FT_3, FT_4 and TSH show subtle age-related changes, and with age FT_3 and TSH decline, whereas FT_4 increases [78].

Subclinical thyroid disease is defined as the presence of abnormal TSH (>4.5 mU/L hypo-; <0.45 mU/L hyper-) and the circulating concentrations of free T4 and free T3 in their respective normal ranges [70, 79]. Increased TSH has been demonstrated resulting from subclinical hypothyroidism and rises further with ageing [80–82], but other studies have shown lower TSH levels with ageing in the absence of thyroid disease [77, 83, 84].

Cognitive Impairment

Thyroid hormones are crucial for brain development and for brain function throughout life [76, 85]. With the cognitive decline often concurrent with ageing and the thyroid hormone concentrations change with age, it is likely that these changes may causally be related to the changes in cognition during normal ageing [76]. Decreased cognitive functioning such as memory and reaction time has been associated with

overt hyperthyroidism and both clinical and subclinical hypothyroidism in middle-aged and the elderly [86].

Several epidemiological studies have demonstrated an association between subclinical hyperthyroidism and low serum concentrations of TSH with dementia [86], but this association has not been substantiated in the elderly [86, 87]. Subclinical hyperthyroidism is the most prevalent thyroid dysfunction in Italian older persons associated with cognitive impairment [88]. Others however have found no dependable evidence of cognitive impairment or decline with subclinical hyper- or hypothyroidism [74].

Treatment

Scientific literature is riddled with uncertainty regarding the treatment of subclinical hypothyroidism. In contrast to the treatment of overt hypothyroidism, the treatment of subclinical hypothyroidism continues to be debated [89]. Several studies have shown that subclinical hypothyroidism is not associated with impairment of cognition or physical function [90, 91] in the elderly. Epidemiological studies have suggested a relationship between hypothyroidism [92] and subclinical hypothyroidism with the risk of dementia [93, 94]. It has also been suggested that subclinical hypothyroidism may be a predisposing factor for depression, cognitive impairment and dementia [95].TSH levels and free thyroxine levels in the oldest old were not associated with cognitive impairment according to the Leiden 85+ study [89]. The Rotterdam study found no association between TSH levels and the risk of Alzheimer disease at 5.5-year follow-up [90].

Studies of the associations of subclinical hypothyroidism and cognitive function in the elderly have yielded inconsistent findings. TSH increases with age even with older people without thyroid disease [75], and a higher TSH may support increased life span [89, 96], and treating older people may do more harm than good [96]. Thus there is insufficient evidence that treatment of subclinical hypothyroidism is beneficial [70]. In the oldest old, TSH is not much of a relevance, and a higher TSH is associated with increased survival.

In older adults subclinical hyperthyroidism is associated with decreased bone mineral density, fractures [97], cognitive impairment [78], coronary heart disease and atrial fibrillation [98]. A serum level of less than 0.1microU per ml was shown to be associated with progression to overt hyperthyroidism, atrial fibrillation and reduced bone density and cardiac dysfunction [70]. However there are reports that subclinical hyperthyroidism is not associated with cognitive impairment in the elderly population, and the progression to overt hyperthyroidism is uncommon [99].

Diabetes Mellitus and Cognitive Impairment

Introduction

Diabetes mellitus (DM) is among the commonest diseases that has the highest number of complications involving various vital organs [100] and resulting in slowly progressive organ damage [101]. Diabetes with dementia and cognitive dysfunction has recently received considerable attention [102]. DM is associated with functional and geriatric syndromes which include falls, frailty, urinary tract infection, pain, depression and cognitive impairment [103–106].With the increase in the life expectancy in the general population [107] and changes in life style [108], type 2 diabetes mellitus (T2DM) is on the rise [109] with increasing global prevalence [110]. It is increasing especially in over 85 years [105, 111]. The overall T2DM increased from 16% to 23% between 1995 and 2004 in residents of nursing care facilities [112]. Of the 328 octogenarians studied, 29.9% had DM with a high prevalence at the 85 years [111].

Pathophysiology

There are many mechanisms through which DM increases the risk of cognitive impairment and dementia. The exact mechanisms are poorly or partly understood [113, 114]. The risk factors that increase include hyper- and hypoglycaemia [113–117], vascular disease [101, 113, 117], vascular risk factors such hypertension and dyslipidaemia [101], insulin resistance [113–115, 117], poor diabetic management [116], duration of disease [101] and glycaemic fluctuations [116]. Several hypotheses have been advanced, and the postulated mechanisms are hyperglycaemia, hypoglycaemia, insulin resistance and vascular advanced glycosylation products (AGEs) and activation of the cytokines.

Hyperglycaemia

The inimical effects of hyperglycaemia can occur through multiple pathways: The polyol pathway, where the glucose is converted to sorbitol and fructose, accumulations of which result in impaired axonal transport and ultimately lead to structural breakdown in the tissues [118]. Protein kinase C pathway plays an important role in the development of diabetic complications, and protein kinase inhibition results in increase in expression of transforming growth factor-beta (TGF-beta) which is a potent prosclerotic cytokine [119]. In diabetes reactive oxygen species generation and expression of proinflammatory cytokines are manifestations of chronic inflammation [120]. In diabetes hyperglycaemia increases

advanced glycation products disturbing biological function of various proteins [121]. Hyperglycaemia activates the hexosamine pathway through increased glucose shunting [114] causing permanent modification of proteins and transcription factors [121]. Diabetes increases oxidative stress resulting in endothelial damage and injury to nerve cell and death [118]. It has been suggested that the same mechanisms may be active in the brain and bring about changes in cognitive function [114].

Hypoglycaemia

Repeated severe hypoglycaemia has been attributed to cause brain damage and cognitive deterioration in several case reports [122]. At the blood glucose below 3 mmol/L, cognitive functioning becomes impaired [122, 123], and cognitive functioning does not return fully until 90 min after blood glucose is restored, but recurrent severe hypoglycaemia may cause cumulative cognitive impairment. In experimental stroke hypoglycaemia is known to induce proinflammatory changes and exacerbate cerebral damage [120]. One of the serious complications of diabetes is intensifying ischaemic brain damage [124]. In the interpretation of the mechanisms of ischaemic brain damage in diabetics, the mitochondria and complex mitochondrial biochemical pathways play an important role [124].

Insulin Signalling and Insulin Resistance

To maintain the health of neuronal cells, to increase their survival and to decrease oxidative stress, insulin signalling is necessary [125]. Glucose uptake and utilization, modulation of acetyl choline levels and amyloid peptide levels are regulated by insulin signalling [126] and the brain signalling systems have an important role in the pathogenesis and aetiology of T2DM and the metabolic system [127]. The brain signalling systems are regulated by insulin, iGF-1, leptin, dopamine, melanocortins and glucagon-like peptide-1 [128].

There is considerable evidence to support the concept that insulin resistance has an important role in the pathogenesis of cognitive impairment and neurodegeneration [128]. Insulin resistance is associated with reduced signalling in the brain [129]. Alzheimer disease is characterised by selective loss of neurons, synaptic connections and accumulation of beta amyloid protein and tau protein [130]. In animal studies peripheral insulin resistance has been shown to accelerate beta amyloid accumulation in the brain [131]. Higher insulin resistance portends reduced grey matter in the medial temporal lobe, prefrontal cortices and other parietal gyri [132]. Hence insulin resistance and impaired insulin signalling are potential mechanisms in the advancement of cognitive impairment [129] and can contribute to the changes seen in AD [126]. AGEs formed due to chronic hyperglycaemia can induce insulin resistance and impede insulin signalling [133]. The effects of insulin signalling predominantly occur in specific regions of the brain where there is a high concentration of insulin receptors such as the hippocampus, prefrontal cortices and cingulate gyrus areas affected in early AD [134]. In T2DM as well as in AD, animal models suggest hippocampal insulin resistance as the potential mediator of cognitive dysfunction [135].

Box 28.1 Possible Mechanisms Involved in Cognitive Decline and Dementia in Diabetes

There are many mechanisms.

The inimical effects of hyperglycaemia are identified through multiple pathways.

Protein kinase C pathway [119].

Hyperglycaemia activates the hexosamine pathway [114].

Diabetes increases oxidative stress.

Reactive oxygen species generation.

Repeated severe hypoglycaemia.

Induces pro-inflammatory changes [120].

Insulin resistance and impaired insulin signalling are potential mechanisms [129].

Vascular disease.

Vascular Disease

Insulin resistance might contribute to cognitive impairment through a vascular mechanism [136]. Longitudinal studies have found a close association between hypertension, cognitive decline and dementia in late life [137, 138]. Long-standing diabetes is associated with damage and dysfunction of large (macrovascular) and small (microvascular) blood vessels resulting in damage to various organs (Box 28.1).

Multiple Choice Questions

1. The following are true of hearing loss in the elderly, EXCEPT:
   A. Hearing loss in older adults is associated with accelerated cognitive decline and incident dementia.
   B. Decline in the peripheral auditory system does not have effects on the central auditory system and function.

Clinical Relevance

Longitudinal studies have shown that hearing loss in older adults is associated with accelerated cognitive decline and incident dementia [19, 22].

Of the older adults who could benefit from treatment, only a small ratio seek help [29]; the remaining suffer from social isolation, a negative impact on health and poor quality of life.

Deficiency of vitamin B12 and folic acid is associated with declining neurocognitive function and atherosclerotic lesions [33].

Randomised controlled trials have not provided any clear evidence that supplementation of folic acid or vitamin B12 had any efficacy in slowing cognitive decline or improving cognitive function though it may normalise homocysteine levels [56].

Decreased cognitive functioning such as memory and reaction time has been associated with overt hyperthyroidism and both clinical and subclinical hypothyroidism in middle-aged and the elderly [86].

There is insufficient evidence that treatment of subclinical hypothyroidism is beneficial [70].

In DM there are many mechanisms through which DM increases the risk of cognitive impairment and dementia.

The risk factors that increase include hyper- and hypoglycaemia [113–117], vascular disease [101, 113, 117], vascular risk factors such hypertension and dyslipidaemia [101], insulin resistance [113–115, 117], poor diabetic management [116], duration of disease [101] and glycaemic fluctuations [116].

C. Adults with hearing loss who were not wearing hearing aids had higher rates of anxiety, depression and psychosocial disorders.
D. In older adults hearing loss may be associated with dementia by decreasing stimulatory input and impeding social interaction.

2. The following are true of B12 and folate deficiencies, EXCEPT:

A. In elderly persons B12 and folate deficiencies are common.
B. Cognitive decline and some forms of dementia including Alzheimer's dementia (AD) are associated with low folate levels.
C. Decreased concentration of homocysteine has been associated with increased prevalence of poor cognitive function and increased risk of developing dementia and AD.
D. The measurement of total vitamin B12 has limitations for it has been shown that the individuals with neurological and vascular abnormalities may present with normal range of B12.

3. The following ate true of thyroid dysfunction, EXCEPT:

A. Decreased cognitive functioning such as memory and reaction time has been associated with overt hyperthyroidism.
B. Decreased cognitive functioning is associated with both clinical and subclinical hypothyroidism in middle-aged and the elderly.
C. In older adults subclinical hyperthyroidism is not associated with coronary heart disease and atrial fibrillation.
D. TSH increases with age even with older people without thyroid disease.

4. The following are true with diabetes, EXCEPT:
A. Repeated severe hypoglycaemia has been attributed to cause brain damage and cognitive deterioration.
B. There is no evidence to support the concept that insulin resistance has an important role in the pathogenesis of cognitive impairment.
C. Studies have found a close association between hypertension, cognitive decline and dementia in late life.
D. One of the serious complications of diabetes is intensifying ischaemic brain damage.

Answers to MCQs

1. B
2. C
3. C
4. B

References

I. Hearing Loss and Cognitive Decline

1. Kravitz E, Schmeidler J, Beeri MS. Cognitive decline and dementia in the oldest-old. Rambam Maimonides Med J. 2012;3(4):e0026. https://doi.org/10.5041/RMMJ.10092.
2. Slavin MJ, Bridaty H, Sachdev PC. Challenges of diagnosing dementia in the oldest old population. Review Article. J Geronto A Biol Sci Med Sco. 2013;68(9):1103–11.
3. Limongi F, Noae M, Siviero P, Crepaldi G, Maggi S. Epidenmiology of aging dementia and age-related hearing loss. Hearing Balance Commun. 2015;13(3) https://doi.org/10.3109/21695717.2015.1013260. Accessed 6 March 2017
4. Cruickshanks KJ, Wiley TL, Tweed TS, Klein BE, Jlein R, Mares-Perlman JA, et al. Prevalence of hearing loss in older adults in beaver dam, wincosin, the epidemiology of hearing loss study. Am J Epidemiol. 1998;148:874–86.
5. Chen W, Lin FR. Prevalence of hearing aid use among older adults in the United States. Arch Intern Med. 2012;172(3):292–3.
6. Solheim J, Shirvaeva O, Kvaerner KJ. Lack of ear care knowledge in nursing homes. J Multidiscip Healthc. 2016;9:481–8.
7. Martini A. Hearing balance and communication problems in the elderly: Editorial. J Hearing Balance Commun. 2015;13(2) https://doi.org/10.3109/21695717.006431.
8. Feder K, Michaund D, Ramage-Morin S, McNamee J, Beauregard Y. Prevalence of hearing loss among Canadians 20 to 79: audiometric results from 2012/2013. Canadian health measures survey. Health Rep. 2015;26:18–25.
9. Davis A, Davis KA. Epidemiology of aging and hearing loss related to other chronic illnesses. www.phonak.com/content/dam/phonak/b2b/Events/conference_proceedings/chicago_2009/proceedings/09_P69344_Pho_Kapital_2_S23_32_pdf. Accessed 6 March 2017.
10. Tavanai E, Mohammadkhani G. Role of antoxidants in prevention of age-related hearing loss: a review of literature. Eur Arch Otorhinolaryngol. 2017;274(4):1821–34.
11. Fujimoto C, Yamasoba T. Oidative stress and mitochondrial dysfunction in age-related hearing loss. Oxod Med Cell Longev. 2014;2014:582849. https://doi.org/10.1155/2014/582849.
12. Martini A, Bovo R, Agnoletto M, Da Col M, Drusian A, Liddeo M, et al. Dichotic performance in elderly Italians with Italian stop consonant-vowel stimul. Audiology. 1988;27:1–7.
13. Yamasoba T, Lin FR, Someya S, Kashio A, Sakamoto T, Kondo K. Current concepts in age-related hearing loss: Epidemoiology amd mechanistic pathways. Hear Res. 2013;303:30–8.
14. Eckert MA, Cute SL, Vaden KL Jr, Kuchinsky SE, Dubno JR. Auditory cortex signs of age-related hearing loss. J Assoc Res Otolaryngol. 2012;13:703–13.
15. Husain FT, Medina RE, Davis CW, Szymko-Bennett Y, Simonyan K, Pajor NM, et al. Neuroanatomical changes due to hearing loss and chronic tinnitus: a combined VBM and DTI study. Brain Res. 2011;1369:74–88.
16. Cardin V. Effects of aging and adult0onset hearing loss on cortical auditory regions. Front Neurosci. 2016;10:199. https://doi.org/10.3389/fnins.2016.00199.eCollection. Accessed 8 March 2017
17. Ouda L, Profant O, Syka J. Age-related changes in the central auditory system. Cell Tissue Res. 2015;36(1):337–58.
18. Rigters SC, Bos D, Metselaar M, Roshchupkin GV, Baatenburg de Jong RJ, Ikram MA, et al. Hearing impairment is associated with smaller brain volume in aging. Front Aging Neurosci. 2017;9:2. https://doi.org/10.3389/fnagi.2017.00002.
19. Lin FR, Ferrucci L, An Y, Goh JO, Doshi J, Metter EJ, et al. Association of hearing impairment with brain volume changes in older adults. NeuroImage. 2014;90:84–92.
20. Wang CH, Wu SB, Wu YT, Wei YH. Oxidative stress response elicited by mitochondrial dysfunction implication in the pathophysiology of aging. Exp Biol Med (Maywood). 2013;238(5):450–60.
21. Seidman MD, Khan MJ, Bai U, Shirwany N, Quirk WS. Biologic activity of mitochondrial metabolites on aging and age-related hearing loss. Am J Otol. 2000;21(2):161–7.
22. Lin FR. Hearing loss and cognition among older adults in the United States. J Gerontol A Biol Sci Med Sci. 2011;66(10):1131–6.
23. Uhlmann RF, Larson EB, Rees TS, Koepsell TD, Duckert LG. Relationship of hearing impairment to dementia and cognitive dysfunction in older adults. JAMA. 1989;261:1916–9.
24. Lin FR, Metter EJ, O'Brien RJ, Resnick SM, Zonderman AB, Ferrrucci L. Hearing loss and incident dementia. Arch Neurol. 2013;68(2):214–20.
25. Martini A, Comacchio F, Magnavita V. Auditory evoked responses (ABR<MLR<SVR) and brain mapping I the elderly. Acta Otolaryngol Suppl. 1990;476:97–103.
26. Lin FR, Yaffe K, Xia J, Xue QL, Harris TB, Purchase-Helzner E, et al. Hearing impairment and cognitive decline in adults. JAMA Intern Med. 2013;173(4):293–9.
27. Panza F, Solfrizzi V, Logroscino G. Age-related hearing impairment – a risk factor and frailty marker for dementa and AD. Nat Rev Neurol. 2015;11:166–75.
28. Ives DG, Bonino P, Traven ND, Kuller LH. Characteristics and comorbidities of rural older adults with hearing impairment. J Am Geriatr Soc. 1995;43:803–80.
29. Lin FR, Thorpe R, Gordon-Salant S, Ferrucci L. Hearing loss prevalence and risk factors among older adults in the United States. J Gerontol A Biol Sci Med Sci. 2011;66:582–90.
30. Kochkin S, Rogin CMA. Quantifying the obvious: The impact of hearing instruments on quality of life. Hearing Review. 2000;7(1):34.
31. Oyler AL. Untreated hearing loss in adults -a Growing National Epidemic. http://www.asha.ord/Aud/articles/Untreated -Hearing-Loss-in-Adults/ Accessed 2 Oct 2015.

II. Vitamin B12 and Folate and the Risk of Cognitive Decline

32. Wahlin A, Backman L, Hultdin J, Adolfsson R, Nilsson L-G. Reference values for serum levels of vitamin B12 and folic aid in a population-based sample of adults between 35 and 80 years ofage. Public Health Nutr. 2002;5(3):505–11.
33. Wolters M, Strohle A, Hahn A. Age-associated changes in the metabolism of vitamin B(12) and folic acid: prevalence, aetiopathogenesis and pathophysiological consequences. Gerontol Geriatr. 2004;37(2):109–35.
34. Tucker KL, Qiao N, Scott T, Rosenberg I, Spiro A III. High homocysteine and low B vitamins predict cognitive decline in aging

men: the Veteran's affaires normative aging study 1′2'3′4. Am J Clin Nutr. 2005;82(3):627–35.
35. Brzozowska A, Sicinska E, Roszkowski W. Role of folates ithe nutrition of the elderly. Rocz Panstw Zaki Hig. 2004;55(2):159–64.
36. Koehler KM, Pareo-Tubbeh SL, Romero LJ, Baumgartener RN, Garry PJ. Folate nutrition ad older adults: challenges and opportunities. J Am Diet Assoc. 1997;97(2):167–73.
37. Flood VM, Smith WT, Webb KL, Rochtchina E, Anderson V, Mitchell P. Prevalence of low serum folate and vitamin B12 in older Australian population. Aust NZ J Public Health. 2006;30(1):38–41.
38. Meziere A, Audureau E, Vairelles S, Krypciak S, Docko M, Monie M, et al. B12 deficiency increases with age in hospitalized patients. A study on 14,904 samples. J Gerontol Abiol Med Sci. 2014;69(12):1576–85.
39. Baik HW. Russel: Vitamin B12 deficiency in the elderly. Annu Rev Nutr. 1999;19:357–7.
40. Andres E, Lukili MH, Noel E, Kaltenbach G, Abdelgheni MB, Perrin AE, et al. Vitamin B12 (cobalamin) deficiency in elderly patients. CMAJ. 2004;171(3):251–9.
41. Pennypacker LC, Allen RH, Kelly JP, et al. High prevalence of cobalamin deficiency in elderly outpatients. J Am Geriatr Soc. 1992;40(12):1197–961.
42. Hausman D, Johnson MA, Davey A, Stabler S. The oldest old: red blood cell and plasma folate in African American and white octagenarians and centenarians in Georgia. J Nutr Health Aging. 2011;15(9):744–50.
43. Risch M, Meier DW, Sakem B, Escobar PM, Risch C, Nydegger U, Risch L. Vitamin B12 and folate levels in healthy Swiss senior citizens: a prospective study evaluating reference intervals and decision limits. BMC Geriatrcs. 15:82. https://doi.org/10.1186/s12877-015-0060-x.
44. Mooijaart SP, Gussekloo J, Frolich M, Jolles J, Stott DJ, Weatendorp RJ, de Craen AJM. Homocysteine vitamin b12 and folic acid and the risk of cognitive decline in old age: the Leiden 85-Plus Study 1'2'3. Am J Clin Nutr. 2005;82(4):866–71.
45. Hutto BR. Folate and cobalamin in psychiatric illness. Comp Psychiatry. 1997;6:305–14.
46. Carney MWP, Toone BK, Reynolds EH. *S*- Sdenosylmethionine and affective disorder. Am J Med. 1987;83(Suppl 5A):104–6.
47. Levitt AJ, Joffe RT. Vitamin B12 and life course of depressive illness. Biol Psychiatry. 1989;25:867–72.
48. Shane B, Stokstad ELR. Vitamin B-12 –folate interrelationships. Annu Rev Nutr. 1995;5:115–41.
49. Lewerin C, Ljungman S, Nilsson-Ehle H. Glomerular filtration rate as measured by serum cystatin C is an important determinant of plasma homocysteine and serum methylmalonic acid in the elderly. J Intern Med. 2007;261(1):65–73.
50. Miller JW. Assessing the association between vitamin B12 status and cognitive function in older adults. Am J Clin Nutr. 2006;84(6):1259–60.
51. D'Anci KE, Rosenberg IH. Folate and brain function in the elderly. Curr Opin Clin Nutr Metab Care. 2004;7(6):659–64.
52. Mischoulon D, Raab MF. The role of folate in depression and dementia. J Clin Psychiatry. 2007;68(Suppl 10):28–33.
53. Ramos M, Allen LH, Mungas DM, Jagust WJ, Haan M, Green R, et al. Low folate states is associated with impaired cognitive function and dementia in the Sacromento area Latino study in aging. Am J Clin Nutr. 2005;82:1346–52.
54. Clarke R, Smith AD, Jobst KA, Refsum H, Sutton L, Ueland PM. Folate, vitamin B12 and serum total homocysteine levels in confirmed Alzheimer's disease. Arch Neurol. 1998;55(11):1449–55.
55. Quadri P, Fragiacomo C, Pezzati R, Zanol L, Forloni C, Tettamanti M, et al. Homocysteine, folate and vitamin B12 in mild cognitive impairment, Alzheimer's disease and vascular dementia. Am J Clin Nutr. 2004;80:114–22.
56. Vogel T, Dali-Youcef N, Kaltenbach G, Andrea E. Homocystene,vitamin B12,folate and cognitive functions: a syatematic and critical review of the literature. Int J Clin Pract. 2009; https://doi.org/10.1111/j.1742-1241,2009.02026x.
57. Hin H, Clarke R, Sherliker P, Atoyebi W, Emmes K, Birks J, et al. Clinical relevance of low serum B12 concentrations in older people: the Babbury B12 Study. Age Aging. 2006;35:4116–22.
58. Lei F, Ng T-P, Chuah L, Niti M, KuaE-H. Homocysteine,folate and vitamin B12 and cognitive performance in older Chinese adults: findings fro the Singapore Longitudinal Ageing Study1'2'3. Am J Clin Nutr. 2006;84(6):1506–12.
59. Allen RH, Stabler SP, Savage DL, Lindenhaum J. Metabolic abnormalities in cobalamin (vitamin B12) and folate deficiency. FASEB J. 1993;7:1344–53.
60. Miller JW, Green R, Ramos MI, Allen LH, Mungas DM, Jagust WJ, et al. Homocysteine and cognitive function in the Sacromento area Latino study on aging. 1′2'3′4. Am J Clin Nutr. 2003;7:441–7.
61. Prins ND, Den Heyer T, Holman A, Kondstaat PJ, Joless J, Clarke R, et al. Homocysteine and cognitive function in the elderly. The Rotterdam Study. Neurology. 2002;59:1375–80.
62. Malouf R, Grimley Evans J, Areosa ASastra A. Folic acid with and without vitamin B12 for cognition and dementia (Cochrane Review). In: et al. The Cochrane Library, Issue 3. Chichester, UK: Wiley & Sons Ltd; 2004.
63. Malouf R, Areosa ASastra A. Vitamin B12 for cognition and dementia (Cochrane Review). In: et al. The Cochrane Library, Issue 3. Chichester, UK: Wiley & Sons Ltd; 2004.

III. Some Aspects of Thyroid Dysfunction in the Elderly

64. Chiovato L, Mariotti S, Pinchera A. Thyroid diseases in the elderly. Bailliere Clin Endocrinol Metab. 1997;11(2):251–70.
65. Faggiano A, Del Prete M, Marciello F, Marrotta V, Ramundo V, Colao A. Thyroid diseases in the elderly. Minnerva Endocrinol. 2011;36(3):211–31.
66. Ozbakir O, Dogukan A, Kelestimur F. The prevalence of thyroid dysfunction among elderly subjects inendemic goiter area of Central Anatolia. Endocr J. 1995;42(5):713–6.
67. Kumar H, Singh VB, Meena BL, Gaur S, Singla R, Sisdiva MS. Clinical profile of thyroid dysfunction in elderly: an overview. Thyroid Res Pract. 2016;13:101–5.
68. Clarnette RM, Patterson CJ. Hypothyroidism : does treatment cure dementia? J Geriatr Psychiatry Neurol. 1994;7:23–7.
69. Formiga F, Ferrer A, Padros G, Contra A, Crbella X, Pjol R, et al. Thyroid status and functional and cognitive status at baseline and survival after 3 tears of follow-up: the OCTABAIX study. Eur J Endocrinol. 2013;170(1):69–75.
70. Wilson GR, Curry RW Jr. Subclinical thyyroid disease. Am Fam Physician. 2005;72(8):1517–24.
71. Mariotti S. Editorial. Thyroid function and aging: Do serum 3,4,3'-triiodothyronine and thyroid-stimulating hormone concentrations give the Janus response? J Clin Endocrinol Metab. https://doi.org/10.1210/jc.2005-2214.
72. Aghini-Lombardi F, Antonangeli L, Martino E, Vitti P, Maccherini D, Leoli F, et al. The spectrum of thyroid disorders in an iodine-deficient community the Pescopagano survey. J Clin Endorinol Metb. 1999;84:51–566.
73. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29:76–131.

74. Wijsman LW, de Craen AJ, Trompet S, Gussekloo J, Stott DJ, Rodondi N, et al. Subclincal thyroid dysfunction and cognitive decline in old age. PloS One. 2013;8(3):e59199. https://doi.org/10.1371/journal.pone.0059199.
75. Mitchell AL, Razvi S, Pearce SH, & 85+Study Core Team. Thyroid function in a cohort of eighty five year olds: the Newcastle 85+study. Endocrine Abstracts. 2009;19:363.
76. Begin ME, Langlois MF, LorrainD CSC. Thyroid function and cognition with aging. Curr Gerontol Geriatr Res. 2008;2008:474868. https://doi.org/10.1155/2008/474868.
77. Mariotti S, Franceschi C, Cossarizza A, Pinchera A. The aging thyroid. Endocr Rev. 1995;16:686–715.
78. Ceresini G, Lauretani F, Maggio M, Ceda GP, Morganti S, Usberti E, et al. Thyroid function abnormalities and cognitive impairment in elderly people: results of the Invecchiare chianti study. J Am Geriatr Soc. 2009;57(1):89–93.
79. Nakajima Y, Yamada M. Subclinical thyroid disease. Nihon Rinsho. 2012;70(11):1865–71.
80. Cooper DS, Biondi B. Sunclinical y=thyroid disease. Lancet. 2012;379:1142–54.
81. Surks MI, Boucai L. Age-and-race-based serum thyrotropin reference limits. J Clin Endocrinol Metab. 2010;95:496–502.
82. Ochs N, Auer R, Bauer DC, Nanchen D, Gussekloo J, Cornuz J, et al. Met-analysis: subclinical thyroid dydfuction ad risk for coronary heart disease and mortality. Ann Intern Med. 2008;148:832–45.
83. Chahal HS, Drake WM. The endocrine system and ageing. J Pathol. 2007;211:173–18.
84. Over R, Mannan S, Nsouli-Marktabi H, Burman KD, Jonklass J. Age and thyrotropin response tohypothyroxinemia. J Clin Endocrinol Metab. 2010;95:3675–83.
85. Benal J. Thyroid hormones amd brain development. Viram Harm. 2005;71:95–122.
86. Annerbo S, Lokk J. A clinical review of the association of thyroid stimulating hormone and cognitive impairment. ISRN Enocrinol. 2013;2013:1. https://doi.org/10.1155/2013/856017.
87. Gan EH, Pearce SHS. The thyroid in mild cognitive impairment and low thyrotropin in older people. J Clin Endocrinol Metab. 2012;97(10):3431–49.
88. Ceresini G, Lauretani F, Maggio M, Cappola AR. Subclinical hyperthyroidism is the most prevalent thyroid dysfunction in older Italians and is associated with cognitive impairment. www.researchgate.net/publication/242589786_subclinical _hyperthyroidism_is_the_most_prevalent_thyroid_dysfunction_in_older_Italians_and_is_associated_with cognitive_impairment.
89. Gesing A, Lewinski A, Karbownik-Lewinska M. The thyroid gland and the process of aging; what is new? Thyroid Research. 2012;5:16. https://doi.org/10.1186/756-6614-5-16.
90. De Jongh RT, Lips P, van Schoor NM, Rijs KJ, Deeg DJ, Comijs HC, et al. Endogenous subclinical thyroid disorders, physical and cognitive function., depression and mortality in older individuals. Eur J Endocrinol. 2011;165:545–54. https://doi.org/10.1530/EJE-11-0430.
91. Park YJ, Lee EJ, Lee YJ, Choi SH, Park JH, Lee SB, et al. Subclincal hypothyroidism (SCH) is not associated with metabolic derangement cognitive impairment depression or poor quality of life (QoL) in elderly subjects. Arch Geronto Geriatr. 2010;50:e68–73. https://doi.org/10.1016/j.arhger.2009.05.015.
92. Ganguli M, Burmeister LA, Seaberg EC, Belle S, DeKosky ST. Association between dementia and TASH. A community based study. Biol Psychiatry. 1996;40:714–25.
93. Van Osch LADM, Hogervorst E, Combrinck M, Smith AD. Low thyroid-stimulating hormone as an independent risk factor for Alzheimer's disease. Neurology. 2004;62:1967–71.
94. Kalmijn S, Mehta KM, Pols HAP, Hofman A, Drexhage HA, Breteler MM. Subclinical hyperthyroidism and the risk of dementia: the Rotterdam study. Clin Endorinol. 2000;53:733–7.
95. Davis JD, Stern RA, Flashman LA. Cognitive and neuropsychiatric aspects of subclinical hypothyrpidism: significance in the elderly. Curr Psychiatry Rep. 2003;5(5):384–90.
96. Pasqualetti G, Tognini S, Polini A, Caraccio N, Monzani E. Subclinical hypothydroism and heart failure in older people. Endocr Metab Immune Disord Drug Targets. 2013;13(1):13–21.
97. Turner MR, Camacho X, Fischer HD, Austin PC, Anderson GM, Rochon PA, et al. Levothroxine dose and the risk of fractures in older adults: nested case –control study. BMJ. 2011;342:d2238. https://doi.org/10.1136/bmj.d2238.
98. Collet TH, Gussekloo J, Bauer DC, den Elzen WP, Cappola AR, Balmer P, et al. Subclinical hyperthyroidism and the risk of coronary heart disease and mortality. Arch Intern Med. 2012;172:799–809.
99. Rosario PW. Natural history of subclinical hyperthyroidism in elderly patients with TSH between 0.1 and 0,.4 mIU/l: a prospective study. Clin Endocrinol. 2010;72:685–8.

IV. Diabetes Mellitus and Cognitive Impairment

100. Mastro A, Caouto JB, Vagula MC. Cognitive impairment and dementia in type 2 diabetes mellitus. US Pharmacis. 2014;39:33–7.
101. Van den Berg E, Kessels RP, Kappelle LJ, de Haan EH, Biessels GJ, et al. Type 2 diabetes cognitive impairment and dementia: vascular and metabolic determinants. Drugs Today (Barc). 2006;42(11):741–54.
102. Dash SK. Cognitive impairment and diabetes. Recent Pat Endocr Metab Immune Drug Discov. 2013;7(2):155–16.
103. Kirkman MS, Briscoe VJ, Clark N, Florez H, Haas LB, Halter JB, et al. Diabetes in older adults: a consensus report. J Am Geriatr Soc. 2012;60:2342.
104. Abbatcola AM, Maggi S, Paolisso G. New approaches to treating type2 diabetes mellitus in the elderly: role of incretin therapies. Drugs Aging. 2008;25(11):913–25.
105. Abbatecola AM, Paolisso G, Sinclair AJ. Treating diabetes mellitus in older and oldest old patients. Curr Pharm Des. 2015;21(13):1665–71.
106. Paolisso G. Pathophysiology of diabetes in elderly people. Acta Biomed. 2010;81(Suppl 1):47–53.
107. Pratley RE, Gilbert M. Clinical management of the elderly patients with type 2 diabetes mellitus. Postgrad Med. 2012;124(1):133–43.
108. Kawamura T. Cognitive impairment in diabetic patients: Can diabetic control prevent.http://onlinelibrary.wiley.com/doi/10.111/j.2040-1124.201.00234.x/full. Accessed 19 March 2017.
109. Saedi E, Gheini MR, Arami MA. Diabetes mellitus and cognitive impairments. World J Diabetes. 2016;7(17):412–22.
110. Du YF, Ou HY, Beverly EA, Chiu CJ. Achieving glycaemic control in elderly patients with type 2 diabetes: a critical comparison of current options. Clin Interv Aging. 2014; https://doi.org/10.2147/CIA.S53482.
111. Ferrer A, Padros G, Formiga F, Pujol R. Diabetes mellitus: prevalence and effect of morbidities in the oldest old. The Octabaix study. J Am Ger Soc. 2012;60(3):462–7.
112. Zhang X, Decker FH, Luo H, Geiss LS, Pearson WS, Saaddine JB, et al. Trends in the prevalence and comorbidities of diabetes mellitus in nursing home residents in the United States. 1995–2004. J Am Geriatr Soc. 2010;58:724.
113. Kodl CT, Seaquist ER. Cognitive dysfunction and diabetes mellitus. Endocri Rev. 2008;29(4):494–511.
114. Vijayakumar TM, Sirisha GBN, Begam MDF, Dhan MD. Mechanism linking cognitive impairment and diabetes

mellitus. https://www.researchgate.nrt/publivation/231537655_Mechanism_Linking_Cognitive_Impairment_and_Diabetes_mellitus. Accessed 19 March 2017.
115. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP Jr, Selby JV. Hypoglycaemic episodes and risk of dementia in older patientstype 2 diabetes mellitus. JAMA. 2009;301(5):1565–72.
116. Ojo O, Brooke J. Evaluating the association between diabetes cognitive impairment and dementia. Int J Environ Res Public Health. 2015;12:8281–94.
117. Iglseder B. Diabetes mellitus and cognitive decline. Wirn Med Wochenschr. 2011;161(21–22):524–30.
118. Clayton W, Elasy TA, Tom A. A review of the pathophysiology classification and treatment of foot ulcers in diabetic patients. Clin Diabetes. 2009;27(2):52–8.
119. Koya KD, Haneda M, Nakakawa H, Isshiki K, Sato H, Maeda S, et al. Amelioration of accelerated diabetic mesangial expansion by treatment with PKC beta inhibitor in diabetic db/db mice, a rodent model of type 2 diabetes. FASEB J. 2000;3:2329–37.
120. Shukla V, Shakya AK, Perez-Pinzon MA, Dave KR. Cerebral ischaemic damage in diabetes an inflammatory perspective. J Neuroinflammation. 2017;14(1):21. https://doi.org/10.1186/s12974-016-0774-5.
121. King KD, Jones JD, Warthen J. Microvascular and macrovascular complications in diabetes mellitus. Amer J Pharm Edu. 2005;69(5):Article 87.
122. Warren RE, Frier BM. Hypoglycaemia and cognitive function. Diabetes Obes Metab. 2005;7(5):493–503.
123. Frier BM. Hypoglycaemia and cognitive function in diabetes. Int J Clin Pract Suppl. 2001;123:30–7.
124. Rehni AK, Natiyal N, Perez-Pinzon MA, Dave KR. Hyperglycaemia/hypoglycaemia- induced mitochondrial dysfunction and cerebral ischaemic damage in diabetics. Metab Brain Dis. 2015;30(2):437–47.
125. Bioemer J, Bhattacharya S, Amin R, Suppiramaniam V. Impaired insulin signaling and mechanism of memory loss. Prog Mol Biol Transl Sci. 2014;121:413–49.
126. Alagiakrishnan K, Sakaralingam S, Ghosh M, Mereu L, Senior P. Antibiotic drugs and their potential role in treating mild cognitive impairment and Alzheimer' s disease. Discovery Medicine. http://www.discovery medicine.com/Kannayiram-Alagiakrishnan/2013/…e-in-treating-mild-cognitive-impairment-and-alzheimers-disease
127. Shapakov AO, Derkach KV, Berstein LM. Brain signalling systems in the Type2 diabetes and metabolic synjdrome: promising target to treat and prevent theses diseases. Future Sci OA. 2015;1(3) https://doi.org/10.4155/fso.15.23.
128. Ma L, Wang J, Li Y. Insulin resistance and cognitivedysfunction. Clin Chim Acta. 2015;444:18–23.
129. de la Monte SM. Brain insulin resistance and deficiency as therapeutic targets in Alzheimer's disease. Curr Alzheimer Res. 2012;9(1):35–66.
130. Cummings JL, Cole G. Alzheimer disease. JAMA. 2002;287(18):2335–8.
131. Park S, Kim DS, Kang S, Moon NR. Bet-Amyloid-induced cognitive dysfunction impairs glucose homeostasis by increasing insulin resistance and decreasing beta-cell mass in non-diabetic and diabetic rats. Metabolism. 2013;62(2):1749–2013.
132. Willette AA, Xu G, Johnson SC, Birdsill AC, Jonaitis EM, Sager MA, et al. Insulin resistance brain atrophy and cognitive performance in late middle-aged adults. Diabetes Care. 2013;36:443–9.
133. Jia X, Olson DJ, Ross AR, Wu L. Structural and functional changes in human insulin induced by methylglyoxal. FASEB J. 2006;20(9):1555–7.
134. Craft S, Watson GS. Insulin and neurodegenerative disease shared and specific mechanisms. Lancet Neurol. 2004;3:169–86.
135. Biessels GJ, Reagan LP. Hippocampal insulin resistance and cognitive dysfunction. Nat Rev Neurosci. 2015;16:660–71.
136. Gerold C, Frisoni GB, Paolissa G. Insulin resistance in cognitive impairment. The InCHANTI Study Arch Neurol. 2005;62(2):1067–72.
137. Duron E, Hanon O. Vascular risk factors cognitive decline and dementia. Vasc Health Risk Manag. 2008;4(2):363–81.
138. Duron E, Hanon O. Hypertension cognitive decline and dementia. Arch Cardiovasc Dis. 2008;101(3):181–9.

Syncope in the Very Elderly: Diagnosis and Treatment

29

Logan Kanagaratnam and Nages Nagaratnam

Introduction

Syncope is a transient loss of consciousness and accompanied by loss of postural tone due to inadequate cerebral perfusion and followed by rapid and spontaneous recovery [1, 2]. Syncope in the very elderly is common. It could be dangerous and disabling, and the cause may be difficult to diagnose. Cardiovascular causes of syncope are more prevalent in the elderly accounting for 33.8% compared to 16.8% in the young [3]. Cardiogenic syncope is associated with higher rates of morbidity and mortality than other causes [4]. One-year mortality for patients with cardiac syncope was 30% in comparison with 12% in those with noncardiac causes [5].

About 3% of the population is affected by syncope [6]. A retrospective analysis of very old institutionalized patients (mean age 87 years) revealed that over a 10-year period, the prevalence of syncope was 23%, and 1-year incidence was 7% [7]. In a prospective study, the incidence of syncope in nursing home residents was 6%, and 30% of these patients had at least one recurrent episode. The Framingham study data suggested that annually 3% of men and 3.5% of women have syncope [8].The Framingham study also revealed that men over the age of 75 had 6% annual incidence of at least one episode of syncope, compared with only 0.7% in the age group 35–44 [8].

Pathophysiology

Any condition that reduces blood pressure either by peripheral vasodilatation or from a decrease in cardiac output may produce syncope. Cardiac output may be transiently affected by myocardial, anatomical or electrical abnormalities. Elderly are especially vulnerable [7]. The common causes of syncope are the neurally mediated syndromes, cardiac and orthostatic.

Neurocardiogenic syncope is due to triggers and responses mediated by the heart and the baroreceptors. The neurally mediated syncope includes vasovagal syncope, situational syncope and carotid hypersensitivity syncope. One study revealed that almost half of cognitively normal elderly patients seen in the emergency with nonaccidental falls have carotid sinus hypersensitivity [9]. When pressure is applied over the carotid artery in the region of the carotid sinus, the normal response is slowing of the heart rate and impaired atrioventricular node conduction. In patients with carotid sinus syncope, accidental mechanical manipulation such as tight collars or head turning can cause an exaggerated reflex. This reflex response known as carotid sinus hypersensitivity has two components. Cardio-inhibitory response gives rise to asystole lasting 3 s or more, and a vasodepressor response causes a fall in blood pressure of 50 mmHg or more, or the response may be mixed [10].

L. Kanagaratnam (✉)
Royal North Shore, Ryde, North Shore Private and Macquarie University Hospitals, University of Sydney,
St. Leonards, NSW, Australia

N. Nagaratnam
Sydney Medical School, The University of Sydney,
Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_29

Orthostatic hypotension occurs when the autonomic nervous system is impaired and may occur with change in position or with hypovolaemia. It occurs in primary and secondary autonomic failure and with medications. The increased susceptibility of elderly to syncope is due to age-related physiological changes which can impede cerebral blood flow. This may be due to impaired baroreceptor response and heart rate response to orthostatic stress. This can also be aggravated by other comorbidities [11, 12]. Renal sodium conservation and intravascular volume maintenance are impaired by age-related decrease in basal and stimulated renin levels and aldosterone production. The elderly are more likely to become dehydrated. They may have a severe response to diuretics leading to rapid volume depletion, postural hypotension and syncope (Fig. 29.1).

Aetiology

The cause of syncope could be determined in less than 50% of the patients following history, examination and electrocardiogram [13]. Broadly, syncope can be categorized as cardiac or noncardiac. The cardiac causes can be subdivided into mechanical and electrical (Table 29.1). In the former

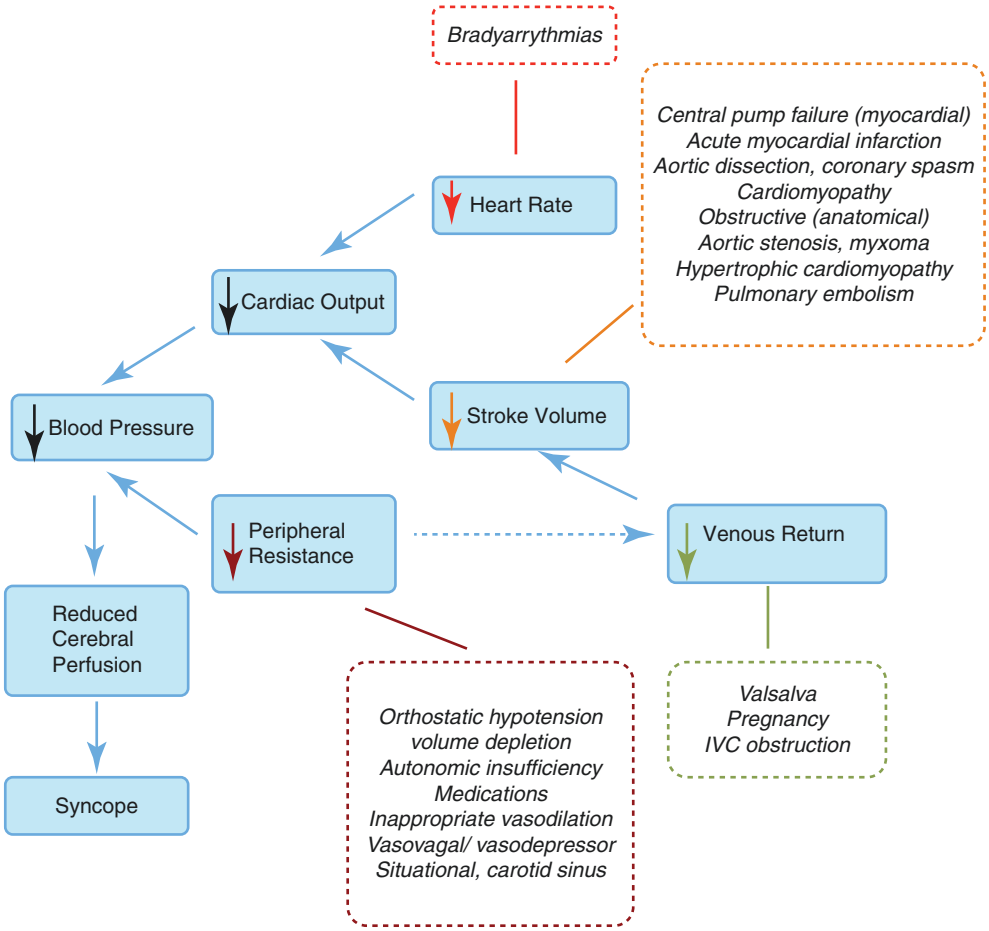


Fig. 29.1 Pathophysiology of syncope

Table 29.1 Syncope causes

Mechanical	Arrhythmia	Postural(Orthostatic) and dys- autonomic	Neurally mediated
Aortic stenosis Hypertrophic obstructive cardiomyopathy Pulmonary embolism Pulmonary hypertension Left atrial myxoma	Sinus node dysfunction Heart block Ventricular tachycardia/ventricular fibrillation Supraventricular tachycardia	Autonomic failure Medication induced Postprandial	Vasovagal syncope Carotid sinus hypersensitivity Situational syncope – Micturition – Cough

blood flow is impeded leading to systemic hypoperfusion and syncope. Conditions like aortic stenosis and hypertrophic cardiomyopathy which cause haemodynamically significant obstruction to the left ventricular outflow tract can be a presenting feature in syncope. It is usually brought on by exertion or exercise. Vigorous exercise and sweating cause vasodilatation, further contributing to the compromise by reduction of venous return leading to hypotension.

Rarely left atrial myxoma which obstructs the mitral orifice, pulmonary embolism and pulmonary hypertension giving rise to right ventricular outflow obstruction may also be associated with effort syncope because of insufficient increase in cardiac output with exercise. Similarly cyanotic congenital heart disease with right to left shunt either by right ventricular outflow obstruction or by pulmonary hypertension could produce exertional syncope. Cardiac syncope could also result from acute myocardial infarction due to low cardiac output or transient severe arrhythmias.

The electrical causes manifest in the form of arrhythmias [14]. They may include bradycardia caused by sinus node dysfunction or bradycardia caused by atrioventricular conduction blocks. Very rapid heart rates also could impair cardiac output and cause syncope. These include ventricular tachycardia and ventricular fibrillation and rapid supraventricular tachycardia. Ventricular arrhythmias can occur in individuals with or without structural heart disease.

Arrhythmias are more frequently diagnosed in the elderly than in younger patients. In a study comparing community-dwelling elderly patients with young persons, arrhythmias were found in 28% of the elderly and only 13% of the young, and several other entities such as aortic stenosis, transient ischaemic attack, myocardial infarction and carotid sinus syncope were primarily found in the elderly [3].

The noncardiac causes include neurally mediated reflex syncope (vasovagal and situational syncope – micturition, postprandial, cough etc.) and orthostatic (postural) hypotension due to autonomic failure. Neurally mediated syncope would still be the commonest cause of syncope in the elderly [15]. In vasovagal syncope, due to external triggers, there is a reflex-mediated transient autonomic failure that may manifest as bradycardia or vasodilatation or both.

Many daily situations such as micturition, defecation, postural changes and meals were found to be associated with syncope in 20% of institutionalized elderly patients [7]. Similarly other situations like strenuous coughing, laughing or swallowing may also cause syncope. Postprandial hypotension is also common among the elderly and could occur during or after a meal and produce syncope [16].

Carotid sinus hypersensitivity was seen in more than half of the cognitively normal older persons presenting to the accident and emergency with nonaccidental falls [9]. A lesion in the bifurcation of the carotid, a tight collar or tumour could produce syncope (carotid sinus syncope) by stimulation of the baroreceptors in the carotid sinus. Carotid massage has its greatest usefulness in the elderly patients [9] and appears to be safe if it is done in patients who do not have carotid bruits, recent stroke, myocardial infarction or a history of ventricular tachycardia [17]. Baroreflex sensitivity decreases with age. When the vagus nerve is stimulated by pain or fright, syncope (vasovagal syncope) could result.

Orthostatic hypotension is an important factor and is common in the elderly and is an important risk factor for syncope. Orthostatic hypotension is defined as a drop of systolic blood pressure of 20 mmHg or more upon standing. Frequently the blood pressure decreases significantly without increase in the heart rate. Prolonged sitting or standing also leads to pooling of blood in the lower extremities. In the elderly orthostatic hypotension is commonly caused by medications. Rarely it is caused by autonomic insufficiency syndromes (idiopathic orthostatic hypotension, Shy-Drager syndrome) (Table 29.1).

Evaluation

The aim of diagnostic evaluation of syncope in the elderly is firstly to identify those who are likely to have life-threatening events or increased risk of death and secondly to prevent recurrent falls [11]. Initially it will be necessary to distinguish true syncope from conditions that can mimic syncope including seizures, narcolepsy, hypoxia, hypoglycaemia, intoxication and functional disorders [18].

For patients presenting to the emergency department with syncope, a short-term risk stratification is utilized to decide whether they need hospital admission. Abnormal ECG and the presence of structural heart disease are associated with increased risk of death in follow-up. Some other factors associated with cardiac syncope include palpitations before syncope, syncope associated with effort or syncope in supine position and absence of autonomic prodromes and absence of predisposing factors [19]. Syncope associated with left ventricular dysfunction, heart failure, severe aortic stenosis and hypertrophic cardiomyopathy also increases the risk of mortality [20].

A number of clinical criteria are available for risk stratification of patients presenting with syncope to emergency department. These include the Risk stratification Of Syncope in the Emergency department (ROSE) rule [21], the San Francisco Syncope Rule (SFSR) [22] and the Boston Syncope Criteria (BSC) among others [23, 24]. They may provide some direction as to who should be admitted to hospital and who are likely to have unfavourable events in the short term.

The ROSE rule is considered positive if any of the following are present, namely, brain natriuretic peptide (BNP) concentration >300 pg/ml, heart rate <50 bpm, positive faecal occult blood, haemoglobin <9.0 g/dl oxygen saturation <94%, chest pain at time of syncope and Q wave on electrocardiogram. Reed et al. [21] reported the ROSE rule had a sensitivity and specificity of 87.2% and 65.5%, respectively, and a negative predictive value of 98.5% for identifying those at high risk.

The San Francisco Syncope Rule criteria include the following: congestive heart failure, haematocrit <30%, abnormal electrocardiogram, shortness of breath and systolic pressure <90 mmHg at triage. An external validation of the SFSR revealed that it is effective in predicting 7-day adverse outcome with a sensitivity of 89% and specificity of 42% suggesting that the rule has limited applicability [25].

Clinical history and examination are the most valuable tools in determining the cause of syncope. The diagnostic yield of history and clinical examination has been quite variable between study populations ranging from 14% to 85% [26, 27].

The syncopal episode is confirmed from the history of abrupt or rapid loss of consciousness lasting a short duration with relatively rapid recovery. The history should be detailed and need to elicit the circumstances when syncope happened including whether patient was standing, sitting, lying or while exercising. It would be important to know whether there was a prodrome (including chest pain or palpitations) and whether there was associated nausea, sweating or vomiting. It is important to know where the syncope happened and whether there were any precipitating factors including fever, dehydration or recent change in medications. In patients with recurrent syncope, it would be essential to look for patterns like relationship to meals or association with micturition. It would also be important to know how quickly the patient recovered and whether there was any fatigue afterwards. If there is an eyewitness available, it would be useful to know whether there was pallor, convulsions, incontinence, tongue biting and the exact duration of the episode. Past history of syncope, heart disease, family and medication should be elicited.

Examination should include heart rate, blood pressure (including postural drop) and presence of cardiac murmur and features of cardiac failure. It is also essential to look for carotid bruit and features of neurological disorders.

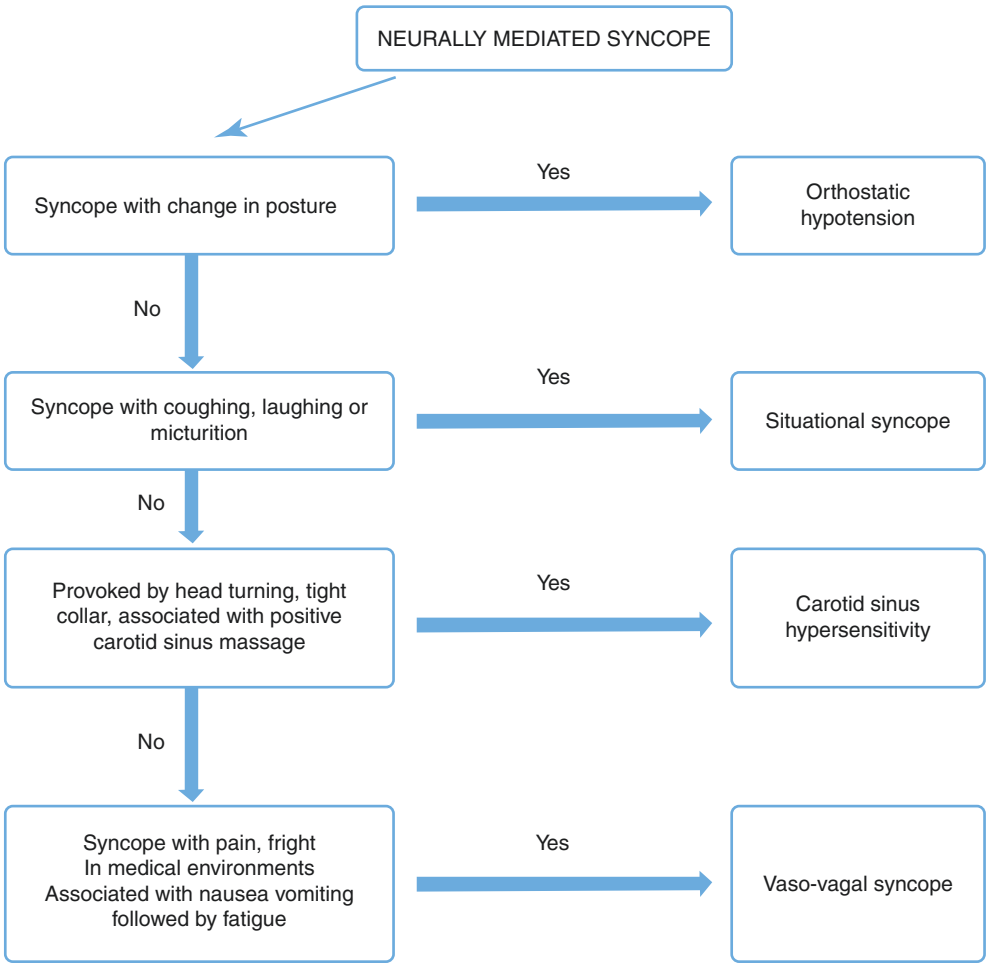
Clinical history alone may be adequate to diagnose neurocardiogenic syncope. These patients often have past history of syncope especially in medical environments or crowded situations. The episodes are often associated with nausea or vomiting. There may be associated sweating, and the episode is often followed by a period of fatigue. However in some elderly neurocardiogenic syncope could occur without these classical features [28].

An ECG would be helpful to look for conduction disturbance, evidence of ischaemia or infarction, left ventricular hypertrophy and conditions like long QT syndrome and Brugada syndrome. Echocardiogram would help to exclude structural heart disease including cardiomyopathy and valvular dysfunction. If no obvious cause is found with basic investigations, further evaluation may be required. Tilt table testing may be useful to diagnose autonomic malfunction, orthostatic hypotension and neurocardiogenic syncope.

Holter monitor is used for 24–48 h of cardiac monitoring (and rarely up to 7 days). Longer duration of cardiac monitoring with event recorder or an implantable loop recorder (ILR) may increase the diagnostic yield [29]. ILR has been made smaller recently. It has a battery life of about 3 years. It can automatically record bradycardia and tachycardia. It also allows patient or carer to activate the device after the event and can retain the heart rhythm few minutes prior to and after activation. In a registry data of patients with syncope who did not have a diagnosis after multiple initial investigations, an ILR was implanted. In this group, after a median follow-up of 10 months, 36% of subjects had a recurrent syncope or significant event, and of these 78% had an ILR-aided diagnosis [30]. A small number of patients may require invasive testing with electrophysiology study. In patients with syncope, neurological investigations are not necessary and have very low diagnostic yield [31]. Algorithms (Algorithms 29.1 and 29.2) outline a diagnostic algorithm for patients presenting with syncope.

Treatment

Treatment would be directed at the specific cause. Bradyarrhythmia may require withdrawal of agents like beta blocker or treatment with pacemaker. Aortic stenosis would require intervention like aortic valve surgery or trans-cathe-



Algorithm 29.1 Neurally mediated syncope

ter aortic valve implantation (TAVI). Neurocardiogenic syncope is prevented by avoidance of dehydration and evasive measures including lying down when patient gets prodromal symptoms. Orthostatic hypotension is treated by withdrawing offending medications and by additional fluid intake. External compression stockings are helpful. Occasional patients may require treatment with fludrocortisone or midodrine.

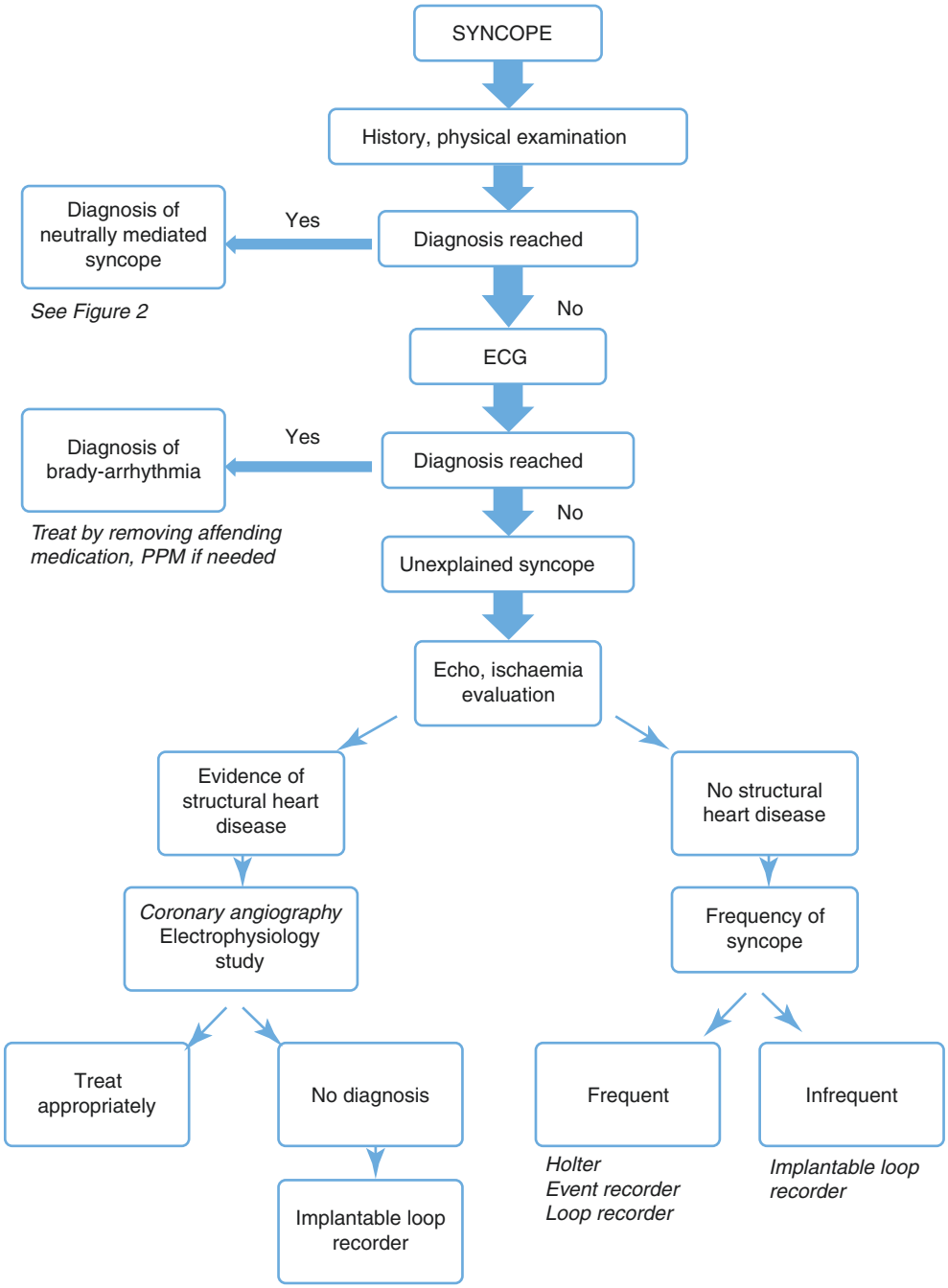
Clinical Relevance

Syncope could be lethal in patients with structural heart disease and warrants prompt evaluation.

Clinical history and examination give vital clues.

Implantable loop recorders and prolonged cardiac monitoring improve diagnostic yield

Algorithm 29.2 Syncope diagnosis



Multiple Choice Questions

Select one appropriate answer for the following situations:

1. An 86-year-old man has had increasing episodes of syncope. They mostly happen when he walks. He also has clinical features of cardiac failure and has a prominent ejection systolic murmur at left sternal edge which radiates to his neck. This is most likely due to:
   A. Sinus node dysfunction
   B. Aortic stenosis
   C. Vasovagal syncope
   D. Carotid sinus hypersensitivity

2. An 80-year-old woman was brought to the hospital emergency after a syncopal episode at church. She was seated during the church service. She felt unwell and nauseated and had a brief syncopal episode. On recovery she vomited and felt tired for quite some time afterwards. This is likely due to:
   A. Sinus node dysfunction
   B. Aortic stenosis

C. Vasovagal syncope
D. Carotid sinus hypersensitivity

3. A 90-year-old man has had recurrent episodes of fainting without any warning. He has had injuries as a result of these episodes. However he recovers very promptly without any associated symptoms. On examination his ECG showed sinus bradycardia at 36/min. The most likely cause of his syncope is:
   A. Sinus node dysfunction
   B. Aortic stenosis
   C. Vasovagal syncope
   D. Carotid sinus hypersensitivity

4. A 76-year-old lady has had recurrent episodes of Syncope. The last episode happened after she had been watching television for 2 hours and when she got up. Prior episodes also happened soon after she stands up from seated positions. On examination her sitting blood pressure was 160/70, and on standing up it was 110/60. There was no significant change in the heart rate from sitting to standing. The most likely diagnosis is:
   A. Orthostatic hypotension
   B. Aortic stenosis
   C. Vasovagal syncope
   D. Carotid sinus hypersensitivity

5. An 82-year-old man complains of recurrent episodes of fainting and near fainting. The episodes often happen when he wears one of his old shirts with tight collar and tie. On some occasions, while he is shaving, also he has felt light-headedness. On examination there was no change in blood pressure from sitting to standing position. The most likely diagnosis is:
   A. Sinus node dysfunction
   B. Aortic stenosis
   C. Vasovagal syncope
   D. Carotid sinus hypersensitivity

6. A 75-year-old lady who had been previously healthy has had four episodes of syncope in the last 6 months. She has also had some breathlessness with change in position. She has had recent joint pains but does not have history of rheumatic fever. She had lost 3 kilograms in weight in the last 3 months. On examination she had elevated jugular venous pressure and a diastolic rumbling murmur at cardiac apex which changed in intensity with change in position. The most likely diagnosis is:
   A. Left atrial myxoma
   B. Postprandial hypotension
   C. Vasovagal syncope
   D. Carotid sinus hypersensitivity

Answers for MCQs

1. B
2. C
3. A
4. A
5. D
6. A

References

1. Forman DE, Rich MW, Alexander KP, Zieman S, Maurer MS, Najjar SS, et al. Cardiac care for older adults: Time for a new paradigm. J Am Coll Cardiol. 2011;57:1801–10.
2. Benditt DG, van Dijk JG, Sutton R, Wieling W, Lin JC, Sakaguchi S, et al. Syncope. Curr Probl Cardiol. 2004;29:152–229.
3. Kapoor W, Snustad D, Peterson J, Wieand HS, Cha R, Karpf M. Syncope in the elderly. Am J Med. 1986;80:419–28.
4. Miller TH, Kruse JE. Evaluation of syncope. Am Fam Physician. 2005;72:1492–500.
5. Kapoor WN, Karpf M, Wieand S, Peterson JR, Levey GS. A prospective evaluation and follow-up of patients with syncope. N Engl J Med. 1983;309:197–204.
6. Kapoor WN, Smith MA, Miller NL. Upright tilt testing in evaluating syncope: a comprehensive literature review. Am J Med. 1994;97:78–88.
7. Lipsitz LA, Wei JY, Rowe JW. Syncope in an elderly, institutionalised population: prevalence, incidence, and associated risk. QJM. 1985;55:45–8.
8. Savage DD, Corwin L, McGee DL, Kannel WB, Wolf PA. Epidemiologic features of isolated syncope: the Framingham study. Stroke. 1985;16:626–9.
9. Davies AJ, Steen N, Kenny RA. Carotid sinus hypersensitivity is common in older patients presenting to an accident and emergency department with unexplained falls. Age Ageing. 2001;30:289–93.
10. Thomas JE. Hyperactive carotid sinus reflex and carotid sinus syncope. Mayo Clin Proc. 1969;44:127–39.
11. Strickberger SA, Benson DW, Biaggioni I, Callans DJ, Cohen MI, Ellenbogen KA, et al. AHA/ACCF scientific statement on the evaluation of syncope: from the American Heart Association councils on clinical cardiology, cardiovascular nursing, cardiovascular disease in the young, and stroke, and the quality of care and outcomes research interdisciplinary working group; and the American College of Cardiology Foundation: in collaboration with the Heart Rhythm Society: endorsed by the American autonomic society. Circulation. 2006;113:316–27.
12. Kenny RA. Syncope in the elderly: diagnosis, evaluation, and treatment. J Cardiovasc Electrophysiol. 2003;14:S74–7.
13. Linzer M, Yang EH, Estes NA 3rd, Wang P, Vorperian VR, Kapoor WN. Diagnosing syncope. Part 2: unexplained syncope. Clinical efficacy assessment project of the American College of Physicians. Ann Int Med. 1997;127:76–86.
14. Seger JJ. Syncope evaluation and management. Tex Heart Inst J. 2005;32:204–6.
15. Brignole M, Menozzi C, Bartoletti A, Giada F, Lagi A, Ungar A, et al. A new management of syncope: prospective systematic guideline-based evaluation of patients referred urgently to general hospitals. Euro Heart J. 2006;27:76–82.
16. Vaitkevicius PV, Esserwein DM, Maynard AK, O'Connor FC, Fleg JL. Frequency and importance of postprandial blood pressure reduction in elderly nursing-home patients. Ann Int Med. 1991;115:865–70.
17. Munro NC, McIntosh S, Lawson J, Morley CA, Sutton R, Kenny RA. Incidence of complications after carotid sinus massage in older patients with syncope. J Am Geriatr Soc. 1994;42:1248–51.

18. Kapoor WN. Current evaluation and management of syncope. Circulation. 2002;106:1606–9.
19. Del Rosso A, Ungar A, Maggi R, Giada F, Petix NR, De Santo T, et al. Clinical predictors of cardiac syncope at initial evaluation in patients referred urgently to a general hospital: the EGSYS score. Heart. 2008;94:1620–6.
20. Olshansky B, Poole JE, Johnson G, Anderson J, Hellkamp AS, Packer D, et al. Syncope predicts the outcome of cardiomyopathy patients: analysis of the SCD-HeFT study. J Am Coll Cardiol. 2008;51:1277–82.
21. Reed MJ, Newby DE, Coull AJ, Prescott RJ, Jacques KG, Gray AJ. The ROSE (risk stratification of syncope in the emergency department) study. J Am Coll Cardiol. 2010;55:713–21.
22. Quinn JV, Stiell IG, McDermott DA, Sellers KL, Kohn MA, Wells GA. Derivation of the San Francisco Syncope Rule to predict patients with short-term serious outcomes. Ann Emerg Med. 2004;43:224–32.
23. Huff JS, Decker WW, Quinn JV, Perron AD, Napoli AM, Peeters S, et al. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with syncope. J Emerg Nurs: JEN. 2007;33:e1–e17.
24. Thiruganasambandamoorthy V, Kwong K, Wells GA, Sivilotti ML, Mukarram M, Rowe BH, et al. Development of the Canadian Syncope Risk Score to predict serious adverse events after emergency department assessment of syncope. CMAJ. 2016;188:E289–98.
25. Sun BC, Mangione CM, Merchant G, Weiss T, Shlamovitz GZ, Zargaraff G, et al. External validation of the San Francisco Syncope Rule. Ann Emerg Med. 2007;49:420–7. 7.e1–4
26. Croci F, Brignole M, Alboni P, Menozzi C, Raviele A, Del Rosso A, et al. The application of a standardized strategy of evaluation in patients with syncope referred to three syncope units. Europace. 2002;4:351–5.
27. Day SC, Cook EF, Funkenstein H, Goldman L. Evaluation and outcome of emergency room patients with transient loss of consciousness. Am J Med. 1982;73:15–23.
28. Linzer M, Pritchett EL, Pontinen M, McCarthy E, Divine GW. Incremental diagnostic yield of loop electrocardiographic recorders in unexplained syncope. Am J Cardiol. 1990;66:214–9.
29. Brignole M, Vardas P, Hoffman E, Huikuri H, Moya A, Ricci R, et al. Indications for the use of diagnostic implantable and external ECG loop recorders. Europace. 2009;11:671–87.
30. Edvardsson N, Frykman V, van Mechelen R, Mitro P, Mohiiddin-Oskarsson A, Pasquie JL, et al. Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: results from the PICTURE registry. Europace. 2011;13:262–9.
31. Pires LA, Ganji JR, Jarandila R, Steele R. Diagnostic patterns and temporal trends in the evaluation of adult patients hospitalized with syncope. Arch Int Med. 2001;161:1889–95.

Sarcopenia, Sarcopenic Obesity and Frailty in Older Adults

30

Nages Nagaratnam and Sai Adithya Nagaratnam

Sarcopenia

Introduction

Sarcopenia is defined as age-related loss of muscle mass [1, 2, 3, 4], changes in muscle strength [5, 6, 7] and muscle quality [8] which accelerates with ageing [9]. The European Working Group in Sarcopenia in Older People (EWGSOP) included both low muscle mass and loss of muscle function (strength or performance) in their definition [10, 11]. EWGSOP further categorised sarcopenia as pre-sarcopenia (decreased muscle mass without decreased strength or function), sarcopenia (decreased muscle mass and strength or performance) and severe sarcopenia (deceased muscle mass, strength and function) [11]. Muscle mass decreases significantly between the ages 50 and 80 years, and muscle strength is halved [12]. The rate and extent muscle changes occur are in some extent genetically determined. If sarcopenia progresses beyond a certain threshold of functional requirements, it leads to loss of function, disability and frailty [13].

It is difficult to compare results of the prevalence of sarcopenia as it varies widely (10–50%) because of the different methods and diagnostic criteria used [14]. It is common in adults over the age of 45 years and increases with age [4]. Using the EWGSOP algorithm, 12.5% of persons were classified as sarcopenic in a sample of persons aged 80 years and older [15]. In community-dwelling older adults, the prevalence was estimated to be as high as 33% [16, 17, 18]. In the United Kingdom using the EWGSOP definition, the Hertfordshire Cohort Study of community-dwelling older people found the prevalence of sarcopenia was 4–6% in men and 7.9% in women [16]. In another study of community-dwelling volunteers, the prevalence in a subgroup 80 years and older was 31.0% in women and 52% in men [4]. In the Tian Liao Old People Study 04 of 549 in a rural community of older Taiwanese, 7.1% was sarcopenic and 5.6% severely sarcopenic [19]. World-wide, based on the operational definition, the estimated prevalence in older women varied from 3% to 30% [18, 20, 21].

N. Nagaratnam (✉)
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

S. A. Nagaratnam
Westmead Hospital, Westmead, NSW, Australia
e-mail: sai@nagaratnam.net

Aetiology

The aetiology is multifactorial [22, 23, 24] and results from a number of age-related changes [25] such as decreased physical function [7, 26, 27], changes in hormonal function such as decreased testosterone and growth hormone [10, 28], decline in alpha-motor neurons [28], insulin resistance [25, 29], age-associated chronic inflammation [10, 29], mitochondrial dysfunction [10], insufficient intake of protein, low vitamin D [3], reduced rate of protein synthesis [23] antioxidants and long-chain polysaturated fatty acids [7] and increased production of catabolic cytokines [24]. The age-dependent muscle degeneration has been attributed to derangements in skeletal myocyte mitochondrial function [30], and more recently it has been suggested that other biological mechanisms such as programmed cell death [31] and changes in the angiotensin system in the ageing skeletal muscle [32] may contribute to the development of sarcopenia. Other factors that are related to muscle loss in the elderly are reduced levels of physical activity [23, 28], increased rates of immobilisation [6], deconditioning and disease. Many old people consume less than the recommended dietary allowance of protein [25]. Older people with diabetes have lower muscle mass and decreased muscle strength and muscle quality [29, 33], and the number of older people with diabetes is increasing [33] (Fig. 30.1).

Fig. 30.1 Near here mechanisms of sarcopenia

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_30

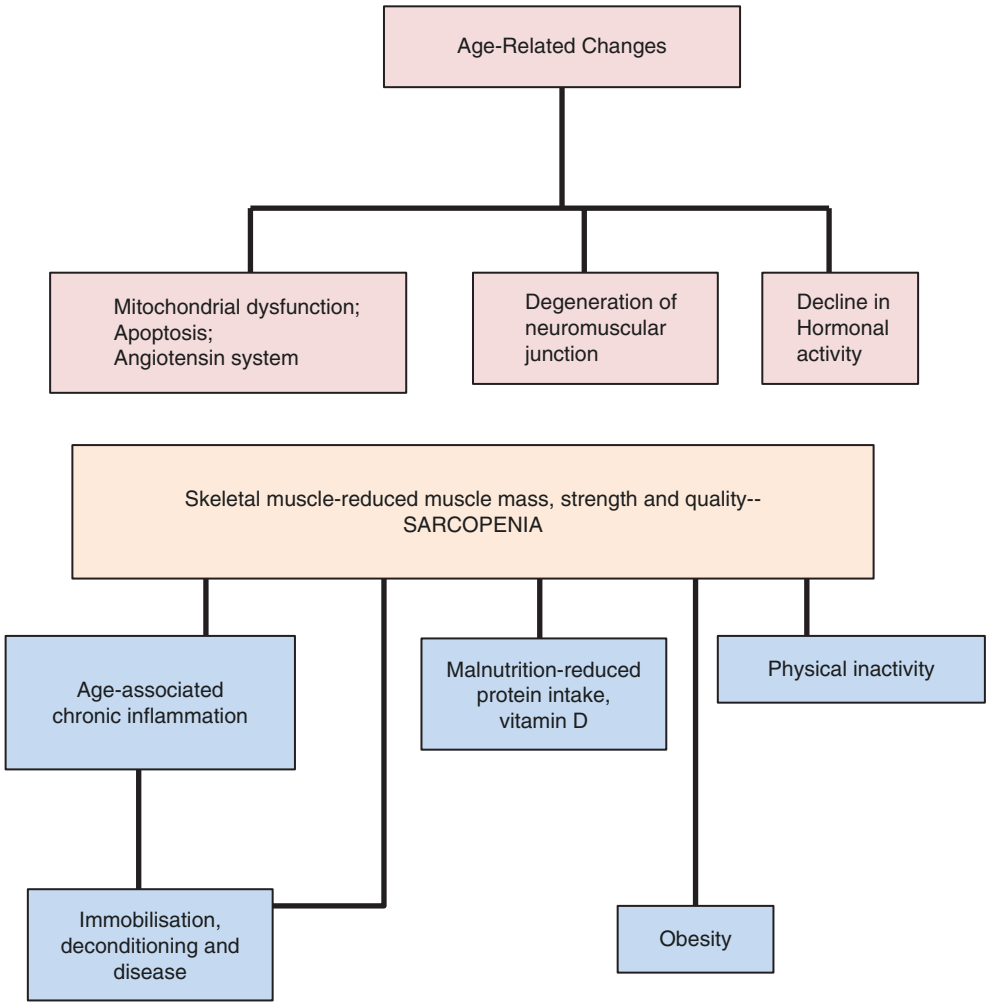


Fig. 30.1 Mechanisms of sarcopenia. (Information sources: [6, 10, 23, 25, 28, 29, 30, 33])

Pathophysiology

Sarcopenia is associated with decreased physical performance, disabilities relating to mobility, increased risk of falls, dependency and mortality [34] independent of age [35]. There is a reduction of muscle mass and strength in all elderly people. Muscle mass and strength reach a maximum in the second and third decades and gradually decline in middle age, and around the age of 80, loss of muscle accelerates leading to progressive weakness [36]. The rate and extent muscle changes occur are in some extent genetically determined. If sarcopenia progresses beyond a certain threshold of functional requirements, it leads to disability and frailty. It is found in 20–30% of elderly over the age of 7 years and increases with advancing age [37].

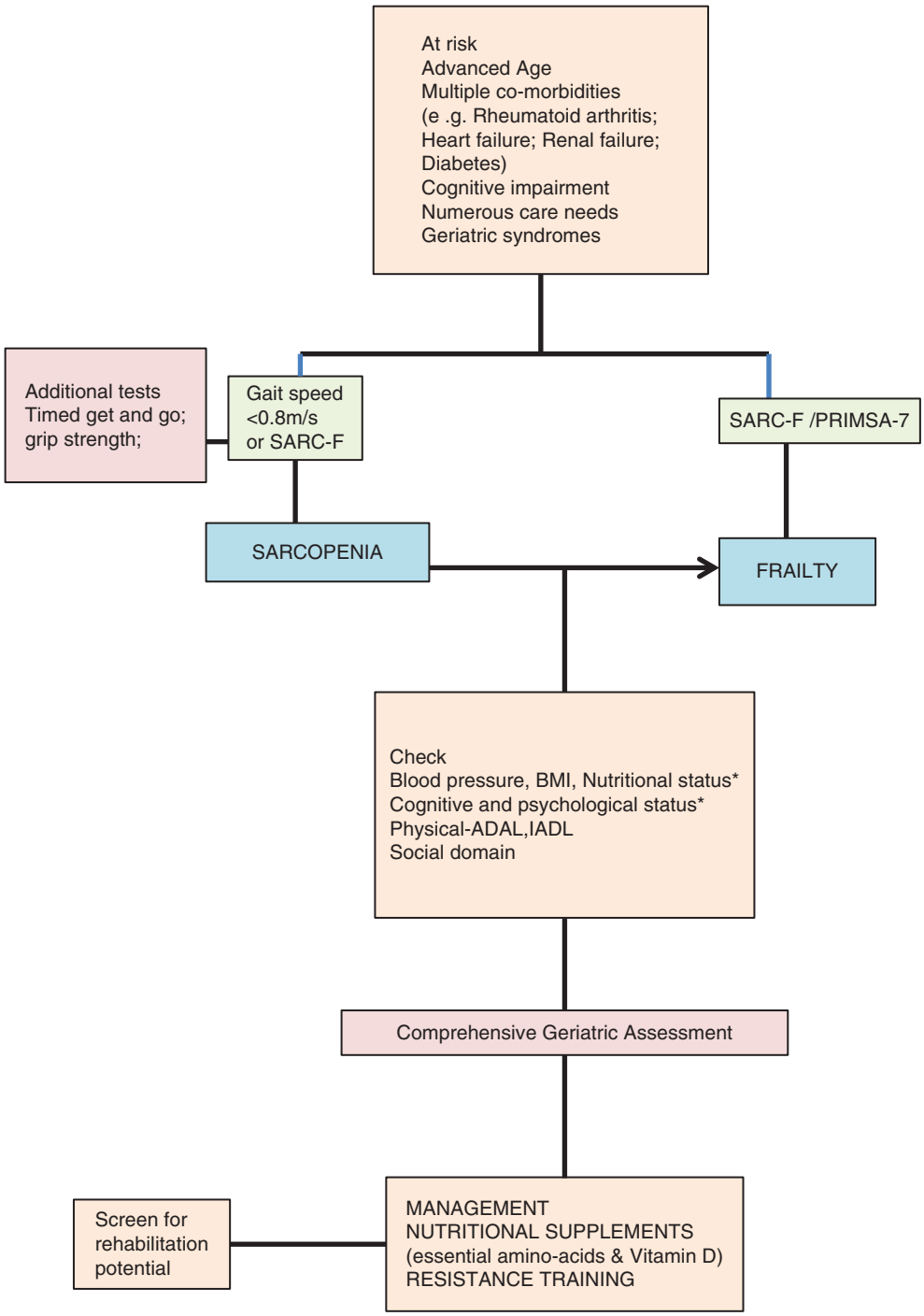
Muscle strength declines 20–30% by 60 years, and voluntary contractile strength of distal and proximal muscles in both men and women is decreased by 20–40% [23]. The decline of muscle strength in old people is directly attributable to physiological and histological changes in the skeletal muscles [38, 39]. With age lipofuscin and adipose tissue are deposited in muscle tissue, and the lost muscle tissue is replaced by fibrous tissue.

Ageing also affects the quality of the muscle. The muscle quality is dependent on fibre composition, contractility, fatigue characteristics and glucose metabolism and uptake [8]. Type II muscle fibres which cause forceful muscle contractions decrease to a greater extent than type I muscle fibres. There is an important relationship between muscle quality and muscle health. The forces generated by muscle contractions can be an important determinant of bone quality [8]. For instance, vertebral compression fractures in postmenopausal women may be due to inadequate support of the vertebral column by the surrounding back muscles [40]. Muscle may be able to attenuate the impact of forces on bone after a fall and alter the susceptibility to fracture [8]. On the other hand, it can augment the mechanical forces on the bone and thereby increase the risk of fracture [8]. Bone mass and density are especially in women after menopause. With age the joints become stiffer and less flexible. Ligaments and tendons decrease in strength. Changes are usually observed in the weight-bearing joints especially parts of the articular

cartilage that are not covered by menisci. It is difficult to differentiate changes due to old age from changes of degenerative processes.

Diagnosis

More recent consensus definitions of sarcopenia incorporate ratios of appendicular mass to height or body weight, muscle strength and physical function [41], and the diagnosis takes the form of measurements of muscle mass and strength or physical performance [42]. The New Mexico health survey measured appendicular muscle mass by dual energy X-ray absorptiometry (DEXA) in 883 Hispanic and non-Hispanic white men and women and defined sarcopenia as a muscle mass of two or more standard deviations below the mean for young healthy participants [43]. There is however a direct structure-function relationship between muscle loss and strength [24] (Algorithm 30.1).



Algorithm 30.1 A practical approach to assessment and management of patients with sarcopenia and frailty. *Cognitive: Mini-Mental State Examination. *Psychological: Geriatric Depression Scale. *Nutritional: Min-Nutritional Assessment –Short Form. (Information sources: Walston et al. [84]; Woo et al. [85]; Morley and Cao [86]; Wells et al. [87]).

Management

Proteins, amino acids and micronutrients have been widely studied as to their effect on muscle synthesis [44] and can improve muscle mass and strength in older adults [45]. The quality of amino acids in the diet is an essential factor in stimulating protein synthesis [46]. There is no pharmaceutical treatments for sarcopenia [47, 48], and so far pharmacological agents have shown nominal efficacy [49], but there is recent evidence of benefits with angiotensin-converting enzyme inhibitors [49]. It has been suggested that there are new pharmacological agents which may reduce the functional decline [50]. Vitamin D, leucine-enriched whey protein [51], beta-OH-beta methyl butyrate, citrulline maleate and isoflavones may have some effect on muscular outcomes [45]. There is considerable evidence to show that resistance training (RT) increases muscle mass, strength and function [27, 47, 48], and this can be enhanced by certain foods and nutritional supplements [47]. The highest consideration in confronting sarcopenia is a combination of resistance training and nutritional interventions [5, 25, 52]. The mechanisms how protein synthesis is increased by mechanical events are unclear [25]. Lifting weight causes the muscle to shorten, whereas lowering weight causes muscle to lengthen, and it has been shown to produce ultrastructural damage and hence stimulates increased muscle protein turnover and triggers a cascade of metabolic events leading to increase in protein synthesis and degradation [25]. Muscle mass and strength increase with protein supplementation during exercise training in both younger and older adults [53]. Much of the trial evidence on the effects of increased exercise or dietary supplementation on muscle mass and function have been evaluated separately, but less is known of the combined effects of the exercise training and with other dietary constituents that have been linked with sarcopenia [7]. There is some evidence that angiotensin-converting enzyme inhibitors in older people can improve physical performance [42].

Sarcopenic Obesity

Sarcopenic obesity is combined muscle loss with increased body fat with age [52, 54]. It manifests as impaired muscle strength and function [50] resulting in increased risk of immobility and disability [41, 55], development of lifestyle-related diseases [54] and early death [50]. Furthermore muscle quality may be adversely affected due to the increased fat mass and accompanying increases in the adipokines and inflammation [41].

The prevalence of obesity in older people is increasing [9, 55], and sarcopenia accelerates with ageing, and both combined have led to a high-risk group [9]. The prevalence of sarcopenic obesity ranges from 0% to 41% in older populations depending on the definition [41].

Management

Energy-restricted diet and exercise are the main lifestyle changes to prevent and treat sarcopenic obesity [54].

Frailty

Introduction

There is still no consensus on a definition [56]. The expert European, Canadian and American Geriatric Advisory Panel (GAP) was unable to arrive at a consensus definition though agreed that frailty is a pre-disability stage [56]. Presently there is insufficient grounds to accept a single definition of frailty [57]. According to Rockwood et al. [58], it is an 'accumulation of impairments'. The most commonly used identifying components of frailty are physical function, gait speed and cognition, and the common outcomes are disability, institutionalisation and death [59]. A successful definition of frailty should have a multidimensional approach [59] with emphasis on its dynamic state, able to identify a group that is susceptible to adverse outcomes [60, 61] and should not include disease, comorbidity or disability [56, 60].

The criteria for frailty and sarcopenia overlap, but in frailty there is weight loss, whereas in sarcopenia there is muscle loss [62], but physical impairment and functional loss are common traits of both [35]. Frailty lacks definition [63], and the definition varies widely [64]. Frailty increases with age [37, 64].

The prevalence of frailty ranges from 5% to 58% [59]. In another study, it was found in 20–30% of the elderly population above the age of 75 years [37] and increases with age [65]. 6% to 25% of free living individuals 65 years and older had many of the elements of frailty [63]. It is higher in women and in African Americans compared to Caucasians and appears to have geographical difference [66].

Aetiology

Its aetiology is complex and multifactorial [66]. Genetic, epigenetic and environmental factors together with advanced age and chronic disease are associated with frailty [61].

Pathophysiology

Several multisystem pathophysiological processes are involved with activation of the inflammatory and coagulation systems [63] and in the endocrine and musculoskeletal systems [66]. Laboratory markers such as IL-6, C-reactive protein (C-RP), 25-hydroxuyvitamin D, insulin growth factor-1 (IGF-1) and D-dimers have been associated with frailty clinical phenotype [37]. Several studies have confirmed the association between frailty and elevated IL-6 levels [67, 68]. Other inflammatory markers such as C-RP and tumour necrosis factor-alpha are also elevated [68, 69]. It has been suggested that in frailty, there is large reduction of anabolic hormones such as IGF-1 and GH (growth hormone) [63]. There is visceral protein depletion resulting from the poor appetite and weight loss in many of the frail individuals [63]. Age-dependent changes in the hormones through their effects on muscle mass and strength and bone density and by activation of catabolic cytokines contribute to the frailty in the elderly [63].

Sarcopenia is also an important pathophysiological contributor to frailty [66]. Osteoporosis and osteopenia have been shown to have direct relationship to frailty [70, 71]. Physical function, gait speed and cognition were the most commonly used identifying components of frailty and disability; institutionalisation and death were common outcomes [59]. IL-6 inhibits erythropoietin and interferes with iron metabolism and thus may contribute to anaemia [72]. Clotting cascade can be activated by the chronic inflammatory state [73]. Frail elderly have been found to have elevated levels of D-dimer, factor VIII and fibrinogen [69]. The likely pathogenesis is multifaceted and includes inflammatory and coagulopathy system with increase in inflammatory cytokines, markers of coagulopathy [63] and hormonal dysregulation [37] and is associated with potential markers such as IL-6,C-RP, D-dimer and 25-hydroxyvitamin D [37]. Frailty is associated with decreased survival [64]. Ageing also affects the quality of the muscle [74, 75].

Clinical Manifestations

Frail old people often have multiple comorbidities [76]. Independent of comorbid conditions, the manifestations of frailty include weight loss, muscle weakness, exhaustion [62], cognitive slowing and impaired performance [77]. The two conditions sarcopenia and frailty overlap, but in frailty there is weight loss, whereas in sarcopenia there is muscle loss [62]. According to Lang et al. [67] in frailty, there is no single symptom crucial in its presentation, but rather it is clearly recognised by clinicians with its multiple manifestations, appearance, nutritional status, performance and health rates, among others. The clinical phenotype manifests as loss of weight, fatigue/exhaustion, weakness, decreased physical activity and immobility [37, 64]. Cognitive impairment is significantly associated with frailty among the oldest old, and frailty is predictive of subsequent mortality [78]. Irrespective of comorbidities, anaemia has been recognised as a significant contributor to mortality in older adults [79]. The prevalence of anaemia is markedly increased in frail older adults and is said to be a potent prognostic indicator for the development of frailty [77].

Identification

Frailty continues to evade a firm diagnosis and is a subject of continuing debate. According to Lang et al. [67], in frailty there is no single symptom crucial in its presentation, but rather it is clearly recognised by clinicians with its multiple manifestations, appearance, nutritional status, performance and health rates, among others. There is no way of knowing at what level of lean mass, sarcopenia is present. Physical function, gait speed and cognition were the most commonly used identifying components of frailty and disability; institutionalisation and death were common outcomes [59]. There are several tools to identify frail older adults. In one study PRISMA-7 questionnaire was the best of five instruments [80], and together with gait speed, timed get up and go test have high sensitivity to identify frailty [81, 82]. In older patients gait speed can be used as a screening test, and there is considerable evidence to support it as a single-item screening tool [56]. The British Geriatric Society Frailty guideline advocates a holistic medical review based on the principle of comprehensive geriatric assessment for all old people to identify frailty [83]. The comprehensive geriatric assessment requires a trained multidisciplinary team, and it is an in-depth assessment across all domains [83] and broadly includes medical, mental health, functional capacity, social circumstances and environment [83]. The SARC-F scale has been shown to effectively screen for sarcopenia [84] based on five domains, namely, muscle strength, walking, stair climbing, chair rising and falls. It is simple to use and takes less than 15 seconds to administer [85].

Management

All elderly are at risk of frailty such that treatments should begin early, before frailty occurs, treatments such as increased physical activity and improved nutrition [81]. Once the elderly patient is identified with frailty, the risk of unfavourable outcomes may be reduced by comprehensive geriatric assessment and implementing a care plan [86]. Frail elderly patients should also be screened for rehabilitation potential [87].

Resistance training (RT)-induced increases in muscle mass, muscle strength [88] and function can be improved by nutritional supplements and certain foods [1, 47].

Clinical Relevance

Sarcopenia is loss of skeletal muscle mass, strength and quality in unison with biological ageing [1–8].

If sarcopenia progresses beyond a certain threshold of functional requirements, it leads to disability and frailty.

Muscle strength declines 20–30% by 60 years, and voluntary contractile strength of distal and proximal muscles in both men and women is decreased by 20–40% [23].

Sarcopenia is associated with decreased physical performance, disabilities relating to mobility, increased risk of falls, dependency and mortality [35].

Multiple Choice Questions

1. The following are true in relation to sarcopenia, EXCEPT:
   A. Sarcopenia is loss of skeletal muscle mass, strength and quality 1in unison with biological ageing.
   B. If sarcopenia progresses beyond a certain threshold of functional requirements, it leads to disability and frailty.
   C. Sarcopenic obesity is increased body fat with age without muscle loss.
   D. Confronting sarcopenia is a combination of resistance training and nutritional interventions.

2. The following are true of frailty, EXCEPT:

   A. Frailty is associated with decreased survival.
   B. Impairment of physical function is a common trait of frailty and sarcopenia.
   C. In frailty there is weight loss, whereas in sarcopenia there is muscle loss.
   D. Frailty is not associated with cognitive impairment.

MCQ Answers

1. C
2. D

References

1. Candow DG. Sarcopenia: current theories and the potential beneficial effect of creatinine application strategies. Biogerontology. 2011;12(4):273–87.
2. Satake S. Sarcopenia in relation to locomotive syndrome and frailty. Clin Calcium. 2012;22(4):67–73.
3. Visvanathan R, Chapman I. Preventing sarcopenia in older people. Maturitas. 2010;66(4):383–8.
4. Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of sarcopenia and prevalence of skeletal muscle mass in healthy older men and women. J Gerontol A Brit Sci Med Sci. 2002;57(12):M722–7.
5. Kim JS, Wilson JM, Lee SR. Dietary implications on mechanisms of sarcopenia: roles of protein, amino acids and antioxidants. J Nutr Biochem. 2010;21(1):1–13.
6. Mulberg W, Sieber C. Sarcopenia and frailty in geriatric patients: implications for training and prevention. Z Gerentol Geriatr. 2004;37(1):2–8.
7. Denison HJ, Cooper S, Sayer AA, Robinson SM. Prevention and optimal management of sarcopenia: a review of combined exercise and nutrition interventions to improve muscle outcomes in older people. Clin Interv Aging. 2015;10:859–69.
8. Dutta C. Significance of sarcopenia in the elderly. J Nutr. 1997;127:992S–3S.
9. Batsis JA, Mackenzie TA, Barre LK, Lopez-Jimenez F, Bartels SJ. Sarcopenia sarcopenic obesity and mortality in older adults: results from the National Health and nutrition examination surveys III. Eur J Clin Nutr. 2014;68:1001–7.
10. Eto. Locomotive syndrome and frailty. Recent advances in sarcopenia. Clin Calcium 2012;22(4):75–79.
11. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing. 2010;39(4):412–23.
12. Prentice AM. Sarcopenic obesity. distributor.tanita.en/uploads/media/1408435942_issue.pdf. Accessed 28 March 2016.
13. Xue QL, Walston JD, FriedLP, Breamer BA. Prediction of risk of falling, physical disability and frailty by rate of decline in grip strength: the women's health and aging study. Arch Intern Med 2011;171:1119–1121.
14. Bijlsma AY, Meskers CG, Ling CH, Narici M, Kurrie Se, et al. Defining sarcopenia: the impact of different diagnostic criteria on the prevalence of sarcopenia in a large middle aged cohort. Age (Dordr). 2012;35:871–81.
15. Legrand D, Vaes B, Mathei C, Swine C, Degryse JM. The prevalence of sarcopenia in very old individuals according to the European consensus definition: insights from the BEFRAIL study. Age Ageing. 2013;42(6):727–34.
16. Patel HP, Syddall HE, Jameson K, Robinson S, Denison HT, Roberts HC, et al. Prevalence of sarcopenia in community –dwelling people in the UK using the European working group on sarcopenia in older people (EWGSOP) definition: findings from the Hertfordshire cohort study (HCS). Age Ageing. 2013;42(3):378–84.
17. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing. 2014;43(6):748–59.
18. Masanes F, Culla A, Navarro-Gonsalez M, NavarroLopez M, Sacanella E, Torres B, et al. Prevalence of sarcopenia in healthy community-dwelling elderly in an urban area of Barcelona (Spain). J Nutr Health Aging. 2012;16:184–7.
19. Wu CH, Chen KT, Hou MT, Chang YF, Chsng CS, Liu PY, et al. Prevalence and associated factors of sarcopenia and severe sarcopenia in older Taiwanese living in rural community the Tian liao Old People study 04. Geriatr Gerontol Int. 2014;14(Supp 1):69–75.
20. Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connor E. Sarcopenia in elderly men and women: the rancho Bernardo study. Am J Prev Med. 2003;25:226–31.
21. Melton LJ III, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, Riggs BL. Epidemiology of sarcopenia. J Am Geriatr Soc. 2000;48:625–30.

22. Boirie Y. Physiopathological mechanism of sarcopenia. J Nutr Health Aging. 009;13(8):717–23.
23. Doherty TJ. Invited review. Aging and sarcopenia J Appl Physiol. 2003;95(4):1717–24.
24. Roubenoff R. Sarcopenia: a major modifiable cause of frailty in the elderly. N Nutr Health Aging. 2000 ;4(3):140–2.
25. Evans WJ. Protein nutrition, exercise and aging.. J Am Coll Nutr.2004;23(6suppl):601S–609S.
26. Robinson S, Cooper C, Aihie Sayer A. Nutrition and sarcopenia: a review of the evidence and implications for preventive strategies. J Aging Res. 2012;:2012:510801.
27. Liu CJ, Latham NK. Progressive resistance strength training for improving physical function in older adults. Cochrane Database Syst Rev. 2009;3:CD002759.
28. Roubenoff R. Sarcopenia and its implications for the elderly. Eur J Clin Nutr. *2000;*54 Suppl 3: S40-S47(b).
29. Umegaki H. Sarcopenia ad frailty in older patients with diabetes mellitus. Geriatr Gerontol Int. 2016;16(3):293–9.
30. Marzetti E, Calvai R, Cesari M, Buford TW, Lorenzi M, Behnke BJ, et al. Mitochondrial dysfunction an sarcopenia of aging: from signalling pathways to clinical trials. Int J Biochem Cell Biol. 2013;45(10):2288–301.
31. Armand AS, Laziz I, Djeghloul D, et al. Apoptosis-inducing factor regulates skeletal progenitor cell number and muscle phenotype. PLoS One.201;6:e27283.
32. Burks TN, Andres-Mateos E, Marx R. et al. Losartan restores skeletal muscle remodelling and protects against disuse atrophy in sarcopenia.asci Transl Med 2011;3:82ra37.
33. Jang HC,. Sarcopenia, frailty and diabetes in older adults. Diabetes Metab J 2016;40(3):182–189.
34. Abellan van Kan G, Rolland Y, Andrieu S, Bauer J, Beauchet O, Bonnefoy M, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an international academy on nutrition and aging (IANA) task force. J Nuthr Health Aging. 2009;13(10):881–9.
35. Landi F, Calvani R, Cesari M, Tosato M, Martone AM, Bernabei R, et al. Sarcopenia as the biological substrate of physical frailty. Clin Geriatr Med. 2015;31(3):367–74.
36. Spirduso WW. Physical dimensions of aging. Campaign Human Kinetics. 1995.
37. Topinkova E. Aging, disability and frailty. Ann Nutr Metab. 2000;52(Suppl 1):6–11.
38. Knight J, Nigam Y. Exploring the anatomy and physiology of aging. Parts-the nervous system. Nurs Times. 2008;104:3518–9.
39. Freemont AJ, Hoyland JA. Morphology mechanisms and pathology of musculoskeletal aging. J Pathol. 2007;211(2):252–9.
40. Limburg PJ, Sinaki M, Rogers JW. A useful technique for measurement of back strength in osteoporotic and elderly patients. Mayo Clin Proc. 1991;68:39–44.
41. Cauley JA. An overview of sarcopenic obesity. J Clin Densitom. 2015;18(4):499–505.
42. Dodds R, Sayer AA. Sarcopenia. Arq Bras Endocrinol Metabol. 2014;58(5):464–9.
43. Encyclopedia of aging. Sarcopenia 2002. website: http//www.encyclopedia.com/doc/1G2-3402200365.html
44. Eglseer D, Poglitsch R, Roller-Wirnsberger RE. Muscle power and nutrition. Z Gerontol Geriatr. 2016;49(2):115–9.
45. Barillaro C, Liperoti R, Martone AM, Onder G, Landi F. The new metabolic treatments for sarcopenia. Aging Clin Exp Res. 2013;25(2):119–27.
46. Rolland Y, Dupuy C. Abellan van Kan G, Gillette S, Vella B. Treatment strategies for sarcopenia and frailty. Med Clin North Am. 2011;96(3):427–38.
47. Phillips SM. Nutritional supplements in support of resistance exercise to counter age-relate sarcopenia. Adv Nutr. 2015;6(4):452–60.
48. Phu S, Boersma D, Duque G. Exercise and sarcopenia. J Clin Densitom. 2015;18(4):488–92.
49. Burton LA, Sumukadas D. Optimal management of sarcopenia. Clin Interv Aging. 2010;5:217–28.
50. Rolland Y, Onder G, Morley JE, Gillette-Guynet S. Abellan van Kan G, Vellas B. Current and future pharmacologic treatment of sarcopenia. Clin Geriatr Med. 2011;27(3):423–47.
51. Bauer JM, Verlaan S, Bautmans I, Brandt K, Donini LM, Maggio M, et al. Effects of a vitamin D and leucine -enriched whey protein nutritional supplement on measures of sarcopenia in older adults, the PROVIDE study: a randomized double-blind placebo-controlled trial. J Am Med Dir Assoc. 2015;16(9):740–7.
52. Benton MJ, Whyte MD, Dyal BW. Sarcopenic obesity: strategies for management. Am J Nurs. 2011;111(12):38–44.
53. Cermack NM, Res PT, de Groot LC, Saris WH, van Loon LJ. Protein supplementation augments the adaptive response of skeletal muscle to resistance type of exercise training and a meta-analysis. Am J Clin Nutr. 2014;96(6):1454–64.
54. Parr EB, Coffey VG. HawleyJA. 'Sarcobesity': a metabolic conundrum. Maturitas. 2013;74(2):109–13.
55. Goisser S, Kemmer W, Porzel S, Volkert, Sieber CC, Bollheimer LC, et al. Sarcopenic obesity and complex interventions with nutrition and exercise in community –dwelling older persons-a narrative review. Clin Interv Aging 2015;10:1267–1268.
56. van Abellan HKG, Rolland Y, Houles M, Gillette-Guyonnet S, Soto M, Vellas B. The assessment of frailty in older adults. Clin Geriatr Med. 2010;26(2):275–86.
57. Rockwood K. What would make a definition of frailty successful? Age Aging. 2005;34(5):532–4.
58. Rockwood K, Song X, McKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(65):489–95.
59. Sternberg SA, Wershof Schewartz A, Krunananthan S, Bergman H, CLarfield MA. The identification of frailty a systematic literature review. J Am Geriatr Soc. 2011;59(11):2129–38.
60. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community dwelling older people. Nurs Outlook. 2010;58(2):76–86.
61. McMillan GJ, Hubbard RE. Frailty in older in patients: what physicians need to know. QJM. 2012;105(11):1059–65.
62. Cederholm T. Overlaps between frailty and sarcopenia : definitions. Nestle Nutr Inst Workshop Sr. 2015;83:65–9.
63. Vanitallie TB.Frailty in the elderly: contributions of sarcopenia and visceral protein depletion. Metabolism. 2003;52(10Suppl2): 22–6.
64. Shamilyan T, Talley KM, Ramakrishan R, Kane RL. Association of frailty with survival: a systematic literature review. Ageing Res Rev. 2013;12(2):71–36.
65. Fried LP, FerruciL, Darer J, Willliamson JD, Anderson G. Untangling the concepts of disability, frailty and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci. 2004;59:255–263.
66. Chen X, Mao G, Leng SX. Frailty syndrome :an overview. Clin Interv Aging. 2014;9:433–41.
67. Leng S, Yang H, Walston J. Decreased cell proliferation and altered cytokine production in frail older adults. Aging Clin Exp Res. 2004;16:249–52.
68. Hubbard RE, O'Mahony MS, Savva GM, Calver BL, Woodhouse KW. Inflammation and frailty measures in older people. J Cell Mol Med. 2009;13:3103–9.
69. Walston J, McBurnie MA, Newman AB, Tracy RP, Kop WJ, Hirsch CH, et al. Frailty and activation of inflammation and coagulation systems with and without clinical morbidities.: results from the cardiovascular health study. Arch Intern Med. 2002;162:2333–41.

70. Fried LP, Hadley EC, Walston JD, Newman AB, Gurainik S, Studenski TB, et al. From bedside to bench: research agenda for frailty. Sci Aging Knowledge Environ. 2005(31):pe24.
71. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C. Gottdiener J, al. Frailty in older adults: evidence for a phenotype J Gerontol A Biol Sci Med Sci. 2001;56:M146–56.
72. Ershler WB. Biological interactions of aging and anaemia: a focus on cytokines. J Am Geriatr Soc. 2003;51(suppl):S18–21.
73. Espinoza S, Walston JD. Frailty in older adults: insights and interventions. Cleveland Clin J Med. 2005;72(12):1105–12.
74. Fragala MS, Kenny AM. Kuchel GA. Sports Med. https://doi.org/10.1007/s40279-015-0315-2.
75. Nair KS. Aging muscle1'2'3'4'5. Am J Clin Nutr. 2005;81(5):953–63.
76. Poudel A, Hubbard RE, Nissen L, Mitchell C. Frailty: a key indicator to minimize inappropriate medication in older people. QJM. 2013;106(10):969–75.
77. Artz AS. Anaemia and the frail elderly. Semin Hematol. 2008;45(4):261–6.
78. Jacobs JM, Cohen A, Ein-Mor E, Maaravi Y, Stessman J. Frailty, cognitive impairment and mortality among the oldest old. J Nutr Health Aging. 2011;15(8):678–82.
79. Robinson SG, Bushinski S. Managing Frailty Syndrome. Today's Geriatr Med. 8 3.30. http://www.todaysgeriatricmedicine.com/archive/0515p30.shtml. Accessed 6 Jan 207.
80. Hoogendijk EO, van der Horst HE, Deeg DJ, Frijters DH, Prins BA, Jansen AP, et al. The identification of frail older adults in primary care: comparing the accuracy of five simple instruments. Age Ageing. 2013;42(2):262–5.
81. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. Age Ageing. 2015;44(1):148–52.
82. Turner G, Clegg A. British geriatrics society: age UK: Royal College of general practitioners. Best practice guidelines for the management of frailty: a British geriatrics society, age UK and Royal College of general practitioner report. Age Ageing. 2014;4(6):744–7.
83. British Geriatric Society. Comprehensive assessment of the frail older patient. http://www.bgs.org.uk/good-practice-guides/resourdes/goodpractice/gpgcgassessment. Accessed 6 Jan 2017.
84. Walston JD, Fried LP. Frailty and its implications for care. In: Morrison RS, Meir DE, editors. Geriatric Palliative Care. New York: Oxford University Press; 2003.
85. Woo J, Yu R, Wong M, Yeung F, Wong M, Lum C. Frailty screening in the community using the FRAIL scale. J Am Med Dir Assoc. 2015;16(5):412–9.
86. Morley JE, Cao L. Rapid screening for sarcopenia. J Cacexia Sarcopenia Muscle. 2015;6(4):312–4.
87. Wells JL, Seabrook JA, Stolee P, Borrie MJ, Knoefel F. State of the art in geriatric rehabilitation: part I. Review of frailty and comprehensive geriatric assessment. Arch Phys Med Rehabil. 2003;84(6):890–7.
88. Cadore EL, Rodriquez-Manas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falling, gait ability, balance in physically frail older adults: a systematic review. Rejuvenation. 2013;16(2):105–14.

Headache in the Elderly

31

Nages Nagaratnam and Gary Cheuk

Introduction

Chronic headache is characterised by the occurrence of headache lasting 15 days or more per month [1] and for more than 3 months [2]. It is important to distinguish those that are life-threatening from those that are benign. Acute headaches include accelerated hypertension, subarachnoid haemorrhage, intracranial disorders (strokes, haemorrhage), infections (meningitis, encephalitis, acute viral illness, acute sinusitis) and acute narrow-angle glaucoma. With the chronic persistent and recurring headaches with advancing age, the prevalence of primary headache such as migraine, tension type and cluster declines, whilst that of the secondary headaches such as intracranial mass lesions, system disease and temporal arteritis increases. In headache symptomatology, for example, migraine may evolve into a pattern of chronic daily headache, and aura may occur without headache [3].

Severe recurrent or constant headaches are experienced by approximately 10% of women and 5% of men at the age of 70 [4, 5]. The prevalence varies with age. Headaches classified as primary headaches are generally due to benign neurochemical factors within the nervous system and include migraine, tension-type headache, cluster headache which may persist in the elderly [6], hypnic headache [4], primary cough headache, exploding head syndrome [7] and other primary headaches. The incidence of primary headache declines with ageing with increase in organic causes especially in 55–60 years of age [8]. Secondary headaches are symptomatic to some underlying conditions [9] and are common with advancing age [10]. Secondary headaches include trigeminal neuralgia, temporal arteritis, post-herpetic neuralgia [10], cervical spondylosis, sleep apnoea, glaucoma, intracranial neoplasm, intracerebral haemorrhage, subarachnoid haemorrhage, post-concussive syndrome [4, 11] and dialysis headache, due to arterial hypertension or hypothyroidism [5].

N. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net

G. Cheuk (✉)
Geriatric Medicine, Rehabilitation and Aged Care Service, Blacktown-Mt Druitt Hospital, Blacktown, NSW, Australia
e-mail: gcheuk@optusnet.com.au

Clinical Manifestations

Primary Headaches

Benign Dysfunctional Headaches

Migraine. In the elderly only 2% of migraines begin after the age of 50 years [12] and are less severe. In individuals over the age of 55 years, the lifetime prevalence of migraine is 20–30% [13]. Migraine with aura occurs in about 28% of the migraine sufferers [14]. More often than not, the symptomatology changes as age advances, for instance, the auras may disappear [15] or the aura can occur in isolation [5], creating difficulties in diagnosis. Late-onset migraine with aura without headache is not rare especially in the elderly [16, 17] and is characterised by visual symptoms followed by sensory, aphasic and motor symptoms [17]. Migraine has a high overall mortality and is associated with increased risk of stroke, heart disease and retinopathies [18, 19].

Dihydroergotamine or triptans should not be used in the elderly because of the risk of coronary artery disease nor should prophylactic agents such as doxepin and amitriptyline because of risks of urinary retention and cardiac arrhythmia [11]. Metoprolol, topiramate and divalproex sodium are recommended as preventive agents in the elderly [11]. It is recommended when starting prophylactic treatment to 'start low and go slow' [20].

Tension headache is common and occurs at any age and is more common in women. Overall, the prevalence of tension headache amongst 65–96-year-olds is comparable, although it is higher in the oldest age groups [21].The headache is of a pressing character and band-like of mild to moderate severity. Nausea is rare and is neither aggravated by physical

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_31

activity nor is there any aura, but like migraine, tension headache is associated with photophobia and phonophobia. According to the European guidelines, a number of medications such as acetaminophen, ibuprofen, diclofenac and acetyl salicylic acid are considered effective [22].

Cluster-type headaches are rare and it affects mainly men and the average age is around 30 years.

Rankin in 1988 [23] described hypnic headache as a rare primary headache also known as 'clockwise' or 'alarm clock' headache [24, 25]. It is exclusively sleep-related and usually starts after the age of 50 years [24, 26]. The pathophysiological mechanism is unclear and continues to be debated but is thought to be associated with hypothalamic dysfunction [26]. It has been included in the headache classification of the International Headache Society (IHS) [27]. The diagnostic criteria include that it is related to sleep, lasts for more than 15 min after waking, occurs >15 times per month, first occurs after the age of 50 years with no autonomic symptoms and other intracranial disorders must be excluded [27]. Caffeine is the first line of treatment both for the acute as well as a prophylaxis, such as a cup of coffee or a caffeine tablet [26, 28]. Lithium has been suggested as a prophylactic [28].

Secondary Headaches

Temporal Arteritis

Temporal arteritis (giant cell arteritis, cranial arteritis) (TA) is a chronic inflammatory disease of the large vessels. It presents more often than not after the age of 50 years, abruptly or insidiously. Headaches have been reported in 60–90% of patients with TA and are felt over the temple [29]. Typically the symptoms are severe headache localised in the arteries of the scalp (temporal and occipital), jaw claudication and muscles of the tongue in two-thirds to half the patients and visual disturbances. The last are due to involvement of either the ophthalmic or posterior ciliary arteries. Visual loss has an abrupt onset and is often preceded by transient visual symptoms such as amaurosis fugax, diplopia, field defects and blurred vision. In more than half the patients, it is accompanied by polymyalgia rheumatica. Systemic symptoms include fever, joint pains, fatigue and loss of weight that occur in the majority of the patients. Low-grade anaemia and subtle changes on the liver function tests may be present. It is another cause of pyrexia of unknown origin or unexplained weight loss. Physical examination reveals the affected scalp vessels to be swollen, tender, thickened, nodular or pulseless. The sedimentation rate (ESR) is usually markedly elevated (often >100 mm/h Westergren method) but could be below 30 mm/h in about a fifth of the cases [30]. The C-reactive protein, by high-sensitivity testing, is now said to be a more reliable diagnostic test than the ESR.

Treatment should commence as soon as temporal arteritis is suspected. Treatment should not be delayed if temporal arteritis is considered even before biopsy is performed. A false-negative result in 5–44% of patients with a superficial temporal artery biopsy [29]. The starting dose usually is 80 mg of prednisolone daily. Based on the response, the dose is tapered down over several weeks till the ESR is normalised to about 10 mg daily thereafter. If the symptoms increase during this period, the dose could be slightly increased. Most patients could be weaned off the prednisolone after a year, but some may require a maintenance dose for several years. The response is dramatic; the headache and other symptoms are relieved within a day or two of commencement of the prednisolone.

Intracranial Headaches

Brain tumours: The incidence of brain tumours over the 1970s has increased sevenfold [31], and the average annual percentage increases with age [32, 33]. In the elderly the incidence of primary brain tumours is higher [34]. Headaches and seizures are the most common symptoms at presentation [35]. Posterior fossa tumours are more likely to produce headache than supratentorial tumours [36]. The headache which may be indeterminate is not particularly aggravated by coughing, exertion or the head-low position and is seldomly accompanied by nausea or other symptoms [37, 38]. Patient often wakes up with headache which soon settles. They are localised and become intense in severity as the tumour progresses, and the seizures can be focal or generalised [35]. Neurological signs include localised limb weakness, sensory changes and speech and behaviour and visual and gait difficulties, depending on the location of the tumour. Focal neurological deficits may be helpful to localise the tumour [35]. In the elderly patients, clinical signs that may suggest the presence of a brain tumour are gait disorders, short-term memory deficits and intellectual decline over a short period of time [39]. In the elderly primary tumours (meningiomas, malignant gliomas, astrocytoma, primary central nervous system lymphomas) and secondaries from the lung and breast are common (Fig. 31.1). Age alone should not preclude the use of aggressive treatment for elderly patients with primary brain tumours, and treatment should be individualised [34].

Chronic subdural haematoma. The chronic syndrome is common in the elderly [40]. A study in North Wales showed the incidence of chronic subdural haematoma (cSDH) in the over 65 years to be 8.2 per 100,000 in that population [41]. The common presentations are altered mental state (42–52%) and focal neurological deficits (46–50%) [40–43]. It often resembles vascular dementia with focal neurological signs and cognitive impairment. There is an increased tendency for fall (57%) [41] due to the presence of cerebral atrophy (which stretches the dural veins) and impaired

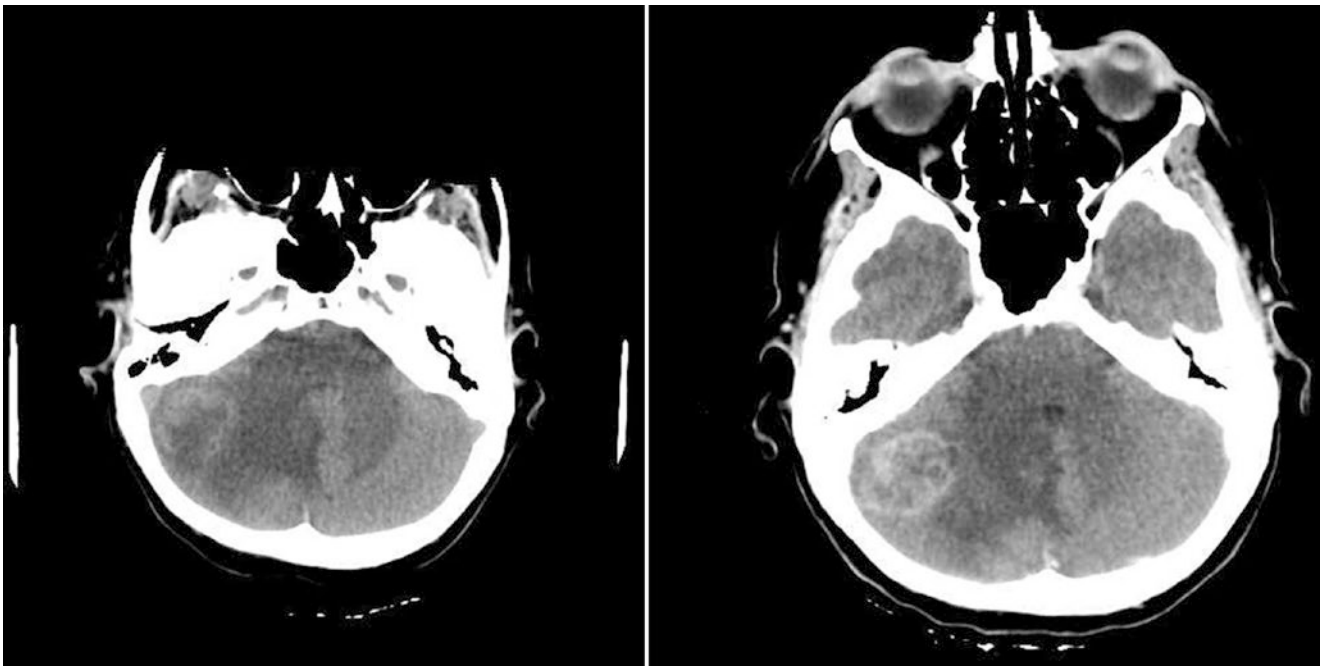


Fig. 31.1 Secondaries. Axial CT scan (right) without contrast. The left image with contrast shows multiple enhancing hyperdense areas. (Reproduced with permission from Dr. Andrew-Owen Jones)

haemostasis (33%) [41]; cSDH is common in the elderly [37]. In patients presenting with cSDH, significant coagulopathy should be reversed [42]. Surgery may restore function or prevent further deterioration of cognitive function. In one study 60% underwent surgical intervention with 4 (17%) deaths [41]. Patients over the age of 85 years are at a greater risk of perioperative complications [44]. These patients are also at higher risk of seizures; evidence to support routine prophylaxis is conflicting [45] (Fig. 31.2).

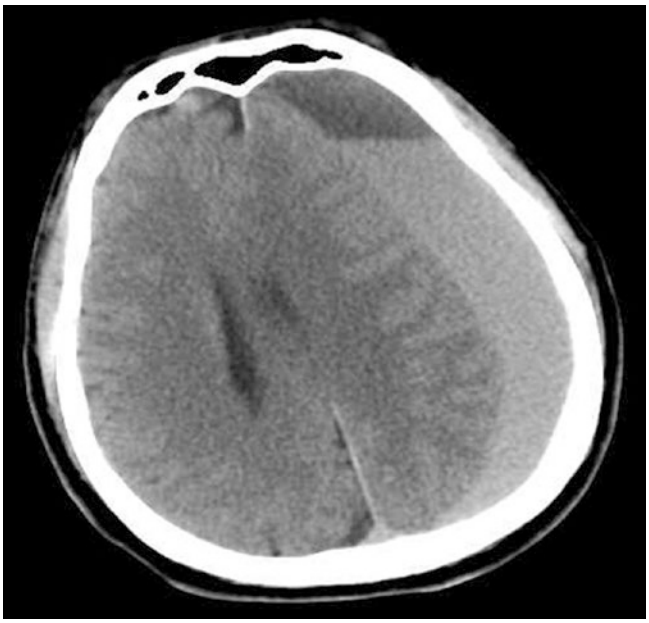


Fig. 31.2 CT scan showing subdural haematoma. (Reproduced with permission of Dr. Andrew-Owen Jones)

Cerebrovascular Disease

Cerebral haemorrhage (subarachnoid and intracerebral) can produce sudden and excruciating headaches. They are potentially life-threatening and may be accompanied by reduced level of consciousness, neurological signs, papilloedema and convulsion and in the case of subarachnoid haemorrhage, meningism, retinal haemorrhage and fever. A very good clinical axiom is that any person presenting with acute onset of severe headache, often the worst in his/her life, is presumed to have an acute subarachnoid haemorrhage, until proven otherwise. The probability of detecting an aneurysmal haemorrhage on the CT scan is 74% on day 3 which gradually decreases to almost zero in 3 weeks [29]. If subarachnoid haemorrhage suspected by imaging is not helpful, a lumbar puncture is mandatory.

Cerebral ischaemia. The headaches are non-specific, dull and usually not severe and may precede the more flagrant signs of brain ischaemia such as hemiparesis, aphasia and sensory changes. About half the patients with vertebrobasilar insufficiency and quarter of those with middle cerebral artery ischaemia have a recurrent but unremarkable headache [37]. A more prominent headache with impairment of consciousness occurs 1–4 days after the onset of cerebral infarction due to surrounding oedema. Headache at the onset of infarction occurs often in cerebral embolism for reasons that are not clear.

Acute meningitis. The elderly are at a higher risk of having acute bacterial meningitis (ABM) than the younger adults [46]. Due to comorbid conditions, the clinical symptoms at presentation and diagnosis are often delayed [46]. Fewer patients present with all three symptoms, fever, neck stiffness and altered mental state [47], but almost all present with least two of the three symptoms [47]. Fever as a symptom varies from 59% [48] and 67% [49] to 100% in other studies [50]. In the elderly there is a greater variety of organisms causing the meningitis, and viral causes are less common [48, 51]. *Streptococcus pneumoniae* is the most common followed by *Listeria monocytogenes* [47, 52, 53], and case fatality for the former is 24% and for the latter 40% [53]. ABM is associated with higher mortality with advancing age [4, 46, 52]. In the elderly with ABM, both neurological and extra-meningeal complications are frequent [46], and patients frequently die of cardiorespiratory failure [54]. Mortality is higher in those with seizures [53].

Drug-Induced Headache

Rebound headache occurs as a result of overusing medications for headache. It is increasingly common and preventable. Drug-induced headaches tend to be dull, diffuse and sometimes throbbing. Medications containing caffeine as ingredient are especially hazardous.

Evaluation

The key to a rewarding evaluation of headaches is a detailed history together with a general and neurological examination. The elderly can experience many types of headaches, and up to two-thirds of the headaches are primary headaches, and the remaining are secondary to systemic disease or primary intracranial lesions. Migraine, tension-type and cluster headaches are still the most frequent headaches in the elderly, but there are others which are of a serious nature. There should be a high index of suspicion for organic disease giving rise to headaches [16], and further evaluation and investigation should be considered as an etiological treatment is often possible. Furthermore life-threatening disorders have to be excluded before concentrating on benign etiologies [55].

A detailed history is the first step to diagnosis. The history should include the location, mode of onset, severity, duration, frequency, precipitating, aggravating factors and associated symptoms. A general examination is followed by a meticulous neurological examination and examination of the head and neck. The choice of the diagnostic tests will very much depend on the findings in the history and examination. The testing should use the most accurate and discriminatory tests. The laboratory investigations include routine blood tests (including C-RP, erythrocyte sedimentation rate), electrolytes, urea, creatinine, serum calcium, magnesium and liver function tests together with imaging (plain X-rays of the neck, sinuses, CT and MRI) and electroencephalogram and lumbar puncture when required. However, the yield of neuroimaging and EEG in the evaluation of patients with headache with a normal neurological examination is low in routine evaluation [29]. A biopsy of the affected vessel is performed if temporal arteritis is suspected. Algorithms 31.1 and 31.2 show evaluation of common acute and chronic headaches.

Treatment

The symptomatic treatment of headaches in the elderly follows the same principles as that of younger patients. However, treatment of elderly patients requires an understanding of the patient's general health, a familiarity with and knowledge of the action of the medications used and above all caution [56]. Headaches that affect the elderly include side effects to the medications, and these can be devastating in a frail person. The elderly do not tolerate medications as well as younger people and suffer from many conditions that contraindicate the use of many of them [56].

Clinical Relevance

It is useful to classify headaches into those with acute onset and those that are persistent and recurrent.

It is important to distinguish those that are life-threatening from those that are benign.

With advancing years the prevalence of primary headaches declines whilst that of the secondary headaches such as intracranial mass lesions and temporal arteritis increases.

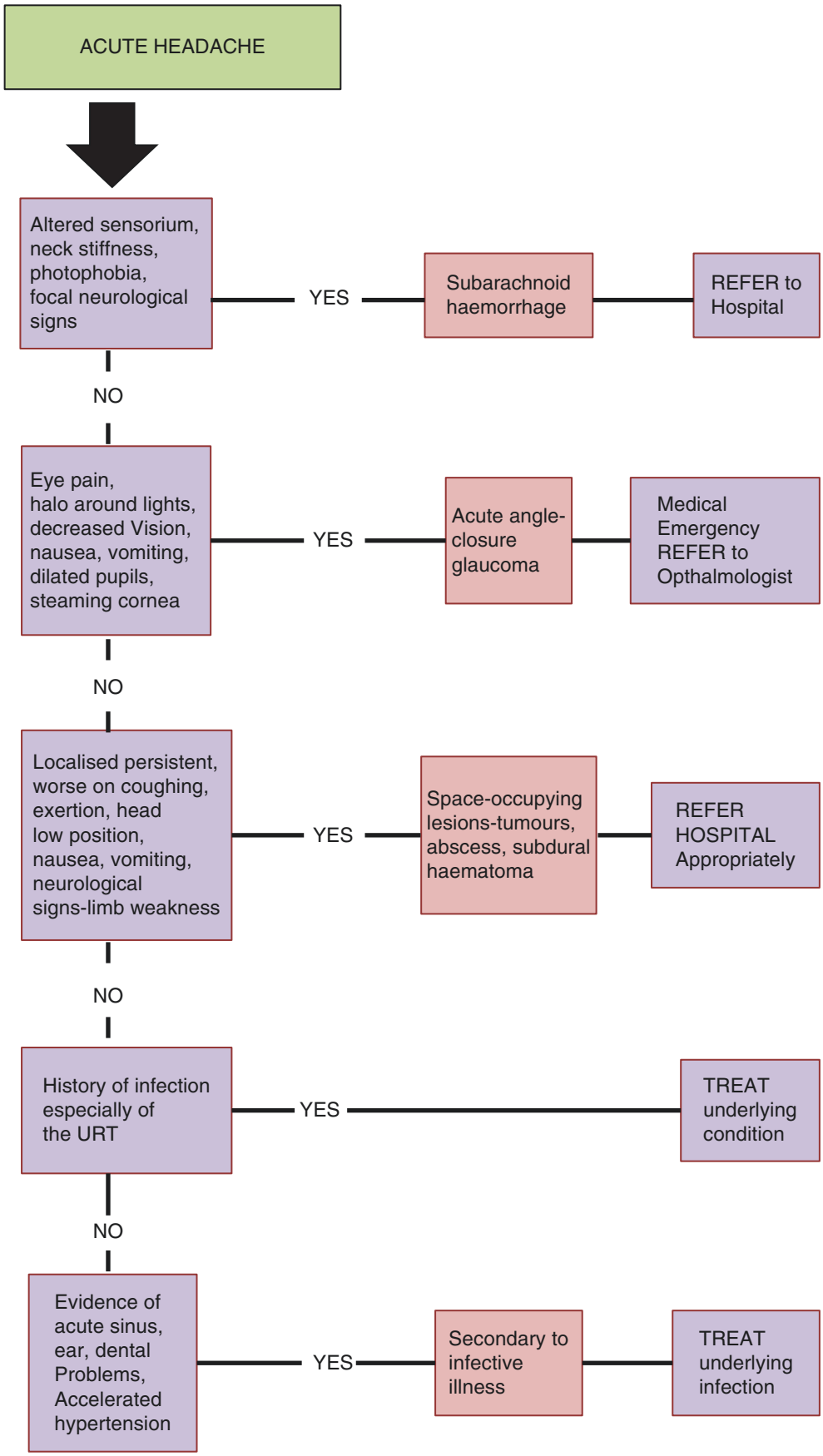
Most alarming complication of temporal arteritis is blindness. Urgent ophthalmological evaluation is mandatory if visual impairment is reported.

Chronic subdural haematoma is common in the elderly and may resemble vascular dementia.

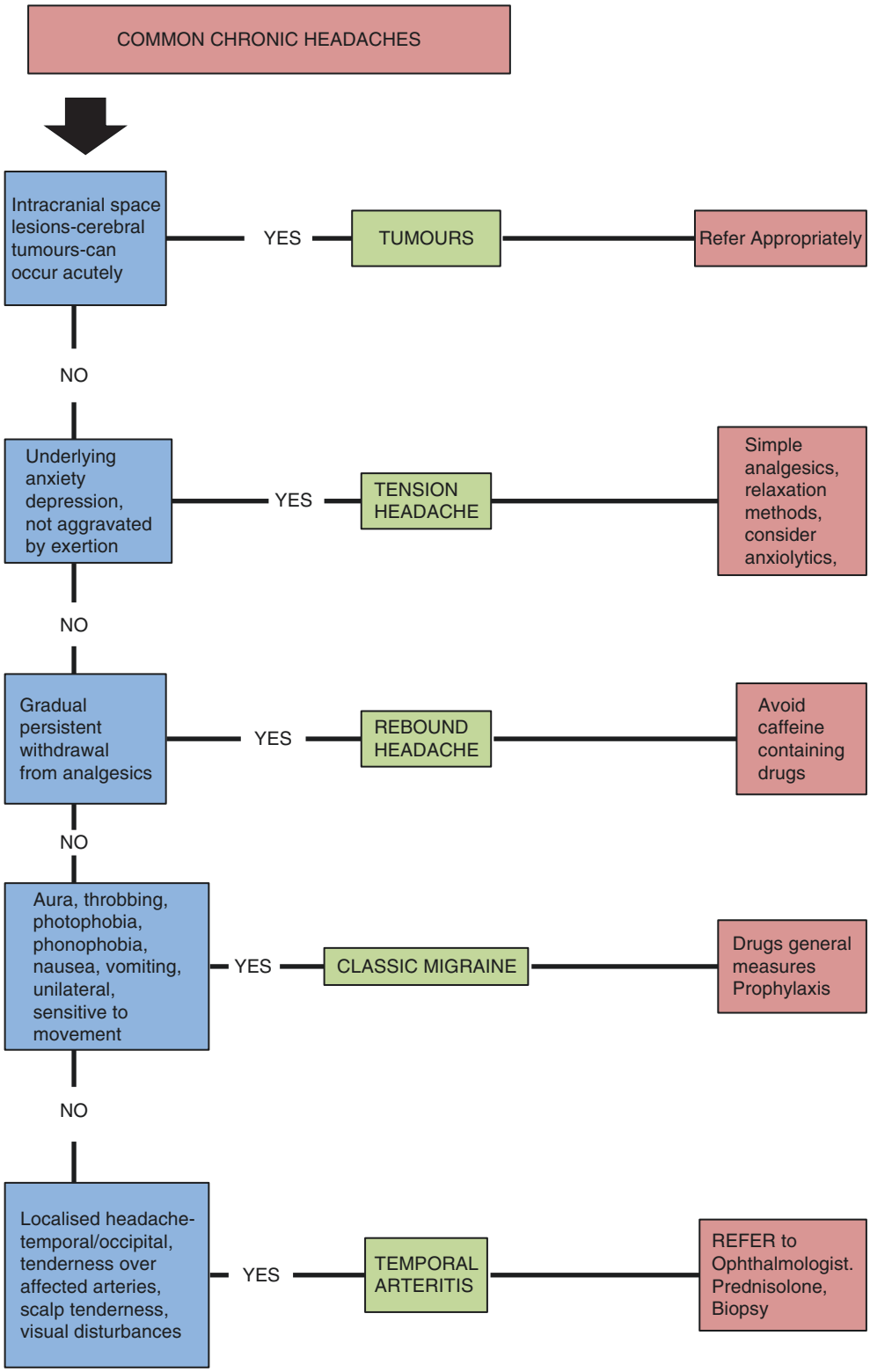
In the elderly primary tumours and secondaries are common.

About 10% of meningitis cases occur in the elderly, and more than 50% of deaths are in the over 60 years group.

Algorithm 31.1 Evaluation of acute headache



Algorithm 31.2 Evaluation of common chronic headaches



Multiple Choice Questions (MCQs)

1. A 72-year-old man was seen in the outpatients accompanied by his son. He lives alone, and according to the son, his father has become forgetful and unsteady on his feet and has had a few falls over the past 3 months. When specifically asked whether his father has had any trauma to his head, he said that his father did knock his head in the past several months earlier. Furthermore the father had complained of headaches on the right side of his head. Physical examination revealed he was alert but had evidence of cognitive impairment and subtle weakness on the left arm and leg. Apart from this the neurological examination was unremarkable.

   Which of the following is the most likely diagnosis?

   A. Vascular dementia
   B. Chronic subdural haematoma
   C. Brain tumour
   D. Normal pressure hydrocephalus

2. A 65-year-old woman was seen in the emergency department complaining of severe throbbing headache over the right temporal and occipital regions for the past 3 days. She further complained of tiredness, fatigue and joint pains, and the scalp was extremely tender when she brushed her hair. Chewing food caused pain in the jaws. She denied any visual disturbances. Physical examination revealed tenderness over the affected scalp. The right temporal artery was not painful on palpation and was thickened.

   Which of the following is the most likely diagnosis?

   A. Herpes ophthalmicus
   B. Carotid artery dissection
   C. Giant cell arteritis
   D. Trigeminal neuralgia

3. A 70-year-old man was seen in the neurological clinic with headaches over the past 2 months. That morning he had developed sudden weakness of the left of his body. The pain was over the right side of his head; throbbing in character was mild at the beginning but now more severe and lasting longer. The headache is worse when lying down and when coughing, sneezing or bending over. There was no history of head trauma. He had been vomiting lately.

   Examination of the nervous system revealed a 6th nerve deficit and weakness of the left arm and leg. The optic fundi showed early papilloedema. Examination of the systems was normal.

   Which of the following is the most likely diagnosis?

   A. Cerebral infarction/haemorrhage
   B. Primary brain tumour
   C. Metastatic tumour
   D. Benign intracranial hypertension (pseudotumor cerebri)

4. The following are true of headaches in the elderly EXCEPT:

   A. Temporal arteritis occurs over the age of 50 years.
   B. Hypnic headaches tend to start before the age of 50 years.
   C. In the elderly 2% of migraine headaches begin after the age of 50 years.
   D. Tension headaches occur at any age.

Answers to MCQs

1. B
2. C
3. B
4. B

References

1. Silberstein SD. Chronic daily headaches. J Am Osteopath Assoc. 2005;105(4 Suppl):23S–9S.
2. Goadsby PJ, Boes C. New daily persistent headaches. J Neurol Neurosurg Psychiatry. 2002;72:ii6–9. https://doi.org/10.1136/jnnp.72suppl_21.6.
3. Lipton RB, Pfeffer D, Newman LC, Solomon S. Headaches in the elderly. J Pain Symptom Manage. 1993;8:87–97.
4. Biondi DM, Saper JR. Geriatric headache: how to make the diagnosis and manage pain. Geriatrics. 2000;55(12):40, 43–5, 48–50.
5. Reinisch VM, Schankin CJ, Felbinger J, Sostak P, Straube A. Headache in the elderly. Schmerz. 2008;22 Suppl 1:22–30.
6. Gobel H, Heinze A. Headache and facial pain in the elderly. Schmerz. 2007;21(6):561–9.
7. Bamford CC, Mays M, Tepper SJ. Unusual headaches in the elderly. Curr Pan Headache Rep. 2011;15(4):295–301.
8. Tanganetti P. Secondary headaches in the elderly. Neuro Sci. 2010;31 Suppl:S73–6. https://doi.org/10.1007/s10072-010-02776.
9. Silberstein SD, Lipton RB. Chronic daily headaches including transformed migraine, chronic tension headache and medications overuse. In: Silberstein SD, Lipton RB, Dalessio DJ, editors. Wolffs. Headache and other head pain. New York: Oxford University Press; 2001. p. 247–82.
10. Bravo TP. Headaches in the elderly. Curr Neurol Neurosci Rep. 2015;15(6):30.
11. Hershey LA, Bednarczyk EM. Treatment of headache in the elderly. Curr Treat Options Neurol. 2013;15(1):56–62.
12. Selby GW, Lance JW. Observations on 500 cases of migraine and allied vascular headache. J Neurol Neurosurg Psychiatry. 1960;23:23–32.
13. Launer LJ, Terwindt GM, Ferrri MD. The prevalence and characteristics of migraine in a population-based cohort-the GEM study. Neurology. 1999;53:537–42.
14. Queroz LP, Friedman DI, Rapoport AM. Characteristics of migraine visual aura in southern Brazil and northern USA. Cephalalgia. 2011;31:1652–8.
15. Wilkinson M. Clinical features of migraine. In: Vinken PJ, Bruyn GW, Klawans HL, et al., editors. Headache. New York: Elsevier; 1986. p. 117–83.
16. Wijman C, Wolf PA, Kase CS. Migrainous visual accompaniments are not rare in late life. The Framingham study. Stroke. 1998;29:1539–43.

17. Vongvaivanich K, Lertakyamane P, Silberstein SD, Dodick DW. Late-life migraine-accompaniments: a narrative review. Cephalalgia. 2015;35:894. http://journals.sagepub.com/doi/full/10.1177/0333102414560635. Accessed 13 Feb 2017.
18. Haan J, Hollander J, Ferrari MD. Migraine in the elderly: a review. Cephalalgia. 2007;27:97–106.
19. Sacco S, Ricci S, Carolei A. Migraine and vascular diseases: a review of the evidence and potential implications for management. Cephalalgia. 2012;32:785–95.
20. Willebrordus P, van Oosterhout J, Cheung A, Haan J. Primary headache syndromes in the elderly: epidemiology, diagnosis and treatment. J Clin Trans Res. 2016;2(2):45–51.
21. Canarda R, Monastero R. Prevalence of primary headaches in Italian elderly: preliminary data from Zabut Aging Project. Neuro Sci. 2003;24 Suppl 2:S122–4.
22. Bendt L, Evers S, Linde M, Mitsikostas DD, Sandrini G, Schoenen J, EFNS. EFNS guideline on the treatment of tension type headache-report of the EFNS task force. Eur J Neurol. 2010;17:1318–25.
23. Raskin NH. The hypnic headache syndrome. Headache. 1988;28(8):534–6.
24. Evers S, Goadsby PJ. Hypnic headache. Pract Neurol. 2005;8:144–9.
25. Newman LC, Lipton RB, Solomon S. The hypnic headache syndrome: a benign headache disorder of the elderly. Neurology. 1990;40(12):1904–5.
26. Obermann M, Holle D. Hypnic headache. Expect Rev Neurother. 2010;10(4):1391–7.
27. International Headache Society (IHS). Hypnic headache [4.5] G44.80. http://ihs-classification.org/en/02_klassification/02teill/04.05.00otherhtml retreived 33.3.2013.
28. Diener HC, Obermann M, Holle D. Hypnic headache: clinical course and treatment. Curr Options Neurol. 2012;14(1):15–26.
29. Evans RW. Diagnostic testing for the evaluation of headaches. Neurol Clin. 1996;14(1):1–26.
30. Ellis ME, Ralston S. The ESR in the diagnosis and management of polymyalgia rheumatica/giant cell arteritis syndrome. Ann Rheum Dis. 1983;42(2):168–70.
31. Greig NH, Ries LG, Yancik R, Rapport SL. Increasing incidence of primary malignant tumours in the elderly. J Natl Cancer Inst. 1990;82:1621–4.
32. Crawford J, Cohen HJ. Relationship of cancer and aging. Clin Geriatr Med. 1987;3:419–32.
33. Legler JM, Reis LA, Smith MA, Warren JL, Heinman EF, Kaplan RS, et al. Cancer surveillance series (corrected) brain and other central nervous system cancers. Recent trends in incidence and mortality. J Natl Cancer Inst. 1999;91:1382–92.
34. Nayak L. I wamoto FM. Primary brain tumours in the elderly. Curr Neurol Neurosci Rep. 2010;10(4):252–8.
35. Cancer Control. Brain tumours in the older person. Medscape. 2000;7(6). http://www.Medscape.com/view article./409013_9. Retrieved 17 Nov 2013.
36. Purdy RA, Kirby S. Headaches and brain tumours. Neurol Clin. 2004;22(1):39–53.
37. Edmeads J. Headaches in cerebrovascular disease. In: Vinken PJ, et al., editors. Hand-book of clinical neurology: headache. 7th ed. New York: Elsevier; 1986. p. 273–90.
38. Forsyth PA, Posner JB. Headaches in patients with brain tumours: a study of 111 patients. Neurology. 1993;43(9):1678–83.
39. Alexander M, Wagner EH, Buchaer DM, Cain KC, Lason EB, et al. Do surgical brain lesions present as isolated dementia ? A population based study. J Am Geriatr Soc. 1995;43:138–43.
40. Tagle P, Mery F, Torreilbe G, Del Villar S, Carmona H, Campos M. Chronic haematoma: a disease of the elderly. Rev Med Clin. 2003;131(2):177–82.
41. Asghar M, Adhiyaman V, Greenway MW, Bhowmich BK, Bates A. Chronic subdural haematoma in the elderly – a North Wales experience. J R Soc Med. 2002;95(6):290–2.
42. Jones S, Kafetz K. A prospective study of chronic subdural haematoma in elderly. Patients. Age Aging. 1999;28(6):519–21.
43. Adhiyaman V, Asghar M, Ganeshram RN, Bhowmich BK. Chronic subdural haematoma in the elderly. Postgrad Med J. 2002;78(916):71–5.
44. Borger V, Vatter H, Oszveld A, Marquadt G, Seifert V, Guresir E. Chronic subdural haematoma in elderly patients: a retrospective analysis of 322 patients between ages of 65-94 years. Acta Neurochir. 2012;154(9):15499–54.
45. Ducruet AF, Grobelny BJ, Zaiharia BE. The surgical management of chronic subdural haematoma. Neurosurg Rev. 2000;35(2):155–69.
46. Domingo P, Pomar V, de Benito N, Coll P. The spectrum of acute bacterial meningitis in elderly patients. BMC Infect Dis. 2013;13:108. https://doi.org/10.1186/1471-2334.
47. Choi C. Bacterial meningitis in adults. Clin Infect Dis. 2001;33:1380–5.
48. Gorse GJ, Thrupp LP, Nadelman KL, Wyle FA, Hawkins G, Cesario TC, et al. Bacterial meningitis in the elderly. Arch Int Med. 1984;144:1603–7.
49. De O Papaiordanu PM, Cadoguns M, Ribeiro R, et al. Bacterial meningitis in the elderly: a 8-year review of cases at two University Hospitals. Braz J Infect Dis. 1999;3:111–7.
50. Behrman RE, Meyers BR, Mendelson MH, Sacks HS, Hirschnar SZ. Central nervous system infections in the elderly. Arch Inter Med. 1989;149:1596–9.
51. Wenger JD, Hightower AW, Facklam RR, Gaventa S, Brome CV. Bacterial meningitis 1986: report of multistate surveillance study. J Infect Dis. 1990;162:1316–23.
52. Laguna -Del-Estal P, Garcia Madero R, Gil-Navarro M, Garcia-Zubiri C, Agud Fernandez AM. Acute bacterial meningitis in older people. Rev Clin Esp. 2010;210(2):57–64.
53. Hussein AS, Shafran SD. Acute bacterial meningitis in adults: a 12 year review. Medicine (Baltimore). 2000;79(6):360–8.
54. Wersfelt M, van de Beek D, Soanjaard L, Reitsma JB, Gans J. Community acquired bacterial meningitis in older people. J Am Geriatr Soc. 2006;54(10):1500–7.
55. Walker RA, Wadman MC. Headache in the elderly. Clin Geriatr Med. 2007;23(2):291–305, v–vi.
56. Edmeads J. Headaches in older people. Postgrad Med. 1997;101(5):91.

Delirium in the Oldest of Old

32

Kujan Nagaratnam

Introduction

Delirium was first described more than 2500 years ago. In spite of this long history, delirium is still poorly understood and under-recognised and its seriousness undervalued. Delirium in simplistic language could be termed 'acute brain failure'. Over the past 30 years, multiple terms had been used depending on the aetiology of the symptoms and signs. These included terms such as encephalopathy, acute brain failure, delirium tremens, acute confusional state and critical illness psychosis [1, 2].

With the advent of formalised classification including DSMs IV and V delirium research networks and consensus meetings, these varied terms have been brought under the term 'delirium'. This has enabled a more structured pathway to not only research but also to provide clinical guidelines, which could be implemented in clinical setting. The latest DSM V classification has also brought into line the divide between hyperactive and hypoactive states of delirium. The latter was previously omitted from the definitions [3].

The prevalence of delirium in the community is 1–2% [4], and this rises to 10% amongst the population aged 85+ years [5]. In hospitalised patients the prevalence is between 11 and 42% [4, 6], and it occurs in up to 50% of the elderly hospitalised inpatients [7, 8]. The prevalence increases in selected groups such as patients from nursing homes and long-term care facilities [9] ranging between 4 and 70% [5]. In intensive care units (ICU), the prevalence is 32.3% [10] increasing to 77% in specialised ICUs, for instance, ventilated burns patients [11] and to 83% in the mechanically ventilated patients [12]. It is identified in 24.3% of elderly patients admitted to the coronary care unit at first assessment within 24 h of admission [13]. In the elderly undergoing elective noncardiac surgeries, the post-operative prevalence ranges from 9% to 87%, whereas those undergoing other forms of surgery the prevalence is 9% [14]. The prevalence and incidence rates in subsyndromal delirium were 23% and 13%, respectively [8].

Risk Factors

With delirium one has to think multiple, for it involves complex interactions between a variety of risk factors. The risk factors can be subdivided into modifiable and non-modifiable risk factors [4, 15]. Risk factors for delirium, all of which are common in the oldest of old, include dementia, older age, multiple comorbidities, psychoactive medication use, polypharmacy, sleep deprivation, dehydration, poor nutritional status, immobility, pain, sensory impairment and hospitalisation [4, 15]. The risk factors of delirium can also be categorised as precipitating and predisposing factors [16]. The precipitating factors include surgery, anticholinergic drugs, alcohol, infections, metabolic abnormalities, pain and admission to ICU [16]. Well-recognised predisposing factors are age, medical comorbidities, cognitive, functional and sensory impairment and institutional residence [16]. Frail older patients present with delirium triggered by multitude medical or surgical problems, often with other predisposing factors; it presents both as a diagnostic and management challenge. As delirium may be the only presenting symptom of a rapidly deteriorating patient, it is a medical emergency (Fig. 32.1).

K. Nagaratnam (✉)
Sydney Medical School, The University of Sydney,
Sydney, NSW, Australia
e-mail: kujan@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_32

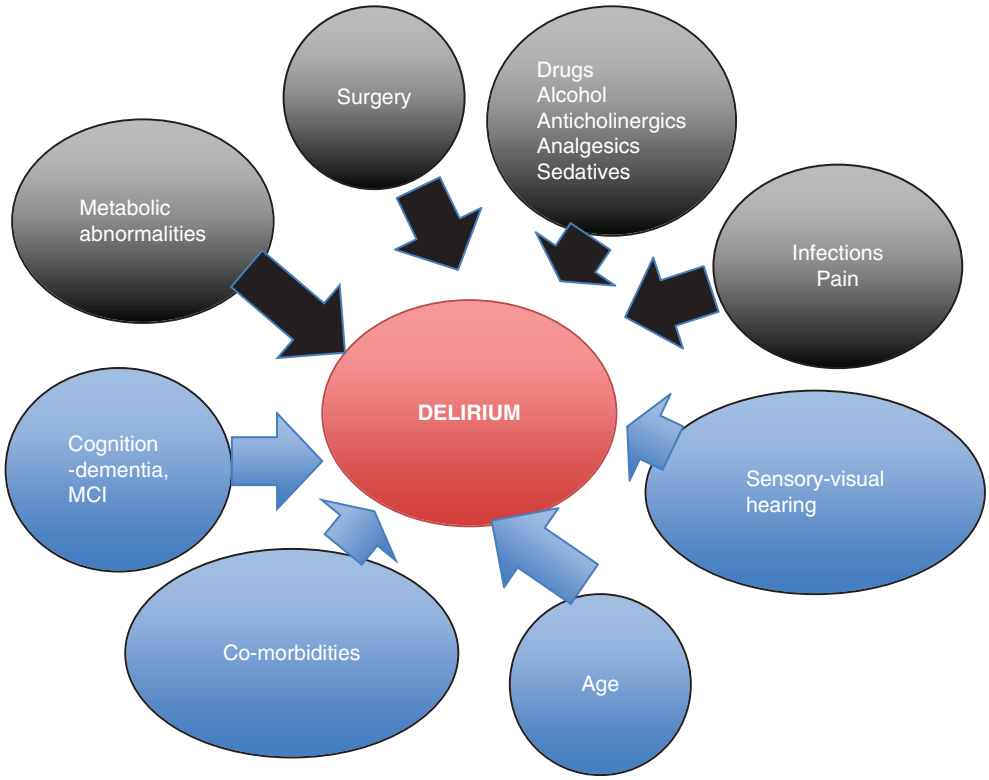


Fig. 32.1 Precipitating and predisposing factors in delirium. (Information sources: Steiner [16])

Pathophysiology of Delirium

The pathophysiology of delirium remains poorly understood for it is complex and involves a diversity of risk factors with dynamic interactions [17]. The difficulty is the complex interplay between multiple factors including external stressors such as hypoxia, metabolic abnormalities, stroke, drug effects [18] infection and surgery with the vulnerable brain, which has network disconnectivity; a low threshold for inflammation; dysfunctional neurotransmission; abnormal metabolism, including that for glucose; and discordance in function including sleep abnormalities. Several theories have been proposed to explain the initial and subsequent development of delirium [19]. Maldonado reviewed the published literature and summarised seven proposed theories and their interrelationship. These included neuroinflammatory, neurotransmitter deficiency, oxidative stress, neuronal ageing, neuroendocrine, diurnal dysregulation and network disconnectivity hypothesis [19].

Inflammatory Hypothesis

According to the inflammatory hypothesis, there is activation of the inflammatory cascade resulting from conditions associated with delirium [17]. In the majority of patients, delirium results from direct brain injury and had been termed as 'direct brain insults' [20]. In some patients, however, it is not that apparent, and mild peripheral infection or injury had been assumed and delirium initiated by the body's response to the insult [18]. Maclullich et al. [18] termed this category of cases of delirium as 'aberrant stress responses'. Acute peripheral inflammatory stimulation induces activation of the brain's parenchymal cells to produce pro-inflammatory cytokines and inflammatory mediators in the central nervous system [17]. Pro-inflammatory cytokines have been shown to be elevated with delirium [21, 22]. In patients with delirium, IL-6 and IL-8 levels are elevated compared to patients without delirium [23]. These inflammatory changes cause neuronal and synaptic dysfunctions which are predisposing factors for cognitive impairments [24].

Neuroendocrine Hypothesis

Olsson et al. [25] studied stroke patients with the possible disturbance at different sites in the hypothalamic-pituitary-adrenal axis. They found that the post-dexamethasone cortisol levels were significantly correlated to the presence of an acute confusional state with extensive limb paresis. They concluded that hypercortisolism was closely associated with cognitive disturbances and extensive motor impairment. High levels of glucocorticoid over long periods can cause neuronal dysfunction.

Network Disconnectivity

The brain is a highly organised and interconnected structure, and in delirium there is an acute breakdown in network connectivity in the brain [26]. Certain brain regions are involved in delirium and have been identified – the prefrontal cortex, the thalamus and the basal ganglia in the non-dominant hemisphere [27] – and that certain anatomical pathways may be more important than others [28]. In the elderly with delirium, imaging has shown marked cortical atrophy in the prefrontal cortex and temporoparietal cortex in the non-dominant hemisphere including the thalamus and basal ganglia [29]. A single-photon emission CT (SPECT) in a prospective study of hospitalised patients with delirium demonstrated frontal and parietal hypoperfusion in half of the patients [30]. Caplan et al. [31] explained differences, in that the inferior parietal structures were associated with 'attentional mechanisms' whereas medial temporal lobe structures with limbic mechanisms with agitation. Attention, sleep and wakefulness are controlled by the reticular formation [32]. Biochemical changes, vascular compromise and or structural damage may be contributory if not causal. It would therefore be reasonable to surmise that delirium and other neuropsychological deficits associated with the right hemisphere can be produced by lesions occurring along the interconnecting neural pathways (a disconnection syndrome) [33].

Neuronal Ageing

The brain of the oldest of old has significant vulnerabilities both by processes of normal ageing and vulnerabilities from disease processes both in the brain and the rest of the ageing body. Besides the loss in brain weight, there is also a reduction in the concentration of a variety of significant neurotransmitters resulting in some slowing of global brain function. Immunosenescence may be a major contributing factor in delirium in the elderly. The immune activity of the innate immune system in later life is evident by the presence of elevated markers of inflammation such as TNF-alpha and interleukin 6(IL-6) [34]. Adaptive changes to acute insults in relation to ageing are characterised by excessive production of pro-inflammatory cytokines by primed microglia together with dysfunction of the brain-immune pathways [35]. Hence minimal stimulation from the multitude of risk factors may set off the inflammatory cascade resulting in delirium.

Neurotransmitter Deficiency

The concept of a 'final common pathway 'is supported by the wide diversity of causes which give rise to the characteristic symptoms of delirium [36]. The final common outcome from the many factors or mechanisms is the alteration in the neurotransmitter synthesis and function that mediates cognitive and behavioural changes [19] with release of cytokines in the brain and consequently delirium. Several neurotransmitter systems have been implicated in the pathophysiology of delirium [37]. It is believed that acetylcholine and serotonin have important roles in common medical and surgical delirium [38]. Dopamine and acetylcholine act in opposite ways, dopamine increases neuronal excitability and acetylcholine decreases [39].

Oxidative Stress

Oxidative stress has been found to occur more frequently in those diagnosed with delirium [40] and may play a role in the pathophysiology of delirium [41].

Diurnal Dysregulation

Poor sleep often occurs sometime prior to the onset of delirium, and the association between delirium and disrupted sleep is the basis for the diurnal dysregulation theory. Melatonin plays an important role in circadian sleep-wake rhythm [42] and is said to play an important role in the pathogenesis of delirium [43]. Sundowning in patients with dementia and alterations in the sleep-wake cycle with delirium could originate from disturbances in the circadian rhythm [44]. In critically ill patients, the sleep pattern is altered; there is loss of circadian rhythms and abnormal levels of melatonin [45]. It has been suggested that there is an association between imbalance in neurotransmitters and alterations in melatonin production, which together contributes to the development of delirium [43] (Fig. 32.2).

Clinical Manifestations

Delirium usually presents with differing subtypes and can be classified as hyperactive, hypoactive and mixed [46]. Patients with hyperactive delirium are agitated, restless, hypervigilant and irritable and often exhibit delusions and hallucinations [4, 47]. In the elderly the hypoactive form occurs frequently and can be mistaken as depression or dementia [4]. They manifest lethargy, reduced alertness and lack spontaneity. The mixed form has characteristics of both hyperactive and hypoactive features [46]. The clinical manifestations can vary according to the precipitating cause [48], for example, with alcohol withdrawal syndrome, patients present with agitation, poor sleep, tremor and tachycardia [49].

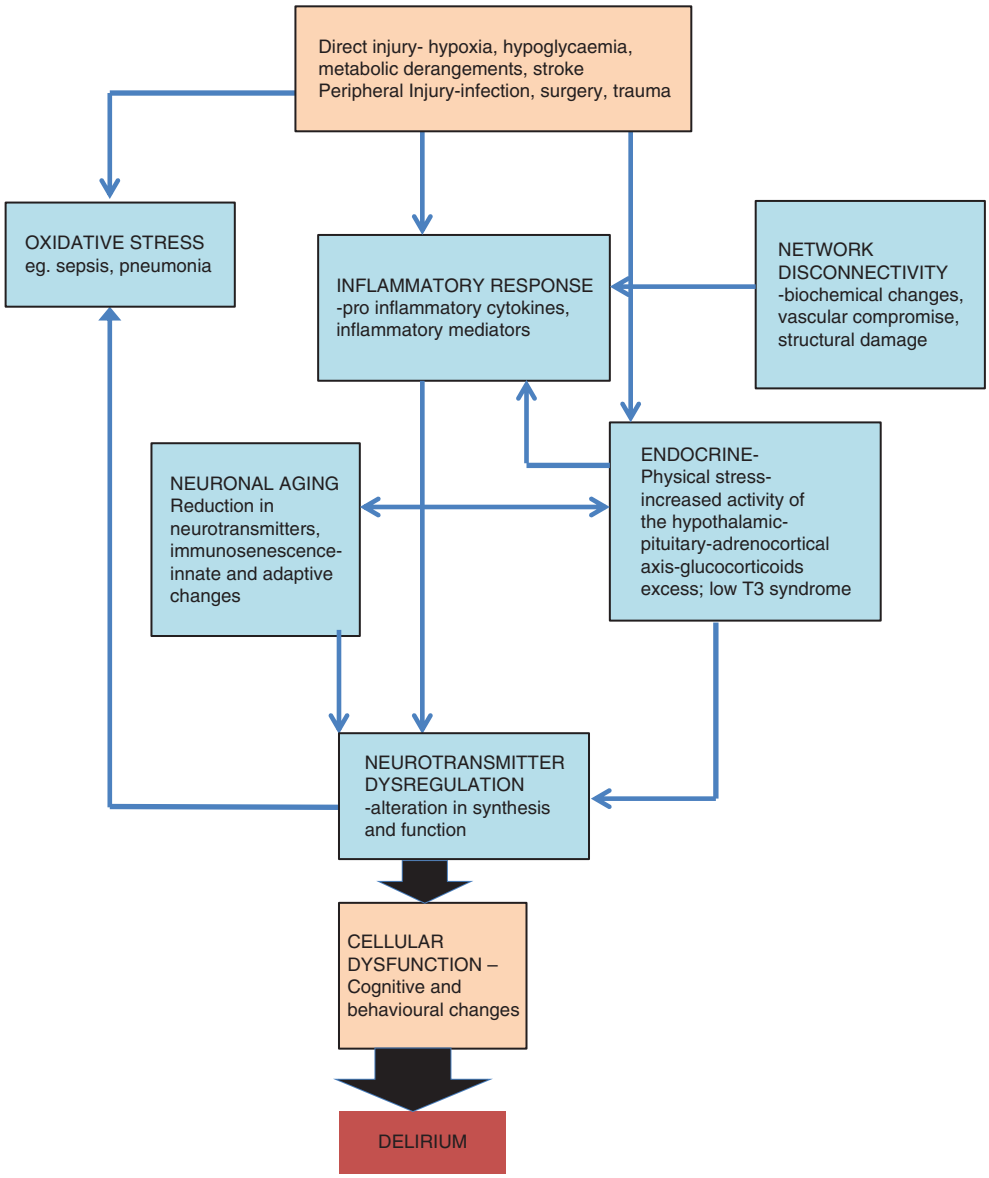


Fig. 32.2 Pathophysiology of delirium. (Information sources: modified form Maldonado [19]. Additional sources: Maclullich et al. [18], Nagaratnam and Nagaratnam [23], Seaman et al. [40])

Diagnosis

Identifying delirium has been a major challenge until now it is due to the lack of awareness and education. There are increasing number of older patients, including the oldest old, admitted to hospitals. A systematic process to screen and monitor for the emergence of delirium through education may be the optimal way of reducing the incidence of or onset of delirium. There are several rating scales, the Mini-Mental State Examination, Dementia Rating Scale-Revised-98, NEECHAM Confusion Scale, Confusion Assessment Method (CAM), CAM-ICU and Delirium Observation Scale. The instruments commonly used for diagnosis, the Confusion Assessment Method (CAM), the CAM-ICU and the Delirium Rating Scale-Revised version (DRS-R-98), are reliable. The CAM and CAM-ICU are validated instruments for diagnosis and have higher specificity than sensitivity [50].

Management

Prevention

Multidimensional interventions have reduced aspects of delirium in hospitalised patients [51, 52] in both medical and surgical settings [52]. Programmes such as the Hospital Elder Life Program (HELP) [53, 54] involves the hospital staff and utilising trained volunteers who address the six major risk

factors for delirium, which are cognitive impairment, immobility, dehydration, visual and hearing impairment and sleep deprivation. They mobilise the patient, reduce sensory deprivation by orientating them, ensure the patient is kept well hydrated and implement a non-pharmacologic sleep regimen, regularly toilet perhaps, thereby limiting the need for urinary catheters and physical and chemical restraints. There are other programmes integrated into the daily clinical practice of the hospital staff [55]. One of the successful programmes over the past decade around the world in reducing the incidence of delirium has been the implementation of the intensive ortho-geriatric services, involving daily geriatrician review starting before surgery which has helped to reduce delirium in hip fracture patients [56]. There is no clear evidence that cholinesterase inhibitors, antipsychotics or melatonin reduce the incidence of delirium [52]. Haloperidol prophylaxis for hip surgery patients had no effect on delirium incidence, but did reduce the severity and duration [57], whereas risperidone after cardiac surgery was found to reduce the incidence of delirium [58].

Treatment

All medications that may cause or exacerbate delirium should be ceased or reduced. In the main, treatment is non-pharmacological and takes the form of supportive care. This includes encouraging mobility, ensuring intake of fluids and providing nutrition, treating pain, addressing incontinence and avoiding physical restraints and catheters [59].

Drugs may be necessary under certain situations such as when the person is jeopardising the safety of others and oneself or preventing the performance of examination or treatment and if there is no improvement from nondrug treatments [59]. There is no conclusive evidence to support pharmacological intervention for the prevention and management of delirium [60]. However, they may be considered for despite unconvincing evidence that antipsychotic reduces the duration and severity of delirium [61]. The main reasons for their use are agitation, aggression, psychiatric symptoms and sleep disturbances [61]. Potential side effects of antipsychotics (typical and atypical) include extra-pyramidal symptoms (EPS) and prolongation of the QTc interval, especially with the use of haloperidol and quetiapine [62]. The risk of dysrhythmia can probably be reduced by prescribing low doses in simple drug regimens [62]. They should be used short term until the delirium subsides [61]. Three studies compared haloperidol with risperidone, olanzapine and placebo in the management of delirium. The results showed that haloperidol in low dosage was in no way different to the atypical antipsychotics, olanzapine and risperidone in efficacy nor had a greater frequency of side effects [63].

I. Intensive Care Unit Delirium

Introduction

Intensive care unit (ICU) delirium once considered benign [64, 65] is now considered a disorder that negatively affects the patient outcomes [64–66]. The disorder was largely under-diagnosed [64, 67] or unrecognised [68] due to the nonavailability of ICU – screening tools [64]. About 32–68% of delirium cases have gone unrecognised by many physicians and nurses [69]. Over the years several tools for detection have been developed for use in the ICU [70, 71].

The prevalence of ICU delirium varies from 20% to 80% [72–74] especially in critically ill patients [66]. It is common in ICU especially in mechanically ventilated patients [46], and a study found an incidence of 83% in mechanically ventilated patients [75]. The prevalence is high in specialised ICUs, for instance, the prevalence was 77% amongst ventilated burn patients [76].

Risk Factors

In 33 studies published for 2000–2014 of critically ill patients for delirium, the investigators [77] found 11 putative factors, namely, age, dementia, hypertension, pre-ICU, emergency surgery or trauma, raised APACHE II score, mechanical ventilation, metabolic acidosis, delirium the previous day and coma. Other studies have implicated severity of illness [64, 73], organ failure [64], metabolic disturbances [72], hypotension [72], hypertension [73], higher APACHE II scores [64, 73, 78], higher age [78], use of mechanical ventilator [78], higher Glasgow Coma Scale [78, 79], hypoalbuminemia [78], effects of sedative [73, 74] and analgesic drugs [73], use of morphine via epidural route [37], smoking [37] and alcoholism [73]. In older trauma patients, physically restrained patients, higher injury severity score and those deeply sedated and mechanically ventilated increased the delirium risk [79]. For every year after the age of 50 years, the chance for delirium increases by 10% [79].

Clinical Manifestations

The clinical manifestations of delirium form a wide spectrum, with restlessness, agitation and emotional lability, [80] at one end to one of decreased responsiveness, withdrawal and apathy [37] and at the other end with a mixed picture in between. The clinical manifestations also may vary according to the precipitating factors [46]. The term subsyndromal has been used to describe an intermediate stage between delirium and normal cognition. Occurring in one-third of the ICU

patients [81, 82], subsyndromal delirium (SSD) is associated with adverse outcome [83], and in older long-term care, residents appeared to last 7–133 days (mean 13.7) and is often recurrent [82].

Outcome

Delirium has a negative influence on outcome [66]. A number of factors influence outcome, namely, in mechanically ventilated patients, there is a 2.5-fold increase in short-term mortality and 3.2-fold increase in 6 month mortality [46]. Prolonged duration of mechanical ventilation [84], prolonged hospitalisation and ICU stay [37, 72, 74, 84, 85] have higher mortality rates.

Diagnosis

There is no specifically designed screening tool for the detection of delirium in acute stroke [32]. The Confusion Assessment Method (CAM) [86] and the Delirium Rating Scale-Revised version (DRS-R-98) [87] are the two screening tools used for the detection of delirium, although CAM has some limitations in the acute stroke setting [88]. When used by a nonpsychiatrist, CAM is equivalent to DRS [89]. Although MMSE scores are influenced by several factors, a low MMSE score may be of some help in identifying patients who are at risk of having delirium [89].

II. Post-stroke Delirium

Delirium is a common complication of stroke [89]. The prevalence of delirium post-stroke ranges from 13 to 48% in general hospitals [90–92] and 10% [93] to 28% in stroke units [91]. In another study the incidence of delirium in general medical wards was 10–25% [94].

Risk Factors

Risk factors for delirium in acute stroke include older age [91–93, 95], pre-existing cognitive decline [91–93, 95], metabolic disturbances [92, 95], infections [92, 93], polypharmacy [92], GCS less than 15 [95] and multiple existing conditions [91, 96].

Specific stroke types may likely to bring on delirium [90]. For example, it is more frequent following intracerebral haemorrhage and infarction in particular areas [91]. It is well known that delirium could occur from focal lesions in the non-dominant hemisphere in the territories of the middle cerebral [97, 98] and posterior cerebral arteries [99, 100]. Milandre et al. [101] in their study of 82 patients with posterior cerebral artery infarction found no difference in the frequency of confusional state between right- and left-sided lesions. Delirium is also known to occur due to lesions in the subcortical structures of the brain, solitary infarcts of the corona radiata, anterior limb and genu of the internal capsule [33, 102], caudate nucleus [33] and thalamus [103] of the non-dominant hemisphere. Furthermore risk factors for post-stroke delirium have been identified with intracerebral haemorrhages [95, 104], cardio-embolic stroke and total anterior circulation infarction [96]. Delirium after stroke probably depends on factors such a localisation of the stroke, size, type of stroke degree of oedema and hypoperfusion apart from the usual predisposing factors [96]. For example, it was predicted by a haematoma in the right hemispheric subcortical white matter and parahippocampal gyrus [105].

Clinical Manifestations

In ischaemic stroke the average duration of delirium is 4 days, and in haemorrhagic stroke it is 3 days with longer duration in women and in patients over the age of 65 years [88]. Delirium is characterised by altered and fluctuating level of consciousness, reduced attention, orientation, memory and behaviour and with a wide spectrum of symptoms from one of apathy, lethargy to one of agitation. The frequent mental changes, fluctuations in the mental state due to cerebral oedema, disturbance in consciousness, neglect and speech disorders after a stroke can cause difficulties in the assessment of delirium [88].

Outcome

Inpatients with post-stroke delirium have a higher mortality [88, 90] and mortality at 12 months compared to non-delirious patients [106]. Higher long-term mortality is seen in patients of advanced age and severe stroke [107]. Functional outcome is poor [95] and more likely to be discharged to a nursing home [90, 106]. It is associated with longer stay in hospital [90, 106].

III. Delirium and Dementia

There is growing evidence that dementia and delirium overlap. Delirium occurs with all types of dementia but is much more prevalent with ex Lewy body disease (LBD). Delirium can occur in pre-existing dementia and has been referred to as ‘delirium superimposed on dementia’ (DSD) [108]. Conversely, it is associated with increased risk of developing dementia [109]. The core features of LBD include fluctuating attention, recurrent visual hallucinations and parkinsonian features, and delirium can be a presenting feature of

LBD. Fluctuating cognition, its severity and prevalence are highest in LBD [110]. Delirium and LBD share a number of clinical similarities including global impairment of cognition, fluctuating attention and perceptual abnormalities, and some cases may typify early or prodromal LBD [109]. It is crucial to differentiate DSD (which has features of both LBD and delirium) from LBD or from delirium [108]. According to Morandi et al. [108], mistaking acute changes as deterioration in patients with LBD would result in under-investigating causes of delirium thereby missing out on the treatment of this potentially medical emergency. On the contrary, misdiagnosing LBD as delirium may result in treating patients with antipsychotics which can worsen LBD or deprive patients of the opportunity to be given a trial of cholinesterase inhibitors.

Case History

An 84-year-old woman presented to the emergency department with her daughter with whom she lived. According to the daughter, her mother was confused from the previous evening. Six to seven months ago, she was confused and was told she had a urine infection and was treated for the same. She had been forgetful for several months, but since that event there was worsening of her memory. More recently she needed help with dressing and showering. Physical examination was unremarkable but for a temperature of 38 °C. The CNS was grossly intact. She was reasonably alert but was markedly inattentive. The attention span was reduced and she was disorientated in time and place. She did poorly on the MMSE with a score of 14/30. She satisfied the criteria for the diagnosis of delirium on the Confusion Assessment Method (CAM). The urine analysis was positive for nitrites and leucocytes. She was treated with antibiotics. When seen again a week later, repeat MMSE revealed a score of 19/30.

Acute delirium is a common complication of medical illnesses and may emerge in the course of dementia or may be the presenting symptom of the disorder. The elderly have a greater susceptibility to infection due to age-related decline in immune responses [111]. One of the top risk factors for delirium in the elderly is infection. The common ones are urinary tract and chest infections. Urinary tract infections (UTIs) are common in the very elderly and account for nearly 25% of all infections [1, 2] as described in the Leiden over 85 trial. The incidence of UTI increases with age in both men and women [3, 112, 113] and increases from 12–29 per 100 person-years at risk in community-dwelling elderly populations [113, 114] to 44–58 per 100 residents per year at risk in long-term care facilities [115, 116]. Several strategies to prevent UTI have been developed, such as treatment of those at high risk with low-dose, long-term antibiotics [117], oestrogens [117] and cranberry products [117]. These strategies have been shown to be effective in preventing UTI in younger women with recurrent UTI [117], but not yet in vulnerable older people.

Clinical Relevance

With delirium one has to think multiple, for it involves complex interactions between a variety of risk factors.

Risk factors for delirium, all of which are common in the oldest of old, include dementia, older age, multiple comorbidities, psychoactive drug use, dehydration, poor nutritional status, immobility, pain, sensory impairment and hospitalisation [4, 15].

Delirium usually presents with differing subtypes which have been classified as hyperactive, hypoactive and mixed [46].

The clinical manifestations can vary according to the precipitating cause [48].

There is growing evidence that dementia and delirium overlap.

Delirium and LBD share a number of clinical similarities including global impairment of cognition, fluctuating attention and perceptual abnormalities [109].

Intensive care unit (ICU) delirium once considered benign [64, 65] is now considered a disorder that can negatively impact patient outcome.

The term subsyndromal has been used to describe an intermediate stage between delirium and normal cognition occurring in one-third of the ICU patients [81, 82].

Higher long-term mortality is seen with advanced age and stroke severity amongst patients with post-stroke delirium [107].

It is crucial to differentiate DSD (which has features of both LBD and delirium) from LBD or from delirium [108].

Multiple Choice Questions

1. The following are true of delirium, EXCEPT:
   A. In delirium the attention is reduced.
   B. The hypoactive form occurs infrequently and often mistaken for depression or dementia.
   C. The clinical manifestations can vary according to the precipitating cause.
   D. Acute delirium is a common complication of medical illnesses.
2. The following are true of delirium, EXCEPT:
   A. The term subsyndromal has been used to describe an intermediate stage between delirium and normal cognition.
   B. Delirium can occur in pre-existing dementia and has been referred to as delirium superimposed on dementia.
   C. Delirium and Lewy body dementia differ largely in their clinical manifestations.
   D. Specific stroke types may likely to bring on delirium.

3. The following are true in the management of delirium, EXCEPT:
   A. Potential side effects of antipsychotics (typical and atypical) include prolongation of the QTc interval.
   B. Antipsychotics should be used short term until the delirium subsides.
   C. Haloperidol in low dosage was in no way different to the atypical antipsychotics, olanzapine and risperidone in efficacy.
   D. There is conclusive evidence to support pharmacological intervention for the prevention and management of delirium.

MCQ Answers

1. B
2. C
3. D

References

1. Francis J, Kapoor WN. Delirium in hospitalized elderly. J Gen Intern Med. 1990;5:65–79. https://doi.org/10.1007/BF02602312.
2. Liston EH. Delirium in the aged. Psychiatr Clin North Am. 1982;5:49–66.
3. The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness safer. European Delirium association and American Delirium Society. BMC Med. 2014;12:141. https://doi.org/10.1186/s12916-014-0141-2.
4. Fong TG, Tuleaev SR, Inouye SK. Delirium in elderly adults: diagnosis prevention and treatment. Nat Rev Neuol. 2009;5(4):210–20.
5. de Lange E, Verhaak PF, van der Meer K. Prevalence, presentation and prognosis of delirium in older people in the population at home and in long term care. Int J Geriatr Psychiatry. 2013;28(2):127–34.
6. Das Gupta M. Cognitive impairment in hospitalised seniors. Geriatrics. 2016;7:4. https://doi.org/10.3390/geriatrics1010004.
7. Rigney TS. Delirium in the hospitalized elder and recommendations for practice. Geriatr Nurs. 2006;27(3):51–7.
8. Cole MG, Ciampi A, Belzile E, Dubuc-Sarrasin M. Subsyndromal delirium in older people: a systematic review of frequency, risk factors, course and outcomes. Int J Geriatr Psychiatry. 2003;28:771–80.
9. Kukreja D. Gunther Ulf, Popp J. Delirium in the elderly: current problems with increasing geriatric age. Ind J Med Res. 2015;142(6):655–62.
10. Salluh JI, Soares M, Teles JM, Ceraso D, Raimondi N, Nava VS, et al. Delirium epidemiology in critical care study group. Delirium Epidemiology in Critical Care Study Group. Delirium in critical care (DECCA) an International Study. Crit Care. 2010;14(6):R210. https://doi.org/10.1186/119333.
11. Agarwal V, O'Neill PJ, Cotton BA, Pun BT, Haney S, Thompson J, et al. Prevalence and risk factors for development of delirium in burns ICU patients. J Burns Care Res. 2010;31(5):706–15.
12. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: validity reliability of the confusion assessment method for ICU. JAMA. 2001;286(21):2703010.
13. Grover S, Lahariya A, Bagga S, Sharma A. Incidence prevalence and risk factors for delirium in elderly admitted to a coronary care unit. J Geriatric Mental Health. 2014;1(1):45–53.
14. Demeure MJ, Fan MJ. The elderly surgical patient and postoperative delirium. J Am Coll Surg. 2006;203(5):752–7.
15. Waas S, Webster PJ, Nair BR. Delirium in the elderly. Oman Med J. 2008;23(3):150–7.
16. Steiner LA. Post-operative delirium. Part: Pathophysiology and risk factors. Eur J Anaesthesiol. 2011;28(9):628–36.
17. Cerejeira J, Firmino H, Vaz-Serra A, Mukaetova-Ladinska EB. The neuroinflammatory hypothesis of delirium. Acta Neuropathol. 2010;119(6):737–54.
18. Maclullich AMJ, Anand A, Davis DH, Jackson T, Barugh AJ, et al. New horizons in the pathogenesis, assessment and management of delirium. Age Ageing. 2013;42:667–74.
19. Maldonado JP. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. Am J Geriatr Psychiatry. 2013;21(12):1190–222.
20. Maclullich AM, Ferguson KJ, Miller T, de Rooj SE, Cunningham C. Unravelling the pathophysiology of delirium: a focus on the role of aberrant stress responses. J Psychosom Res. 2008;65:229–38.
21. Cunningham C, Campson S, Lunnin K, Murray CL, Woods JF, Deacon RM, et al. Systemic inflammation induces acute behavioural and cognitive changes and accelerates neurodegenerative disease. Biol Psychiatry. 2009;65:304–12.
22. van Munster BC, Korevar JC, Zwinderman AH, Levi M, Wiersinga WJ, de Rooij SE. Time-course of cytokines during delirium in elderly patients with hip fractures. J Am Geriatr Soc. 2008;56:1704–9.
23. de Rooij SE, van Munster BC, Korevaar JC, Levi M. Cytokines and acute phase response in delirium. J Psychosom Res. 2007;2(5):521–5.
24. Murray S, Sanderson DJ, Barkus C, Deacon RM, Rawins JN, Bannerman DM, et al. Systemic inflammation induces working memory deficits in the primed brain: relevance for delirium. Neurobiol Aging. 2012;33(3):603–16.
25. Olsson T, Marklund N, Gustafson Y, Nasinen B. Abnormalities at different levels of the hypothalamic –pituitary adrenocortical axis early after stroke. Stroke. 1992;23(ii):1573–6.
26. Sanders RD. Hypotheses for the pathophysiology of delirium: role of base; line brain network connectivity and changes in inhibitory tone. Med Hypotheses. 2011;77(1):140–3.
27. Veiga Fernandez F, Cruz JJ. Delirium: etiology and pathophysiology. Rev Esp Geriatr Gerontol. 2004;43(Suppl 3):4–12.
28. Alagiakrishnan K. Delirium. Medscape http://emedicine.medscape.com/article/288890-overview. Accessed 20 July 2017.
29. Burns A, Gallagley A, Byrne J. Delirium. J Neurol Neurosurg Psychiatry. 2004;75:362–7.
30. Fong TG, Bogardus ST Jr, Daftary A, Auerbach E, Blumenfeld H, Modur S, et al. Cerebral perfusion in older delirious patients using 99mTc HMPA O SPECT. J Gerontol A Biol Sci Med Sci. 2006;61:1294–9.
31. Caplan LR, Kelly M, Kase Hier DB, White JL, Tatamichi T, Mohr J, et al. Infarction of the inferior division of the right middle cerebral artery. Neurology. 1986;56:1015–28.
32. Dostovic Z, Smajlovic D, Dostovic E, Ibrahimagic OC. Risk factors for delirium in the acute stroke. https://www.intechpen.combooks-…/risk-factors-for-delirium-in–the-acute-stroke. 2012. Accessed 23 July 2017.
33. Nagaratnam N, Nagaratnam K. Subcortical origins of acute confusional states. Eur J Int Med. 1995;6:55–8.
34. Bruunsgaard H, Pedersen M, Pedersen BK. Aging and proinflammatory cytokines. Curr Opin Haematol. 2001;8:131–6.
35. Cerejeira J, Lagarto L, Mukaetova-Ladinska EB. The immunology of delirium. Neueoimmunomodulation. 2014;21(2–3):72–8.
36. Trzepacz PT. Is there a final common neural pathway in delirium? Focus on acetylcholine and dopamine. Semin Clin Neuropsychiatry. 2000;5(2):132–48.
37. Girard TD, Pandharipande PP, Ely WE. Delirium in the intensive care unit. Crit Care. 2008;12(suppl 3):S#. https://doi.org/10.1186/cc6149.

38. Flacker JM, Lipitz LA. Neural mechanisms of delirium: current hypothesis and evolving concepts. J Gerontol A Biol Sci Med Sci. 1999;54(6):B239–46.
39. Bogovic TZ, Tonkovic D, Sekulic A, Bandic-Pavlovic D, Baronica R, Bogovic M, et al. Pathophysiology of delirium. Acta Med Croatica. 2012;66(1):61–6.
40. Seaman JS, Schillerstrom J, Carroll D, Brown TM. Impaired oxidative metabolism precipitates delirium: a study of 101 ICU patients. Psychosomatics. 2006;47:56–61.
41. Egberts A, Fekkes D, Wijnbeld EHA, van der Ploeg MA, van Saase J LCM, Ziere G, et al. Disturbed serotonergic neurotransmission and oxidative stress in elderly patients. Dement Geriatr Cogn Dis Extra. 2015;5(3):450–58.
42. De Rooij SE, van Munster BC. Melatonin deficiency hypothesis in delirium: synthesis of current evidence. Rejuvenation Res. 2013;16(4):273–8.
43. Figueroa-Ramos MI, Arroyo-Novoal M, Lee KA, Padilla G, Puntillo KA. Sleep and delirium in ICU patients and review of mechanisms and manifestations. Intensive Care Med. 2009;35:781–5.
44. De Jonghe A, Korevaar JC, van Munster BC, de Rooij SE. Effectiveness of melatonin treatment on circadian rhythm disturbances in dementia: are there implications for delirium? A systematic review. Int J Geriatr Psychiatry. 2010;25(12):1201–8.
45. Bellapart J, Boots R. Potential use of melatonin in sleep and delirium in the critically ill. Br J Anaesth. 2012;108(4):572–80.
46. Liptzin B, Levkoff SE. A empirical study of delirium subtypes. Br J Psychiatry. 1992;6:843–5.
47. Jain G, Chakrabarti S, Kulhara P. Symptoms of delirium: an explanatory factor for analytic study among referred patients. Gen Hosp Psychiatry. 2011;33(4):377–88.
48. Cavallazzi R, Saad M, Marik PE. Delirium in the ICU: an overview. Ann Intensive Care. 2012;2:49. https://doi.org/10.1186/2110-5820-2-49.
49. Hall W, Zador D. The alcohol withdrawal syndrome. Lancet. 1997;349(9069):1897–900.
50. Shi O, Warren L, Saposnik G, Macdermid JC. Confusion assessment method: a systematic review and meta-analysis of diagnostic accuracy. Neuropsychiatr Dis Treat. 2013;9:1359–70.
51. Inouye SK, Bogardus ST Jr, Charpentier PA, Leo Summers L, Acampora D, Holford TR, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1999;340:669–76.
52. Siddiqi N, Harrson JK, Clegg A, Teale EA, Young J, Taylor T, et al. Interventions to prevent delirium in hospitalised patients, not including those on intensive care units. http://www.cochrane.org/CD005563/DEMENTIA_interventions-prevent-…hospitalised-patients-not–including-those-intensive-care-units. Accessed 1 Aug 2017.
53. (www.hospitalelderlifeprogram.org (http://www.hospitalelderlifeprogram.org))
54. Inouye SK, Bogardus ST Jr, Baker DI, Leo-Summers L, Cooney M Jr. The hospital elder life program: a model of care to prevent cognitive and functional decline in older hospitalised patients. J Am Geriatr Soc. 2000;48:1679–170.
55. Vidan MT, Sanchez E, Alonso M, Montero B, Oritz J, Serra JA. An intervention integrated into daily clinical practice reduces the incidence of delirium during hospitalisation of elderly patients. J Am Geriatr Soc. 2009;57:01292036.
56. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc. 2001;49:516–22.
57. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreewijk R, Egberts TC, Burger BJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc. 2005;53:1658–66.
58. Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. Anaesth Intensive Care. 2007;35:714–9.
59. Mayo Clinic. Delirium. www.mayclinic.org/disease-cnditions/deiroium.basics/tratment/con_20033982.
60. Holroyd-Leduc JM, Khandwala F, Sink KM. How can delirium best be prevented and managed in older patients in hospital? Can Med Assoc J. 2010;182(5):465–70.
61. Chan PKY. Clarifying the confusion about confusion: current practices in managing geriatric delirium. BCMJ. 2011;53:409–15.
62. Taylor DM. Antipsychotics and QT prolongation. Acta Psychiar Scand. 2003;107:85–95.
63. Lonergan E, Britton AM, Luxenberg J, Wyller T. Antipsychotics for delirium. Cochrane Database Syst Rev. 2007;(2):CD005594.
64. Roberts B, Rickard CM, Rajbhandari D, Turner G, Clarke J, Hill D, et al. Multicentre study of delirium in ICU patients using a simple screening tool. Aust Crit Care. 2005;18(1):6,11–4.
65. Bruno JJ, Warren ML. Intensive care unit delirium. Crit Care Nurs Clin North Am. 2010;22(2):161–78.
66. Delvin JW, Brummel NE, Al-Qadheeb NS. Optimising the recognition of delirium in the intensive care unit. Best Pract Res Clin Anaesthesiol. 2012;26(3):385–93.
67. Van Eijk MM, Slooter AJ. Delirium in intensive care unit patients. Semin Cardiothorac Vasc Anesth. 2010;14(2):141–7.
68. Miller RR 3rd, Ely EW. Delirium and cognitive dysfunction in the intensive care unit. Semin Respir Crit Care Med. 2006;27(3):210–20.
69. Pandharipande P, Jackson J, Ely EW. Delirium: acute cognitive dysfunction in the critically ill. Curr Opin Crit Care. 2005;11(4):360–8.
70. Grover S, Kate N. Assessment scales for delirium: a review. World J Psychiatry. 2012;2(4):58–70.
71. Gusmao-Flores D, Salluh JL, Chalhub RA, Quarantini LC. The confusion assessment method fot the intensive care unit(CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies. Crit Care. 2012;16(4):R115. https://doi.org/10.1186/cc11.
72. Burkhart CS, Birkner-Binder D, Steiner LA. Delirium in the intensive care unit. Ther Umsch. 2010;67(2):75–8.
73. Quimet S, Kavansgh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. Intensive Care Med. 2007;33(1):66–73.
74. Morandi A, Jackson JC. Delirium in the intensive care unit: a review. Neurol Clin. 2011;29(4):749–63.
75. Ely EY, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). Crit Care Med. 2001;29(7):1370–9.
76. Agrawal IJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. Crit Care Med. 2015;43(1):40–7.
77. Zaal IJ, Devlin JW, Peelen LM. Slooter AJ.A systematic review of risk factors for delirium in the ICU. Crit Care Med. 2015;43(1):40–7.
78. Sharma A, Malhotra S, Grover S, Jindal SK. Incidence, prevalence, risk factor and outcome of delirium in intensive care unit: a study from India. Gen Hosp Psychiatry. 2012;34(6):639–46.
79. Bryczkowski SB, Lopreiato MC, Yonclas PP, Sacca JJ, Mosenthal AC. Risk factors for delirium in older trauma patients admitted to the surgical intensive care unit. J Trauma Acute Care Surg. 2014;77(6):944–51.
80. Meagher DJ, Trzepacz PT. Motoric subtypes of delirium. Semin Clin Neuropsychiatry. 2000;5:75–85.
81. Serafim RB, Soaes M, Bozza FA, Silva LE, Dal-Pizzol F, et al. Outcomes of subsyndomal delirium in ICU: a systematic review

and meta-analysis. Crit Care. 2017;21(1):179. https://doi.org/10.1186/s13054-017-1765-3.
82. Cole MG, McCusker J, Voyer P, Monette J, Champoux N, Ciampi AA, et al. He course of subsyndromal delirium in older long-term care residents. Am J Geriatr Psychiatry. 2013;21(3):289–96.
83. Ouimet S, Riker R, Bergeron N, Cossette M, Kavanagh B, Skrobik Y. Subsyndromal delirium in the ICU: evidence for a disease spectrum. Intensive Care Med. 2007;33(6):1007–13.
84. Pandaharipande PP, Patel MB, Barr J. Management of pain, agitation and delirium in critically ill patients. Pol Arch Med Wewn. 2014;124(3):114–23.
85. von Haken, Gruss M, Plaschke K, Scholz M, Engelhardt R, Brobeil A, et al. Delirium in the intensive care unit. Anaesthetist. 2010;59(3):235–47.
86. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A method for detection of delirium. Ann Intern Med. 1990;113:941–8.
87. Trzepaez PJ, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-Revised-98. Comparison with the Dementia Rating Scale and Cognitive test for Delirium. J Neuropsyhiatry Clin Sci. 2001;13:229–42.
88. Dostovic Z, Smajlovic D, Sinanovic O, Vidovic H. Duration of delirium in the acute stage of stroke. Acta Clin Croat. 2009;48(1):13–7.
89. McManus J, Pathansali R, Hassan H, Ouldred E, Cooper D, Stewrat R, et al. The evaluation of delirium post-stroke. Int J Geriatr Psychiatry. 2009;24(11):1251–6.
90. McManus J, Pathansali R, Stewart R, Macdonald A, Jackson S. Delirium post-stroke. Age Aging. 2007;36(6):613–8.
91. Martin JJ. Confusion agitation and delirium. Front Neurol Neurosci. 2012;30:46–9.
92. Oldenbenving AW, de Kort PL, Jansen BP, Roks G, Kappilla LT. Delirium in acute stroke: a review. Int J Stroke. 2007;2:270–5.
93. Dahl MH, Ronning OM, Thommissen B. Delirium in acute stroke-prevalence and risk factors. Acta Neurol Scand. 2010;122(s190):39–43.
94. Siddiqi N, House AO, Holmes TD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. Age Aging. 2006;35:350–64.
95. Sheng AZ, Shen Q, Cordato D, Zhang YY, Yan Chan OR. Delirium within 3 days of stroke in a cohort of elderly patients. J Am Geriatr Soc. 2006;54(8):1192–8.
96. Dostovic Z, Dostovic E, Smajlovic D, Ibrahimagic OC, Avdic L, Becirovic E. Predictors for post-stroke delirium outcome. Mater Sociomed. 2016;28(5):382–6.
97. Mesulam MM, Waxman SG, Geschwind N, Sabin T. Acute confusional state: with right-sided cerebral artery infarctions. J Neurol Neurosurg Psychiatry. 1976;39:84–9.
98. Caplan LR, Kelly M, Kase CS, Hier DB, White JL, Tatemichi TK, et al. Infarction of the right middle cerebral artery. Neurology. 1986;36:1015–20.
99. Devinsky O, Bear D, Volpe BT. Confusional states following posterior cerebral artery infarction. Arch Neurol. 1988;45:601–6.
100. Nicolai A, Lazzarino LG. Acute confusional states secondary to infarctions in the territory of the osterior cerebral artery in elderly patients. Italian J Neurol Sci. 1994;15(2):91–6.
101. Milandre L, Brosset C, Botti G, Khalil R. A study of 82 cerebral infarction in the area of the posterior cerebral arteries. Rev Neurol. 1994;150:133–41.
102. Tatemichi TK, Desmond DW, Prohovnik I, Cross DT, Gropen TI, Mohr JP, et al. Confusion and memory loss from capsular genu infarction: a thalamocortical disconnection syndrome? Neurology. 1992;42:1966–79.
103. Santamaria J, Blesa R, Tolsa ES. Confusional syndrome in thalamic stoke. Neurology. 1984;34:168.
104. Caeiro L, Ferro JM, Albuquerque R, Figueira ML. Delirium in the first days of acute stroke. J Neurol. 2004;251(2):17–8.
105. Naidech AM, Polnaszek KL, Berman MD, Voss JL. Haematoma locations predicting delirium symptoms after intracerebral haemorrhage. Neurocrit Care. 2016;24(3):397–403.
106. Shi Q, Persutti R, Selchen D, Saposnik G. Delirium in acute stroke. Stroke. 2012;42:645–9.
107. Melkar S, Laurila JV, Vataje R, Oksala N, Jokinen H, Pohjasvaara T, et al. Post-stroke delirium in reaction to dementia and long term mortality. Int J Geriatr Psychiatry. 2012;27(4):401–8.
108. Morandi A, Davis D, Bellelli G, Arora RC, Caplan GA, Kamholz B, et al. The diagnosis of delirium superimposed on dementia: an emerging challenge. J Am Med Dir Assoc. 2017;18(1):12–8.
109. Gore RL, Vardy ER, O'Brien JT. Delirium and dementia with Lewy bodies: distinct diagnosis or part of same spectrum. J Neurol Neurosurg Psychiatry. 2015;86(1):50–9.
110. Walker MP, Ayre GA, Cummings JL, Wesnes K, McKeith IG, O'Brien JT, et al. Quantifying fluctuation with dementia with Lewy bodies, Alzheimer' dementia, vascular dementia. Neurology. 2000;54:1616–162.
111. Grubeck-Loebenstein B, Della Bella S, Iorio AM, Michel JP, Pawelec G, Solana R. Immunosenescence and vaccine failure in the elderly. Aging Clin Exp Res. 2009;21(13):201–9.
112. Burkle A, Casell G, Franceschi C, Mariani E, Sansoni P, Sansoni A, et al. Pathophysiology of ageing, longevity and age related disease. Immunity Aging. 2007;4:4. https://doi.org/10.1186/1742-4933-4-4.
113. Campisi J. The biology of replicative senescence. Eur J Cancer. 1997;33(5):703–9.
114. Vasto S, Colonna-Romano G, Larbi A, Wikby A, Caruso C, Pawelec G. Role of persistent CMV infection in in figuring T cell immunity in the elderly. Immun Ageing. 2007;4:2. https://doi.org/10.1186/1742-4933-42.
115. Gruver AL, Hudson LL, Sempowski GD. Immunosenescence of ageing. J Pathol. 2007;211(2):144–56.
116. Alberts B, Johnson A, Lewis J, Raff M, Robrts K, Walter P. Helper T cells and lymphocyte activation. In: Molecular biology of the cell. 4th ed. New York: Garland Science; 2002.
117. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalised elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA. 1996;275(11):852.

Prescribing to the Oldest Old

33

Vasi Naganathan

Introduction

When prescribing to younger people, there are clinical guidelines that can be used to guide prescribing, especially for common diseases. These guidelines are based on the evidence from clinical trials conducted on participants who are of middle age or older people whose physical and cognitive functions are good enough to volunteer to participate in clinical trials. As a result, older people especially frail older people and older people with comorbidity are poorly represented in clinical trials [1]. Compared to younger people, older people are more likely to suffer the adverse effects of medications. In this context, the challenge when prescribing to older people is to do more good than harm. This chapter will provide some guidance of the factors to consider and processes to follow to achieve optimal medication regimens for older patients.

A Comprehensive Understanding of the Patient and the Medications They Are Taking Is the Key to Optimal Prescribing

The information obtained from a comprehensive geriatric assessment (see Chap. 5) is vital for formulating optimal medication regimens. It is important to know about all medical problems and how they are being managed. Details on medications currently taken and taken in the past should be obtained from multiple sources. Ideally, the patient and/or the person administering the medications should show the packets and boxes of the medications they are taking and show which medications they are taking and when. It is important to ask about how medicines are being taken and if medication administration aids are being used. Even medicines packed in dosette boxes or blister packs may not be taken as prescribed. It is important to ask about over-the counter-medications, complimentary medicines, vitamins and other supplements as well as about 'borrowed' medications. Many older patients find large tablets difficult to swallow. Chewable tablets can be difficult to take for someone with poor dentition. Poor hand dexterity can make inhalers or pumped sprays difficult to use. Failure to recognise discrepancies between the medication regimen prescribed and what medicines are actually taken can result in adverse consequences.

Older people are not necessarily less compliant with medication regimens or prescriber's instructions, but prescribers should be aware of some of the risk factors associated with non-compliance. These risk factors include cognitive impairment, polypharmacy, living alone, using more than one community pharmacy, complex medication regimens, experience of side-effects and poor knowledge of medicines.

When taking a history about current symptoms, it is important to ask about symptoms that could be due to the adverse effects of medications. For an example ask about postural dizziness in anyone who is taking medications that can lower blood pressure. As people become frailer and acquire new diseases, a previously safe and tolerated medication regimen may now be causing harm. A simple but effective strategy is to look at each medication being prescribed and think about what benefit or potential benefit exists for the patient to continue taking the medication. Then check if there are any adverse effects of the medication, keeping drug–disease and drug–drug interactions in mind.

A comprehensive geriatric assessment includes physical examination and assessment of cognition, psychological status, functional status, living circumstances, role of carers and community services. All of these can influence medication use and medication prescription. The management plans that follow a comprehensive geriatric assessment should always include a medication regimen management plan. With the patient's medical history, examination findings and functional and social history in mind, make sure that the patient

V. Naganathan (✉)
Centre for Education and Research on Ageing, Faculty of Medicine and Health, The University of Sydney and Ageing and Alzhiemer's Institute, Concord Hospital, Sydney, NSW, Australia
e-mail: vasi.naganathan@sydney.edu.au

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_33

is getting the right drugs for their medical condition. The medication regimen may need to be altered if it is found that medical conditions are not being adequately treated. Any change in medication regimen should prompt close monitoring and a follow-up assessment by someone who is able to assess for benefit and harm.

The mediation regimen management plan should also include plans for how the medications will be taken. Providing more information about taking medicines in general and about specific medicines, simplifying medication regimens and implementing strategies to help medication administration are all helpful in improving medication compliance and avoiding harm as a result of medication not be taken correctly.

As is often the case with comprehensive geriatric management plan, the skills of other health professionals should be utilised. Pharmacists have an important role in helping collect medication-related information and can help in formulating sensible prescribing plans and optimising medication plans. Occupational therapists and social workers can help with medication administration plans, and speech pathologists can provide advice when there are problems swallowing tablets.

Goals of Treatment

Optimal prescribing cannot be done without knowing the overall goals of treatment for the individual patient. The prescribers should ask themselves 'What do I hope to achieve with the medication regimen being prescribed?' The prescriber should therefore have insight into what their patient, and if appropriate their carer, hopes to achieve by taking the medications that are prescribed and what their priorities are. Good communication between the prescriber and the patient is the key to achieving the medication regimen that meets the patient's goals.

The goals of treatment in a healthy well-functioning 80-year-old person is clearly different from that of an 80-year-old person with advanced dementia who is bed bound and unable to communicate. The healthy 80-year-old can potentially live for many more years so preventive medications such as antihypertensive, lipid-lowering agents and osteoporosis drugs may be appropriate. For the person with advanced dementia, the goals of treatment would be to focus on minimising any discomfort. Medications aimed at prolonging life are unlikely to be of any value and, if anything, only have the potential for harm.

The following common examples illustrate how the goals of medications for common medical problems may be subtly different for a frail older patient compared to a healthy older person:

(a) In a frail older diabetic patient, avoidance of hypoglycaemia is the priority even if it means less than ideal blood sugar control. Older people are unlikely to live long enough to see the benefits of tight glycaemic control but are at higher risk of the harmful effect of tight blood sugar control. Even in younger people, there is evidence of harm from intensive tight blood sugar control [2].
(b) In a frail older patient who has symptomatic postural hypotension but high blood pressure when lying down, if the problems of postural hypotension such as dizziness, syncope and falls are troublesome, then avoidance of these problems becomes the priority even if it means high blood pressure when sitting or lying down.
(c) In a frail older patient with Parkinson's disease, it can be difficult to formulate a Parkinson's disease medication regimen that helps motor symptoms without adversely affecting cognition and making postural blood pressure worse. One should not assume that motor symptoms are the priority, as some patients will say that they would like to have "clearer thinking" even if it means that they are physically more dependent.
(d) In a frail older person, who has lost weight and has muscle weakness, statins to lower cholesterol may not be appropriate as increasing weight or maintaining weight is the priority and statins could be contributing to muscle weakness.
(e) In a frail older person with advanced dementia who is bed bound and nearing the end of their life, preventative medications like antihypertensive medications, lipid-lowering agents and osteoporosis medications can be stopped. There is no evidence that they are of any benefit in this situation.

Under-prescribing

Well-functioning older people are often under-prescribed medications. The lack of direct evidence for medications in older people should not be a reason to deny older people medications that have the potential to improve their function and quality of life. For an example, older people are often under-prescribed medications that can relieve pain or are prescribed weak analgesics. There is little evidence that these less potent analgesics are any safer, but they are less effective in controlling pain. Optimal treatment of heart failure to minimise symptoms such as breathlessness can have a big impact on the everyday function and overall quality of life of an older person. Even preventative medications should not be denied to older people on the basis of age alone. There is more evidence now for the benefits of

treating high blood pressure even in people over the age of 80 [3]. With regard to anticoagulation to prevent stroke in older people with atrial fibrillation, there is evidence that older people are "undertreated" on the basis of age alone rather than risk of bleeding [4]. The key is not to undertreat older people on the basis of age alone but to choose medications that are less likely to have adverse events, start at low doses and monitor closely for benefit and harm. There may be good reasons not to treat or to de-prescribe medications, but these decisions should be made on the basis of comorbidity, prognosis and function rather than simply on the basis of chronological age.

The Screening Tool to Alert doctors to the Right Treatment (START) criteria, which is part of the STOPP/START tool (see below), lists potential prescribing omissions by organ systems [5]. It lists drug therapies that should be considered when omitted for no valid clinical reason(s) assuming that specific contraindications to the recommended drug therapies are observed. The following are some examples of common drug therapies on the list:

(a) Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation
(b) Antihypertensive therapy where systolic blood pressure is consistently >160 mmHg and/or diastolic blood pressure is consistently >90 mmHg
(c) Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end of life or age is >85 years
(d) Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol or carvedilol) with stable systolic heart failure
(e) Proton pump inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation
(f) Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (bone mineral density T-scores - >2.5 in multiple sites) and/or previous history of fragility fracture(s)
(g) Laxatives in patients receiving opioids regularly
(h) Seasonal trivalent influenza vaccine annually

In the acute setting, determining the cause of the acute deterioration in health can be a challenge as older people often present in an atypical fashion. This can result in delay in treatment. Particularly if infection is suspected, it is important to treat older people as early as possible and at the correct doses to be effective. Treatment may have to be started before all the reasons for the acute deterioration and the results of investigations are known.

Identifying Adverse Effects of Medications and Avoiding Adverse Effects

The key principle to keep in mind when prescribing to older people is that older people are more likely than younger people to suffer adverse drug reactions (ADRs) and when they do it can be more serious and is more likely to lead to hospitalisation [6]. There are a number of reasons for why older people are more vulnerable to the adverse effects of medications; these include the pharmacokinetic and pharmacodynamic changes that occur with ageing, the presence of multiple diseases, and polypharmacy.

Many ADRs are preventable as around 80% of ADRs are dose-related and predictable. To minimise the possibility of ADRs, it is a good idea to take a 'start slow, go slow' approach when prescribing medications to older people. If possible start only one new medication at a time, at the lowest dose possible, and increase the dose slowly while being vigilant for possible adverse effects of the medication.

It is important to question and examine older people for possible ADRs. Often the symptoms can be non-specific, such as falls or confusion. An ADR such as postural hypotension can easily be missed if not asked about. When asking about ADRs, it is important to ask if any of the existing diseases and problems have got any worse after any medication changes. It also important to be aware of the common problems that can be caused by specific classes of drugs [Box 33.1] and specifically ask about and look for these adverse effects. The prescriber should also be aware of drugs that have a narrow therapeutic window and/or a long half-life as these drugs are more likely to cause harm.

Box 33.1 Common Problems Due to Medications and the Drugs that Can Cause Them

Confusion
Tricyclic antidepressants
Anticholinergics used to treat urinary incontinence
Antipsychotics
Opioid analgesics
Benzodiazepines
Anticonvulsants
Antiparkinsonian
Corticosteroids (high dose)
Cardiovascular, e.g. digoxin, metoprolol
Antibiotics, e.g. ciprofloxacin, acyclovir
Falls
Antipsychotics
Benzodiazepines

Antidepressants
Neuroleptics
Diuretics
Bleeding
Non-steroidal anti-inflammatory drugs
Antiplatelet agents, e.g. aspirin
Anticoagulants, e.g. warfarin
Hypothermia
Antipsychotics
Tricyclic antidepressants
Parkinsonism or movement disorders
Metoclopramide
Stemetil
Antipsychotic
Selective serotonin reuptake inhibitors
Electrolyte abnormalities
Diuretics
Selective serotonin reuptake inhibitors
Renal failure
Diuretics
ACE inhibitors and angiotensin receptor antagonists
NSAIDs
Allopurinol

Adapted with permission from IP Communications. Naganathan and Le Couteur [7]

There need to be a clear indication and strong likelihood of benefit to prescribe or continue medications such as those listed in the tables above. These medications should be prescribed with care, and their continued use always questioned. There may be of course a good reason for prescribing these medications specifically.

There are now tools that can be used to identify potentially inappropriate medicines in older people. The American Geriatrics Society Beers criteria for Potentially Inappropriate Medication (PIM), which was last updated in 2015 [8], provides lists of PIMs as follows:

(a) Medications to avoid for many or most older adults
(b) Medications to avoid for older adults with specific diseases or syndromes
(c) Medications to be used with caution
(d) Potentially clinical important non-anti-infective drug–drug interactions
(e) Non-anti-infective medications to avoid or the dosage of which to be adjusted based on the individual's kidney function
(f) Drugs with strong anticholinergic properties

Some commonly used mediations appear on these lists. For example, the BEERS criteria states that digoxin should be avoided as first-line therapy for atrial fibrillation or heart failure and should not be prescribed in daily doses great than 0.125 mg for any indication. Proton pump inhibitors should be avoided beyond 8 weeks without justification. Opioids are on the list of central nervous system medications that should be avoided in individuals with a history of falls or fractures. It is recommended that antipsychotics should be avoided to treat behavioural problems of dementia or delirium unless non-pharmacological options (e.g. behavioural interventions) have failed or are not possible and the older adult is threatening substantial harm to self or others. The BEERS criteria serve as a 'warning light' about medications which have an unfavourable balance of benefits and harms, and there may be situations in which use of medications included in the criteria is appropriate. The criteria are designed to support, rather than supplant, good clinical judgement. The BEERS criteria do not apply to individuals in palliative care or hospice settings.

The other well-known tool to identify inappropriate prescribing is the STOPP/START criteria which was developed in Europe and was last updated in 2015 [5]. Along with the START criteria, mentioned above in the section on under-prescribing, it includes a list of PIMs called the Screening Tool of Older Persons' Prescriptions (STOPP). The following are some examples of prescriptions on the list:

1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)
2. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)
3. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer)
4. Initiation of tricyclic antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).
5. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy)
6. Long-term use of NSAID (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief)

A systematic review found that the STOPP criteria reduced PIM rates in all fours clinical trials included in the review [9]. There was also some evidence from specific trials that use of the criteria reduced falls, delirium episodes,

hospital length-of-stay, care visits (primary and emergency) and medication costs.

Prescribers should be aware of the 'prescribing cascade'. This is where failure to recognise the side-effect of medications results in the prescribing of more medications to treat the adverse effects of the original mediation regimen, which in turn leads to more adverse drug reactions. An example of a prescribing cascade is shown below:

Non-steroidal anti-inflammatory drug → causes nausea → metoclopramide prescribed for nausea → causes extrapyramidal signs resembling Parkinson's disease → levodopa prescribed for extrapyramidal signs → causes hallucinations → antipsychotic prescribed for hallucinations.

Polypharmacy

Polypharmacy is usually defined as the use of five or more medications. There are a number of reasons why polypharmacy is more prevalent in older people. Older people are more likely to have several chronic diseases for which they are often seeing more than one prescriber. It is unclear whether applying all the relevant disease-specific guidelines in patients with multiple diseases does more good than harm [10]. Polypharmacy also occurs if prescribers fail to review medication regimens to discontinue unnecessary medications. Sometimes more medications are prescribed when it hasn't been recognised that a poor therapeutic response has been due to poor compliance.

Polypharmacy is associated with a number of problems. The more medicines someone takes, the harder it is to obtain an accurate medication history. Medication management becomes more difficult and compliance is more likely to be poor. The likelihood of an ADR increases, and the potential for drug–drug interactions and drug–disease interactions increases. The more medicines an older person is taking, the more likely it is that they are taking at least one 'high-risk' medicine such as sedatives or medicines with anticholinergic effects. Polypharmacy in older people is associated with impaired cognition, frailty, falls, disability and increased mortality [11–14].

Polypharmacy should alert the treating doctor to have a close look at the medication regimen. The goals of treatment should be re-evaluated. Ask for and look for any ADR, keeping drug–disease and drug–drug interactions in mind. Medication management is particularly important to address in someone taking a lot of medications. Sometimes it is possible to simplify the medication regimen. Strategies can be used to assist people with taking medication, such as a dosette box or having the pharmacy pack medications in a blister medication pack.

De-prescribing

The presence of polypharmacy, adverse drug reactions, potentially inappropriate medicines, geriatric syndromes and advanced end-stage disease or terminal illness is just some of the reasons to consider reducing an older person's medication – de-prescribing. De-prescribing has been defined by Scott et al. [14] as 'a systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient's care goals, current level of functioning, life expectancy, values, and preferences' [14]. Dose reduction and switching to a safer medication can also be considered part of the de-prescribing process. A systematic review that aimed to determine if de-prescribing was a safe, effective and feasible intervention to modify mortality and health outcomes in older adults found that patient-specific de-prescribing interventions (as opposed to educational programmes) resulted in a significant reduction in mortality (OR 1.21, 95% CI 0.86–1.69) [15]. Individual clinical trials have shown that psychotropic mediation reduction results in less falls in community living people [16] and mortality benefits in people with Alzheimer's disease living in residential care [17]. Importantly the evidence to date suggests that de-prescribing can be done safely without an increase in adverse drug withdrawal events or increased mortality. In addition, the withdrawal of unnecessary medication that occurs during the de-prescribing process may prompt the prescription of more appropriate medication with a greater likelihood of benefit.

A number of tools and algorithms, in addition to the BEERS and STOPP/START criteria described above, have been developed to assist clinicians in the de-prescribing process. These appear in publications [14, 18, 19] and online resources (such as http://deprescribing.org/ and http://medstopper.com). Reeve et al. outlines in more detail available resources and tools to aid de-prescribing [20]. The reasons that a medication could be considered for de-prescribing include:

(a) ADE due to the medication.
(b) No clear indication for continued use.
(c) Adverse effect or potential adverse effects outweigh symptomatic benefit or potential future benefit.
(d) In medications for symptoms, the symptoms are now stable or non-existent.
(e) In preventative medications, the potential benefit is unlikely to be realised because of limited life expectancy.

To identify these reasons and to have the information needed to successfully de-prescribe medications require a

comprehensive understanding of patient and the medications they are taking, an agreement between patient and prescriber on the goals of treatment and recognition of possible of adverse effects of medications. Usually medications that are responsible for ADE are targeted first. In other instances, medications that are easiest to discontinue or those that the patient is most willing to discontinue may be targeted first. Medications with low likelihood of withdrawal symptoms or disease recurrence can be discontinued by simply stopping the drug. On the other hand, if withdrawal symptoms or disease recurrence is possible if the mediation is stopped, doses should be tapered and the patient monitored for adverse drug withdrawal effects.

There are a number of barrier and enablers of de-prescribing. Reeve et al. [20] in a narrative review on de-prescribing provide a detailed summary on the research to date in this area. The attitudes of patients, their carers and those prescribing medications to mediations in general and de-prescribing specifically play a big role in influencing whether de-prescribing can occur or not. Studies suggest that the vast majority of patients are hypothetically willing to have a medication de-prescribed. It is important to involve the patient, their caregiver (if appropriate), other prescribers and those involved in medication management (e.g. pharmacists, nurses in residential care) in the de-prescribing process. Jansen et al. [21] describes the key steps to enhance shared decision making about de-prescribing between patient and the prescriber as follows: creating awareness that options exist and a decision can be made, discussing the options and their potential benefits and harms, exploring preferences for (attributes of) different options and making the decision.

Conclusion

Appropriate and safe prescribing to older people is challenging. There are many things to consider when prescribing to older people, especially if they are frail. Both under-prescribing and over-prescribing of medications are seen in older people. Box 33.2 provides some rules to follow when prescribing to older people that will help the prescriber achieve appropriate medications regimens for their older patients.

Box 33.2 Rule to follow when prescribing to older people

1. Take into account the information obtained from a comprehensive geriatric assessment.
2. Set goals of treatment.
3. Understand and apply the evidence appropriately.
4. Avoid under-prescribing medications that are likely to have symptomatic and functional benefits.
5. Be vigilant for the adverse effects of medications and potentially inappropriate medicines
6. Specifically look for drug–drug and drug–disease interactions.
7. Identify medications that could potentially be de-prescribed.
8. Discuss the potential benefits and harms with patient, family and carers.
9. Choose medications wisely and then ‘start low and go slow’.
10. The prescription of medication should be seen as a ‘n of 1’ trial so try to avoid starting many medications at once.
11. Use available resources and tools to aid de-prescribing.
12. Involve the other people that have a ‘stake’ in the mediation regimen such as carers, specialists and pharmacists.
13. Formulate and implement a plan to achieve optimal medication management.

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Clinical Relevance

Polypharmacy is common in older people.

Older people are vulnerable to the adverse effects of medications.

There are medications that are more likely to result in adverse effects in older people.

A good knowledge about medications that should be prescribed and should be avoided in older people results in more appropriate prescribing and better health outcomes.

Case Study

An 84-year-old lady came into an outpatient clinic for review after a fall which resulted in a fractured wrist. She has had three falls in the last 12 months. She describes dizziness when standing. She has pain in both knees when walking and suffers from intermittent constipation. On examination, she is frail (thin and has quadriceps wasting and weakness), has osteoarthritis of both knees and walks slowly with a walking stick. Blood pressure is 155/80 lying and 125/60 standing with associated dizziness. She is on the following medications:

lisinopril 5 mg daily, amlodipine 5 mg daily, sertraline 25 mg daily, temazepam 10 mg nocte, simvastatin 20 mg nocte and aspirin 100 mg daily.

The following are the important considerations when thinking about her medication regimen:

- On six regular medications (polypharmacy).
- Sertraline and temazepam are psychotropic medications and are associated with increased risk of falling.
- On further questioning the sertraline was started 3 years ago when she had low mood after her husband passed away. She has never had clinical depression and has no symptoms suggestive of clinical depression now.
- She has been taking temazepam for years for insomnia but does not really think it helps.
- Has symptomatic postural hypotension and is on two antihypertensive medications.
- Amlodipine can cause constipation.
- No history of ischaemic heart disease, stroke or peripheral vascular disease so is on aspirin and simvastatin as primary prevention.
- Statins can contribute to muscle weakness.
- Has had a minimal trauma fracture and therefore should be on osteoporosis treatment.
- Paracetamol has helped the knee pain in the past.

With the above considerations in mind, the following is an appropriate medication regimen plan:

- Take as needed or regular paracetamol for knee pain.
- Start osteoporosis treatment if bone mineral density is low and vitamin D replacement if vitamin D level is low.
- Stop aspirin, simvastatin and amlodipine.
- Start weaning sertraline by reducing dose to 25 mg on alternate days or if she is wary about stopping then start weaning by advising not taking it 1 day of the week and then ceasing it on another day of the week 2 weeks later and so on,
- Discuss non-pharmacological methods to manage insomnia with view to weaning temazepam.

Multiple-Choice Questions

1. An 85-year-old man presents with delirium due to a urinary tract infection. He is taking the following medications: lisinopril, metoprolol, paracetamol, diazepam and Oxybutynin. Which medication should be stopped in view of the delirium?
   A. Lisinopril
   B. Metoprolol
   C. Paracetamol
   D. Diazepam
   E. Oxybutynin
2. An 85-year-old woman came into clinic complaining of increased breathlessness and oedema of the legs consistent with an exacerbation of heart failure. Which of the following of her regular medications has the highest potential to promote fluid retention and exacerbate heart failure (drug–disease interaction)?
   A. Non-steroidal anti-inflammatory drug (NSAID)
   B. Proton pump inhibitor
   C. Angiotensin-converting enzyme inhibitor
   D. Beta-blocker
   E. Nitrates
3. For which of the following medication and indication for its use is there strongest evidence of benefit and prescribing of this medication would be consistent with the STOPP/START criteria?
   A. Statins in 85-year-old with no history in ischaemic heart disease or stroke
   B. Antihypertensive in 80-year-old with BP 160/95
   C. Antipsychotics in 80-year-old with behavioural symptoms due to dementia
   D. Digoxin in 83-year-old for heart failure with preserved systolic function
   E. Tricyclic antidepressant in 80-year-old with major clinical depression

MCQs Answers

1. E
2. A
3. B

References

1. Zulman DM, Sussman JB, Chen X, Cigolle CT, Blaum CS, Hayward RA. Examining the evidence: a systematic review of the inclusion and analysis of older adults in randomized controlled trials. J Gen Intern Med. 2011;26(7):783–90.
2. Action to Control Cardiovascular Risk in Diabetes Study G, Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358(24):2545–59.
3. Group SR, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med. 2015;373(22):2103–16.
4. Bajorek B. Utilisation of antithrombotic therapy for stroke prevention in atrial fibrillation in a Sydney hospital: then and now. Int J Clin Pharm. 2012;34(1):88–97.
5. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015;44(2):213–8.
6. Beijer HJM, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. Pharm World Sci. 2002;24(2):46–54.

7. Naganathan V, Le Couteur D. Prescribing medications to older people. In: Caplan G, editor. Geriatric medicine – an introduction Victoria. Australia: IP Communications; 2014. p. 258–69.
8. By the American Geriatrics Society Beers Criteria Update Expert P. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015;63(11):2227–46.
9. Hill-Taylor B, Sketris I, Hayden J, Byrne S, O'Sullivan D, Christie R. Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. J Clin Pharm Ther. 2013;38(5):360–72.
10. Multimorbidity AGSEPotCoOAw. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians: American Geriatrics Society expert panel on the Care of Older Adults with multimorbidity. J Am Geriatr Soc. 2012;60(10):E1–E25.
11. Shah BM, Hajjar ER. Polypharmacy, adverse drug reactions, and geriatric syndromes. Clin Geriatr Med. 2012;28(2):173–86.
12. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol. 2012;65(9):989–95.
13. Jyrkka J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Polypharmacy status as an indicator of mortality in an elderly population. Drugs Aging. 2009;26(12):1039–48.
14. Scott IA, Hilmer SN, Reeve E, Potter K, Le Couteur D, Rigby D, et al. Reducing inappropriate polypharmacy: the process of deprescribing. JAMA Intern Med. 2015;175(5):827–34.
15. Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD. The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016;82(3):583–623.
16. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. J Am Geriatr Soc. 1999;47(7):850–3.
17. Ballard C, Lana MM, Theodoulou M, Douglas S, McShane R, Jacoby R, et al. A randomised, blinded, placebo-controlled trial in dementia patients continuing or stopping neuroleptics (the DART-AD trial). PLoS Medicine / Public Library of Science. 2008;5(4):e76.
18. Garfinkel D, Zur-Gil S, Ben-Israel J. The war against polypharmacy: a new cost-effective geriatric-palliative approach for improving drug therapy in disabled elderly people. Isr Med Assoc J. 2007;9(6):430–4.
19. McGrath K, Hajjar ER, Kumar C, Hwang C, Salzman B. Deprescribing: a simple method for reducing polypharmacy. J Fam Pract. 2017;66(7):436–45.
20. Reeve E, Thompson W, Farrell B. Deprescribing: a narrative review of the evidence and practical recommendations for recognizing opportunities and taking action. Eur J Intern Med. 2017; 38:3–11.
21. Jansen J, Naganathan V, Carter SM, McLachlan AJ, Nickel B, Irwig L, et al. Too much medicine in older people? Deprescribing through shared decision making. BMJ. 2016;353:i2893.

Dementia in the Oldest Old

34

Nages Nagaratnam and Kujan Nagaratnam

Introduction

The 'oldest old' now refers to people who are 90 years old or older, for it is argued that the earlier description of 'oldest old', that is, those 85 years and older, is no longer appropriate [1]. The 90 years and older are the fastest growing segment of the population in the United States [2] and is growing at a faster rate than the 85–89-year-old group [3]. In the United States, in 2010, there were 5.5 million Americans aged 85 years and older [4], and this will increase from less than 2% in 2010 to over 4% in 2050 [5]. By the middle of this century, 5.5% of the combined population from the more developed countries of the world will be aged 85 years or more [6]. A wide variety of changes have been described in normal ageing and dementias, but their relationship to one another is obscure. The distinction between age-related process and ageing-related disease becomes indistinct as age advances. In the oldest old, age is the only risk factor that is persistently associated with dementia [3, 7].

Incidence, Prevalence and Demographic Characteristics

In a large sample of patients, Corrada and colleagues [8] presented data showing the incidence rate of dementia increased exponentially from 12.7% per year for 90- to 94-year-olds to 40.7% per year for persons aged 100 years and older but only for women. The prevalence of dementia in the oldest old was more common in women than in men so was doubling of prevalence seen in women but not in men according to the 90+ Study [3]. In men the prevalence of dementia remained stable increasing from 21% in the low 90 age group to 33% in the aged over 100. In women, however, 27% of the women aged 90–91 were diagnosed with dementia, and this rose to 70% of the women aged 98–99 [9]. In contrast, other studies have shown a slowing of dementia incidence after the age of 90 [10–13]. This would indicate that age may not be related to dementia in the oldest old but to other age-associated factors and diseases [14]. Currently there has been a shift to the earlier view that dementia continues to rise and the incidence and prevalence are highest in the oldest old [15]. The prevalence rates of dementia in the oldest old range between 50% [16] and over 60% [17, 18]. Alzheimer's disease and vascular dementia are the most common subtypes. In a neuropathological study of 137 autopsied subjects with dementia dying 95 years and over, the investigators found those with clinical dementia (80%) demonstrated AD pathological features with coexisting neurodegenerative and vascular disease and in those without clinical dementia had degenerative neuropathology including plaques, hippocampal sclerosis, vascular disease, Lewy bodies and argyrophilic grain pathology [19]. The increase in the incidence rates of dementia in the very old appears to be due to AD, and the rates for vascular dementia remained relatively constant [20].

The prevalence and incidence rates for dementia across Asia, China, Europe and the United States are comparable, but the types of dementia tend to vary. Cerebrovascular disease is a relatively important cause in East Asia than in Western countries [21]. In cognitively impaired aged subjects, the prevalence of vascular dementia (VaD) was 8–10% in the Western clinic-based series [22] and in autopsy series with reasonable values of 8–15% and in Japan 22–35% [22].

N. Nagaratnam (✉) · K. Nagaratnam
Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
e-mail: nages@nagaratnam.net; kujan@nagaratnam.net

N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5_34

Neuropathology

With ageing there are decrease in brain weight, atrophy and ventricular dilatation. Brain ageing is pathologically characterised by neurofibrillary tangles and neuritic plaques together with neuronal and synaptic loss [23]. These occur in both cognitively intact and patients with Alzheimer's disease (AD). Ageing affects different brain regions differently [24, 25]. Similarly the effect of ageing on the type of cell (neurones or glial cells, their numbers and branching) and the site of action (synapse) varies. White matter may decline with age, and age-related changes in the white matter (leucoaraiosis) occur in zones of low density and show a predilection for the frontal regions [26] and may progress with increasing age to the posterior areas [27]. The hippocampus shows the most significant age-related atrophy with advancing age.

Savva and colleagues [18] in their study found the prevalence of moderate-severe AD-type pathology progressively increased with age in both the cortex and hippocampus in individuals without dementia. In comparison with increasing age, the prevalence of such pathology remained constant or decreased in patients with dementia. The findings imply that moderate-severe AD pathology was more strongly associated with dementia in those 80 years or lower, and this decreased as age advanced and attenuated in the oldest old. This lack of correlation in the oldest old indicates that AD pathology is not a requisite occurrence of increasing chronological age. These investigators [18] further found moderate to severe atrophy (a measure of neuronal loss) in the cortex and hippocampus which correlated with dementia across all age groups. One reason for the failure of the relationship between AD-type pathology and dementia in the oldest old may be the coexistence of other pathologies notably cerebrovascular disease. The brains of the oldest old usually have a mix of pathologies associated with dementia, the commonest being Alzheimer's disease-related brain changes, and other pathologies include infarcts, hippocampal sclerosis, white matter disease and Lewy bodies [28]. Autopsy studies in advanced old age found AD pathology with moderate neuritic plaques in 62% and some hippocampal NFTs in every case, hippocampal sclerosis in 20% and Lewy body pathology in 17% [29]. Other studies however had shown weaker association with AD pathology and other pathologies such as hippocampal sclerosis and vascular dementia [18, 30, 31]. Hippocampal sclerosis affects 20% of the oldest old and is strongly associated with cognitive impairment [29, 32]. It is strongly associated with TDP-43 pathology [32].

The 90+ Study established that close to half of demented oldest old do not have any known pathology to account for their cognitive deficits [33]. Cognitively impaired oldest old have a preference to involve the anterior part of the CA1 field of the hippocampus unlike that of young old who manifest severe NFT formation within the inferior temporal and frontal association areas [34, 35]. Furthermore, in the oldest old, the extent of neuronal loss in the CA1 field and the entorhinal cortex was significantly lower compared to that of younger AD cases [36–38]. This disparity between pathology and dementia in the oldest old has drawn awareness to the significance of neuronal than to the accumulation abnormal protein deposits in causing cognitive impairment [7]. Synaptic loss which is a feature of ageing and dementia may help to separate oldest-old subjects with and without dementia [7].

Neuropathological changes in vascular dementia with cognitive impairment included multifocal and/or diffuse disease and focal lesions: multi-infract encephalopathy, white matter lesions or arteriosclerotic subcortical (leuko)encephalopathy, multi-lacunar state, mixed cortico-subcortical type, watershed lesions, post-ischaemic encephalopathy and hippocampal sclerosis [22].

Box 34.1 Neuropathology

Moderate-severe AD pathology was more strongly associated with dementia in those 80 years or lower, and this decreased as age advanced and attenuated in the oldest old [18].

The brains of the oldest old usually have a mix of pathologies associated with dementia [28].

Hippocampal sclerosis, which affects 20% of the oldest old, is strongly associated with cognitive impairment [29, 32].

It is strongly associated with TDP-43 pathology [32].

Cognitively impaired oldest old have preference to involve the anterior part of the CA1 field of the hippocampus [34, 35].

One reason for the failure of the relationship between AD-type pathology and dementia in the oldest old may be the coexistence of other pathologies notably cerebrovascular disease.

Risk Factors

The 90+ Study showed that about half of the demented oldest old had no cerebral pathology and the ApoE-e4 allele is a risk factor for women only [39]. ApoE-e4 loses its importance predicting AD as age progresses [40]. The continuous decreasing frequency of e4 allele in AD patients has been reported for Northern and Southern European regions [41].

Low level of education, low level of physical activity, midlife poor health, depression and delirium have been linked with dementia in the oldest old [9]. ApoE-e4 genotype, late-life hypertension, hyperlipidaemia and elevated inflammatory markers are indeterminate [9].

Differential Diagnosis

DSM-5 removed the subcategories 'early onset' (onset at age 65 years and below) and 'late onset' specifying that since there is no difference in the underlying pathology, the differentiation into early and late onset has little scientific grounds for retaining this distinction. We believe this distinction should be retained, for evaluating oldest old with cognitive impairment requires special consideration because the features of dementia are unique to the 90 years and older population [3]. Hence a wider differential diagnosis is necessary for the oldest old. Dementia must be differentiated from age-associated memory impairment (AAMI) which is defined as a symptomatic memory change in people over 50 years old and may involve not only memory but other cognitive functions and with a negative effect in daily life activity which is within the age-associated norms of cognitive performance. It seems to be more frequent with affective disorders from low sociocultural status [42]. There is no progression however towards cognitive decline characteristic of dementia [43]. Another is mild cognitive impairment (MCI). Patients with MCI perform relatively poorly on formal tests of memory and often show mild difficulties in other cognitive functions to an extent beyond that expected for age and individual background. Individuals who meet the criteria for MCI are at a greater risk than those with AAMI to develop dementia. In a study of dementia in people aged 90 years and older, the investigators [44] found the incidence was highest for amnestic MCI (31%) and other cognitive impairment (39.9% per year). naMCI had an incidence of 14% per year. The oldest old with cognitive impairment had higher dementia incidence rates [44]. In another study of oldest-old women, 23% had MCI and 18% had dementia with a combined cognitive impairment prevalence of 41% [45]. Depression is known to cause cognitive symptoms. Chronic substance abuse can induce persistent dementias.

Diagnosis

In 2013 the American Psychiatric Association published its fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) [46]. What was classified as 'Delirium, Dementia, Amnestic and other Cognitive Disorders' in DSM-IV is now called 'neurocognitive disorders'. DSM-5 has replaced the term 'dementia' with 'major neurocognitive disorder (NCD) or mild neurocognitive disorder' but accepts 'dementia' as an agreeable alternative. The purpose of this change is to lessen the stigmatisation associated with the word 'dementia' towards elderly individuals and to bring the diagnostic guidelines in step with present-day practice [47]. However, if the physician prefers, the term dementia can still be referred to by their accustomed names, for example, Alzheimer's dementia, vascular dementia or frontotemporal dementia [48], and in fact, DSM-5 has included 'or dementia' in parentheses when referring to major NCD [47].

The American Psychiatric Association [46] defined dementia as a disorder characterised by a decline in cognition involving one or more cognitive domains. The DSM-5 details six cognitive domains, namely, attention, executive function, learning and memory, language, perceptual-motor function and social cognition. The deficits represent a decline from previous level of function, leading to an incapacity for personal and instrumental activities. Dementia poses special difficulties with behavioural and psychological symptoms and debilitating psychological distress that caregivers may experience.

Dementia can pose problems in diagnosis more so in the mild end of the spectrum. Progressive deterioration of cognitive function is a characteristic feature of dementia. The cognitive changes that occur can be indexed by measures of global cognitive scales such as the Mini-Mental State Examination (MMSE). The MMSE is a clinical scale designed for screening, diagnosis and serial assessment of geriatric patients and is a relatively comprehensive measure of cognition including orientation, memory, concentration, language and design copying, but it lacks the ability to assess perceptual ability and abstract thinking and may be supplemented by such items as the ability to abstract and calculate and perceptual abilities. There are challenges of diagnosing dementia in the oldest old. Determining the cognitive impairment in the oldest old can be baffling because of the high prevalence of sensory loss, comorbidities, disability, frailty [3] and polypharmacy [49]. Vision loss is frequent in the oldest old with a frequency of 59% [50]. Hearing loss is equal to or more striking than vision loss, and the 90+ Study showed that 72% of the subjects had significant vision loss, hearing loss or both [51]. Other factors common to the oldest old are frailty and fatigue which may interfere with the subjects' cognitive and functional performance [3].

The diagnosis of dementia results from a comprehensive evaluation which includes a history obtained from different sources substantiated by a reliable informant and should aim at specific cognitive, behavioural and mood changes and on

symptoms relating to medical, neurological and psychiatric illnesses. Drugs should be reviewed and a family history of dementia, depression, stroke or related conditions obtained. The clinical history should include an evaluation of the patient's functional abilities in his activities of daily living (ADL) and instrumental activities of daily living (IADL). Evaluation of the functional capacity can be challenging because of the increased frequency of cognitive impairment, physical disability or both in the oldest old [3]. To determine accurately the functional disability information must be sought from a variety of sources [3].

A thorough physical and neurological examinations followed by mental status screening which includes assessment of cognitive and affective states. Haematological and biochemical investigations involve complete blood count, tests for thyroid function, vitamin B12 levels screening for infectious disease such as neurosyphilis. Neuroimaging (computed tomography (CT), magnetic resonance imaging (MRI)) of the brain is used to exclude structural lesions (such as cerebral tumours, normal pressure hydrocephalus, cerebral infarction, subdural hematoma) that may subscribe to dementia.

Treatment

High cholesterol has been associated with improved memory function in earlier studies [52]. Evans et al. [53] reported that hypercholesterolaemia was not associated with dementia, but statin users were at reduced risk of dementia. More recently it has been reported that late-onset hypertension was associated with a lower dementia risk after the age of 90 [54]. There is dearth of drug trials, and information on the oldest old are scanty as they are often left out from research. The high prevalence of increased mixed pathologies and multi-comorbidities indicates that multiple preventive and therapeutic means are necessary to protect the brains of the oldest old [55]. A trial with donepezil at 10 mg and 23 mg dose in 116 patients aged 85–90 years with moderate to severe dementia found a higher rate of side effects, urinary tract infections, diarrhoea, fatigue and somnolence with increasing age in the 23 mg group [56]. In another study, donepezil appeared to be clinically effective in patients with mild to moderate AD even at an advanced age and was well tolerated when continued for 6 months in 56% of the participants [57]. For patients with frontotemporal and vascular dementia, there is so far no proven treatment [58].

More than half of the people with dementia experience behavioural and psychological symptoms (BPSD) [59], and the prevalence may range from 20% to 90% [60]. It occurs in all types of dementia [61], and it is important though often difficult to differentiate Lewy body disease from AD [62]. BPSD occurs in most elderly people at some stage of the illness and [63] includes psychotic symptoms such as delusions, hallucinations, aggression or mood disorders [62]. It has been suggested [62] that there is a relationship between bipolarity (BT) and psychological symptoms of dementia (BPSD) [64, 65]. Some disturbances such as agitation, aggressiveness and wandering can be disturbing, distressing, disruptive and dangerous to the patient and their caregivers. When making the diagnosis of dementia, it is crucial to assess BPSD in detail to establish symptoms causing distress to patient and/or caregiver [63]. It affects the quality of life of both patient and caregiver and increases the need for professional care [66]. It is important that when prescribing cautious consideration is given to risk versus benefit [67]. Furthermore, it is vital before prescribing to exclude precipitating factors such as infection, pain, delirium [59], psychiatric or drug-related problems [66].

While non-pharmacological approaches may be successful in managing these patients, very often pharmacological treatment is needed [68]. There are number of drugs used in BPSD including antipsychotics, antidepressants, anticonvulsants, anxiolytics, cholinesterase inhibitors and NMDA modulators. Atypical antipsychotics have often been widely used to treat BPSD as the first-line drug approach [61] and are effective in controlling aggression, anger, agitation and psychotic symptoms such as delusions [60, 63]. Studies have shown that they target multiple neurotransmitter systems, and there is significant evidence that BPSD symptoms are not the result of a single neurotransmitter imbalance [60]. Risperidone, olanzapine and quetiapine are better tolerated and as effective as conventional antipsychotics and have lower proclivity for extrapyramidal symptoms [63] and less somnolence [69] and have different side effect profiles [63]. Although they may cause fewer adverse effects [69] before the patient is prescribed antipsychotic medication, the patient should be screened for risk factors for cardiovascular disease and stroke [67]. Antidepressants are used for mood disorders although their efficacy in depression associated with dementia is unproven [58] and anticonvulsants for nonpsychotic agitation [63].

Behavioural disturbance contributes to the burden experienced by caregivers [70], and very often it is the disturbed behaviour that brings the patient to the clinician's attention and caring becomes unbearable and the carer seeks. Education, support and behavioural training of the caregiver may help in alleviating the BSPD [63]. BPSD is often a decisive factor that precipitates institutionalisation. AD consists of a full panoply of memory impairment, paranoid delusions, hallucinations, screaming and bizarre behaviour [71]. It would be useful to consider clusters of symptoms rather than single behaviours to equate with neurochemical measures and the treatment be directed to them rather than to individual behaviour [72]. For example, there is considerable evidence to link psychotic symptoms with aggression.

Clinical Relevance

A wider differential diagnosis is necessary for the oldest old.

Determining the cognitive impairment in the oldest old can be baffling because of the high prevalence of sensory loss, comorbidities, disability and frailty [3].

Evaluation of the functional capacity can be challenging because of the increased frequency of cognitive impairment, physical disability or both in the oldest old [3].

The high prevalence of increased mixed pathologies and multi-comorbidities indicates that multiple preventive and therapeutic means are necessary to protect the brains of the oldest old [53].

More than half of the people with dementia experience behavioural and psychological symptoms (BPSD) [59].

Behavioural disturbance contribute to the burden experienced by caregivers [70].

Case Study

An 89-year-old man had been living with his son and family after the death of his wife 6 months before. Behavioural changes began insidiously with restlessness, sleep disturbance, nocturnal wandering and poor memory. He has had more recent onset of paranoid ideation, fear of being 'put away'. He further exhibited agitation, aggression and often hitting out. He was treated with olanzapine with some amelioration of his symptoms.

Comment

Among behavioural symptoms, often symptom clusters or subsyndromes emerge. It is important to identify target behaviours plus coexisting behaviours. This patient had a number of behavioural symptoms, the more important being aggression and paranoid symptoms. In treating, drug classes should be favoured for initiation in certain subsyndromes because they have evidence of benefit in particular coexisting conditions (e.g. aggression, psychotic symptoms and violence).

Multiple Choice Questions

1. The following neuropathology in dementia of the oldest old are true, EXCEPT:
   A. Moderate-severe AD-type pathology progressively increased with age in both the cortex and hippocampus in individuals without dementia.
   B. The brains of the oldest old usually have a mix of pathologies associated with dementia.
   C. In the oldest old, the extent of neuronal loss in the CA1 field and the entorhinal cortex was significantly higher compared to that of younger AD.
   D. Cognitively impaired oldest old have a preference to involve the anterior part of the CA1 field of the hippocampus.
2. The following are true of dementia in the oldest old, EXCEPT:
   A. The oldest old with cognitive impairment had higher dementia incidence rates.
   B. ApoE-e4 loses its importance predicting AD as age progresses.
   C. Low level of education, low level of physical activity, mid-life poor health, depression and delirium have been linked with dementia in the oldest old.
   D. About half of the demented oldest old had no cerebral pathology, and the ApoE-e4 allele is a risk factor for men only.
3. The following are true of dementia in the oldest old, EXCEPT:
   A. Frailty and fatigue in the oldest old may interfere with the subjects' cognitive and functional performance.
   B. To determine accurately the functional disability information must be sought from a variety of sources.
   C. Determining cognitive impairment in the oldest old can be difficult because of the high prevalence of sensory loss, comorbidities, disability and frailty.
   D. Progressive deterioration of cognitive function is not a characteristic feature of dementia in the oldest old.

Answers

1. C
2. D
3. D

References

1. He W, Muenchrath MN. 90+ in the United States,2000-2008. The United States. In: Census Bureau, editor. American community survey reports;ACS-17. Washington DC: US Government Printing Office; 2011.
2. United States Census Bureau Projections of the population by Selected Age Groups and Sex for the United States: 2010. Available at. http://tinyurl.com/4sv5i2.
3. Bullain SS, Corrada MM. Dementia in the oldest old. Continuum (Minneap Minn). 2013;19(2Dementia):457–69.
4. Howden LM, Meyer JA. Age and sex composition:2010.2010 census briefs. Washington, DC: US Census Bureau; 2011.
5. United States Census Bureau. National population projects (based on census (2002). Table 12.Projections of the population by age and sex for the United States: 2010 to 2050, 2008.
6. United Nations, Department of Economic and Social Affairs, Population division world population prospects. The 2010 Revision, 2011.
7. Kravitz E, Schmeidler J, Beeri MS. Cognitive decline and dementia in the oldest-old. Rambam Maimonides Med J. 2012;3(4):e0026. https://doi.org/10.5041/RMMJ.10092.

8. Corrado MM, Brookmeyer R, Paganini-Hill A, Berlau D, Kawas CH. Dementia incidence continues to increase with age in the oldest old: the 90+ study. Ann Neurol. 2010;67:114–21.
9. Gardner RC, Valcour V, Yaffe K. Dementia in the oldest old: a multi-factorial and growing public health issue. Alzheimers Res Ther. https://doi.org/10.1186/azrt181.2013.
10. Hagnell O. L, Rorsman B. Incidence of dementia in the Lundby Study. Neuroepidemiology. 1992;11(suppl11):61–6.
11. Canadian Study of Health and Aging Working Group. The incidence of dementia in Canada. Neurology. 2000;55:66–73.
12. Miech RA, Breitner JC, Zandi PP, Khachaturian AS, Anthony JC, Mayer L. Incidence of AD may decline in the early 90s for men, later for women: the Cache County study. Neurology. 2002;58: 209–18.
13. Fichter MM, Schroppel H, Meller I. Incidence of dementia in a Munich Community sample of the oldest old Eur Arch Psychiatry. Clin Neuro Sci. 1996;246:320–8.
14. Hall CB, Verghese J, Sliwinski M, Chen Z, Katz M, Derby C, et al. Dementia incidence may increase more slowly after 90: results from the Bronx Aging Study. Neurology. 2005;65:882–6.
15. Lucca U, Garri M, Nobili A, et al. Risk of dementia continues in the oldest old: the Monzino 80-plus study. Alzheimers Dement. 2009;5(4):381.
16. Green MS, Kaye JA, Ball MJ. The Oregon brain aging study: neuropathology accompanying healthy aging in the oldest old. Neurology. 2000;54:105–13.
17. Poon IW, Woodard JL, Stephen Miller L, Green R, Gearing M, Davey A, et al. Understanding dementia prevalence among centenarians. J Gerontol A Biol Sci Med Sci. 2012;67:358–65.
18. Savva GM, Wharton SB, Ince PG, Forster G, Matthews FE, Brayne C, et al. Age, neuropathology and dementia. N Engl J Med. 2009;360:2302–9.
19. Camsari GB, Graff-Radford N, Petersen R, Knopman D, Boeve B, Parisi J, et al. The neuropathology of patients with dementia and non-dementia in the oldest old (I9-1B). Neurology. 2015;84(14 suppl 19-1B) http:www.neurology.org/content/84/14_Supplement/19-1B.
20. Brayne C, Gill C, Huppert FA, Barkley C, Gehlhaar E, Girling DM, O'Connor DW, et al. Incidence of clinically diagnosed subtypes of dementia in an elderly population. Cambridge project for later life. Br J Psychiatry. 1995;67(2):255–62.
21. Jorm AF, Korten AE, Henderson AS. The prevalence of dementia quantitative of the literature. Acta Psychiatr Scand. 1987;76:465479.
22. Bellinger KA. The enigma of vascular cognitive disorder and vascular dementia. Acta Neuropathol. 2007;113(4):349–88.
23. Gunten V, Ebbing K, Imhof A, Giannakppoulos P, Kovari E. Brain aging in the oldest-old. Curr Gerontol Gertatr Res. 2010; https://doi.org/10.1155/2010/358531.
24. Raz N, Rodrique KN. Differential aging of the brain: patterns cognitive correlates and modifiers. Neurosci Biobehav Rev. 2006;30:730–48.
25. Troller J, Valenzuela M. Brain ageing in the new millennium. Aust NZJ Psychiatry. 2001;35:788–805.
26. Raz N, Rodrique KM, Acker D. Hypertension and the brain: vulnerability of prefrontal regions and executive functions. Behav Neurosci. 2003;17:1169–80.
27. Artero S, Tremeir H, Prins ND, Sabatier R, Breteler MM, Ritche K, et al. Neuroanatomical localisation and clinical correlates of white matter lesions in the elderly. J Neurol Neurosurg Psychiatry. 2005;75:1304–8.
28. Kawas CH, Kim RL, Sonneen JA, Bullain SS, Trieu T, Corrada MM. Multiple pathologies are common and related to dementia in the oldest old. The 90+ study. Neurology. 2015;85(6):535–42.
29. Neltner JH, Abner EL, Jicha GA, Schmitt FA, Patel E, Poon LW, et al. Brain pathologies in extreme old age. Neurobiol Aging. 2016;37:1–11.
30. Silve MH, Newell K, Brady C, Hedley-White ET, Perls TT. Distinguishing between neurodegenerative disease and disease-free aging: correlating neurophysiological evaluations and neuropathological studies in centenarians. Psychosom Med. 2002;64:493–501.
31. Crystal HA, Dickson D, Davies P, Masur D, Grobe E, Lipton RB. The relative frequency of "dementia of unknown etiology" increases with age and is nearly 50% in nonagenarians. Arch Neurol. 2000;57:713–9.
32. Nelson PT, Smith CD, Abner EL, Wilfred BJ, Wang WX, Neltner JH, et al. Hippocampal sclerosis of aging, a prevalent and high-morbidity brain disease. Acta Neuropathol. 2013;126(2):161–77.
33. Kawas CH, Corrado MM. Alzheimer's and dementia on the oldest-old: a century of challenges. Curr Alzheimer Res. 2006;3(5):411–9.
34. Giannakopoulos P, Hof PR, Kovari E, Vallet PG, Herrman FR, Bouras C. Distinct patterns of neuronal loss and Alzheimer's disease lesion distribution in the elderly individuals older than 90 years. J Neuropath Exp Neurology. 1996;55(12):1210–20.
35. Delaere P, He Y, Fayet G, Duyckaerts C, Hau JJ. Beta A4 deposits are constant in the brain of the oldest old: an immunocytochemical study of 20 French centenarians. Neurobiol Aging. 1993;14(2):191–4.
36. Gomes-Isla T, Price JL, McKeel DW Jr, Morris JC, Growdon JH, Hyman BT. Profound loss of layer ii entorhinal cortex neurons occurs in very mild Alzheimer's disease. J Neurosci. 1996;16(14):4491–500.
37. Hof PR, Bussiere T, Gold G, et al. Stereologic evidence for persistence of viable neurons in layer II of the entorhinal cortex and CA1 field in Alzheimer's disease. Neuropath Exp Neurology. 2003;62(1):55–67.
38. Kril JJ, Patel S, Harding AJ, Haliday GM. Neuron loss from the hippocampus of Alzheimer's disease exceeds extracellular neurofibrillary tangle formation. Acta Neuropathol. 2002;103(4):370–6.
39. Kawas H, Corrada MM. Alzheimer's and Dementia in the oldest old: a century of challenges. Curr Alzheimer Res. 2006;3(5):411–5.
40. Breitner JC, Wyse BW, Anthony JC, Welsh-Bohmer KA, Steffens DC, Norton MC, et al. APOE-epsilon 4 count predicts age when prevalence of AD increases, the declines : the Cache County Study. Neurology. 1999;53:321–31.
41. Panza F, Solfrizzi V, D'Introno A, Capurso C, Colacicco AM, Torres F, et al. Genetics of late-onset Alzheimer's disease: vascular risk and beta –amyloid metabolism. Recenti Ptrog Med. 2002;93(9):489–97.
42. Koivisto K, Reinikainen KJ, Hanninen T, Vanhanen M, Hekala EL, Mykkaren L, et al. Prevalence of age-associated memory impairment in a randomly selected population from eastern Finland. Neurology. 1995;45:741–7.
43. Hanninen T, Hallikainen M, Kolvisto K, Helkala EL, Reinikainen KJ, Soininen H, et al. A follow up study of age-associated memory impairment: neuropsychological predictions of dementia. J Am Geriatr Soc. 1995;43:1007–15.
44. Peltz CB, Corrada MM, Berlau DJ, Kawas CH. Incidence of dementia in oldest-old with amnestic MCI and other cognitive impairments. Neurology. 2011;7(21):1906–12.
45. Yaffe K, Middleton LE, Lui LY, Spira AP, Stone K, Racine C, et al. Mild cognitive impairment, dementia, and their subtypes in the oldest old. Arch Neurol. 2011;68(5):631–6.
46. American Psychiatric Association, DSM-5 Task Force. American psychiatric association diagnostic and statistical manual of mental diseases. 5th ed. Arlington: APA; 2013.
47. Bellinger J. DSM-V. Continuing the confusion about aging. Alzheimer's and Dementia. http://historypsychiatry.com/2010/03/19dsm-v-continuing-the-confusion-about-aging-alzheimer's-dementia/. Accessed 13 Jul 2016.
48. Simpson JR. DSM-5 and Neurocognitive disorders. J Am Acad Psychiatry. 2014;42(2):159–64.

49. Giulioli C, Amieva H. Epidemiology of cognitive aging in the oldest old. Rev Investig Clin. 2016;68(1):33–9.
50. Gussekloo J, deCraen AJ, Oduber C, van Boxtel MP, Westendorp RG. Sensory impairment and cognitive functioning in oldest-old subjects: the Leiden 85+ Study. J Geriatr Psychiatry. 2005;13:781–6.
51. Kahle-Wrobleski K, Corrada N, Kawas C. Dementia and cognition in the oldest-old. In: Miller BL, Boeve BF, editors. The behavioural neurology of dementia. Cambridge: Cambridge University Press; 2009. p. 254–63.
52. West R, Beri MS, Schmeidler J, Hannigan CM, Angelo G, Grossman HT, et al. Better memory functioning associated with higher total and low density lipoprotein cholesterol levels in very elderly subjects without the apolipoprotein e4 allele. Am J Geriatr Psychiatry. 2008;16:7810785.
53. Evans M, Kawas C, Corrada M. Cholesterol statins and the risk of dementia in the oldest old: The 90+ Study (S58.003). Neurology. 2014;82(10Suppl S58.003)
54. Corrado MM, Haysen RM, Paganini-Hill A, Bullain SS, DeMoss J, Aquire C, et al. Age of onset of hypertension and risk of dementia in the oldest old: The 90+ Study. Alzheimer's Dement. 2017;13(2):103–10.
55. Tanskanen M, Makea M, Notkola I-L, Myllykangas L, Rastas S, Oinas M, et al. Population-based analysis of pathological correlates of dementia in the oldest old. Annal Clin TransNeurology. 2017;4:154. https://doi.org/10.1002/acn3.389.
56. Farlow M, Veloso F, Moline M, Yardley J, Brand-Schieber E, Bibbiani F, et al. Safety and tolerability of donepezil 23 mg in moderate to severe Alzheimer's disease. BMC Neurol. 2011;11:57. https://doi.org/10.1186/1471-2377-11-57.
57. Aagiakrishnan K, Wong W, Blsnchette PL. Use of donepezil patients with Alzheimer's, disease-a Hawaii based study. Hawaii Med J. 2000;59:57–9.
58. Schwarz S, Froelich L, Burns A. Pharmacological treatment of dementia. Curr Opin Psychiatry. 2012;25(6):542–50.
59. Hersch EC, Falzgraf S. Management of the behavioural and psychological symptoms of dementia. Clin Interv Aging. 2007;2(4):611–21.
60. Kalman J, Kalman S, Pakaski M. Recognition and treatment of behavioural and psychological symptoms of dementias: lessons from the CATIE-AD study. Neuropsychopharmacol Hung. 2008;10(4):233–49.
61. Gabryelewicz T. Pharmacological treatment of behavioural symptoms in dementia patients. Przegl Lek. 2014;71(4):215–20.
62. Hori K, Hosoi M, Konishi K, Haschisu M, Tomioka H, Sodenaga M, et al. Pharmacotherapies for behavioural and psychological symptoms of dementia with Alzheimer's disease: two subcategories of these symptoms. Brain Disord Ther. 5:225. https://doi.org/10.4172/2168-975X.10000225.
63. Lawlor BA. Behavioural and psychological symptoms in dementia: the role of atypical antipsychotics. J Clin Psychiatry. 2004;65(Suppl 11):5–10.
64. Ng B, Camacho A, Lara DR, Brunstein MG, Pinto OC, et al. A case series on the hypothesized connection between dementia and bipolar spectrum disorders: bipolar type VI. J Affect Disord. 2008;107:307–15.
65. Dorey JM, Beauchet O, Anterion AC, Rouch I, Krolak-Salmon P, et al. Behavioural and psychological symptoms of dementia and bipolar spectrum disorders: review of the evidence of a relationship and treatment implications. CNS Spectr. 2008;13:796–603.
66. Gillabert C, Desmeules J, Vogt-Ferrier N, Dayer P. Behavioural and psychological symptoms of dementia (BPSD): pharmacological management. Rev Med Suisse. 2006;2(61):970–5.
67. Bullock R. Treatment of behavioural and psychiatric symptoms in dementia: implications of recent warnings. Curr Med Re Opin. 2005;21(1):1–10.
68. Goldberg RJ, Goldberg J. Antipsychotics for dementia-related behavioural disturbances in elderly institutionalised patients. Clin Geriatr. 1996;4:58–68.
69. Van Iersel MB, Zuidema SU, Koopmans RT, Verhey FR, Olde Rikkert MG. Antipsychotics for behavioural and psychological problems in elderly people with dementia: a systematic review of adverse events. Drugs Aging. 2005;22(10):845–58.
70. Rabins PV, Mace NL, Lucas MJ. The impact of dementia in the family. J Am Med Assoc. 1982;248:333–5.
71. Alzheimer A. Uber eine eigenartige Erkrankung der Himrinde. Allg Z Psychiatr Gericht Med. 1907;146-8(translation):64.
72. Hope T, Keene J, Fairburn C, Shane R, Jacoby R. Behavioural changes in dementia.2.Are there behavioural syndromes? Int J Geriatr Psychiatry. 1997;12:1074–8.

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N. Nagaratnam et al. (eds.), *Advanced Age Geriatric Care*, https://doi.org/10.1007/978-3-319-96998-5