European Manual of Medicine

Hans-Jörg Oestern · Otmar Trentz
Selman Uranues *Editors*

General Trauma Care and Related Aspects

Trauma Surgery II

W. Arnold · U. Ganzer *Series Editors*

Springer

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Foreword

The *European Manual of Medicine* was founded on the idea of offering resident and specialized clinicians the latest and most up-to-date information on diagnosis and treatment in Europe. In contrast to existing textbooks, the *European Manual of Medicine* aims to find a consensus on the demands of modern European medicine based on the "logbooks" recommended by the Union of European Medical Societies (UEMS). Therefore, for each discipline those diagnostic and therapeutic principles that are generally considered best practices are presented as "recommended European standards."

To fulfill these demands we—together with Springer—recruited editors who are well established and recognized in their specialties. For each volume at least three editors from different European countries were invited to present the high clinical and scientific standards of their discipline in this book.

Wherever possible the volume editors were asked to follow a standardized structure for each chapter so as to provide readers quick and easy access to the material. High-quality illustrations and figures serve to provide additional useful information. Detailed references allow interested readers to further investigate areas of individual interest.

The Series Editors wish to express their sincere gratitude to Springer-Verlag, especially to Gabriele Schroeder and Sandra Lesny, for their support and assistance in the realization of this project from the beginning.

The fifth volume of our *European Manual of Medicine* series is dedicated to *Trauma Surgery* and will be published in three parts. The second part presented here focuses on general trauma care and related aspects. The first part deals with head, thoracic, abdominal, and vascular injuries and the third part will report bone and joint injuries. One of the main aims of this volume is to provide the resident and specialized clinicians, especially trainees, with a comprehensive yet condensed guide to the core knowledge required in this broad surgical field and give them the ability to work in their specialty anywhere in the European Union.

The volume editors Prof. Hans-Jörg Oestern (Celle, Germany), Prof. Otmar Trentz (Zurich, Switzerland), and Prof. Selman Uranues (Graz, Austria)—leading European experts in trauma surgery—recruited contributors from different European countries to compile a textbook that conforms to our original concept of the *European Manual of Medicine* series.

Munich, Germany — Wolfgang Arnold
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Preface

Trauma care depends on good organization, an understanding of trauma as a surgical disease, awareness of potential complications, and the ability to cope with them. Focusing only on the repair of anatomic lesions will not meet the requirements of good clinical practice.

This second volume in the *Trauma Surgery* series deals with General Trauma Care and Related Aspects and covers optimization of trauma management, handling of physiological derangement in major trauma, and typical posttraumatic complications. Soft tissue injuries, burns, muscle and tendon lesions, and plastic surgery for post-traumatic defects also receive due attention.

General and trauma surgeons who want to brush up or to prepare for the EBSQ Trauma Surgery exam will find this volume invaluable. The contributing authors are all highly experienced trauma surgeons and specialists in their fields with a strong commitment to trauma care.

We express our sincere gratitude to all the contributing authors for sharing their expertise.

Special appreciation is due to Springer Publishing and in particular to Gabriele Schroeder for putting this book in the works and to Martina Himberger for publishing it. Finally, we are very much indebted to Sandra Lesny for her support of both the editors and the authors.

Celle, Germany — Hans-Jörg Oestern
Zurich, Switzerland — Otmar Trentz
Graz, Austria — Selman Uranüs

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M. Hofman and H.-C. Pape

1.1 Introduction

1.1.1 History [1]

Historically, the development of trauma care and trauma care systems is based on the experiences provided by conflict and war situations all over the world. Military emergency care has led the way to the systematic approach to trauma care for the severely injured patient.

In the early 19th century, during the Napoleonic wars, Dominique Larrey as surgeon-in-chief of the Napoleonic armies developed the "flying ambulances" as the first exponents of prehospital trauma care. These flying ambulances were staffed with trained medical crews who transported the wounded soldiers to battlefield hospitals using a "scoop-and-run" concept.

Subsequently, during the American Civil War later in the 19th century, battlefield hospitals providing different levels of care were established according to a hierarchical structure because it was not practical to treat every injury in a similar way.

In 1888, a first European onset of specified trauma care took place by opening the world's first, oldest, and also largest emergency hospital, the "Bergbau-Berufsgenossenschaftliche Krankenanstalten Bergmannsheil" in Bochum, Germany, to provide medical care for injured miners.

During World Wars I and II, motorized vehicles were put to use; therefore the prehospital transportation time was decreased to a few hours. In the early 20th century, mortality and morbidity rates also decreased as a result of medical research, use of blood transfusions, and the introduction of antibiotics and antiseptics in medical care. Additionally, the treatment of specific injuries during the American Civil War had been documented and allowed for the development of standardized treatment.

In 1925, Dr. Lorenz Böhler founded the first civilian trauma system in Europe, located in Austria. In the United Kingdom, the Birmingham Accident Hospital, which claimed to be the world's first Trauma Center was established in April 1941 by William Gissane; it remained the only trauma center in the United Kingdom until 1991, but was closed in the mid-1990s.

During the Korean and Vietnam Wars in the second half of the 20th century, the use of helicopters further decreased the prehospital transport time to less than 1 h. The medical teams were better trained and therefore were able to triage and treat the soldiers in a better and more adequate way, which led to a high survival rate among the severely injured soldiers arriving at the surgical facility.

In the USA, the first trauma centers were established in 1966 at the San Francisco General Hospital in California and the Cook County Hospital, in Chicago, Illinois. This was followed by an expansion of trauma centers across the country, which, led to the establishment of the first trauma care system in the USA in 1969: the Maryland System of Trauma Care.

During the 1970s, these medical care configurations were incorporated in the German health care system through the establishment of trauma centers with helicopter and ambulance access in the vicinity of

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motorways to guarantee swift evacuation of patients to a hospital of definitive care.

The development of trauma care systems began simultaneously with the return of military medical personnel from the Vietnam War in the 1960s and 1970s, initiated by the publication of "Accidental Death and Disability, the Neglected Disease of Modern Society" by the National Academy of Sciences in the USA. The recommendations proposed in the article in 1976 were guidelines from the American College of Surgeons Committee on Trauma entitled "Optimal Hospital Resources for Care of the Injured Patient."

In the same year, orthopedic surgeon Dr. J.K. Styner developed the Advanced Trauma Life Support (ATLS) course as a result of his own experiences with the American health care system after an airplane crash experienced by him and his family in 1976.

1.1.2 The Last 40 Years

In 1976 the American College of Surgeons developed criteria for classifying acute care hospitals according to the level of care that they can provide (levels I–V), and since that time, trauma care systems have evolved throughout the world [2].

The implementation of trauma systems is a difficult and time-consuming business because every system must be adjusted to the unique requirements of the population served. These population-based needs differ greatly throughout different regions of the world, or even within one country, depending on rural, suburban, or urban populations. Additionally, the types of injuries differ throughout the world; in Europe, most injuries are a result of blunt trauma whereas and in the USA and the Republic of South Africa there are more injuries that result from penetrating trauma.

Even though, many studies have proved that by the implementation of trauma care systems over the past 40 years the outcomes of severely injured patients have improved, the development of nationwide trauma systems progresses slowly because of organizational and pecuniary difficulties. The studies mainly looked at the reduction of mortality, which decreased by 15–20 % after the implementation of trauma care systems (Table 1.1). The positive results of trauma system implementation were contradicted by only a few studies until 2010 [15, 16].

More than 50 % of the reduction of mortality is a result of reduction in prehospital time, trauma center designation, better prehospital triage of patients, and shortened time to definitive treatment within the structured organization of a regional trauma care system [4]. Furthermore, within a trauma care system, the mortality of severely injured patients decreases inversely to the level of trauma care provided by facilities where the patient is treated [4].

At the same time, mortality is predicted more accurately by the severity of the injury (age, injury severity score [ISS] > 15, hypotension, severe head injury, and penetrating injury mechanism) than by the surgeon's experience or annual surgeon case volume [10]. It is, therefore, important to realize that it takes time to optimize the care provided in all aspects of a trauma care system and to make the system more effective [17]. However, the ultimate goal of each trauma care system should be the improvement of overall functional outcome of severely injured patients [18]. This effect of trauma systems on functional outcome and quality of life is not evidence based and should be subject to further studies [1].

Because from an economic point of view it is not lucrative to provide trauma care for severely injured patients at a high level, over the past decade it was difficult for many trauma systems throughout the world to maintain their standards of care. This problem will become greater in the future because of the growing aging population. The rising costs of regular health care as a result of age-related diseases are also seen in the trauma care system because the elderly (> 65 years old) are at higher risk for injuries requiring expensive care and prolonged hospitalization.

1.1.3 Definitions

A trauma system combines the cooperation of prehospital, hospital, and rehabilitation facilities within a defined geographic area integrated with a regional public health system. The goal of the system is to provide the best possible care to traumatically injured patients, according to the severity of their injuries, in the fastest possible way. Such care will be provided by designated trauma centers with different levels of care.

There are two different types of trauma systems. The most common trauma systems are ranged around hospitals with the highest possible level of care (the so-called level I trauma centers). Mainly, these

Table 1.1 Literature review on mortality of severely injured patients in trauma care systems

Author(s)	Journal	Title	Conclusion
Jurkovich and Mock [3]	*J Trauma*, 1999	Systematic review of trauma system effectiveness based on registry comparisons	Eight of 11 articles reviewed (period 1987–1997) provided comparable data and consistently demonstrated a 15–20 % reduction in the risk of death comparing trauma system outcomes with major trauma outcome study norms
Sampalis et al. [4]	*J Trauma*, 1999	Trauma care regionalization: a process-outcome evaluation	This study produced empirical evidence that the integration of trauma care services into a regionalized system reduced mortality
Nast-Kolb et al. [5]	*Unfallchirurg*, 1999	Quality management in the early clinical treatment of severely injured patients	Since the 1970s, the mortality of severely injured patients could be reduced by approximately 20 % by optimizing the pre-clinical and clinical treatment of severely injured patients In the United States, the preventable death rate of severely injured patients was reduced to 1–2 % through the implementation of regionalized trauma systems
Celso et al. [6]	*J Trauma*, 2006	A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems	The results of the meta-analysis showed a 15 % reduction in mortality in favor of the presence of a trauma system
Papa et al. [7]	*J Trauma*, 2006	Assessing effectiveness of a mature trauma system: Association of trauma center presence with lower injury mortality rate	Trauma center counties had significantly lower motor vehicle crash (MVC) death rates than non-trauma center counties. This association was independent of age, alcohol use, speed, rural/urban location, and pre-hospital resources
Lansink and Leenen [8]	*Curr Opin Crit Care*, 2007	Do designated trauma systems improve outcome?	Designated trauma centers and trauma systems do improve outcome. Inclusive trauma systems outperform exclusive trauma systems in terms of survival of the severely injured
Cameron et al. [9]	*Med J Aust*, 2008	A statewide system of trauma care in Victoria: effect on patient survival	Introduction of a statewide trauma system was associated with a significant reduction in risk-adjusted mortality. Such inclusive systems of trauma care should be regarded as a minimum standard for health jurisdictions
Haut et al. [10]	*Arch Surg*, 2009	Surgeon- and system-based influences on trauma mortality	These data support the belief that in a structured trauma program, surgeons with vastly different levels of training can safely provide care and obtain equivalent outcomes
MacKenzie et al. [11]	*J Trauma*, 2010	The value of trauma center care	Our findings provide evidence that regionalization of trauma care is not only effective but also cost-effective
Twijnstra et al. [12]	*Ann Surg*, 2010	Regional trauma system reduces mortality and changes admission rates	Implementation of an inclusive trauma system in the Netherlands results in more efficient triage of trauma patients among hospitals and is associated with a substantial and statistically significant risk reduction (16 %) of death
Meisler et al. [13]	*Acta Anaesthesiol Scand*, 2010	Triage and Mortality in 2,875 consecutive trauma patients	Increased survival of severely injured patients can be achieved through early transfer to highly specialized care
Gabbe et al. [14]	*Ann Surg*, 2011	The effect of an organized trauma system on mortality in major trauma involving serious head injury: a comparison of the United Kingdom and Victoria, Australia	Management of the severely injured patient with an associated head injury in England and Wales, where an organized trauma system is absent, was associated with increased risk-adjusted mortality compared with management of these patients in the inclusive trauma system of Victoria, Australia

"exclusive" trauma systems prioritize the care of the most severely injured patients needing immediate treatment [8, 12].

The other type of trauma system is the "inclusive" trauma system that aims to provide adjusted care to all injured patients within a certain area, and therefore this system incorporates all acute care facilities at all levels, within that area [8].

The principle target of an inclusive trauma system is to provide the right level of care, conform to the specific requirements of a patient's injuries, avoid over-referral of patients with minor injuries to level I trauma centers, and thereby making efficient use of available health care resources [12].

There are studies that state that the more inclusive a trauma system is, the better the effectiveness of the system, but there is no clear evidence that one system is superior to the other [2].

1.2 Trauma Care Systems in Different Parts of the World

The main goal of trauma care systems is to optimize the care given to trauma patients in a particular region. By facilitating all phases of trauma care (from patient transport to patient rehabilitation), it provides better adjusted treatment that will benefit patients the most in terms of outcome.

To achieve this goal, it is necessary for all facilitators (political and medical) and trauma care providers to cooperate within the system. The development of a good trauma care system is a difficult process that depends on many factors and many different authorities. The important factors are health care insurance systems, organization of (pre-) hospital care, injury type, and the geographic and demographic situation. Throughout the world, these factors are subject to regional differences and are coordinated by different authorities [19]. Trauma care is more developed in the 'Western' countries and therefore the differences in trauma care organization between developed and developing countries are many, but even in countries where trauma care is good, there is still great regional variation in trauma care organization.

A good example of these international differences can be found in the European Union (EU), which includes 27 countries. There are no standard criteria within the EU for how trauma care should be organized. Consequently, in practically every country, there is a different approach to the organization of (pre-)hospital care, trauma teams, and rehabilitation. The training standards for trauma surgeons are also different in these countries. In some countries, trauma surgery is a separate department (e.g., in Austria) but in other countries is integrated with other specialties such as orthopedic surgery (e.g., Belgium, Switzerland) and general surgery (e.g., Italy, The Netherlands). Another variant is that trauma care is covered by different specialties, each with its own area of responsibility (e.g., France, Germany, Portugal, Scandinavia, The United Kingdom) [20, 21]. Overall, in Europe, trauma care appears to be more developed in the central European countries than in the United Kingdom and the Scandinavian and Mediterranean countries [21].

In this chapter we will not focus on a single trauma care system because there is no consensus on which trauma care system is the best and it is probably more important that trauma care has been organized in a certain region rather than how it is organized. In this chapter we provide an overview and comparison of trauma care systems in countries throughout the world where the health care services are of a high standard.

1.2.1 USA

The biggest efforts to initiate standards for trauma care systems in the world were made in the 1970s in the United States of America. At first, the emphasis of trauma care was on high-level trauma centers within exclusive trauma care systems, since the 1990s American trauma systems have become more inclusive as a result of "The Model Trauma Care System Plan" released in 1992 by the Health Resources Services Administration [18].

The trauma care facilities within a trauma care system in the United States are classified and designated, by the American College of Surgery (ACS), Committee on Trauma into different levels of care (levels I–V) according to the updated criteria for trauma center verification listed in the *Resources for Optimal Care of the Injured Patient*: *2006*. In some states, the process of evaluating trauma care facilities is performed by the state government or local emergency medical services, and in those cases,

verification by the ACS is not necessary. Furthermore, some states still provide trauma care through a limited number of designated level I and level II trauma centers, whereas other states have classified every acute trauma hospital according to the levels of care they can provide.

In 2010, a total of over 1,600 trauma centers in 40 states were classified and certified. They included 203 level I, 271 level II, 393 level III, 765 level IV or V, and 43 pediatric trauma centers.

1.2.2 Canada [4, 22]

The trauma care in Canada is organized around the 17 medical universities across the country, and the designation of trauma centers is organized by every province. There is currently no nationwide designation and verification process.

The geographical situation of Canada resembles that of the United States, with major metropolitan areas sometimes having more than one trauma center, and large rural areas with no (pre-)hospital trauma care at all. The central areas and the districts in the Rocky Mountains particularly have problems with prehospital transportation times.

Since 1999, several trauma managers and coordinators in Canada have been organizing meetings and programs to improve the trauma care organization in Canada. In 2008 they founded the Interdisciplinary Trauma Network of Canada.

The designation of trauma care facilities by the Trauma Association of Canada (TAC) started in 2005 and their guidelines were last updated in June 2011. Since 2005, 25 trauma centers have been accredited, of which 13 are level I, one is level II, five are level III, and four are level IV or V. Only four of the 10 provinces took part in the designation process and of the 13 level I centers, nine are situated in the province of Ontario, illustrating the geographical problems mentioned above. The trauma centers are all funded by the provinces and are responsible for leading the trauma care in their regions and act as referral facilities.

Even with the widespread education of ATLS®, the high quality of in-hospital trauma care, and the efforts of the TAC, there is still no countrywide trauma care system in place.

1.2.3 Australia [23]

The Australian mainland consists of five states and three territories, with two of the territories being very small (i.e., Australian Capital Territory and Jervis Bay Territory). The mainland has a nationwide trauma care system as all states have a trauma care system with designated trauma centers. The Northern Territory has only one major trauma center, located in Darwin; the Australian Capital Territory has one major trauma center located in Canberra, but only covers ca. 2,350 km^2 of the mainland and is fully enclosed within the state of New South Wales. The Jervis Bay Territory covers only 73 km^2 of land and has therefore no trauma care system.

The implementation of trauma care systems in Australia began in the early 1990s in New South Wales and is currently still developing. One of the biggest problems for trauma care systems in Australia is (as in Canada) the particular geography and demography of the nation. It is the sixth largest country in the world with just a little less surface area than the USA, but has only just over 21 million residents, who are concentrated in the urban and metropolitan areas in the coastal regions. In consequence, the 'outback' of Australia is large and not provided with health care. This causes a high mortality rate among traumatically injured patients, although the unique organization of the Royal Flying Doctor Service of Australia (RFDS) can reach every resident in the 'outback' within a 2 h flight, which puts the "golden hour" of trauma care in another perspective.

The trauma care systems in Australia are initiated and developed by individual states and the acute care facilities are designated by either the regional health service or the state Department of Health. Currently there are ca. 16 level I trauma centers for adult care and ca. seven level I trauma centers for pediatric care assigned throughout the five states and two territories. The Royal Darwin Hospital has also been designated as the National Critical Care and Trauma Response Centre because of the fact that it is the first Australian hospital accessible from South East Asia in the event of a mass casualty or disasterous event. This seems to be in keeping with the concept of many trauma care systems to designate one reference center per one million inhabitants, but when we look at the geographical location of these so-called major trauma services, we

find the centers are concentrated in only one city or metropolis in almost every state or territory. Therefore, the organization of trauma care in rural areas is very important. There are six levels of acute trauma care in Australia, divided over two types of trauma networks (i.e., the metropolitan and the rural). In the metropolitan trauma network, the following levels of care are designated: Major Trauma Service (level I), which provides the full spectrum of care and function as a tertiary referral center; Metropolitan Trauma Service (level II), which provides initial assessment and stabilization, and when warranted, initiates transfer to a Major Trauma Service; and Urban Trauma Service (level III), which provides care to patients with minor-to-moderate injuries at local communities in urban areas. The rural trauma network is established on three other levels of care: the Regional Trauma Services provide definitive care of non-major trauma according to the availability of local expertise; the Rural Trauma Services, which have 24 h availability of an on-duty medical practitioner; and the Remote Trauma Services, serving people in remote areas from small hospitals with no immediately available general practitioners.

1.2.4 Germany [24]

The statewide trauma system in Germany is one of the best organized trauma systems in Europe and includes all aspects of trauma care: prevention, (pre-) hospital care system, trauma center designation, rehabilitation units, and a quality control system. According to the current information of the German Society for Trauma Surgery (DGU), there are over 850 acute care facilities registered, forming 57 regionalized trauma networks, of which 17 are already officially certified. Although the overall improvement of trauma patients after the establishment of the trauma system in 1970 is remarkable, the trauma register shows great differences between different trauma care systems throughout Germany due to geographic, demographic, and organizational infrastructure differences. This is why in 2004, the DGU laid the foundation for an improved structure of the statewide trauma systems, the TraumaNetwork[D]. The main aims were to increase the quality of trauma care, improve cooperation among acute care facilities, and shorten the pre-hospital time to less than 30 min. This was enforced in 2006 by the 'White Paper on Trauma care', in which recommendations and strict guidelines for all aspects of acute trauma care are listed.

1.2.5 United Kingdom [21]

After the establishment of the Birmingham Accident Hospital as the first trauma center, which functioned from 1941 until the 1990s, the first pilot trauma care system was launched at the North Staffordshire Hospital in Stoke-on-Trent. This study was initiated by the Royal College of Surgeons in England, and showed bad outcomes in major trauma care in acute care hospitals [25]. The results of the study were not convincing [26], although it showed a decreasing trend in mortality, and in consequence there was much criticism. The development of trauma care was postponed until after the Military Medical Services returned from their missions in Afghanistan and Iraq with proof of excellent results of the trauma care they provided to severely injured soldiers [27]. This led to the establishment of the London trauma system in 2010. This system encompasses four inclusive trauma care systems with approximately four level I trauma centers and facilities with a lower care level. Initiatives to develop a trauma care system at the Birmingham Accident Hospital have also been taken.

1.2.6 The Netherlands [28]

Since the first impetus given by the Dutch Trauma Society in the early 1990s, The Netherlands have developed an excellent, functioning, nationwide, inclusive trauma care system. In 1997, the Ministry of Health, Welfare and Sport established 11 level I trauma centers that are the reference centers in 10 inclusive trauma care systems that cover The Netherlands. The reference centers play a key role in the development of guidelines for trauma care and quality control within each region. Every reference center has a specialized Medical Mobile Team that provides pre-hospital care for polytraumatized patients in addition to the normal paramedic-based ambulance system.

Although this has resulted in enhanced quality of care in all aspects, from pre-hospital care to improvement of facility coordination to the foundation of a national trauma registration, the system also has its imperfections. The biggest concerns in

The Netherlands are the shortage of intensive care beds and the organizational shortcomings of pre-hospital care.

1.2.7 France

In France, the emphasis of the trauma care systems is on pre-hospital care, with well- organized physician-based emergency care. The designation of hospitals in France is different from that in the USA but there is also a difference in the level of care. There are three different types of emergency departments: (1) The *Service d'Accueil des Urgences* (*SAU*) can provide a high level of care because they can rely on the following 24 h specialties: intensive care, internal medicine, cardiology, anesthesia/intensive care, and visceral-, gynecological-, and orthopedic surgery. These SAU departments are situated in the *Hôpital de reference* (level I trauma center) or *Hôpital de recours* (level II trauma center), and the centers are found in university hospitals (32 in France) or bigger general hospitals throughout France. (2) The *Pôle Spécialisé d'Accueil des Urgences* can provide the same high level of care as the SAU departments but are specialized in a certain area of health care, for instance, pediatrics. (3) The *Unité de Proximité d'Accueil*, *d'Orientation et de Traitement des Urgences* are found in smaller district hospitals, the *Hôpital de proximité* (level III trauma centers) where at least one physician (24 h/day), a state-registered nurse, and technical facilities enabling standard imaging and laboratory tests are available. The facilities have limited resources but can stabilize critically ill patients before transferring them to facilities with higher levels of care. The role of the level IV and level V trauma centers is overtaken by the physician-based Service d'Aide Médicale Urgente (SAMU) Organizations.

There are no specialized hospitals in France for trauma care but the designated trauma centers each other at the regional level throughout France.

1.3 The "Ideal" Trauma Care System [29]

As a result of improving diagnostic and therapeutic options in recent times, the demands and expectations of medical trauma care are becoming increasingly higher. Although there are a few studies showing that inclusive trauma systems perform better than exclusive trauma systems in terms of outcome, the key components of the systems are the same.

To guarantee the best possible care for each trauma patient and to have the right trauma patient at the right time, at the right place, an 'ideal' functioning trauma care system is needed. The 'ideal' trauma care system includes the following components that will be discussed in the next section: (1) Prevention of trauma. (2) Pre-hospital care. (3) In-hospital care. (4) Rehabilitation facilities. (5) Internal and external quality control. (6) Education and research programs.

There is a seamless transition between each phase of care in an effective trauma care system that results in getting the right patient, at the right time, to the right place. This will eventually result in the reduction of disability, mortality, and costs and thereby an increase in productive working years. However, in every system there is always a small percentage of preventable deaths and inexplicable treatment deviations that lead to complications in the trauma population served, even in the most developed and 'ideal' trauma care system [5].

1.3.1 Prevention

Prevention of trauma is the first, and possibly most important, component of trauma care systems. This part of the trauma care system can intervene in the first peak of the trimodal death distribution of trauma, in which one third to one half of all traumatic deaths occur. Although the implementation of trauma care centers can make a big difference in death and disability rates from trauma injuries, trauma prevention has more opportunities for decreasing the impact of trauma on both the personnel and community level [8]. Because the trauma care systems we discuss in this chapter are systems in developed Western countries, the main issues of prevention have already been dealt with. In both Europe and North America, traffic safety is improved by safety measures such as traffic rules, road signs, safer cars, seatbelts, and motor helmets. Such prevention prevents injuries from blunt trauma, which is the main cause of death and disability in European countries.

In North America, and particularly in the United States, penetrating injuries continue to be the greatest cause of death and disability resulting from trauma.

Prevention of penetrating injuries is a difficult issue to address in the American community, where the possession of weapons is still common. Even after several tragedies over the past 20 years (e.g., the massacres at Waco, Columbine, and Virginia Tech), it is still not really a point of discussion.

In conclusion, prevention of blunt trauma continues to evolve even though it is highly developed in all the countries discussed here. On the other hand, prevention of penetrating injuries is a difficult issue, particularly in the United States, where it is common.

1.3.2 Pre-hospital Care

The pre-hospital care plays a very important role in the second peak of the trimodal death distribution in trauma. It is being repeatedly proved that reduced pre-hospital time results in favorable outcomes for severely injured patients.

In some remote areas of countries with extended rural regions such as Australia, Canada, and the USA, there is no professional acute care system present. In some of these areas, there are groups of motivated people, sometimes organized in special occupational groups, who are trained to provide first aid in a basic or even advanced form. In some areas, some of these groups can even transport seriously injured patients to an acute care facility in special vehicles; it is the only possible alternative to a professional pre-hospital care system in such areas.

A second level of pre-hospital care that is implemented in the most effective pre-hospital care systems throughout the world is provided by emergency medical technicians (EMTs) who can rescue, immobilize, and transport patients without giving real medical treatment.

In populated regions of middle- and high-income countries, the main part of pre-hospital emergency care is performed by specially trained paramedics. The standards of training for paramedics show great country-by-country and even regional variation because it is not a protected title. Therefore, although we use the term ‘paramedic’ for this group of pre-hospital emergency care providers, the care they are allowed to provide sometimes differs and depends on their level of education. In some countries, even physicians are involved in the pre-hospital emergency care system.

In the Western world there are two prominent models of the pre-hospital care system. The first is the “Anglo-American model”, in which normal pre-hospital care is provided by emergency medical technicians and paramedics of varying levels of skill who staff the ambulances to transport trauma victims. Physicians are only (when at all) involved in the pre-hospital trauma care in severe and complex cases. Physicians in this system can play a consultant role for the ambulance crew to provide medical back up or overview in the triage process within a trauma system. In some systems, the paramedics need consent from a physician to perform certain interventions or administer medication. In some of these systems, as in the United Kingdom, The Netherlands, and Australia, a paramedic is a recognized professional who does not need consent from a physician.

1.3.2.1 USA

In the USA, pre-hospital emergency care is provided by EMTs and paramedics with different levels of training who treat patients according to their competences and according to recorded algorithms [19]. However, even in a highly developed country such as the USA, there are areas that are so remote that professional emergency care is not present and the pre-hospital time is often very long. This problem is still not addressed by trauma care systems throughout the United States.

Helicopter emergency medical services (HEMS) began functioning in the early 1980s. There are approximately 870 emergency medical service helicopters and ca. 310 medical fixed wing aircraft operating in the USA today and the staff on board differ across the country. Most helicopters (71 %) fly with one nurse and one paramedic on board, some fly with two nurses on board, and only 5 % of HEMS fly with a physician on board. This is especially surprising because most studies on this topic report that in ca. 25 % of cases, a physician’s presence is needed and that physicians can administer more medical procedures than non-physicians, without compromising pre-hospital time [30].

1.3.2.2 Canada

The pre-hospital emergency care in Canada is almost exclusively provided by paramedics, though in some areas such as the Montreal metropolis there are a few physicians taking part in the emergency medical service; but this is more or less an exception. This is based on the idea that the “scoop and run” method is more

effective than the "stay and play" method, which was supported by several studies in Canada at the Montreal McGill University, which showed that physicians were not as effective as paramedics in pre-hospital emergency care.

The medical crews are transported by land-bound ambulances in urban regions and by helicopters or fixed wing aircrafts in rural regions. Because Canada is a large country with vast distances, the helicopter services, as in Europe and the USA, are often not viable because the range for helicopters is too small. That is why the fixed wing aircraft-based transport has developed, not only for major trauma cases but also for minor injuries and non-trauma patients [31–33].

1.3.2.3 Australia

The Australian pre-hospital care system is also paramedic-based, and the treatment is orientated to the Pre-Hospital Trauma Life Support (PHTLS) algorithm [19]. Every ambulance is staffed with at least one paramedic, for whom the training level varies, and in some regions is very high.

Pre-hospital emergency care in many areas of Australia is supplemented by volunteers or employees of enterprises in the event of work-related accidents, and in 1928 Reverend John Flynn recognized the problem of emergency health care in the wide outback of the country and established the famous RFDS of Australia.

With only approximately 60 aircrafts to cover over seven million square kilometers (80 % of Australia), the time for delivering physician-based staff to the injured is often longer then the "golden hour" of trauma, and therefore, remote outposts and telemedicine are the only solutions for initial care. To support telemedicine care, medical chests with numbered medication have been placed in remote areas and can be used upon instructions from a physician [10]. In addition to this rural oriented air rescue system, there are statewide aeromedical services such as the Aeromedical and Medical Retrieval Service and the Newborn and Paediatric Emergency Transport Service, which transport patients from all rural and urban regions. These paramedic-based retrieval services utilize land-bound ambulances, helicopters, and fixed wing planes [34].

1.3.2.4 United Kingdom

Pre-hospital emergency care in the United Kingdom is based on the American model. The ambulance has an emergency technician and a paramedic on board, and helicopters have two paramedics on board. These helicopters (30 in England) and fixed wing planes have paramedics on board and work in conjunction with the Emergency Medical Retrieval Service, staffed by consultants, nurses, and paramedics providing advice and retrieval services. In some areas, the emergency service uses rapid response vehicles staffed with one experienced paramedic who can provide advanced life support and supports the ambulance teams.

An exception to this system exists within the London trauma care system in that the normal ambulance service is supported by a mobile medical team, such as is used in The Netherlands. These teams always include a senior trauma physician and a specially trained paramedic, and operate 24 h a day. During daylight hours they operate via helicopter and during the night, by rapid response vehicles in order to arrive at the scene as quickly as possible.

1.3.2.5 The Netherlands

Pre-hospital emergency care in The Netherlands, in contrast to neighboring countries, is organized like the Anglo-American system. Since 1973, a nationwide ambulance system has been anchored by law, and the country is currently divided into 25 regional ambulance services that coordinate ambulance care.

With the establishment of the ten trauma care systems in 1997, the ground-bound pre-hospital, paramedic-based ambulance care can get support from the Mobile Medical Teams (MMTs) that are transported by helicopter or by special busses. Each trauma region has a physician (anesthesiologist or surgeon)-based MMT that provides pre-hospital trauma life support at the scene. Four trauma regions have the ability to send MMTs 24 hours a day, 7 days a week by helicopter to provide a nationwide air rescue system. The fact that only four MMTs can be transported day and night by helicopter is one of the big concerns of the system. At the nation's boundary, the air rescue system is bilaterally supported by teams from Germany and Belgium. The air rescue system is also involved in mass casualties and in secondary inter-hospital transport of patients.

The second model of pre-hospital care is the "Franco-German model" and is a physician-based system. All emergency cases requiring more than basic life support are treated by physicians. In some systems, the ambulances are staffed with a physician,

a paramedic, and a driver; in other systems the ambulance is only staffed by a paramedic and a driver, and the physician is dispatched in a separate rapid response vehicle to provide medical support to multiple ambulances.

The level of training of paramedics is diverse and some paramedics are allowed to provide only basic life support and heavy lifting services, while other paramedics are advanced life support (ALS)-trained and are allowed to provide ALS, although mostly only under supervision of a physician or in acute life threatening situations.

Generally, these ambulance vehicles are fully equipped to provide care according to the "stay and play" principle because the physician is brought to the patient. However, it is the decision of the physician to take the "scoop and run" approach for those patients for whom further pre-hospital interventions could deteriorate outcome.

1.3.2.6 Germany

The German-speaking countries in middle Europe (Austria, Switzerland, and Germany) have organized their pre-hospital emergency care on a physician-based system. In this system, emergency medical technicians and paramedics have a role in only basic life support, and only sometimes in advanced life support (only in life-threatening situations). The emergency physician (Notarzt) is specially trained in pre-hospital acute care and usually provides ALS on the scene. The way the ambulances are staffed in these countries is determined by the federal states.

They also have an excellent helicopter air rescue system, which was first developed in Switzerland, followed by Austria and Germany. The system covers the entire national area, and the border regions sometimes work in conjunction with foreign helicopter services (i.e., The Netherlands, Belgium, and France).

1.3.2.7 France [12, 21]

In 1956, the Service Mobile de Reanimation (SMUR), the first pre-hospital emergency system with ambulances equipped for stabilization of non-traumatic medical emergencies to provide care to patients with poliomyelitis, was established. In the 1960s, the physician-based "Service d'Aide Medicale Urgente" (SAMU) was established, which also treated traumatic emergencies.

Each of the 96 departments in France has its own regional SAMU, with a center to coordinate the dispatch of two physicians. The centers are typically situated in a level I trauma center with several surrounding acute care facilities. There are no paramedics within the system and the physician supervisor at the coordination center can decide whether to dispatch a basic life support (resuscitation) (BLS) provider team or a physician-based team to provide extensive care. An SMUR team consisting of a physician intensivist, a nurse anesthetist, and an ambulance driver begins the first phase of treatment at the site and transports patients in specially equipped ambulances appropriate for that particular geography (land ambulances or helicopters) [35].

Patients picked up by a BLS provider team and in cases of peripheral or single trauma are taken to the nearest hospital with an accident and emergency department. Polytraumatized patients and patients with specific solitary injuries are taken directly to referral centers [35].

The main goal of including pre-hospital emergency care in trauma care systems is to transport injured patients to the most appropriate acute care facility as quickly as possible in the best possible condition. In regionalized trauma care systems it is possible for pre-hospital care providers to bypass the nearest hospital and to transport the patient to a more appropriate facility with higher levels of care [36]. However, there is still debate about which pre-hospital emergency care system is the most effective, the physician-based or the paramedic-based system.

Studies have shown that although paramedics do not have as much experience as physicians do in life-saving procedures, they spend less time with trauma victims at the scene because their care is based more on standardized protocols [37, 38]. These guidelines are efficient for standard pathology, but in the pre-hospital setting, major trauma patients are not often presented in standard situations with standard injuries [39]. In those cases, it is especially important to have a thorough knowledge of trauma care management and invasive procedures. Physicians, and particularly anesthesiologists, have such knowledge because they are extensively trained and encounter airway and sedation problems that they must solve daily [38]. On the other hand, other studies show that physicians involved in pre-hospital care do not always receive extensive training in pre-hospital trauma care as do paramedics, and

they tend to spend too much time treating patients at the scene [38, 39].

As a corollary to this, invasive procedures in the pre-hospital setting are not only time consuming but are also related to risks and complications that can deteriorate the condition of the patient. Intrinsically, it is not the procedure as such, although there has been much discussion on the use of endotracheal intubation in the pre-hospital emergency care, that influences the outcome but rather the skills of the medical personnel and the pre-hospital conditions that can affect outcome [38].

The time measured from arrival of the pre-hospital care team until arrival at the hospital correlate with the risk of mortality. Data from one study indicate that with every extra pre-hospital minute, the odds of the patient dying increase by 5 % [4].

Another study has shown that pre-hospital time factors did not affect outcome, as long as the pre-hospital time did not exceed the first hour after injury [38]. However, pre-hospital time in severely injured patients is determined by the reaction time of the emergency care services, extrication time, and time for immediate life-saving procedure and therefore 1 h of pre-hospital time is easily consumed without exaggerated procedures. The time required for medical treatment evaluation at the scene takes up only 20 % of the total scene time, a fraction of the total pre-hospital time [40].

Another important issue is pre-hospital patient triage to the most appropriate hospital because patients who were secondarily transferred within a trauma care system have a 30 % increased risk of mortality in comparison with patients who were transported directly to the appropriate facility. Physicians are more skilled in the proper acute care facility for triage patients, but in the paramedic-based system, triage is established using scoring systems and telemedicine whereby paramedics can consult a physician [18, 41].

Moreover, in a study comparing the Anglo-American and the Franco-German system, overall mortality of severely injured patients did not differ significantly, but as mentioned previously, this is still a subject of discussion in the medical world [12].

We believe that the real issue is not whether the basis of the system is the presence of physicians or paramedics, but rather on how to deliver a patient to the appropriate facility within a short period of time and in the best possible condition. The situation will depend on the level of training of the pre-hospital care providers and their competence in dealing difficult environmental and medical situations as well as possible complications. To facilitate such pre-hospital care, standards of triage, care, and transport within a trauma care system must be established.

1.3.3 In-Hospital Care and the Role of the Team Leader

In-hospital care and the role of the team leader can influence the second and third peak of the trimodal death distribution, mainly through good communication and structural organization within a facility as well as between the different facilities within a trauma system.

In-hospital trauma care will be improved by the implementation of acute care facilities, arrangement of effective trauma teams led by a trauma leader that focus on damage control surgery, and the provision of excellent intensive care treatment. It is additionally important to have inter-hospital transfer agreements in place because sometimes a severely injured patient is triaged to a hospital with an inappropriate level of care, and subsequently the patient must undergo a secondary transport to another hospital within the trauma care system [18]. This issue is particularly important because several studies have shown that outcome of severely injured patients improves when treated in tertiary trauma centers [4].

Designation of acute care facilities is essential in a trauma care system and should always be established based on the care that can be provided by each facility. This process started in the USA with the designation of hospitals into different levels (levels I-V). In countries where trauma care systems are implemented, similar classifications are used, although the specific levels can differ. In this classification system, level I trauma centers represent the highest level of care and function as tertiary referral facilities. Basically, they can provide definitive care to the complete spectrum of trauma patients, and have a coordinative function within the trauma system with regard to education and research. Level II trauma centers can also provide definitive care of the severely injured, as they have of all subspecialties and diagnostic tools, but do not necessarily have a neurosurgical and burn department at their facility. A level III trauma center can provide initial diagnosis and

Table 1.2 Pre-hospital care organization

	Paramedic-based					Physician-based	
	The USA	Canada	Australia	The UK	The Netherlands	Germany	France
Basic life support	Paramedic + EMT	Paramedic + EMT	Paramedic + EMT	Paramedic + EMT	Paramedic + EMT	Paramedic + EMT	Paramedic + EMT
Advanced life support						Physician + Paramedic (Notarzt-team)	Physician + Paramedic (SMUR-team)
Pre-hospital trauma life support	(Physicians in 5% of helicopter emergency medical service (HEMS))	(Physicians only in Montreal area)	(Remote areas: RFDS-Physician)	(Physicians only in London trauma system)	Physician + Paramedic (Mobile medical team)		

EMT emergency medical technician, *RFDS* Royal Flying Doctor Service, Helicopter Emergency Medical Service *HEMS*

stabilization of trauma patients and can admit patients who are stable or who show improvement in their condition. Levels IV and V trauma centers can provide initial basic trauma diagnosis and stabilization of the patient before transferring them to a higher level trauma center.

An ideal tertiary trauma center requires the following services: a trauma team, 24-hour a day and 7 days a week coverage by all subspecialties (including neurosurgery and cardiothoracic surgery, burn unit, and hemodialysis unit), a well-organized intensive care unit, full radiological diagnostics, 24/7 operating room and laboratory capacity, among others.

An ideal trauma team consists of at least a team leader, an anesthetist, a trauma surgeon, and a nursing team [42]. Other staff such as neurosurgeons, thoracic surgeons, plastic surgeons, and radiologists should be available to the trauma team in an emergency.

It is also important that every member of the trauma team receive special training in trauma care management. The training can be provided by ATLS, training for medical doctors; and the Trauma Nurses Core Courses (TNCC), training for nurses.

The team leader is responsible for stabilizing and treating a severely injured patient. He/she plays an important role in optimizing and planning the diagnostic and therapeutic trajectory, although he/she should not touch the patient. Therefore, it is necessary that the person who takes over this role is trained and experienced in trauma care management [42]. Most often this role is performed by an emergency medicine or intensive care physician in Australia, the United Kingdom, and France, or surgical physicians in Germany and The Netherlands, as well as the USA. In Canada, that role is divided between emergency care physicians and surgeons. In all cases, it is important that an anesthesiologist and surgeon are present in the emergency room because airway and circulation are the first and most important concerns in trauma management.

The type of surgical physicians who are involved in trauma care differs from country to country with regard to training, background, and subspecialty (Table 1.2). In Europe, several systems need to be discerned. In Germany, trauma care was formerly totally in the hands of trauma surgeons, who specialized in general surgery, with a subspecialty in orthopedic trauma surgery. Currently, because the training of trauma and orthopedic surgery have been merged, the German system resembles the systems in the United Kingdom and France, where trauma of the musculoskeletal system is handled by orthopedic trauma surgeons and trauma of the body cavities by general surgeons. General surgeons take over the responsibility of trauma care surgery in The Netherlands, including fracture treatment, but because the orthopedics also cover fracture care there are different arrangements in different hospitals regarding which cases of fracture treatment and polytrauma should be treated by the orthopedic surgeons. In Europe, the role of the general trauma surgeon, who performs all surgical trauma care, is slowly being taken over by subspecialties that are responsible for their own area of trauma care. This is possible in Europe because distances are relatively short. In Australia, Canada, and the USA, the same system is principally used as in the United Kingdom, where the locomotor system injuries are treated by orthopedic trauma surgeons and the body cavity injuries by general trauma surgeons. However, while in these countries distances are sometimes immense, it is not always possible to provide all subspecialized care by different surgeons, and in these circumstances a general surgeon must often take care of every injury.

1.3.4 Rehabilitation

The ultimate goal of trauma care is to improve the patient's function and quality of life to pre-injury status. After the initial care of pre-hospital and in-hospital emergency management and definitive care, the patient will ideally be discharged to a rehabilitation facility. Rehabilitation facilities can reduce the length of hospital stay, the number of readmissions, and the costs for health care overall. In a trauma care system, the rehabilitation period is an important last stage of care for each trauma patient. Unfortunately, this area of care is underrecognized because there is no evidence for the superiority of any particular trauma rehabilitation model (early integrated vs. late referrals).

In some countries (e.g., France, The Netherlands, Australia) rehabilitation facilities are located across the country, but these services are restricted to certain types of injuries such as spinal cord injuries and for polytraumatized patients; however, patients with severe isolated injuries can also benefit from a rehabilitation period [35].

In the United Kingdom, the spread of rehabilitation centers is not adapted to the regional needs, and the facilities are not considered by authorities in the review of emergency health care in the country.

In Australia there are some state trauma plans that acknowledge the need for polytrauma rehabilitation services. Traditionally, rehabilitation services in Australia have been utilized for patients in the severely disabled or impairment groups, including brain and spinal cord injury, amputations, and major multitrauma. Both public hospital and private hospital rehabilitation units submit data to the Australasian Rehabilitation Outcomes Centre (AROC), which currently records a total of greater than 50,000 rehabilitation episodes per year. Of these cases, between 15 % and 20 % are a result of trauma [4, 43]. Additionally, 73.5 % of all MMT rehabilitation in Australia is undertaken in the 160 public hospital rehabilitation units [37, 44].

Rehabilitation centers in the United States often provide care for a specific kind of injury or subpopulation, but since the wars in Iraq and Afghanistan, the need for multidisciplinary rehabilitation facilities has been recognized. Currently, many veteran rehabilitation centers offer polytrauma rehabilitation services and treatment to civilians as well. Such centers are now located in five states in the USA [45].

In Germany, rehabilitation facilities are well integrated with trauma care. In-hospital rehabilitation is mainly handled by physiotherapists, however, after discharge, patients are transported to rehabilitation facilities across the country. Patients with less severe injuries or even single fractures can also follow an in- or outpatient rehabilitation program.

1.3.5 Quality Control

It cannot be overemphasized that in order to improve and maintain the quality of care provided, all components of a trauma care system must have some type of review and validation. This quality control concerns the establishment of clear and unambiguous guidelines to standardize trauma care and trauma registries as a feedback mechanism for trauma care. The provision of personnel and technical resources is also an essential part of quality control.

The inspection and review of trauma centers within a trauma care system should be executed every few years by independent and designated authorities. In Australia, there is the opportunity for hospitals which are not yet part of a trauma care system, to be visited on a voluntary basis by a multidisciplinary team of trauma clinicians who assess that hospital's capacity to provide trauma care, and then assist and advise that hospital on how to develop trauma management.

It is important to organize interdisciplinary quality meetings to discuss the course and results of trauma management of specific trauma cases within a facility to evaluate the performance of the pre-hospital emergency team and the in-hospital trauma team. The use of data and video documentation in the emergency room is very useful.

The organization of trauma care education for all trauma care providers within a trauma care system is another initiative that should be developed to improve trauma care quality. Trauma registries (Table 1.3) are important tools for improving the quality of trauma management, and can also be used for research purposes (Table 1.4).

1.3.5.1 The USA [46]

The National Trauma Data Bank® (NTDB) is the largest aggregation of trauma registry data ever assembled. The 2010 register contained 681,990 cases. Because

Table 1.3 Role of trauma care surgeons throughout the world

	The USA	Canada	Australia	The UK	The Netherlands	Germany	France
Trauma team leader	General surgeon	General surgeon, Emergency-/ ICU- physician	Emergency-/ ICU-physician, General surgeon	Experienced consultant	General surgeon	Orthopedic trauma surgeon, General surgeon	Emergency-/ ICU-physician
Locomotor trauma	Orthopedic trauma surgeon	Orthopedic trauma surgeon	Orthopedic trauma surgeon	Orthopedic trauma surgeon	Trauma surgeon, Orthopedic surgeon	Orthopedic trauma surgeon	Orthopedic trauma surgeon
Body cavity trauma	General surgeon	General surgeon	General surgeon	General surgeon	General surgeon	General surgeon	General surgeon

ICU intensive care unit

Table 1.4 Trauma registries throughout the world

Country	Trauma registry	First patient	Number of hospitals	Patients per year
The USA	National Trauma Data Bank® (NTDB)	2003	682	ca. 682,000
Canada	Canadian National Trauma Registry (CNTR)	1994	107	ca. 14,000
Australia	National Trauma Registry Consortium (NTRC)	2003	43	ca. 6,900
The United Kingdom	Trauma Audit and Research Network (TARN)	1990	114	ca. 27,000
Germany	Trauma Registry (TR-DGU®)	1993	300	ca. 13,000
The Netherlands	National Trauma Registry (NTR)	2004	53	ca. 6,000

trauma system configurations vary between states in the United States, data supplied to the NTDB are also diverse. Some states only submit trauma data from tertiary trauma centers and other states submit data from every acute care facility within the trauma system.

1.3.5.2 Canada [22, 47]

The National Trauma Registry in Canada was founded in 1994 and is managed by the Canadian Institute for Health Information (CIHI). This national register gets data from the provincial trauma registers. Because there are great differences between the trauma care organizations in the different provinces, the data supplied also varies.

Between 2008 and 2009, over 14,000 cases from 107 facilities (25 level I centers, 32 level II centers, and 48 levels III–V centers) in eight provinces were entered into the National Trauma Registry; two provinces did not provide data.

1.3.5.3 Australia

The National Trauma Registry Consortium, founded in 2003, obtains its data from all pre-existing state-based and individual hospital-based trauma registries in Australia and New Zealand.

1.3.5.4 The Netherlands

The 11 level I trauma centers are associated with the National Network for Acute Care, which had made big efforts to establish the National Trauma Register. The trauma register was established in 2004 and every reference center is responsible for supplying all trauma data from its region to the national registry.

1.3.5.5 Germany

In 1993, the German Trauma Registry was founded by the DGU through the development of a nationwide trauma care system; this registry is fairly complete for cases with an ISS >15 throughout Germany.

1.3.6 Education

The perspective of trauma surgery is changing in all civilized countries. In blunt trauma, the number of killing injuries has dropped over the last decade. This general trend has been caused by the influence of road safety measures, rescue conditions, passive car safety, and also by the improvement of emergency medical care and the development of trauma care systems.

In Europe, the education for residents has changed. Qualification for the orthopaedist no longer requires 6 years of surgery. Instead, common trunk education includes emergency medicine, intensive care, and orthopaedic traumatology or elective orthopaedic surgery. Vascular surgery, plastic surgery, and general surgery are not required fields any longer. This has tremendous impact on the skills of orthopaedic surgeons because intra-operative complications may be treated only in the presence of a subspecialty expert. Thereby, it has become dangerous to treat complex fractures, except in centres that cover all subspecialties.

In the USA, a contrary trend is seen. The development of an "acute care surgery" fellowship might in the future enable general surgeons to cover a broader spectrum of injuries, including orthopaedic injuries. This fellowship widens the expertise and skills of the general surgeon. It also underlines a close cooperation between general surgery and orthopaedic surgery.

Within trauma care systems, education of health care professionals is very important. Trauma care courses such as the PHTLS, ATLS, Early Management of Severe Trauma, Advanced Paediatric Life Support, and Definitive Surgical Trauma Course for doctors and the TNCC and the Trauma Nurse Program for nurses contribute to the improvement of trauma care. These courses are increasing across countries with and without trauma care systems.

1.4 The Future

Inherent to the development and success of a trauma system is a complete injury management program, incorporating the vital components of data management, injury prevention, research, education and training. Each major trauma center should be responsible for developing a trauma system to support outreach programs and provide expert support to the peripheral hospitals in their geographic area, including ongoing trauma education and training to build a sustainable trauma workforce [40].

On the contrary, it is clear from history and this review that trauma care and trauma care systems are in their infancy worldwide. Some countries are advanced in comparison with others, but few, if any, can claim that they have a perfect system. Furthermore, in some of the Western countries, a large number of patients do not have access to a trauma care system or even a trauma center.

There are a few fundamental problems in establishing effective and comprehensive trauma care systems, which normally takes several years.

First, particularly in the last decade, because of the economic crisis, health care authorities are reluctant to provide sufficient resources for the development of trauma care systems in all its aspects. Such funding is essential to implement a statewide or regional trauma care system. There are growing concerns regarding the financial solvency of trauma centers as a result of increasing costs and many of them are closing or downgrading their level of care in order to boost profits [1].

Another aspect that contributes to this discussion is the increase in the elderly patient population. There is already a bimodal death distribution because of trauma. Mortality rates among elderly trauma patients with an ISS > 15 is 3.5 times higher than for their younger counterparts. The elderly spend more time in the intensive care unit, and the rehabilitation potential is lower. Therefore, the costs are higher and the outcome is lower.

Furthermore, there is the perception among many small non-designated centers that they will lose income if they participate in a trauma care system and therefore they resist such inclusion [2].

For example, even if all hospitals across the United Kingdom participate in trauma systems, the estimated costs of running eight 'ideal' trauma care centers to serve the whole country is at the upper limit of, or exceeds, the equitable sum available within the National Health Service [42].

Moreover, over the past years, there has been a work force shortage developing across all levels of care and this shortage will not be relieved by the introduction of physician extenders, including nurse practitioners and physicians' assistants. For the surgical specialty, a lack of interest by residents for this profession is a big problem. The main objections are the undesirable lifestyle with long working hours, the impossibility of combining a professional career with the role of parent, and incompatibility with a private practice for trauma surgeons.

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Prehospital Trauma Care

2

Bertil Bouillon

2.1 The Chain of Rescue

The overall aim of trauma care is to ensure survival and good quality of life for the injured patient. Optimal trauma care begins at the site of the accident and ends with a good rehabilitation program and reintegration into society. The term "*chain of rescue*" reflects the idea that optimal trauma care can be achieved only if all parts of the chain deliver excellent care and interact effectively. The overall result can only be as good as the weakest part of the chain. Therefore, in-hospital trauma care providers should take interest in the quality of prehospital care, as well as the quality of the rehabilitation program, following acute in-hospital care.

The pathophysiological concept of trauma care recognizes three main determinants of patient outcome: (1) the **primary injury**, (2) the **secondary injury**, and (3) the **individual biologic** *response* or physiologic reserves of the patient. The term "*primary injury*" describes the initial injuries caused by the accident, such as a subdural hematoma, a splenic rupture, or a femur fracture. They define the best achievable outcome of the patient if optimal care is delivered. The term "*secondary injury*" describes all the injuries or consequences caused by second hits that occurred after the initial trauma. Many of these second hits are caused by complications and delayed or suboptimal treatment. Examples of second hits are postoperative complications, nosocomial infections, inadequate fracture stabilization, and secondary ischemic brain injury caused by insufficient oxygenation or hypoxia as a result of incorrect intubation. The term individual biologic response describes the fact that identical primary injuries can have very different outcomes depending on the physiologic reserves of a patient. An initial epidural hematoma, splenic rupture, and femoral shaft fracture in a 20-year-old healthy athlete will probably have a better outcome than the same primary injury in a 60-year-old who is taking aspirin and clopidogrel because of a heart attack he experienced 3 months earlier. The individual biologic response depends not only on comorbidities and age, but also on many other individual factors.

These three variables mainly define outcome. Even more important is to reflect on which of these variables can be modified through trauma care. The primary injury can be influenced only by prevention programs. Once the accident has occurred, it can no longer be changed. The individual biologic response can be supported, but the patient cannot be changed. The only possibility of improving outcome is minimizing secondary injuries. This is the main focus of trauma care throughout the rescue chain.

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2.2 Prehospital Care

Writing a chapter on prehospital trauma care in a European trauma manual is a challenge because there are several regional differences throughout Europe.

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The systems differ with respect to the level of care provided (basic life support [BLS] vs advanced life support [ALS]), the personnel delivering care (paramedic vs nurses vs physician-staffed ambulances), and mode of transportation (ground vs air).

There is no conclusive evidence substantiating which system is best with respect to the outcome of the trauma patient [1–7]. In a review article, Liberman [3] stated that "the type of pre-hospital care available to trauma patients is determined by regional policies that are dictated by local political, cultural, and economic factors as well as the influential opinion of local and international experts."

With respect to prehospital interventions, different types of controversial concepts have been discussed worldwide. The two main concepts that are often described are "scoop and run" and "stay and stabilize" [5].

The overall aim of "scoop and run" is to save time until hospital admission. Supporters of this approach believe that if a trauma patient is in danger it is because of an uncontrolled hemorrhage. Airway and breathing should be controlled and secured if necessary. Starting intravenous lines and replacing large volumes of fluids are unnecessary. If the patient is bleeding, fluid replacement will cost time, increase bleeding and coagulopathy, and thereby worsen outcome. In uncontrolled hemorrhage, rapid surgical control of the bleeding in the operating room is the only option.

The overall aim of "stay and play" is to secure oxygenation. Airway and breathing should be controlled and early intubation should be initiated. Volume should be replaced in order to maintain organ perfusion and tissue oxygenation. Time is not considered a primary focus.

This chapter will focus on the most important prehospital interventions and will discuss their indication and the evidence behind them. It will also point out the latest evidence-based guidelines that have been published in Germany in 2011 [1, 8]. These interdisciplinary clinical practice guidelines have been developed by 97 authors from 11 medical societies. The guidelines are evidence- and consensus-based and include 264 key recommendations for the prehospital setting, the emergency room, and for initial emergency surgery. According to the evidence and consensus available, the recommendations were graded (GoR) with A (must), B (should), and 0 (can). Sixty-six of the recommendations pertain to the prehospital setting.

2.3 The Goals of Prehospital Trauma Care

Prehospital trauma care has four main goals:

1. To quickly detect all life-threatening injuries
2. To treat these life-threatening injuries as quickly as possible
3. To bring the correct patient to the right hospital
4. To save time until definitive care

Advanced trauma life support (ATLS) provides a well-established and accepted concept of rapid evaluation of the trauma patient in the emergency room, followed by a priority-oriented treatment. Derived from the ATLS concept of prehospital trauma, life support and other programs such as the European Trauma Course have adopted the initial assessment of a trauma patient in the prehospital setting [4, 9]. The initial assessment consists of a **primary and a secondary survey**. The primary survey addresses the vital status, checking if a patient has an A, B, C, D, or E problem. The secondary survey tries to detect the relevant anatomical injuries on the basis of a complete anatomical body check.

The evaluation of a trauma patient at the scene begins with a general impression [4]. Paramedics or emergency physicians obtain this general impression when they approach the injured patient. They notice if the patient is breathing, is awake or unconscious, or moves spontaneously. As soon as they reach the patient it makes sense to ask him what happened. If the patient answers normally, he or she probably does not have an acute A, B, C, D, or E problem and the primary survey can be completed. If the patient does not respond normally, a formal primary survey checking the A, B, C, D, and E is necessary.

2.3.1 Primary Survey

The primary survey addresses checking the vital status to find out if a patient has an A, B, C, D, or E problem [4, 9].

A – Airway and cervical stabilization
B – Breathing
C – Circulation and bleeding control
D – Disability and neurological deficit
E – Exposure, environment, temperature control

Airway and breathing should be checked with auscultation of the thorax, measuring the oxygen saturation by pulsoxymetry, and calculating the respiratory rate. If all three variables show normal values and if the patient is not unconscious, then there is

no “A” or “B” problem. If one of the variables shows abnormal values, further evaluation is necessary in order to check if the patient has an “A” or “B” problem.

Life-threatening “A” problems that must be detected are impairments of the airway that prevent oxygen intake. Unconscious patients with a Glasgow Coma Scale (GCS) of 3–8 also have a potential “A” problem. Their airway is not safe because they can aspirate as a result of impaired reflexes. The treatment of choice is rapid sequence endotracheal intubation. It is important to reevaluate the patient after each intervention to ensure success.

Good Clinical Practice (GCP) Guideline: Key recommendations for airway [1]	Grade (GoR)
Emergency medical services personnel must be regularly trained in emergency anesthesia, endotracheal intubation, and alternative ways of securing an airway (bag-valve-mask, supraglottic airway devices, emergency cricothyroidotomy)	GoR A
Multiply injured patients with apnoe or a respiratory rate below 6 must be anesthetized, intubated endotracheally, and ventilated in the prehospital setting	GoR A
Emergency anesthesia, endotracheal intubation, and ventilation should be carried out in the prehospital phase in multiply injured patients with the following indications: Hypoxia (SpO_2 < 90 %) despite oxygenation after exclusion of a tension pneumothorax Severe traumatic brain injury (GCS < 9) Trauma-associated hemodynamic instability (BP_{sys} < 90 mmHg) Severe chest injury with respiratory insufficiency (respiratory rate > 29 breaths per minute)	GoR B
The multiply injured patient must be preoxygenated before anesthesia	GoR A
After more than three attempts of endotracheal intubation, alternative methods must be considered for ventilation and securing an airway	GoR A
Alternative methods for securing an airway must be available when anesthetizing and endotracheally intubating a multiply injured patient	GoR A
When endotracheal intubation and emergency anesthesia are performed, electrocardiogram, blood pressure measurement, pulse oxymetry, and capnography must be used to monitor the patient	GoR A
During endotracheal intubation in the prehospital and in-hospital setting, capnometry/capnography must be used for monitoring tube placement and ventilation	GoR A
Normoventilation must be carried out in endotracheally intubated and anesthetized trauma patients	GoR A
For endotracheal intubation in multiply injured patients, emergency anesthesia must be carried out as rapid sequence induction because of the usual lack of a fasting state and risk of aspiration	GoR A
Manual in-line stabilization should be carried out for endotracheal intubation with the cervical spine immobilization device temporarily removed	GoR B

Life threatening “B” problems that must be detected are a tension pneumothorax or relevant pneumothorax or hemothorax that result in cardiorespiratory impairment. A tension pneumothorax will usually show reduced breath sounds, a reduced oxygen saturation, distended neck veins, and dyspnoea if the patient is awake. The treatment of choice for a tension pneumothorax or a relevant pneumothorax or hemothorax is placement of a thoracic drain. In case of a tension pneumothorax, fast needle decompression can be a good option, followed by placement of a thoracic drain. It is important to reevaluate breath sounds and oxygen saturation after the intervention to ensure that the treatment has a positive effect. In patients with a suspected minor pneumothorax without cardiorespiratory impairment, close reevaluation of the patient is appropriate.

GCP Guideline: Key recommendations for breathing [1]	Grade (GoR)
A suspected diagnosis of pneumothorax and/or hemothorax must be made if breath sounds are weaker or absent on one side (after checking correct placement of the tube). Absence of such auscultation largely rules out a larger pneumothorax, especially if the patient is normopneic and has no chest pain	GoR A
The potential progression of a small pneumothorax that cannot initially be diagnosed in the prehospital phase should be taken into consideration	GoR B
A suspected diagnosis of tension pneumothorax should be made if auscultation of the lung reveals no breath sounds unilaterally (after checking correct placement of the tube) and, in addition, typical symptoms are present, particularly, severe respiratory disorder or distended neck veins, in combination with arterial hypotension	GoR B
A clinically suspected tension pneumothorax must be decompressed immediately	GoR A
A tension pneumothorax should be decompressed by needle decompression, followed by placement of a chest drain	GoR B
A pneumothorax diagnosed on the basis of auscultation in patients not on ventilation should usually be managed by close clinical observation	GoR B
A pneumothorax diagnosed on the basis of auscultation in a patient with positive pressure ventilation should be decompressed	GoR B
A pneumothorax should be treated with a chest drain provided the indication exists	GoR B

Life-threatening “C” problems that must be detected are sources of uncontrolled bleeding. The variables used to check if the patient has a “C”

problem are blood pressure, pulse rate, and capillary refill. A systolic blood pressure below 90 mm Hg and tachycardia above 100 beats per minute indicate presence of shock. Shock in trauma patients is usually a result of bleeding. Typical bleeding sources are abdominal injuries, thoracic injuries, pelvic and long bone fractures, and open wounds with arterial bleeding. If the bleeding source is detected, the emergency personnel must check if control of the bleeding is possible. Bleeding from extremity injuries can be controlled by pressure or application of tourniquets. Bleeding from pelvic injuries can often be controlled by application of simple pelvic binders combined with fixed inner rotation of the legs. Abdominal or thoracic bleeding usually cannot be controlled. Limited application of fluids and a rapid transportation to a facility that can provide surgical control of the bleeding in the operating room is important. Administration of large amounts of fluids has been shown to deteriorate outcome by increasing blood loss because of increased blood pressure and impaired coagulation.

GCP Guideline: Key recommendations for circulation [1]	GoR
Volume replacement should be initiated in multiply injured patients. In patients with uncontrolled bleeding, volume replacement should be performed at a reduced level	GoR B
In hypotensive patients with traumatic brain injury, volume replacement should be carried out with the goal of restoring normotension	GoR B
Normotensive patients do not require volume replacement, but venous lines should be started	GoR B
Crystalloids should be used for volume replacement in trauma patients	GoR B
Anti-shock trousers must not be used for circulatory support in multiply injured patients	GoR A

Life-threatening "D" problems that must be detected are clinical signs of increased cranial pressure as a result of intracranial bleeding. Any deterioration in the patient's consciousness and abnormal pupillary reaction are important clinical signs that necessitate rapid transportation to an institution that allows rapid evaluation of the cranium with computed tomography. If a patient is unconscious and if the GCS is 8 or lower, the patient by definition, has an "A" problem and needs endotracheal intubation.

Glasgow Coma Scale (GCS) [10]	Score
Best eye opening (E)	
Spontaneous	4
To speech	3
To pain	2
None	1
Best verbal response (V)	
Oriented	5
Confused conversation	
Inappropriate words	3
Incomprehensible sounds	2
None	1
Best motor response (M)	
Obeys commands	6
Localizes pain	5
Normal flexion (withdrawal)	4
Abnormal flexion (decorticate)	3
Extension (decerebrate)	2
None (Flaccid)	1
GCS Score = E + V + M (best possible score = 15, worst possible score = 3)	

GCP Guideline: Key recommendations for disability [1]	GoR
The level of consciousness, papillary reaction, and the GCS must be recorded and documented at repeated intervals	GoR A
The goal in adults should be arterial normotension with a systolic blood pressure not below 90 mm Hg	GoR B
A fall in arterial oxygen saturation below 90 % should be avoided	GoR B
If severely elevated intracranial pressure is suspected at the scene, particularly with signs of transtentorial herniation (pupil widening, decerebrate rigidity, extensor reaction to painful stimulus, progressive clouded consciousness), the following treatments can be considered:	GoR 0
Hyperventilation	
Mannitol	
Hypertonic saline solution	

Life-threatening "E" problems that must be detected are hypothermia or exposure to toxic agents such as inhalation trauma after burn injuries. In case of penetrating injuries, the penetrating object should be left in situ.

2.3.2 Secondary Survey

After completion of the primary survey, the patient should be stabilized with respect to his vital functions [4]. The secondary survey is then initiated by

performing a quick body check, searching for relevant anatomic injuries such as unstable pelvic fractures, spine fractures, long bone fractures, open fractures, or neurovascular injuries to the extremities.

If pain, hematoma, or crepitation is diagnosed during the secondary survey, a fracture must be suspected. Any injury to the extremity must be checked for neurovascular damage. In injuries to the extremities that bleed, the bleeding should be stopped by local compression or application of tourniquets if necessary. In suspected unstable fractures of the pelvis on the basis of the clinical examination, a pelvic binder should be applied. Grossly dislocated fractures of the extremities should be reduced and stabilized with splints after pain treatment has been initiated. Any open fracture should be covered with a sterile dressing. Multiply injured patients should be fixed on a long spine board or a vacuum matrace depending on local availability.

GCP Guideline: Key recommendations for injuries to the extremities [1]	GoR
Severely bleeding injuries to the extremities that could impair vital functions must be given first priority	GoR A
The management of extremity injuries must avoid further damage and not delay the rescue time if additional threatening injuries are present	GoR A
The extremities of any injured patient should be examined in the prehospital phase	GoR B
Extremities with suspected injury should be immobilized against rough movement before transportation of the patient	GoR B
If possible, and particularly with concomitant ischemia in the extremity concerned/with a long rescue time, grossly dislocated fractures and dislocations should be reduced in the prehospital phase	GoR B
Each open fracture should be cleaned and covered with a sterile dressing	GoR B
Active bleeding should be treated according to the following stepwise approach: Manual compression/pressure dressing Elevation Tourniquet	GoR B

The emergency medical services (EMS) team should screen injured patients to exclude spine injuries. If the secondary survey of a conscious patient shows no pain in the spine region and if the neurologic exam is normal, a severe injury of the spine can usually be excluded. If pain or a hematoma in the spine region is present an injury to the spine must be suspected. In any unconscious patient, a spine injury must be suspected and the patient must be treated accordingly. The most important treatment of suspected spine injury in the prehospital setting is immobilization. At the level of the cervical spine, immobilization is achieved with application of a cervical spine immobilization device. At the level of the thoracic or lumbar spine, immobilization is achieved with a long spine board or a vacuum matrace.

GCP Guideline: Key recommendations for injuries to the spine [1]	GoR
A thorough physical examination including the spine and the functions associated with it must be carried out	GoR A
Acute pain in the spinal region after trauma indicates injury to the spine	GoR B
In unconscious patients, the presence of a spine injury must be suspected until it is ruled out	GoR A
An instable spine injury can be excluded if the following five criteria are absent: Impaired consciousness Neurologic deficit Spinal pain Intoxication Trauma to the extremities	GoR A
If an injury to the cervical spine is suspected, the cervical spine must be immobilized before technical rescue	GoR A
Transportation of spine-injured patients should be as gentle as possible and free of pain	GoR B
Patients with a neurologic deficit and suspected spine injury should be transported to a trauma center with spine surgery facilities	GoR B

The EMS team make a decision as to which hospital the patient should be transported (level of trauma center) and how the patient should be transported (air vs ground). Variables that can influence the decision are local availability of resources, distances, the injuries of the patient, and the status of the patient's vital functions [1, 4, 5, 11].

The aim is to get the right patient to the appropriate hospital in time. It would not make sense if every injured patient was sent to a level I trauma center. This would result in an inefficient use of resources. The evidence available suggests that severely injured patients have a better outcome when treated in trauma centers. In countries with regional trauma care, criteria have been suggested for patients to be transferred from the site of the accident to a trauma center [4, 11]. These criteria may vary from country to country.

All experts unanimously agree that prehospital time should be as short as possible. Interventions such as endotracheal intubation, placement of a thoracic drain, or starting intravenous lines, and volume replacement should only be performed if indicated and not "de principe". In uncontrolled bleeding and in penetrating trauma, all guidelines suggest that time is of utmost importance.

GCP Guideline: Key recommendations for transportation [1]	GoR
Severely injured patients should primarily be transferred to a trauma center	GoR B
Helicopter rescue can be used in the prehospital management of severely injured persons because it can result in a survival advantage, particularly for medium- to high-severity injuries	GoR 0

2.4 Summary

Optimal trauma care begins at the site of the accident and ends with a good rehabilitation program and reintegration into society. The term "chain of rescue" reflects the idea that optimal trauma care can only be achieved if all parts of the chain deliver excellent care and interact effectively. The types of prehospital care differ among countries and regions. There is no conclusive evidence pertaining to which system (ALS vs BLS) is best with respect to outcome of the trauma patient. The evidence available suggests that vital functions need to be evaluated and stabilized, if endangered. The controversial discussions regarding the different approaches "scoop and run" vs "stay and stabilize" seem to gravitate toward the "treat and go" approach.

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Trauma Scores

3

Rolf Lefering

3.1 What Is a Trauma Score?

A score in medicine is a one-dimensional value that describes a rather complex situation. A score is usually a combination of several aspects of the complex situation, each of which is also expressed as a value or category. For example, the critical state of a patient admitted to an intensive care unit represents a complex clinical situation. This situation is determined by the patient (age, sex, chronic diseases), his or her history (myocardial infarction, surgery, emergency), the actual physical state (circulation, blood gases, organ function), and the current treatment (ventilation, dialysis). If the severity of such a case and the circumstances must be described, it should be done literally and consider only the individual instance (e.g., if a patient is to be transferred to another ward). However, if groups of patients are considered, such as in clinical studies, scientific reports, or benchmarking statistics for quality audits, this approach would not work. The severity of the case must be described in a way that makes it possible to compare the individual case with many other cases.

In this situation, scores are a feasible and widely accepted option to describe severity. Different aspects are considered (e.g., blood pressure), the degree of deviation from normal function is graded (e.g., 8 points for blood pressure 40–69 mmHg), and the points from different aspects are added to build the final score value. The above example is from the Simplified Acute Physiology Score III [1]. The higher the point, the greater the severity of the patient's illness. If required, these score values could be transformed into an estimator of the probability of survival. Such estimators are usually derived from a large number of observations.

Trauma scores follow a similar principle but take into consideration only trauma victims. Some trauma scores focus on the prehospital setting, where they are used to support the decision to bring a patient into an appropriate trauma center (triage scores). Other scores are more complex; they include several aspects of a case and involve sophisticated mathematical formulas to provide a more exact prognosis for survival. Such prognostic data, for example, are used for interhospital comparisons.

Trauma scores now have a history of approximately 40 years. One of the first scoring systems, the Injury Severity Score (ISS), was published in the early 1970s. Most interestingly, this score is still the most frequently used scoring system in trauma research because it has become a type of common language among trauma surgeons.

3.2 What Are Trauma Scores Used for?

Trauma scores are developed to describe the severity of injuries, or the prognosis of a patient, and correlate with severity.

The so-called *triage scores* are simple systems made from only a few items. Categories are preferred over exact measurements. Triage scores can usually be determined without using a calculator or a computer. Sometimes a simple scoring sheet supports the calculation of the score value (e.g., the Trauma Associated

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Severe Hemorrhage [TASH] Score). Triage scores are intended to give supportive information for decision making. Such decisions might be whether to transport a patient to the nearest hospital or to a trauma center. Trauma team activation can also be based on certain levels of severity.

Trauma severity scores describe the injury pattern in a comparative fashion, where injuries might affect organs, bones, or whole body regions. Injuries are graded according to the extent of damage and multiple injuries usually receive higher scores than isolated injuries. A typical score of this type is the ISS.

Severity scores are frequently used to describe groups of trauma patients (e.g., in scientific publications or presentations), but they can also be used to define inclusion and exclusion criteria in clinical trials and trauma registries.

Prognostic scores are similar to the above-mentioned severity scores but they further derive a probability of survival (or risk of death) estimator from the score value. The estimates are used to evaluate the observed outcome (survival or mortality rate) in groups of patients.

Trauma registries use prognostic scores to compare different time periods or different hospitals. The reason for using scores for this purpose is that unless there are sufficiently powered randomized trials, there will be differences in the case mix of trauma populations regarding demographic data and injury severity. Thus, direct comparison of mortality rates can be misleading. However, comparing observed and predicted mortality rates of different populations would allow for drawing conclusions regarding the quality of care. This approach is used in quality audit reports and in the evaluation of therapeutic and diagnostic measures. Huber-Wagner et al., for example, compared patients with and without whole-body computed tomography using prognostic scores [2]. In this regard, scoring systems can make situations more comparable in instances where they initially were not. This is an important aspect in an area where randomized clinical trials are difficult to perform.

Susan P. Baker, founder and first director of the Johns Hopkins Center for Injury Research and Policy and 'mother' of the ISS, once said: *'If you have never felt the need for any type of severity scoring system, then you probably have never had to explain how it is that survival rate of 85% in your trauma center is actually better than the survival rate of 97% in some other hospital where the patients are much less seriously injured'*.

3.3 Examples of Trauma Scores

The following is a list of trauma scores, but it does not provide details for the calculation of the scores. For this purpose we refer the reader to the original publications, or to articles with an extended overviews [3, 4]. The list includes short descriptions of the different scores and what they are used for.

3.3.1 Glasgow Coma Scale (GCS)

The GCS measures unconsciousness by considering three different aspects of the patient: eye opening (1–4 points), verbal response (1–5 points), and motor response (1–6 points). High values (maximum is 15) are associated with a normal mental function. This rather old score (first published in 1974 by Teasdale and Jennett [5]), developed for the initial evaluation of cases with head injury, is actually used in many other scores such as the Acute Physiology and Chronic Health Evaluation score, Simplified Acute Physiology Score, or organ failure score.

3.3.2 The Revised Trauma Score (RTS)

The RTS is based on blood pressure, consciousness (GCS), and respiratory rate [6]. Each of these three physiological aspects is recorded in five categories (0–4 points each) and added. High scores correspond to normal values. This simple 0–12 points scale could be used as a triage score. The final RTS score value is calculated as the logistic function of a weighted sum of these three components. The RTS only covers the physiological response to an injury and does not directly measure the extent or severity of injuries.

3.3.3 ISS

The ISS is one of the first trauma scores created, and was published in 1974 [7]. This anatomical severity

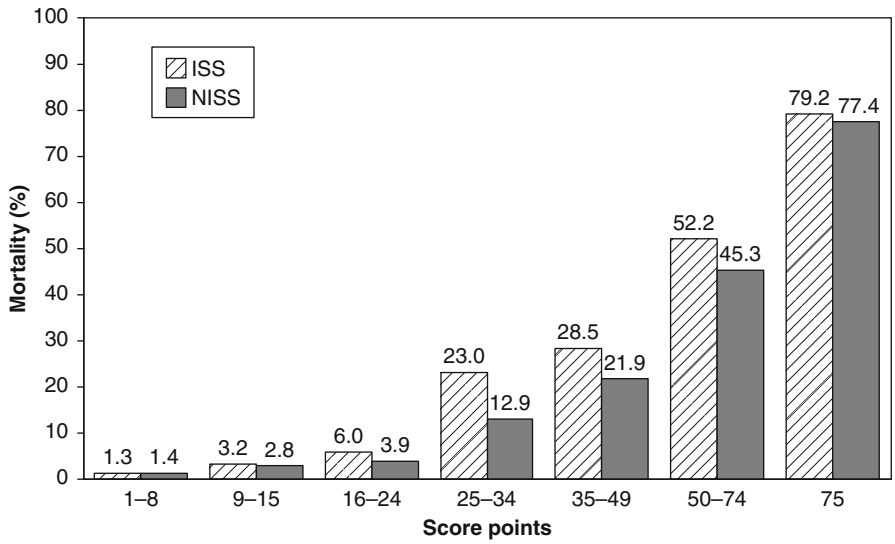

Fig. 3.1 Association of Injury Severity Score (ISS) and New Injury Severity Score (NISS) with hospital mortality. Results are based on 88,480 patients from the TraumaRegister German Society for Trauma (DGU)

score is based on the three most severe injuries in different body regions. The six body regions considered are: head, face, thorax, abdomen, extremities (including pelvis), and soft tissue. All injuries are graded according to the Abbreviated Injury Scale as minor (1), moderate (2), serious (3), severe (4), critical (5), or maximal (6). The three worst injuries from different body regions are squared and then added to obtain the ISS. Thus, the ISS ranges from 1 to 75 (Fig. 3.1).

Although still the most frequently used injury severity measure, the ISS is also criticised for not adequately regarding multiple injuries in the same body region. In order to compensate for that, and to make the calculations easier, Osler et al. suggested using just the three worst injuries without regard to the body region [8]. This score is referred to as the New ISS and its predictive ability is somewhat better, but it still does not conform with the worldwide standard of the ISS.

3.3.4 Trauma and Injury Severity Score (TRISS)

TRISS is the result of the Major Trauma Outcome Study [9]. It combines the following three most important and independent predictive factors: (1) anatomic injury severity, quantified as ISS; (2) the physiological response to these injuries, quantified as RTS; and (3) the age of the patient. However, age is only considered as < / ≥55 years. Different formulas for patients with blunt and penetrating injuries provide a probability of survival as the final TRISS score. Many trauma registries use the TRISS or updated and modified versions of this score.

3.3.5 Revised Injury Severity Classification (RISC)

RISC was developed in a large trauma registry (Trauma Register of the German Trauma Society) to improve outcome prediction [10]. In addition to age, physiology, and injury severity, it also takes into consideration the first laboratory values upon admission, such as base deficit or coagulation marker (partial thromboplastin time, international normalized ration, hemoglobin) and prehospital cardiac arrest.

Other trauma registries such as the British Trauma Audit and Research Network (TARN) also use predictive models to estimate the prognosis. The TARN model includes fewer variables but is updated every year; the actual version can be retrieved from their web site.

3.3.6 TASH

Finally, scores can not only be used to predict mortality or survival, but also to predict other conditions. As an example, the TASH score determines the probability of a patient needing a mass transfusion (defined as

10 or more units of blood) [11]. This easy-to-calculate score could increase the preparedness for blood transfusion when a patient with severe bleeding is admitted, or it can easily be included in treatment algorithms. The score uses blood pressure, heart rate, hemoglobin, base deficit, initial ultrasound results, femur/pelvic fracture, and male gender as predictive factors.

3.4 Quality of Scores

What is a 'good' score? A good trauma score should be able to discriminate between patients with minor and severe injuries. Severity, however, is usually associated with mortality and other unfavorable outcomes (Fig. 3.1). Thus, predicted and observed mortality rates are frequently used to evaluate trauma scores. The following four aspects should be analyzed when the quality of a score is measured:

- Discrimination
- Precision
- Calibration
- Validation

Discrimination describes the ability of a score to separate survivors from non-survivors. Therefore, mean score values (or predictions) should be as different as possible in the two groups. The most frequently used measure for discrimination is the area under the receiver operating characteristic curve (AUC of ROC), a summary measure where all possible score values are used for prediction of survival (or death). Each score value is used as a cut-off value for prediction of death, and sensitivity and specificity (or true and false positive rate) are determined and plotted in the diagram. AUC of ROC values range from 0.5 to 1.0, and the higher the value, the better the outcome. AUC of ROC values of different scoring systems derived from the same dataset are appropriate tools for comparing their discriminating power. However, if results come from different publications or datasets, comparability is limited because the AUC strongly depends on the portion of easy-to-predict cases. In populations where 95 % of cases survived, AUC ROC values were much higher than those obtained in more severely injured patients.

Precision is the extent to which a prognostic score (i.e., a score that provides a risk of death estimate for each case) is able to closely predict the mortality rate actually observed. Deviations of precision can occur if a rather old score is applied to actual data (i.e., if the mortality today is lower than 20 or 30 years ago). A lack of precision will also be observed when a score is applied in a less-developed health care system.

Calibration is the extent to which the above-mentioned precision is equally valid for low-risk and high-risk patients. Calibration is usually measured by the Hosmer-Lemeshow (HL) statistic which evaluates the precision in ten different subgroups of increasing risk of death. The derived HL statistic should be as small as possible. It uses chi square distribution, and both values, HL statistic and *p* value, are usually reported.

Finally, there should be *validation* of the score. Validation means that the properties of a score (discrimination, precision, calibration) are evaluated on a different set of data. Developers of a score sometimes use only one part of their data for developing the score, and the remaining data for validation. A valid scoring system will show similar results in both datasets.

3.5 Limitations

The usefulness of scoring systems in scientific research cannot be disputed. Scores are used for description, inclusion of cases, and even evaluation of outcome. Also, in comparative quality audits, scores are used to compare institutions with a varying case mix of patients. However, in routine care, the role of scoring systems is limited.

Prognostic estimates derived from a score should be carefully considered when applied to individual patients. What does it mean if a patient with an initial risk of death of 10 % (derived from a score) finally died? Was the score wrong? Was the treatment not optimal? These questions cannot be answered. A 10 % risk of death means that on average, one out of ten similar patients would die. But the score cannot predict which patient will die. If such deaths in low-risk patients occur more frequently than one in ten, then it could be a matter of treatment quality. But in the individual case, this decision is not acceptable.

In conclusion, a variety of trauma scores exist and new scores will continue to be developed in the future. Scores are used mainly in clinical studies and audit of care. Their application to an individual patient is limited; however, some well-known

scoring systems have become a type of common language for communication.

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Response to Major Incidents and Disasters: An Important Part of Trauma Management

4

Sten Lennquist

4.1 Definitions

Ever since disaster medicine was established as an academic discipline, many attempts have been made to define the term *disaster* from a medical point of view. A wide range of definitions have been proposed and discussed, but many of these proposals have been only constructions of words and do not entail any practical function, neither as a basis for decision making in the process of alert nor as a basis for evaluating and comparing various incidents.

In order to achieve this, more practical and useful terminology originating from the term *Major Incident (MI)*, defined as *any situation where available resources are insufficient for the immediate need of medical care*, has been developed during recent years for the health care sector. MI is not related to any specific number of critically ill or injured patients, or to any specific level of resources, but rather to the balance between resources and need. The term is used only in the acute situation where lack of resources can cause immediate loss of life or severe impairment of health – a "chronic" discrepancy between recourses and need that might be present within an increasing part of the present health care system is not classified as MI.

The text in this chapter is to a part based on the textbook Lennquist S. (Ed): Medical Response to Major Incidents and disasters, Springer 2012, with permission from the publisher.

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The impact on the health care system is related to the *MI level*.

1. *MI Level 1*: By adjusting organization and methodology, we can attain the level of expectation of our medical care and rescue all patients who can be saved. Alternative definitions are *Major Incidents* or *Major Accidents*, *Major Emergencies*, and *Compensated Incidents*.
2. *MI Level 2*: The number of casualties is so high that even with adjusting organization and methodology we cannot attain the level of expectation, meaning that all patients cannot be saved. Alternative definitions are *Mass-Casualty Incidents*, *Disasters*, or *Decompensated Incidents*.
3. *MI Level 3*: The same as level 2, but combined with destruction of the infrastructure in a region. This means even higher demands on triage, as well as demands on other types of support, requiring national assistance from outside the affected region.
4. *MI Level 4*: The same as level 3, but affecting a country where the entire national infrastructure is impaired or where the national resources are insufficient to handle the situation and international assistance is needed. Alternative definitions for levels 3 and 4 are *Complex Emergencies* or *Compound Incidents*.

The advantage of this terminology is that it provides a direct practical base for decisions in response to the alert.

Level 1 means that disaster plans should be activated and the methodology of working adjusted to that, but the goal can still be to save all patients.

Level 2 means upgrading the degree of alert and preparedness, giving a lower priority to casualties with minimal prospects of cure to be able to save patients with a better chance of survival (i.e., use of the triage category "expectant").

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Level 3 means mobilizing national resources from outside the affected region, including support functions for supply of water, electricity, food, and temporary accommodation, and transport facilities both for evacuation of casualties and for delivery of personnel and material resources.

Level 4 has the same meaning as level 3 but on an international basis, indicating activation of international relief organizations.

When this terminology was introduced, levels 3 and 4 were combined into level 3. Recognition of incidents that can be handled nationally in spite of destroyed infrastructure and the need for clear indications for activation of international relief operations has led to the proposal for separating the last level into two separate categories (levels 3 and 4).

Most incidents in high-technology countries, or countries with good health care resources, fall under the category *MI level 1*. From a medical point of view, the World Trade Center terrorist attack of 2001 can be included in this category, even if, in general terminology, it has been classified as a disaster. The primary mortality on the scene was so high that there was an ambulance for every surviving casualty, and the hospital resources were more than adequate.

An example of an *MI level 2* situation is the Estonia Ferry Incident in the Baltic in 1994, where in a storm and cold water the resources were sufficient enough to rescue only a limited number of passengers from the cold water, with a total of 852 casualties; the evacuation of those with signs of life was restricted, leaving hypothermic and "normally" rescuable casualties on the rafts.

Examples of *MI level 3* are the floods after Hurricane Katrina in the United States in 2005 and the earthquake/tsunami disaster in Japan in 2011. Examples of *MI level 4* are the tsunami disaster in the South East Ocean in 2004 and the earthquake in Haiti in 2010.

Even though an internationally uniform terminology is desirable, there will probably be variations in definitions between countries, based on differences in resources, potential scenarios, community structure, culture, and traditions. Regardless of terminology, it is important that the definitions used are not only a theoretical construction of words, but practical and useful for basing decisions and performance in such situations, and they should be well known to health care staff at all levels.

4.2 Risks of MIs in Modern Societies

It has been clearly shown that the possibility of situations where available resources are insufficient for immediate medical care has increased significantly during the past decades and continues to increase in parallel with the development of the community:

- The *global population* has increased from 1.6 to 6 billion people during the past century, and with the current annual increase of 1.33 %, the calculated number for the year 2050 is 8.9 billion, which is a risk factor in itself.
- *Continuing urbanization* means increasing numbers or people in crowded areas, both for permanent living and gathering for different public events. Such areas are also a potential target for terrorist actions.
- *Increasing movement* of people, whether permanent or by travelling. As an example, of the 9 million inhabitants of Sweden, more than 400,000 are in other countries at any given time of the year, in many cases, traveling in areas known to be a focus of natural disasters and/or terrorist activity.
- Production, transport, and use of *hazardous material* has greatly increased over the past decades; only in Sweden, 18 million tons of flammable, explosive, chemical, or toxic agents are transported over roads every year, with an additional 3 million tons transported by rail.
- Hazardous material also includes *radioactive substances* that modern society has been increasingly dependent on for supply of energy, which involves risks that cannot be ignored.
- *Global terrorism* has apparently come to stay, partly replacing armed conflicts. This means that at any time, at any place, regardless of active involvement in any conflict, and without warning, we can be faced with large numbers of severely injured people. The goal of the terrorists is to gain attention for their own interests, with killing being the easiest way and having the biggest effect, regardless of whether innocent people are killed.
- Even if the risk for a global war has decreased temporarily, history speaks for itself, and *armed conflicts* are continuously occurring all over the world and will probably continue to occur, with increasing political tensions, accelerated by increasing divisions between poor and rich populations.

- It is today agreed that the ongoing climatic changes have generated an escalation of so-called *natural disasters* and that the effects of such disasters with regard to loss of health and life have the potential to increase, subsequent to the increased global population and increased concentrations of people in limited areas.

The World Disaster Report 2007 showed a 60 % increase of occurrence of incidents defined as "disasters" during the decade 1997–2006. During that period, the reported deaths from such incidents increased from 600,000 to more than 1,200,000, and the number of affected people increased from 230 to 270 million.

Reviews of MIs occurring in the world during the past few decades clearly show that wherever we live or work in the world and however safe and peaceful the area may seem, we can at any time face a situation requiring all the knowledge and preparedness described below to be able to reduce loss of health and life, as well as suffering, of people who depend on and trust the competence of experts in this field.

For a review of recent MIs, experiences, and lessons learned, the reader is referred to text books on medical response to MIs.

4.3 Demands on Health Care in Major Incidents

Parallel to the increasing risk for MIs wherever we live in the world, we can – as a paradox – identify an *increased vulnerability of our health care system* to these kinds of situations.

- Reduced reserve capacity because of increasing demands on efficiency, with continuous optimal utilization of all available resources
- Increased dependence on advanced technology
- Increased specialization, with reduced ability to deal with conditions outside one's own specialty

The goal of the health care system during MIs is to *reduce* (*as far as possible*) *or eliminate loss of life and health and physical and psychological suffering as consequences of the incident*.

The following are required to achieve this goal:

- Relocating of available resources to where they are most needed and rapid mobilization of additional resources (personnel and material).
- Optimal utilization of available resources by accurately prioritizing between patients and diagnostic and therapeutic measures and the use of simplified methods for diagnosis and treatment.

Relocation and mobilization of resources require *planning and preparedness*, including a prepared structure for coordination and command, defining the positions responsible for decisions on different levels.

Optimal utilization of available resources requires *education and training* for all the staff involved in responding to the incident, possibly the most important part of preparedness.

Planning, education, and training require *development and research* within this field, as in all other fields of medicine.

4.4 Prehospital Response

4.4.1 Demands on Prehospital Response in MIs

This situation is different from the "normal accident" where an ambulance (at least within a short time) can be expected to be available for every patient needing transport, with a varying number of patients now having to wait for transport. Evacuation may be delayed by time-consuming extrication, difficulties in obtaining access to the scene, and/or lack of rescue staff in relation to the need. All these points generate a need for *additional medical functions* at the scene:

- Leading and coordinating the medical activities at scene in conjunction with other organizations (rescue service, police);
- Continuous communication with the medical coordination center (the alarm center, ambulance dispatch center, or regional medical command center, depending on local organization), reporting expected need for care, and requesting resources according to needs;
- Triage on the scene (i.e., deciding in what order the patients should be treated and evacuated);
- Treatment at the scene because evacuation is delayed, but also because treatment may permit lower priority for some casualties, saving ambulances for those requiring immediate hospitalization;

- Transport to hospitals, with estimation of available hospital resources, which requires communication with a coordinating medical center.

These demands result in an immediate need for medical staff at the scene who (1) can lead and coordinate the work according to the above and (2) can start triage as a basis for transport priority.

Regardless of organization, these tasks are always primarily performed by the crew of the first ambulance at the scene.

Incidents with many casualties and/or delay in evacuation require additional medical staff at the scene for the tasks described above. Planning for MIs must include preparedness for them. It is important for the medical officer in command at the scene to identify such needs at an early stage so that prehospital teams can be mobilized for this function and ambulance crews can instead be utilized for transport.

4.4.2 Structural Variations Among Countries

The type of organization on the scene naturally varies among countries depending on structural differences among communities with regard to involved participants and their responsibilities, national traditions, geography and culture, economy, and political system. However, the basic principles are the same and will be described based on what is common practice in at least most European countries, but also with emphasis on where alternative ways of organization may exist. Some basic rules that are important to follow regardless of type of organization will be particularly emphasized, as well as the most common mistakes.

A concept that will be referred to, because it is frequently used in European courses in this field, is the Major Incident Medical Management and Support (MIMMS) concept, originating from the United Kingdom. It is influenced by British organization, which differs somewhat from the organization in Central Europe, but parts of it are valid for any organization and it is educationally well presented, using acronym-based poems to support memory in critical situations.

It is important that all medical personnel who might be deployed for work at the scene of MIs are familiar with their own local organization, have postgraduate education and training in the positions they may be expected to have in a MI.

4.4.3 Terminology

As the organization at the scene varies on some points between countries, there are also variations in terminology. With the aim of avoiding continuous repetition of alternative terminology, which can cause confusion, only one form of terminology will be used in the following text, explained below with mention of alternatives. Regarding organization, it is important for all medical personnel to learn and use the terminology adopted in their own country; hopefully it will be possible sometime in the future to come to an agreement on an internationally uniform terminology.

MIC Medical Incident Commander. Leads and coordinates the medical work at the scene. Alternative term: *Ambulance Incident Officer*.

RIC Rescue Incident Commander. Leads and coordinates the rescue work at the scene. Alternative term: *Fire Incident Officer*.

PIC Police Incident Commander. Leads the police work at the scene.

TRO Triage Officer. Medical officer responsible for the primary triage. The term is not used in all organizations.

ALO Ambulance Loading Officer. Leads and coordinates transport of casualties from the scene. Alternative terms: *Transport Officer*, *Transport Leader*, *Chief of Transport*.

RMC Regional Medical Command Center. Leads and coordinates the whole medical response to the incident. In some countries, this is a specially prepared function staffed by medical and administrative officers. In other countries, this function is covered by other organizations: *Alarm Center*, *Ambulance Dispatch Center*, or a defined hospital in the area, and in some countries it does not exist.

RVP Rendezvous Point. Point where all incoming units in the rescue action are directed to stand by for access to the scene. Alternative terms: *Check Point*, *Break Point*.

4.4.4 First Unit at the Scene

4.4.4.1 The First Report

The first unit at the scene always has an important role, even more so in MIs. Regardless of what type of information has already been relayed to the coordinating center, this will be the first report from medical staff,

which is of critical importance for further activation of the entire medical response chain: Mobilizing transport facilities, equipment and prehospital teams, and alerting hospitals. Delay in this report will cause a delay in the response that can have fatal consequences for the victims of the incident.

The first report is commonly referred to as "Window report"–*it should* ***not*** *try to be complete*, but is *only a primary indication of how great the need for medical care is expected to be*, and therefore in many cases can be based on what can be seen through the window of an arriving vehicle. Possible information at this stage may be restricted to "*Many injured, probably many dead, need both medical support at scene and transport facilities*"–enough to pull the trigger for MI and start activation of the medical response.

According to the MIMMS concept, the acronym-based word for the first report is *METHANE*:
*M*ajor incident declared (or standby)
*E*xact location
*T*ype of incident
*H*azards
*A*ccess
*N*umber of casualties
*E*xtra resources

This concept is used as standard in some countries, but is not always easy to translate into other languages. It is based on the British system where the first ambulance crew may declare a Major Incident, whereas in many countries this is the responsibility of a coordinating medical center. The difference may be of theoretical interest; the probability is that no coordinating center would object if the first arriving ambulance evaluates the situation as a MI. However, *it is important that it is clearly stated in the disaster plan to which position the authority* (*and responsibility*) *to declare a MI is connected*, *so that confusion on this point does not delay the decision and thereby the alerting of resources*.

If an MI is apparent and immediate contact cannot be established with the coordinating center, the first ambulance crew at the scene should act according to the action cards for MI (see Table 4.1) until contact has been established.

Table 4.1 Action card for medical incident commander (example)

Action card MIC
1. *Deliver window report* to alarm center (rough estimation of number of casualties, estimated need of transport and medical care on scene)[a]
2. *Confirm MI*. If MI is not already declared but apparent on arrival, inform alarm center, act according to MI until contact from *RMC*[b]
3. *Park ambulance*, take on *tabards* for *MIC* and (other crew member) *TRO*
4. *Contact RIC* (if arrived) direct or by Channel X
Request information about:
Estimated number of injured and dead
Risk zones(hot, warm) and other risks at the scene
The most urgent need of care
Required and expected resources from rescue service
Decide together with RIC location of casualty-clearing and ambulance-loading zones
5. *Decide* if incoming ambulance crews should be retained at the scene for medical support, and if so how may and for which tasks
6. *Dispatch* TRO to start primary triage according to action card
7. *Make quick survey* of the scene and:
Estimate again number and severity of casualties
Need of support in injury zone (trapped). Identify urgent needs
8. *Decide Level of MI* as guideline for medical work, inform all staff and re-evaluate this level continuously
9. *Contact RMC* Channel X (if no contact with RMC, Alarm center or ADC) and:
Deliver second report based on the information above
Request prehospital teams to scene if needed
Request helicopters if needed and not already alerted
Request distribution key for transports to hospital
10. *Start transport* of patients triaged by TRO. Until distribution key given, start to send severely injured according to:
Six to Major City University Hospital
Four to Small Town Regional Hospital
Two to Small Town County Hospital

(continued)

Table 4.1 (continued)

Action card MIC
11. *Organize casualty-clearing and ambulance-loading zones* for primary and secondary triage and dispatch teams according to that, and also teams to injury zone when needed (to risk zone = not without communication with RIC)
12. *Appoint ALO* for transport coordination
13. *Repeat contacts with RMC*, update reports from scene, request updated distribution keys, request additional support and equipment when needed
14. *Maintain contact with RIC and PIC*, in big incidents establish Command Place
15. *Decide* "*MI* Stand Down" on scene in agreement with RMC when all injured are evacuated. Inform RIC, PIC, and all medical staff at the scene. Lead *debriefing* for all medical staff before departure from scene

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[a]If "METHANE" is used as guideline for this report, insert it here
[b]In some countries, MI is declared by the first arriving ambulance at the scene

Fig. 4.1 The crew in the first ambulance at the scene in a major incident takes the roles of Medical Incident Commander (MIC) and Triage Officer (TRO). They wear tabards with these markings, available in all ambulances, unload medical equipment needed on the scene, and follow the action cards for these positions, also available in all ambulances (Table 4.1). Their ambulance is not used for transport but stays on the scene as a *command ambulance*, in some countries indicated by keeping the blue light on (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, with permission)

4.4.4.2 Taking Command

When an MI is declared, the first arriving ambulance will not be involved in transport of casualties, but will stay at the scene. One of the officers will take the role of *Medical Incident Commander* (*MIC*) and the other, the primary role of *Triage Officer* (*TRO*) and immediately prepare the ambulance loading zone and triage the first casualties for transport to the first available ambulances.

In some organizations with very good access to ambulances, both officers in the first ambulance take administrative roles, but with such an urgent need of medical care at this stage, it is often difficult to have two administrators.

In most organizations, the ambulances are equipped with tabards labeled with the positions referred to above (Fig. 4.1). The labeling may vary between countries, but the most generally internationally accepted colors for medical staff are green and yellow. The figure also illustrates the need of personal protection clothes and is valid for all medical staff working in the field.

The MIC should have a prepared *action card for MIC* telling what steps to take, and in which order (see Table 4.1). Such action cards should also be included in the equipment of all ambulances.

The acronym-based word used in the MIMMS concept to summarize the contents of the action card is *CSCATTT*, standing for "*C*ommand, *S*afety, *C*ommunication, *A*ssessment, *T*riage, *T*reatment, *T*ransport". This can be good support for memory if the action card is lost or not found.

Fig. 4.2 Police Incident Commander (*left*), Rescue Incident Commander (*middle*) and Medical Incident Commander (*right*). These officers constitute the Command group at the scene and stay in continuous communication during the response, and a command place is usually established that can be at a vehicle or, in extensive incidents, in a special command wagon (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, with permission)

4.4.4.3 Coordination with Collaborating Agencies

The leader of the rescue operation in most countries is the officer in charge of the first fire brigade that arrives, the *Rescue Incident Commander* (*RIC*), and in some countries the officer in charge of the first police unit to arrive, the *Police Incident Commander* (*PIC*). In some countries, the rescue leader has overall command of rescue operations, whereas in others, every organization involved is on its own. This difference is mainly theoretical because no chief of rescue or police would give orders with regard to medical care, and medical staff naturally respect the advice of police and fire brigade with regard to security matters.

Regardless of organization, the *RIC* has authority to request any type of resource needed for the rescue work, including private property (even if he/she has to answer for it afterward).

If the *RIC* (in most places clearly marked with tabard and helmet [see Fig. 4.2]) has arrived at the scene before the first ambulance, one of the first steps is to establish contact, request available information (Table 4.1), request resources for medical care, and agree on location for triage and ambulance loading zones, which should be as close together as possible, but outside potential risk zones.

The *RIC*, *PIC*, and *MIC* normally constitute the *command group on the scene*. In complex incidents, or incidents extended in time, a command center is established from where this command group can coordinate the operation.

4.4.4.4 Safety

The *MIC* is responsible for the safety of the medical staff, and a dead or injured medical officer is of no benefit to the victims. Communication with the *RIC* with regard to possible risks in the area (Table 4.1) is mandatory as a basis for dispatching medical staff onto the scene.

The rescue service commonly uses the terminology *hot*, *warm*, and *cold* zones:

Hot zone = risks for life and health so high that only rescue staff with special equipment and training should go in (fire, smoke, or high concentrations of hazardous material).

Warm zone = medical staff can go in, but only if they are wearing protective equipment and are trained for it (smoke or hazardous material in concentrations so low that simple protection equipment is sufficient).

Cold zone = no risks requiring special equipment or training (not excluding other risks).

In some countries, the *RIC* decides who is allowed to enter warm or hot zones; in other countries the *MIC* decides on medical staff, but should nevertheless respect the advice of the *RIC*.

In incidents caused by, or involving, criminal activities such as terrorist attacks, riots, or gunfire, the police are also responsible for security and making decisions

with regard to which zones can be entered by rescue and health-care staff without risk of being injured from such activities.

4.4.4.5 Overview of the Scene

Before delivering the next report, the *MIC* should make a *quick scene reconnaissance* (1–3 min) to get the first medical overview of the scene and identify urgent needs of care such as need for medical support for extrication of trapped, and make a preliminary estimation of the number of severely injured. This offers a personal knowledge of the conditions at the scene, valuable as a basis for leading the work and for dispatching medical staff within the area.

In bigger incidents, the *RIC* usually organizes the scene in *sectors* (part of a building, one or more wagons in a train) with a rescue officer responsible for each sector. If there is a need for medical support at the scene, it would be wise to dispatch medical staff to make contact with the responsible rescue sector officers to obtain information and establish collaboration.

4.4.4.6 Second Report

The second report is the *confirming report*, coming after the first "window report". *It is important that this report come as soon as possible*. At this stage, the whole medical organization, triggered by the first alert, is awaiting more information as a basis for a decision regarding the level of alert and steps to be taken within every unit. Therefore, again, there should be no details, no attempts to give the anatomical distribution of injuries, just the information that can be extracted from communicating with other units at the scene, and from the rapid reconnaissance of the area.

4.4.4.7 Decision of Strategy for the Medical Work

At this stage, the *MIC* should be able to estimate the relation (or discrepancy) between the need for medical care at the scene and available resources. Based on this estimate a decision about strategy must be made: Is this a situation where the normal level of medical care can be maintained with the steps:

- taken as above (= *MI Level 1*: all potentially rescuable can be saved, what is called a *compensated incident*), *or*
- Is the load of casualties so high that the standard of care must be lowered to be able to save as many as possible (= *MI Level 2*: *decompensated incident*)?

It is difficult for medical staff at the scene to obtain the overview needed to make such judgments and this is therefore the task of the MIC. Decisions with regard to strategy should be clearly communicated to all the staff involved as a guideline for triage and can be changed, depending on incoming resources or initially undiscovered needs.

4.4.4.8 Establishing Continuous Contact with the Regional Medical Coordinating Center (RMC)

After following these first steps on the action card, the *MIC* should take a position where he/she is not involved in medical care or decisions with regard to triage and establish repeated contacts with the RMC to:

- Request information on hospital capacity
- Request additional support at the scene if needed (transport resources, equipment, staff)
- Report casualty load at the scene and departed transports

4.4.5 Building up the Structure at the Scene

4.4.5.1 The Need for Simplicity

As stated in Chap. 1, *simplicity is the key to successful management of MIs* and that is valid also for the operations at the scene. It should be remembered that the majority of MIs occur in densely populated areas with good access to ambulances and short distances to hospitals. The first ambulance is often at the scene within 5–15 min after the alarm and then the medical work begins, and with many ambulances within close range, the evacuation from the scene can (and should) start a few minutes later.

This does not allow time for building up a complex organization. Schedules of organization that are too complex with too many boxes, too many levels of command and decision, and too many ranks and titles, will involve a risk that "the war is over" before the organization is built up.

It is an understandable temptation to transfer experiences from a military organization to a civilian one because military personnel are (and must be) good organizers, using a clear and strict hierarchy. However, there are significant differences between the civilian MI and the combat situation with regard to (1) time for preparation, (2) demands on endurance:

- A war rarely commences without warning, which allows for a long preparation time. However, the organization must have the ability to run on a high

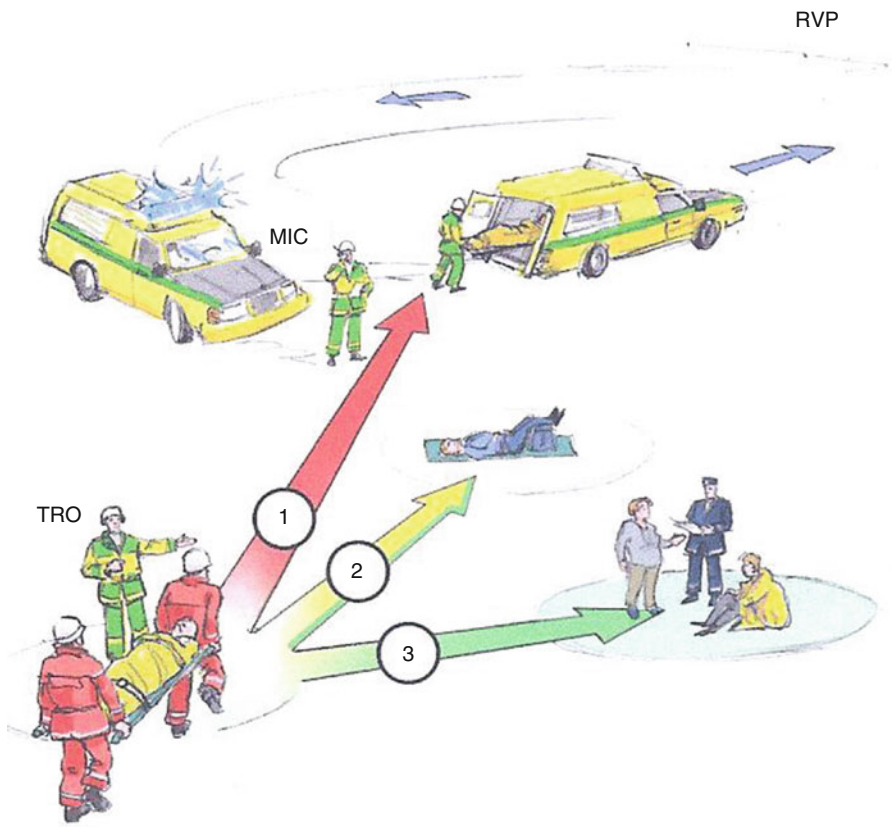


Fig. 4.3 The organization on scene is built up step by step, the first step when the first ambulance arrives. The Triage Officer (*TRO*) makes only a simple primary triage and sorts the patients according to three routes: (*1*) Severely injured, can go with available ambulance, necessary resuscitation done by ambulance crew. (*2*) Need ambulance transport, but can wait. (*3*) Do not need ambulance transport. The Medical Incident Commander (*MIC*) at this stage has the role as transport coordinator and decides the destination for the first patients. *RVP* Rendezvous Point (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012. Artwork Lats-Ake Pettersson, with permission)

capacity for a long time, days, weeks, months, or even years.

- An MI in peace time in a civilian community, on the other hand, occurs at any time, without any warning at all, and within a few minutes, an organization fully occupied with routine medical care must have the ability to deal with a number of severely injured, far exceeding available capacity, regardless of whether any of the available staff has any experience of such situations. However, the peak of the casualty load usually passes within a few hours (exceptions exist, of course).

This means higher demands on existing facilities than in the combat situation. There is no time to build up a new organization, only to adapt the existing organization to the specific demands of the MI.

4.4.5.2 The First Step: Starting Triage and Transport

The tasks of the first medical unit at the scene have already been described, illustrating that one of the officers in the first unit will be fully occupied with the important role of *MIC*.

At the same time, it is of critical importance that the transports to hospitals begin as soon as possible – "*no fully staffed ambulance should be standing waiting*", and the sooner they get moving, the sooner they come back.

Therefore, the triage process must start as soon as there are ambulances at the scene, and this is the reason to use the second officer in the first ambulance as primary triage officer = *TRO*.

The first step in organizing relief work, based on the presence of only one ambulance staff, is illustrated in Fig. 4.3. The *TRO* sorts the patients into three routes of evacuation: (1) Should go with the first available ambulance, (2) needs ambulance but can wait, and (3) injured but without need of ambulance transport. A very simple system should be used for this *primary triage*, for example *Triage Sieve* (see below under triage).

In this phase, the *MIC* may also have the role of transport coordinator and direct available (staffed) ambulances to hospitals. The principles for the distribution between hospitals are described below under "Transport".

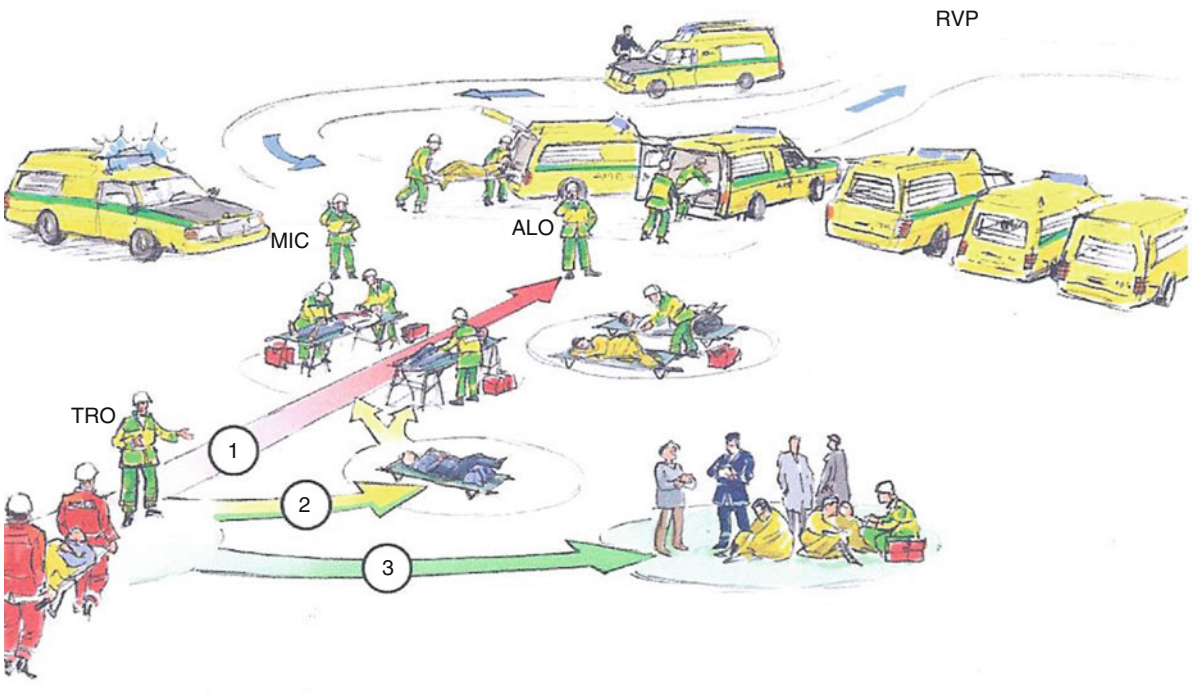


Fig. 4.4 When it is apparent that there are additional patients needing ambulance transport than there are available ambulances, the organization is extended with a *second step*: Patients who are not ready to depart, or cannot depart because of lack of available ambulance, now follow line (*2*) to teams devoted to necessary resuscitation/treatment and secondary triage before transport. An additional medical officer/team surveys patients waiting for transport, and another is dispatched for secondary triage/survey of patients estimated not to need ambulance transport. The *Medical Incident Commander* is now replaced by another ambulance officer having the role as Ambulance Loading Officer (*ALO*) (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012. Artwork Lats-Ake Pettersson, with permission)

As soon as casualties in route (2) begin to accumulate, or need surveillance, additional medical staff at the scene is mandatory and that is the task of the *MIC*. Thereby the organization is transferred to the next step.

4.4.5.3 The Second Step: Completing Casualty and Ambulance Loading

There is now access to additional medical staff at the scene, either ambulance crews from arrived ambulances or deployed prehospital teams (they usually take longer to arrive on the scene).

This means that the second route of evacuation goes to one or more teams for *secondary triage*, including measures of resuscitation needed before transport (Fig. 4.4). Two staff members in each such team are preferable to, for example, one ambulance crew, or a prehospital team with a physician and a nurse. For this secondary triage a system with better discriminative capacity than Triage Sieve is recommended, for example *Triage Sort* (see below under "Triage").

If there is congestion in the evacuation area and no immediate access to ambulances for high priority patients, staff are needed to attend to and help casualties awaiting transport (Fig. 4.4).

At this stage, evacuation of casualties not needing ambulance transport should also be begun, and they must be examined and re-triaged by medical staff before departure (Fig. 4.4).

The *MIC* should be released to assume the position of transport coordinator as soon as possible and replaced by another ambulance officer (*ALO*, Fig. 4.4).

4.4.5.4 The Third Step: Completing the Organization at the Scene

The Injury Zone

As mentioned above, the need for medical support in MIs is usually not restricted to the casualty-clearing

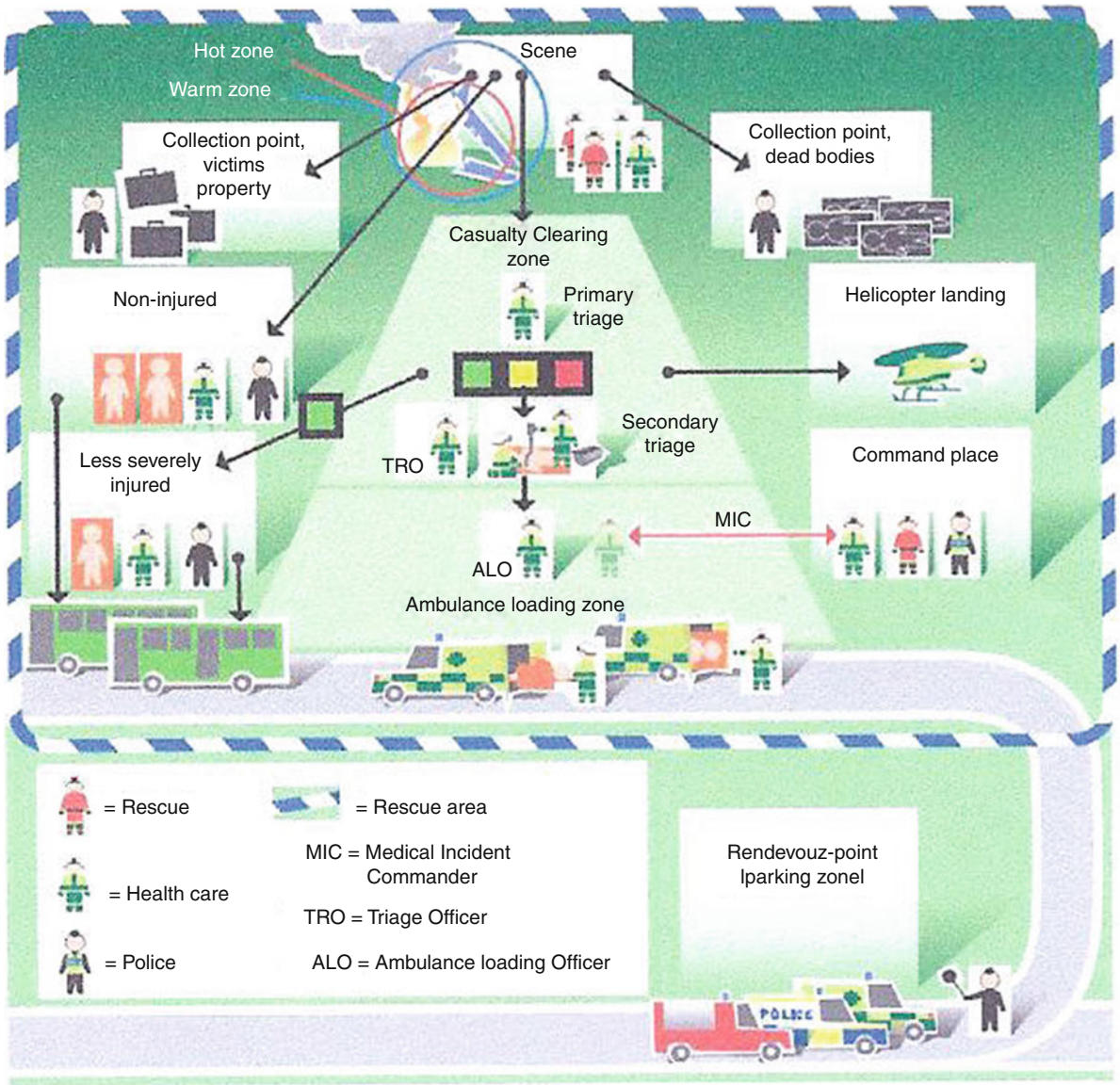


Fig. 4.5 The organization at the scene in a greater incident completely built up (see further the text) (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, Artwork Typoform, with permission)

and ambulance-loading zones, even if, as a general principle, the work should begin there to have the transport going as soon as possible. There may also be an urgent need for resuscitation and triage where the injured are located, the *injury zone* (Fig. 4.5) and may be in the wreck after an airplane, rail, or bus crash; in a collapsed building; or in an area of explosion. One of the objectives of the rapid overview of the scene performed by the MIC immediately upon arrival is to identify such needs and deploy staff to the location as soon as possible. Note that there can be *risk zones* (see above) within the injury zone; do not deploy staff there without communicating with the *RIC*.

Non-injured People

People who survive an MI without physical injuries are also victims. Exposure to a situation like this is a severe psychological shock for most people, and even if the reactions are not apparent immediately, they may appear later. In addition, many of the non-injured people may have lost contact with friends and relatives,

or seen them killed or injured, and they may have lost their property and/or be far from home. This group of people cannot just be sent away, but need to be taken care of.

Additionally, the same considerations are valid with regard to potential severe injuries here as for the group primarily triaged as "less severely injured" (see below): They should also be examined by a medical officer, if possible, before departing from the scene.

The police have the responsibility of taking care of those who were not injured. They must be registered and taken to a prepared zone where they can be given protection and obtain transport to a location where they can get psychosocial support, information with regard to lost friends and relatives, and help with further transport (Fig. 4.5).

The Dead at the Scene

Management of dead victims on the scene is the responsibility of the police. In most countries, only doctors are allowed to declare patients dead, unless death is apparent: Head separated from the rest of the body or the patient totally crushed or burned. Victims who are apparently dead should be left where they are found to facilitate identification and investigation by the police. For management of the dead, the reader should consult text books on medical response to MIs.

Other casualties without any signs of life should be labeled as low priority patients until they can be examined by a doctor and death confirmed. Note the hazard of differentiating between hypothermia and death: *In a cold environment*, *no one should be declared dead until warm and dead*! For triage and management of hypothermic casualties, the reader should consult text books on medical response to MIs.

Helicopter Landing Area

Helicopters are a useful resource in MIs, not only for evacuation of casualties (see below under "Transport") but also for transport of equipment and staff to the scene. In incidents where the benefit of helicopters is apparent and there is access to them, they should be alerted early for this purpose, and a *helicopter landing area* prepared and clearly marked out. It should be located at such a distance from the casualty-clearing zone that ambulance transport to the helicopters is not necessary, but not so close that it disturbs the work in the casualty-clearing zone (a distance of approximately 50 m is recommended for standard helicopters).

Cordoning Areas Off and Traffic Control

The first task of the police is to cordon off the area to prevent access to all traffic not involved in the rescue action.

If all rescue and transport vehicles arriving at the area should proceed into it, it would soon create a congested and chaotic situation where no vehicle can move. One of the first tasks of the incoming rescue leader is to decide a *check-point* or *rendezvous point* (*RVP*) in conjunction with the police: A place easy to identify on the map, well connected to routes for both entrance and evacuation, and with space enough to park waiting vehicles.

This point is often decided already before arrival of rescue units, based on local knowledge of the area, and information about it should be forwarded to all alerted units. Traffic control at this point should be handled by the police.

Figure 4.5 illustrates the principles for a fully developed organization at the scene of an MI, with many injured and need of medical support both in the injury zone and in the casualty-clearing and ambulance-loading zones. The figure illustrates a scene with immediate access to a road which is the case in most, but not all, MIs. Long distances from the injury zone to a road require off-road transport between casualty-clearing and ambulance-loading zones, which puts even higher demands on the rescue organization.

Inflatable tents can be life-saving measures in severe climatic conditions with delayed evacuation, but also involve a potential risk of congestion: They give the impression of being in a field hospital with a temptation to extend the treatment to more than is absolutely necessary before transport, which may create a congestion of waiting patients and also non-utilized ambulances (Fig. 4.6). *If tents are used*, *it is of vital importance that the structure and principles of working as described above are maintained*.

4.4.6 Triage

4.4.6.1 General Principles

Triage in MI situations must meet the following requirements:

- Triage is, and must be, *a dynamic process*, which means that it can and should be reevaluated at every stage in the chain of response and adjusted to:
  - The patient's condition
  - Effects of performed treatment

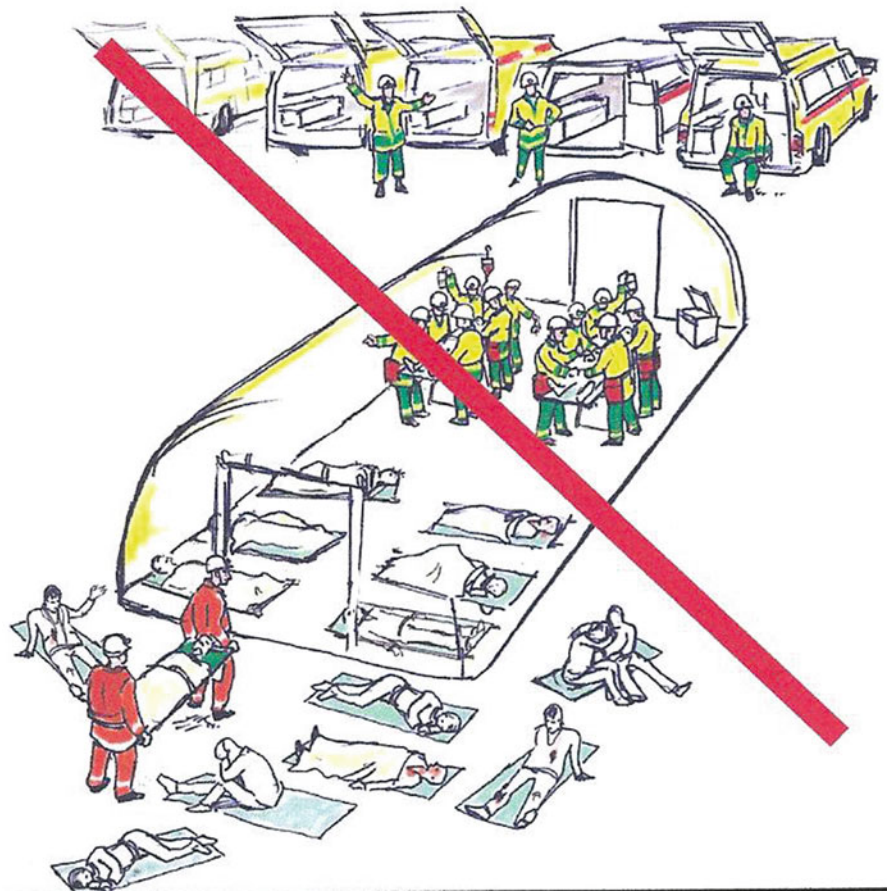


Fig. 4.6 The use of inflatable tents for protection of casualties and staff may be necessary in extreme climatic conditions and delayed evacuation. Even if such tents are used, it is important to maintain the simplicity of the structure and not fall for the temptation to overdo treatment with the feeling of being in a field hospital. What, as seen in this figure, could also be the effect of exercises performed without real times, giving the impression that everything can be done without consuming any time (From Lennquist S (ed) (2012) Medical response to major incidents. Springer, Artwork Lats Ake Pettersson with permission)

  - Position in the chain of response (prehospital, transport, different levels in the hospital response).

This means that a patient may be at different priorities at different levels of the chain of management.

- *Standardized systems* for triage, based on simple physiological criteria, make the triage more independent of the level of competence of the staff performing it, and may thereby be the method of choice in the front line of the response, where senior experience in most cases is not available.
- The *system used must be adapted* to
  - The level in the chain of management at which it is done
  - The competence of the responder doing it

This means that different systems may be used at different levels of the response.

- The *categories of priority must be clearly defined and a uniform terminology used* by all staff involved in the same incident. Internationally uniform terminology is desirable.
- The priority given to a patient must be *clearly marked* though it is *possible to change it rapidly and simply* according to the demand that triage must be a dynamic process.

4.4.6.2 Categories of Priority

The categories used today in most European countries, introduced by the North Atlantic Treaty Organization (NATO), are described in Table 4.2. Two different systems are used, depending on the MI level: The P-system in incidents corresponding to level MI 1, and the T-system in incidents corresponding to levels MI 2 – MI 4.

The *P-system* includes three categories:

- P 1 = Immediate treatment is required to save life
- P 2 = Severely injured, but can wait for a limited time (30–60 min)
- P 3 = Can wait without risk for life and health

The *T- system* includes five categories of priority:

- T 1 = As P 1 above, with the difference that patients with possibilities of survival considered very limited, are now referred to as category T 4 (see below)

Table 4.2 Triage classifications used by NATO

		Label	
Priority	Color	P-system	T-system
Immediate	Red	P 1	T 1
Urgent	Yellow	P 2	T 2
Delayed	Green	P 3	T 3
Expectant	Black/green	T 4	
Dead	White/black	T 0	

The P-system is used in incidents corresponding to MI Level 1 and the T-system in incidents corresponding to MI Levels 2–4

- T 2 = As P 2 above
- T 3 = As P 3 above
- T 4 = Can wait ("expectant"); Patients with very severe injuries where the possibility of survival is considered so limited that the resources they would consume for treatment should instead be used for those who can be saved.
- T 0 = Dead

4.4.6.3 Indication of Priority

There is currently a lack of agreement on an internationally uniform system and a wide variety of colors and symbols are used. This can be dangerous because the same color can have different meanings in different countries. For example, black is used for the category "expectant" as mentioned above in some countries, whereas in other countries it is used only for casualties declared dead by a doctor, and the consequences of misinterpretation are easy to understand.

Triage is a dynamic process, which means that the priority must be reevaluated – and changed when justified – at all stages in the chain of response. The system for indicating priority must then have the possibility to change in both directions: Upgraded or downgraded. There are still systems in use in Europe in which this is not possible and as a result, the triage process cannot be dynamic, which interferes with optimal utilization of resources.

Most systems for indicating priority are based on colors. At a workshop held already during the First Congress of the World Association for Disaster and Emergency Medicine (WADEM) in Mainz, Germany in 1977, the following colors were agreed upon:
Red: Immediate
Yellow: Urgent but can wait
Green: Shall wait
Black: Dead

Since that time, the need of a fourth category has been increasingly recognized, particularly in MI levels 2–4: Casualties with such small possibilities of survival that the resources they would consume for treatment should be used for those who can be saved, as described above. In the NATO system they are categorized as "T4" and are labeled with black and green. In the British system, they are categorized as "Expectant" and labeled with blue color. Most European countries have adopted the British color system, in part influenced by the MIMMS courses, but also by the fact that the color blue offers a better contrast to the other colors.

The introduction of this fourth category is not without controversies and many countries have still not introduced it but it has gained an increasing support in recent years and has been considered justified, particularly in MI levels 2–3. A reasonable European standard would therefore be to add this fourth category:
Blue: Expectant (= shall wait, as long as resources do not permit curative treatment of all casualties)

How these color indicators are applied to casualties also widely varies among countries and among regions; therefore, an internationally uniform standard would be desirable. As already mentioned, it should be a system that permits easy change of priority in both upgrading and downgrading, and disqualifies many systems used today. For different examples of priority markings the reader is referred to text books on medical response to MIs.

4.4.6.4 Triage in Incidents of Physical Trauma

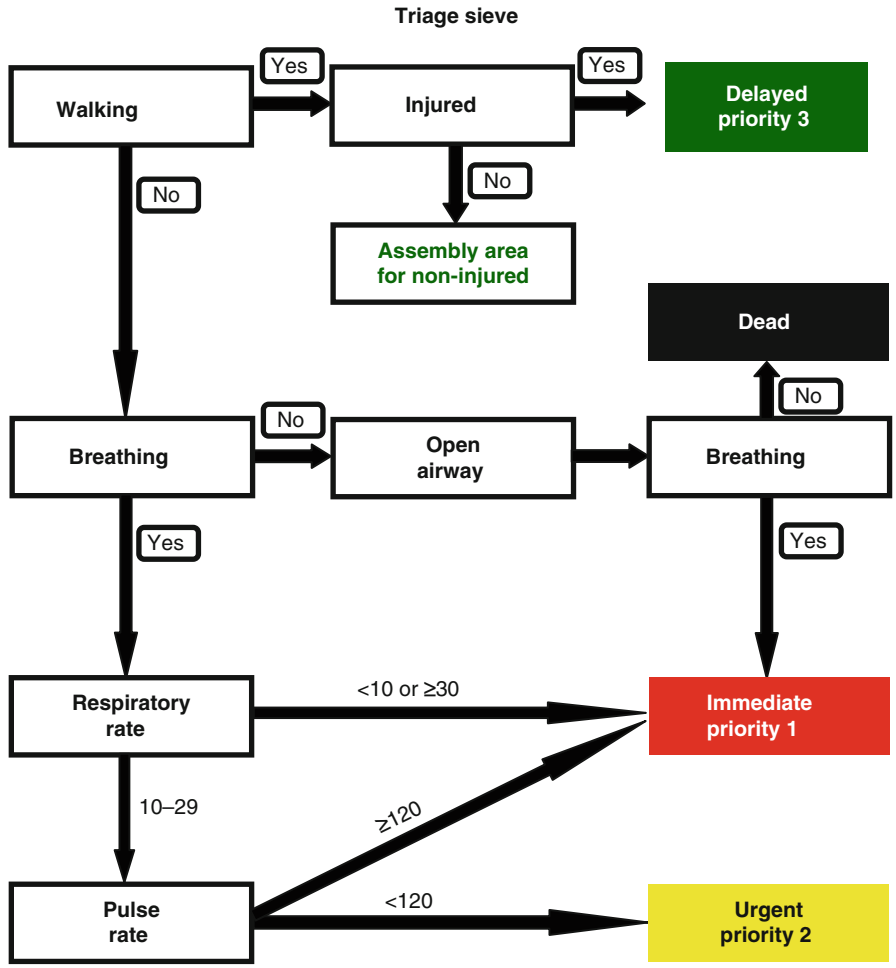
Triage at the scene of MIs caused by physical trauma is typically done in different steps according to the structure illustrated in Figs. 4.3, 4.4, and 4.5.

Primary triage by the primary TRO (or team) with the aim of

- Sorting out those who do *not* need ambulance transport
- Give those who *need* ambulance transport priority for either
  - resuscitation at the scene and secondary triage, or
  - resuscitation and departure in immediately available ambulances.

This primary triage can be based on very simple criteria such as sorting those able to walk from those who are not, or by using a system based on simple criteria

Table 4.3 Algorithm for triage sieve. This method is based on simple physiological criteria and is suitable for primary triage. The original version was based on capillary refill, not always easy to determine under field conditions; the figure illustrates a modified version based on pulse rate



From TG Associates, with permission

of the patients' condition ("physiological triage"), for example *Triage Sieve* (Table 4.3). This can be done quickly and also by a person with limited medical experience, if no experienced staff is available. However, it must be emphasized that this is only a first rough categorization and *those given low priorities in this primary triage must be re-evaluated before evacuation*: Even a patient with dangerous internal bleeding can primarily be walking.

Secondary triage, by the next triage teams, with the aim of:

- Performing a secondary and more thorough examination and evaluation of the victims' condition
- Perform resuscitation and the treatment necessary before transport
- Confirm or adjust priority, based on the results of the above steps, also considering access to transport facilities and estimated time to hospitals.

At this level, a triage system with a higher discriminative capacity is preferred, for example *Triage Sort*, a physiological triage system based on the Revised Trauma Score (Table 4.4), and, if possible, combined with "anatomical triage" (see below).

In incidents with many casualties and/or limited access to transport resources, it may be necessary to *re-evaluate priorities before transporting*, as a basis for the order in which patients should be evacuated. If possible, this triage should be *anatomical* (i.e., based on injuries possible to diagnose at this level and consideration of the potential clinical course of the

Table 4.4 Algorithm for triage sort, based on revised trauma score

TRIAGE SORT

Physiological Variable	Value	Score
Respiratory rate	10-29	4
	>29	3
	6-9	2
	1-5	1
	0	0
Systolic blood pressure	>90	4
	76-89	3
	50-75	2
	1-49	1
	0	0
Glascow coma scale	13-15	4
	9-12	3
	6-8	2
	4-5	1
	3	0

A total score of	12	indicates	T3
	11		T2
	10-1		T1

After Champion et al. (1989)

injuries). This requires clinical competence and experience in trauma. Recently published comparisons between anatomical and physiological triage have shown that anatomical triage performed by staff with such competence gains a better outcome, which emphasizes the importance of bringing such staff to the scene in incidents where delay in evacuation can be expected.

For the principles of anatomical triage for different injuries on different levels in the chain of management, the reader is referred to text books on medical response to MIs.

4.4.6.5 Triage in Scenarios Other than Those Caused by Physical Trauma

For triage in incidents caused by fire or toxic gases, cold and wet climate, hazardous material, irradiation, nature and climate, and infectious diseases, the reader is referred to text books on medical response to MIs.

4.4.7 Indications for Treatment at the Scene

How much medical treatment should be offered on the scene? Is it not a better option to get the injured to the hospitals as soon as possible, where the facilities for diagnosis and treatment are always far better than in the field?

There is an old, and still on-going, debate with regard to which is the best strategy in MIs:

- *Load and go* (*or* "Scope and run") = Transport the patient from the scene without any delay caused by treatment that not is immediately necessary to save a life
- *Stay and stabilize* (*or* "Stay and play") = Not only life-saving, but also more advanced procedures on scene with the goal to
  - Get the patient in the best possible condition before transport
  - Make it possible to give lower priority to some patients, saving transport facilities for those with more urgent need.

As in other fields of medicine, the truth is not black and white: Selection of a strategy must be adapted to the situation, and what is right in one situation might be totally wrong in another. Factors influencing the strategy in MIOs are (in addition to the patient's condition):

- Time to hospital
- Access to transport facilities
- Access to resources on scene

The need of simple, life-saving procedures before transport is apparent and not controversial: Clearing and securing of airway, stopping major external bleeding, simple shock prevention, immobilization of fractures. The controversies apply to more time-consuming procedures such as intravenous lines, intravenous fluids, and tracheal intubation. Such procedures can however be both justified and of critical importance when:

- Expected transport time to hospital is extensive (>30 min as a guide-line)
- Delayed evacuation form the scene (trapped patients and/or many injured)
- Limited access to transport facilities (waiting time for ambulance/helicopter)

When the transport time is <30 min, prehospital intravenous fluid hardly has any effect, then it is better to get the patient to the hospital quickly. Overuse of fluids such as crystalloid solutions can also have negative affects. In case of extensive internal bleeding, the only possibility to save a life may be to get rapid surgical control of the bleeding in the hospital, and any delay might be fatal.

However, as stated above, in the "normal" accident there are also situations where more advanced

prehospital treatment is justified. Increasing ambulance crew competence and having them be better equipped has made that possible. Equally important as the skills for performing treatment in these situations is the ability to make accurate decisions with regard to what to do, and not to do. A good rule to follow is: "The hospital is always the best place for the severely injured patient, and if you stay out there to do things before transport, you must have a very good reason for it".

In *MIs* on the other hand, many of the indications for the more extensive prehospital treatments listed above may be present:

- The transport times to hospital are longer because it may be necessary to send patients to hospitals of longer distance from the scene for capacity reasons
- The evacuation from the scene is delayed because of trapping, limited access, or a high number of casualties in relation to available staff
- The available transport facilities are insufficient in relation to the need

Therefore, preparedness for MIs should include preparedness for treatment of casualties on scene, both with regard to competence and equipment. Good medical competence is also of critical importance for triage of casualties for the most effective utilization of available resources.

For indications and principles for prehospital treatment of different injuries in MIs, the reader is referred to consult text books on medical response to MIs.

4.4.8 Transport of Casualties

With regard to evacuation of casualties from the scene in an MI situation, there is an old misconception that the only important thing is to get all the patients evacuated as soon as possible and when all the patients are in hospital, all the problems are solved. This kind of thinking does in fact still exist. One reason for it is that MI-exercises often stops at the hospital entrance because of practical problems in bringing casualty-actors into the hospital. This means that no one knows what would have happened to all these patients if they really had been brought to hospitals according to the information in the records.

Another reason is that the development within the health care system during the last decades has not been recognized by the prehospital organization. Going back 20–25 years, the situation in the hospitals with regard to capacity for unexpected high loads of casualties was different: It was much easier to find available room and ventilators, and many patients in the wards were in such a condition that they could be sent home earlier if needed. The increasing demands on efficiency (parallel to increased costs for health care) have led to every resource being optimally utilized: During office hours every room in a big hospital is occupied, often for time-consuming heavy surgery, every ventilator in the ICU is in use, and hospital beds are used only for those needing advanced care or surveillance.

If a patient needing immediate surgery or ventilator use arrives at a hospital with no room or ventilator available, the patient may be lost – even in a big hospital – because there is neither time, nor immediately available resources for secondary transport to another hospital.

This can never be understood if rescue exercises are limited to the prehospital part of the response. Every exercise should illustrate the whole chain of management, which can never be achieved without using simulation systems, which is the only effective way to illustrate the hospital response. Live field exercises might be justified, but should always include simulation of transport and hospital response in real times and with real resources.

To summarize, as a consequence of the current development within the health care system, it is of critical importance that the patient be directed to the appropriate hospital facility from the beginning, meaning a hospital where immediately needed resources are immediately available.

Figure 4.7 illustrates what can happen if this is not properly facilitated. An incident has occurred in an area with four hospitals within a relatively close range; all hospitals are alerted and activate their plans. The ALO wants to use the ambulances in the most efficient way and sends all of them to the nearest hospital, thereby getting them back quickly, and the scene can be evacuated in a relatively short time – with the problem over for the transport officer.

However, the nearest hospital in this case does not have enough ORs or ventilators for all patients needing them, patients are lost, while all ambulances are circulating between this hospital and the scene, and the other hospitals are not utilized.

Such a "maldistribution" of patients is one of the most common recently reported errors of MIs.

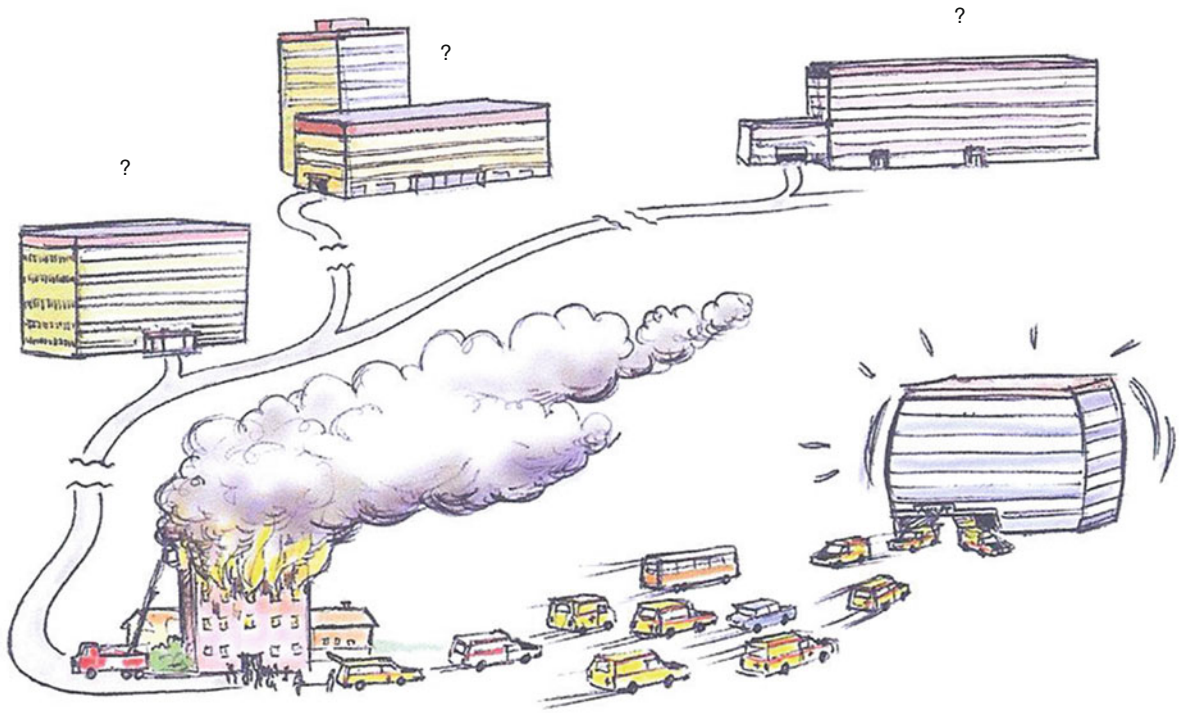


Fig. 4.7 An example of "maldistribution" of patients between hospitals. Instead of distributing the patients between the hospitals in the area of the incident considering hospital capacity, all ambulances are sent to the nearest hospitals to get them back quickly. Because "reserve capacity" for sudden high loads of casualties in hospitals today is limited, this will lead to mortality that could have been avoided (see text) (From Lennquist S (ed): Medical response to major incidents. Springer 2012, with permission)

To achieve an accurate distribution of patients among available hospitals with regard to their immediate capacity requires establishment of communication between the scene and the receiving hospitals as quickly as possible. Communication between the scene and every hospital is not realistic, considering the well-known difficulties of establishing a functioning communication under these circumstances. The communication must be mediated through a coordinating center that is well-equipped with communication lines and staffed by competent medical personnel. It is easier to establish communication with the command groups of involved hospitals from this coordinating center. This coordination is schematically illustrated in Fig. 4.8.

4.4.9 Registration on Scene

4.4.9.1 Medical Documentation

In most countries there is a legal obligation within the health care system to document treatment and decisions made by medical staff outside the hospital, and this is also an important part of patient management. There is still no internationally uniform system, and many countries do not even have a nationally uniform system.

The medical registration is a balance between the need to evacuate the patient from the scene as soon as possible and document as much as possible. As a principle, registration should not cause any unnecessary delay in evacuation; many of the cards used for documentation have space for a lot of information, and it must not be an end in itself. However, medication administered to the patient, including analgesia, must always be documented, and certain data are important for diagnosis and decision making later in the chain (i.e., level of consciousness in head injuries), but everything need not be filled in if it delays transport.

4.4.9.2 Identification and Destination

A part of the medical registration card that should always be filled in is the destination of the patient,

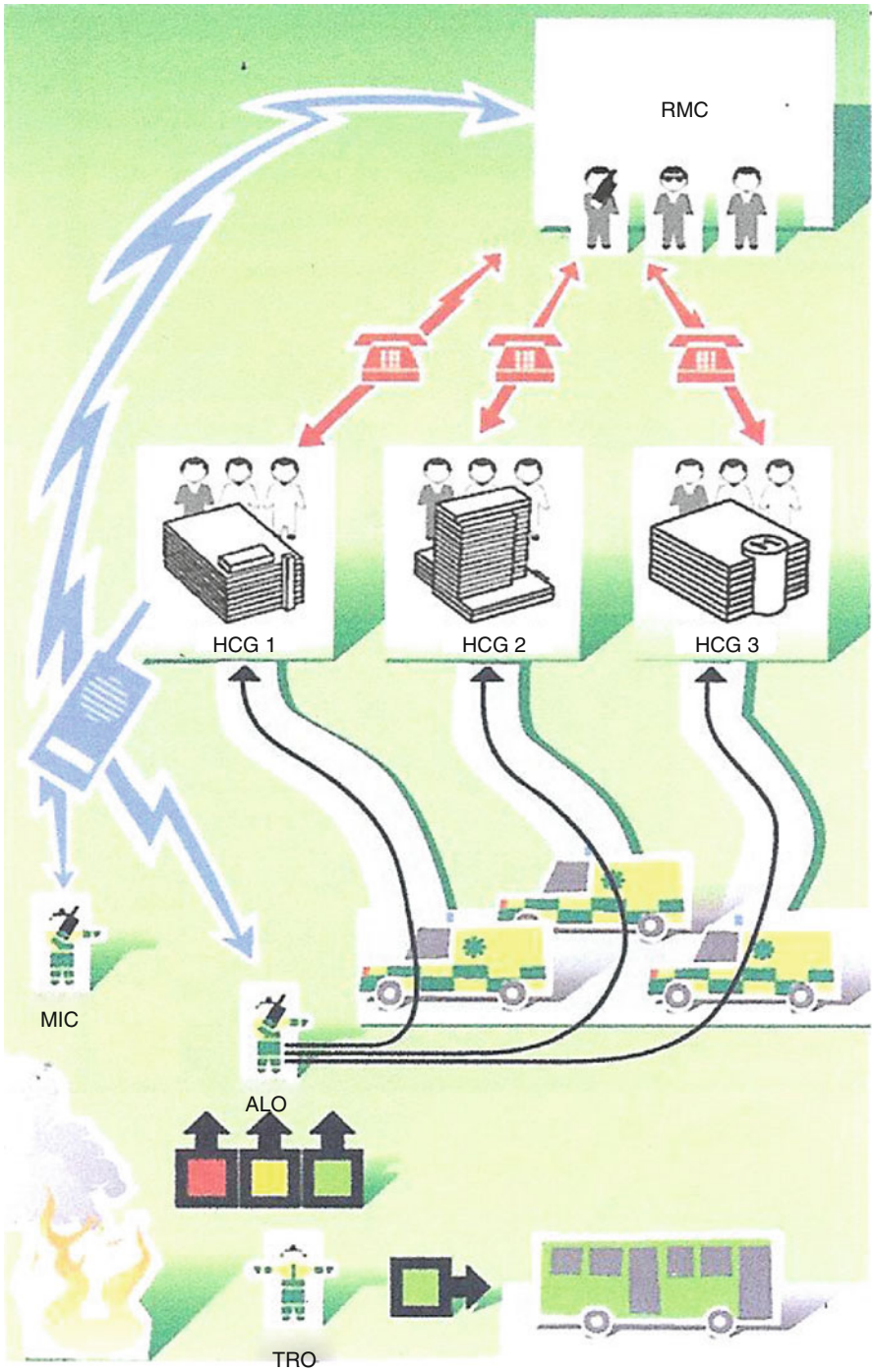


Fig. 4.8 Schematic illustration of the medical "command structure" and coordination of transports to hospitals. The Ambulance Loading Officer (*ALO*) has radio communication with the Regional Medical Coordination Center (*RMC*), which in its turn has telecommunication with the Hospital Command Groups (*HCG*). One of the tasks of the HCG is to report capacity for immediate treatment (room, intensive care unit) at latest 15 min after alert and then continuously after activating disaster plan. Based on this, *RMC* gives a "distribution key" for distribution of casualties between hospitals. A prerequisite for this is that both the *RMC* and *HCG* are based on medical staff on duty or on call (From Lennquist S (ed): Medical response to major incidents. Springer 2012, Artwork Typoform, with permission)

which is also the basic information to relatives. Every card usually has a registration number so if the name cannot be identified or given, the destination can be connected to the registration number.

It is desirable for many reasons that as many patients as possible are identified by name before departing, so that information with regard to which patient goes to which hospital (or another destination) is available as soon as possible. In a heavy load of casualties, it is not practical to assign this task to medical staff. In most countries, this is done by the police. A common registration system for police and medical staff should be a natural goal, but has so far been possible to achieve in very few countries. The police also have the task of

registering non-injured victims and those dead on the scene.

Whichever system is used, it is of critical importance that the registration does not delay the evacuation from the scene; the organization responsible for this must devote sufficient resources to avoid congestion at departure.

4.4.10 Communication

A functioning communication is an absolute prerequisite for a successful MI response and this is valid for all organizations involved in the response. At the same time, the most commonly reported problems in the evaluation of MI response are failures in communication. These failures are of three different types:

1. Deficient functioning of available communication systems, for example, insufficient covering, overload of systems, or technical failures
2. Deficiencies in handling of these systems (human factor), for example, lack of training of medical staff in the use of communication devices or charging of batteries
3. Deficiencies in communication technique: Forget to report (common), unnecessary or unnecessarily long communication, deficiencies in verbal technique

As a golden rule, no organization should be dependent on one single system; alternative systems must be established and available and the involved staff must be trained to use them, which means that communication techniques must be included in the training of medical staff for these situations. For a description of the different available communication systems, and when and how to use them, the reader is referred to text books on medical response to MIs.

4.4.11 Special Considerations in Terrorist Actions in Areas of Violence

In civilian incidents caused by terrorist actions in regions with political tensions and continuous violence, there may be remaining threats on the scene immediately following the incident: Casualties, rescue staff, and medical staff may be exposed to threats even during the response (shooting, explosions). In such cases, safety must take priority and casualties must be evacuated as quickly as possible, even without triage and with minimal resuscitation at the scene.

For the special organization and considerations required for such situations, the reader is referred to text books on medical response to MIs.

4.5 The Hospital Response

4.5.1 Functions of Critical Importance for the Capacity of the Hospital

The capacity of the hospital to receive casualties from an MI is often referred to as the *surge capacity*, the capacity to receive a certain number of injured or critically ill per time unit. Which are then the most common factors limiting this capacity?

The continuously reduced number of *beds* available in hospitals, because of more and more efficient use of available beds, is often referred to as a limiting factor for this capacity. However, all available data show that *the number of beds is rarely or never the limiting factor*, there is always space, there are often supplies of extra beds and patients can even sleep on the floor on mattresses if necessary. Alerting staff not on duty will in most cases bring a sufficient number of staff to take care of a high load of extra patients needing in-patient care for a limited time.

The *emergency department* (ED) a not a limiting factor either. For the severely injured or ill, the ED is just a transfer station through which the casualties should pass as quickly as possible on their way to surgery, ICU, or other wards. The triage and primary treatment at this time should be led by staff with the highest possible level of clinical competence within the actual field; for example, in trauma, by specialists within the surgical and anesthesiologic disciplines; for less severely injured patients on the other hand, the ED is in many cases the final destination, but this category is less resource demanding and not a critical capacity-limiting factor.

Factors of critical importance for the capacity of the hospital are, *actually*, *surgical and ICU capacity*; *the number of available ORs and ventilators*, *and staff to handle them*. As already mentioned, every available OR-theatre is occupied during office hours in a big hospital by (often time consuming) surgery, and it can be very difficult to find a single ventilator for a patient needing it unexpectedly. If these resources are not

available for an injured patient needing them urgently, the patient may die.

Planning and preparing the hospital response must be based on the awareness about which functions are critical in reality, and staff representing these functions must have a major role in the process of planning as well as in the leading of the hospital response.

4.5.2 The Disaster Plan: Goals and Structure

4.5.2.1 Demands on a Functioning Plan

In most countries, there currently is a legal obligation for all hospitals responsible for and authorized to receive patients in the fields of trauma and emergency surgery and medicine to have a functioning disaster plan. A "functioning plan" means not only that there should be a written plan somewhere in an office, but a plan that is continuously updated and tested, and known by all staff potentially involved in the response to MIs.

To meet the demands of a functioning plan requires:

- A responsible committee within the hospital with authorization to request the involvement and contributions needed from all units in the hospital with regard to planning, preparedness, and education
- Informing all staff about the plan as a part of the employment process
- Systematic and repeated training of staff who have important functions in MI response

4.5.2.2 The Need for Simplicity

Equally important is to have a plan to avoid "overplanning": The goal should *not* be to build up a new organization, only to make necessary adjustments to the already existing organization to divert resources to where they by definition are insufficient (i.e., to the treatment of victims). The plan created must be one that can be activated in a few minutes, at any day of the year, and at any time of the day, regardless of who is on duty, and it must be simple:

Simplicity is the key to accurate and realistic planning!

A disaster plan should *not* be a "monument of words" built up through administrative ambitions. There are unfortunately many examples of plans that have been so extensive and complex that no one has taken time to read them, and so they cannot work. At evaluations after MIs, it can sometimes be heard: "Yes we had a plan, but we did not use it," and when you see the plan, you easily realize why.

4.5.2.3 The Content of the Disaster Plan

Plans may look different for various hospitals depending on variations in hospital size and capacity, geographic conditions, and local traditions and there is not, and probably should not be, any uniform "standard plan". However, the structure of the plan should be as uniform as possible, at least within the same country, both for educational reasons (staff is moving between hospitals) and to facilitate collaboration between hospitals during a response – everyone should use the same terminology. Involvement of many hospitals, possibly from different regions, in a response has also been increasingly necessary because of the reduced reserve capacity mentioned above. The following structure is recommended:

I. *General information*

This part should be read and known by all staff and therefore should be restricted to a maximum of five to ten pages. It should include:

- *Alerting the hospital*
  - How the hospital is alerted
  - What to do when receiving the alarm
  - Where to go when alerted
  - What to do when alerted
  - Cancelling of the alert
- *Levels of alert*
  Definitions and indications – when to use a particular level
- *Coordination and command*
  - Overall (regional) command of the response
  - Hospital command:

Who is responsible for a particular decision?

II. *Action cards*

Action cards should be created and available for all staff involved in the response. Every staff member must know the information on his/her own action card, but all action cards can be attached to the plan for information purposes.

III. *Information about special types of incidents, or those involving only specific categories of staff*

- Incidents involving hazardous material
- Incidents involving irradiation

- Incidents involving infectious diseases of biological agents
- Incidents involving large numbers of burns
- Incidents primarily involving the hospital
  - Threats
  - Fire
  - Technical disturbances

4.5.2.4 What Every Staff Member Should Know

As previously mentioned, *Part* (*I*) = "General information" should be known by every staff member and it is recommended that this part be included in the introduction at the time of employment. It is therefore important that this part not be burdened with information that is not absolutely necessary for all staff.

The next part that every staff member should know is his/her own *action card* (see below for examples). The action card for a certain position can be put in a visible place in the office, or as some hospitals do, given out laminated in "pocket format" to staff members in key positions.

All staff should also know where to find information about special types of incidents, including those primarily involving the hospital.

Some categories of staff need specific training:

- Those included in the hospital command group
- Those who might be deployed to prehospital teams (see Chap. 3)
- Those responsible for decontamination of victims from incidents with hazardous material or irradiation

4.5.2.5 The "All-Hazard" Concept

Even if the plan must include certain information about specific types of incidents, this does not mean that there should be specific plans for these types of incidents – this would make the planning much too complex. Instead, *the same structure of plan should be used in every kind of incident*: alert process, levels of alert, coordination, and command. However, staff with special functions in specific types of incidents (for example, decontamination) need special action cards for those types of incidents.

4.5.3 The Alert Process

4.5.3.1 Receiving the Alarm

An incoming alarm should immediately be connected to a defined position in the hospital, clearly described in the plan, usually the senior nurse on duty in the Emergency Department, who is always available. Her/his task is to:

- Collect and register information
- Transfer this information to the person (position) responsible to make decisions with regard to level of alert and to take primary command

In this situation it is easy to miss information of critical importance. The person receiving the alarm therefore should have a *check list for receiving alarm*, listing information important to record. If the receiver is the senior nurse on duty in the Emergency Department, the check list should be on the wall in her/his office along with the action card for this position.

In the MIMMS concept, the same acronym as used at the scene, METHANE, is recommended. It can be used instead of a check list, but is not entirely adapted to the need for information in the hospital; that is why a check list according to the above is recommended.

4.5.3.2 Decision of Level of Alert

It must be clearly stated in the plan which person (= position) has the authorization/responsibility to decide the *level of alert for the hospital* (see below).

In some countries, the alerting organization (RMC or Alarm Center) has this responsibility and if so, it should be included in the message of alert, and thereby also included in the check list of the receiving person.

In other countries, this decision is made by the medical officer primarily in charge in the hospital. This model is recommended, because this is the person who has immediate overview of the present situation in the hospital. For example, if an MI occurs during office hours when all staff are in the hospital and a number of room and ventilators happen to be available, a lower level of alert may be sufficient; in another situation outside office hours and with all available rooms and ventilators occupied, the same incident may require a higher level of alert.

Regardless of which position this responsibility/authorization is connected to, it must be clearly stated in the plan, and included on the action card for that position.

4.5.3.3 Further Processing of the Alarm

An alarm is spread within the hospital according to the principle of "rings-on-the water": The primarily alerted staff alerts other staff/positions, ending up by all alerted units alerting or calling in their own staff. For this purpose, regularly updated files with home telephone

numbers and alternative numbers should be available in all units. To avoid misuse of such lists, they can be kept safe (sealed envelope) until they are needed for this purpose.

To make processing of the alarm possible, it must be clearly stated on the action card for each position as to whom to alert further, with given paging and telephone numbers (see Tables 4.5 and 4.6). *An absolute prerequisite is that everyone should know where to find his/her action card, and that is a keystone in preparedness and education*.

4.5.4 Levels of Alert

To have just one level of alert (which still is the case in some countries) might appear as the most simple. However, this would mean that many steps would need to be taken as soon as there was a suspicion of an MI. The consequences of this would be either a number of "overalerts" (i.e., initiating many procedures that would turn out to be not needed) or absence of alert when it really is needed because of fear of overalert.

Avoiding this requires a system based on different levels of alert. There is still no internationally uniform standard. The system presented here is an example, originally developed by the author, and for many years used as the national system in Sweden and introduced in an increasing number of countries. It is used as a model in the Medical Response to Major Incidents (MRMI) courses organized by the European Society for Trauma and Emergency Surgery (ESTES).

This system is based on three levels of alert:

Green alert = "Stand by"
Yellow alert = "Partial mobilization"
Red alert = "Full mobilization"

4.5.4.1 Green Alert ("Stand by")

Used when:

An accident has occurred or a threat has come up, but it is not yet known whether or to what extent the hospital will accept casualties

Means:

- Activation of the Hospital Command Group (HCG)
- Information of critical functions in the hospital, simultaneous investigation of present capacity
- Report of present capacity of the RMC
- *Considering* "freezing" of planned treatments that can wait (done if something has happened, not in threats)

= *Green alert is minimally resource-consuming but increases the preparedness significantly and should be used with wide indications*

4.5.4.2 Yellow Alert ("Partial Mobilization")

Used when:

It is confirmed that the hospital will receive casualties, but within a limit that does not request full response.

Means:

As above plus:

- "Freezing" of all non-started treatments that can wait
- Alert of a (in the plan defined, and limited) number of emergency room nurses, emergency physicians, surgeons, orthopedic surgeons, anesthesiology teams (physician + nurse), and operating room nurses
- Alert of HCG support group (see below under "command & coordination")

Point (2) above depends on the size and location of the hospital and should be clearly defined in the plan. Example from a medium-sized hospital without emergency physicians in the organization (as in many places in Europe):

> 6 emergency room nurses, 4 surgeons, 2 orthopedic surgeons, 6 anesthesiology teams, and 6 OR nurses

Yellow alert is sufficient to cope with the majority of MIs during peace time (additional staff in key functions can be mobilized later, within this level, by decision of the HCG).

4.5.4.3 Red Alert ("Full Mobilization")

Used when:

It is confirmed or suspected that the hospital will receive a large number of casualties within a short time, requiring its full capacity.

Means:

As above, plus automatic alert of all available staff within emergency and supporting disciplines according to a prepared alarm schedule ("rings-on-the-water" system).

Red alert in a major hospital is a level to be used only on rare occasions = with a very high load of casualties expected and short distance to the scene.

4.5.4.4 The Need for Three Levels

Green alert is needed as a level to activate on very wide indications, as soon as there is even a small suspicion of an MI, and therefore it should remain as a level consuming minimal resources. A common mistake is to "burden" this level with additional steps, but that might create a hesitation to activate it and then the intention is lost. Just the steps included above significantly increase the preparedness for response by having:

- The HCG group in place and activated
- Critical functions (Emergency Department, OR, ICU) informed
- Capacity of critical functions investigated, ready to report to RMC

Yellow alert is clearly justified as being enough to cope with the vast majority of MIs during peace time.

Red alert, even if indicated only on rare occasions in a major hospital, is needed in situations where the hospital is expected to be flooded by casualties within a very short time; there is no time to think of what to alert or not, and *red alert* means automatic mobilization of large numbers of staff and other resources. It must be considered, however, that taking care of all incoming staff also consumes resources, and preparedness for this should be reflected in the action cards for *red alert*.

4.5.5 Coordination and Command

4.5.5.1 Demands on a Clear Command Structure

Most MIs occur in rural or densely populated areas with short distances to hospitals and good access to ambulances. The first ambulances are at the scene often 10–15 min after the alarm and the transport of casualties to hospitals can begin. The importance of getting the patient primarily to a hospital where requested resources are immediately available has already been emphasized. This means that transport of patients as soon as possible must be based on capacity reports from the hospitals. The HCG collects and delivers these reports. *The demand on the HCG should be that it is in action not later than 15 min after the alarm has reached the hospital*.

This means that the hospital response to MIs requires a well-prepared leadership structure based on staff who:

- Are immediately available during non-office hours
- Have a clearly defined responsibility as well as authorization to make the necessary decisions in the initial phase of the response
- Are trained specifically for this difficult task

4.5.5.2 The Medical Officer in Charge in the Hospital

Immediately available on a 24-h basis at a senior level are the senior physicians on call within surgical specialties, anesthesiology, or ED (if the hospital has emergency physicians). Who of these should be the primary Medical Officer in Charge (*MOC*) is not important; however, it is important that:

- It is clearly stated in the disaster plan to which position this task is connected
- Everyone holding this position should have special training for this difficult and important task

Many hospitals use the senior surgeon on call for this task for several reasons:

- He/she automatically has an immediate overview of the critical functions = OR and ICU
- The senior anesthesiologist is needed to prioritize the ICU and the senior emergency physician to prepare the Emergency Department, and the senior orthopedic surgeon is more likely to immediately be involved in patient management.

This is valid for the initial (primary) phase of the response. When more staff are called in, a more senior physician with more experience and also more training for this purpose often takes over the difficult role as *MOC*, especially if the response is extended in time.

4.5.5.3 The Hospital Command Group (HCG)

The *MOC should be the operative leader* of the HCG. The HCG should include administrative staff for support and for decisions with regard to economy and hospital security. Usually this *administrative officer in charge* (*AOC*) is a senior administrative officer available on call, who later may be replaced by the ordinary director/manager of the hospital. However, to make pure administrative staff responsible for the primary operative decisions is not realistic, considering the usually much longer response times for this category of staff.

Because of the many tasks connected to the HCG during the initial critical 15–30 min of the response, it is preferable to dispatch more medical staff to this group whenever possible. They can be senior medical officers on call in other specialties and the details vary among hospitals but, again, it should be clearly stated in the plan.

Fig. 4.9 Hospital command room (example). The room should be located centrally in the hospital, close to the Emergency Department, and always be prepared for action. The equipment should include telephones (internal lines + direct external lines), radio for communication with the ambulance services and, in case of failure in telephone communication, with the regional command center, computers, radio and television receiver to record media broadcasts, plotting boards with maps and disaster plans for the region and the hospital (see further the text) (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, with permission, Photo University Hospital, Lin Köping)

Secretarial staff specially trained for this purpose should also be working with this group as soon as possible.

Because staff in this position should have special training for this task, for a more detailed description of the coordinating functions in the hospital, the reader is referred to text books on MI response.

4.5.5.4 The Major Incident Command Room

It is mandatory that the HCG has a specially prepared room to go to, which is equipped with:

- Telephones for each staff member, both internal and direct external lines
- Communication – radio with channels for communication with the RMC, the MIC at the scene, and the ambulance service (see Chap. 3)
- Radio and TV sets for following information in the media
- Maps
- Disaster plans for hospitals in the region
- Prepared whiteboards for continuous documentation of information
- Computers

For an example of such a room, see Fig. 4.9.

It is important that the HCG staff go to this room immediately after the alarm. A lot of questions come up in the hospital, there is a need for somewhere to call, and many calls will come to the HCG room within the first minutes after the alarm. That emphasizes the immediate need for secretarial staff.

4.5.5.5 Medical Staff in Charge in Different Functions

During the MI response, it must be clear who has the coordinating responsibility for all critical functions in the hospital. It is one of the initial tasks of the HCG to define or appoint the leaders for different functions, in some cases a nurse, and in some cases a physician and a nurse. Such staff should be clearly labeled with tabards or arm badges.

Table 4.5 Action card for surgeon on duty (example)

Surgeon on duty
Alarm received by: senior nurse ED
When receiving alarm:
Contact senior surgeon on call, report the content of the alarm and the present situation in the hospital with regard to surgery, anesthesiology, and ICU. Senior Surgeon on call makes decision with regard to level of alert
If the Senior Surgeon on call is not immediately available, the surgeon on duty can make this decision
Green alert 1. Inform senior nurse ED (beeper/telephone….) that "green alert" is activated 2. Inform Senior Anesthesiologist on duty (beeper/telephone….) that "green alert" is activated 3. Inform hospital telephone board that "green alert" is activated 4. Inform Senior Nurse OR (beeper/telephone….) that green alert is activated. Simultaneously, investigate the present situation in OR: Theatres available for surgery? Occupied until when? 5. Inform Senior Orthopedic surgeon on duty (beeper/telephone….) that green alert is activated 6. If the senior surgeon on call is not in the hospital or not immediately available, go to hospital command center and follow action card for HCG until senior surgeon on call is available for this position. When and if senior surgeon on call is available, go to ED and accelerate treatment and evacuation of surgical patients
Yellow alert As under "green alert" 1–5 with addition of: 7. Request senior nurse OR to: "Freeze" all non-started surgery that can wait Call 4 OR teams from staff not on duty Call 4 surgeons from staff not on duty according to alarm list
Red alert As under "yellow alert" with addition of: 8. Request Senior Nurse OR to alert all surgeons and all OR staff not on duty according to alarm list

From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, with permission

4.5.6 Action Cards

As already emphasized, the most important components in hospital preparedness for MIs are the action cards for all positions involved in the response.

What you need to know as a staff member is

- Which level of alert is activated – green, yellow, or red?
- Where is my action card?

Then you can put your index finger in the left margin of the card and follow it step by step, in chronologic order. The telephone and pager numbers you need should be there. *Following this procedure*, *you cannot fail to fulfill your task in the alert and preparatory phase of the response* (= *simplicity is the key to a functioning disaster plan*).

An example of an action card for staff in the "front line" is given in Table 4.5. It is a recommended policy to print the action cards separately, put them on the wall in offices and laminate them in pocket-format for key staff.

4.5.7 Preparing the Hospital

Transferring from a structure designed for ordinary patient care to a structure designed to receive a large number of casualties from MIs is a process that must progress quickly and therefore must be prepared and trained. The action cards, telling all staff members what to do and in what order, is a help in this process. However, other forms of preparation are equally necessary:

- Rooms in the ED where patients should be received, triaged, and primarily treated, must be prepared and all equipment needed for this stored in places known to everyone and with easy access.
- Special material needed, such as cards/records for registration of victims and triage tags and tabards/arm-badges for staff in charge and in key functions, must be prepared and easily available.
- Signs for identification of different zones and pathways in the hospital must be prepared to be set up according to a prepared schedule, usually a task for porters.

- Extra supplies for fluid, disposable material, and beds must be prepared and easily available.
- A room for the HCG must be prepared (see above)
- A room and organization for the hospital information center (see below) must be prepared

All these points are examples of things that must be prepared *before* the incident occurs; otherwise it will not work.

4.5.8 Receiving of Casualties

4.5.8.1 Primary Triage

As a general rule, all casualties should enter the hospital at the same place, a prerequisite for accurate registration. This is usually the ambulance entrance of the Emergency Department. It is important that the hospital is constructed so that there is a wide open area available adjacent to this entrance, used for other purposes under normal conditions but possible to rapidly evacuate on alert (Fig. 4.9). That area will function as the *zone for primary triage*, supplied with:

- Experienced staff responsible for the first triage, with the goal to:
  - Separate the less severely injured who are transferred to the zone for this, usually waiting rooms and offices for ambulatory care of emergency patients
  - Set priority for the severely injured to be taken care of by prepared teams (see below) for primary treatment and secondary triage
- Staff responsible for registration of all arriving casualties

In MI levels 2 and 3, a big entrance hall may be too small for all casualties waiting for triage. This should be considered in the planning and an adjacent area prepared. In countries with a warm climate, this can be an outdoor area; in countries with harsher climates, some sort of indoor facility should be prepared for this (dotted line, Fig. 4.10).

A "must" in all major hospitals receiving emergency and trauma patients is a *decontamination unit in the hospital* for decontamination of patients exposed to hazardous material or irradiation. Theoretically, all such decontamination should be done at the scene before evacuating the casualties for transport to hospitals. In practice, however, there is no guarantee that this is always done. Patients may evacuate themselves spontaneously before rescue and healthcare staff arrive and take control of the scene (this has occurred in MIs during recent years). To bring in one single contaminated patient into the ED may paralyze not only the ED, but many other critical functions in the hospital. Therefore, a decontamination unit should be prepared in connection to, but ventilatorily separated from, the hospital (Fig. 4.11), and the staff should be trained to perform decontamination and work in protective clothes (Fig. 4.11).

4.5.8.2 Severely Injured

The management of the severely injured must run through several *parallel lines*; otherwise the ED will be a keyhole creating congestion. For this purpose, the staff must be organized in teams, working parallel in areas prepared for this (Fig. 4.10).

It is important that these teams are well staffed. Normally, severely injured patients are taken care of by *Trauma Teams*; such a team usually consists of two to three physicians and three to four nurses, all responsible for different functions. With a heavy load of casualties and need of many parallel teams, it may be difficult to afford that many staff in every team. On the other hand, a single physician and nurse are not enough for this task. A recommended model is special *Major Incident Resuscitation* (*MIR*) *teams* for severely injured or critically ill victims with a minimum staff of four persons that includes two physicians and two nurses. In MIs caused by trauma, at least one of the physicians should have clinical experience of trauma and at least one of the nurses should have trauma experience. The rest of the team may in this situation be available physicians and nurses from any specialty.

The first task of the staff in charge of this position is to recruit staff to these MIR teams and appoint *team leaders* according to the principles mentioned above. Some hospitals label these teams with arm badges with numbers so they can be easily identified.

The areas/rooms where these teams can work should be defined as a part of the planning process and supplied with necessary equipment: suction, oxygen, sufficient illumination, and trays with necessary instruments and material. A bigger hospital should have prepared space for at least 6–8 such parallel teams, including the regular trauma bays that of course are suitable for this purpose.

The task of the MIR teams is to make a complete survey of the patient according to the Advanced

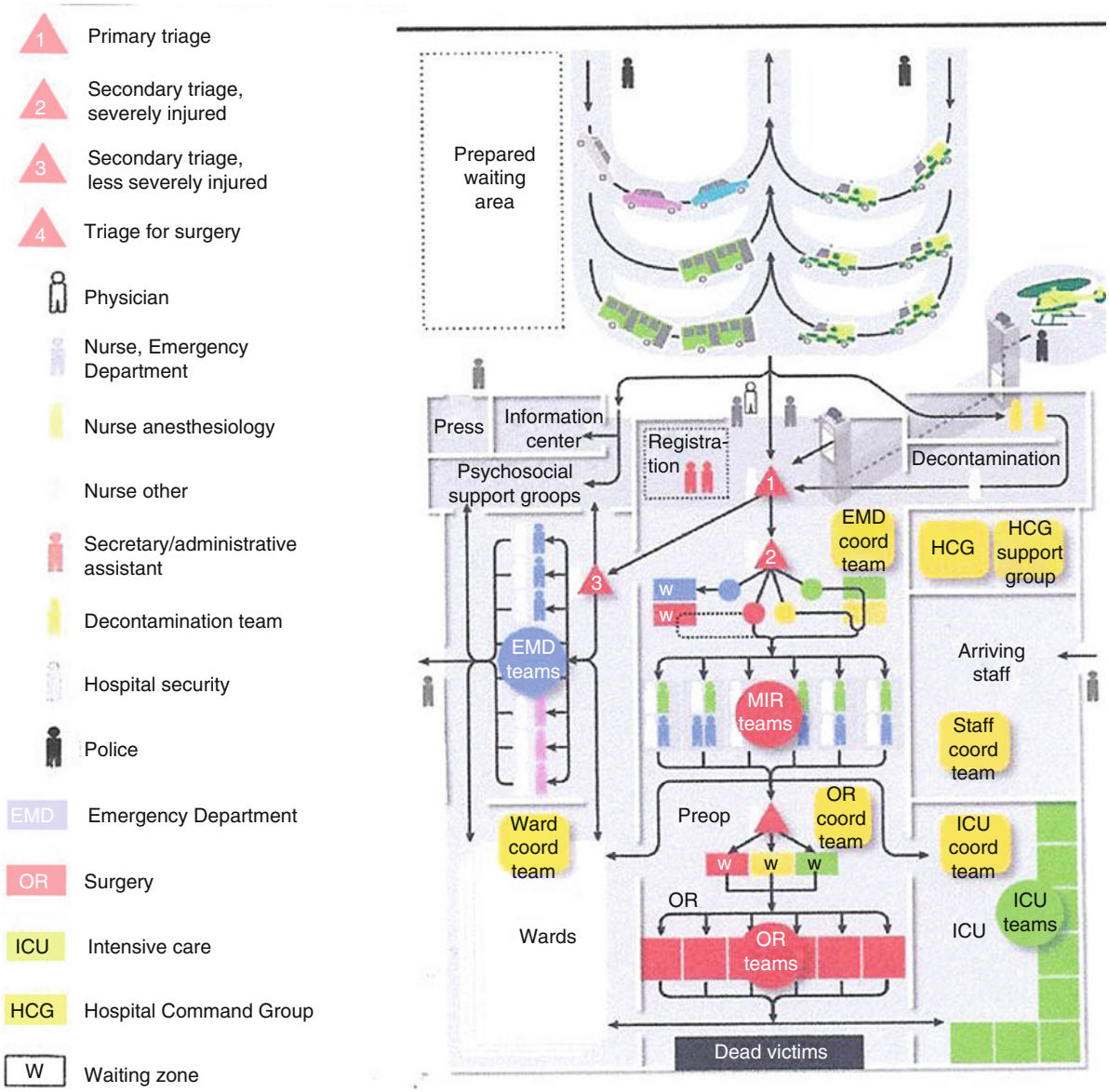


Fig. 4.10 Schematic illustration of the organization of the hospital during an MI response. Areas normally used as entrance hall. (**a**) Emergency Department (**b**) and Postoperative unit (**c**) are now according to a prepared plan rapidly transferred to areas for receiving and triage of casualties (**a**) management of severely + less severely injured casualties (**b**) and preoperative zone with triage/waiting for surgery (**c**). Offices and meeting rooms (**d**, **e**) are in the same way transferred to command rooms and area for arriving staff (**d**) and information-and media center and psychosocial support functions (**e**). Coordinating staff are appointed for all these functions, responsible also for their preparation and staffing. The *red triangles* indicate primary triage on arrival (*1*), secondary triage of severely injured (*2*), secondary triage of less severely injured (*3*) and triage for surgery (*4*). The *arrows* indicate the flow of casualties. See further the text (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, Artwork Typoform, with permission)

Trauma Life Support (ATLS) principles, perform necessary resuscitation, perform investigations necessary for decisions and immediately necessary treatment, re-evaluate priority (= secondary triage) and then transfer the patient to the next destination as soon as possible, which might be the preoperative zone, the ICU, or in some cases, a ward (Fig. 4.10).

Fig. 4.11 The figure shows a decontamination unit in a major hospital. The unit should be located in connection to, but ventilatorily separated from, the rest of the hospital, with special evacuation routes for decontaminated air and water. The staff who may have to work here must be specially trained in how to perform decontamination and how to use the special protection equipment for this, based on over-pressure of air into the suites (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, Photo Södersjukhuset, Stockholm with permission)

Radiograph examinations should in this situation be used very restrictively. Even if CT is available in the ED, it cannot be used for all patients and in many cases needs to be replaced by simpler examinations. Plain radiographs of fractures can be done at a later time with mobile units in the preoperative zone or in wards.

4.5.8.3 Less Severely Injured

Those categorized as less severely injured must also be carefully and systematically examined; even a walking patient can have internal bleeding. The staff assigned to this should have trauma experience and can be consulted when needed.

Some of these patients may be transferred to wards for observation or later surgery (for example, fractures that can wait after temporary reduction and stabilization). Others may be ready to be dismissed after treatment. However, it must be considered that these patients, even if they have minor injuries, have gone through a shocking experience and cannot just be sent home. They must have the opportunity to meet with psychosocial support staff (see below) where contact for future needs can be established. These patients can also have lost relatives or friends, they may have relatives among the severely injured, and they may be far from home and have lost their personal property or clothes. An organization to take care of them must therefore be prepared (Fig. 4.10).

Patients who have received some form of treatment must also have a plan for follow up in their home hospital if they are away from home.

4.5.8.4 Non-Injured

Non-injured victims may also come to the hospital, either accompanying injured relatives or friends, or

psychologically shocked, or just because they are far from home and have nowhere else to go. A special area must be prepared for this category of victims, away from the ED and with access to psychosocial support staff as well as access to information to search for relatives and friends (Fig. 4.10). Voluntary organizations such as the Red Cross often play an important role in the support of this category of victims.

4.5.8.5 Dead

Patients who have died during transport or after arrival to the hospital should be transferred to a prepared area for deceased victims, usually in connection with the department of pathology (Fig. 4.10). It is important that this area has rooms where relatives can see their dead in a calm and harmonious atmosphere, and with access to staff from the psychosocial support group.

For information about management and identification of dead casualties, the reader is referred to text books on medical response to MIs.

4.5.9 Registration of Patients

To avoid congestion when a high number of casualties arrive at the hospital within a very short time, *a simple and rapid system for registration and documentation is needed*. This is best achieved by using prepared "fill-in" documents. Many hospitals use the same registration as for trauma patients which works well for incidents caused by physical trauma but not for other types of incidents (hazardous material, irradiation). Other hospitals have a special registration system for MIs covering all types of incidents, including additional information valuable for evaluation of the response. From a scientific point of view, an internationally uniform system should be a goal to work toward.

Regardless of which system is used, it must be a system that meets the demands of simplicity and speed, all staff involved in registration must be familiar with it, and it must be prepared so that the needed documents are available in sufficient number.

It is important that the registration *documents from the scene* are kept together with the hospital registration documents. They may contain valuable information, and as medical documents they must be preserved for medico-legal reasons.

4.5.10 Psychosocial Support

The need for psychosocial support is important both during and after the response to an MI, and many different categories may need such support:

- Injured patients
- Non-injured hit by the incident
- Relatives/friends of injured patients
- Relative/friends of dead victims
- Staff of all categories

Such support therefore must be available at many positions in the chain of management:

- In the assembly area for patients who have been treated and are ambulatory and are ready to be dismissed
- In the assembly area for non-injured, but psychologically shocked victims
- In wards where casualties from the incident are treated
- At the ICU (waiting room for relatives)
- In the area for management of dead for support to relatives/friends
- In the hospital information center

Staff from all categories should have the opportunity to receive psychological support, but the primary support should always be given within their own unit. Persons in charge should have the responsibility of gathering all staff before following a response to discuss what occurred, what was bad and what was good in the response, and what has been learned for the future. This *primary debriefing* is not a task for only psychologists; everyone should be made aware that reactions and feelings are natural and not pathologic. However, it is also important to identify whether any staff member requires psychological support at this point, and if so, to see that it is provided. All staff should be aware that such support can be obtained later if necessary, and whom to contact about it.

The *coordinator of psychosocial support*, who can be a psychiatrist or a psychologist, is responsible for the psychosocial support functions in the hospital. Staff involved in this work can be:

- Psychiatrists
- Psychologists
- Social workers
- Priests

For methodology of psychosocial support in MIs, the reader is referred to text books on medical response to MIs.

4.5.11 Hospital Information Center

After an MI, there is need for information to relatives and friends of people who have been involved, or may have been involved, in the incident. Many call just because they believe that their relatives have been in the area of the incident, others know that their relatives were on the plane, or in the train, that crashed. The total number of calls is too great to be handled by the hospitals and another organization is needed to sort out questions about those who are registered as casualties and to which hospital they have been taken, so that these calls can be transfered to the appropriate hospital.

In most countries, the dissemination of primary information is handled by the police, who immediately after the incident open a *police information center* well staffed with people who can take all the calls (hundreds, sometimes even several thousand) within a short period of time following the incident. This requires a well-prepared organization. The number(s) to call are usually given in the media at an early stage after the incident.

When such calls come to the hospitals, the operator should confirm that the person making the inquiry has been in contact with the police information center and if not, refer them there.

If contact has been made with the police information center and it has been confirmed that the person being inquired about has been taken to the hospital, the operator should forward the call to the *hospital information center*, which is a necessary function in the hospital and must be prepared as an important part of the planning process.

This unit should be located in a place well supplied with telephones and staffed by persons who have received special training for this purpose. A common way to staff this center is by using secretaries working together with nurses from out-patient clinics who are not medically involved in the incident; this staff works in teams of two, one answering the call and one searching for the patient, following the files continuously delivered from registration.

4.5.12 Contact with Media

There are many reasons to establish a constructive collaboration between health care and media in these situations. The health care staff are interested in getting information delivered, for example, request for staff of certain categories to go to the hospital, request for blood – donors, request to people not absolutely needing to go to the hospital to wait, or go to primary care stations. Representatives of the media should, like all other categories in the community, see it as their task to give support in this difficult situation; they also have a responsibility to disseminate the correct information.

Unfortunately, this collaboration is sometimes ruined by "hunting a scope", in order to obtain sensational photograph ps of wounded casualties or crying relatives. However, it is the responsibility of the health care staff to protect patients and relatives in this situation. Even if they agree to be photographed, it is a well-known fact that this can cause considerable psychological harm in the aftermath. This creates a potential conflict between health care staff and media.

The best ways to cope with this is to have:

- Discussions with representatives of the media *before* an incident occurs so that both sides understand each other. Some hospitals organize regular seminars with their local media representatives concerning matters as a daily routine, including MI response and problems associated with that. This is an effort that usually pays well in the long run.
- A senior person (*Information officer*) responsible for media contact, who takes an active role in informing the media representatives, showing them around in an organized way, and giving them the facilities needed, for example, a press room with access to telephones where they can also be continuously informed.

Staff who are in the position of obtaining a role as Information Officers should go through special training in media management.

A good strategy in the initial phase after the alarm is to give a *press release to the hospital telephone operator*. It might appear strange that this measure is given such a high priority in the critical phase immediately after the alarm. However, as soon as information about the incident reaches the media (which occurs quickly today), they will call the nearest hospital and ask for information, and it is not only one call, it is dozens of calls within a few minutes. The hospital operator has to transfer these calls to the HCG – *unless* he/she has a short written message to read, for example: "The hospital has at 10:25 am received an alarm

informing about a train crash between A and B city, many injured. We have activated the plan for MIs and are preparing the hospital according to that, but casualties have not yet arrived. Next press release will occur at 11:00 am." This simple step "protects" the HCG group from a flood of incoming calls, and later the Information Officer can handle this.

4.5.13 Supplies

Most hospitals are currently working with very limited supplies because it is considered an economic advantage not to have big stores of supplies in the hospital and some of the material also has expiry dates. With the current technology, it is relatively easy to continuously refill supplies according to expected needs.

However, this creates new problems during MIs, where the need for specific types of supplies can reach high volumes within a few hours, possibly during non-office hours. Especially sensitive areas are disposable material, fluids, and drugs. For disposable material, many hospitals have supplies only for a few days of routine activity that will run out quickly during an MI.

Preparedness for this must include:

- Reserve supplies of certain materials of critical importance (fluids and certain drugs), even if it is means additional costs
- Agreements with suppliers of material (fluids, drugs, disposables) to have access to supplies in case of emergency within a short time frame, even after business hours
- Certain stock of non-disposable material that can be sterilized and re-used, for example syringes, scalpel blades, linen

4.5.14 Technical Functions

Hospitals today are highly dependent on technology, and the more advanced the technology is, the more sensitive it is to disturbances. Unfortunately, such disturbances are very likely to occur in connection with MIs, either because of simultaneous damage to the infrastructure of the community, or just by overloading. Preparedness for this is therefore an important part of the process of planning and preparedness.

4.5.14.1 Electrical Power

Every hospital today has reserve power systems that automatically take over if the supply by the ordinary net is interrupted. However, it is important that:

- These systems are regularly tested.
- They really cover all functions necessary for an MI response, such as the areas prepared for receiving casualties in the ED, and also administrative functions such as the HCG command room and the information center. During an MI, the interruption of power supply can be long.

Supplies of flashlights and battery head lights in designated areas are also part of the preparedness for this.

4.5.14.2 Water

Very few hospitals have reserves of water supply and because this is dependent on electrical power, long-lasting disturbances are a serious threat. Generally, this is something that should be looked at more precisely. A simple step is having reserve tanks for storing water for a threatening long-lasting interruption of electric supply.

4.5.14.3 Computer Support

Most medical staff have probably experienced a failure of the hospital's central computer system and know what happens: the hospital becomes totally paralyzed. It is suddenly not possible to obtain laboratory test results, in some cases not even possible to request fluids or blood, or diagnostic procedures such as radiographs. Additionally, the entire system of patient registration fails. In routine medical care, such failures are often corrected within a few hours, but in MIs, they can last long and prove fatal for the hospital's ability to respond.

Back-up and reserve systems are mandatory as a part of the process of MI planning and preparedness. This may be the weakest point of current planning, and very few hospitals have such systems, possibly because the consequences of failures are not yet completely understood (the technical development within this field has proceeded quickly).

4.5.14.4 Communication

A well-functioning line of communication is of vital importance for a hospital's MI response. Historically, the old hospital switch boards were sensitive to overloading and could collapse because of a heavy inflow of calls. Following some incidents where this occurred, this could be solved technically and the problem was

forgotten, until the new digital, computer-based systems were introduced a few years ago and the same problem appeared again, this time on a central level and outside the control of the hospitals. This is still not solved and has been reported following a number of recent MIs. The hospital is suddenly isolated from telephone contact both to and from the world outside.

This is also something that must be included in the process of planning and preparedness. Access to cell phones for all key staff is pertinent as long as it works, but this system can also collapse because of the overloading in these situations. One possibility is to secure certain cell phones for key functions (see Chap. 3), but this must be done during the planning stage.

For communication within the hospital, internal lines can be used as well as runners transferring information in written or oral form (something voluntary organizations can be used for if it is planned in advance).

For external communication, the HCG group must have access to radios and be trained in their use (see Chap. 3). Another solution for external communication is runners who can deliver messages between the scene and the hospital and also to the RMC, depending on distance.

4.5.15 Incidents Primarily Involving the Hospital

In the description of the contents of the disaster plan above, a separate part dealing with incidents primarily involving the hospital was also included. This can be:

- Fires, accidental or intentional
- Threats
- Collapsed buildings, as in earthquakes
- Incidents with hazardous material or irradiation
- Floods
- Terrorist actions
- Armed conflicts, exposing the hospital to gun fire

Several *fires* in hospitals have been reported over the past years. It is mandatory that hospitals have special plans for this, including evacuation lines, and everyone knows where to find them, but it also should be regularly tested with the fire department; the staff has a big responsibility to save not only themselves, but the patients, including those severely ill and with ongoing treatment.

Threats to hospitals, for example bomb threats by terrorists, have been reported with increasing frequency and should always be taken seriously. A special action card for dealing with threats should be included in the plan.

4.5.16 The Recovery Phase

A hospital's response to an MI involves many functions in the hospital and sometimes means maximum utilization of all available resources during a (during peace time) usually limited period. However, the response is not over because all patients have left the ED. Primary surgery may continue for many days for casualties who initially were given low priority. Primary surgery is often Damage Control – surgery = temporary life-saving procedures, followed later by definitive surgical repair. This "secondary surgery" is done one or several days after primary surgery, unless the patient is transferred to another hospital. This means that the surgical activity, with all that is connected to it, may fully occupy available OR facilities several days after the incident. During this period, everything in the normal routine that had to be postponed during the incident must also be dealt with. It also takes time to restore supplies, and the staff need rest.

During this phase, it is also extremely important to start the *evaluation process*, which is a part of the debriefing with the staff on all levels. It is important to have the opportunity to discuss how the response fulfilled its goals and what could be planned better for the future. This is also the golden occasion to put together a report of the response from which others will benefit. To make possible scientific evaluation and comparison of such reports, they should be standardized as far as possible, that is, follow the same protocol, and efforts to come to an agreement on such protocols are currently going on, for example in the Section of Disaster & Military Surgery within ESTES.

4.6 Treatment Principles in MIs

Triage, diagnosis, and treatment under these conditions have in common for all scenarios that it often must be done

- Under time pressure
- With limited or no access to specialists
- With limited or no access to advanced technology
- With impaired technical support functions

- With limited supplies
- With long intervals between injury and treatment
- With limited possibilities of follow-up

In addition, the mechanisms of injury are often different from those seen in routine medical care. This puts demands on:

- Simplified methods with emphasis on safety
- Knowledge among medical staff about the principles for triage and primary management of injuries/diseases outside their own specialty
- Knowledge about the principles of treatment of injuries/conditions common in MIs (high-energy trauma, blast injuries, burns, hypothermia, injuries caused by hazardous material, irradiation or biologic agents).

This should also be a part of education and training in disaster medicine (see below).

For the principles of triage, diagnosis, and treatment of different types of injuries at various levels of the chain of management in different scenarios of MIs, the reader is referred to text books on medical response to MIs.

4.7 Education and Training

4.7.1 The Need for Training

To cope with such situations, it is not enough that we as medical staff can do our ordinary job, and continue to do it as efficiently as possible. Additional knowledge and skills of different kinds are needed to accurately respond to the specific demands in these situations. We must be able to:

- Use simplified methods for diagnosis and treatment.
- Primarily treat emergencies outside our own specialty, at least those commonly occurring in these situations.
- Perform triage (i.e., make rapid and accurate decisions with regard to priority between patients and between diagnostic and therapeutic measures, also in a heavy load of casualties).
- Work as an integrated part of an organization where resources rapidly must be redistributed depending on needs, which requires knowledge about the organization.
- Work with limited supplies.
- Use reserve systems if computer or telecommunication systems, or other advanced technical systems, fail.

In addition, specific types of incidents require special knowledge: management of patients contaminated by hazardous material, biological agents or irradiation, or with specific injuries more rarely occurring in our daily care such as high-energy missile fragment injuries, blast injuries, and severely contaminated injuries.

4.7.2 Who Should Be Trained?

Because any medical staff, regardless of specialty, any day at any time, can be faced with a large number of severely injured or critically ill patients with no specialists or expertise available, the basic principles for working during MIs must be taught through special courses during the basic training of doctors and nurses, which is the case today in Europe, with very few exceptions. This is the responsibility of universities and nursing academies and is a prerequisite for a good standard of training.

Staff specializing in emergency disciplines need additional training in their positions that usually is the responsibility of the hospitals, or in some countries, counties or regions, often with government support because this is a matter of security for the population. Staff expected to be given leading or coordinating roles need even further training in these difficult tasks, training that usually is given by a few regional training centers in every country.

Working under austere conditions in areas with highly limited resources or in "chronic" disaster zones with severe public health problems, requires specific knowledge in fields such as nutrition, infectious diseases, and management of refugees and displaced populations. All this requires specific education and training for those deployed to serve in such areas.

4.7.3 Methodology of Training

Education and training in this field is very demanding. Being different from other parts of medicine, the problems and the methods to deal with them can only to a very limited extent be demonstrated on patients, and the real incident is not the place for education or training. This requires simulation models of different kinds. Practical field field exercises are the most common way of teaching and training, but they have had a tendency to become more spectacular events, possibly filling the purpose to illustrate chaotic situations, but giving limited feedback to the trainee: *What would my decision and performance have led to in reality*?

The key element in education and training in Disaster Medicine is decision making:

Correct decisions must be made under time pressure on all levels, from coordination and command: "Which resources to alert? How to use them best?" to individual patient management: "What to do with this patient in this particular situation, when and how to do it, and in what priority?"

Characteristic for this field is that the patient may not get another chance if the wrong decision is made once.

We act as computers, we receive a large amount of information, analyze it and deliver the decision, which leads to a result. To train and evaluate decision making requires that:

- All information on which the decision should be based is available.
- All consequences of the decision are illustrated.

This requires advanced simulation models in which all components in the chain of management (scene, transport, hospital, coordination, and command) are simultaneously handled because they are linked to each other in determining the outcome. It is also the coordination between these components that often fails in reality, illustrating the importance that this be included in the training. The need for such models has been recognized during recent years and they are to an increasing extent replacing the old fashioned form of training with field exercises, which was also more expensive.

An example of a course model meeting the demands described above, is the MRMI course developed by ESTES. The courses are based on a simulation system originally developed for scientific evaluation of methodology, MACSIM (www.macsim.se). They are totally interactive (Fig. 4.12a, b) and include simultaneous training of the whole chain of response, and they also give a measurable outcome of the response that can be used as a basis for improvement with further training, or by adjusting methodology or organization.

Fig. 4.12 Pictures from a Medical Response to Major Incidents (MRMI) course. The course is totally interactive with all participants working in their normal positions. The simulation system is based on injuries from real incidents and everything is run with real consumption of time and resources. The whole chain of response is trained simultaneously. (**a**) A hospital set up with (from the *left* to the *right*) area for arrival and primary triage, ED, preoperative zone, surgery and intensive care. Wards indicated with plastic pouches along the bottom of the boards. The instructor (*yellow arm-badge*) records every decision for later evaluation. (**b**) The coordinating centers are built up on distance from the hospitals. The picture illustrates the Regional Command Center, communicating by radio to the scene and by telephone to the hospital command groups (From Lennquist S (ed): Medical Response to Major Incidents, Springer 2012, with permission)

Fig. 4.12 (continued)

For a further description of different educational methods, the reader is referred to text books on MI Response.

4.8 Development and Research

Development and evaluation of methodology is as necessary in this field as in all other fields of medicine. Examples of important scientific areas are:

- Analysis of risks for MIs and disasters as a basis for planning and preparedness
- Continuous and consequent collection and analysis of experiences and results from MIs and disasters as a basis for development and evaluation of methodology
- Development and evaluation of simplified methods for diagnosis and treatment to be used in these situations
- Development and evaluation of a reserve system for technical support, communication, and information technology
- Development and evaluation of criteria on good preparedness for quality assurance
- Development, evaluation, and validation of educational methods

For a further review of the different areas for development and research, the reader is referred to text books on MI Response.

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Polytrauma: Pathophysiology, Priorities, and Management

5

Otmar Trentz

5.1 Definition

Polytrauma is a syndrome of multiple injuries exceeding a defined severity (Injury Severity Score [ISS] ≥ 17) with sequential systemic reactions that can lead to dysfunction or failure of remote organs and vital systems, which have not themselves been directly injured.

5.2 Importance of Fractures

Fractures frequently occur in polytrauma patients. These fractures can be considered as wounds of the bone and soft tissue, giving rise to physiologic stress, pain, and hemorrhage. They can be contaminated if open wounds are present and cause compartment syndrome with ischemia-reperfusion injury. The instability of the skeleton renders the patient immobile and denies the option to select the nursing position most suitable for intensive care of brain and chest injuries.

5.3 Pathophysiological Background

Wounds (i.e., around fractures) are inflammatory foci, consisting of dead tissue in an ischemic or marginally perfused hypoxic zone. Such foci behave like endocrine organs, locally releasing mediators and cytokines to tissue macrophages as well as into the circulatory system causing systemic reactions. In severely injured patients, the lung is one of the first major immunological contact and response organs (Fig. 5.1). By releasing these substances, a cascade of local and systemic defense mechanisms is activated and immunocompetent cells are directed to control, débride, and repair the tissue defects.

Stress and pain are potent stimuli [1] for neuroendocrine, neuroimmunological, and metabolic responses. In addition, if hemorrhage, contamination, and ischemia-reperfusion injury complicate fractures, or if these are caused by associated injuries, systemic reactions to trauma produce a systemic inflammatory response syndrome (SIRS) [2]. SIRS is associated with a general capillary leak syndrome and high-energy consumption demanding a hyperdynamic hemodynamic state (flow phase) and an increased availability of oxygen. This flow phase generates an intense metabolic load with significant muscle wasting, nitrogen loss, and accelerated protein breakdown. This hypermetabolic state is accompanied by an increase in core body temperature and by thermal dysregulation.

If adequate and timely resuscitation is neither permitted (by the severity of trauma) nor provided (by the quality of care), the high-energy consumption will lead to “burn out”. This process moves from depletion of immunocompetent cells and acute-phase proteins to critical immunosuppression and sepsis, then onward via increased cell damage, to a multiple organ dysfunction syndrome (MODS), and ultimately lethal multiple organ failure [3–5].

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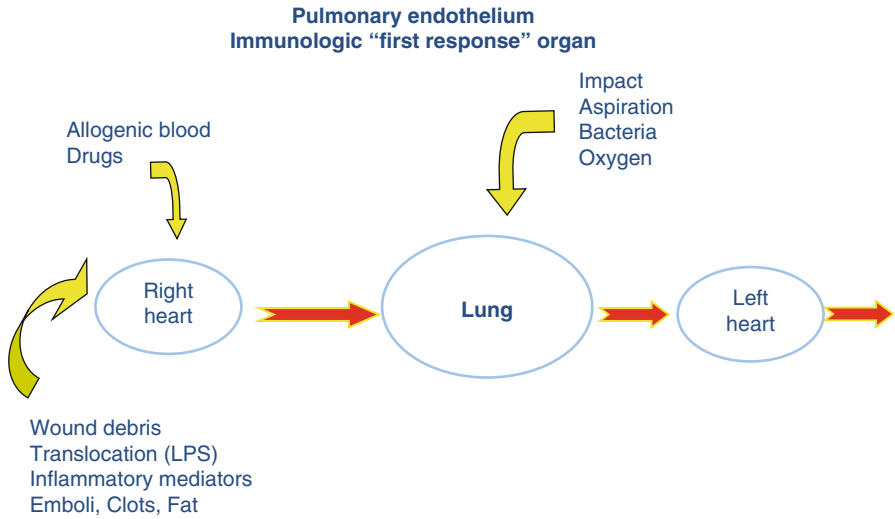

Fig. 5.1 Traumatic and interventional antigenic load on the pulmonary endothelium and alveolar epithelium in severe trauma conditions

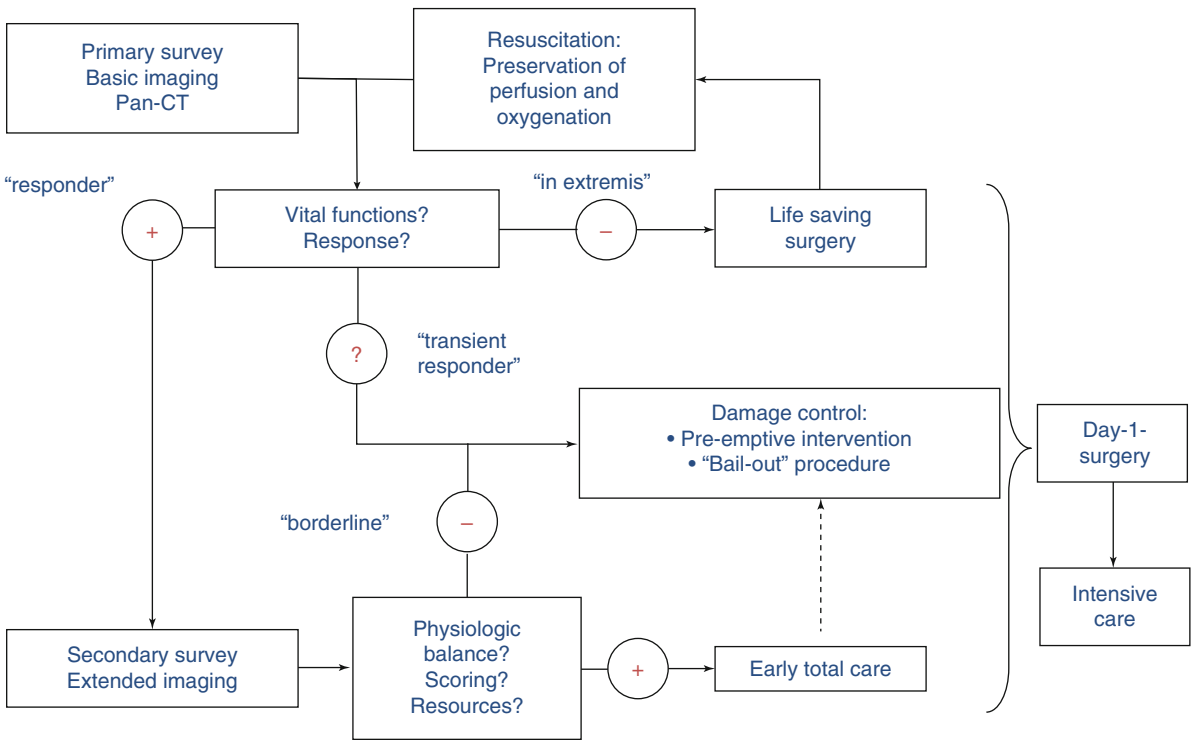

Fig. 5.2 Algorithm for resuscitation, assessment, and acute surgery in polytrauma

5.4 Timing and Priorities of Surgery (Fig. 5.2)

The primary objective during initial care of polytraumatized patients is survival with normal cognitive function. The first priority is resuscitation to ensure adequate perfusion and oxygenation of all vital organs. This can usually be accomplished by conservative means such as intubation, ventilation, and volume replacement according to the Advanced Trauma Life Support (ATLS®) protocol. If the response to such measures is not successful, *immediate life-saving surgery* is necessary:

- Decompression of body cavities (tension pneumothorax, cardiac tamponade, epidural hematoma);
- Control of exsanguinating hemorrhage (massive hemothorax or hemoperitoneum, crushed pelvis; whole limb amputation, mangled extremity).

If there is poor response to resuscitation or ongoing physiological weakness in the patient, definitive surgery should be avoided and the concept of *damage control* applied. The rationale behind this concept is saving the life by deferring repair of anatomical lesions and focusing on restoring physiology [6–9].

Briefly stated, there are two different conditions for selecting *damage-control surgery*:

1. *Physiological criteria*: hypothermia, coagulopathy, and acidosis; patient "in extremis".
2. *Complex pattern of severe injuries*: expecting major blood loss and prolonged reconstructive procedures in an unstable patient.

Damage control can be utilized in two ways:

1. *Reactively*: "bail-out" surgery, which means aborted termination of procedures in a patient at imminent risk of death;
2. *Pre-emptively*: calculated early decision to accomplish definitive repair in staged sequential procedures because of a high risk of physiological deterioration.

Damage control procedures such as control of hemorrhage, source control, irrigation, packing, external fixation of long bones and pelvic ring, and provisional closure of wounds or abdominal cavity are followed by stabilization of the physiological systems in the intensive care unit (ICU). After physiological restoration in the ICU, *staged definitive surgery* can take place under improved and safer conditions. With regard to fracture repair, there is a "window of opportunity" between day 5 and 10 post-trauma. Damage control surgery is indicated in about one third of polytrauma patients.

- *If there is a positive response to resuscitation and the patient remains stable during the "secondary survey", then "early total care" can begin according to the general principles of fracture care.*

Fracture fixation must have a high priority within the scope of this algorithm:

- Limb-threatening and disabling injuries (including open fractures) require at least damage control: débridement, fasciotomies, reduction, stabilization, and revascularization [10].
- Long bone fractures (especially femoral shaft fractures), unstable pelvic injuries, highly unstable large joints, and spinal injuries require at least provisional reduction and fixation. Definitive fixation may have to wait. A better option would be temporary stabilization by means of an external fixator followed by scheduled, definitive osteosynthesis (intramedullary nailing) during a window of opportunity between day 5 and 10 [10].

There is evidence, from clinical experience as well as in the literature, that early fracture fixation in polytrauma is beneficial in terms of mortality and morbidity [11–13].

The arguments and experience in favor of early fixation of femoral fractures and unstable pelvic-ring injuries are:

- Reduction of the incidence of acute respiratory distress syndrome (ARDS), fat embolism and pneumonia, MODS, sepsis, and thromboembolic complications;
- Facilitation of nursing and intensive care: Upright chest position, early mobilization, use of less analgesia.

Definitive osteosynthesis as day 1 surgery is advisable only when all the endpoints of resuscitation [14] have been accomplished.

Between the fifth and tenth day post-trauma an immunological window of opportunity exists, when the phase of hyperinflammation is followed by a period of immunosuppression and when new cell recruitment and de novo synthesis of acute-phase proteins are taking place.

- *During the "window of opportunity", scheduled definitive surgery of long bone fractures (shaft and articular) can be performed relatively safely.*

This period of immunosuppression lasts for about 2–3 weeks; therefore, secondary reconstructive procedures can be planned for the third or fourth week post-trauma (Fig. 5.3).

Physiology	Surgery	Time
Response to resuscitation:	– Life saving surgery ? "Damage control" + Delayed primary surgery	Day 1
Hyper-inflammation	"Second looks", only!	Days 2–3
"Window of opportunity"	Scheduled definitive surgery	Days 5–10
Immunosuppression	Emergencies, only !	
Recovery	Secondary reconstructive surgeries	Weeks 3–4

Fig. 5.3 Roadmap for timing of surgeries according to the physiological status of the patient

5.5 General Aims and Scopes of Fracture Management in Polytrauma

Fractures can have an important impact on the severity of systemic traumatic reactions as a result of

- *Hemorrhage*: Prolonged states of shock as well as exsanguinating hemorrhage are frequently associated with open or highly unstable pelvic ring injuries or femoral shaft fractures.
- *Contamination*: Open fractures must always be considered as contaminated. If a wound can only be débrided after some delay or if débridement is not radical enough, bacterial nutrients will develop in the wound. A second or even third débridement is therefore mandatory.
- *Dead, ischemic tissue with a marginally perfused hypoxic zone*: In unstable, displaced fractures, particularly after high-energy impact, a radical soft-tissue débridement is necessary as soon as possible in order to control the source of the inflammatory reaction.
- *Ischemia-reperfusion injury*: Prolonged hypovolemic shock and compartment syndromes related to fractures with or without vascular injuries are prone to ischemia-reperfusion injury with microvascular damage because of oxygen radicals. Blunt tissue contusions may activate xanthine oxidase; ischemia will produce the substrate xanthine/hypoxanthine, and reperfusion will add co-substrate oxygen. A dangerous triad is thus established.
- *Stress and pain*: Unstable fractures cause pain and stress, which via afferent input [1] to the central nervous system, stimulate a neuroendocrine, neuroimmunological, and metabolic reflex arc.
- *Interference with intensive care*: Unstable fractures prevent effective patient postures (upright chest) and pain-free handling in intensive care.

The general aims and scope of fracture management are:

- Control of hemorrhage;
- Control of sources of contamination, removal of dead tissue, prevention of ischemia-reperfusion injury;
- Pain relief;
- Facilitating intensive care.

These concepts can be realized by hemostasis, débridement, fasciotomy, fracture fixation, and tension-free wound coverage.

For stabilization of long bones, external and internal fixation as well as plates and nails are options depending on the circumstances.

5.6 Pros and Cons of Different Fixation Methods

Intramedullary nailing is, from the biomechanical point of view, the method of choice for shaft fractures of the femur and tibia. However, femoral nailing, reamed as well as unreamed, bears the risk of pulmonary embolization [15].

The main reason for this is the manipulation of the content of the medullary canal by opening, insertion of guide-wire, reaming, and placement of a nail. This increases the intramedullary pressure so that emboli of bone marrow content, fibrin clots, and debris are introduced into the pulmonary circulation. Embolization also causes activation of coagulation and other cascade systems.

The immense clearing capacity of the pulmonary endothelium may already be compromised by a lung contusion, a massive transfusion of allogenic blood, a spill over of cytokines and mediators from large wounds with dead tissues, or an incomplete resuscitation from shock. In this situation, the additional insult arising from iatrogenic embolization can crucially damage pulmonary function (Fig. 5.1). Furthermore, it is important to realize that simple fracture types (transverse and short oblique) in a young patient with a narrow medullary canal and well-developed muscle envelope are more prone to be followed by pulmonary embolization after intramedullary nailing than complex fractures with extensive fragmentation of the femoral shaft, or fractures in elderly individuals with poorer muscles and a wide medullary canal. Currently, there is no evidence that intramedullary nailing without reaming is less dangerous than intra-medullary nailing after reaming.

Plating requires a major surgical approach and is usually technically more demanding. However, it permits simultaneous débridement and fasciotomies.

External fixation minimizes additional surgical trauma. As a fixing and time-saving procedure, it prevents compartment syndrome. The drawbacks are insufficient stability for definitive treatment, pin-track infections, and limitation of plastic soft-tissue procedures.

In summary, every fixation method has its biological advantages and disadvantages. Rigid protocols should therefore be avoided when timing and choice of implant are considered.

5.7 Fracture Management Under Specific Conditions

5.7.1 Massive Hemorrhage as a Result of a Crushed or Disrupted Pelvis [16, 17]

Open or closed crush or disruption of the pelvic ring ("open book", "vertical shear" injuries) can produce exsanguinating hemorrhage into the retroperitoneum, the peritoneal cavity, or to an open or closed (semi-) circular degloving injury (Morel-Lavallee syndrome). In addition to aggressive fluid replacement, these patients require immediate reduction and fixation of the pelvic ring by an external fixator or a pelvic compression clamp. If the hemodynamic response is good, the diagnostic work-up can be completed and pelvic reconstruction can be performed as staged surgery.

However, if the patient remains unstable, emergency laparotomy is mandatory to stop the bleeding. In such circumstance the pelvic ring must be stabilized by pelvic binders, external or internal fixation, followed by surgical hemostasis, tight pelvic packing, and provisional closure of the abdomen. Angiographic embolization may be of assistance at this juncture. The possibility of abdominal compartment syndrome must be kept in mind [18, 19]. After recovery in the ICU, one or two "second-look" procedures are mandatory, followed by definitive stabilization of the pelvis and closure of the abdominal wall (Fig. 5.4a–c).

5.7.2 Early Fracture Fixation in Patients with Severe Brain Injury

In traumatic brain injury (TBI), it is of paramount importance to prevent secondary brain damage [20, 21] resulting from hypotension and hypoxemia, and to maintain optimal cerebral perfusion. Epidural or acute subdural hematomas require urgent surgical evacuation and hemostasis. Patients with TBI and Glasgow Coma Scale < 9 after craniotomy require intracranial pressure monitoring immediately after life-saving surgery [22]. Given a good response to resuscitation (stable hemodynamics and adequate oxygenation), early fracture fixation has a positive effect [23] in brain-injured patients because it facilitates nursing care, reduces painful stimuli (afferent input), and decreases the need for sedation and analgesia.

Concerns that early fixation of major fractures in TBI patients may–under the circumstances just described–increase mortality rate are not evidence based [23].

- *Time-consuming fracture reconstructions should be postponed to the fifth to tenth day during the window of opportunity following initial damage control with external fixation.*

5.7.3 Early Fixation of Femoral Shaft Fractures in Severe Polytrauma Patients or Polytrauma Patients with Chest Injury

Several studies have documented the advantages of early fixation of long bone fractures, particularly of the femoral shaft in polytrauma. These advantages include:

- Facilitation of nursing care;
- Early mobilization with improved pulmonary function;
- Shorter time on the ventilator;
- Reduced morbidity and mortality [6, 11–13, 24].

Locked intramedullary nailing has become the standard method in closed and open femoral shaft fractures. However, there is abundant experimental and clinical evidence of a considerable increase in intramedullary pressure during the nailing procedure, especially in simple types A and B fractures. This leads to a significant release of mediators as well as to the passing of emboli to the lung. The latter can be demonstrated by transesophageal echocardiography [15]. While the side effects of nailing can be disregarded in patients with isolated fractures, they are likely to cause rapid pulmonary deterioration in the multiply injured patient when the procedure begins [6, 25, 26].

Other stabilization procedures such as plating or application of an external fixator can also initiate mediator release, though to a lesser extent. In order to protect pulmonary function, intramedullary nailing (the biomechanically better method) should not be done. The application of an external fixator is less

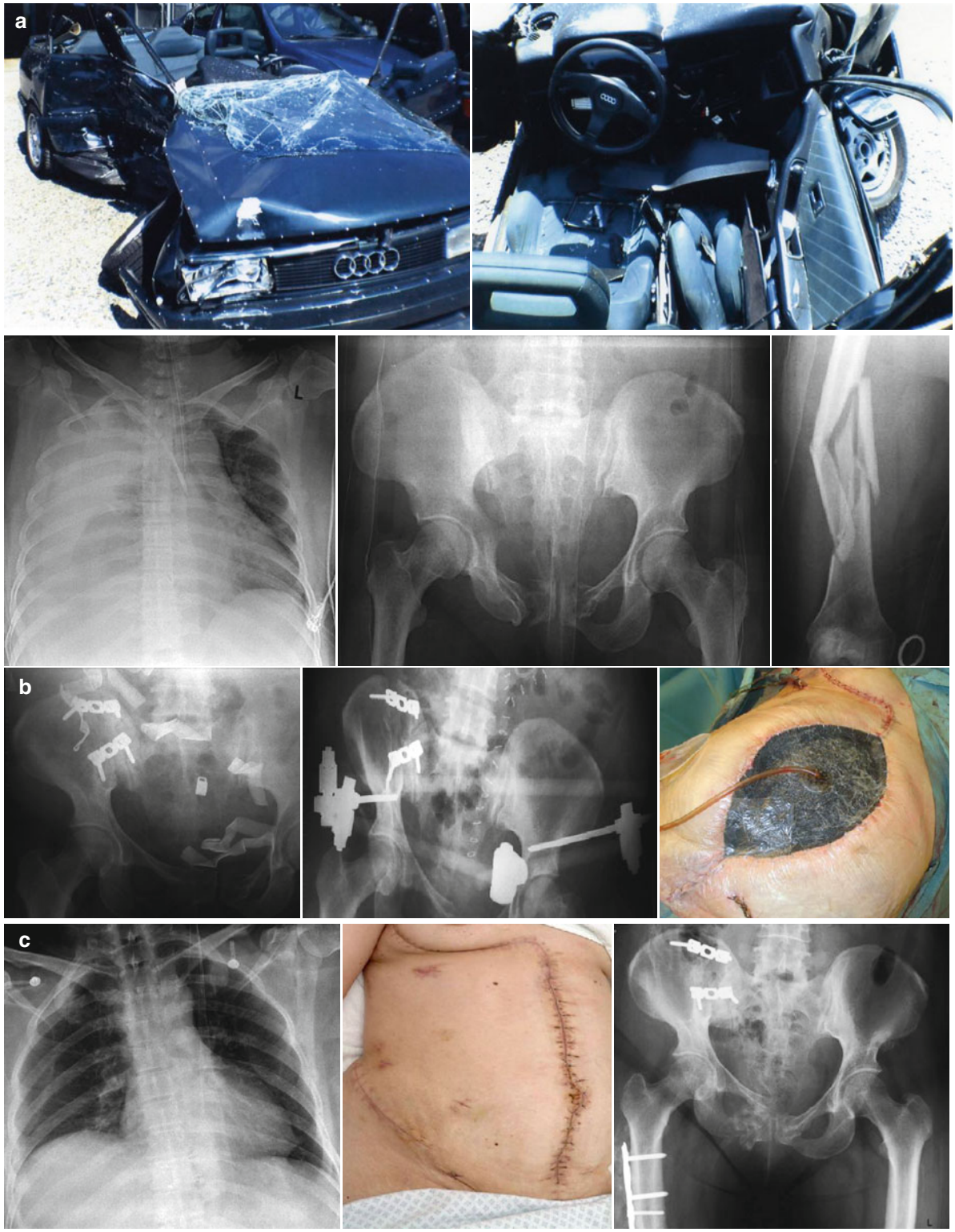

Fig. 5.4 (**a**) A 45 year old female crushed in the right front seat during an automobile accident with severe right side impact. Injuries included thoraco-abdominal trauma, pelvic fracture, bladder injury, femoral shaft fracture, and severe shock. (**b**) Damage control: bleeding and source control, fixation of posterior pelvic ring, packing abdomen and pelvis, abdomen left open, external fixation of femur. Second look: Removal of packs, anterior external fixator pelvis, vacuseal abdomen. Day 6: definitive plate fixation femur, repeat vacuseal abdomen. (**c**) Status after definitive wound healing

distressing to already compromised endogenous defense systems and the pulmonary endothelium.

- *Primary intramedullary nailing of the femur* (*especially in types A and B fractures*) *can only be recommended for polytraumatized patients without significant chest injury* (*ISS <25*). *If the ISS exceeds 40 points*, *primary stabilization is still essential*, *but should be performed only with external fixators* [6].

Plating can be a good alternative when ISS values are between these limits, particularly if the soft-tissue conditions require débridement, fasciotomy, and active control of hemorrhage. Seriously compromised soft tissues may respond to additional distraction with a further reduction of perfusion, enhancing the possibility of a compartment syndrome. In such situations, a temporary shortening of a limb must occasionally be accepted.

In complex type C fractures with extensive comminution, the range of indications for nailing can be extended because no substantial pressure increase can occur. As clinical and experimental data indicate that the application of solid nails with smaller diameters and without reaming may also cause relevant pulmonary impairment, their use has no significant advantage over reamed nails.

Solid nails should therefore predominantly be used for open fractures (no dead space) and are recommended particularly if a scheduled definitive change from external to internal fixation is intended. Any switch to a biomechanically better procedure should be performed early, ideally between the fifth and tenth day after trauma.

This concept of staged surgery in a subset of patients in critical conditions appears to be generally accepted by most authors in Central Europe. In contrast, a number of investigators from North America continue to argue that all femoral shaft fractures should have primary nailing performed regardless of the patient's clinical status [12, 27, 28]. These retrospective studies, however, have several inconsistencies regarding patient selection and comparability of study groups. However, a prospective randomized trial recently performed suggests that most polytraumatized patients with femur fractures with or without chest injury can be safely treated with intramedullary fixation [29]. A low rate of ARDS was demonstrated in all groups.

5.7.4 Limb Salvage Versus Amputation

The development of microsurgical techniques for free vascularized tissue transfer has increased the chances of saving mangled extremities or nearly amputated limbs [30]. For polytrauma patients, however, such salvage procedures are rarely indicated because they increase the systemic inflammatory load. The mangled extremity severity score can assist in decision making [31]. There are only rare indications for heroic salvage attempts. These require a multi-stage concept with initial débridement, revascularization, fasciotomies, and fracture fixation, followed by repeated débridements and early soft-tissue reconstruction during a "window of opportunity".

When the decision is to amputate, the amputation should be performed at a level of healthy tissue combined with primary open wound management.

5.8 Summary

Polytrauma must be considered as a systemic surgical problem.

Successful management requires

1. A firm understanding of pathophysiology;
2. Complete patient resuscitation;
3. Correct triage and timing;
4. Trauma algorithms.

Algorithms optimize the physiological state of patients prior to life-saving surgery and provide procedures that are safe, simple and quick, and well executed.

The primary objective is survival of the patient. Early fixation of major fractures – performed under the correct parameters – has proved to be an important tool in achieving this primary objective.

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Anesthesia and Pain Relief in Trauma Patients

6

Hans Anton Adams

6.1 Fundamentals

6.1.1 Introduction and General Pathophysiology

Analgesia and anesthesia have long posed a medical challenge that goes far beyond the administration of analgesics and anesthesia. The basic analgesics of *personal attention and positioning* should be used by everyone, including physicians.

Pain does not cause mental suffering alone; beyond that, it has a negative effect on the body, especially in the respiratory and cardiocirculatory systems, that can delay healing. When pain leads to shallow breathing and the inability to cough up phlegm, atelectasia can develop and lead to pneumonia, while activation of the sympatho-adrenergic system with tachycardia, increase in blood pressure, peripheral vasoconstriction, and greater myocardial oxygen demand can cause myocardial ischemia.

Concern is often expressed that analgesia could obscure the diagnosis; however, if the medical history is documented carefully and symptoms are ordered systematically, this concern is unfounded and should be relegated to the past.

The hope that the postoperative stress reaction could be clearly reduced with suitable pain therapy has not been fulfilled. It has been found that pain therapy that is subjectively judged to be excellent is not necessarily related to a decrease in endocrine stress parameters [1]. At least in the immediate postoperative period, and surely in the preclinical phase as well, pain is not the decisive stressor, and freedom from pain is not to be equated with freedom from stress. There are apparently stressors other than pain that dominate. These humoral and neural stressors originate in traumatized tissue with the liberation of a number of mediator substances that cannot be neutralized even with the best peripheral or central blockade; this nonetheless does not cast any doubt on the value of pain therapy.

Analgesia does not require any further justification and can considerably improve the patient's respiratory and cardiovascular situation as a whole. In contrast, anesthesia is not a simple entity and is only indicated when, upon careful review, the patient's condition is seen to absolutely demand it.

6.1.2 Endocrine Stress Reaction and Stress Concepts

Current stress concepts are based on the work of Claude Bernard, Walter Cannon, and Hans Selye. Claude Bernard (1813–1873) coined the term *milieu*

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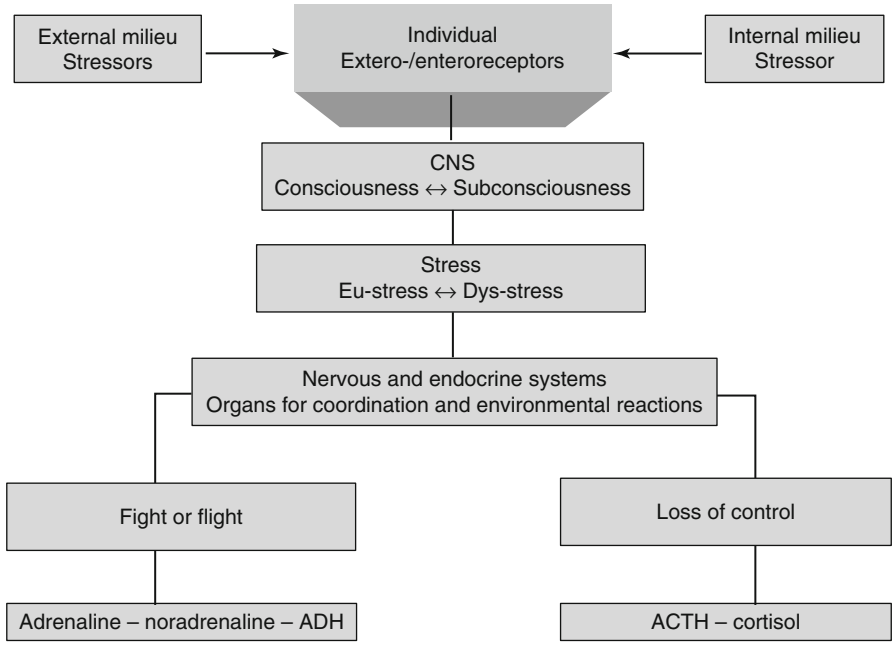

Fig. 6.1 Stress and stress reaction. *ACTH* adrenocorticotropic hormone, *ADH* antidiuretic hormone

intérieur. Walter Cannon (1871–1945) provided the definition of homeostasis and developed the concept of "fight or flight," with emphasis on the role of the catecholamines [2]. Hans Selye (1907–1982) characterized stress as a "general adaptation syndrome," distinguished between "eu-stress" and "dys-stress," and emphasized the role of the glucocorticoids [3, 4].

Selye separated the stress reaction into three sequential phases:

- The alarm reaction (corresponding to Cannon's "fight or flight")
- Phase of resistance
- Phase of exhaustion

J. Henry took the endocrine-metabolic aspects into consideration and saw a dual stress response with two main components [5] that were not necessarily sequential but could run a parallel course (Fig. 6.1); this response is described as follows:

- Activation of the sympathoadrenergic system with release of catecholamines is an immediate and active response to the stressor; release of the antidiuretic hormone is also a component of the immediate stress response.
- In contrast, activation of the hypothalamus-hypophysis-adrenal cortex axis focuses on tolerance and adaptation and, with a protracted course, is to be seen as a sign of loss of control in the confrontation with the stressor.

Later concepts emphasize organic responses to interior and exterior stressors that serve to maintain homeostasis [6]. A distinction is made between homeostatic systems in the narrow sense (e.g., oxygen concentration in the blood, body temperature) that allow changes only within very narrow limits and so-called allostatic systems that allow a wider range of responses. This is described as "maintaining stability through change (allostasis)" [7]. Allostasis as a basic function of bodily stress modulation thus reacts quickly via the sympathoadrenergic system and slowly via the hypothalamus-hypophysis-adrenal cortex axis.

> Afferent neuronal stimuli and humoral factors are of great importance in modulating the surgical stress reaction.

The neural facilitation of the stress response to tissue trauma is explained by afferent impulses from nociceptive, somatosensitive, and sympathetic pathways, whereby the relative importance of the somatosensitive nervous system in comparison with the sympathetic nervous system remains unclear. The nociceptive afferents modify the neuroendocrine function of the hypothalamus and trigger the endocrine surgical stress response. A stress reaction can, however, also be induced by physiological factors (e.g., anxiety).

Humoral mediators of the stress response include prostaglandins, bradykinin, substance P, histamine, and serotonin, which are released upon tissue trauma. Among the mediators secreted by macrophages, interleukin-1 and tumor necrosis factor-α are especially important [8].

For all trauma patients – as for all critically ill patients – the effects of analgesia and anesthesia on the stress reaction must be borne in mind. The acutely injured patient is in the "fight or flight" stage, directly confronted with the trauma-induced stressors. Because the life-preserving stress reaction depends on catecholamines, the effect of anesthetics on the sympathoadrenergic system demands special attention. The goal of anesthesia and analgosedation is to preserve the stress reaction without suppression or overactivity.

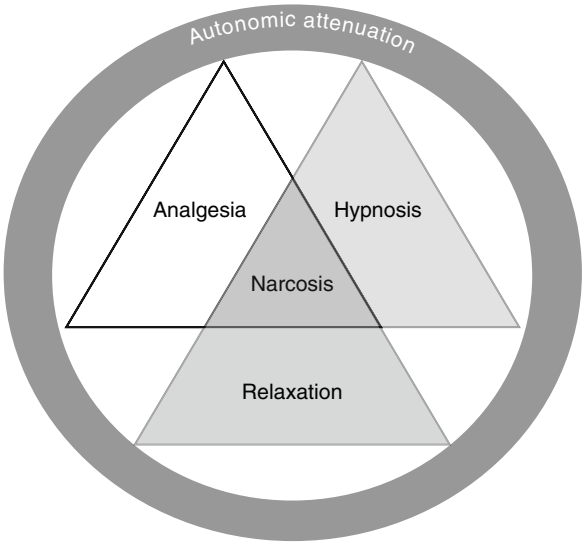

Fig. 6.2 Components of anesthesia – the specific effect sought should always be borne in mind

6.1.3 Basic Concepts in Anesthesiology

6.1.3.1 Definitions

The following definitions will be used [9]:

- *Anesthesia* is the Greek-Neo Latin word for insensitivity or lack of sensation and applies not only to the *state* of an iatrogenically induced reversible insensitivity that aims to make an intervention possible, but also to a medical *procedure* to induce such a state.
- *General anesthesia* affects the entire organism, while *local anesthesia* is limited to particular areas.
- *Narcosis* (Greek: torpor) is general anesthesia with central exclusion of pain and consciousness induced by anesthetics. "Narcosis" is synonymous with "general anesthesia" and extends the term anesthesia to cover exclusion of consciousness or hypnosis while simultaneously disallowing the term partial narcosis that is sometimes used (e.g., for spinal anesthesia).
- "Narcosis" expands the term "anesthesia," while "analgesia" limits it to the pain component by excluding sensitivity to position, touch, and temperature. *Analgesia* eliminates sensitivity to pain, producing painlessness. By definition, a properly "narcotized" patient cannot sense pain, therefore the term "analgesia" in the context of narcosis is problematic. Because a lack of specific inhibition of the nociceptive system in a narcotized patient is mentally and physically noxious, "antinociception" for specific blockade of the nociceptive system [10] is an essential component of adequate general anesthesia.
- Local anesthesia, or more precisely, local insensitivity, with its sequence of sympathetic, sensory, and when necessary, motor blockade, is more than analgesia and thus a form of anesthesia. Local anesthesia implies regional exclusion of pain in the area of the nerve endings or nerve tracts without affecting consciousness.

6.1.3.2 Components of Anesthesia

Traditionally, anesthesia comprises three main components (Fig. 6.2):

- Analgesia as *exclusion of pain* only
- Hypnosis as *loss of consciousness*
- *Attenuation of autonomic nervous activity*

Muscle relaxation is a further component that is usually required for surgery. A clear distinction cannot be made between analgesia and hypnosis, as the respective medications interact. Analgesia and hypnosis have attenuation of autonomic nervous activity in common as an additional effect.

6.1.4 Anesthetics and Anesthetic Procedures

Anesthetics, in the broader sense, are all those medications that are specifically used to induce general or local anesthesia. The substances in their main groups

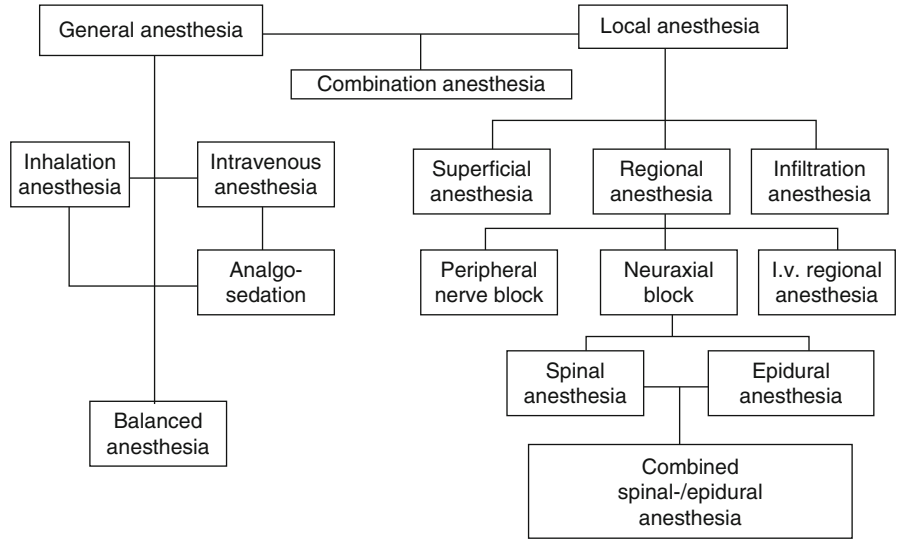

Fig. 6.3 Schematic of anesthesia techniques

of *general anesthetics* and *local anesthetics* are classified according to their mode of application:

- Local anesthetics are applied to the immediate vicinity of their target area.
- General anesthetics are classified according to their mode of application as inhalation and intravenous anesthetics.
- Inhalation anesthetics include volatile substances such as sevoflurane or desflurane and the gases nitrous oxide (laughing gas, N_2O) and xenon.
- Intravenous, better described as injectable anesthetics, because some may be administered intramuscularly, are the hypnotics, sedatives and analgesics, and ketamine.
- Because of their lack of analgesic and hypnotic effect, muscle relaxants can only be considered as anesthetics in the widest sense.

The classification of anesthetic procedures [9] depends on their mode of administration, as shown in Fig. 6.3.

6.2 Preclinical Analgesia and Anesthesia

6.2.1 Medications

6.2.1.1 General

For medical and logistic reasons, only a few tried and true medications are suitable for the preclinical situation (Table 6.1). In regard to the administration of anesthesia, the concrete effect (analgesia or sedation) that is desired of the respective medication must be taken into account (Fig. 6.2).

During embryogenesis and the early fetal period (until about the 16th week of gestation), analgesics and anesthetics are contraindicated except in special cases.

- Metamizole is contraindicated in the first and third trimesters; in the second trimester it is limited to exceptional cases. Inhibition of prostaglandin can lead to early closure of ductus arteriosus in the newborn.
- Morphine, fentanyl, and esketamine (the latter only in high doses >1 mg/kg body weight (BW)) administered to the mother shortly before birth can cause respiratory depression in the newborn.
- Midozalam administered to the mother in high doses shortly before birth can cause "floppy infant" syndrome with flaccid muscle tone and respiratory depression.
- Use of analgesics and anesthetics during lactation is generally not at issue because the mother's illness will usually preclude nursing.

The abbreviation RAD used below indicates the recommended dose for an adult weighing about 75 kg, but the dose should be adjusted to the individual patient.

Table 6.1 Medications for analgesia, sedation, and anesthesia

Medication	Indications	Dosage	RAD
Metamizole	Analgesic for mild to moderate pain	6–12.5 (–30) mg/kg BW IV	0.5–1.0 (–2.5) g IV
Morphine	Analgesic for severe pain	0.05–0.1 mg/kg BW IV	4–8 mg IV
Fentanyl	Highly potent analgesic for TIVA with ventilation	Analgesia with spontaneous respiration (*cave* respiratory depression) 0.6–1.8 µg/kg BW IV	0.05–0.15 mg IV
		For analgosedation 3–15 µg/kg BW/h	up to 1.0 mg/h
		Initial TIVA 1.25–3.75 µg/kg BW IV	0.1–0.3 mg IV
Esketamine	Analgesic and anesthetic	Analgesia 0.125–0.25 mg/kg BW IV (if needed 0.25–0.5 mg/kg BW i.m.)	10–20 mg IV (if necessary 20–40 mg i.m.)
		Analgosedation with spontaneous respiration 0.3–0.5 mg/kg BW/h	25–40 mg/h IV
		Analgosedation of ventilated patients 0.3–1.5 mg/kg BW/h	25–125 mg/h
		Anesthesia 0.5–1.0 mg/kg BW IV (if necessary 2.5 mg/kg BW IM)	40–80 mg IV (if necessary 200 mg IM)
Etomidate	Induction for generally stable patients	0.25–0.5 mg/kg BW IV	20–40 mg IV
Midazolam	Standard sedative for sedation, analgosedation and TIVA	Sedation 0.03–0.1 mg/kg BW IV	Boluses of 1–2 mg
		Induction 0.1–0.2 mg/kg BW IV	7.5–15 mg IV
Succinylcholine	Depolarizing muscle relaxant for rapid induction	1.0–1.5 mg/kg BW IV	100 mg IV

RAD recommended dose for an adult of about 75 kg body weight (BW), that should be adjusted for each individual case, *TIVA* total intravenous anesthesia

6.2.1.2 Metamizole

Metamizole is a pyrazolone derivative for analgesia for mild to moderate pain (e.g., soft-tissue injuries) with antipyretic and anti-inflammatory properties.

The effect begins within a few minutes and lasts for about 2 h. Side effects (SE) are decrease in blood pressure and tachycardia (that can lead to shock) when administered too quickly intravenously (IV).

- The single analgesic dose is 6–12.5 mg/kg BW IV (RAD 0.5–1.0 g).
- For severe pain, up to 30 mg/kg BW (2.5 g) is injected IV.

6.2.1.3 Morphine

Morphine is the standard analgesic for extremely severe pain.

The effect sets in within minutes and lasts about 4 h. SEs are respiratory depression, nausea, vomiting, and release of histamine with hypotonia. Naloxone is available as a specific antagonist.

- The individual dose is 0.05–0.1 mg/kg BW IV (RAD 4–8 mg).

6.2.1.4 Fentanyl

Fentanyl is a highly potent synthetic µ-receptor antagonist for profound analgesia with total IV anesthesia (TIVA) and airway management. It can also be used for analgesia with spontaneous breathing; however, that is off-label use.

It is effective within 2–3 min and remains so for 20–40 min. The most important SE is a potentially life threatening respiratory depression. Naxolone is the specific antagonist.

- For analgesia with spontaneous breathing, 0.6–1.8 µg/kg BW (RAD 0.05–0.15 mg) are administered IV in selected cases (*cave* respiratory depression, if necessary use breathing on command or a breathing mask).
- Depending on the patient's general condition, 1.25–3.75 µg/kg BW (RAD 0.1–0.3 mg) is injected IV.

6.2.1.5 Esketamine and Ketamine

Esketamine is the dextrorotatory isomer of the ketamine racemate. It has double the analgesic and anesthetic potency of the racemic mixture as well as a higher elimination rate with shorter time to awakening. The dosages for esketamine are given below; if the ketamine racemate is used, the dose should be doubled.

> Esketamine is an anesthetic with a strong analgesic and weak hypnotic effect. Depending on the dosage, it can be used for analgesia and analgosedation as well as anesthesia that, because of its typical effects, is termed dissociative anesthesia.

Centrally modulated activation of the sympathetic nervous system by the substance increases blood pressure, heart rate (HR), and myocardial oxygen demand. Spontaneous breathing is usually maintained. After IV administration and after a circulation time, the analgesic effect sets in and persists for some 15 min. After intramuscular (IM) injection, the effect commences within 2–5 min and lasts for up to 30 min.

No relevant increase in intracranial pressure (ICP) is to be expected with controlled normoventilation. SE include dreams and nightmares and hypersalivation. It is contraindicated for patients with hypertension, coronary heart disease, preeclampsia, and eclampsia. Dream reactions and excessive circulatory effects can be diminished or avoided with combination with midazolam; atropine combats hypersalivation.

- For *analgesia*, 0.125–0.25 mg/kg esketamine (RAD 10–20 mg) is injected IV; this can be followed by half of the initial dose when necessary. If there is no venous access, 0.25–0.5 mg/kg BW (RAD 20–40 mg) can be injected IM.
- For *analgosedation with spontaneous breathing*, 0.3–0.5 mg/kg BW/h esketamine (RAD 25–40 mg/h) is injected IV by pump, or an IV drip with 0.5 mg esketamine/ml (1 ml = 20 drops) can be used. Dosage depends on the effect. For sedation, midazolam is administered in a lower fractionated dose (1–2 mg) IV, or alternatively, 0.03 mg/kg BW/h (RAD 2.5 mg/h) is administered by injection pump. Before the IV drip is started, adequate analgesia and sedation should be secured with IV boluses of esketamine and when needed, midazolam.
- For *monoanesthesia* for rapid sequence induction (RSI) of patients in a poor general condition (e.g., in shock) 0.5 mg/kg BW (RAD 40–50 mg) is injected IV.
- For *TIVA*, esketamine is typically combined with midazolam. For RSI as is often necessary for emergency medical service, depending on the patient's condition, first up to 0.1 mg/kg BW midazolam (RAD 8 mg) is injected IV, followed by 0.5–1.0 mg/kg BW esketamine (RAD 40–80 mg) and when necessary, 1.5 mg/kg BW succinylcholine (RAD 100 mg). When necessary, further injection of half of the initial dose of esketamine can be administered, but further midazolam injections are seldom required.
- For *IM induction* – as a last resort when there is no venous access – about 2.5 mg/kg BW esketamine (RAD 200 mg) is injected along with 0.01 mg/kg BW atropine (up to 0.5 mg). Anesthesia sets in within a few minutes and a venous access should be established immediately.
- For management of special cases of uncooperative patients, 1.25–2.5 mg/kg BW esketamine (RAD 100–200 mg) is injected IM to enable venipuncture and further measures.

6.2.1.6 Etomidate

> Etomidate is an induction hypnotic without analgesic potency or significant effect on the circulatory system. It is used for induction in generally stable patients.

- For induction, depending on the patient's general condition 0.25–0.5 mg/kg BW (RAD 20–40 mg) is injected IV. Typically, fentanyl or esketamine is also needed.

> Etomidate suppresses cortisol (hydrocortisone) synthesis in the adrenal cortex for approximately 1 day and a single dose increases mortality in septic patients.

6.2.1.7 Midazolam

> Midazolam is a benzodiazepine with sedating, anxiolytic, and amnestic effects. It is used alone as a sedative or in combination with esketamine or fentanyl for TIVA.

The effect is seen quickly and usually lasts about 30 min. There can be severe respiratory depression in elderly patients and those in poor general condition. With careful dosage, cardiovascular SEs should not be expected. Flumazenil is the specific antagonist.

- For *sedation*, a fractionated IV dose of small boluses of 1–2 mg is administered until the patient slurs his or her speech or is sleepily responsive (total dose 0.03–0.1 mg/kg BW).
- For *induction*, 0.1–0.2 mg/kg BW (RAD 7.5–15 mg) is injected combined with esketamine or fentanyl.

6.2.1.8 Succinylcholine

Succinylcholine is a depolarizing muscle relaxant that has the shortest onset time (30–45 s) and the shortest action time of all muscle relaxants.

SEs are sinus bradycardia, other arrhythmias (especially in children), triggering of malignant hyperthermia (MH), and increased serum potassium. Because of the danger of hyperkalemia, it is contraindicated in patients with neuromuscular diseases (particularly extensive paralysis), longer immobilization, and predisposition to MH.

- Dosage is 1.0–1.5 mg/kg BW IV (RAD 100 mg).

6.2.1.9 Vecuronium

Vecuronium is a moderately long-acting, nondepolarizing muscle relaxant without any particular SEs that is easily stored in its dry form.

- The initial dose is 0.1 mg/kg BW IV (RAD 8 mg) followed by 0.025 mg/kg BW IV (RAD 2 mg) if necessary.

Other moderately long-acting relaxants are also suitable. In all, the indications for these substances are limited (e.g., prevention of bucking and pressing in spite of adequate anesthesia with head injury).

6.2.2 Practical Procedure

6.2.2.1 General Aspects of Analgesia and Anesthesia

In the preclinical situation, analgesia or anesthesia should be applied conservatively and only after careful consideration. Anxious nontreatment and noncritical overtreatment are both to be avoided.

The following basic aspects should be borne in mind:

- Whenever possible, all medications should be administered by drip through a safe venous access.
- Analgesics should be *titrated*, beginning with one half the normal dose or less, depending on the patient's condition. With opioids and benzodiazepines, the physician should wait until the medication takes effect before administering additional doses, and this requires patience. Anesthesia in contrast generally requires *RSI with high doses* of anesthetics to preclude defensive reflexes and movements.
- All patients who have received analgesics and sedatives generally are given oxygen (at least 5 l/min via a face mask or nasal tube).
- The patient must be closely observed for state of consciousness, skin color and perfusion, and breathing pattern; blood pressure measurement, pulse oxymetry, ECG, and with ventilated patients, capnometry/capnography are essential.

6.2.2.2 Preclinical Anesthesia

Any emergency physician should be able to intubate a profoundly unconscious patient, but induction of anesthesia in a patient who is breathing spontaneously – to improve oxygenation and for analgesia when required – should be decided on a case-to-case basis [11]. Anesthesia is generally only considered with vital or urgent indication: the patient is not fasting, is in poor condition, and must be treated by limited personnel and equipment in unfamiliar surroundings. This is true to a lesser extent for analgesic treatment protocols.

Induction of anesthesia in emergencies

1. **Prepare and check material**
   - Anesthetics
   - Bag valve mask and oxygen source
   - Suction
   - Laryngoscope
   - Tube (e.g. ID 7.5 mm) with guide wire and Luer lock-tip syringe
2. **Preparing the patient**
   - Secure venous (if necessary intraosseous) access
   - Take advantage of every opportunity for preoxygenation
   - Apply ECG and pulse oxymeter, measure blood pressure
   - Check the situation for intubation, inspect oral cavity
3. **Depending on the patient's condition, rapid i.v. injection of**
   - Up to 0.1 mg/kg BW midazolam (RAD up to approx. 8.0 mg); no midazolam when the patient is in very poor condition
   - 0.5 – 1.0 mg/kg BW esketamine (RAD 40–80 mg); low dose for patient in very poor condition
   - If necessary, 1.5 mg/kg BW succinylcholine (RAD 100 mg)
4. **Rapid orotracheal intubation as soon as relaxation sets in**
   - Mouth can be opened with little resistance
5. **Block tube and ventilate**
   - Check tube position (auscultation of the epigastrium and thoracic flanks, capnometry/-graphy)
   - Fix tube securely
6. **Administer oxygen (FiO_2 1.0)**
7. **Monitor patient**
   - Pulse, ECG, pulse oxymeter, blood pressure, capnometry/-graphy
9. **Have anesthetics at hand for further administration**

Fig. 6.4 Rapid sequence induction (RSI) of emergency anesthesia. FiO_2 inspiratory oxygen fraction

The physician must be attentive and cautious. If intubation is expected to be difficult or the physician is inexperienced, alternative airway management (especially larynx tube) should be considered, or the patient should be turned on his or her side and given oxygen with a face mask. Alternative measures for securing the airway that require experience include laryngeal tube and mask; coniotomy should be the last resort.

The practical procedure for obligatory *RSI* of anesthesia (Fig. 6.4) – for which temporary respiration with a face mask should be avoided whenever possible – is as follows [12]:

- Carefully check the material and lay it out; a powerful vacuum pump should be available.
- From the onset, use every possibility for preoxygenation and give the patient oxygen at a high flow with a mask. Washing nitrogen out of the lung (denitrogenization) and filling the intrapulmonary oxygen reserve creates an important safety margin.

- Briefly check the situation for intubation and inspect the oral cavity if possible (Is the mouth open far enough? Is the uvula visible? Is there bleeding or vomiting?)
- A Magill tube with a 7.5 mm inner diameter is standard. It should have a guidewire so that the curve of the tube can be corrected without delay if needed.
- Depending on the patient's condition, anesthesia is induced with up to 0.1 mg/kg BW midazolam (RAD up to 8.0 mg), 0.5–1.0 mg/kg BW esketamine (RAD 40–80 mg), and 1.5 mg/kg BW succinylcholine (RAD 100 mg) IV. Etomidate (dose 0.2–0.3 mg/kg BW IV; RAD 15–20 mg) or a similar substance can be used instead of midazolam, and fentanyl (dose 1.25–3.75 μg/kg BW IV; RAD 0.1–0.3 mg) instead of esketamine.
- Midazolam and etomidate are not administered to patients in very poor condition and manifestly in shock; they should only receive esketamine in a dose of approximately 0.5 mg/kg BW (RAD 40–50 mg) IV. In this case, succinylcholine can be dispensed with.
- Hyperextension of the head should be kept at a minimum for intubation. An assistant stabilizes the cervical spine with the hands on both sides of the neck. Any neck support device should be opened but left in place.
- After intubation, the patient is ventilated – regardless of the arterial oxygen saturation by pulse oxymeter (SpO_2) – with an inspiratory oxygen fraction (FiO_2) of 1.0 and a positive end expiratory pressure (PEEP) of about 5 mbar.
- After intubation, the end tidal CO_2 partial pressure is monitored with capnometry/capnography (target value 35–40 mmHg), but this value will be limited in polytrauma patients by inadequate perfusion and abnormal gas exchange in the lungs.

At first, many severely injured patients do not need any further analgesics or sedatives after induction of anesthesia their sensitivity to pain is apparently diminished. In these patients, the life-preserving endocrine stress reaction must not be suppressed by unsuitable administration of anesthetics.

With clinical signs of insufficient anesthesia (furrowed brow, tearing, defensive movements), anesthesia is optimized with injection of one half of the initial dose of esketamine or an opioid such as fentanyl (in boluses of approximately 0.2 mg); there can also be further sedation with midazolam as needed.

When *pneumothorax* is suspected in a ventilated patient, immediate insertion of a thorax drain (approximately 24 Ch.) is indicated. As hematothorax cannot be diagnosed with certainty on a clinical basis alone; a drain (approximately 28 Ch.) should be inserted pre-hospital only when ventilation cannot be otherwise secured (e.g., with increasing respiratory pressure and decreasing SpO_2) and not prophylactically.

The endotracheal tube, vascular accesses, and drains should be securely fixed in place to prevent dislocation.

When possible, a history of previous illness and surgeries, as well as current medications being used should be sought so that effects and interactions of medications can be taken into consideration.

Inadequate *documentation* of the pre-hospital care can have serious medical and legal consequences.

In particular, the neurological status (Glasgow Coma Score [GCS], pupil status, motor function of the individual extremities) should be assessed before induction of anesthesia, as well as the nature and localization of pain before administration of analgesia. Other important parameters are the courses of blood pressure and HR, and the volume requirement. Anesthetics and other medications administered should be documented carefully [11].

6.2.2.3 Special Aspects with of Polytrauma Patients

Unconscious and deeply somnolent patients (GCS persistently <9) should generally be intubated and ventilated. Endotracheal intubation and ventilation will assure optimal oxygenation (FiO_2 normally

1.0) and at the same time protect the airway from aspiration. Analgesia is less important because polytrauma patients often have little need for pain medication.

> Oxygenation – not pain relief – is the first aim of anesthesia for polytrauma patients.

- *RSI* of patients with manifest hypovolemic shock – whenever possible after preoxygenation – is with esketamine and if necessary, with succinylcholine; thereafter, the patient is ventilated (FiO_2 1.0 und PEEP 5 mbar).
- Maintenance of anesthesia depends mainly on the blood pressure. With hemodynamic instability, often no further anesthetics are needed. The patient is monitored carefully; when there are signs of insufficient depth of anesthesia (see above), minimal doses of esketamine and midazolam are injected when necessary. If the patient is hemodynamically stable (e.g., after volume replacement), fentanyl and midazolam are administered in small, and then increasing doses; a muscle relaxant (e.g., Vecuronium) is given only when necessary and the depth of anesthesia is sure to allow it.
- To preserve clotting function, normothermia [13, 14] and avoiding acidosis [15–17] have high priority; the negative effects of these parameters on coagulation are often underestimated.

6.2.2.4 Trapped Patients

> With a *trapped person* – as long as there is no free access to the patient – anesthesia and even analgesia must be avoided as far as possible.

- For analgesia, esketamine is administered in the smallest dose IV (alternatively IM) if necessary.
- An unavoidable anesthesia is performed as RSI with esketamine, and if necessary, succinylcholine.

6.2.2.5 Traumatic Brain Injury

> Before induction, the neurological situation should be assessed and documented.

- As isolated traumatic brain injury is often not accompanied by hypovolemic shock. RSI with etomidate, and if necessary succinylcholine, is indicated.
- In cardiovasculary stable patients, anesthesia is optimized with enough fentanyl and midazolam to prevent coughing and bucking with increase in ICP. Vecuronium can be added as a muscle relaxant.

6.2.2.6 Other Trauma

- When a fracture needs to be reduced, small doses of esketamine (up to 0.5 mg/kg BW IV) work well, usually after sedation with midazolam. Esketamine works faster than fentanyl or morphine and there is a less risk of respiratory depression.
- With burns, analgosedation with esketamine and midazolam often suffices. Induction, also with those two drugs, should be considered with care and will possibly be best administered after hospital admission, (e.g., with inhalation trauma or a burned body surface of more than 20 %).

6.2.2.7 Procedure with Children

Children preferably receive small doses of esketamine, or even morphine. Anesthesia is performed – as in adults – with esketamine, fentanyl and midazolam.

6.3 Anesthesia After Hospital Admission

6.3.1 Receiving the Patient

> Correct oral and written procedures for handover of the patient by the emergency physician is imperative. The emergency physician informs all the admitting physicians simultaneously, and not separately. The emergency physician's protocol can be completed, or additions made to it after the handover.

Basic anesthesiological care in the shockroom includes [18]:

- With intubated patients, the position of the endotracheal tube should be checked immediately by inspection of thoracic movement and auscultation (epigastrium and thorax flanks); this is to be repeated every time the patient's position is changed.
- Any vascular accesses should be checked for correct position, particularly with regard to backflow.
- An anesthesia protocol should begin immediately, as well as documentation of at least blood pressure, HR, and SpO_2 at the time of handover.
- Sufficient venous accesses (at least two large-lumen peripheral venous accesses) are essential.
- When possible, a multi-lumen central venous catheter (CVC) with high flow rate should be inserted to allow sufficient volume therapy as well as measurement of central venous pressure (CVP) and central venous sO_2. The catheter must be inserted in the subclavian or internal jugular vein because the femoral vein does not allow valid measurement of CVP and central venous sO_2.
- The *CVP* [11] provides valuable information on the volume status as well as right ventricular preload and compliance. The general target value is 5–10 mm Hg. A lesser value points to a lack of volume, while the target value does not guarantee sufficient preload. Higher values may be required to optimize cardiac output (e.g., with chronic right heart load). In ventilated patients, PEEP should also be taken into account, although it does not follow the CVP in a linear-additive manner.
- Arterial puncture for *invasive arterial pressure measurement* to monitor circulation beat by beat and for arterial blood gas analysis (BGA) should be performed as soon as possible but without substantially delaying patient care that is more essential. Arterial measurement does not improve a state of shock, therefore, the cause should better be sought. Respiratory fluctuations in the arterial pressure curve indicate a lack of volume.

Even if urgent action is called for, the *basic rules of hygiene* must be followed. This is especially true for insertion of a thorax drain or a CVC with Seldinger technique. Trauma patients are potentially immune compromised and must not be subjected to any avoidable additional antigen load.

6.3.2 Intrahospital Transport

Patient transportation within the hospital often entails gaps in surveillance and other risks such as inadequate ventilation or dislocation of vascular accesses.

- Transportation within the hospital demands careful clinical and technical surveillance (see above); furthermore, the patient must be protected from chill.
- Patient ventilation with FiO_2 of 1.0 and PEEP of about 5 mbar should be monitored regularly. As oxygen toxicity takes hours to become relevant, an FiO_2 of 1.0 is harmless and is an important safety factor with disconnections.
- Keeping an eye on the clock prevents unnecessary time loss.

6.3.3 Continuation of Anesthesia

Further anesthesiological procedure [18] is limited here to the basics:

- Anesthesia is maintained – with an eye on the target blood pressure value – with midazolam (RAD some 5 mg) and fentanyl (RAD some 0.2 mg) IV as needed. Particularly for patients with a head injury, a relaxant is indicated to prevent an increase in ICP as a result of coughing or bucking. Because of their pronounced sympatholytic effect, propofol and remifentanil are to be avoided in unstable patients.

- Continuous treatment of shock with volume replacement and blood components is imperative.
- Administration of catecholamines should only be considered in special situations, for example, when lack of volume cannot otherwise be brought under control.
- Until proven otherwise, it is to be assumed that the spine of the polytrauma patient is unstable; this should be kept in mind particularly when the patient is repositioned.

Other measures during in-hospital transport, diagnostic procedures, and subsequent care in the operating room include:

- Regular checks of the position of the tube
- Regular auscultation of the thorax
- Monitoring of respiratory pressures
- Monitoring of the circulatory situation and urine output
- Regular checks of pupil reaction
- Avoiding chilling and active rewarming of the patient as needed

6.3.4 Contribution of Anesthesia to Overall Care

In the individual case, the following factors can help to optimize overall care, whereby all the parameters in the previous and expected course are to be considered and included in the total clinical setting (trauma, age, previous illnesses, etc.) [18].

- Assessing pulmonary function and gas exchange, particularly FiO_2 and BGA throughout the course.
- Evaluating circulatory function, taking into account previous IV drip and transfusion requirements, as well as the course of blood pressure, HR, and CVP. The target is a systolic arterial pressure (SAP) >90 mm Hg with an HR <100/min; in head injury patients the SAP should be >120 mm Hg. Further critical values are a pH (preferably taken from a CVC) <7.25, a base excess (also preferably taken from a CVC) of −6 mmol/l or worse, a lactate concentration >2.5 mmol/l, and central venous sO2 < 70 %.
- Evaluation of renal function: hourly urine output <0.5 ml/kg BW is critical.
- Evaluation of coagulation status: critical signs are a decrease in thrombocytes, Quick value, antithrombin (AT) and fibrinogen concentration over 50 % and doubling of prothrombin time (PTT) or thrombin time (TT).
- Measuring body core temperature; values <35 °C are critical, especially for coagulatory function.

6.4 Perioperative and Postoperative Pain Therapy

6.4.1 Fundamentals

Efficient perioperative and postoperative pain therapy [19] can only be achieved with clear organizational guidelines and orientation to objectifiable standards such as the exemplary German-language guideline, S3-Leitlinie "Behandlung akuter perioperativer und posttraumatischer Schmerzen" [20].

Immediate postoperative pain therapy is often ordered by the anesthesiologist using the anesthesia protocol and begun in the recovery room. This makes sense as the anesthesiologist can best evaluate the transition from intra- to postoperative analgesia and the initial success of the latter. When the patient is transferred from the recovery room, responsibility for the continuation and monitoring of the treatment ordered by the anesthesiologist passes to the nursing staff. The primary physician is responsible for any changes in the suggested treatment plan.

The respective surgical service is responsible for the general perioperative (not immediately postoperative) analgesic care of patients, possibly with the support of a consultant, or with treatment directed by an acute pain service. In any case, responsibility for treatment during this phase must be clarified.

The most important ground rules for practical analgesic care are:

- Before surgery, the patient should be informed of possible postoperative pain and its treatment. This can be

Table 6.2 Mode of application, dosage, and main indication of common analgesics for postoperative pain therapy

Medication	Application	Dosage	Main indication
Acetylsalicylic acid	Oral; IV	RAD 0.5–1.0 g every 6–8 h MDD 3 g	Mild to moderate pain, fever
Paracetamol	Oral, rectal	RAD 0.5–1.0 g every 6–8 h MDD 50 mg/kg BW	Mild to moderate pain, fever
Diclofenac	Oral, rectal, (IM)	RAD 50 mg (−100 mg) every 8–12 h; single dose of 75 mg IM MDD 100 mg (initial 150 mg)	Rheumatic and nonrheumatic pain
Metamizol	Oral, rectal, IV, (IM)	MDD 0.5–1.0 g (20–40 drops) every 6–8 h (up to 2.5 g IV) MDD 5 g	Acute moderate and severe pain, colic, high fever
Tramadol	Oral, IV, (IM, s.c.)	RAD 50–100 mg or 20–40 drops MDD 400 mg or more	Moderate to severe pain
Tilidin-naloxone	Oral	RAD 50–100 mg or 20–40 drops every 4–8 h MDD 600 mg	Severe and very severe pain
Morphine	IV (s.c., IM)	RAD 5–10 mg IV, 10–20 mg IM or s.c. every 4–6 h MDD no information available	Severe and most severe pain

RAD Recommended dose for an adult of about 75 kg body weight (BW), *MDD* maximum daily dose, *s.c.* subcutaneous

done by the anesthesiologist or the surgeon, if the former is involved in the postoperative pain therapy.

- Pain is a subjective matter that is to be evaluated regularly by the patient himself/herself as it can be misestimated by physicians or nursing staff.
- The visual analog scale (VAS) has proved useful for evaluating subjective pain intensity. The patient selects a value between 0 and 100 (or 10) on a 10 cm long ruler indicating degree of pain from "no pain" to "unbearable pain." The VAS is especially useful for objectifying treatment success.
- In individual cases and beside clinical surveillance of the patient, a technical monitoring (ECG, pulse oxymeter, blood pressure) is necessary even on the ward to register respiratory depression due to opioids, systemic effects of local anesthetics (LA) or rostral diffusion of neuraxial anesthesia. It may also be necessary to administer oxygen. With extreme pain, at least the initial analgesia should be given in the intermediate care unit.

6.4.2 Systemic Analgesia

Systemic analgesia is fast and uncomplicated and is the basis of perioperative analgesia.

6.4.2.1 General

The substances used in systemic perioperative pain therapy can basically be given IV, IM, orally, sublingually, rectally, or transdermally. The following general rules should be observed:

- For fast treatment and to avoid incalculable resorption phenomena, analgesics are best administered via a drip using a reliable venous access; other modes of administration are usually used for chronic pain.
- First, a bolus injection is given for fast pain relief. The injections should be titrated, depending on the patient's condition to avoid under- or overdosage. Patience is needed with opioids in particular, to let the full effect develop and avoid overhasty further injections.
- The initial freedom from pain is maintained with an IV drip or further scheduled doses to avoid analgesic gaps.

6.4.2.2 Medications

Analgesics are classified as non-opioids and opioids. The analgesics that are commonly used to treat postoperative pain are listed in Table 6.2, with information on mode of application, dosage, and main indication.

Non-opioids mainly work peripherally and were previously called "peripheral analgesics." Their analgesic effect is based mainly on inhibition of prostaglandin (PG) synthesis in traumatized tissue but they

also have some additional central effects. Their SEs are clear. With short-term use, gastrointestinal disorders such as bleeding and activation of ulcers can occur, along with asthma attacks in predisposed persons, resulting from the absence of bronchodilating PG. Relative contraindications are kidney and liver disease as well as hemorrhagic diathesis. Use in the third trimester of pregnancy is normally contraindicated because inhibition of PG synthesis can lead to premature closure of the ductus arteriosus and bradytocia; acetylsalicylic acid (ASS) and diclofenac can increase the risk of bleeding in mother and child.

The non-opioid analgesics are the basis of perioperative pain treatment and are indicated for mild to moderate pain. Because of their limited analgesic potency, they are often combined with opioids. They are valued mainly for their antipyretic and anti-inflammatory effects, particularly when the musculoskeletal system is involved.

Opioids are natural or synthetic morphine derivatives, acting on various opioid receptors. Because these receptors can also be expressed in traumatized tissue, the term "central analgesics" is not completely correct. The opioids used in perioperative pain control are usually morphine agonists that mainly affect the μ-opioid receptor; their effect is felt within a few minutes and persists for several hours. Typical SEs are respiratory depression, emesis, constipation, and miosis, which currently cannot be separated from the analgesic effect. Morphine agonists can be displaced at the receptor by naloxone and so antagonized.

As extremely potent analgesics, opioids basically fulfill all clinical requirements. Their main SE is respiratory depression. As the transition from sufficient analgesia to relative overdosage with dangerous respiratory depression is insidious ("silent death"), experience as well as careful surveillance and monitoring of the patient are essential.

6.4.2.3 Patient-Controlled Analgesia

Patient-controlled analgesia (PCA) is a method in which the patient controls his/her own pain medication using an injection pump programmed by the physician. This can have optimal results with a patient who is willing and able to understand and apply the technique.

After titrated boluses have produced adequate analgesia, the physician programs the injection pump with the amount of the single dose (bolus) and the interval between doses (blocking period); a maximum dose can also be programmed. The injection pump is then connected to the patient. Although many opioids are suitable, it is suggested that only medications in regular use at the particular institution be used; the following is an example:

- Fill a 50 ml-syringe with 50 mg morphine in 50 ml NaCl 0.9 %; 1 ml of this solution corresponds to 1 mg morphine
- Bolus 2,5 ml (= 2,5 mg)
- Blocking time 15 min
- Maximal dose 25 mg morphine in 4 h

If satisfactory analgesia has not been achieved within an hour, the bolus dose is increased; if that does not produce the desired effect, the second step is to decrease the blocking time. It may be necessary to add non-opioids such as diclofenac or metamizole. Additional opioids may be administered in exceptional cases only, with the agreement of the physician responsible for PCA and surveillance of the vital functions (*cave* respiratory depression).

Metoclopramide is often prescribed for prophylaxis and treatment of nausea and vomiting. If the venous access for the PCA is also used for a gravity drip, this should have a backup valve to prevent accidental infusion of the opioid into the drip solution. Naloxon should be immediately on hand to quickly counteract an opioid overdose.

6.4.3 Regional Analgesia and Anesthesia

6.4.3.1 Fundamentals

Regional analgesia or anesthesia is usually highly effective and avoids the SEs of higher doses of systemic opioids.

In addition to the actual analgesic effects, regional administration has the following *general advantages*:

- The patient's general well-being is largely uncompromised.
- Sympathicolysis resulting from LA improves perfusion in the affected area.
- Thoracal and lumbal peridural analgesia or anesthesia considerably attenuates the systemic endocrine stress response – in this case the sympathoadrenergic reaction in particular [1] – that is of particular benefit to patients with cardiocirculatory and metabolic disorders (coronary heart disease, diabetes mellitus).

Regional administration can occur preoperatively (e.g., 3-in-1 block with fractures in the hip area), intraoperatively for anesthesia and subsequent analgesia (e.g., blockade of the axillary plexus), or postoperatively. Planning should be anticipatory, in close cooperation with the specialists involved.

The catheter technique allows the blockade to be continued over a longer period of time so that once-only blockades are the exception. LA are used for analgesia and, in the vicinity of the spinal cord, opioids. The substances are given as a bolus or a continuous drip.

With both the catheter technique and once-only blockade, the first injection should be administered by the physician who performed the puncture. Subsequent bolus injections should also be administered by the physician. Continuous infusion with an injection pump helps to avoid analgesic gaps and further allows patient control, especially for patient-controlled epidural analgesia. Axillary plexus blockade and others can also be continued on a patient-controlled basis.

Regional techniques are absolutely contraindicated with infections in the area of the planned puncture. Peripheral nerve damage or other neurological diseases (e.g., diabetic neuropathy) are *relative contraindications* because patients can potentially blame persistent neurological symptoms on previous regional anesthesia. If necessary, the patient should be referred to a neurologist for documentation of the initial status.

There are no particular hemostasiological prerequisites for *peripheral blockades*, including axillary plexus anesthesia, except with clinically manifest coagulation disorders. This is not the case, however, *in neuraxial techniques* with spinal anesthesia or analgesia, epidural anesthesia or analgesia (EDA), and combined spinal and epidural anesthesia. There is the danger of intraspinal bleeding with subsequent neurological damage and even paraplegia, so that the relevant national [21] and international [22] guidelines should be followed.

6.4.3.2 Substances

The *LA* used for spinal and peripheral blockades differ in their time to take effect and duration of effect.

- Mepivacaine and prilocaine are LA with medium-term effect (up to 2 h) that are mainly used intraoperatively and seldom for postoperative pain treatment. Although it forms methemoglobin, prilocaine is less toxic than mepivacaine and penetrates tissue particularly well.
- Bupivacaine and ropivacaine have a longer effect (5–6 h and more) but take longer to take effect. Ropivacaine is less cardiotoxic, and in low concentrations allows better distinction of sensory and motor blockade (differential blockade).

After a catheter has been inserted, a fast-acting substance is often injected to check for correct positioning. A long-acting substance is then used, generally for the above-mentioned differential blockade. With painful measures (physiotherapy, etc.) the blockade can be reinforced with a short-acting LA.

Opioids are used alone or in combination with an LA for catheter EDA (C-EDA). Sufentanil and morphine are approved for EDA; morphine is also approved for intrathecal application with spinal anesthesia, but this does not play any particular role in normal perioperative pain therapy.

Metamizole and diclofenac are usually used as comedication for insufficient analgesia.

6.4.3.3 Procedures and Indications

Of the many possible options for postoperative regional analgesia, only the most important are mentioned here:

- Thoracal C-EDA is normally used for thoracotomy and serial rib fractures.
- Lumbal C-EDA is used with extensive laparotomies (with the addition of morphine for adequate rostral diffusion), as well as for pain in the pelvic area and lower extremities.
- Continuous blockade of the axillary plexus is usually via the axillary or vertical infraclavicular plexus (VIP) access and allows analgesia in the entire upper extremity. VIP also eliminates pain in the shoulder joint.

- The 3-in-1 block is indicated particularly for knee operations (including endoprosthetic procedures), as well as for hip fractures and hip joint replacement.
- A foot block is an option for pain in the mid- and forefoot.
- The ulnar, radial, and median nerves can also be targeted for blockade.

6.4.3.4 Surveillance and Monitoring

Because of the danger of primary or secondary displacement of the catheter and the SEs that can follow, every continuous regional anesthesia should be carefully monitored.

With all regional techniques, there can be unnoticed intravasal application of LA either *primarily* during the bolus application or *secondarily* after displacement of the infusion catheter, with systemic signs such as tingling and paresthesia in nonsupplied areas (often perioral), cardiac arrhythmias, clouded consciousness, and convulsions; ultimately there can be coma and cardiocirculatory failure.

- Accidental intrathecal LA administration through an epidural catheter leads to ascending paresis with the danger of respiratory failure ("total spinal anesthesia").
- Unnoticed intrathecal administration of opioids is more insidious, with central respiratory depression and "silent death."

Care of patients with neuraxial analgesia via C-EDA poses problems because of the danger of secondary intrathecal or intravasal dislocation of the catheter. In many hospitals, C-EDA with LA and opioids is limited to intensive or intermediate care conditions. In the ward, only LA (and no opioids) are used and patients should be monitored every 15–30 min.

The following rules apply for the surveillance of the regional techniques ("pain catheter") used for postoperative pain treatment (for basic information see the section "Organization and general practice"):

- There should be written orders for every patient that include the substances to be administered, dosage intervals, procedure for insufficient effects, and the intervals for replacing filters and syringes.
- These orders should be discussed, preferably daily, with the acute pain service as well as with the medical and nursing team and changed when necessary.
- When dressings are changed, punctures and catheter insertion points should be examined for any erythema, swelling, or secretion.
- Catheters that have not been used for 2 days and that are not expected to be needed further (no physiotherapy, etc., scheduled) are to be removed.
- The acute pain service should always be consulted in any cases of doubt until neurology has completely normalized and the puncture site is painless. Furthermore, the patient should be evaluated daily by a physician or a specially trained member of the acute pain service.

Patients with C-EDA for pain therapy should be monitored carefully. New symptoms, especially one-sided neurological ones and pronounced back pain, indicate an intraspinal space-occupying process (bleeding, abscess) and demand immediate clarification using magnetic resonance imaging (MRI) (computed tomography, if MRI is not available).

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Contemporary Intensive Care Treatment for Patients with Severe Multiple Trauma

7

Reto Stocker, Philipp M. Lenzlinger, and John F. Stover

7.1 Introduction

The primary reason for mortality in patients younger than 40 years is still severe injuries induced by multiple trauma. Improvement of the rescue system with shorter intervals for rescue and transport and early respiratory and circulatory support significantly reduced early death resulting from brain damage, hypoxia, and the typical reasons of death such as exsanguinating hemorrhage in combination with acidosis, hypothermia, and coagulopathy, referred to as the "lethal triad." Consequently, complex and sequential multiple organ dysfunction (MOD) and multiple organ failure (MOF) have advanced to being the predominant reasons for increased mortality. Interestingly, the triggers for subsequent MOD/MOF are the same as those factors that accounted for the early casualties.

On the basis of the realization that multiple trauma is not characterized by the sum of the individual injuries, but predominantly reflects the consequences of severe systemic changes that expand the severity of the initial injuries, the preclinical management and emergency room management (e.g., advanced trauma life support), including surgical treatment concepts (damage control surgery, bail-out surgery), were developed (Fig. 7.1). The improvements substantially influence the subsequent intensive care of patients suffering from multiple trauma.

Apart from the basic treatment concepts of intensive care medicine (e.g., volume management, lung-protective respiratory support, nutrition, and anti-infectious therapy), treating physicians must be familiar with the trauma-induced cascades and trauma-associated MOD/MOF (e.g., coagulopathy, metabolism, thermoregulation). Insufficient cognition will promote mortality and morbidity caused by the alterations inherent to MOD/MOF.

7.2 Pathophysiology of Trauma

Severe trauma is characterized by a systemic reaction characterized by immunologic, neuroendocrine, microcirculatory, and coagulatory alterations. The functionally interwoven cascades are activated sequentially and in parallel. The typical findings are:

- Acute phase reaction with the goal of activating the immune system, initiating a host defense and promoting reparative processes
- Hyperinflammation (i.e., systemic inflammatory response syndrome [SIRS]) and increased endothelial permeability
- Hypoinflammation progressing to immunoparalysis (i.e., compensatory anti-inflammatory response [CARS]) subsequent to the initial SIRS
- Recruitment of leukocytes
- Activation of the plasmatic coagulation cascades
- Neuroendocrine response and metabolic alterations

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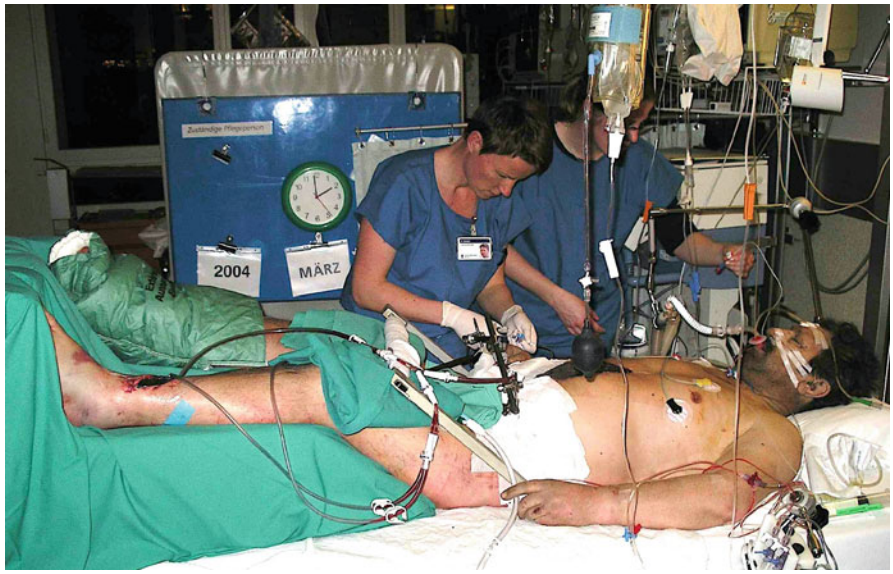

Fig. 7.1 Polytrauma patient after damage control surgery: Pelvic clamp, external fixator, open abdomen with Vacu-seal

Triggering, as well as modulation, of these trauma-related reactions results from disturbed microcirculation and alterations induced by ischemia/reperfusion.

To date, these trauma-induced cascades are best explained by a so-called two-hit model. While the first hit is induced by the initial trauma with soft-tissue damage, organ injury, and fractures, the second hit is triggered by the subsequent SIRS [1]. The second hit is caused by secondary insults resulting from endogenous or exogenous causes. Endogenous reasons are hypoxia, repetitive cardiovascular instability/hypovolemia, metabolic acidosis, ischemia/reperfusion, tissue necrosis, and infections associated with an antigenic load that activates the immune response (Fig. 7.2). Common exogenous reasons are extensive surgical interventions with additional tissue damage, extensive blood loss, disturbed coagulation, hypothermia, acidosis, mass transfusions, inadequate or delayed surgery, and inadequate or delayed intensive care treatment. Insufficient timely surgery and intensive care are reflected by the term "neglected trauma".

These diverse alterations amplify inflammatory, neuroendocrine, and metabolic reactions [2].

The trauma and subsequent "antigenic load" induce local and systemic liberation of primary pro-inflammatory mediators followed by subsequent or parallel release of anti-inflammatory mediators.

The resulting extensive SIRS that can induce multiple organ dysfunction and progress to MOF substantially contributes to an increased morbidity and mortality. In this context, levels of cytokines as well as duration of elevated cytokine concentrations correlate with the severity of injury and are associated with an increased susceptibility to subsequent infections and mortality [3, 4]. In addition, the subsequent impaired cellular immunocompetence is clearly associated with an increased risk of developing sepsis that in turn is associated with an aggravated mortality following trauma [5, 6]. This explains why additional insults known to amplify destructive cascades must be avoided. Furthermore, perfect timing of potentially damaging interventions is indispensable.

Apart from the more obvious findings that can be measured and observed at the bedside, several additional factors have been identified. In this context, genetic predisposition and gender dependency influence morbidity and mortality:

- Men show an increased morbidity and mortality compared with women [7]
- Men show a significantly increased incidence of bacterial infections [8]
- Women develop a sepsis significantly less often and thus have a better prognosis [9]
- Male gender is a risk factor for developing pneumonia and septic complications following trauma [10]
- Polymorphism of the interferon-γ-receptor-1-Gens is closely correlated with posttraumatic infections [11]

Aimed at reducing the "antigenic load" and thereby decreasing release of trigger factors, novel surgical strategic concepts during primary surgical care were developed and implemented in clinical routine. In this context, "damage control" has advanced to being an integral component in contemporary surgery [12]. A central element is to postpone the definitive surgical

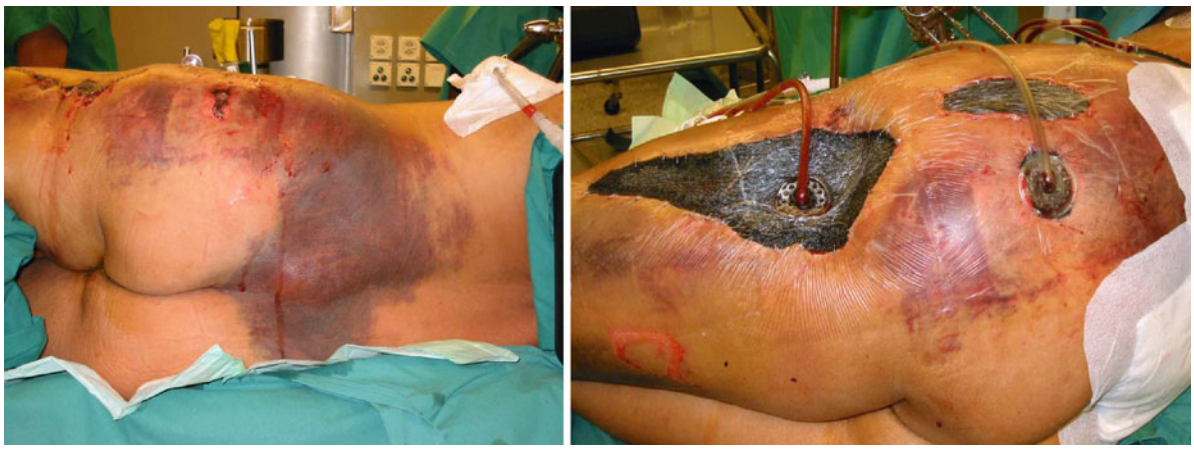

Fig. 7.2 Morel-Lavallee lesion of the pelvis (subcutaneous degloving) after débridement and vacuum sealing

care of the severely injured patient and to initially perform less invasive primary surgical stabilization procedures (i.e., external fixation, tamponade for hemostasis). Definitive surgical care should be performed after the patient has been stabilized in the ICU. The different surgical steps are strongly influenced by the individual reactions with their individual temporal development (SIRS, CARS, infections, sepsis, and hemodynamic and cardiopulmonary instability) [13]. Consequently, intensive care is crucial in stabilizing and improving the condition of the patient, thereby preparing the patient for subsequent surgical interventions.

7.3 Intensive Care

In close cooperation with trauma surgeons, intensive care medicine entails the following duties and responsibilities:

- Maintenance and restoration of vital and organ functions, including homeostasis concomitantly avoiding overcorrection
- Optimization of overall condition for subsequent surgical treatment
- Defining optimal time point for subsequent surgical treatment in cooperation with the trauma surgeons
- Stabilization, prevention, and early diagnosis and treatment of general as well as trauma surgery-related complications

Successful treatment of severely injured patients in the ICU is comprised of different parts that can only be performed using an interdisciplinary approach. The following points are of particular importance:

- *Intensive nursing care/surveillance*: Support of, and where necessary, taking over of activities of daily life (e.g., food intake, personal hygiene, movement, bedding) and medical attention and actions (e.g., analgesia, administration of fluids and drugs, complete control of vital functions and organ systems based on clinical surveillance, registration of monitored vital signs, handling of devices, etc.). Standardized physiotherapy aimed at improving and reinstituting breathing, mobilization, and movement.
- *Intensive care therapy*: Consists of supporting the endogenous compensation mechanisms and reparative processes by optimizing substrate delivery (e.g., oxygenation, perfusion, nutrition), temporary artificial support of organ functions in the event of reversible organ failure, and prevention of secondary damage. The overall purpose is to create a condition allowing subsequent healing and recovery.

In this context it is of utmost importance to practise a holistic approach (i.e., to understand the patient) in its complete complexity and to guarantee an adequate and timely flow of information between the different disciplines involved. For the trauma patient, the interdisciplinary approach is indispensable to identify problems quickly, to react adequately, and to develop a strategy based on individual development and regression.

Many new procedures are considered impossible without contemporary intensive care medicine. A good example of this is the non-surgical management of patients with injuries to the liver, spleen, and kidney and is considered the best approach in hemodynamically stable patients. As recently reported, this non-surgical management of patients who are not actively bleeding is successful in >90 % of patents with isolated trauma and

94 % of multiply injured patients. This is only possible in the event of minimal volume administration, absence of brain injury, and additional abdominal trauma, as well as additional injuries requiring surgery and age below 55 years [14]. This, however, requires a continuous, competent, dedicated, and immediate readiness in the ICU.

7.4 Special Aspects in Trauma Intensive Care

Patients with traumatic brain injury (TBI), severe trauma, and multiple injuries are usually incapable of providing detailed information regarding the circumstances of the accident and their own personal medical history. Thus, additional injuries as well as concomitant pre-existing diseases and regular medication will remain unknown during the early posttraumatic phase and can be overlooked if information is not gathered from relatives and the treating general practitioner.

7.4.1 Hemorrhage

During the early posttraumatic phase, longstanding volume deficit and the hypovolemic-hemorrhagic shock are the most deleterious alterations that determine subsequent development and incidence of potentially devastating consequences. The most prominent pathophysiologic consequence is microcirculatory impairment, resulting from hypovolemia and subsequent sympathic-adrenergic precapillary vasoconstriction. These changes are accompanied by nitric oxide-induced vasodilation that in turn causes shunts and impairs nutritive capillary perfusion, explaining heterogenous capillary perfusion. As a consequence, impaired organ perfusion with evolving tissue acidosis and lactate production with sustained increase in endothelial permeability will aggravate the underlying condition as a result of progressive edema formation. In case of persisting ischemia, degradation of energetically rich phosphates in conjunction with free oxygen radical induced mitochondrial damage will result in irreversible structural and functional cell injury. The degree of the damage strongly depends on the extent and duration of the underlying hypovolemia. Reperfusion injury resulting from restored perfusion is feared for its generation of highly toxic free oxygen radicals. These, in turn, are known to damage cell membranes by peroxidation of cell membrane lipids, accounting for resulting vasoplegia and swelling.

The criteria defining diagnosis of hemorrhagic shock have been refined over the years. The early definition of hemorrhagic shock consisting of a lost blood volume of 1–2 l [15] was substituted by the systolic blood pressure <90 mmHg [16] and the vital parameters were used to estimate prognosis [17]. Based on the observation that the cardiovascular system is able to maintain an adequate systolic pressure by a compensatory increase in heart rate despite a progressive volume loss, the so-called shock index was introduced [18]. The shock index consists of an easy-to-calculate formula dividing systolic blood pressure by heart rate. A shock index <1 is highly suggestive of hemodynamic instability resulting from hypovolemia. In addition to the absolute values, duration of shock is also of crucial importance. In this context, a threshold of 70 min appears to be clinically relevant [19, 20]. Additional predictive factors are heart and breathing frequency upon admission to the hospital [21–23]. Especially in younger patients with well preserved compensation mechanisms macrocirculation (blood pressure, heart frequency, filling pressures) may appear "normal" although microcirculation still is impaired (i.e. serum lactate concentrations 12 hours after admission). This condition is referred to as "occult" hypoperfusion and is accompanied by an increase in infectious and other complications [24–25].

Diuresis can also be used as a parameter to estimate volume depletion, provided urine production and urine release are not hampered by pre-existing renal disease and injuries to the urinary tract system.

The overall accepted goal is to swiftly restore sufficient circulation, maintain hemodynamic stability by improving organ perfusion and microcirculation using volume administration via large bore catheters, and by reducing further temperature loss. The primary goal is quantitative restoration guided by hemodynamic parameters, restoration of peripheral perfusion, restitution of sufficient diuresis (0.5–1 ml/kg body weight, >2 ml/kg body weight in case of rhabdomyolysis, that is, creatin kinase (CK) >5,000 IU/ml), and reduction or normalization of arterial lactate, pH, and base excess values. In this context, lactate >2.5 mmol/l and negative base excess that has a higher negativity than – 8 mmol/l represent important threshold values of acidosis (pH<7.2), and negative base excess values were shown to significantly predict outcome in traumatized patients [26].

Because low pH values did not unanimously correlate with the outcome, pH alone should not be used as a basis to limit therapeutic interventions. Predictive sensitivity is increased by the presence of other factors such as blood loss, hypothermia, increased lactate levels with negative base excess, and coagulopathy.

Perhaps more important than the absolute values is how long it takes to normalize lactacidosis and negative base excess during adequate treatment consisting of volume management, hemodynamic support, and rewarming. Persisting negative base excess and lactacidosis exceeding 24 h is clearly associated with significantly increased morbidity and mortality [24, 27]. Lactate-guided volume management was associated with significant reduction in mortality despite absence of improved signs of vasopressor-driven hemodynamic stabilization determined by measurements using the pulmonary artery catheter [24, 28].

7.4.2 Hypovolemia and Management of Hypovolemic/Hemorrhagic Shock

Qualitative volume replacement consists of substituting oxygen carriers (hemoglobin), factors of hemostasis (plasmatic coagulation factors, platelets), and correcting existing intravascular volume depletion. While a hemoglobin target of 9–10 g/dl had been targeted for many years, a lower hemoglobin count of approximately 7 g/dl was shown to improve outcome [29]. In this context, bedside point of care analysis of hemoglobin as well as glucose and lactate have significantly influenced morbidity and mortality and have reduced the number of resources consumed [30].

7.4.3 Disturbed Coagulation

Loss of coagulation factors and platelets as a result of uncontrolled hemorrhage, as well as dilution of coagulation factors and platelets resulting from excessive fluid replacement and reduced ionized calcium concentrations, hypothermia, and acidosis, in conjunction with the type and extent of injury (e.g., brain) all contribute to disturbed hemostatic mechanisms [31]. Contrary to the diffuse intravascular coagulopathy which includes thrombus formation we are confronted with traumatic intravascular coagulopathy (TIC) in which coagulation is hampered. In this context, the clinical picture of coagulopathy is not always reflected by laboratory values in a timely fashion. It is critical to base the subsequent administration of various coagulation factors on clinical judgment that, in turn, is strongly influenced by individual experience. Obvious bleeding requires immediate correction during the process of obtaining laboratory values that can take up to 60 min before results of plasmatic coagulation can be integrated into the fine-tuning of correcting TIC. Bedside analysis using thrombelastography may aid in faster and differentiated decision making. It is important to keep in mind that other elements apart from the concentration of coagulation factors and platelets are responsible for hemostatic failure [32]. An important devastating factor is underlying hypothermia that will disturb the entire coagulation cascade [33]. Inhibition of enzymatic reactions is reflected by prolonged prothrombin- and thromboplastin time during hypothermia even when the measured coagulation factors are normal. Another important technical detail is that functional coagulation tests are performed at 37 °C and not corrected for the actual temperature of the injured patients. This, in turn, will underestimate the extent of disturbed coagulation [34]. In addition, platelet function is impaired by hypothermia via reversible, temperature-dependent disturbance of thromboxane B2 production that will prolong the hemorrhage time [35]. Additional changes of the enzyme kinetics will delay initiation and propagation of platelet aggregation despite adequate platelet substitution [36]. This, in turn, explains the often seen poor correlation between platelet count and progressive bleeding in patients receiving massive transfusions and can be seen as an indication for platelet transfusion despite normal platelet count [37].

The following additional and preexisting coagulation disorders can aggravate the acute coagulation disorder:

Release of tissue factors because of severe TBI, pharmacologic anticoagulation, functional disturbance of platelet functions due to pharmacological and endogenous (hepatic and renal insufficiency) influences, hemophilia and deficit in von Willebrand factor. Moreover, consumption of factors due to massive transfusions (MT) and underlying hemorrhage resulting in low 2,3-DPG concentrations, low activity of factors IV (ionized calcium), V, VIII, and XIII, low fibrinogen levels, dilution thrombocytopenia, functional platelet disturbance, hypothermia, and acidosis have to be taken into consideration. Massive transfusion is thought to increase citrate concentration which chelates calcium that in turn will impair the coagula-

tion cascade and is also believed to increase protein C that can inhibit plasminogen activator inhibitor, thereby resulting in sustained activation of plasminogen; which can generate hyperfibrinolysis, and in turn, promote the development of microvascular hemorrhages at the mucosa, injuries, puncture sites, and sutures. Microvascular hemorrhages generally result from dilution coagulopathy and an increased consumption of hemostatic factors that can lead to diffuse bleeding that cannot be managed surgically. Consequently, the diagnosis of such a hemostatic disturbance must be made early to allow timely correction and prevention of aggravated complications. The diagnosis of such a hemostatic disturbance strongly depends on the vigilance and experience of the treating physicians in all involved disciplines.

Contrary to dilution coagulopathy, the combination of consumption and dilution coagulopathy will result in more severe disturbances seen in laboratory parameters reflected by a larger decrease in platelets, international normalized ratio, and fibrogen, as well as a pronounced prolongation of the activated prothrombine time (aPTT). Therefore, in patients requiring massive transfusion use of fresh frozen plasma (FFP) in order to provide a balanced set of activating and inhibitory coagulation factors (including Factor V) still may be indicated particularly because blood donors carrying a higher risk for induction of transfusion-related lung injury have been identified and excluded from FFP donation. This procedure is supported by a meta-analysis published in 2010 reporting that plasma infusion at high plasma: RBC ratios in patients undergoing MT was associated with a significant reduction in the risk of death [odds ratio (OR), 0.38; 95 % confidence interval (CI), 0.24–0.60] and multiorgan failure (OR, 0.40; 95 % CI, 0.26–0.60) [38]

Correction of disturbed coagulation occurs by supplementing the different components. To date there has been considerable controversy regarding correction strategies of impaired coagulation in trauma patients. Whereas in slight or moderate bleeding, targeted supplementation of coagulation factors monitored by means of thrombelastography or preferably thrombelastomety (i.e. ROTEM) as point of care testing (POCT) might be feasible, in severe and life-threatening bleeding this approach might fail because of the time lag between sample drawing and availability of the results. Therefore, as mentioned above use of fresh frozen plasma (FFP) in severe bleeding still is an important option in order to achieve hemostasis. However, certain factors, frequently fibrinogen and sometimes factor XIII must be additionally supplemented because provision by FFP alone might be insufficient. Factor XIII is a protein responsible for stabilizing the formation of a blood clot. In the absence of Factor XIII, a clot will still develop but it will remain unstable. If Factor XIII is deficient, the tenuously formed clot will eventually break down and cause recurrent bleeds. Suspicion in Factor XIII deficiency should be raised if in a patient with clinical relevant bleeding (i.e. diffuse micro vascular bleeding without clearly identifiable bleeding source if FXIII-activity is below 60 %). In such circumstances administration of FXIII in a dose of 30 IE/kg BW may be indicated. Furthermore, in trauma patients a positive influence on the development of the systemic inflammatory response syndrome (SIRS) could be demonstrated [39, 40, 41].

7.4.4 Hypercoagulability

Apart from possibilities of uncontrolled bleeding, trauma patients are exposed to a considerably elevated risk of thromboembolic complications in part because of an imbalance of pro- and anticoagulating factors and an increase in pro-coagulant factors (i.e., fibrinogen) resulting from a post-traumatic acute phase reaction.

Venous thromboembolic complications lead to a significant increase in morbidity and mortality and present in two forms:

- Deep vein thrombosis
- Lung embolism

A prophylaxis in trauma patients is important because clinical investigations for establishing a diagnosis are not sensitive enough. In a meta-analysis of 73 studies, however, it was found that none of the prophylaxis used was superior to another, even compared with no prophylaxis. Moreover, spinal injuries, spinal cord injuries, and age were identified as major risk factors for thromboembolic complications [42]. A prophylactic placement of caval filters may reduce the incidence of lung embolism [43, 44]. Our own experience demonstrates that cava filters can temporarily be inserted and removed in a high percentage of patients, and that they provide reliable protection against clinically relevant lung embolism [45–47].

7.4.5 Quantitative Volume Substitution

The choice of the type as well as of the amount of volume substitutes is still a matter of controversy. Young, healthy, trauma patients generally tolerate large amounts of intravenous fluids. In elderly patients, on the other hand, fluid and sodium overload may induce congestive heart failure, impaired blood–gas exchange, and hypoxia leading to the classic day 3 myocardial infarction and increased mortality, particularly if they are already suffering from a preexisting heart condition or renal insufficiency [48, 49].

It must be stressed that the classic 0.9 % sodium chloride solution is somehow toxic because it leads to hyperchloremic and dilution acidosis that exacerbates the existing acidosis in patients [48, 50, 51]. If the situation goes unrecognized, the attempt to correct the acidosis with additional fluid replacement will lead to a volume overload, with all its consequences [44, 52]. Additional unwanted effects of pure crystalloid fluid replacement are the decrease of cardiac output [53] and stroke volume by as much as 20 % even if adequate end diastolic pressure is achieved [44]. Furthermore, it has been shown that after pure crystalloid infusion – as opposed to higher concentration hydroxy ethyl starch – higher concentrations of proinflammatory cytokines, a depression of peritoneal macrophage function, and a higher expression of adhesion molecules can be found [54].

Patient's microcirculation is very vulnerable to become compromised during the acute phase. Once a SIRS is induced, fluid overload and edema potentiate capillary leak leading to a local loss of control of inflammatory mediators and an increase of edema [55]. Furthermore, volume substitution with crystalloids alone leads to a reduced colloidosmotic pressure by up to 50 % with a consecutive fourfold increase of pulmonary transendothelial flux. Corrective administration of colloid fluids will consecutively reduce inflammation and edema [56–58].

In summary, volume expansion will improve cardiac output to a certain point via the Starling mechanism. Beyond that point it will, however, worsen cardiac function and promote edema formation, particularly if based solely on crystalloids [59]. Therefore, monitoring of stroke volume and cardiac output before and after fluid challenge is a more reliable alternative than assessing heart frequency and blood pressure alone [60–62].

7.4.5.1 Fluid Replacement and the Bowel System

In recent years, several studies have shown that an increased administration of sodium and water may have numerous detrimental effects on the gastrointestinal system: The edema in the splanchnic area leads to an increase in intraabdominal pressure that in turn can lead to a decrease of tissue oxygenation. Apart from intestinal permeability dysfunction, which is suspected to account for increased bacterial translocation, a protracted dysmotility of the bowel can be observed, causing intolerance to enteral nutrition. The resulting gastrointestinal dysfunction increases the risk of ventilation-associated pneumonia and therefore increases morbidity and mortality, as well as length of stay in the ICU and time to discharge [49, 59]. It is well recognized that the excessive use of crystalloids constitutes a risk factor for the development of abdominal compartment syndrome (ACS) in trauma patients. It has been shown that supranormal volume replacement, as it is often applied, will lead to an increase of the amount of crystalloid fluids infused, an increased incidence of ACS, and an elevated rate of MOF with a consecutively higher mortality rate [63–66]. Liberal infusion of crystalloid fluids in young trauma patients may lead to the secondary development of ACS even in the absence of abdominal injuries [67]. In most studies, the mortality rate resulting from ACS-induced lung failure or MOF is more than 50 % despite aggressive surgical abdominal decompression [63–66]. Administration of more than 3 l of crystalloid fluids prior to transfer of the patient from the Emergency Department to the ICU is highly predictive for the development of primary or secondary ACS.

Given these pathophysiological effects of crystalloid fluid infusion, alternative volume replacement strategies are warranted using colloid fluids or hypertonic saline, and considering early administration of vasopressors in order to restore vascular tone [63–66, 68].

7.4.6 Hypothermia

There is an increased risk for hypothermia leading to elevated mortality during volume substitution particularly during massive transfusions, commonly necessary in multiple trauma patients. It has been shown that prolonged hypothermia during volume therapy has deleterious effects on cardiovascular parameters and

hepatocellular function, and additionally leads to an upregulation of cytokines. Conversely, heating to 37 °C during volume restitution improves cardiovascular and hepatocellular function and reduces cytokine concentrations [69]. Furthermore, rewarming increased hepatic blood [70]. Heating of the patient to normothermia, therefore, must accompany volume substitution following traumatic hemorrhage.

Thermal homeostasis depends on the balance of factors leading to heat loss (conduction, convection, evaporation, and radiation) and the capacity of the body to produce heat. It is important to note that heat loss and the drop in body temperature begin immediately following trauma and are further propagated by hypoperfusion, shock, prolonged exposure, immobility, and old age. If preventive measures are not implemented, cooling continues in the emergency department and the ICU, especially if the injured patient is exposed in a temperature gradient of more than 15 °C and if he or she is not immediately covered by warm blankets. A drop of core body temperature to 35 °C is regarded as being clinically significant, and a drop to below 34 °C indicates that early intraabdominal packing may be warranted [20]. More than 20 % of trauma patients and 50 % of injured patients undergoing laparotomy are hypothermic upon exit from the operating room [71]. These patients require significantly more volume substitutes and transfusions, and their need for catecholamine is increased, which leads to a higher incidence of organ dysfunction, a longer stay (LOS) in the ICU, as well as a higher mortality [72]. However, hypothermia may possibly be a surrogate marker for the severity of the injury and the consecutive shock, making it difficult to account for the true effect of hypothermia alone in the clinical setting [73].

Rewarming of the patient in the ICU can be achieved through warming of ventilation gas, warmed intravenous fluids, heating blankets, or by invasive heating devices (i.e., Cool Guard®).

7.4.7 Acidosis

Acidosis resulting from hypovolemia can contribute to coagulopathy, which in turn may promote hemorrhage and hypovolemia. Correction of coagulopathy therefore requires not only hemostasis but also restoration of tissue perfusion and oxygenation through adequate volume substitution, transfusion, and pharmacological circulatory support. Apart from clinical signs (e.g., peripheral perfusion and adequate diuresis) the endpoints of restoration of sufficient tissue perfusion are normalization of serum lactate levels, base deficit, and central venous O_2 saturation. However, they remain controversial [74–76].

7.4.8 Prophylaxis and Therapy of Organ Damage

7.4.8.1 Circulation

Volume substitution for stabilization of the circulatory system is not an issue only at the start of intensive therapy. Apart from the primary hypovolemia resulting from hemorrhage, secondary trauma reactions can cause protracted hypovolemia and fluid distribution disturbances. They include vasodilation and a capillary leakage because of posttraumatic inflammation caused by inflammatory mediators (SIRS). The use of vasopressors is often unavoidable because of SIRS-associated vasodilation.

Despite adequate volume substitution, intractable shock, particularly in the context of thoracic trauma, may indicate cardiac injury (valvular injuries, cardiac tamponade, or coronary dissection) or acute cardiac decompensation resulting from concomitant heart disease (coronary heart disease, cardiomyopathy). Transesophageal echocardiography has proved to be a useful bedside examination in such situations.

7.4.8.2 Respiration

Respiratory failure primarily resulting from pulmonary insufficiency or from extrapulmonary causes is commonly encountered in the trauma patient. If the cause is of extrapulmonary origin (abdominal hypertension, left heart failure, etc.), these problems should be addressed and non-invasive ventilatory support strategies should be employed. Respiratory failure resulting from a pulmonary disturbance (lung contusion, aspiration), endotracheal intubation, and ventilation using positive end expiratory pressure often cannot be avoided. In general, however, modern ventilation strategies aim at keeping ventilator support as short and least invasive as possible. Therefore, controlled ventilation of the trauma patient is mandatory only if an acute TBI is present or in cases of severe hypovolemic shock. In the latter case, maintaining spontaneous ventilation will require a blood flow of 20–30 % of cardiac output. Therefore, relieving the respiratory muscles by controlled ventilation is essential in this phase. In all other cases of respiratory insufficiency, the goal currently is to preserve at least parts of

spontaneous breathing activity or the use of non-invasive support [77, 78].

Restriction of controlled ventilation lies in the fact that it causes a myriad of undesired effects and carries risks (circulatory depression, ventilator-associated pneumonia, alveolar volutrauma and barotraumas, etc.) that can lead to increased morbidity and mortality, as well as a prolonged LOS in the ICU and hospital. Recent studies have shown that assisted spontaneous breathing (ASB), as opposed to controlled mechanical ventilation, increases gas exchange, systemic blood flow, and tissue oxygenation. Computed tomography studies have revealed that the improved gas exchange is a result of a re-distribution of ventilation and end expiratory gas distribution in dependent lung areas. ASB, therefore, avoids the unwanted cyclic end expiratory alveolar collapse in dependent zones [79]. Another advantage lies in the lower requirement for sedation, which again may lead to a shorter LOS in the ICU [78]. Early ASB calls for intensive support such as breathing and physical therapy, posturing, and early mobilization. Therefore, surgical treatment must aim for early fracture stabilization, even if only temporary (e.g., by external fixation).

In the event of controlled mechanical ventilation, lung injury as a result of the ventilation, must be avoided. Central elements comprise limitation of tidal volume to 6 ml/kg body weight, depending on the severity of lung injury, in order to avoid volutrauma, as well as limiting peak inspiratory pressure to below 30 mbar to avoid barotrauma (so-called "Lung Protective Ventilatory Strategy") [80]. Switching to assisted spontaneous breathing modes as early as possible should remain a high priority in these cases.

Techniques such as pumpless extracorporeal lung assist up to extracorporeal mebrane oxygenation (ECMO) (Fig. 7.3) may be needed in order to allow for sufficient gas exchange obeying lung protective ventilatory strategies.

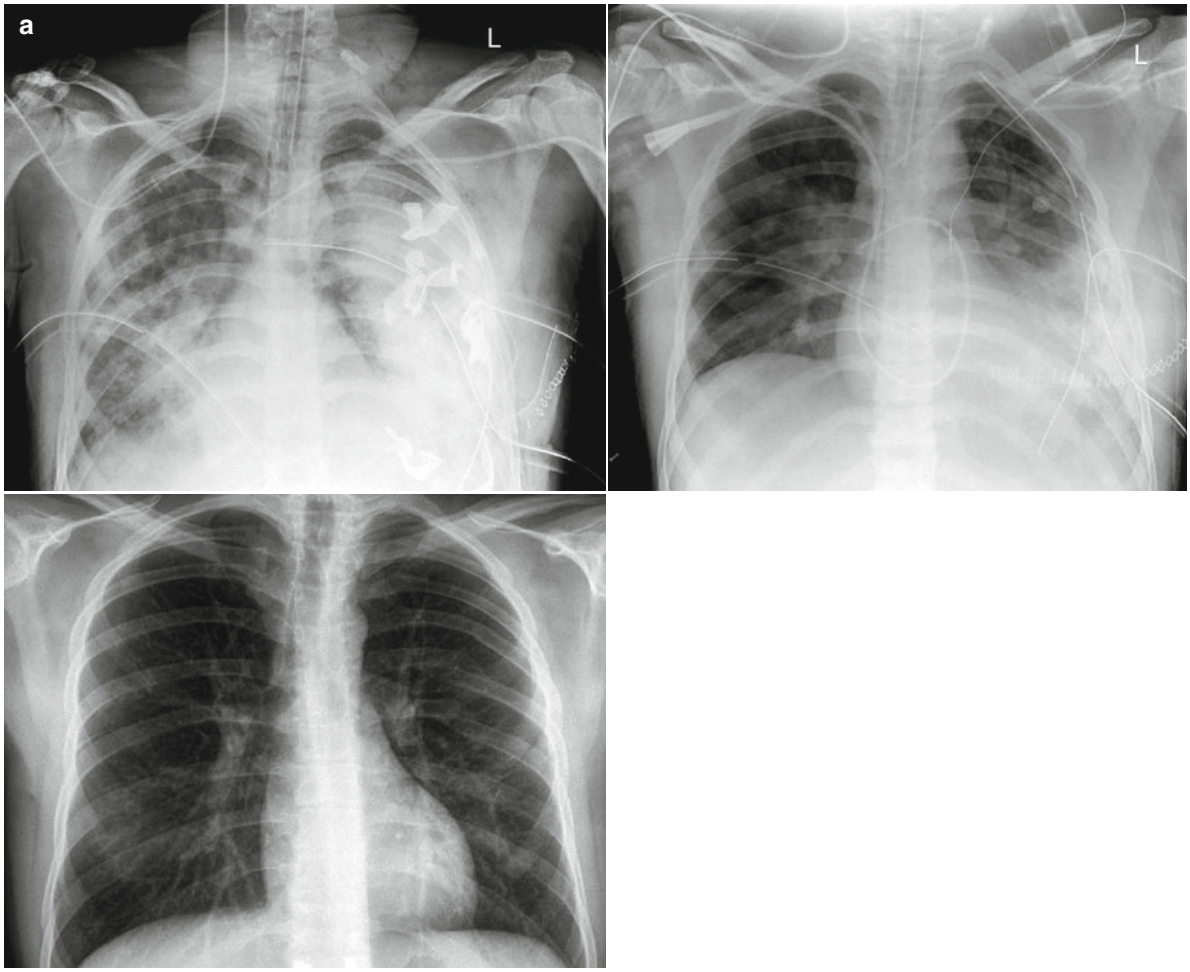

Fig. 7.3 (**a**) Severe chest trauma: Sequence of chest radiographs. (**b**) Patient with PECLA (Pumpless ExtraCorporal Lung Assist)

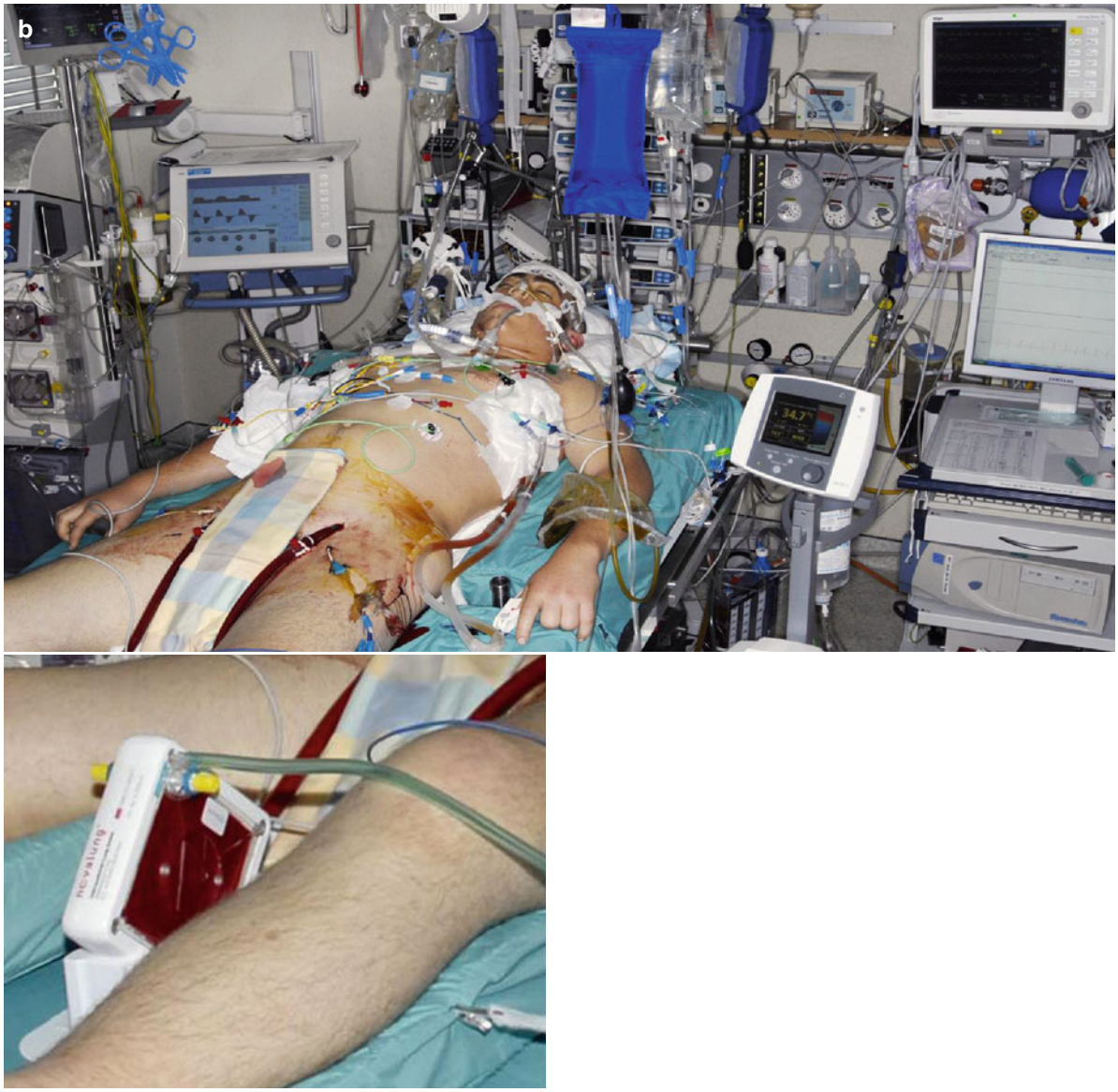

Fig. 7.3 (continued)

7.4.8.3 Bowel System

The bowel system acts a classic shock organ and is rather inaccessible to clinical diagnostic tests and leads to compromising events that are not being noted and treated in a timely manner. The occurrence of stress ulcers is often the result of organ dysfunction because of a relative or absolute hypoperfusion of the splanchnic area. It can therefore not be prevented by a pharmaceutical ulcer prophylaxis.

Complications such as SIRS, severe infections, or sepsis are characterized by a splanchnic hyperperfusion and increased oxygen transport caused by a stress hormone and cytokine-induced hypermetabolism, as well as an increased hepatic gluconeogenesis. Various cytokines, such as Interleukin-6, induce an acute phase reaction with synthesis of acute phase proteins by the liver. This hypermetabolism in turn can lead to a mismatch between actual oxygen consumption and availability.

The gut mucosa, lined with enterocytes, probably plays an important role in the pathogenesis of MOF, and is a controversial topic [81]. In order to limit damage to the mucous membrane, restoration of splanchnic

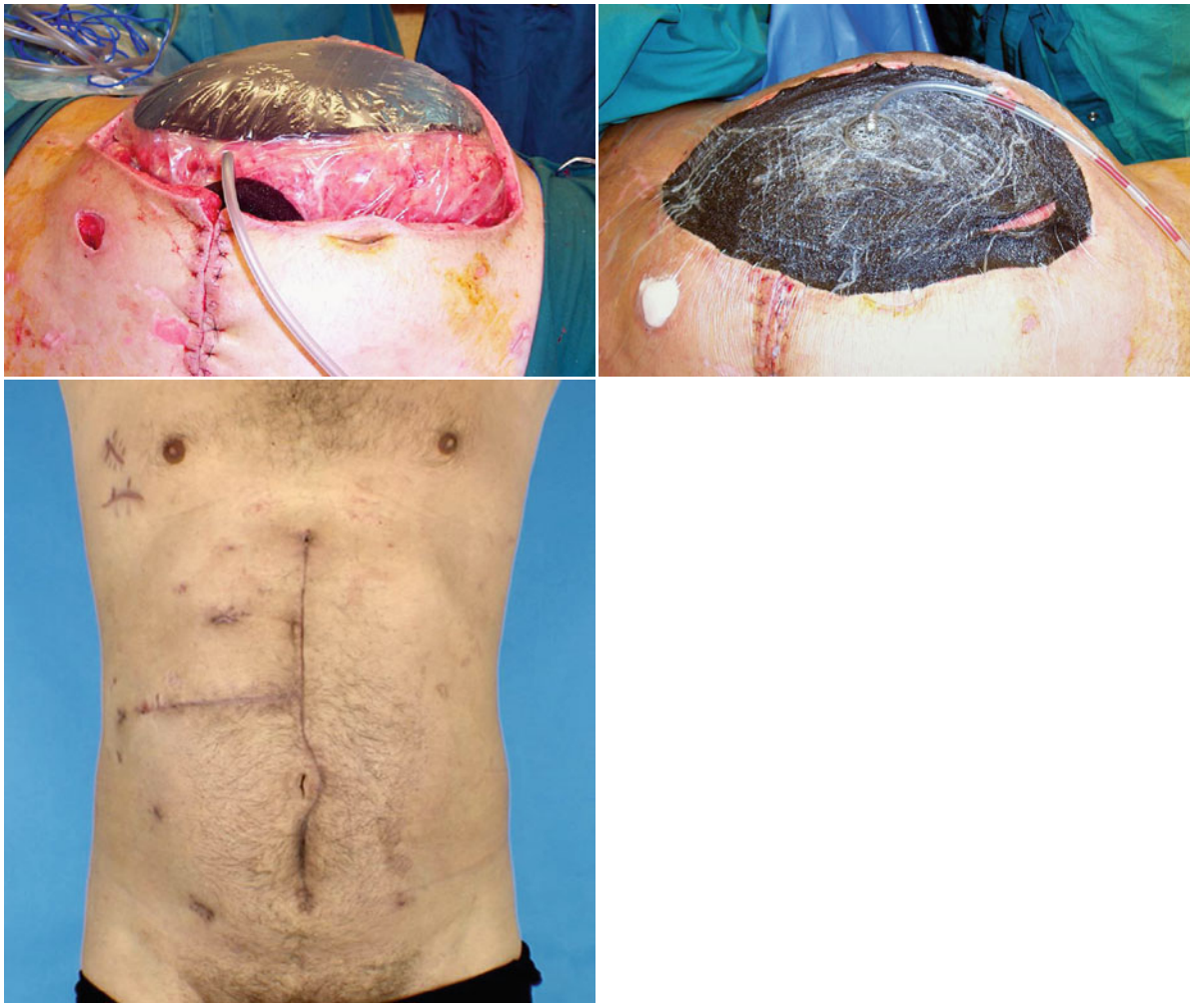

Fig. 7.4 Abdominal gunshot wound, perihepatic packing, open abdomen with Vacu-seal. Healed abdominal wall

perfusion through volume therapy and shock treatment, as well as endoluminal administration of substrates by early enteral nutrition, is essential.

Abdominal Compartment Syndrome

An elevated intraabdominal pressure, termed ACS, may heavily impair systemic circulation and perfusion of abdominal organs [82].

ACS can be induced by abdominal trauma with consecutive gut edema, intra- and retroperitoneal hematomas, intra-abdominal packing (in damage control surgery) (Fig. 7.4), and by excessive infusion of crystalloid fluids (see above). Venous backflow decreases because of direct compression of the inferior vena cava and venous pooling of blood in the pelvic area and the lower extremities. Additionally, elevated intra-abdominal pressure leads to diaphragmatic elevation and a relative increase of cardiac afterload, causing a decrease of cardiac output [83].

Visceral blood flow to the liver, the gut, and the kidneys is impaired. Renal function is particularly at risk because elevated intra-abdominal pressure also impairs renal run-off and also because the kidneys are particularly vulnerable to direct organ compression, leading to an elevated vascular resistance, and therefore, further impairment of kidney perfusion [84]. So renal dysfunction up to anuria is a common complication of ACS.

Elevated intra-abdominal pressure causes a decrease of thoracic volume and pulmonary compliance. Ventilation-perfusion mismatch and impaired blood oxygenation follow.

Perihepatic packing as a damage control procedure may be a reason for a significant ACS. Compression of

the suprarenal vena cava impairs kidney function, in which case a second look at abdominal decompression through hematoma evacuation and/or (partial) removal of the packing may be necessary [83, 85]. This will also improve visceral perfusion, cardiac function, and respiratory mechanics [86]. In the absence of ACS, packing should be left in place until the patient is hemodynamically stable, acidosis has been corrected, the patient is normothermic, and sufficient coagulation has been restored. Premature removal of abdominal packing may otherwise only be warranted in order to decrease the risk of abscess formation if the abdominal cavity has been substantially contaminated [87]. Moreover, ACS still can occur even if an open abdomen strategy has been applied. This is referred to as "tertiary ACS" and also may require premature return to the operating theatre for decompression (i.e. exchange of soaked packing tissue).

Kidneys

The pathophysiology of acute renal insufficiency in the polytrauma patient is driven by shock resulting from hypovolemia. Ischemia, focal hypoxia, and dysfunction of the coagulation system lead to functional and structural damage presenting itself clinically as oligo/anuria. Therefore, a central element of preventing acute renal failure is urgent as also decisive correction of hypovolemia and avoiding hypotensive states. There are no other possibilities of protecting the kidney; neither application of dopamine nor administration of diuretic drugs has any scientific basis. On the contrary, it is most likely that such interventions will lead to a deterioration of renal function (e.g., because of worsening of renal energy homeostasis).

A trauma-specific form of renal failure known as crush syndrome is the result of the destruction of large amounts of muscle mass where myoglobin reaches the intravascular space. Myoglobin is toxic for the kidneys because it is filtrated and may then mechanically clog the tubular system because of precipitation. Additionally, small amounts of myoglobin can be absorbed through endocytosis into the tubular cells which will lead to the formation of highly toxic hydroxyl radicals through the release of porphyrin complexes of iron [88]. The standard therapy for crush syndrome entails the liberal administration of large quantities of isotonic crystalloid fluids (correction of hypovolemia, increase of diuresis), bicarbonate (increases solubility of myoglobin in the urine through alkalinization), and mannitol (increases tubular urinary flow). As long as systemic arterial blood pressure can be maintained, substances (i.e. calcium antagonists) may be used to inhibit the myoglobin-induced vasoconstriction (i.e., calcium antagonists). Any type of vasoconstriction during hypovolemic shock is detrimental and worsens the prognosis of acute renal insufficiency.

In the event of acute oligo/anuric renal failure, continuous renal replacement therapy should be employed. It has been shown that for crush syndrome, continuous hemofiltration is superior to dialysis.

7.5 Summary

As the trauma surgeon is responsible for all surgical aspects of trauma and decides whether, and at what stage of treatment, support from other specialties is needed, the trauma ICU specialist aims for restitution of vital and physiological functions taking into account the specific host response by the patient. Major goals in the initial phase include rewarming, correction of coagulation, acidosis, hypovolemia, monitoring/avoidance of compartment syndromes in order to optimize oxygenation, and tissue perfusion. Therapy is later directed toward reestablishing physiological functions, including early enteral nutrition, infection control, and avoiding secondary injuries and complications.

Consultation between the trauma surgeon, ICU staff, and other medical specialties guarantees optimal assessment, diagnostics, and treatment tailored to the specific needs of the individual patient. The major goal is maintenance and/or restoration of all functions that are needed to assure a good long-term quality of life.

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Systemic Infections and Sepsis

8

Marius Johann Baptist Keel

8.1 Introduction

Sepsis as a clinical syndrome occurs when a local infection with an appropriate inflammatory response becomes amplified, leading to organ dysfunction or risk of secondary infection. A continuum exists from a low-grade systemic response with a self-limited infection to a marked systemic response with solitary or multiple organ dysfunction syndrome (MODS) or finally multiple organ failure (MOF) in severe sepsis or septic shock. Sepsis is the most common cause of death in intensive care units or among severely injured patients surviving the first 3 days after trauma.

The following definitions of systemic infections and sepsis were determined by a consensus conference of the American College of Chest Physicians and the Society of Critical Care Medicine in 1991:

- Infection: microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.
- Bacteremia: presence of viable bacteria in the blood.
- Systemic inflammatory response syndrome (SIRS): systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions:
  1. Temperature >38 °C (fever) or <36 °C
  2. Heart rate >90 beats/min. (tachycardia)
  3. Respiratory rate >20 breaths/min. (tachypnea) or $PaCO_2$ <32 mmHg
  4. White blood cell count >12,000/mm^3 (leukocytosis), <4,000 mm^3, or >10 % immature (band) forms.
- Sepsis: systemic response to infection, manifested by two or more SIRS criteria.
- Severe sepsis: sepsis associated with organ dysfunction, hypoperfusion (lactic acidosis, oliguria, acute alteration in mental status), or hypotension (systolic blood pressure <90 mmHg or a reduction of ≥40 mmHg from baseline in the absence of other causes for hypotension).
- Septic shock: sepsis-induced hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities or treated by inotropic or vasopressor agents.

The introduction of this nomenclature is important to understand the pathophysiology of this clinical syndrome and to describe the different manifestations of clinical symptoms. In addition, it has aided in determining the prognosis of sepsis and the design of randomized, controlled trials during the past decade.

8.2 Epidemiology

Severe sepsis is common (3 cases per 1,000 person-years) and is associated with a high mortality rate (25–30 %). Necrotizing soft-tissue infection (NSTI), one of the most serious examples of severe sepsis in adults, has an incidence of 0.04 cases per 1,000 person-years. It has increased during the past decade as a result of increased microbial virulence and resistance because of excessive use of antibiotics. In an analysis of almost 1,000 severely injured patients surviving the first 3 days after trauma,

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infection was diagnosed in the mean 11 days after the trauma in 46 % of all patients. The most frequent type of infection was pneumonia (34 %), followed by bacteremia (15 %), wound infection (13 %), catheter-related infection (11 %), urinary tract infection (9 %), intracranial (6.5 %) or intraabdominal (3.3 %) infections, bone or joint infection (1.4 %), and other unknown infections in 6 %. Of the isolated microorganisms, 49 % were gram positive, 49 % were gram negative, 2 % were fungi, and 0.1 % were viruses. The most commonly recovered pathogens included *Staphylococcus aureus* (16 %), coagulase-negative *Staphylococci* (14 %), *Pseudomonas aeruginosa* (10 %), *Enterococcus* species (10 %), *Escherichia coli* (9 %), and *Enterobacter* species (8 %). Fifty one percent of all infected patients developed septic episodes, of which most were associated with pneumonia (51 %), bacteremia (13 %), wound infection (9 %), catheter-related infection (5 %), or intracranial infection (5 %). In NSTIs, 55–75 % result from type I infections (polymicrobial) and the remainder are monomicrobial infections (type II). The leading microbial causes are gram-positive cocci (*S. aureus* [22 %], *Streptococcus* species [17 %]), followed by gram-negative rods (*Klebsiella* species [10 %], *E. coli* [7 %]), anaerobic bacteria (7–18 %), and *Clostridia* species (gram-positive rods).

8.3 Predisposing Risk Factors

The risk for postoperative or posttraumatic sepsis is influenced by five factors:

- Patient factors
- Local tissue factors
- Systemic factors
- Injury factors
- Therapeutic factors

Patient-specific factors include the patient's sex and genetic predisposition regarding inflammation and coagulation cascade. In a cohort of severely injured patients with an Injury Severity Score (ISS) ≥25 points, the incidence of sepsis was 31 % for males and 17 % for females, whereas age had no significant effect. The immunosuppressive function of androgens seems to be responsible for this phenomenon. Gene polymorphisms with increased mortality of septic patients were observed for tumor necrosis factor B2/B2 and heat shock protein 70-2A/A genotypes. Other patient-specific factors are diabetes, alcohol and drug abuse, immunosuppression, renal insufficiency, and chronic obstructive airway diseases.

Tissue necrosis or hematoma in the wound and local hypoperfusion through contusions, lacerations, vascular injuries, or compartment syndromes of organs or soft tissues influence the local immunity and tissue integrity. Hypoperfusion leads to oxygen deficit in local endothelial, parenchymal, or immune competent cells, which is partially compensated for by the intracellular degradation of the energy-store adenosine triphosphate (ATP) to adenosine diphosphate and monophosphate (AMP). Through the ATP-consumption, disturbances of membrane permeability and energy-dependent Na^+/K^+-ATPase-pump arise with an intracellular Na^+ increase and cellular swelling. Finally, generation of hypoxanthin leads to a deficit of the cellular second messenger cyclic AMP. The ATP-deficit is further responsible for an increase of cytosolic Ca^{2+} with metabolic disturbances of glucose, proteins, release of neurotransmitters or hormones, and an activation of phospholipases, proteases, and endonucleases with membrane disintegration and DNA damage. Of more importance for secondary tissue damage and organ dysfunction is the reperfusion phase (ischemia-reperfusion injury). During this postischemic phase, hypoxanthine is degraded to xanthine and finally to urea acid by xanthine oxidase with generation of superoxide anions (O_2^-) from reavailable oxygen. Superoxide anions are further reduced to hydrogen peroxide (H_2O_2) and hydroxyl ions (HO^-) by superoxide dismutase. These free oxygen radicals enhance disturbances of the intracellular Ca^{2+} homeostasis and induce lipid peroxidation, membrane disintegration, and DNA damage with apoptosis and necrosis of local endothelial, parenchymal, and immune cells.

The severity of trauma as measured by the ISS increases the severity of posttraumatic SIRS and the incidence of septic complications. In addition, the extent of hemorrhagic shock predicts the incidence of infectious complications. Severe hemorrhagic shock (grades 3 and 4 according to the shock classification of Advanced Trauma Life Support [ATLS®]) on admission in patients surviving the first 3 days after trauma is associated with a higher rate of infections (73 %) and sepsis (43 %) compared with mild hemorrhagic shock (43 %, respectively 22 %). For this reason, severely injured patients with insufficient 24 h-lactate-clearance have a high rate of infection. The number of units of packed red blood cells is also an independent risk factor for posttraumatic SIRS and infections. Furthermore, the intensive care unit stay predicts the occurrence of subsequent nosocomial

infections. The high rate of respiratory tract infections is a consequence of frequent ventilator support in trauma patients, particularly in patients with chest, abdominal, and head injuries. With respect to the site of injury, patients with abdominal and pelvic injuries have the highest rates of septic complications.

Furthermore, therapeutic factors regarding the management of severely injured patients influence the risk for posttraumatic infections. They are called secondary endogenous and exogenous hits. The first hits are the trauma impact (trauma load), determining primary organ or soft-tissue injuries and fractures. Typical endogenous (antigenic load) second hits are respiratory distress with hypoxia, repeated cardiovascular instability, metabolic acidosis, ischemia/reperfusion injuries, vital tissues, contaminated catheters, tubes, or wounds. Surgical interventions with severe tissue damage, hypothermia or blood loss, inadequate or delayed surgical or intensive care after neglected or missed injuries, as well as massive transfusions represent exogenous second hits (interventional or surgical load).

8.4 Pathophysiology

Sepsis is the culmination of complex interactions between the infecting pathogens and the host immune response. Bacteria, viruses, parasites, and fungi in combination with traumatic tissue injuries initiate the host immune response through complex intracellular signal-transduction pathways with release of proinflammatory mediators and induction of acute phase reaction and plasmatic cascade system consisting of the complement cascade, kallikrein-kinin system, and coagulation cascade. The interaction of leukocytes, particularly the polymorphonuclear leukocytes (PMNLs) as cells of the first defense line, with endothelial cells, plays a crucial role in the inflammation-mediated injury. The key determinant of survival in sepsis is limiting excess systemic inflammatory and coagulopathic damage, while retaining the benefits of controlled antimicrobial clearance and localized clot formation.

8.4.1 Host Response Initiation

Host defenses can be categorized according to innate and adaptive immune system responses. The innate immune system responds rapidly to pathogens, mediated by various sets of pathogen-associated molecular patterns (PAMPs) and pattern recognition receptors (PRRs). PRRs also serve as receptors for endogenous danger signals such as hemodynamic changes in sepsis (tissue hypoperfusion and ischemia/reperfusion) or traumatic tissue damage (fractures and organ injuries). Heat shock proteins-60, -70, -90, fibrinogen, fibronectin, hyaluran, or high mobility group box-1 (HMGB-1), and recently formyl peptides, mitochondrial DNA, or glycosaminoglycans from apoptotic or necrotic cells have been identified as danger-associated molecular patterns (DAMPs) that are relevant for sepsis. PAMPs or DAMPs bind to three different families of PRRs: (1) toll-like receptors (TLRs); (2) nucleotide-oligomerization domain leucine-rich repeat (NOD-LRR) proteins; and (3) cytoplasmatic caspase activation and recruiting domain helicases such as retinoic-acid-inducible gene I (RIG-I)-like helicases (RLHs). Multiple positive feedback loops between PAMPs, DAMPs, and their receptors may represent the molecular basis for the observation that infections as well as damaged tissue or nonspecific stress factors can trigger flares in systemic inflammatory response. TLR expression on antigen presenting cells is up-regulated in patients with sepsis. TLR-2 recognizes a peptidoglycan of gram-positive bacteria, whereas TLR-4 recognizes lipopolysaccharide of gram-negative bacteria. Mitochondrial DAMPs activate PMNLs through formyl peptide receptor-1 and TLR-9. Binding of TLRs activates intracellular signal-transduction pathways that lead to the activation of transcriptional activators such as phosphoinositide 3-kinase (PI3K) or cytosolic nuclear factor-kappa B (NF-kB). PI3K can function either as a positive or negative regulator of TLR signaling. As a positive mediator of TLR signaling, PI3K, along with p38 and extracellular regulated kinase 1/2 mitogen-activated phosphokinases, lead to production of proinflammatory cytokines interleukin (IL)-1β, IL-6, and IL-8. On the other hand, along with the downstream serine/threonine kinase Akt PI3K/Akt, the signaling pathway acts as an endogenous negative feedback mechanism to limit proinflammatory and apoptotic events in immune cells during sepsis through generation of anti-inflammatory cytokine IL-10. NOD proteins recognize common fragments of bacterial peptidoglycan, whereas RIG-I or RLHs primarily recognize viral nucleic acids.

In addition, microorganisms stimulate specific humoral and cell-mediated adaptive immune responses that amplify innate immunity. B cells release

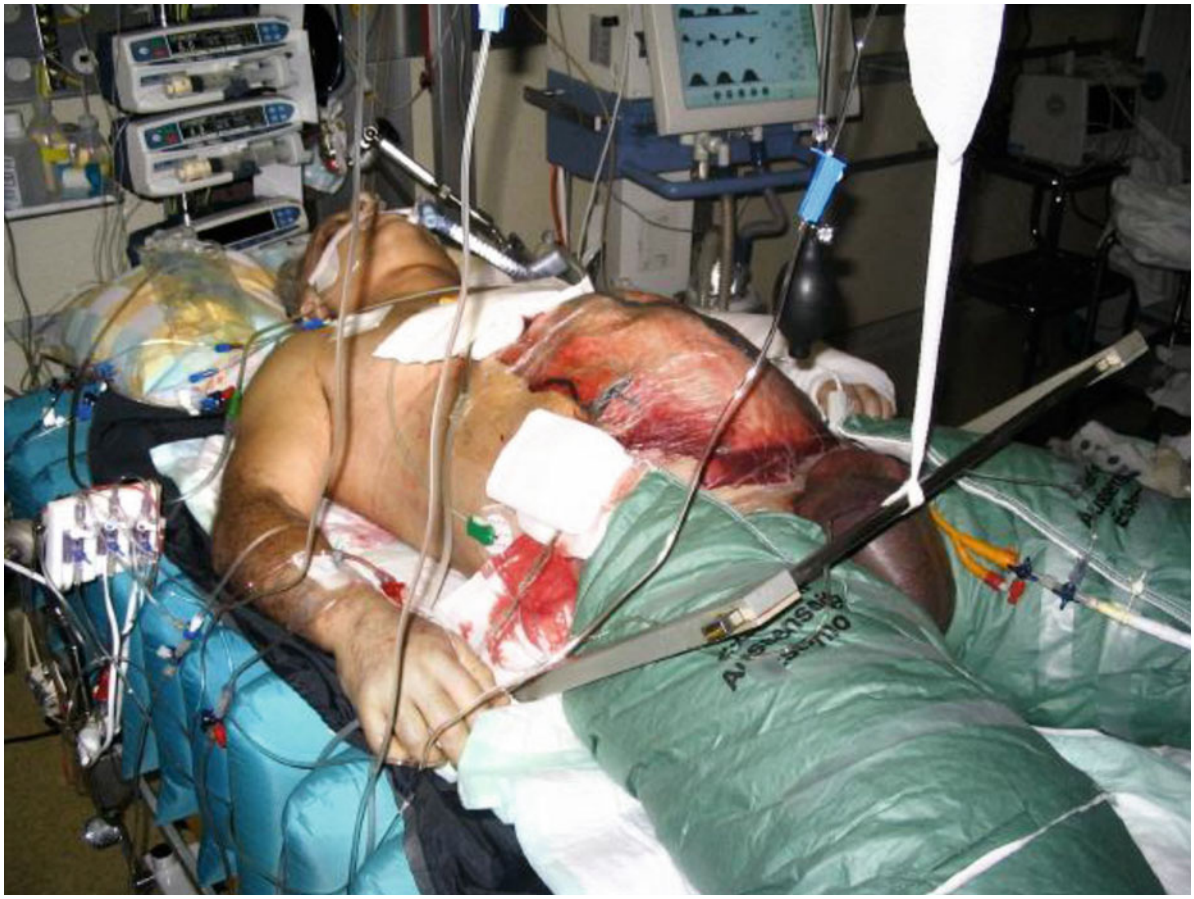

Fig. 8.1 Systemic inflammatory response syndrome after polytrauma

immunoglobulins that bind to microorganisms, facilitating their delivery (opsonization) by antigen-presenting cells (antigen presentation) to natural killer (NK)-cells and PMNLs that can kill the microorganisms.

In contrast to ordinary bacterial infections, microbial subtypes of NSTIs are characterized by the production of endo- and exotoxins that cause tissue ischemia, liquefactive necrosis, and systemic illness. The *Clostridium* species produce α-toxin, which causes extensive necrosis and cardiovascular collapse. *Staphylococcus aureus* and *Streptococci* elaborate surface proteins M-1 and M-3, exotoxins A, B, C, streptolysin O, and superantigen. The M proteins increase the microbes' ability to adhere to tissue and escape phagocytosis. Toxins A and B with streptolysin stimulate $CD4^+$ cells and macrophages to produce large bursts of cytokines (e.g., tumor necrosis factor [TNF]–α). Superantigens stimulate a cytokine release through direct binding with the major histocompatibility complex (MHC) class II receptor on antigen presenting cells and the Vβ-chain of T-cell receptors without time-consuming antigen presentation process, activating complement and coagulation cascades.

8.4.2 Hyperinflammation: SIRS

PMNLs, monocytes, tissue macrophages (e.g., alveolar macrophages), lymphocytes, NK-cells or parenchymal cells are involved in a complex network of the host defense response. An overwhelming proinflammatory response (hyperinflammation) leads to the clinical manifestation of SIRS (Fig. 8.1), and finally to host defense failure (MODS, MOF).

Cytokines are polypeptides and act in a para- or autocrine manner. They are capable of exerting many effects on an array of cell types (pleiotropy). In addition to hyperacute proinflammatory cytokines such as

TNF-α or IL-1β with an effect after 1–2 h there exist subacute (secondary) cytokines such as IL-6, IL-8 (neutrophil activating peptide), macrophage migratory-inhibitory factor (MIF), HMGB-1, as well as IL-12 and IL-18, two interferon-γ-modulating cytokines. MIF has a pivotal role in regulating systemic and local inflammatory responses by activating macrophages and T-cells. MIF is unique among cytokines in that it links the immune system with the endocrine system. In response to stress, MIF is secreted by the hypothalamus, the anterior pituitary gland and the adrenal glands and antagonizes the anti-inflammatory effect of endogenous steroids. HMGB-1 increases the proinflammatory effect of IL-1β through binding of these mediators. Recently, the IL-17 cytokine family was discovered. IL-17A interplays between innate and adaptive immune responses. This proinflammatory cytokine is mainly produced by T_H17 cells, but also by other immune cells. It triggers the production of many other cytokines and provides crosstalk between lymphocytes and phagocytes.

Through the influence of antigens, T-helper lymphocytes (T_H cells, $CD4^+$ cells) differentiate two phenotypes, the T_H1 and T_H2 lymphocytes (adaptive immunity). T_H1 cells support the proinflammatory cascade through secretion of IL-2, interferon-γ (IFN-γ) and TNF-β, whereas T_H2 cells are important producers of anti-inflammatory mediators. Monocytes/macrophages are involved in the differentiation of T_H1 cells through secretion of IL-12. Depressed IL-12 production after trauma correlated with a shift of the T_H1/T_H2 ratio toward T_H2-type pattern with an adverse clinical outcome.

As described, mechanical and hypoxic cellular damages lead to an increase of intracellular Ca^{2+} levels with an activation of phospholipase A_2 (PLA_2) and phospholipase C. These enzymes catalyze the release of arachidonic acids from membrane phospholipids. Through the activation of cyclooxygenase and 5-lipooxygenase prostaglandin E_2, respectively, leucotriene B_4 and thromboxane A_2 are produced. These metabolites are involved in the recruitment of inflammatory cells, regulation of vascular permeability and motility, as well as aggregation of thrombocytes. Additionally, PLA_2 induces the release of the platelet-activating factor. It supports the activation of macrophages, their interaction with endothelial cells, and the activation and aggregation of thrombocytes.

8.4.3 Hypoinflammation: Compensatory Anti-inflammatory Response Syndrome

T_H2-cells and monocytes/macrophages release IL-4, IL-10, IL-13 or transforming growth factor-β. In addition, different cytokines (e.g., IL-6) have shown a dual effect with pro- and anti-inflammatory activities. Serum levels of IL-10 or natural inhibitors of receptors, such as soluble TNF receptors (TNF-RI (55 kD) and TNF-RII (75 kD) or IL-1 receptor antagonist correlate with the incidence of posttraumatic septic complications. Furthermore, the responsiveness of blood monocytes from septic patients to release proinflammatory cytokines is decreased in in vitro studies after stimulation with gram-negative (endotoxin, lipopolysaccharide [LPS]) or gram-positive bacterial products (e.g., peptioglycan, lipoteichonic acid). This phenomenon is called "endotoxin tolerance" and is explained through IL-10–mediated depression of the activity of intracellular transcription factors (NF-κB). Antigen-presenting cells such as monocytes/marcrophages show a depressed expression of the MHC class II molecule human leucocyte antigen-DR with a correlation to posttraumatic infections.

During the early phase of the posttraumatic course, a lymphocytopenia can be observed and is associated with morbidity after trauma. It can be related to increased apoptosis triggered by stress hormones (steroids) and cell death proteins. Apoptosis is characterized morphologically by cell shrinking with cytoplasmatic condensation (apoptotic bodies), nuclear condensation (pycnosis), and DNA-fragmentation (DNA laddering). The cell membranes stay primarily intact and no surrounding inflammatory signs can be observed in contrast to necrosis.

An overwhelming anti-inflammatory response (hypoinflammation) seems to be responsible for immunosuppression with a high susceptibility to secondary infections. This immunological status is called compensatory anti-inflammatory response syndrome (CARS). However, it does not resemble a compensatory mechanism in a biphasic model. A few hours after a first hit, anti-inflammatory mediators (e.g., IL-10) are detectable in the serum. It seems that the host defense response tries to find a fine balance between SIRS and CARS to induce reparative mechanisms and limit entry or overload of microorganisms and to avoid autoaggressive inflammation with secondary tissue

damage and susceptibility to infections. These mixed inflammatory mechanisms are called mixed antagonistic response syndrome.

8.4.4 Complement System

Complement activation is an early event in sepsis. The classical pathway of activation is induced by antigen-antibody (immunoglobulins M or G) complexes or activated coagulation factor XII (FXIIa), whereas bacterial products (e.g., LPS) activate the alternative pathway. Cleavages of C3 by C3 convertase and C5 by C5 convertase lead to the formation of opsonins, anaphylatoxins C3a and C5a, C4a and the membrane-attack complex (also known as C5b-C9). The opsonins C3b and C4b are involved in the phagocytosis of cell detritus and especially bacteria by covalent binding of pathogen surfaces (opsonization). The anaphylatoxins C3a and C5a support different inflammatory mechanisms, the recruitment (chemotaxis) and activation of phagocytic cells (PMNL, monocytes, macrophages), the enhancement of the hepatic acute phase response, the degranulation of mast cells and basophils with release of vasoactive mediators such as histamine as well as the adhesion of leukocytes to endothelial cells leading to increased vascular permeability with edema. In addition, C5a contribute to immunoparalysis, imbalances in the coagulation system, MOF, septic cardiomyopathy and apoptosis of parenchymal cells. In clinical studies of sepsis, increased concentrations of C3a, C4a, and C5a in the plasma linked to poor outcome. In contrast, the C1-Inhibitor, produced by hepatocytes, endothelial cells, monocytes, and macrophages, is decreased during sepsis through degradation by PMNL-elastases. Dual blockade of the two C5a receptors (C5AR and C5L2), rather than blockade of C5a alone, seems to be an encouraging strategy for clinical trials in sepsis.

8.4.5 Coagulation Cascade

Coagulation contributes significantly to the outcome in sepsis with concurrent down-regulation of anticoagulant systems and fibrinolysis. Dysregulation of coagulation during sepsis can range from a moderate coagulopathy to the occurrence of disseminated intravascular coagulation (DIC). In addition, inflammation-induced coagulation in turn contributes to further inflammation.

In primary haemostasis, platelet-derived microparticles (MPs) express functional adhesion receptors including P-selectin on their surface, attach to the site of injury on the vessel wall, and support the rolling of leukocytes in the presence of shear stress. The adhesion of platelets is stabilized by von-Willebrand-factor (VWF) proteins. VWF is synthesized in endothelial cells and released in the plasma as unusually large VWF multimers that are rapidly degraded into smaller VWF multimers by the modulator ADAMTS-13 (a disintegrin-like and metalloproteinase with a thrombospondin type-1 motifs 13). Deficiency of ADAMTS-13, observed during severe sepsis, increases the level of large VWF multimers and leads to platelet aggregation and thrombus, resulting in microvascular failure.

In secondary hemostasis, the complex cascade of complement factors activation results in the formation of fibrin strands, which further strengthen the platelet plug. Two pathways of coagulation cascade are described and converge on the activation of thrombin.

- The intrinsic coagulation system is linked to the contact activation system (contact factor pathway). The plasma proteins FXII, prekallikrein, kininogen, and the factor XI (FXI) represent this system. They are characterized by the fact that they can be activated by negative charged cellular surfaces (contact activation). FXII and prekallikrein activate mutually and form FXIIa and kallikrein. FXIIa stimulates the complement cascade on the classical pathway and amplifies the prothrombotic events during sepsis through the formation of FIXa by FXIa. Kallikrein induces fibrinolysis through conversion of plasminogen to plasmin or activation of the urokinase-like plasminogen activator. The tissue plasminogen activator works as a cofactor. In addition, kallikrein stimulates the formation of bradykinin from kininogen. Kinins are vasodilators, increase the vascular permeability and inhibit the functions of thrombocytes. A consumption of FXII and FXI is observed during sepsis, whereas plasma levels of enzyme-inhibitor-complexes such as FXIIa-C1-inhibitor are increased. C1-inhibitor and α1-protease-inhibitor represent the inhibitors of the intrinsic coagulation system.
- However, the coagulation system is primarily activated over the extrinsic pathway (tissue factor pathway) with an increased expression of the tissue factor (TF) on endothelial and subendothelial cells, fibroblasts, and monocytes induced by bacterial cell wall fragments

and proinflammatory cytokines (TNF-α, IL-1β). The FVII-TF-complex stimulates the coagulation cascade with formation of aFX and finally thrombin (FIIa) from prothrombin (FII). Thrombin activates FV, FVIII, and FXI leading to an enhanced formation of thrombin. After cleavage of fibrinogen by thrombin, fibrin monomers polymerate to stable fibrin clots through support of aFXIII. The consumption of coagulation factors is further enhanced through the proteolysis of fibrin clots to fibrin fragments by the protease plasmin (fibrinolysis). To control the consumption of coagulation factors antithrombin (ATIII) produced by hepatocytes inhibits thrombin and FXa through formation of a thrombin-antithrombin complex. This effect can be enhanced by heparin. Furthermore thrombin inhibits the factors IXa, XIa and XIIa. Other inhibitors are the tissue factor pathway inhibitor and the activated protein C (APC). Protein C is synthesized in the liver, keratinocytes and the endothelium and is activated by thrombin bound to the thrombomodulin complex and by endothelial protein C receptor (EPCR). After dissociation from EPCR, APC binds to its cofactor protein S, resulting in the inactivation of clotting factors Va and VIIIa. Levels of APC, protein C and protein S are depleted in sepsis. APC is a central endogenous anticoagulant protein with antithrombotic, antiinflammatory, antiapoptotic, and profibrinolytic (through inhibition of plasminogen activator inhibitor 1) activities. APC can cleave and activate protease activated receptor-1 (PAR-1)-dependent cellular pathways in endothelial cells in competition with thrombin.

The DIC represents the most serious dysfunction of coagulation cascade during sepsis. In the initial phase of DIC, thrombin activation in combination with a reduced fibrinolytic cascade results in intra- and extravascular (e.g., intraalveolar in adult respiratory distress syndrome [ARDS]) fibrin clots (hypercoagulability) and an increased interaction of endothelial cells and leukocytes is observed. The consumption of the coagulation factors (hypocoagulability) and dysfunctions of thrombocytes are responsible for diffuse bleedings (hemorrhagic diathesis). In the late phase of DIC, intravascular fibrin clots lead finally to microcirculatory disturbances with hypoxia-induced cellular damage and multiple organ failure. Another consequence of DIC is the inhibition of fibrinolysis. As DIC develops, inflammation and coagulation interact in a bidirectional manner. Thrombin, FXa, and FVII-TF-complex interact with PAR1-4 system on endothelial cells, platelets and leukocytes and promote proinflammatory cytokine release generation of C5a, and expression of adhesion molecules by endothelial cells, platelets and leukocytes.

8.4.6 Acute Phase Reaction

The local (Kupffer-cells) and systemic release of proinflammatory cytokines induce the acute phase reaction in the liver to enhance tissue protective and antimicrobial mechanisms. The synthesis of positive APPs in hepatocytes such as C-reactive proteins (CRP), α1-antitrypsin, α2-makroglobulin, caeruloplasmin, LPS-binding protein (LBP), fibrinogen, prothrombin, and C4BP is increased, whereas the production of negative APPs such as albumin, high-density lipoproteins, protein C, protein S and ATIII are reduced. CRP increases the expression of TF on PMNLs and monocytes/macrophages and enhances therefore the activation of the extrinsic coagulation cascade. α1-antitrypsin inactivates proteases, secreted by PMNLs or macrophages, whereas α2-macroglobulin and caeruloplasmin neutralize free oxygen radicals and proinflammatory cytokines. LBP suppress the effects of LPS in high concentrations, whereas in small quantities an enhancement of the LPS-effects can be observed. Serum levels of LBP are increased during sepsis. The elevated ratio of positive to negative APPs accelerates the development of DIC.

Procalcitonin (PCT), a new representer of positive APPs, is a precursor of calcitonin, which is normally produced in the C-cells of the thyroid. Hepatocytes as well as immune cells are also capable of secreting PCT. The biological function of this APP is still unclear. However, increased levels of PCT can be observed after trauma and especially with a complicated course with sepsis or MODS. Recently, pancreatic stone protein, known from the pathogenetic cascade of pancreatits, was detected as positive APP in sepsis with an influence on adhesion molecules on PMNLs.

8.4.7 Leukocytes Recruitment and Oxidative Stress

The infiltration and accumulation of PMNLs and macrophages at the local side of infection with large stores

of proteolytic enzymes (elastase, metalloproteinase) and with the capacity to rapidly generate reactive oxygen (ROS), the so-called respiratory burst or oxidative stress, and reactive nitrogen (RNS) species represent a crucial event for degradation of internalized pathogens.

- Leukocyte/endothelial cell interaction (adherence) involves two sets of adhesion molecules. During the initial phase of adherence, selectins on leukocytes (L-selectin, leukocyte adhesion molecule-1) and endothelial cells (E-selectin, endothelial leukocyte adhesion molecule-1) are responsible for the "rolling" of PMNLs. In the second step, an up-regulation of integrins on PMNLs (CD11a-c/CD18 complexes) and intercellular adhesion molecules (ICAM-1) or vascular cell adhesion molecules (VCAM-1) on endothelial cells are involved. The interaction of these adhesion molecules leads to a stable cell-to-cell contact with a PMNL-attachment, the so-called "sticking" of PMNLs. Through shedding increased levels of adhesion receptors (selectins, soluble ICAM-1 (sICAM-1) or sVCAM-1) are detectable in serum of injured patients with a predictive value for the development of septic complications. Finally, the migration (diapedesis), accumulation, and activation of leukocytes in tissue are mediated by chemoattractant factors, such as chemokines (IL-8, macrophage inflammatory protein-1α) and complement anaphylatoxins (C3a, C5a) after binding to their corresponding receptors.
- Neutrophil elastase has the capacity to degrade most proteins in the extracellular matrix and important plasma proteins. Its proteolytic activity is regulated by endogenous protease inhibitors (PI) such as α1-antitrypsin, α2-macroglobulin or α1-PI. In addition, neutrophil elastase induces the release of proinflammatory cytokines.
- Stimulated PMNLs produce ROS and RNS through the membrane associated nicotinamide adenine dinucleotide phosphate (NADPH)-oxidase complex, myeloperoxidase and xanthine oxidorductase and represent a defense mechanism against invading microorganisms. Superoxide anions (O_2^-) are generated by NADPH-oxidase, which is activated by proinflammatory cytokines, arachidonic acid metabolites, complement factors and bacterial products. Thereafter, O_2^- are reduced in the Haber-Weiss reaction to hydrogen peroxide (H_2O_2) by superoxide dismutase in cytosol (SOD 1), mitochondrium (SOD 2) or cell membrane (SOD 3). H_2O_2 is the substrate for the myeloperoxidase, which forms the high toxic and bacterizid hypocholorous acid (HOCL) and chloride anion (Cl^-). In addition, accumulated H_2O_2 is transformed to hydroxyl ions (OH^-) in the Fenton reaction. The free ROS induce lipid peroxidation, cell membrane disintegration and DNA-damage of endothelial and parenchymal cells. Furthermore, oxygen radicals and HOCL activate PMNL to release proteases and collagenase and inactivate PIs. In addition, the capacity of non-enzymatic antioxidants such as vitamins E or C (scavenger) or enzymatic antioxidants such as SOD, katalase, or glutathione peroxidase are reduced during sepsis.
- RNS are also involved in the pathogenesis of secondary tissue damages. Nitric oxide (NO) is generated from the amino acid L-arginine by inducible nitric oxide synthase (iNOS) in PMNLs or vascular muscle cells and by endothelial nitric oxide synthase (eNOS) in endothelial cells. NO induces vasodilatation through increase of guanosine 3′,5′-cyclic monophosphate by activation of the guanylate cyclase. The activity of iNOS is stimulated by cytokines and toxins, and eNOS by mechanical shearing forces or acetycholin. O_2^- in the presence of NO generates peroxynitrite ($ONOO^-$), a key player in the pathogenesis of sepsis-induced organ dysfunction. The results for the vascular dysfunctions by oxygen radicals and NO are a generalized edema, clinically manifested as capillary leakage syndrome with a disturbance of nutritional and metabolic exchange, cell swelling and cellular dysfunctions.

8.4.8 Leukocytes Apoptosis

The accumulation of PMNLs and macrophages is accelerated by colony-stimulating factors such as granulocyte-colony stimulating factor and granulocyte macrophage-colony stimulating factor enhancing monocyte- or granulocytopoiesis and reducing the apoptosis of PMNLs during sepsis. As neutrophils kill pathogens using ROS and RNS and a mixture of lytic enzymes, delayed clearance of PMNLs in sepsis can potentially contribute to cell and organ injury ("Janus face" of PMNLs). However, the highly proapoptotic nature of PMNLs is designed to maintain a balance between antimicrobial effectiveness and the potential for neutrophil-mediated tissue damage. PMNLs can

undergo apoptosis via intrinsic (mitochondrial) and extrinsic (activation of death receptors) pathways. Extrinsic signals (TNF-α, Fas ligand [CD95 ligand]) bind to their receptors (TNF-R, Fas antigen [CD95 antigen]) and trigger intracellular signaling, leading to caspase-8 and finally caspase-3 activation. Phagocytosis of apoptotic PMNLs by macrophages inhibits the release of proinflammatory cytokines and promotes the secretion of anti-inflammatory mediators. The recognition of apoptotic cells is dependent on the cell surface appearance of an anionic phospholipid, phosphatidyl-serine (eat-me sign), which is normally confined to the inner leaflet of the plasma membrane.

8.4.9 Microcirculatory Dysfunction

Microcirculation as functional unity, consisting of terminal arterioles, capillaries, and venules, regulates nutritional and metabolic exchange in organs and tissues. Microcirculatory dysfunction during systemic inflammation is primarily determined through the sympathetic-adrenal reaction leading to a vasoconstriction of arterioles and venules. However, through a decrease of the catecholamine effect on arterioles a reduced capillary flow with an increased hydrostatic pressure can be observed. This microcirculatory alteration in combination with the cytokine and NO mediated capillary leakage, is responsible for a secondary hypovolemia and hemoconcentration with agglutinations of erythrocytes (red sludge) and thrombocytes (white sludge). The sludge phenomenon evokes an obstruction of the microcirculation with a failure of the transcapillar exchange. The cellular oxygen deficiency and the accumulation of metabolic products (hidden acidosis) are finally responsible for tissue and cell damages. In addition, NO (vasodilatation) and endothelin (vasoconstriction) induce a shock specific microcirculatory change with a shunting of some organ or tissue areas enhancing the damage.

8.4.10 Autonomic Nervous System and Neuroendocrine Reaction

Advances in neuroimmunology have shown that the nervous system and the immune system communicate during inflammation. The main pathways involved in this crosstalk are the hypothalamic-pituitary-adrenal axis and the autonomic nervous system (ANS).

The ANS maintains homeostasis in the body by controlling vital functions (heart rate, respiration rate, digestion, perspiration, body temperature) and has three components.

- The sympathetic (adrenergic) branch of ANS consists of sympathetic neurons and the adrenal medulla. The early phase of sepsis is characterized by high concentrations of catecholamines, which boost the inflammatory response. Signals in the hypothalamic area sympathica evoke a release of catecholamines from the marrow of the adrenal gland. Adrenalin stimulates the cardiac output (increase of 40–90 %) through an increase of the heart contractility, the heart rate and the preload (Frank-Starling mechanism) (hyperdynamic phase). Thereafter, the blood pressure is elevated by the increased peripheral vascular resistance (vasoconstriction of arterioles) and a centralization of the blood in favor of vital organs such as the heart and brain is established through a decrease of the perfusion of splanchnic area, kidneys and muscles. Furthermore, catecholamines influence the metabolism with an increase of the energy expenditure, hepatic glycogenolysis and gluconeogenesis (glucose-lactate [Cori-cycle] and glucose-alanin cycles) as well as release of free fat acids. Later, in septic shock (hypodynamic phase) through apoptosis of adrenal medullary cells, the production of catecholamines is insufficient for stabilization of the cardiovascular system and administration of catecholamines is needed. Leukocytes are also an abundant source of catecholamines and express adrenergic receptors. Stimulation of these receptors influences lymphocyte trafficking, release of proinflammatory cytokines, vascular perfusion, and cell proliferation or apoptosis.
- The parasympathetic (cholinergic) branch is the vagus nerve and is mediated by acetylcholine and its receptors. Activation of α_7-nicotinic acetycholine receptors (α_7nAChRs) on macrophages decreases intracellular cytokine synthesis. The branch of the vagus nerve that innervates the spleen is crucial for the suppression of cytokine synthesis in sepsis. In experimental studies, activation of this cholinergic anti-inflammatory pathway inhibited the production of HMGB1 or TNF-α and increased survival.
- The enteric nervous system controls the gastrointestinal system. The gut can produce large amounts of catecholamines during sepsis, which are released in the portal vein system and contribute to the release of proinflammatory cytokines by Kupffer cells and

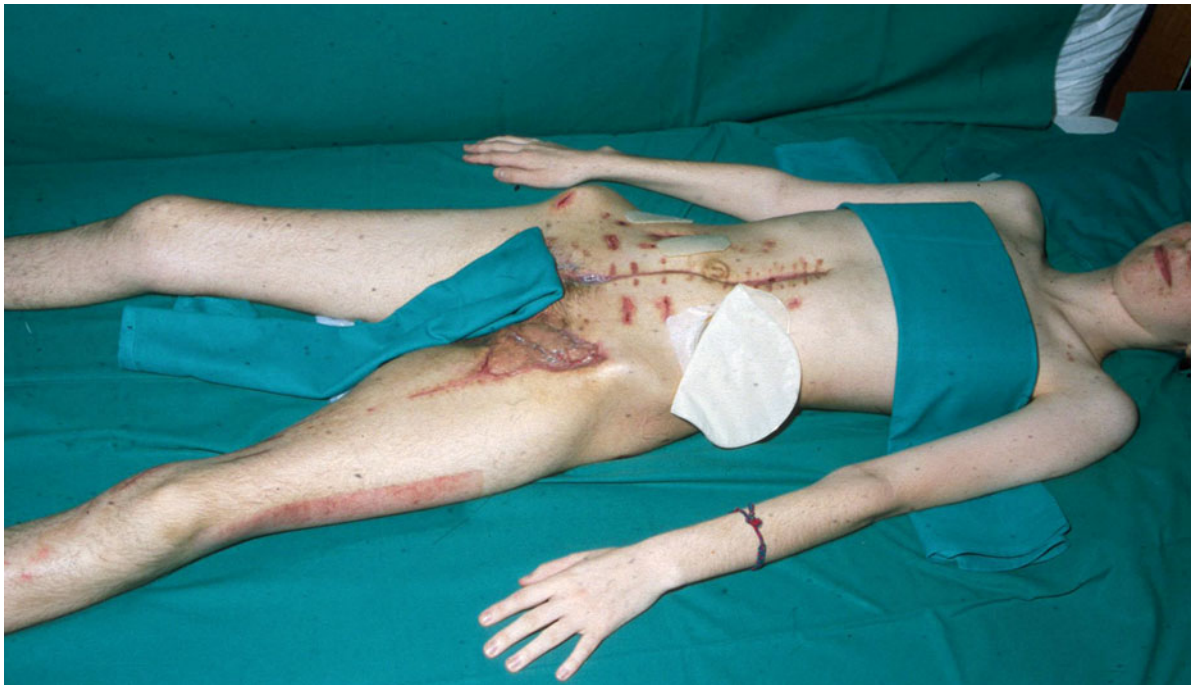

Fig. 8.2 Katabolic state with wasting of muscles after severe trauma and sepsis

hepatocytes. In addition, it seems that resident immune cells in Peyer's patches and lymph nodes of the intestinal tract are involved in catecholamines, cytokine, and acute phase protein release.

Primary (bleeding) and secondary (capillary leakage) hypovolemia trigger through aortic or carotic baro receptors a sympathic-adrenal response and through juxta-glomerular baroreceptors an activation of the renin-angiotensin system to support the perfusion of vital organs. Angiotensin II is an effective vasoconstrictor, induces a renal retention of sodium and fluids and stimulates the adrenal release of aldosteron. In addition, osmotic receptors in the hypothalamus are responsible for the secretion of the antidiuretic hormone by the posterior lobe of the hypophysis (neurohypophysis). Pain, stress and fear evoke the hypothalamus to release the corticotropin-releasing hormone leading to a secretion of adrenocorticotropic hormone (corticotropin, ACTH) from the anterior lobe of hypophysis (adenohypophysis). ACTH stimulates the cortex of the adrenal gland to release glucocorticoids (cortisol) or mineralocorticoids (aldosteron). Glucocorticoids have different effects on the metabolism such as hepatic gluconeogenesis, glycogenesis, inhibition of protein synthesis, increase of protein degradation in muscles, and mobilization of free fatty acids by lipolysis. In addition, they limit cellular inflammatory processes of mononuclear cells and suppress the production of antibodies. In contrast, the spontaneous apoptosis of PMNLs is reduced by cortisol. Aldosteron increases the renal resorption of sodium associated by fluid retention.

8.4.11 Metabolic Alterations

The metabolic disorders after trauma or at the beginning of septic shock are initially characterized by a reduced metabolism for about 24 h (acute, shock, or ebb phase). It is followed by a flow phase (hypermetabolism) with a katabolic metabolism (Fig. 8.2), for up to 2 weeks, and a final reparative phase with a turnover from a katabolic to an anabolic metabolism. In the second phase, all energy storages such as glucose, fatty acids (lipemia of sepsis), and proteins are made available for the host defense response. The increase of the energy expenditure is maximum after 5–10 days. The increased levels of amino acids are needed for the synthesis of acute phase proteins in the liver and inflammatory mediators in mononuclear cells. In addition, glutamate represents a neurotransmitter and is the most important substrate for the metabolic processes of enterocytes and immune cells conserving the immune

integrity of the intestinal wall to avoid a bacterial translocation. Furthermore, various cytokines (TNF-α, IL-1β) increase the expression of glucose transport systems (insulin-like activity). The increased intracellular glucose is oxidated to pyruvate and finally reduced to lactate (stress lactate acidosis) and contributes to the elevated lactate levels caused primarily by the metabolic lactate acidosis (cellular hypoxia).

8.4.12 Multiple Organ Dysfunction or Failure

Endothelial cell damage, dysfunctions of vascular permeability with capillary leakage, microcirculatory dysfunctions with cellular hypoxia, and finally apoptosis of parenchymal cells by cell-associated or free cell death proteins and/or necrosis of parenchymal cells are involved in MODS or MOF. The clinical manifestation of MODS varies in affected organs and dysfunction severities. Different scores such as MOF score (Goris score), MODS score (Marshall score), or Sequential Organ Failure Assessment score are available to describe dysfunctions of seven systems: respiratory, cardiovascular, renal, hepatic, gastrointestinal, hematologic, and central nervous system[8,63,73,119]. For the diagnosis of acute lung injury (ALI) or ARDS bilateral lung infiltrations on thoracic radiography and a decrease of the Horowitz ratio must be observed (P_aO_2/F_iO_2 ratio < 300 corresponds to an ALI, <200 to an ARDS). Renal and gastrointestinal systems are sensitive to microcirculatory disorders leading to necrosis of renal tubular necrosis with increase of serum creatinine concentrations and oliguria (<0.5 mL/kg/h) or anuria necrosis of intestinal villi respectively. The alteration of the intestinal mucosa seems to be responsible for a bacterial translocation and explains the high rate of bacteremia without detection of infectious focus in lethal sepsis (gut hypothesis). The gastrointestinal tract often the source of secondary multiple organ failure after trauma, where as the liver represents the engine with an acute phase and cytokine response and a decreased function of hepatocytes (increase of serum bilirubin concentration).

8.5 Diagnosis

The diagnosis of sepsis is a challenge. Clinical and standard laboratory tests are not helpful because most severely injured patients (>80 %), or postoperatively, develop some degree of SIRS, whether or not they have sepsis. Even microbiological assessment is unreliable as many culture samples do not yield microorganisms in these patients.

In patients with NSTI, local erythema in combination with swelling and pain is the most common sign. However, 35 % of cases are initially misdiagnosed as simple cellulitis or nonnecrotizing skin infection. Crepitus or skin necrosis, often thought to be the sine qua non of NSTI, is present in only 30 % of patients (Fig. 8.3).

Currently, as many as 170 different biomarkers in sepsis have been evaluated in more than 3,300 studies. Of the many proposed markers for sepsis, acute phase proteins have been most widely assessed.

- Elevated concentrations of serum CRP are correlated with an increased risk of organ failure and death, and the study of its time course may be helpful in evaluating the response to therapy in septic patients.
- PCT has been used extensively in recent years. Elevated early serum PCT on days 1–5 post trauma was strongly associated with the subsequent development of sepsis and MODS, but not with non-septic infections in severely injured patients. However, PCT can be useful to rule out sepsis, rather than rule it in with a high negative predictive value of 99 % at a cut-off value of 0.2 ng/mL. In addition, PCT levels are useful in guiding therapy and reducing antibiotic use.

Another group of compounds that has been widely assessed as potential biomarkers is cytokines (i.e., TNF-α, IL-6, IL-8, IL-10, or IL-18). However, blood concentrations are rather erratic and their time course is not clearly in concert with the course of sepsis. The kinetics of IL-6 are similar to those of PCT but differentiated between infected and non-infected patients after day 5 following trauma. Its use in the early distinction between SIRS and sepsis has further facilitated the identification of patients requiring antibiotic therapy or surgical intervention to control infectious foci. CD64 and CD11b had the highest sensitivity and specificity for the early diagnosis of sepsis in adults. However, the combinations of several biomarkers may be more effective than single biomarkers, but this requires further evaluation.

Radiographic testing plays different roles in diagnosis of expected infectious focus. Chest radiographs are the golden standard for the diagnosis of pneumonia or ARDS. Computed tomography (CT) of the thorax for empyema or of abdomen for intraabdominal abscess

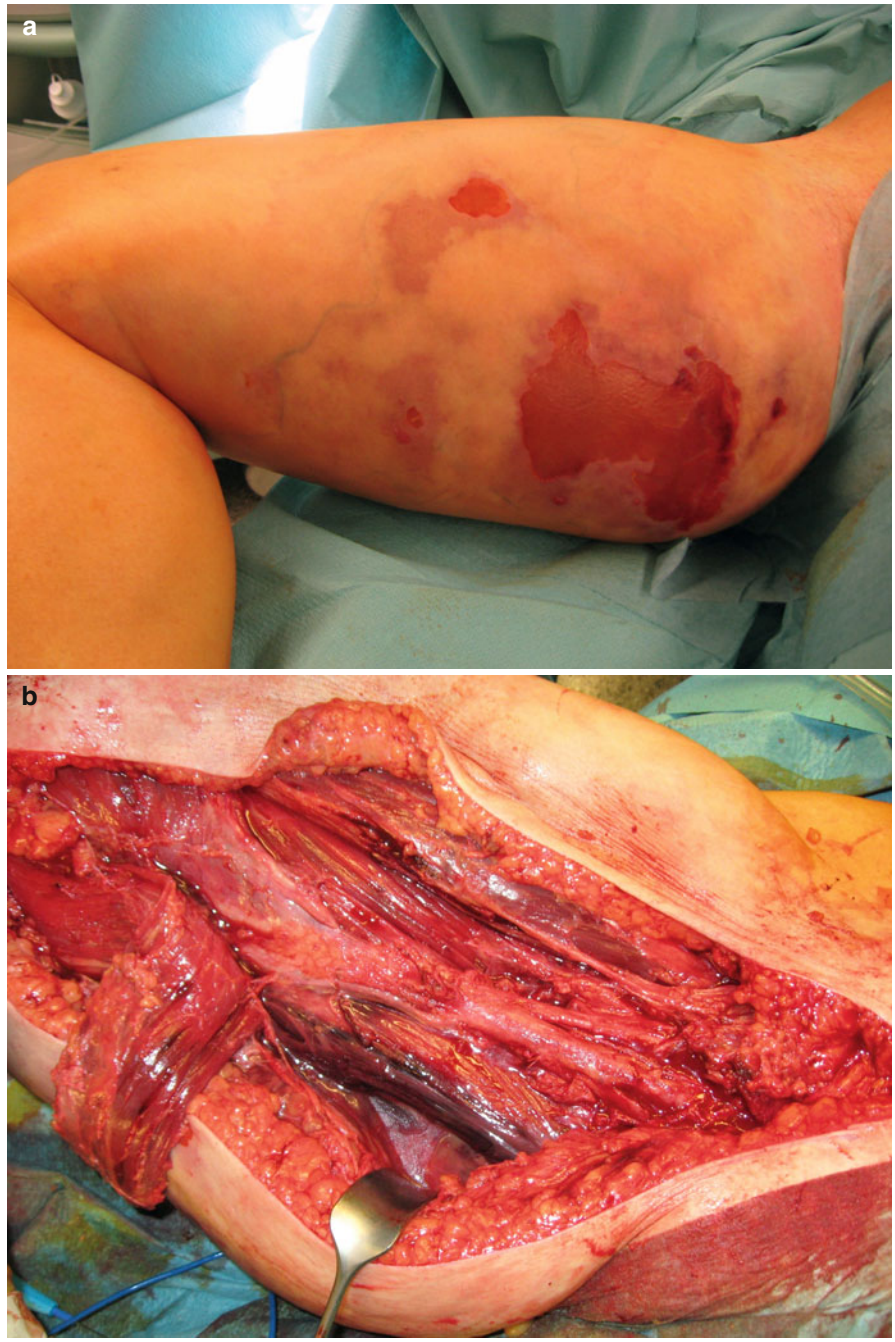

Fig. 8.3 Clinical manifestation of a necrotizing soft-tissue infection (NSTI). (**a**) Local erythema, swelling, and skin necrosis of the right medial thigh. (**b**) Intraoperative situs shows muscle necrosis

are essential. CT has 80 % sensitivity for the diagnosis of NSTI, whereas magnetic resonance imaging (MRI) has a sensitivity of 90–100 %. Characteristic findings include soft-tissue or fascial thickening on T2-weighted images with enhancement after administration of contrast. However, the use of MRI should not delay the immediate surgical intervention in patients with the clinical diagnosis or suspicion of NSTI.

8.6 Therapy

8.6.1 Preventive Interventions

Postoperative or posttraumatic sepsis with multiple organ failure is associated with a high mortality and should be prevented by prophylactic interventions and an adequate treatment concept in the early

postoperative or posttraumatic course. Prolonged hypoxia and hemorrhagic shock as second hits are crucial for the development of severe systemic inflammation and the increased incidence of systemic infections and sepsis. Therefore early oxygenation through intubation and early assisted ventilation as well as adequate volume therapy play an essential role in preventing sepsis. However, the large-volume loading scheme is controversially discussed for severe hemorrhagic shock. Patients with blood loss of more than 2 l should not be overwhelmed by kristalloids or kolloids until surgical management of bleeding is performed to avoid a reduced O_2 transport capacity, coagulopathy, as well as hypothermia.

Patients with a borderline state after primary survey according to the guidelines of ATLS© or patients with a high trauma impact or at risk for adverse outcome such as head injury, bilateral lung contusions, multiple long bone fractures, acidosis, coagulopathy, hypothermia, or a presumed operation time >6 h after the further work up in the secondary survey should be supplied with a staged sequential surgical management as damage control to avoid or limit the influence of second hits (interventional or antigenic loads) for the host defense response. Damage control includes:

- Hemorrhage control.
- Reduction of contamination of hollow organ injuries or open wounds and fractures.
- Resection of vital tissue.
- Decompression of compartments of the extremity by fasciotomy, or of the abdomen by decompressive laparotomy.
- Temporary stabilization of pelvic and long bone fractures or dislocations of large joints by fast assembled external fixators contribute to a limited antigenic load with reduced pain and neuroendocrine reaction. In addition, early (within 48 h after trauma) posterior stabilization of severe spinal instabilities allows mobilization and optimal care in the intensive care unit.

The surgical time in the initial treatment algorithm determines the rate of surgical site infections (SSI): <6 % wound infection after 1 h operation, >17 % after >6 h operation time. The time point for definitive surgery should be planned for the end of the first posttraumatic week, after recovery from the proinflammatory overwhelming proinflammatory response and before the onset of the immunodepression (window of opportunity). During the vulnerable period between the second and fifth day after trauma, only necessary second look operations for thoracic, abdominal, or wound injuries and open fractures with removal of tamponades or débridement of vital tissue should be done.

A single shot of antibiotics (cephalosporine) before surgical treatment of closed fractures, and therapy with antibiogramm-adapted antibiotics for open fractures over 5 days decreases wound infections. An early enteral nutrition through gastric or duodenal tubes reduces the accumulation of pathogenic bacteria in the intestinal tract and prevents an atrophy of intestinal mucosa, an essential bacterial barrier. Additional arginine, glutamine, nucleotides, or unsaturated omega-3-fatty acids (immune-enhanced enteral nutrition) reduce the posttraumatic hypermetabolism and improve immune competence. To reduce the risk for pneumonia or catheter sepsis, extubation and removal of catheters should be done as early as possible.

8.6.2 Therapeutic Interventions

The therapy of sepsis is based on a quick clinical and microbiological diagnosis and source localization of infection. There are five pillars for managing patients with sepsis. The first three should be approached simultaneously.

1. Timely administration of appropriate antimicrobial therapy
2. Source control of infection (elimination of septic focus)
3. Hemodynamic resuscitation by early goal-directed therapy (EGDT)
4. Damage control of infection (limitation of progression of infection)
5. Supportive interventions for organ dysfunctions
    - The effective use of antimicrobial agents is central to the optimization of outcome in life-threatening infections in critically ill patients. Inappropriate initial antimicrobial therapy for septic shock occurs in about 20 % of patients and is associated with a fivefold reduction in survival. Early after suspicion or clinical diagnosis of sepsis empiric intravenous broad-spectrum antibiotics should be implemented according to the location of infection begin (ambulatory or nosocomial), to the expected source of sepsis (pneumonia, catheter, wound, intrabdominal, soft tissue), to the timepoint after trauma respectively stay of the severely injured patient on the intensive care unit, to the immune status of the

patient (comorbidities, sepsis with or without granulocytopenia), and to the organ dysfunctions with limited drug clearance (liver, kidney). Each hour delay in appropriate antimicrobial administration after onset of hypotension during sepsis (septic shock) is associated with an average increase in mortality of 8 %. The early empiric antibiotic strategy should be replaced as early as possible with focused antibiotic therapy according to the culture results and the antibiogram. The antibiotic-based therapy for sepsis consists of betalactams (imipenem, meropenem) or pseudomonas, effective aminoglycosids and parenteral cephalosporines (cefepim, ceftazidime), or piperacillin with beta-lactamase-inhibitor (tazobactam). Quinolones offer excellent soft-tissue penetration and can be used to cover gram-negative organisms. However, even if the offending microorganism is correctly identified, administering an appropriate antibiotic to the patient is becoming more problematic because of the increasing antimicrobial resistance such as in the multiply resistant pathogens *Pseudomonas aeruginosa*, *Acinetobacter species*, and *Klebsiella pneumonia*. If methicillin-resistant *Staphylococcus aureus* infection is suspected, vancomycin should be administered additionally. Clindamycin remains a useful agent because it covers anaerobic organisms well and inhibits M protein and exotoxin synthesis by group A *Streptococcus*.

- Source control of infections includes surgical resection and débridement of infected tissue with extended irrigation for SSIs or arthroscopically in hematogenous joint infections. In localized intrathoracic or abdominal infections, drainages can be placed endoscopically, via sonography, or a CT-guided technique. A temporary, diverting colostomy should be considered in cases of perineal or perianal NSTI or colonic infections. In NSTI, the fascia from all muscle compartments of the extremities (highways for infections) and necrotic muscles must be resected to prevent torso involvement, which has a mortality rate of over 90 %. Amputation can be necessary if the infection has rendered most muscle groups necrotic, thereby resulting in a useless extremity. In infections associated with fracture-fixation devices, the nature of surgical intervention depends on the type of device (external fixator, plate, nail) and in late infections the presence or absence of bone union. Necrotic bone fragments must be resected. Where there is insufficient fracture healing, bridging of the fracture site with external fixation is done. The optimal method of initial wound management after débridement is debated. Vacuum-assisted closure (VAC) has become a common method of treating large wounds. However, coagulopathy represents a contraindication for VAC and a wet-to-dry dressing should be applied initially. In cases of catheter sepsis, catheters have to be removed and if necessary replaced.
- The resucitation components of EGDT were derived from the practice parameters for the hemodynamic support of sepsis recommended by the American College of Critical Care Medicine in 1999. The EGDT uses central venous pressure (CVP) measurements instead of pulmonary capillary wedge pressure to address preload. Over the first 6 h, the patients receive greater amounts of fluids (kristalloids and kolloids) to restore the intravascular volume if the CVP is below 8 mmHg. In the next step, vasoactive agents are needed in cases with a mean arterial pressure (MAP) below 65 mmHg to support the perfusion. After correcting CVP and MAP the EGDT protocol addresses the resolution of global tissue hypoxia. This is treated by reversing the imbalance between oxygen delivery and oxygen consumption, as measured by the surrogate central venous oxygen saturation ($ScvO_2$). The combination of anemia, global tissue hypoxia and the accompanying comorbidities (cardiovascular disease) provides the physiologic rationale for transfusion of red blood cells (RBC's) during the delivery-dependent ($ScvO_2$ <70 % and lactate >4 mmol/L) phase of the resuscitation of patients with severe sepsis and septic shock. If the $ScvO_2$ is still <70 % after correcting the anemia until the hematocrit is greater than 30 %, dobutamine (vasodilatator) is used to increase inotropy, optimize contractility and aid oxygen delivery. EGDT results in a significant modulation of pro-, antiinflammatory, apoptotic and coagulation biomarkers in patients treated with EGDT versus standard therapy. The relative risk reduction for mortality through EGDT exceeds 25 % and absolute risk reduction exceeds 9 % in all peer-review

publications. In addition, EGDT decreases intensive care unit length of stay, hospital length of stay, duration of mechanical ventilation, renal replacement therapy, vasopressor therapy, and pulmonary artery catheterization with 23 % reduction in hospital costs.

- Damage control procedures for infections include serial débridements with resection of necrotic tissue and extended irrigation. Bacterial focus is rarely eradicated after a single debridement, particularly in NSTI or fracture site infections. An average of three débridements spaced 12–36 h apart are needed to obtain control of gross infection. Amputation must be considered if the extent of severe soft-tissue infections includes a joint or the infection is rapidly spreading toward the torso despite aggressive attempts at surgical control.
- Supportive interventions for organ dysfunctions in the treatment of sepsis have led to slowly improved outcomes in the past few decades. Lung-protective ventilation – meaning the use of relatively low tidal volumes (6 mL/kg of ideal body weight) – or early continuous renal replacement therapy have become standard practice in intensive care units. However, some therapies, such as intensive insulin therapy, administration of corticosteroids, and the use of APC, remain controversial.
  - Injured patients with increased blood glucose on admission or throughout the hospital stay had a higher mortality, longer duration of ventilation and intensive care unit stay, and a higher rate of hospital-acquired infections. Therefore, the goal of insulin therapy is to control hyperglycemia while preventing episodes of hypoglycemia. In reviewing clinical trials and meta-analyses, liberal targeted blood glucose range (140–180 mg/dL) appears favorable because of the lack of mortality benefit and subsequent increased hypoglycemia rate associated with intensive glucose control (80–110 mg/dL).
  - Patients with septic shock with baseline plasma cortisol levels of ≤34 mg/dL and a change in cortisol levels of >9 mg/dL with corticotropin stimulation had the best probability of survival. However, recent meta-analyses have shown that regardless of the dose or duration and the responsiveness to corticotropin, use of corticosteroids did not affect mortality in sepsis, but low-dose corticosteroids, in the form of hydrocortisone, appear to be beneficial in severe sepsis refractory to intravenous fluid and vasopressor support.
  - Low levels of circulating protein C are associated with poor outcome in severe sepsis. Therefore, the replacement of APC should modify the coagulation and inflammation changes in severe sepsis. In 2001, the Recombinant Human Protein C Worldwide Evaluation in Severe Sepsis study group reported an absolute reduction of 6 % in the risk of death in 1,690 patients. However, in a 2005 study in patients with less severe sepsis no significant benefit, but a higher risk for serious bleeding were observed (Administration of Drotrecogin Alfa [Activated] in Early Stage Severe Sepsis study group). APC should be reserved for patients with severe sepsis with a high risk of death Acute Physiology and Chronic Health Evaluation II score >25 points).

Despite thorough insights into pathophysiological mechanisms of systemic inflammation and sepsis, earlier recognition of sepsis by biomarkers, and hopeful results of animal studies in multiple prospective clinical trials performed in the past decades have failed to provide the benefit of anti-inflammatory, anti-coagulant, or antioxidant strategies with regard to mortality, whereas the incidence of secondary infections or MODS has partially decreased. However, the magic bullet still has not been and probably will not be found. The study protocols have focused on single mechanisms, whereas the immune network is more complex and individual (gene polymorphism, sexual dimorphism) than described above. In addition, inappropriate timing of administration and suboptimal drug levels at the target site are reasons for these equivocal results.

8.7 Prognosis

The mortality rate for severe sepsis still ranges from 25 % to 30 % and that of septic shock ranges from 40 to 70 %. Nosocomial infection-associated septic shock has a higher overall mortality risk than community-acquired infection-associated sepsis. Patients with septic shock associated with gram-positive cocci and gram-negative bacilli infection have similar survival chances. The time to the initiation of effective

antimicrobial therapy, and in cases of NSTI, the time to surgical intervention are the critical determinants of outcome in patients with septic shock. The choice of an appropriate empiric antimicrobial agent and the adequacy of initial débridement are key elements in effecting rapid initiation.

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Necrotizing Soft-Tissue Infections

9

Thomas Kossmann
and Cristina Morganti-Kossmann

9.1 Introduction

Necrotizing soft-tissue infections (NSTIs) are a heterogeneous group of life- and limb-threatening infections with the following characteristics:

- Fulminate progression
- Occur in immune-compromised patients
- High mortality
- Caused often by Streptococci
- Synergistic with Staphylococci and other bacteria and fungi

NSTI has been referred to in ancient history. Galen mentioned these infections more than 2,000 years ago. Over the past 150 years, different forms of NSTIs have been described. During the American Civil War, military doctor Joseph Jones systematically described NSTI as "hospital gangrene." Since 1884, infections of the perineum and scrotum have been labeled as "Fournier gangrene." In 1924, Meleny identified hemolytic Streptococci as the cause of necrotizing infections of the skin and soft tissues and described in detail the systemic toxicity of the infections. Wilson coined the term *necrotizing fasciitis* in 1952, specifically referring to a single form of NSTI that is within the subcutaneous tissue on top of the muscle fascia. Wilson recognized that the severe toxic effects of the infections resulted in a high mortality rate and that skin necrosis is a late clinical sign in the infections.

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9.2 Predisposing Factors

Patients with NSTI usually have preexisting systemic diseases, which compromise their immune system. Patients at risk of developing NSTI are those who suffer from:

- Diabetes mellitus
- Obesity
- Chronic alcoholism
- Drug abuse
- Chronic obstructive lung disease
- Posttraumatic immune suppression
- Chronic venous or lymph insufficiency with tissue edema.

Malnourished HIV-positive patients using intravenous drugs have a high incidence of NSTI, most likely resulting from multiple skin infections caused by bacteria, fungi, and parasites.

Local predisposing factors for NSTI are the presence of a foreign body in the wound, necrotic tissue formation around the wound, or both. Tissue ischemia caused by tight sutures, hematomas, peripheral angiopathy, irradiation, and extensive burns have also been associated with NSTI.

Often these life- and limb-threatening infections appear after small injuries to the skin (e.g., excoriations, lacerations, and injections). Some are small and are initially treated inadequately (so-called neglected trauma). In some patients the entry site cannot be identified at all, and even a sore throat has been identified as the initial entry point for bacteria.

NSTIs have been described after

- Blunt or penetrating trauma
- Postoperative complications

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- Incarcerated inguinal hernias
- Perianal abscesses
- Urological and gynecological operations
- Injection of drugs (e.g., corticosteroids, subcutaneous insulin)
- Animal bites
- Coloncutaneous fistula
- Renal calculi
- Idiopathic causes

The clinical signs of NSTI can be masked or appear delayed in cases of previous treatment with non-steroidal and anti-inflammatory medications because these drugs suppress the classic signs of inflammation and reduce cellular and humoral immunological reactions. An initial harmless infection can be protracted by these medications and then suddenly appear hyperacute.

9.3 Clinical Appearance of NSTI

The initial clinical picture of most NSTIs is unspecific and may appear as a simple skin or subcutaneous infection. However, NSTI should be considered for the following clinical signs:

- In the early progression of these devastating infections, patients are experiencing excruciating pain, which is disproportional in relation to the clinical appearance.
- Classic signs of skin infection may occur later in the form of hyperemia, fluctuation, exudates with none or unspecific odor, and lymph node involvement.
- The rapid deterioration of the patient's overall condition.
- Appearance of large hemorrhagic bullae.
- The skin may then turn to red-blue resulting from vascular thrombosis and consequent formation of skin necrosis.
- Pain will cease suddenly and sensory and/or motor deficits may be present.
- Gas-producing bacteria cause crepitus of the skin on palpation ("bubble wrap paper").
- Several anatomical sites and different tissue layers can be affected simultaneously.
- NSTIs can spread extremely quickly directly on top of the fascia ("highway to hell") because most of the bacteria responsible for these devastating infections produce proteolytic enzymes allowing tissue destruction. Vascular thrombosis is cutting off the host's own defense mechanisms.
- The infections tend to spread into areas of least resistance in the patient. For example, the initial start of NSTI in the perineal region can spread to distant regions such as the inner surface of the thigh, hypogastric and ischiorectal space, lesser pelvis, and retroperitoneal fat up to the kidneys or through the mesothorax and moving up to the neck.

9.4 Types of Necrotizing Soft-Tissue Infections

NSTIs can appear in many different clinical forms:

- They can begin as a simple superficial bacterial skin infection and then progress to severe NSTI of the muscle compartment with fatal outcome.
- The clinical appearance depends on the organism(s) responsible for NSTI, the immune status of the patient, and the time until the recognition of infection.
- NSTI can be found superficially in the subcutaneous tissue but also in deeper muscle compartments.
- Many different aerobic and anaerobic species have been identified in patients with NSTI (Table 9.1).
- The cause of severe NSTI can be multi-bacterial.
- The different bacteria may act in synergy.
- In limb infections, only a single microorganism can be found, usually from the skin flora of the host, such as *Staphylococcus pyogenes*.

Under these circumstances the classification of NSTI is challenging. Ahrenholz developed a practical differentiation based on the classification by Lewis. The differentiation takes into account:

- The level of the affected soft tissue, which determines the surgical intervention(s)
- The responsible bacteria, which dictates the antibiotic therapy

9.4.1 NSTI of the Skin, Subcutaneous and Fascia Level

9.4.1.1 Cellulitis

Cellulitis caused by group A Streptococcus or *Staphylococcus aureus* is an acute infection of the skin and underlying soft tissues originating mostly from wound ulcer(s) or dermatosis. The classic sign of the infection is a hot, red, oedematous, sharply defined area. The patient may have fever, with lymphangitis and lymphadenitis possibly appearing later.

Table 9.1 Microorganisms isolated in NSTI

Gram-positive aerobic bacteria	Gram-negative aerobic bacteria	Anaerobic bacteria	Marine vibrio
Group A Streptococcus	*Escherichia coli*	*Bacteroides* sp.	*Vibrio vulnificus*
Group B Streptococcus	*Pseudomonas aeruginosa* sp.	*Clostridium* sp.	*Vibrio parahaemolyticus*
Staphylococcus aureus	*Enterobacter cloacae*	*Peptostreptococcus* sp.	*Vibrio damsela*
Coagulase-negative Staphylococci	*Klebsiella* sp.	*Peptococcus* sp.	*Vibrio alginolyticus*
Enterococci	*Proteus* sp.		
Bacilli	*Serratia* sp.		
	Acinetobacter		
	Citrobacter freundii		
	Pasteurella multocida		

9.4.1.2 Synergistic Necrotizing Cellulitis

This type of infection is a variation of necrotizing fasciitis, which will be described later, and is caused by a combination of anaerobic bacteria and Enterobacteria. Synergistic necrotizing cellulitis is predominantly found in elderly patients with diabetes and cardiovascular and renal diseases, affecting mostly the lower extremities and the perineum, showing multiple cutaneous ulcers producing a reddish-brown fluid.

9.4.1.3 Clostridia Cellulitis

Clostridia is the cause of a specific type of cellulitis and typically appears 3–5 days after trauma. Characteristics are severe pain and the development of bullae that contain a reddish-brown fluid emitting a typical foul smell. In contrast to clostridia myositis, severe systemic septic-toxic reactions are absent.

9.4.1.4 Hemolytic Streptococcal Gangrene

Hemolytic streptococcal gangrene, described by Meleney in 1924, is characterized by a rapid spreading of infection and high fever developing within a short period of time. The local clinical signs are hyperemia, swelling, redness, and severe pain of the affected area. The skin is initially intact but within 2–4 days, the color changes from red to blue as a sign of ongoing subcutaneous spreading of infection with vascular thrombosis, ending in patchy skin gangrene. β-hemolytic Streptococcus is usually responsible for these infections and produces a number of toxins such as hemolysins, streptolysins O and S, and leukocidins, which cause local but severe systemic symptoms such as high fever, cardiovascular collapse, and respiratory problems.

9.4.1.5 Fournier's Gangrene

In 1883, Fournier described a type of NSTI of the skin and soft tissue of the perineum and scrotum that progresses rapidly (<24 h) from the onset of the infection to the development of skin gangrene. The testicles are usually not affected. Patients complain about excruciating pain and show severe systemic toxic symptoms in the form of multiple organ dysfunction and eventually multiple organ failure frequently requiring intensive care treatment. Multiple organisms can cause this form of NSTI, but often the underlying cause is unknown. In 45 % of cases the infection originates from the urogenital system, in 33 % from the rectum, and in 21 % a local skin infection can be responsible for this form of infection.

9.4.1.6 Necrotizing Fasciitis

Necrotizing fasciitis is divided into types I and II. Type I necrotizing fasciitis is caused by mixed anaerobic bacteria (Enterobacteria and Streptococcus with Lancefield group A), whereas type II is caused by Streptococci with or without *Staphylococcus*. The synergism between these bacteria determines the progression of the infection. In contrast to β-hemolytic Streptococcus gangrene, this type of infection is not characterized by severe excruciating pain, and patients complain of only dull pain. In the early stage, systemic signs such as tachycardia, low blood pressure, and feeling unwell can be present. The spread of the

infection within the subcutaneous level is always more extensive than it appears from the visible skin changes. On inspection, the tissue is grey or grey-green, while the muscle is initially not affected. The infection then rapidly progresses along the fascia ("highway to hell") causing thrombosis of the subcutaneous blood vessels. At this stage the pain may decrease significantly as a result of the necrosis of the skin nerves. The nonexisting blood circulation within the skin causes necrosis, which is a late clinical sign in the infection.

9.4.2 NSTI of the Muscle

In this category NSTI are differentiated between
- Myositis caused by Streptococcus
- Myonecrosis caused by Clostridia

Often, in this type of NSTI, an entry point into the muscle layer cannot be identified. Most likely these infections are caused by hematological dissemination from a distant source within the body, in most cases an infected throat can be identified as the source.

9.4.2.1 Streptococcal Myositis

Streptococcal myositis is caused by Streptococcus of Group A and initially presents without myonecrosis. In some cases, a synergistic infection with *Staphylococcus aureus* has been described. The affected muscle tissue is discolored and swollen, but still functionally intact. At this early stage, the muscle tissue is not (yet) necrotic, however this type of infection is regarded as an NSTI because of the systemic reaction, which can deteriorate into a "Streptococcal toxic shock syndrome."

9.4.2.2 Myonecrosis Caused by Streptococcus

Group A Streptococcus can cause myonecrosis, often in combination with *Staphylococcus aureus* and progress rapidly (<24 h). The affected muscle is unresponsive to stimulation and changes its normal color from red to grey. Because the vessels are thrombosed, no bleeding occurs in these necrotic areas unless the débridement reaches healthy muscle. The necrotic muscle areas are macerated, have lost their typical structural integrity, and can be easily débrided from the intact tissue. The margin of the infection is indicated by the appearance of bleeding, red color, and responsiveness of the muscle fibers to touch.

9.4.2.3 Clostridium Myonecrosis

Infections of muscle with *Clostridium perfringes*, novyi, and septicum can be found after severe agricultural accidents, perforating injuries, or in patients with intestinal tumors (Fig. 9.1). Clostridia are part of our normal environment and intestinal flora. The clinical features are severe pain and profound systemic reactions in the form of septicemia with high fever, coagulopathy, and initially, multiple organ dysfunction, often developing into a multiple organ failure. The main characteristic is a sweet-foul smell from the wound secretion. Clostridia produce α-toxin (lecithinase), which causes cell membrane rupture leading to hemolysis and deactivation of white blood cells. It has also a cardiotoxic effect. This form of NSTI progresses quickly. Within hours, the skin, which is initially edematous, changes from pale to blue with the appearance of hemorrhagic bullae filled with non-purulent fluid. The texture of the affected muscle is edematous and pale in color, before it becomes gangrenous and black. Characteristically, the affected muscle is unresponsive to stimulation and extremely friable. Patients with diabetes or angiopathy are more susceptible to this type of NSTI. Increase in serum creatinine kinase and urine myoglobin values indicate muscle involvement in this type of infection. Gram staining of the fluid from the affected area shows the characteristic form of Clostridia (i.e., boxcars). Positive blood cultures for Clostridia may be found in only 15 % of patients.

9.4.3 Toxic Shock Syndrome

Willoughby and Greenberg introduced the definition of "Streptococcal toxic shock syndrome" in 1983, similar to the definition of the Staphylococcal toxic shock syndrome. Several consensus criteria must be satisfied for the diagnosis of this syndrome, such as isolation of Streptococcus strains from the patient and certain clinical signs such as erythema, muscle necrosis, hypotension, renal insufficiency, coagulopathy, liver dysfunction/failure, and adult respiratory distress syndrome.

Toxic shock syndrome (TSS) develops in 50 % of the patients who suffer from necrotizing fasciitis as a result of Streptococci infections, and 60 % of the infections originate from the skin or urogenital tract. In other instances, a translocation of bacteria from the pharynx into the bloodstream is responsible for the infections.

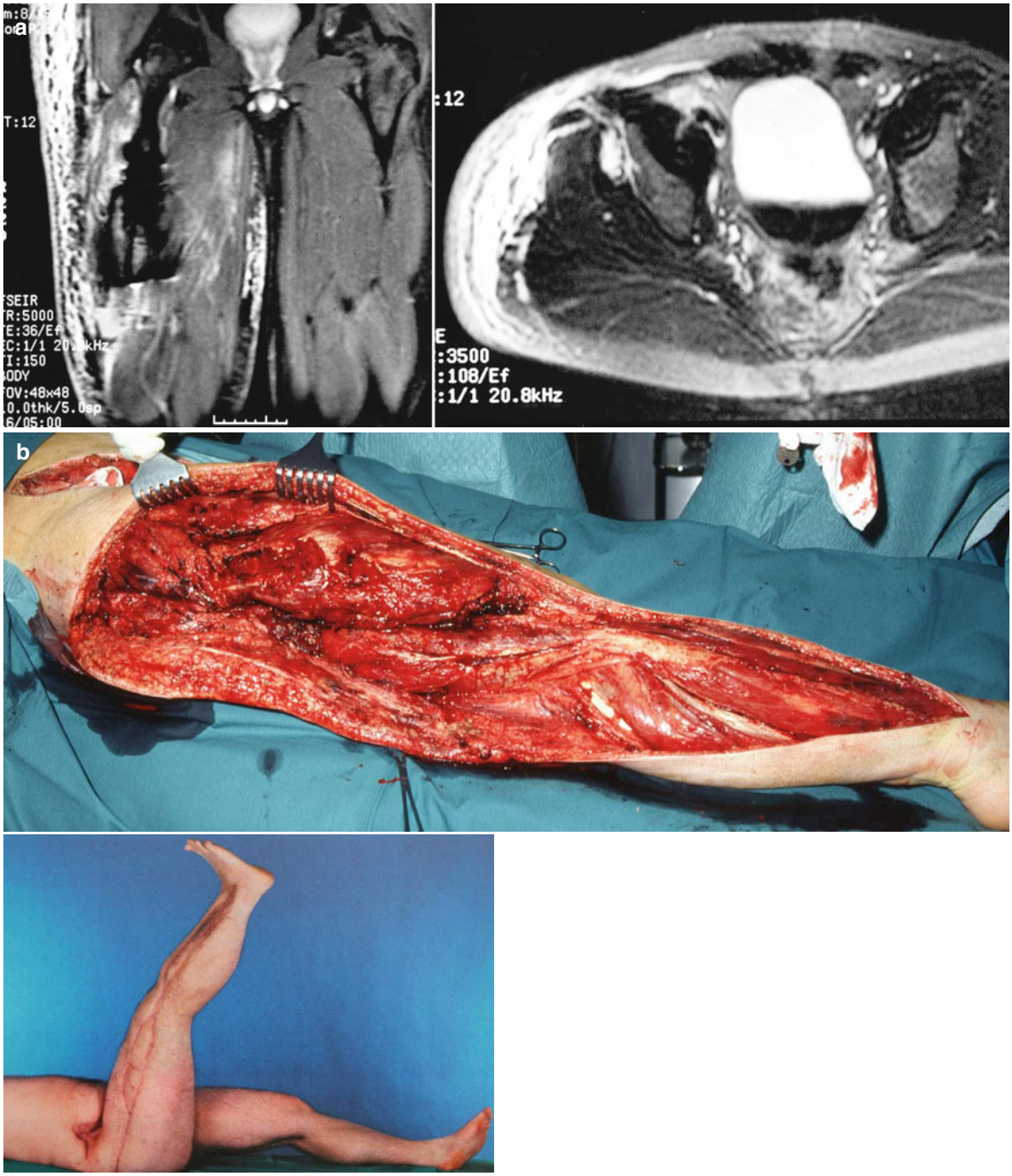


Fig. 9.1 (**a**) Myonecrosis of right thigh because of *Clostridium perfingens*: MRI at admission. (**b**) Status after radical débridement including right retroperitoneal space, several "second-look" procedures, and the final result after wound healing and skin grafting

Three clinical phases of TSS:

- In the first phase, the symptoms are unspecific and present as generalized or localized muscle pain, vomiting, general malaise, and diarrhea. The shock symptoms can develop hyper-acutely within hours, but can also take several days, depending on the causative bacteria, the localization of the infection, and the immune status of the patient.

- In the second phase, the pain and swelling increase in the affected side. Patients show systemic toxic signs such as tachycardia, tachypnea, and high fever. Rarely is lymphangitis or lymphadenitis seen.
- Without adequate therapy the infection progresses to the third phase, which is a severe TSS with multiple organ failure. An important fact is that TSS has been seen in patients with and without skin gangrene.

The shock symptoms are caused in part by so-called "superantigens", which are proteins produced by certain group A Streptococci, but also by Staphylococci (exotoxine type A, B, C, D, F, MF, SSA). The difference of these proteins as compared with conventional antigens is that they are not controlled by the major histocompatibility complex of T cell receptors. The consequence is that normal T cell activation is bypassed and massive and uncontrolled amounts of immune mediators (e.g., tumor necrosis factor-α, interleukin-1, -2, -6, -8, -12, and interferon-γ) are liberated into the circulation of the affected patient, causing the described shock symptoms.

9.4.4 Diagnosis

9.4.4.1 Clinical Signs

Early diagnosis of NSTI is often difficult because of the lack of typical clinical signs and the absence of characteristic skin changes. As a general rule, skin necrosis is a late sign of NSTI. However, the survival of patients with NSTI depends on early diagnosis, which can only be made by a physician who approaches the patient with a high suspicion for NSTI, if the following clinical signs are present:

- Symptoms of severe local or systemic infection
- Systematic toxicity
- Radiograph showing subcutaneous gas
- Histology with characteristic changes for ongoing severe infections
- Positive microbiology

One feature in particular that must always alert a clinician for considering NSTI is pain that is disproportionate to the clinical findings. Sudden decrease in pain or anesthesia at an apparent site of infection is a late change and is a result of necrosis of the skin nerves.

In patients in whom NSTI is suspected, all body surfaces must be inspected during the physical examination.

The skin must be examined for:

- Erythema
- Tense skin edema
- Grayish or other discolored wound drainage
- Vesicles or bullae
- Necrosis
- Ulcers
- Crepitus

Bullae with serous fluid appear as an early clinical sign during the course of the infection, whereas large hemorrhagic bullae, skin necrosis, crepitus, and sensory and motor deficits are late signs. Migration of the margins of erythema and increasing skin induration despite the use of intravenous antibiotics is another indication of NSTI.

Clinical symptoms such as hypotension, fever (temperature > 38 °C), tachycardia, tachypnea, mental disturbance, and tremor may or may not be present or appear suddenly without any warning. Marked increase in white blood cell count and metabolic acidosis often occur at a later stage and reflect severe sepsis.

9.4.4.2 Radiology

NSTIs can cause subcutaneous gas produced by bacteria that can be detected using various radiography techniques. Gas in soft tissue may be visible on conventional radiographs, ultrasonography and computed tomography (CT). Compared with plain-film radiography or ultrasonography, CT and magnetic resonance imaging (MRI) are superior for detecting tissue inflammation and necrosis. Gadolinium-enhanced MRI demonstrates not only gas within the soft tissue, but marks the extent and the involvement of the different tissue layers. It is important to understand that these examinations show the extent of the infection at the time of the examination, but the infection continues to progress at a high speed. The area of NSTI may continue to increase until the patient has been transported to the operating room for surgical treatment.

9.4.4.3 Laboratory Tests

Patients with NSTI have

- Abnormal blood values
- Elevated polymorphonuclear leucocyte counts
- Anemia
- Hypocalcaemia

- Acidosis
- Decreased platelet counts
- Increased prothrombin and partial thromboplastin time
- Elevated serum creatinine phosphokinase

The combination of local symptoms, systemic toxicity, radiological results, and pathological laboratory tests should raise the suspicion of NSTI.

9.4.4.4 Tissue Specimen and Microbiology

The definite diagnosis of NSTI and the responsible bacteria must be obtained through:

- Blood sampling
- Intraoperative collection of tissue samples and swabs

To identify the bacteria responsible for NSTI and the level of the affected tissue, the following procedures must be performed:

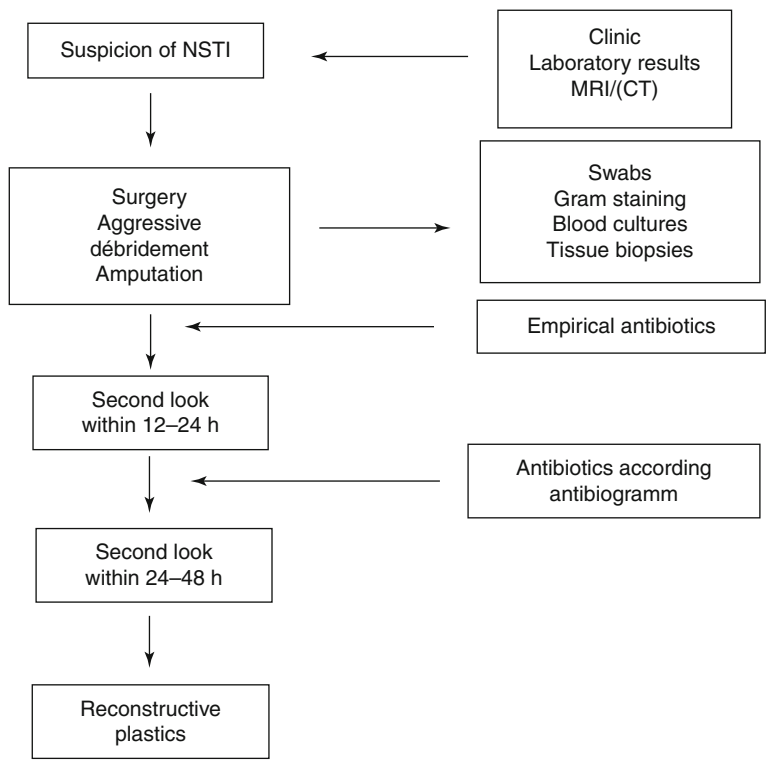
- Specimens (tissue and swabs) must be taken from the penumbra area of the infection to obtain an up-to-date view of the infection and its progress
- Specimens and swabs taken from the center of the necrosis may produce negative results
- Intraoperative tissue samples are obtained for culture and frozen-section biopsy
- The biopsy must include all tissue layers (cutis, subcutis, fascia, and muscle) to define the extent and depth of the infection
- Immediate gram staining of specimens taken during surgical intervention is advised to identify the involved bacteria and adopt an antibiotic treatment
- Fine-needle and punch biopsy are recommended only if a thorough débridement is performed at the same time

Despite all efforts, the causative bacteria(s) for NSTI may never be identified. The antibiotic therapy is then guided by the clinical appearance of the infection and progress of the patient's condition.

9.4.5 Therapy

The key in saving a patient with NSTI is to understand the clinical symptoms with all its variation(s). Only early therapy gives the patient a chance for surviving these devastating infections, or lowers the risk of losing a limb. Nearly all NSTI must be treated surgically, with the exemption of superficial cellulitis (Table 9.2).

Table 9.2 Diagnostic and therapeutic algorithms for NSTI



9.4.5.1 Treatment of Superficial NSTIs

The treatment of cellulitis is primarily conservative, with antibiotics and splinting if a limb is affected. Surgical intervention is only necessary if the infection spreads further and signs of systemic toxicity occur. The moderately severe form is managed with oral penicillinase-resistant penicillins or cephalosporins. More serious infections require intravenous treatment with cloxacillin plus aminoglycoside or third-generation cephalosporin, quinolone, or tircacillin plus clavulanic acid. In cases of infected human or animal bites as the source of cellulitis, the administration of cloxacillin has been recommended.

9.4.5.2 Surgical Treatment of Rapidly Spreading NSTI

The overall high mortality and morbidity of rapidly spreading NSTI can only be prevented by

- Surgery performed without delay and without compromise
- Triple regime of high-dose antibiotics
- Life support
- Hyperbaric chamber treatment (if available)

During surgery, the infected area must be inspected carefully and all necrotized tissue must be removed:

- Necrotized skin, subcutaneous fat, fascia, muscles, vessels, and nerves must be removed until healthy bleeding tissue is encountered.
- Depending on the clinical conditions, surgical débridement must be repeated several times during the course of a short time period.
- Amputation is the treatment of choice in severely affected limbs and should be considered if the infection is spreading rapidly or the toxic symptoms are not under control.
- Limb amputation should also be considered if extensive muscle necrosis and excision would leave the patient with poor or no limb function.
- Remaining cavities that have no natural way of draining after the débridement must be drained with large caliber drains.
- The débrided wound should be kept open.
- Vacuum sealing can be used. However, the negative pressure must be adjusted to low levels to ensure that only the excessive exudate is evacuated from the wound and no additional bleeding from the débrided area is facilitated.
- During the postoperative period, regular control (on an hourly basis) of the area operated on is mandatory to detect excessive drainage and delayed onset of bleeding.
- Scheduled inspections initially every 12–24 h are advised.
- If the patient is showing signs of systemic toxicity or the infection is spreading, further débridement within a shorter time frame may be necessary.
- However, if the patient shows improvement, the time lag between débridement may be extended.

For Fournier's gangrene, daily radical débridement of all necrotized tissue must be performed until complete infection control has been achieved, followed by plastic reconstructive operations. The testicles are usually unharmed because their blood supply is of a different origin. Colostomy should be considered early in order to deflect stool from the infected area.

9.4.6 Life Support

Following surgery, most patients with NSTI require intensive care treatment with intubation, intravenous fluid resuscitation in large volumes, and monitoring of the cardiovascular system to correct:

- Anemia
- Electrolyte disturbances
- Platelet deficiencies
- Coagulopathy

Patients with NSTI may display multiple organ dysfunction, which may progress to multiple system organ failure and may require intermittent dialysis for renal dysfunction. Patients with NSTI require enteral feeding with high calorie and protein intake to counter auto-cannibalism and electrolyte and vitamin substitutions. Regular bowel emptying must be achieved, on a daily basis if possible, to facilitate enteral feeding and to avoid internal bacterial overgrowth and potential translocation into the blood stream.

9.4.7 Antibiotics

In rapidly spreading NSTI, antibiotics are used in addition to surgery. Antimicrobial therapy may help to prevent the further spread of NSTIs. However, only tissue that is well perfused and not affected by thrombosed blood vessels can be reached by antibiotics. Without surgery, antibiotics alone will not ensure survival of patients with NSTI.

Initially, the antibiotic treatment is empirical with three different antibiotics to cover the multi-bacterial origin of these infections.

- Penicillin plus b-lactamase inhibitor against *Enterococcus*, *Peptostreptococcus*, and Clostridia
- Metronidazole against anaerobes
- Clindamycin against *Streptococcus*, *Peptostreptococcus*, and anaerobes

Clindamycin is recommended because it inhibits the bacteria protein synthesis and the production of toxins and M-proteins. M-proteins protect bacteria against phagocytosis. Continued administration of clindamycin prevents the secretion of immune mediators from leucocytes, the main mediator responsible for the toxic shock syndrome.

The antibiotic treatment must be adjusted once microbiological cultures have been evaluated and the bacteria identified. It is important to avoid the development of bacterial resistance against the administered antibiotics during the treatment.

In the event of detection of methicillin-resistant *Staphylococcus* or vancomycin-resistant *Enterococcus*, the patient may need to be treated in isolation with special precautions for nursing procedures and restrictions for visiting relatives.

9.4.8 Hyperbaric Oxygen

Hyperbaric oxygen (HBO) is advocated as an adjunct in the therapy of NSTI because the effect of HBO in the treatment of NSTI has not been proved. HBO seems to help improve leukocyte cytotoxic and bactericidal functions, maintaining viability of marginally perfused tissue, and is thought to improve wound healing. However, surgical débridement must never be delayed in favor of hyperbaric oxygen treatment.

9.4.9 Reconstruction of Soft-Tissue Defects

The size of the postsurgical tissue defect and the resulting functional disability is not of concern during débridement(s). The surgical therapy has only one purpose, which is to enable the patient to survive. The surgery must be radical and follow the paradigm: "Limb for life". Functional or cosmetic improvements can be considered later and must only be performed during the safe recovery phase, when the acute infection is well under control and the patient is out of danger. Amputated limbs require good soft-tissue coverage to enable good prosthetic fit. Soft-tissue correction or adjustment of the length of the stump may be done at a later stage. In necrotizing fasciitis, the involved subcutaneous tissue and fascia are removed. In most cases the muscles remain unharmed. The soft-tissue defect is normally covered with split skin graft. In cases of extended abdominal deficits, split-thickness skin grafts are applied as soon as the infection has subsided. Once the patient has recovered, a reconstruction of the abdominal wall using a non-absorbable net should be performed. Large defects may require either direct or free soft-tissue flaps.

9.4.10 Prognosis and Mortality

NSTI is a surgical disease and survival can be achieved only if the surgical treatment is quick and aggressive. Delay in surgery will increase mortality or the risk of limb loss. Mortality due to NSTI has been reported in about 35 % of cases when the infection is limited to limb(s). The mortality rises to 60 % in cases with gas gangrene. The mortality of NSTI located at the trunk is close to 100 %.

Early death of patients with NSTI is in most cases a result of septic shock; later death is a result of multiple organ insufficiency/failure.

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Soft-Tissue Trauma

10

Hans-Jörg Oestern

10.1 Introduction

Open fractures are often high-energy injuries with a high risk of infection, delayed union, and nonunion.

The incidence of open fractures including small bones is 30.7 per 100,000 population per year. The incidence for open long bone fractures is 10.9/100,000/year. Open lower-limb fractures had an incidence of 3.4/100,000/year: 45 % were Gustilo type III and, of these, 51.3 % were type IIIA, 45.4 % type IIIB, and 3.4 % type IIIC.

10.2 Etiology, Mechanism of Injury, and Radiography

1. Severe open fractures usually occur as a result of direct, high-energy trauma. The energy (E_k) dissipated at the time of injury is proportional to the mass (m) and the square of the velocity (v) according to the formula $E_k = mv^2/2$.
2. In low-energy trauma (torsional fractures) the skin will be perforated from the inside.
3. Extensive displacement, comminution, and radiographic changes in soft-tissue structures (foreign bodies, air inclusions, soft-tissue defects) can in themselves be an indication of the severity of the soft-tissue injury. On the other hand, even a simple-looking fracture can be accompanied by extensive soft-tissue damage because a spontaneous or manual reduction of the fracture at the accident scene can cause initial radiographic findings to be deceptive. However, smooth transverse fractures and even segmental fractures of the tibia are usually the result of direct violence and thus will be associated with characteristic soft-tissue lesions.

10.3 Classification

The simple classification of fractures as "open" or "closed" seems to be the only universally accepted scheme but is not enough for therapeutic decision-making, quality control, and scientific comparison of different soft-tissue lesions. Therefore, a differentiated classification for closed and open fractures is needed. Closed fractures are divided into four grades of severity according to Tscherne and Oestern, whereas open fractures are classified into three grades and three subgrades in type III fractures according to Gustilo and Anderson [1] (Table 10.1).

10.4 Closed Fractures (Tscherne and Oestern) [2, 3]

Soft-tissue damage in closed fractures might often be more severe than open fractures. Grade 0 closed fractures (*Fr. C 0*) Soft-tissue damage is absent or negligible. The fracture is caused by indirect violence and has a simple configuration (Fig. 10.1). Torsion fractures of the tibia in skiers are typical of this category.

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Table 10.1 Classification of soft-tissue injuries in closed fractures according to soft-tissue damage, fracture severity, and contamination

Classification	Skin open + closed –	Soft-tissue damage	Fracture mild + severity mod ++ sev. +++	Contamination
Fr. C 0	–	–	+	–
C I	–	+	+ to ++	–
C II	–	++	+ to +++	–
C III	–	+++	+ to +++	–

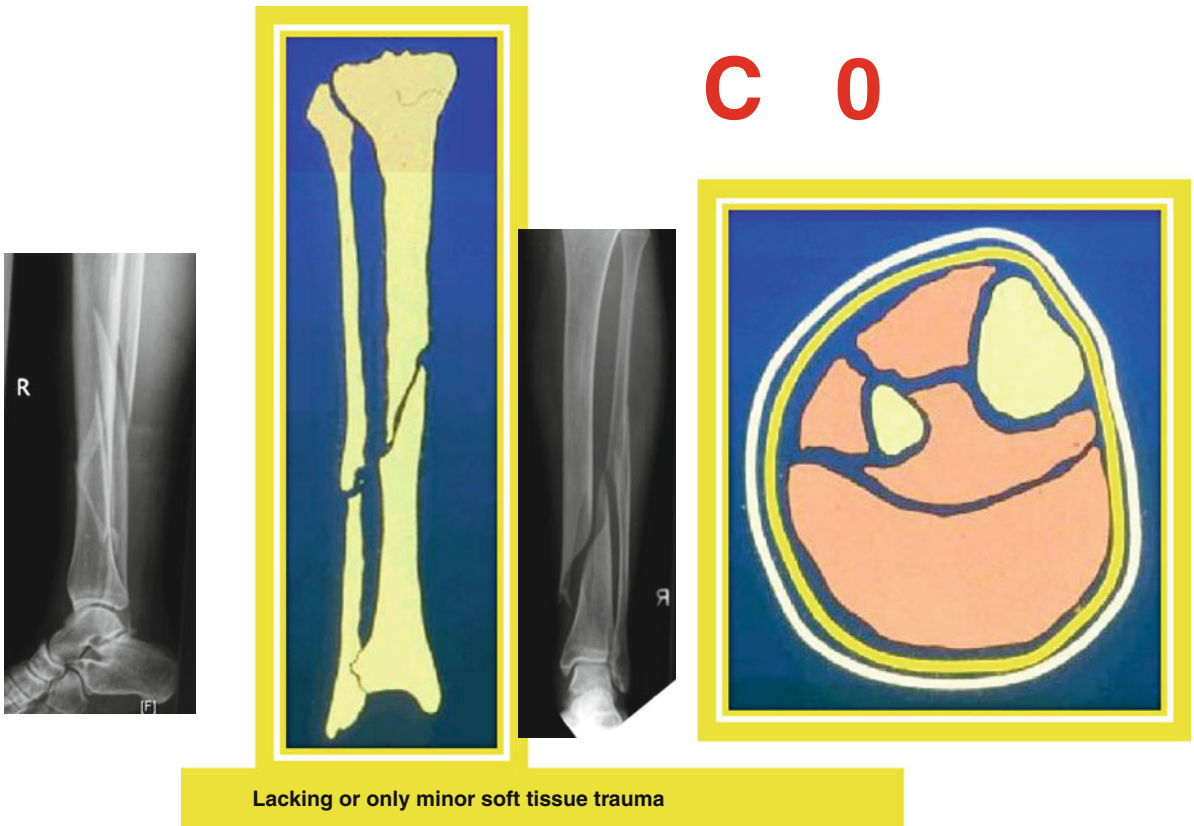


Fig. 10.1 Grade 0 closed fracture (Fr. C 0): Simple fracture configuration with little or no soft-tissue injury

Grade I closed fractures (*Fr. C I*): There is a superficial abrasion or contusion caused by fragment pressure from within. The fracture itself is of a mild to moderately severe configuration (Fig. 10.2). A typical example is the pronation fracture-dislocation of the ankle joint, in which soft-tissue lesions are caused by pressure from the fractured margin of the medial malleolus.

Grade II closed fracture (*Fr. C II*): There is a deep, contaminated abrasion associated with localized skin or muscle contusion from direct trauma (Fig. 10.3). Impending compartment syndrome is included in this category. Generally, there has been direct violence producing a moderately severe fracture configuration. Segmental "bumper" fractures of the tibia are an example. Given the mechanism of injury, the soft-tissue lesions must be at least Fr. C I but are usually Fr. C II.

Grade III closed fracture (*Fr. C III*): The skin is extensively contused or crushed, and muscle damage can be severe. Other criteria for this category are subcutaneous avulsions, decompensated

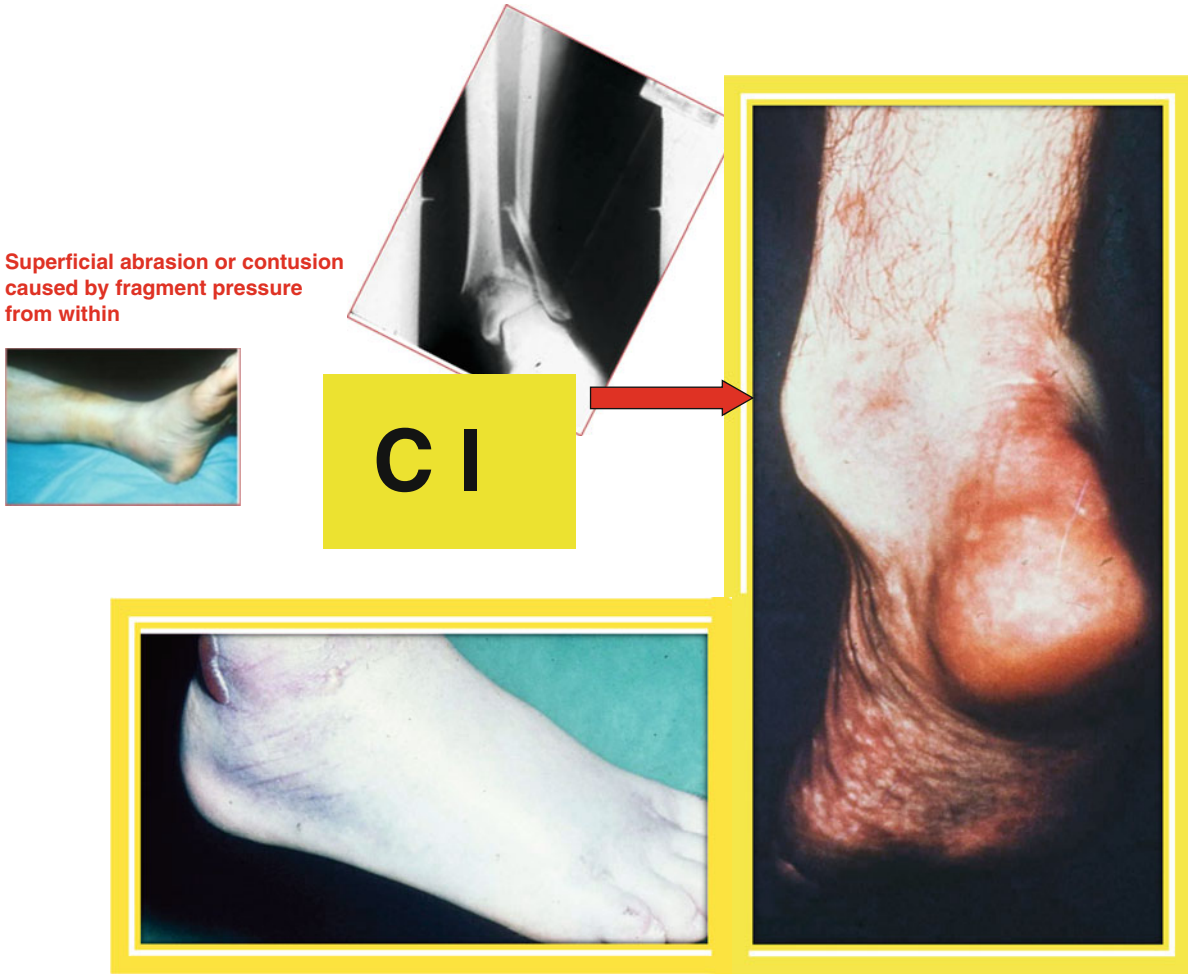


Fig. 10.2 Grade I closed fracture (Fr. C I): Superficial abrasion (*shaded area*), mild to moderately severe fracture configuration

compartment syndrome, and rupture of a major blood vessel associated with a closed fracture (Figs. 10.4, 10.5, and 10.6). The fracture configuration is severe or comminuted. The contusional damage makes treatment of the soft-tissue injuries more difficult than in grade III open fractures [2].

10.5 Open Fractures

The evaluation and treatment of open fractures is governed both by the extent of soft-tissue injuries and by the level of wound contamination. The primary concern is *not* the size of the skin wound, but the degree of soft-tissue damage and extent of muscle contusions. Consequently, it may not be possible to make a definitive classification until the wound has been explored. In addition to classifications such as those of Tscherne and Oestern [3] and the AO classification, the most used classification for open fractures is the Gustilo and Anderson classification [1].

10.5.1 Classification (Gustilo and Anderson) [2]

Type I:

- Wound is less than 1 cm with minimal soft-tissue injures.
- Wound bed is clean.
- Fracture is usually a simple transverse, short oblique fracture, with minimal comminution.

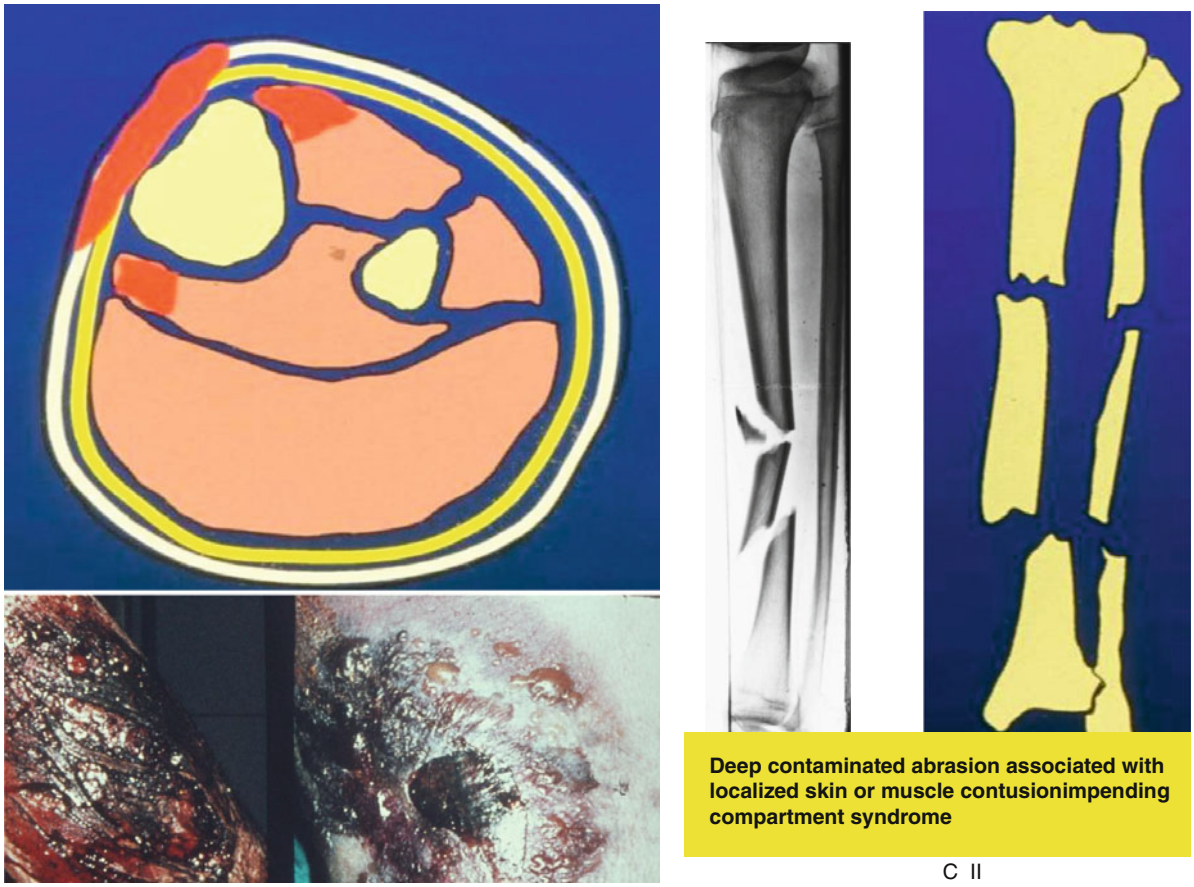


Fig. 10.3 Grade II closed fracture (Fr. C II): Deep, contaminated abrasion with local contusional damage to skin or muscle (*shaded area*), moderately severe fracture configuration (e.g., closed segmental fracture of the tibial shaft)

Type II:

- Wound is greater than 1 cm with moderate soft-tissue injury
- Fracture is usually a simple transverse, short oblique fracture, with minimal comminution

Type III:

- Fractures that involve damage to the soft tissues, including muscle, skin, and neurovascular structures
- Often accompanied by a high-velocity injury or a severe crushing component
- Special patterns classified as Type III

  Subtype IIIA
  - Adequate soft-tissue coverage despite soft-tissue laceration or flaps or high-energy trauma irrespective of the size of the wound
  - Includes segmental or severely conminuted fractures

  Subtype IIIB:
  - Extensive soft tissue lost with periosteal stripping and bony exposure
  - Usually associated with massive contamination; needs local or free flaps for coverage of the defect

  Subtype IIIC:
  - Fracture in which there is a major arterial injury requiring repair for limb salvage

There are age and comorbidities (i.e., diabetes, pulmonary insufficiency, malignant disease, systemic immunodeficiency) and compromising factors (i.e., nicotine abuse) that are of importance regarding prognosis and risk of infection.

10.5.2 Treatment Algorithm of Open Fractures

10.5.2.1 Primary Treatment at the Scene

The fracture should be reduced at the scene. Reduction means decompression of the soft tissue to avoid further soft-tissue damage. The extremity is splinted using a vacuum bandage. The wound is covered with sterile

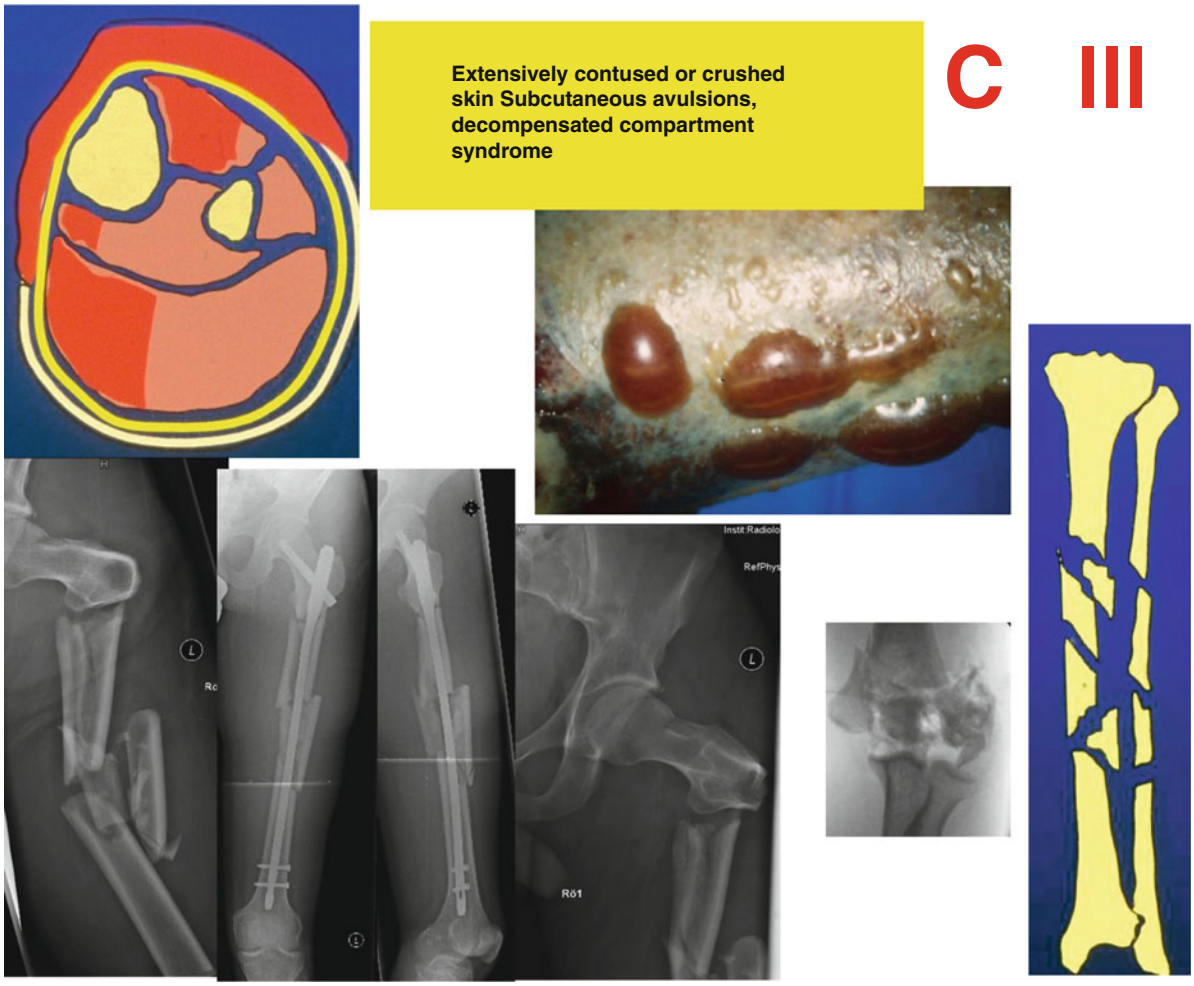


Fig. 10.4 Grade IIII closed fracture (Fr. C III): Extensive contusion or crushing of skin or destruction of muscle (*shaded area*), severe fracture

dressing. The dressing should only be removed in operating room.

10.5.2.2 Emergency Room

Assessment

Vascularity and circulation, neurological function, and musculotendinous continuity must be assessed. Radiographs are obtained of the proximal and distal joint. History is documented: When happened and what was the cause of the accident? What were the surroundings? What was the mechanism of injury?

10.5.2.3 Surgical Treatment

Surgical Preparation

With the patient under anesthesia, the dressings are removed under sterile conditions. Bacteriological probes are taken. The skin is cleaned using a soapy solution. The proximal and distal joints are carefully examined [2, 4].

Antibiotics

Antibiotics should be administered as soon as possible and certainly within 3 h after injury

The choice of antibiotic is dictated by the potential bacterial contaminant. First- or second-generation cephalosporins have a broad spectrum of activity and are suitable for most wounds. In type III open fractures, aminoglycide can be added. Antibiotics should be given until soft-tissue closure, or a maximum of 72 h.

Definitive Assessment

A tourniquet should be applied, but not inflated. Full evaluation of the wound demands a detailed assessment of the true extent of the zone of injury. This usually requires enlargement of the window by surgical extension of the skin wound, or on occasion, another incision to create a second window.

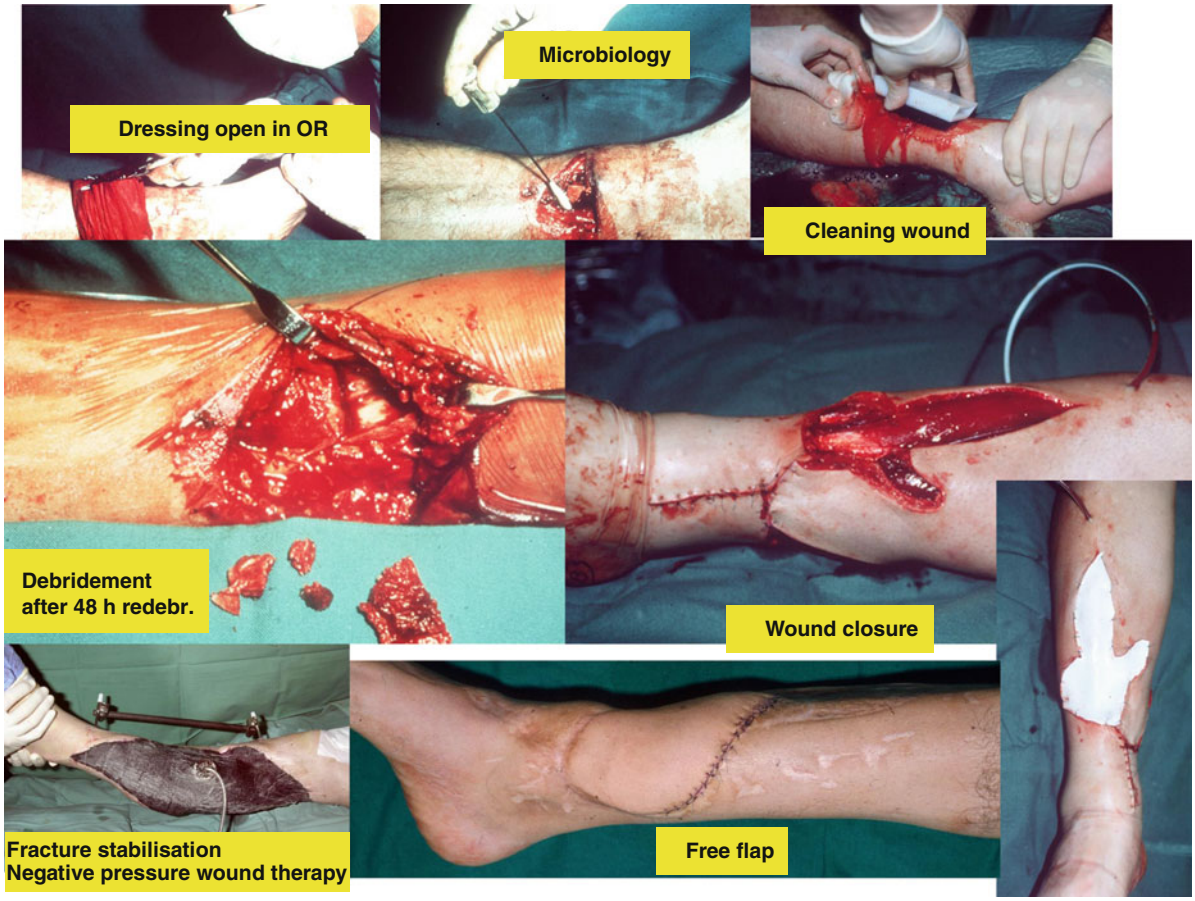


Fig. 10.5 Steps in the management of open fractures: (1) Sterile dressing of the wound at the scene; (2) General assessment in the emergency room; (3) Removal of the dressing and cleaning the wound with a soapy solution; (4) Administration of antibiotics; (5) Débridement; (6) Fracture fixation; (7) Redébridement; (8) Primary or secondary wound closure

Wound Irrigation

Sterile saline solution is typically used either alone or with an additive such as bacitracin (100,000 units).

Low-pressure pulsatile lavage (14 lb psi and 550 pulsations per minute) is used in most instances. Use of high-pressure pulsatile lavage (70 lb psi 1,050 pulsations per minute) has some side effects (i.e., more bone damage, bacterial propagation into the medullary canal, increased depths of bacterial contamination, and reduction and promotion of stem cells, more so to the adipocyte type than to the osteoblast type).

Débridement

Surgical débridement demands meticulous excision of all dead and devitalized tissues. A second investigation should be routinely performed after an interval of 48–72 h. Débridement should thus be regarded as a staged procedure. Skin that is manifestly dead and macerated should be excised. Skin of dubious viability can safely be left until the second look, when viability will be obvious. All muscle of dubious viability must be resected to pink bleeding edges that contract when gently pinched. Detached, avascular bone fragments should be discarded. The dreaded "3 Ds" of dead bone, dead tissue, and dead space are the greatest enemies to an open fracture. Major neurovascular structures should be preserved and repaired if necessary.

Care must be taken to ensure complete removal of all non-viable tissues while at the same time preserving blood supply to others. A photo should be taken after débridement for documentation and later comparison [2, 4].

Fracture Stabilization

The fracture in a type I injury can be treated in the same way as a comparable closed fracture. Type II and type III open fractures are almost inevitably displaced and unstable.

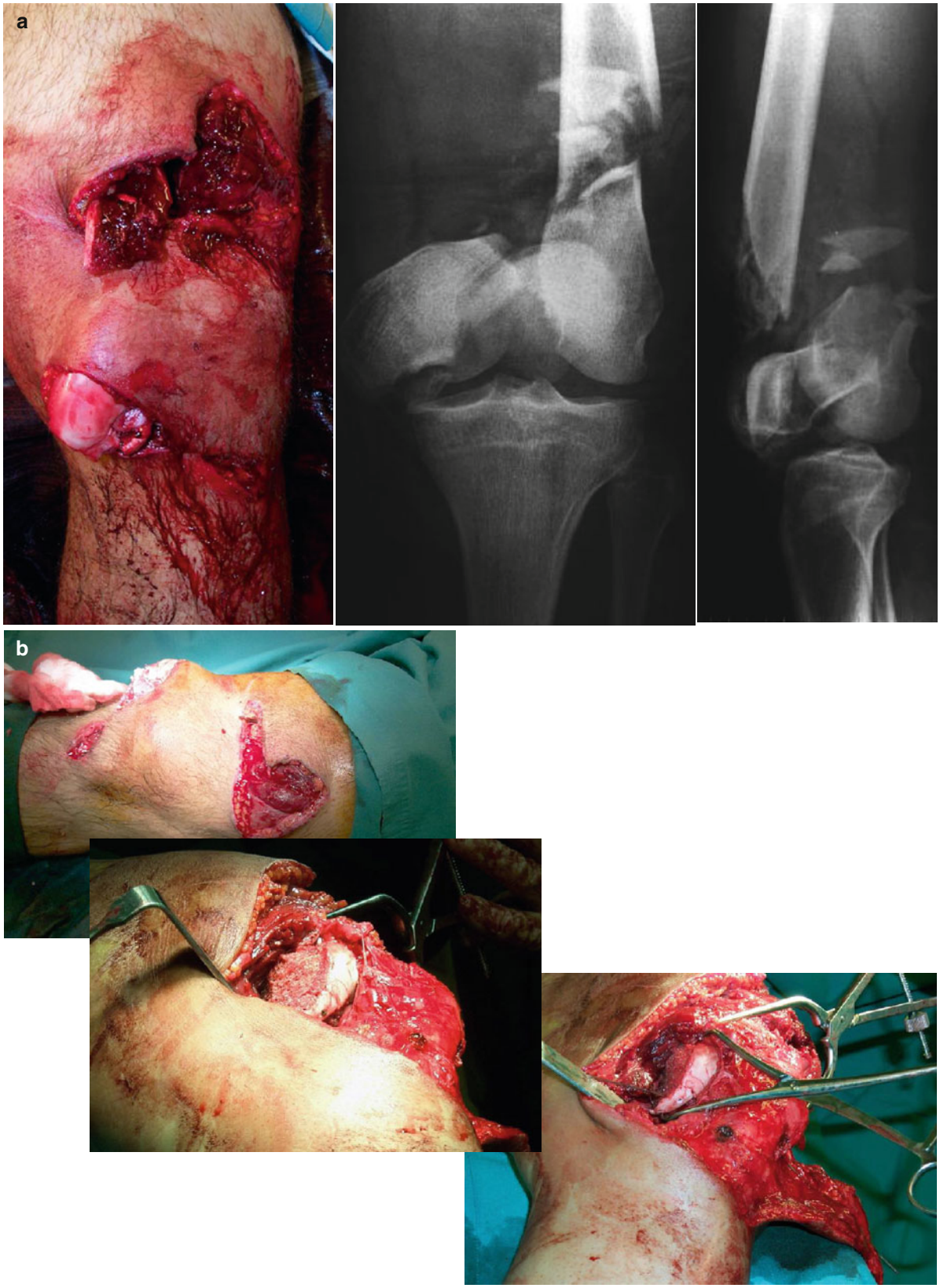
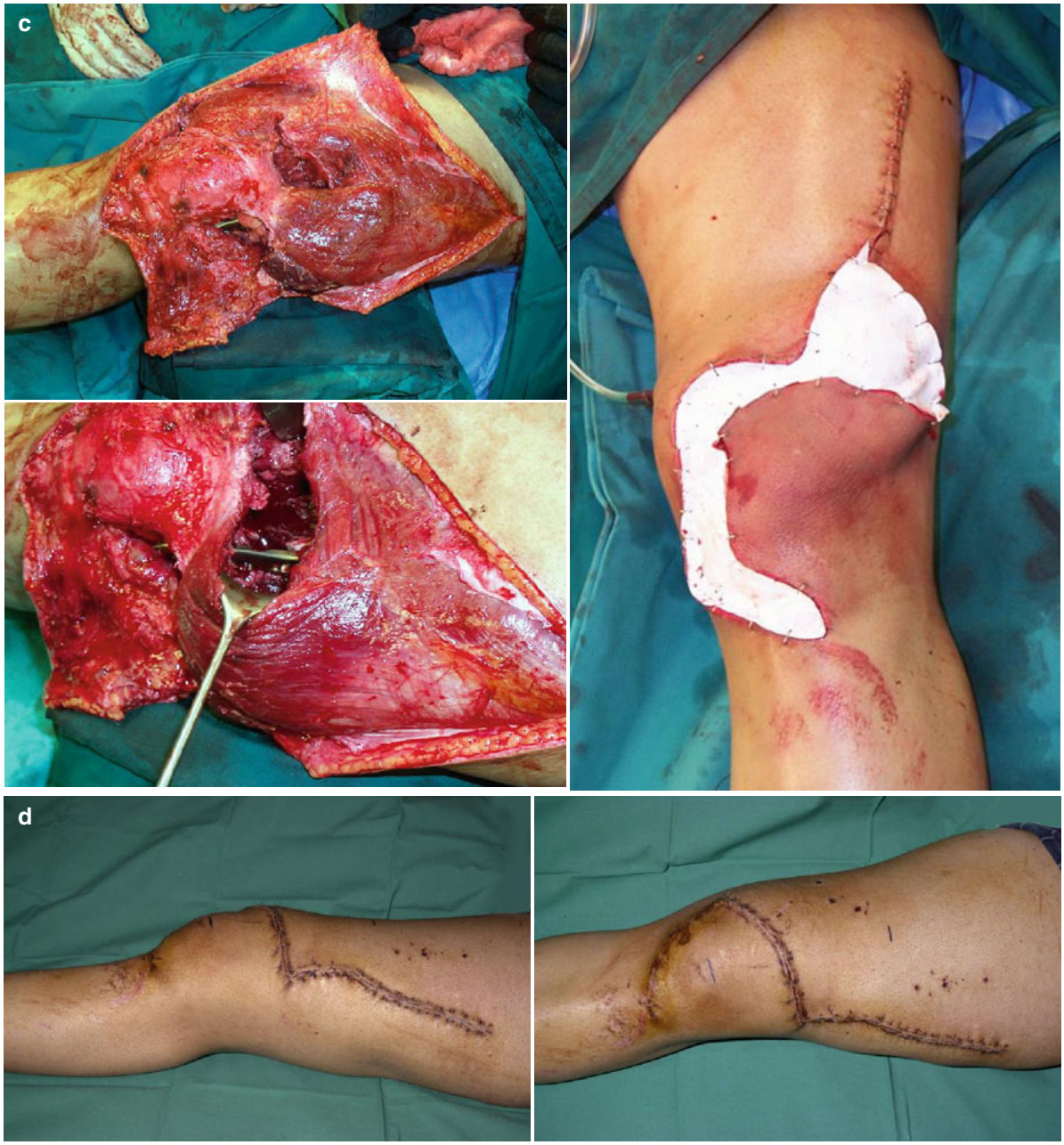


Fig. 10.6 (**a**) Grade III A open distal femur fracture with bone loss. (**b**) After débridement reconstruction of the articular fractures. (**c**) Reduction and submuscular implantation of a less invasive stabilization system (LISS) plate temporary wound cover with Epigard. (**d**) Definitive closure after redébridement cancellous bone grafting. (**e**) Radiograph control 6 weeks after injury



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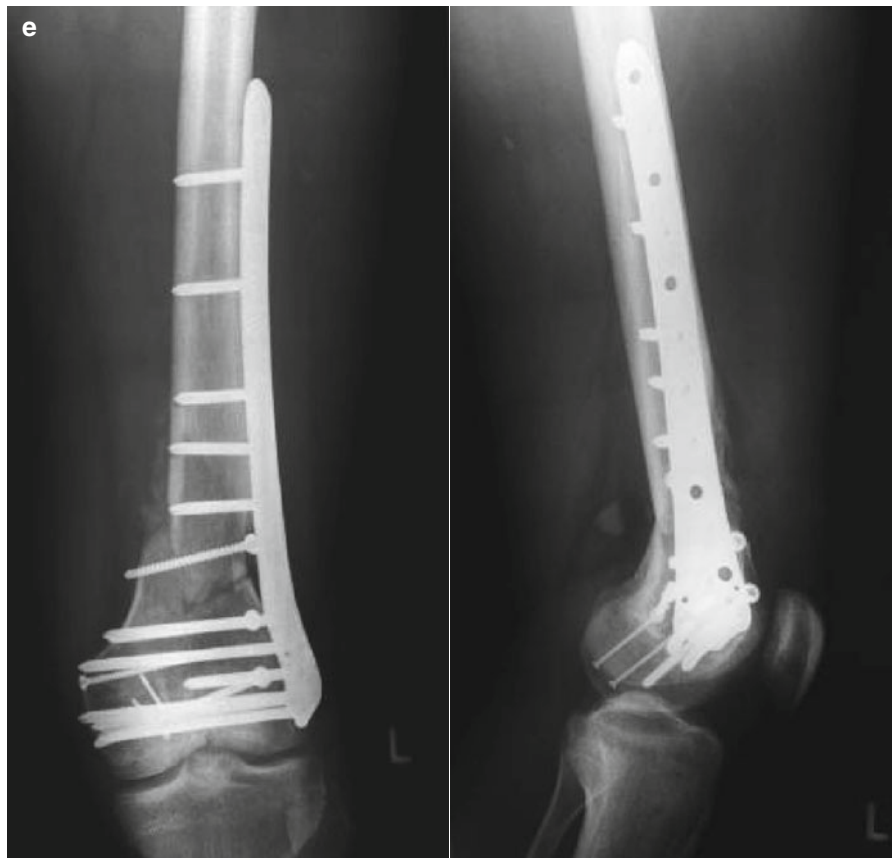

Plates

Plates remain the definitive choice for fixation of open metaphyseal fractures. They are also particularly useful in diaphyseal fractures of the forearm where the soft-tissue sleeve makes them relatively safe and where no other fixation device can provide the stability required to maintain the important anatomical length, axis, and rotation.

Restoration of length and correction of bony deformity facilitates anatomical alignment and tensioning of the soft-tissue structures, thereby reducing dead space and hematoma volume. Stability at the fracture site prevents further damage from mobile bone fragments. However, there is experimental evidence to suggest that fracture stability can be helpful in inhibiting bacterial proliferation. Implants should, wherever possible, be applied through the wound while respecting the need to cover metal with soft tissue.

Intramedullary Nails

The unreamed nail has been developed with the purpose of reducing the disruption of the medullary blood supply. Experimental work demonstrating a reduction in cortical blood supply of 30 %, compared with 70 % after medullary reaming, suggests that these goals have been successfully achieved. Reaming of the medullary canal has been shown to stimulate fracture healing, although insertion of solid nails without reaming has been recommended for open fractures in the hope of reducing the infection.

External Fixation

External fixators are particularly useful when wounds and soft-tissue characteristics contraindicate direct surgical access to the fracture. They are usually the device of choice in severely soiled and contaminated wounds where metallic implants, with the risk of bacterial adherence, are best avoided. The development of ring fixators has extended the indications to include periarticular and intra-articular fractures. In most cases, a change to an internal implant is performed within the first 10 days after the accident.

Wound Closure

Primary closure, delayed closure, and secondary closure are the possible methods for wound closure.

Primary closure: Absolute contraindications are heavily contaminated wounds, large soft-tissue defects, and puncture wounds. Temporary vacuum-assisted closure can be used until secondary wound closure. Negative pressure wound therapy works through at least three primary mechanisms:

1. Increased blood flow and/or angiogenesis
2. Mechanical stretching of cells, leading to the secretion of cytokines and growth factors associated with wound healing
3. Reduction of edema. Delayed closure can be performed using skin grafts, local flaps, free flaps, and tissue expansion. Infection rate is low because early definitive wound closure can be performed.

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Compartment Syndrome

11

Hans-Jörg Oestern

11.1 Definition

Compartment syndrome is a condition in which increased pressure within a limited space compromises the circulation and function of the tissues within the space [1].

11.2 Etiology

Most compartment syndromes are associated with traumatic insults, but the condition also occurs after reperfusion, following a period of ischemia, burns, prolonged limb compression after drug abuse, or poor positioning during prolonged surgical procedures. The most common fractures causing a limb compartment are those of the tibial shaft (40 %) and of the forearm (18 %). About 23 % are caused by soft-tissue injuries without fracture. It is important to recognize that open fractures can develop a compartment syndrome, both in the closed compartments and those compartments opened by the injury.

11.3 Pathophysiology

Compartment syndrome results primarily from increased intracompartmental pressure. The mechanism involved in the development of increased pressure depends on the precipitating event.

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Two distinct types of compartment syndromes have been recognized. The first type is associated with trauma to the affected compartment, as seen in fractures and muscle injuries. The second type, called exertional compartment syndrome, is associated with repetitive loading or microtrauma related to physical activity. Thus, compartment syndrome can be acute or chronic in nature [1–3]. Tissue perfusion is proportional to the difference between the capillary perfusion pressure (CPP) and the interstitial fluid pressure, given by the following formula

$$\mathrm{LBF} = (\mathrm{PA} - \mathrm{PV}) / \mathrm{R},$$

where LBF is local blood flow, PV is local venous pressure, PA is local arterial pressure, and R is local resistance. Normal myocyte metabolism requires a 5–7 mm Hg oxygen tension that can readily be obtained with a CPP of 25 mm Hg and an interstitial tissue pressure of 4–6 mm Hg. The rising intracompartmental pressure causes the venous pressure to rise and the capillaries to collapse. This activates histamine-like substances that increase vascular permeability and also increase sludging in the capillaries. Reperfusion activates neutrophils and the production of free oxygen radicals, producing a simultaneous double hit injury that causes damage and dysfunction of cellular membranes and further acceleration of intracellular and extracellular edema. Nerve conduction decreases and the switch to anaerobic metabolism occurs. Myoglobin release occurs and then progresses to renal failure, contributing to loss of limb and life [4, 5].

When intracompartmental pressure rises above 30 mm Hg, fasciotomy is advocated. Delta p is a

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measure of perfusion pressure (diastolic pressure-intracompartmental pressure). There is an urgent need for fasciotomy when the level is 30 mm Hg.

11.4 Diagnosis

Six main symptoms of compartment syndrome exist (the 6 Ps): pain, paresthesia, paresis, pain with stretch, pulse examination, and pink skin color. These signs can be elicited only in the fully conscious patient. Early diagnosis is difficult in patients with central nervous system compromise, in the very young and the very old patients, and in patients with substance abuse. To distinguish between ischemic pain and pain caused by fracture, contusion, or muscle injury can sometimes be difficult. The presence of distal pulses never excludes compartment syndrome.

The deep peroneal nerve lies in the anterior compartment in the leg with its four compartments (anterior, lateral, deep posterior, and superficial posterior). Its sensory territory is confined to the web space between the first and the second toes and it subserves active dorsiflexion of the toes. The superficial peroneal nerve runs through the lateral compartment and supplies sensation to the dorsum of the foot, except to the first web space. The posterior tibial nerve lies in the deep posterior compartment, providing sensation to the plantar surface of the foot, its motor function being flexion of the toes. The superficial posterior compartment can be examined by testing the sural nerve sensation along the lateral border of the foot [3–6].

11.4.1 Chronic Exertional Compartment Syndrome (CECS)

CECS is another subset of compartment syndrome that has been described as a reversible muscle ischemia in an osteofascial compartment secondary to muscular volume increase during exercise. CECS has been defined as preexercise intracompartmental pressures of 15 mm Hg, followed by a 1-min posterxercise pressure reading of greater than 30 mm Hg, and a 5-min postexercise pressure reading greater than 20 mm Hg. These findings along with clinical symptoms lead to the diagnosis.

11.4.2 Laboratory Parameters

Seriously elevated levels of creatinine phosphokinase can indicate severe muscle damage or ischemia. In the absence of clinical signs, it may indicate an unsuspected compartment syndrome. For early diagnosis, it is clearly not helpful.

11.4.3 Compartment Pressure

Measuring the compartment pressure should only be undertaken when the clinical signs are unclear and only in patients whose consciousness level is impaired. A needle technique and a catheter technique are possible. The catheter systems provide a continuous pressure recording for up to 24 h.

11.5 Treatment

If compartment syndrome is suspected, all circumferential dressings should be removed and normal blood pressure should be achieved by dealing with any cause of hypotension. The extremity should not be elevated because that reduces the already impaired blood flow. Supplementary oxygen to improve tissue oxygenation is helpful [2, 7, 8].

11.5.1 Upper Arm

Decompression of the anterior and posterior compartment on the upper arm is performed either by a lateral or, in case of vascular injury, a medial approach.

11.5.2 Forearm

The volar compartment is decompressed by a volar-ulnar incision. The lacertus fibrosus must be incised. The superficial and deep flexor compartments must be decompressed. The transverse carpal ligament must be

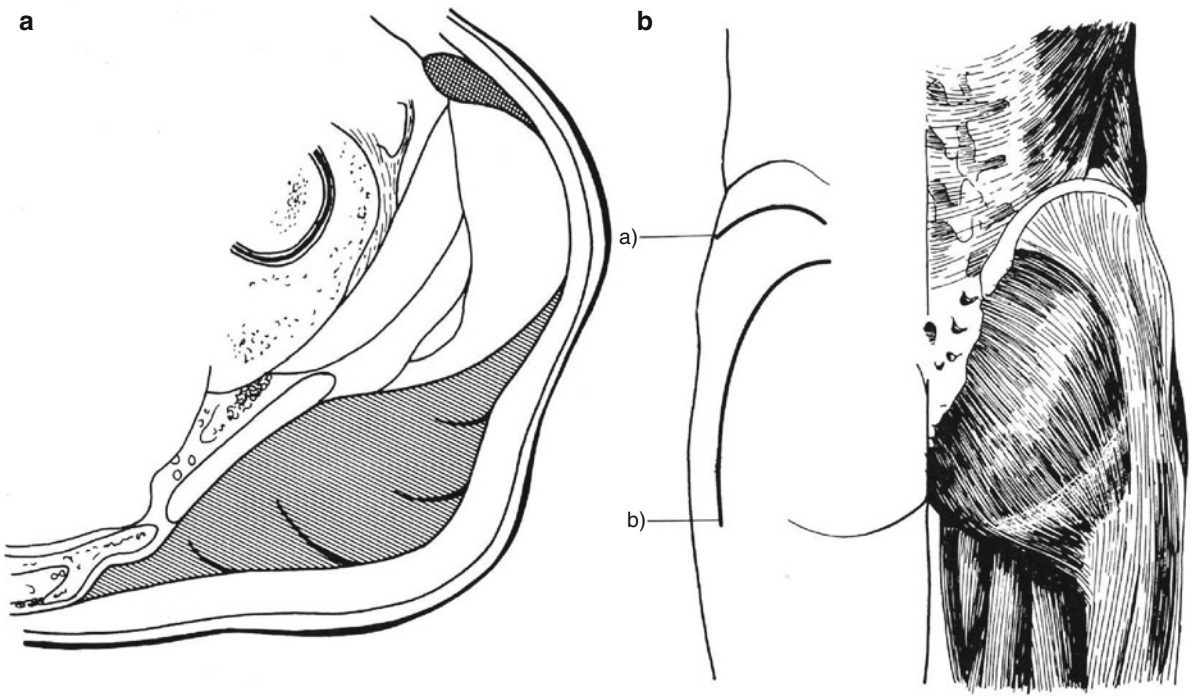

Fig. 11.1 Compartment of the gluteal region. (**a**) Transverse section through the gluteal region showing the compartments of tensor fasciae latae (*darkly shaded*), gluteus medius and minimus (*unshaded*), and gluteus maximus (*lightly shaded*). (**b**) Skin incision for decompressing the gluteal muscles. *a* Distal and parallel to the iliac crest. *b* Posterior approach to the hip joint

divided. The extensor compartment is decompressed by an incision from the dorsal side.

11.5.3 Hand Compartment

For decompression of the interosseous compartments, a dorsal in-line incision or an s-shaped incision over the second and fourth metacarpals is recommended. Thenar and hypothenar compartments are decompressed by a volar approach. Carpal tunnel and retinaculum are released. Extra care should be taken with the motor branch of the median nerve.

11.5.4 Gluteal Compartment

The approach is in line with the posterior approach to the hip joint. In addition to the fasciotomy of the gluteal maximus compartment, decompression of the gluteus medius and minimus compartment is essential (Fig. 11.1).

11.5.5 Thigh Compartment Syndrome

The surgical approach for thigh fasciotomy depends on the muscle groups involved [1]. However, Matsen noted that all muscle compartments of the involved limb must be relieved at fasciotomy to eliminate the risk of subsequent ischemic changes. A lateral incision is recommended to decompress the three compartments (flexor, extensor, and adductor).

11.5.6 Lower Leg

Decompression can be performed either by a single lateral incision or by combined anterolateral and posteromedial incisions. A double incision can

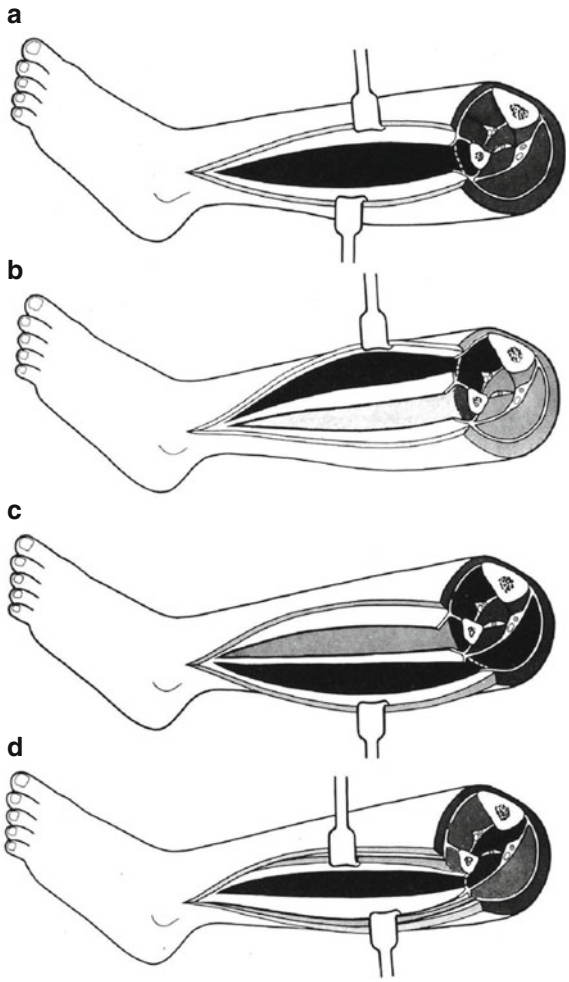

Fig. 11.2 Four-compartment parafibular decompression according to Matsen [1]. (**a**) The lateral compartment is opened at the level of the skin incision. (**b**) The anterior compartment is reached by retracting the anterior skin. (**c**) The superficial posterior compartment is opened by retracting the posterior skin. (**d**) The deep posterior compartment is reached by retracting the peroneal muscles anteriorly and the triceps surae posteriorly

reduce soft-tissue support for the fracture. The parafibular incision must extend the entire length of the lower leg. The intramuscular septum between the lateral and superficial posterior compartment should be identified and should be split longitudinally. Care must be taken not to injure the common and superficial peroneal nerves. The skin is dissected anteriorly and the anterior compartment opened. After retracting the peroneal muscles anteriorly, the fascia of the deep posterior compartment becomes visible and must be split along the entire length (Figs. 11.2, 11.3, and 11.4).

11.5.7 Foot

11.5.7.1 Dorsal Approach

On the assumption that the interosseous compartments are the most affected compartments, Mubarak and Owen recommended a dorsal dermatofasciotomy [9]. The approach can be modified to two dorsal incisions over the second and fourth metatarsals .This approach allows direct access to all compartments and provides exposure for open reduction and internal fixation of Chopart or Lisfranc fracture dislocations and tarsometatarsal fractures.

11.5.7.2 Medial Plantar Approach

The necessity for calcaneal compartment decompression requires a medial plantar approach in combination with the dorsal approach to decompress all foot compartments. The medial incision begins at the origin of the abductor hallucis (approximately 3 cm above the plantar surface and 4 cm from the posterior aspect of the heel) and is extended parallel to the plantar surface for 6 cm. Untreated compartment syndrome with ischemia of the lower leg or foot can lead to muscle contractures resulting in deformity and functional impairment. Additionally, nerve damage can cause weakness or paralysis of the four affected muscles and a dysfunctional painful extremity.

11.6 Prognosis

The outcome depends on both the diagnosis and the time from injury to intervention. Complete recovery can be reached if fasciotomy is performed within 6 h.

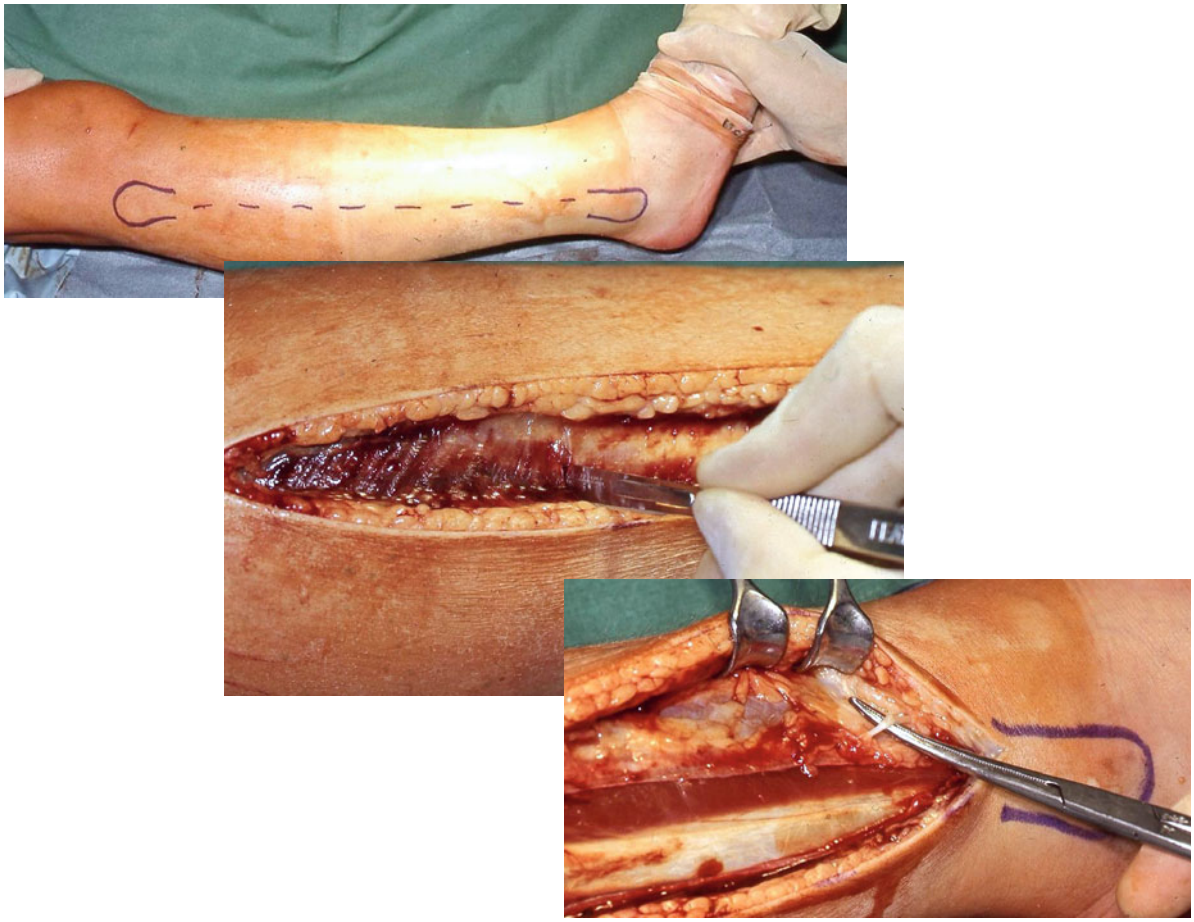

Fig. 11.3 After decompression of the lateral compartment the superficial peroneal nerve is identified. Thereafter the anterior compartment is decompressed

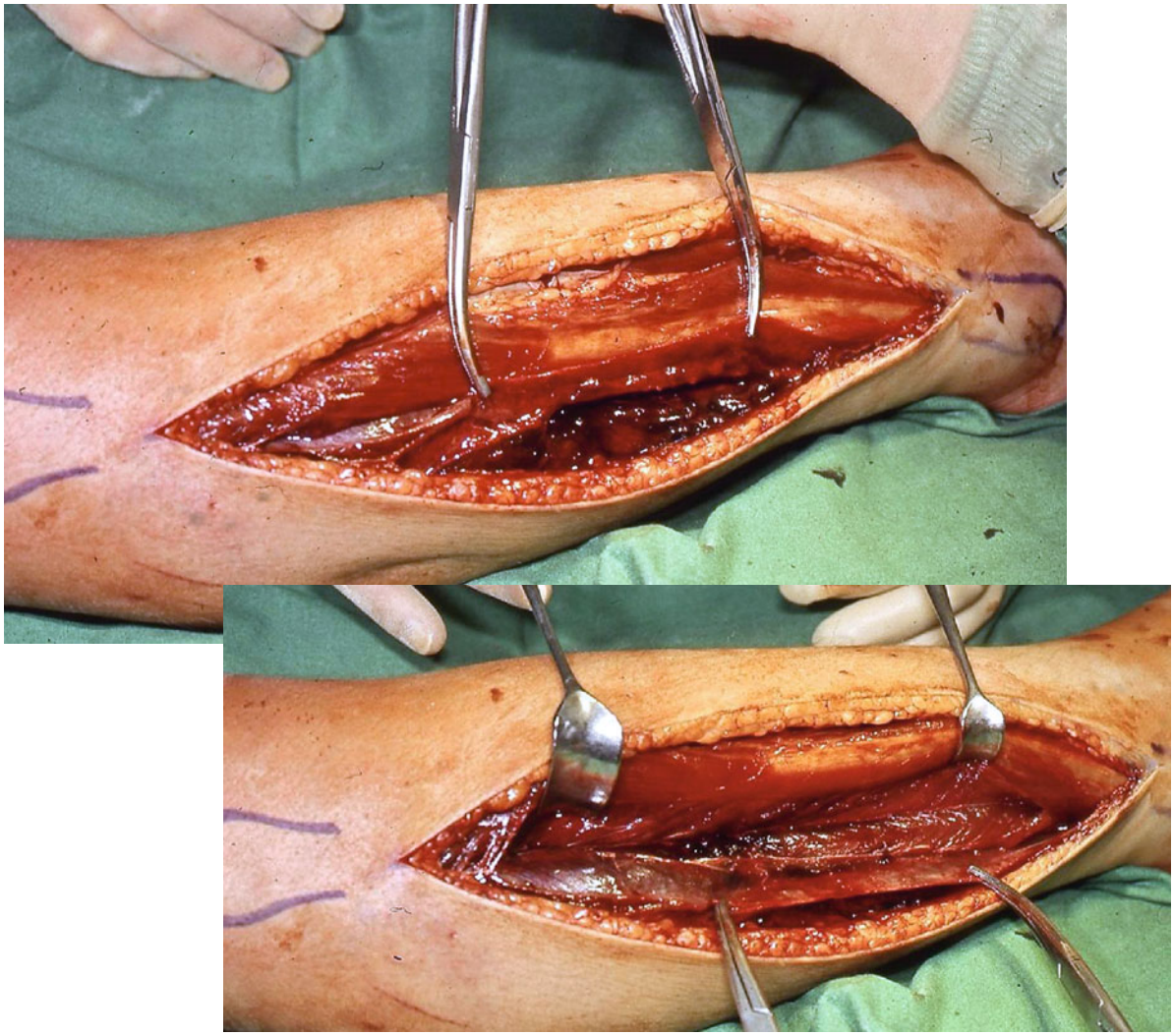

Fig. 11.4 Fasciotomy of the superficial and deep posterior compartment after retraction of the peroneal muscles (*below*)

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Plastic Surgery in Trauma

12

Heiko Sorg and Peter Maria Vogt

12.1 Interdisciplinary Collaboration

The most interesting part of plastic surgery, of all its subcategories, is the correction or restoration of body form and function. For this, plastic surgery is based on myriad different techniques that are uniquely associated with this area of expertise but originate from other medical specialties too. Because plastic and reconstructive surgery is one of the most interdisciplinary medical specialties, it makes it necessary for the reconstructive surgeon to keep up to date with new techniques as well as refine and critically appraise the currently available methods. The restoration of complex soft-tissue injuries combined with closed or open fractures resulting from severe trauma poses a significant clinical challenge. These injuries often are associated with significant clinical complications including wound infection, loss of soft tissue, compartment syndrome, nonunion fractures, pain, stiffness, protracted course of treatment, joint contracture, osteomyelitis, chronic pain syndromes, and amputation of the involved extremity. A solid and cooperative team approach is indispensable to obtain initial tissue integrity as well as the respective organ function of the patient with a focus on the complexity of the respective injury, complications that may arise, and the diversity of treatment options.

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12.2 Ladder of Reconstruction: Reconstructive Clockwork

The reconstruction methods of traumatic soft-tissue injuries vary from skin grafts to free, vascularized tissue transfer (Table 12.1). The reconstructive surgeon should be familiar with each of these techniques; however, a truly skilled surgeon should know when and where to apply the best treatment option for a successful outcome. The concept of the reconstructive ladder (Table 12.1), introduced by Mathes and Nahai in 1982 [1], and the reconstructive elevator by Gottlieb and Krieger [2], address the treatment of tissue defects, first by primary or secondary closure, followed by split-thickness skin grafting, regional or local pedicled flaps, tissue expansion, and finally free tissue transfer. In 2010, Knobloch and Vogt [3] introduced reconstructive clockwork (Fig. 12.1) to cope with the tremendous achievements in this sector in the past several years. The clockwork considers potential new techniques such as tissue engineering, robotics, and composite tissue allotransplantation (CTA) and thus proposes a simultaneous rather than consecutive use of the respective techniques.

Table 12.1 Options for reconstruction of soft-tissue following trauma

Healing by secondary intention
Primary closure
Skin grafting
Local flaps
Distant pedicled flaps
Tissue expansion
Free tissue transfer

H.-J. Oestern et al. (eds.), *General Trauma Care and Related Aspects*, European Manual of Medicine,
DOI 10.1007/978-3-540-88124-7_12,

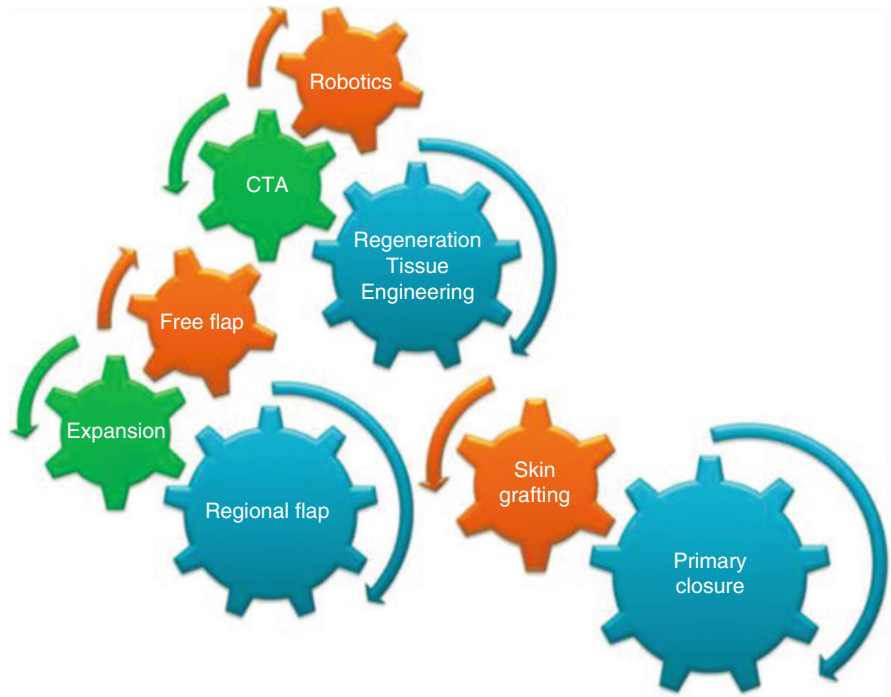

Fig. 12.1 Reconstructive clockwork as a refinement of the reconstructive ladder. *CTA* composite tissue allotransplantation (From Knobloch and Vogt [3])

12.3 Zone of Injury and Reconstructive Units

Mangled limbs resulting from high-velocity injuries develop a zone of soft-tissue injury that is greater than the visible wound or might increase dramatically within the first hours after trauma [4, 5]. The direct trauma contact area is characterized by a zone of necrosis with an adjacent zone of stasis surrounded by a hyperemic region. Marginally viable soft tissue during the initial trauma might die or will be replaced by fibrous scar tissue, particularly within large soft-tissue defects. The initial management, therefore, requires a fast and effective examination of the patient and should be supported by imaging techniques such as ultrasound, radiography, angiography, magnetic resonance imaging, or other specific imaging procedures. In addition, the early treatment of soft-tissue and osseous defects should prevent an increase of the soft-tissue damage, dead space, infection, nonunion, osteomyelitis, pain, malfunction, or complete tissue or limb loss.

To apply the best treatment method for the patient, the reconstructive surgeon should be familiar with the regional specific physiological vascularization. Furthermore, the type of skin incision that should be parallel to the Langer or resting tension lines, should be considered. Transverse running scars might functionally and aesthetically bother the patient. For reconstruction of soft-tissue defects it has been established that there is a difference between reconstructive and functional (skin) units with respect to local factors such as function, mechanical demands and aesthetics as well as the different possibilities of defect coverage. Additionally, the localization of the defect must be considered with regard to the locoregional demands as well as the respective treatment options. Palmar skin, for example, differs greatly in its mechanical capacity and sensibility from that of the back of the hand. Attention should also be paid to zones of low resistance where the bone is better located directly beneath the skin without any muscle padding.

12.3.1 Defect Description

Determining the severity of injury to the soft tissues is a central component of patient assessment and affects the management of surgical intervention. The reconstructive surgeon can choose from among a variety of techniques for optimal treatment; however, the surgeon needs to know the exact description of the defect as well as distinct patient- and therapy-imminent criteria (Table 12.2). The defect can be differentiated as acute and chronic soft-tissue defects according to its

Table 12.2 Decision criteria for the coverage of tissue defects using plastic reconstructive techniques

Defect-associated factors	Patient-associated factors	Therapy-associated factors
Etiology	Acute patient condition	Goal of reconstruction
Localization	Age	Timing
Skin defect	Sex	Reconstruction method (Table 12.1)
Soft-tissue defect	Intelligence/compliance	Sequence of reconstruction
Soft-tissue and osseous defect	Job	
Character of the wound	Social background	
	Other diseases	
	Patient wishes	

Table 12.3 The Oestern and Tscherne classification for soft tissue in closed and open fractures

Grade	Closed fractures	Open fractures
0	Minimal soft-tissue damage Indirect injury to limb (torsion) Simple fracture pattern	
I	Superficial abrasion or contusion Mild fracture pattern	Small puncture wound without skin contusion Negligible bacterial contamination Low-energy fracture pattern
II	Deep abrasion Skin or muscle contusion Severe fracture pattern Direct trauma to limb	Minor skin and soft-tissue contusions Moderate contamination Variable fracture patterns
III	Extensive skin contusion or crush injury Severe damage to underlying muscle Compartment syndrome Subcutaneous avulsion	Heavy contamination Extensive soft-tissue damage Associated arterial or neural injuries
IV		Incomplete or complete amputations

etiology. Special forms are the combined soft and osseous tissue defect and the soft-tissue defect resulting from a multiple trauma injury. Furthermore, the surgeon must verify whether a tissue dehiscence is the result of tissue elasticity or edema, or whether it is true soft-tissue loss. To rapidly define the extent of the tissue damage, the defect can be classified as type a (defect reaching the fascia), type b (mixed skin-muscle and other soft tissue defects), and type c (combination of soft-tissue and bony defect). A more detailed determination of the soft-tissue injury in combination with closed or open fractures can be obtained using the classification of Tscherne and Oestern, grouped into four categories according to severity (Table 12.3; [6]).

12.3.2 Timing

The proper timing and adequate planning of wound closure in soft-tissue traumas helps to limit further soft-tissue injury and facilitates its rapid recovery. Therefore, the surgeon should also have clear-sighted vision and not pass up a chance for other treatment possibilities if complications arise. The response of soft tissue to injury involves microvascular and inflammatory processes that produce localized tissue hypoxia and acidosis. Incisions placed through such compromised tissue, particularly in blunt soft-tissue injuries, can lead to wound breakdown and deep infection. Therefore, recognizing the signs of soft-tissue injury is the basis for successful management [7].

In any soft-tissue injury, especially of the limbs, an initial radical débridement of damaged and necrotic tissues is necessary within the first 6 h after trauma. The débridement can also be performed in scheduled second- or third look surgeries after 48–72 h. On the one hand, surgical débridement supports the phagocytic activity of the macrophages and reduces the risk of hypoxia and infection within the inflammatory

phase of wound healing [8]. On the other hand, it helps to clearly evaluate the extent of injury for the subsequent treatment regimen. The width of the débridement might sometimes be hard to accept by the operating surgeon because of additional tissue loss, but it is necessary to prevent the above-mentioned complications (i.e., zone of injury).

Appropriate timing for soft-tissue reconstruction and wound closure is a matter of controversy. The recommendation of Godina clearly reveals the advantage of aggressive débridement and closure of the wound with vascularized tissue within 72 h. Through adherence to this timeframe, severe complications can be decreased significantly [9]. A special form of a conservative treatment regimen in local wound support can also be obtained from vacuum assisted closure. Because of the optimization of the wound milieu via continuous wound cleaning, spontaneous regeneration processes will be accelerated and definitive wound closure can be reached significantly faster. Furthermore, the flap reconstruction can also be performed beyond the quoted critical time interval of 72 h with results similar to those of immediate reconstruction [10].

12.3.3 Special Co-injuries

12.3.3.1 Bone Injury

A stable osseous condition is an indispensable prerequisite for successful soft-tissue coverage [11]. For that reason, fractures and bone dislocations must be stabilized, even if only provisionally to restore the essential mechanical stability, to prevent further soft-tissue injury and to limit perfusion problems (Figs. 12.2, 12.3, 12.4, and 12.10). In unclear or severe cases of soft-tissue injury combined with fractures, it has proved valuable to proceed stepwise for definite osteosynthesis. First, on the day of injury, the fracture is adjusted by external fixation with regard to the applied reconstruction techniques, which may cover the defect. Internal fixation should be avoided; however, when there is need for large soft-tissue reconstruction, recent studies have not shown differences in internal versus external fixation [12]. Time and technique of the definite fracture treatment depend on the extent of the soft-tissue injury after demarcation, the extent of the bone defect, the infection, and the defect localization.

12.3.3.2 Tendon Injury

Tendon injuries should initially be treated by primary tendon suture. In case of severe substance defects it is important for the tendon to slide freely. If there is adequate skin coverage, a primary suture with tendon or fascia transplants can be performed. Otherwise, the tendon reconstruction can be performed in a two-step operation with an initial implantation of a silicon bar with definite reconstruction after full wound coverage.

12.3.3.3 Nerve Injury

In the event of a combination of skin and nerve injury with no mass destruction, primarily adapting of the nerve endings should be initiated. Alternatively, the nerve must be reconstructed with nerve transplants from the sural nerve or from the amputated limb. If there is a combination of tendon and nerve injury, the tendon should be reconstructed first, as tendons must be treated with immediate dynamic training, while nerve reconstructions can be postponed for 6–8 weeks.

12.3.3.4 Vessel Injury

Severe injuries are frequently associated with vessel injuries that result in perfusion problems of the supplying area. If not obviously visible, pulsation of vessels proximal and distal to the zone of injury, temperature, capillary refill, and color should be checked and can be completed by Doppler flow assessment. In order to restore the perfusion, vessels should be adapted as quickly as possible to reduce ischemia time as well as reperfusion injury, development of a compartment syndrome, and the possibility of a final amputation of the limb. In the case of impossible primary adaptation, autologous venous transplants should be used and can be taken from the forearm, the lower leg, or from the amputated limb. The reconstruction of vessels needs immobilization for 2–4 weeks and the patient should receive sufficient thrombosis prophylaxis.

12.3.4 Wound Coverage Techniques and Possibilities of Defect Closure

For the reconstruction of the skin and soft tissue, in most cases the surgeon can take a decision based on many options as summarized in Table 12.1. The use of split-thickness skin grafts is only limited to areas with a good vascular bed such as well-perfused wound

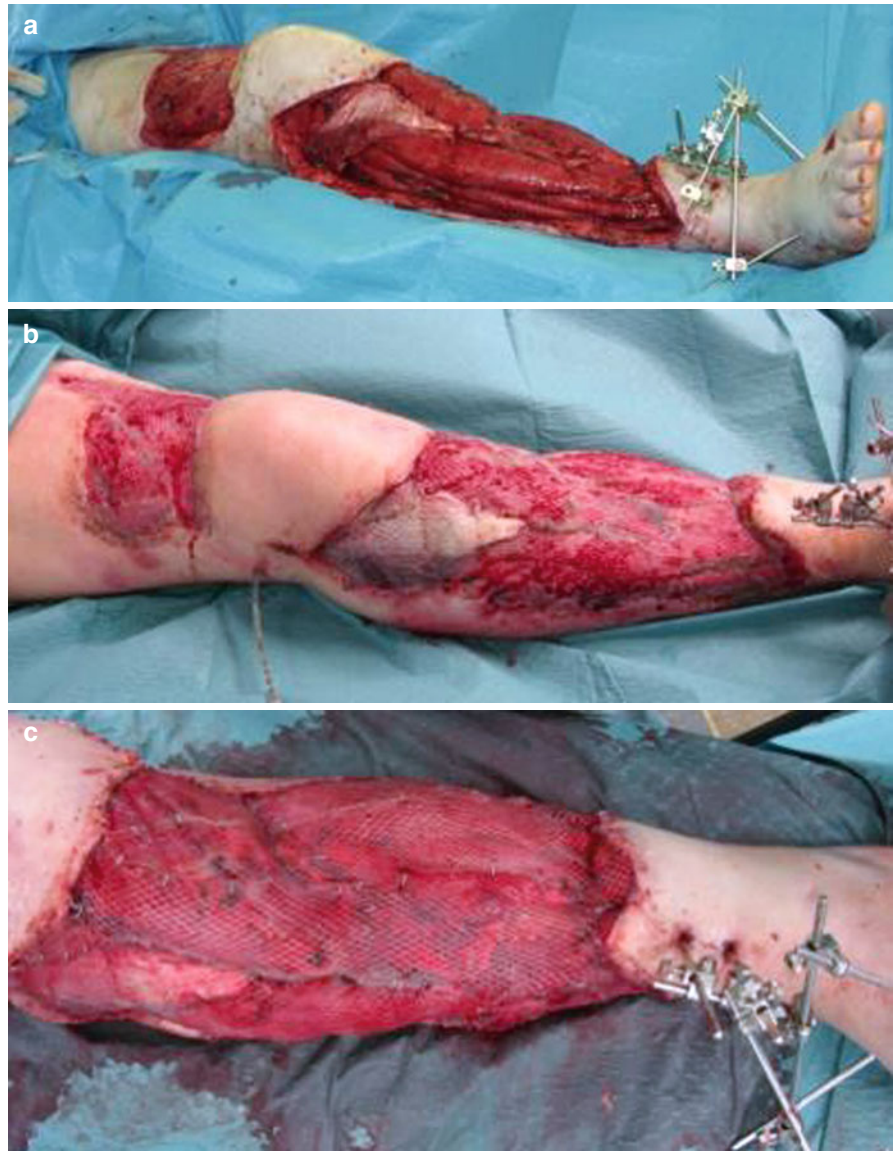

Fig. 12.2 Ankle tibial fracture with a combined severe soft-tissue trauma with a complete loss of skin in the ventral lower leg and proximal knee region (**a**). The entire defect can be covered by meshed split thickness skin grafts because of the vital muscular wound bed (**b**, **c**)

granulation or muscle tissue (Figs. 12.2, 12.5, and 12.6). Areas with exposed bone, cartilage, tendon, or neurovascular bundles forbid skin grafting. For local random pattern flaps it must be ensured that the ratio of length to width does not exceed 1:1.5, because of the perfusion conditions particularly at the lower limb. Furthermore, it is of importance for flap planning that defects in convex areas are larger than expected. A discussion of all the currently available flaps, including their anatomies and surgical preparations, is well beyond the scope of this chapter and for this reason we will focus on the commonly applied options and techniques for the reconstruction of skin and soft-tissue defects in the upper and lower limbs. The aforementioned alternatives such as tissue engineering and CTA are currently still under intensive investigation and will not be discussed in detail here, but might offer many new potential possibilities for trauma and reconstructive surgery.

Proximally pedicled lateral arm island flaps can easily cover medium-sized defects in the proximal and frontal region of the shoulder. For defects in the dorsal shoulder region, the pedicled scapula or parascapula flap is recommended, which can be rotated from 90° to 180°. Local fasciocutanenous flaps can be used in small defects in the upper arm region.

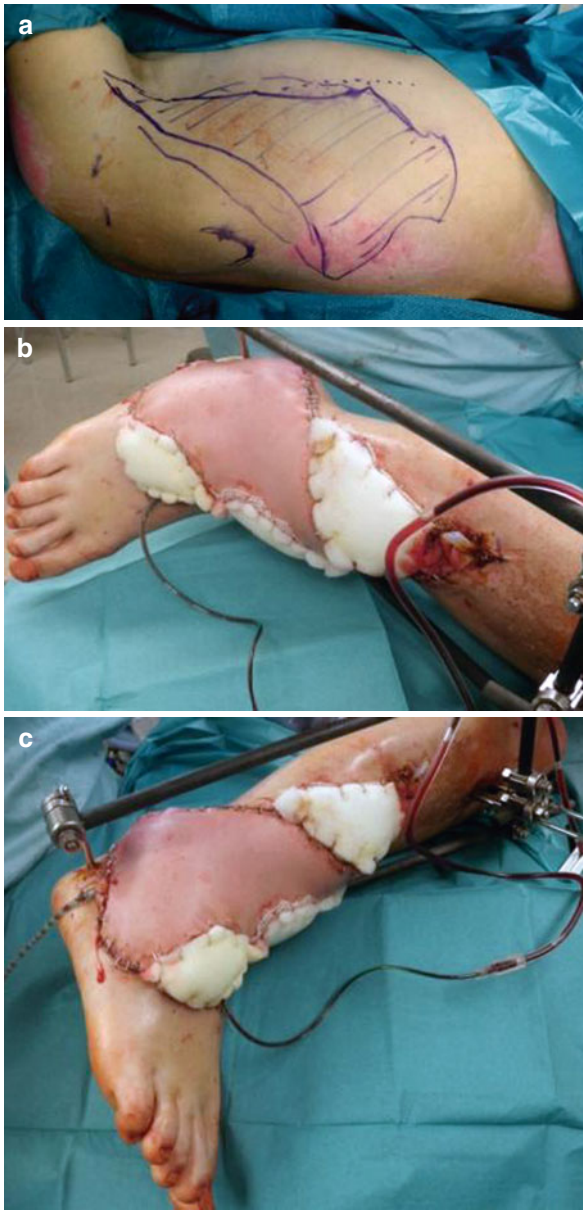

Fig. 12.3 A 35-year-old man suffered from a pilon tibiale and ankle fracture with a severe soft-tissue defect after a motorbike accident. The defect could only be covered with a free microvascular latissimus dorsi flap. (**a**) The flap design on the back is marked. (**b**, **c**) The postoperative result is demonstrated

The lateral, medial, or posterior upper arm flaps are available for larger defects but should be used cautiously in young patients because of large donor site defects developing. Furthermore, the flaps of the subscapular artery basin can be used as a first-choice method. Through the use of a pedicled latissimus dorsi flap, a missing function of the triceps or biceps muscle might be reconstructed in a one-step operation. The dorsal and lateral areas of the elbow, as well as the distal third of the ulna, are zones of low resistance where primary closure can be successfully achieved only with good wound conditions, also via mobilization of the wound edges. Secondary wound healing cannot be recommended in this region as a result of long-term immobilization that is consecutively associated with long-term inability to work. Moreover, secondary wound healing might result in insufficient and unaesthetic scar formation requiring further surgical intervention. The first choice of treatment for defects of the dorsal elbow is the proximally pedicled radial artery flap [13]. Outside of these low resistance zones, split skin grafts can safely cover small wounds and might further be supported by allogenic skin substitutes (Alloderm®, Integra®, Matriderm®).

The indication for pedicled or free tissue transfer is given in the case of large soft-tissue defects with the exposure of periost free bone, denudated tendons, blood vessels, or nerves. Local flaps might cover small- to medium-sized defects in the cubital fossa. Alternatively, particularly in older patients, the radial recurrent artery flap might be a second choice for wound coverage; however, it is characterized by a large donor site defect.

The brachioradial muscle flap has become an established procedure for covering deep and narrow defects with the exposure of bone or an opened elbow joint allowing a rotation distance from the lateral part of the elbow joint to the olecranon. To avoid the sacrifice of the radial artery, this flap should be elevated and rotated at the proximal pedicle. The mid third of the lower arm is particularly efficient for split-thickness skin grafts because of its well-perfused muscular layer.

A posterior interosseus artery flap can cover defects of 4–6 cm in the distal two thirds of the lower arm. Larger defects need to be rectified using a radial artery flap or even free tissue transfer (Table 12.4).

In special circumstances, a pedicled abdominal wall flap might also be an alternative. Skin defects in the palmar hand/wrist are commonly associated with scar contractures or traumatic lesions (suicidal injuries). Some cases require revascularization or cushioning of the median nerve. For this purpose, the ulnodorsal flap (as described by Becker and Gilbert) or the pronator quadratus muscle flap are recommended [14].

Defects of the thigh can often been treated with local flaps from the surrounding tissue. In addition to

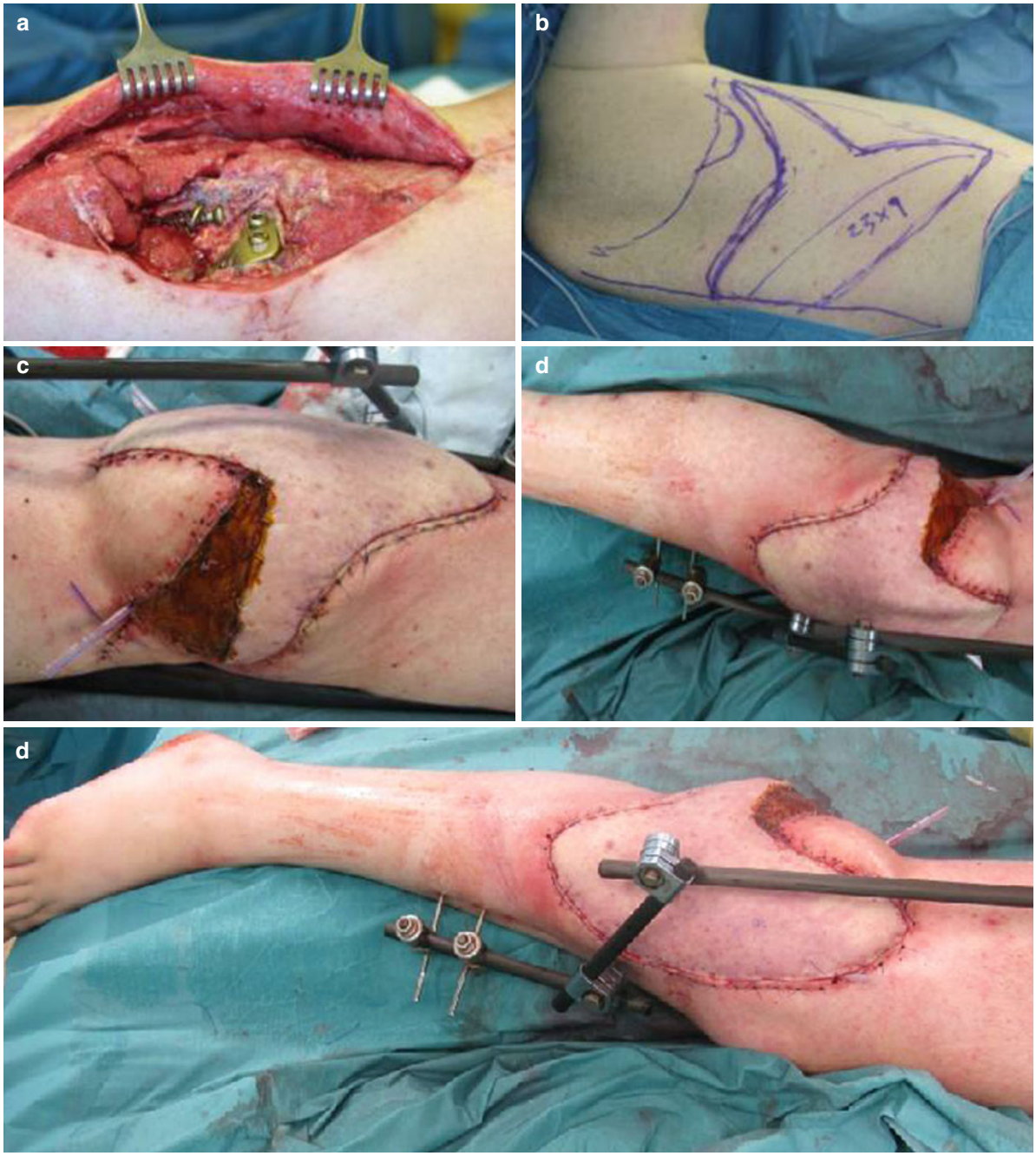

Fig. 12.4 After a shot gun injury in the knee area, this young man suffered a soft-tissue defect with exposed osteosynthetic material (**a**). (**b**) The flap design of a free latissimus dorsi flap is marked on the right back of the patient. (**c**–**e**) The respective postoperative results are shown. Marked with *asterisk* is a small area that could not be covered by the back skin and was then covered by a split-thickness skin graft

the above-described random pattern flaps, almost every muscle at the thigh can be used for a pedicled muscle flap, to some extent also with the respective skin area (Table 12.5).

Defect coverage at the proximal and lateral thigh region can be achieved using the tensor fascia lata flap. For defects in the proximal and ventral thigh, the rectus femoris flap is appropriate. A gracilis flap can be

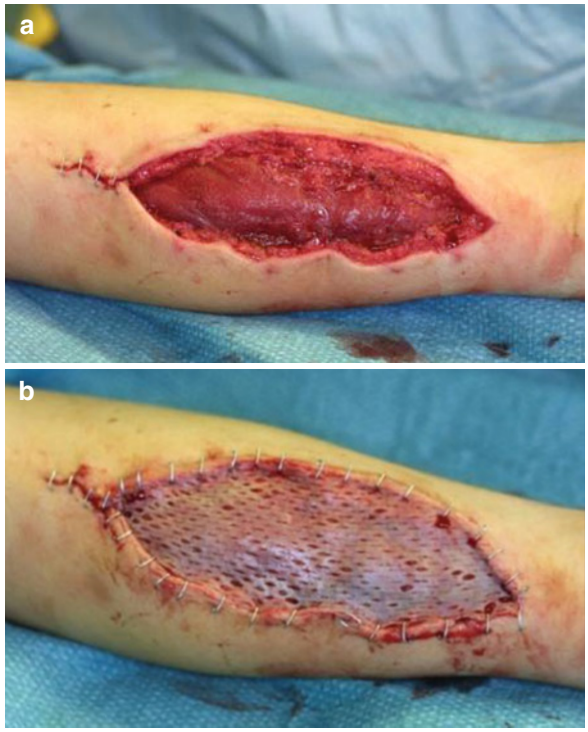

Fig. 12.5 Soft-tissue defect of the lower arm after a distal radius fracture. (**a**) After débridement, showing a well-prepared and vital wound bed, in order to transplant split thickness skin grafts (**b**)

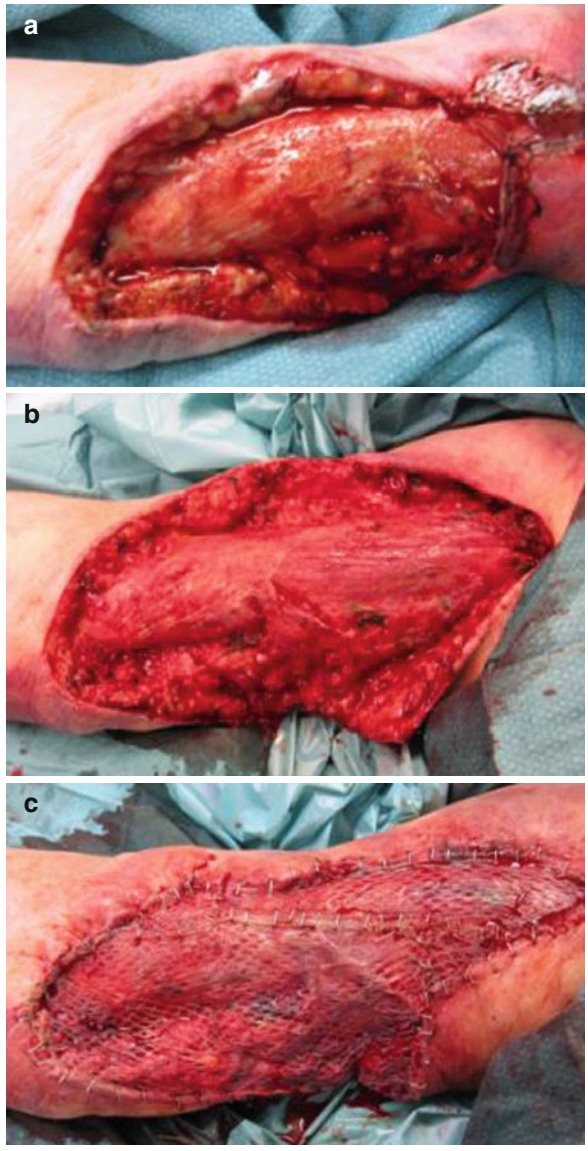

Fig. 12.6 (**a**) A severe soft-tissue defect of the upper arm after hematoma and skin necrosis resection in a 66-year-old woman after a car accident. (**b**) The defect after débridement, with vital musculature in order to cover the defect with meshed split-thickness skin grafts (**c**)

used in the inguinal region, whereas the biceps femoris muscle flap is used in dorsal thigh defects.

In the event that the above-mentioned techniques are impossible, defects in the proximal thigh and inguinal area can also be covered with a pedicled rectus abdominis muscle flap with a transverse or vertical skin part. A pedicled gastrocnemius flap can be transferred to cover the distal part of the thigh. Larger defects profit from free microvascular tissue transfer such as the reconstruction with the latissimus dorsi flap (Table 12.5).

Osseous femur defects can be reconstructed during a one-step free microvascular fibula transfer. The fibula is then transplanted as a spare bone transplant or as an osteofasciocutaneous flap pedicled at the fibular artery. For better stability, the fibula might also be adjusted in a doubled way into the defect [15, 16].

Split skin grafts are not recommended in the knee region because of the risk of the development of contractures. Fasciocutaneous or muscle flaps should be applied in the ventral and dorsal part of the knee (Table 12.5). A commonly used fasciocutaneous flap in the popliteal fossa is the proximally pedicled soleus or hemisoleus flap. Blood perfusion

Table 12.4 Various possibilities for covering skin and soft-tissue defects in the shoulder and arm region

Supraclavicular region	Lateral shoulder region	Axillar region	Upper arm region
Scapula-/parascapula flap	Proximally pedicled lateral upper arm flap	Small- to medium-sized defects: Limberg flap	Small defects: local (pedicled) flaps
Latissimus dorsi flap	Scapula-/parascapula flap	Posterior upper arm flap	Medium-sized defects: lateral or posterior upper arm flap
	Latissimus dorsi flap	Defects exceeding the axilla: latissimus dorsi flap	Large defects: latissimus dorsi flap
		Thoracodorsal artery perforator flap	Scapula/parascapula flap
		Scapula/parascapula flap	Free fibula transfer (osseous defects)

Table 12.5 Various possibilities for covering skin and soft-tissue defects in the thigh, knee, and lower leg region

Thigh region	Knee region	Lower leg region	Foot region
Tensor fascia lata flap (lateroventral thigh)	Gastrocnemius flap (Fig. 12.7)	Gastrocnemius flap	Soleus flap
Rectus femoris flap (proximal and ventral thigh)	Soleus flap	Soleus flap	Dorsalis pedis flap
Anterior lateral thigh flap	Vastus medialis flap	Posterior tibialis flap	Posterior tibialis flap
Biceps femoris flap (dorsal thigh)	Vastus lateralis flap	Peroneus brevis flap	Sural nerve flap (Fig. 12.9)
Gracilis flap (inguinal region and dorsal thigh)	Posterior tibialis flap	Dorsalis pedis flap	Lateral calcaneal flap (Fig. 12.10)
Rectus abdominis flap (proximal thigh)	Latissimus dorsi flap (Fig. 12.4)	Extensor digitorum longus flap	Latissimus dorsi flap
Gastrocnemius flap (distal thigh)	Scapula/parascapula flap	Sural nerve flap (Fig. 12.8)	
Latissimus dorsi flap		Latissimus dorsi flap (Fig. 12.3)	
Free fibula transfer (osseous defects)			

is ensured via the accompanying vessels of the sural nerve. The donor site of the flap must be covered by a split-thickness skin graft. As a standard muscle flap, the gastrocnemius flap is applied to cover defects in the proximal third of the lower leg as well as in the knee area (Fig. 12.7). Because of the larger operating distance and the wide rotation possibilities, the medial part of the gastrocnemius muscle is most frequently used.

It is recommended to use distally pedicled flaps in the distal third of the lower leg because the muscles in the proximally pedicled flaps might not fully reach the covering area and thus, lead to perfusion problems because the tensile strength is too high. Following the soleus flap [17], the distally pedicled peroneus brevis muscle flap is one of the safest procedures to perform in this area and can also be used for defect coverage in the Achilles tendon area [18]. Larger defects in the knee, lower leg, and the ankle joint region can be covered by using sural nerve flaps (Figs. 12.8 and 12.9). The sural nerve flap (Fig. 12.9) as well as a lateral calcaneal flap can cover respective defects in the heel area. According to the reconstructive ladder, the free microvascular tissue transfer is also an option in the event of good donor vessels in the lower leg and foot region (Table 12.5; Fig. 12.3).

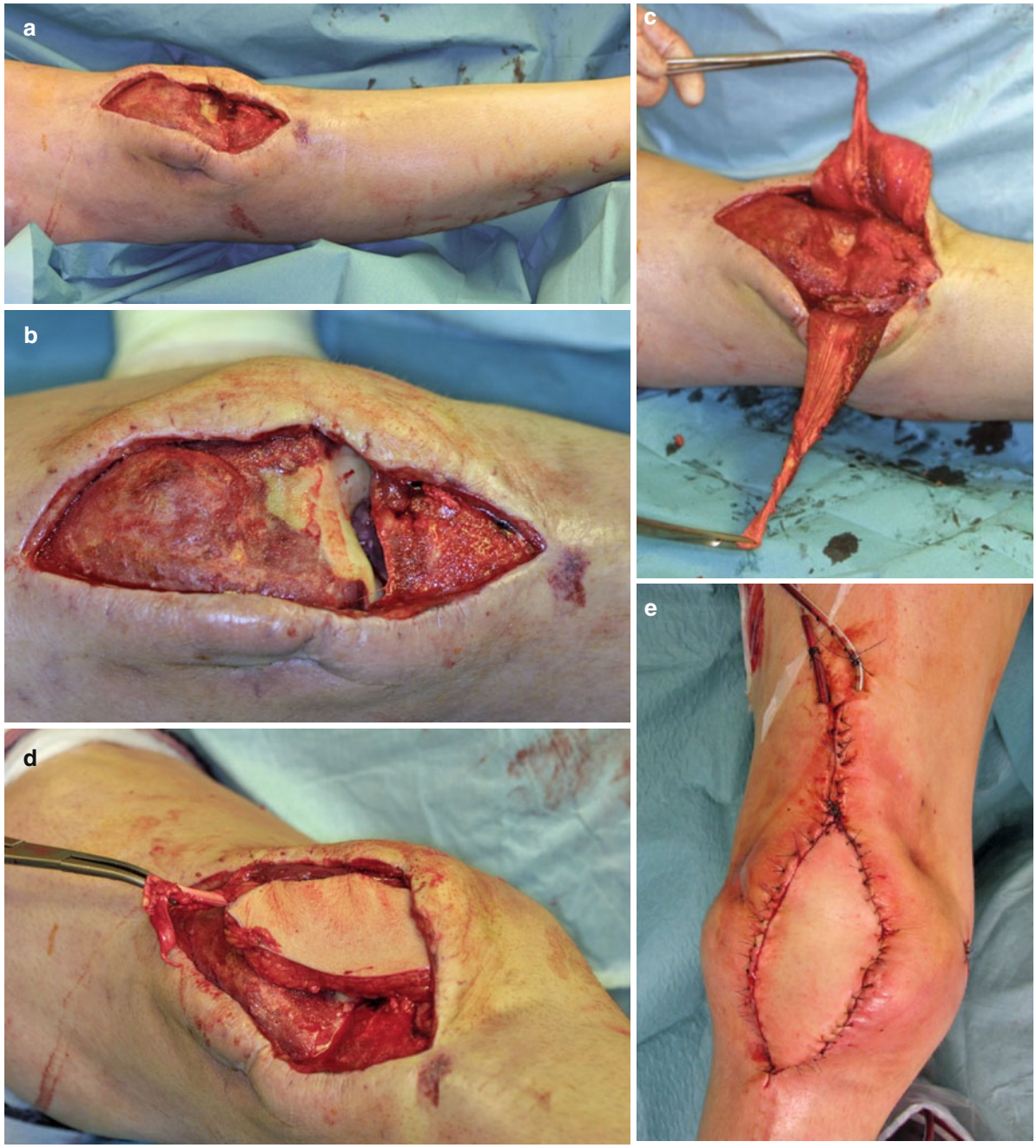

Fig. 12.7 (**a**, **b**) A 40-year-old man who suffered from a horse accident, with an approximately 15 × 5 cm defect in the patella region with an open knee joint. (**c**–**e**) The defect was covered with a bilateral gastrocnemius flap with skin

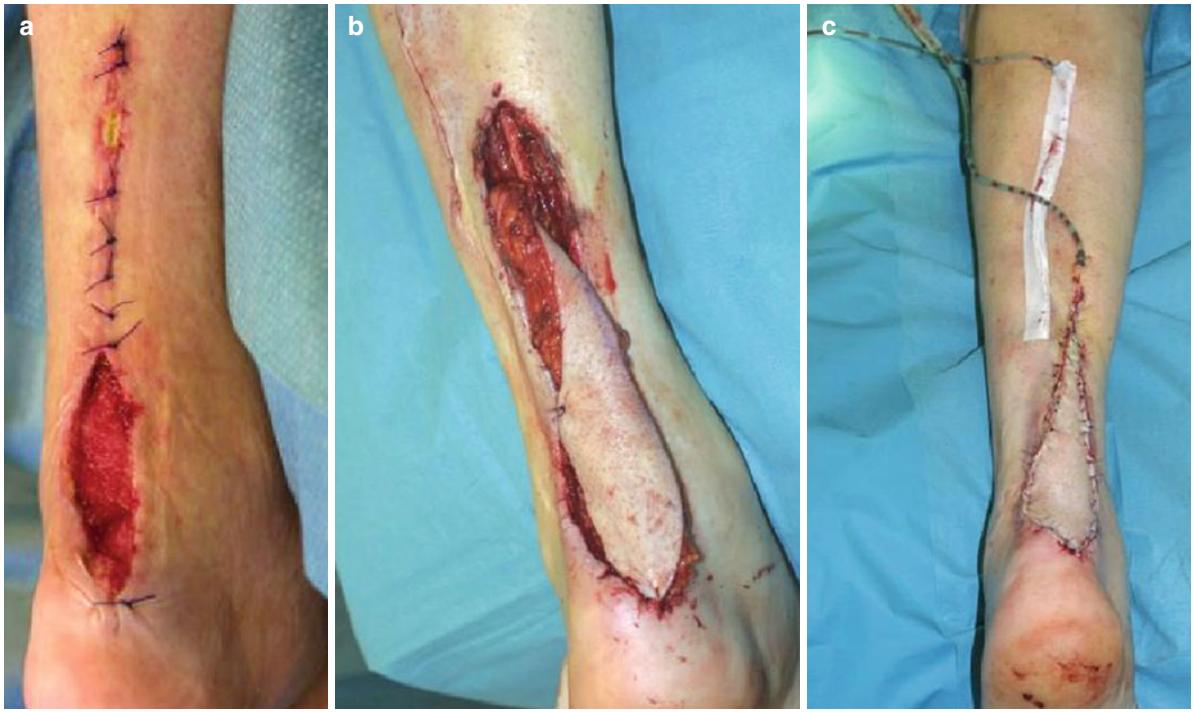

Fig. 12.8 (**a**) Soft-tissue defect in the Achilles region of a 48-year-old man after traumatic reconstruction of the Achilles tendon 2 weeks prior. (**b**, **c**) The defect was covered using a sural nerve flap

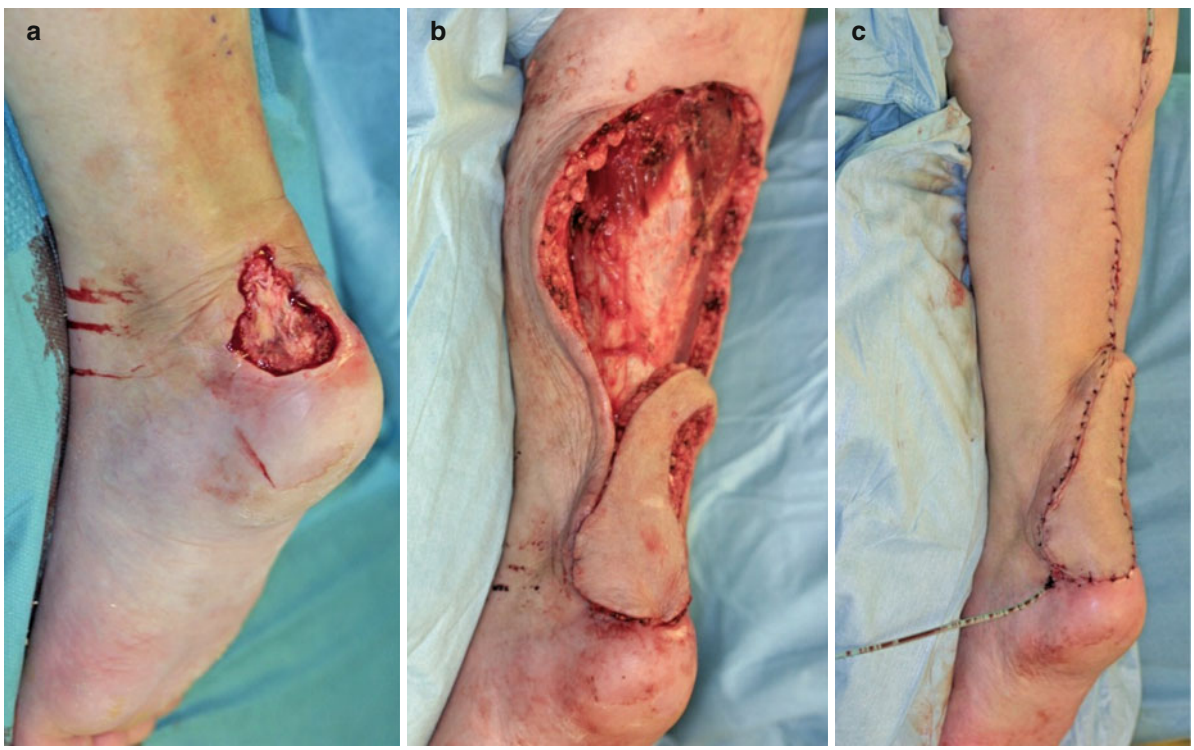

Fig. 12.9 (**a**) Soft-tissue defect of the heel in a 69-year-old woman who fell down on an icy street during winter using a sural nerve flap. (**b**, **c**) The defect was covered using a pedicled local flap

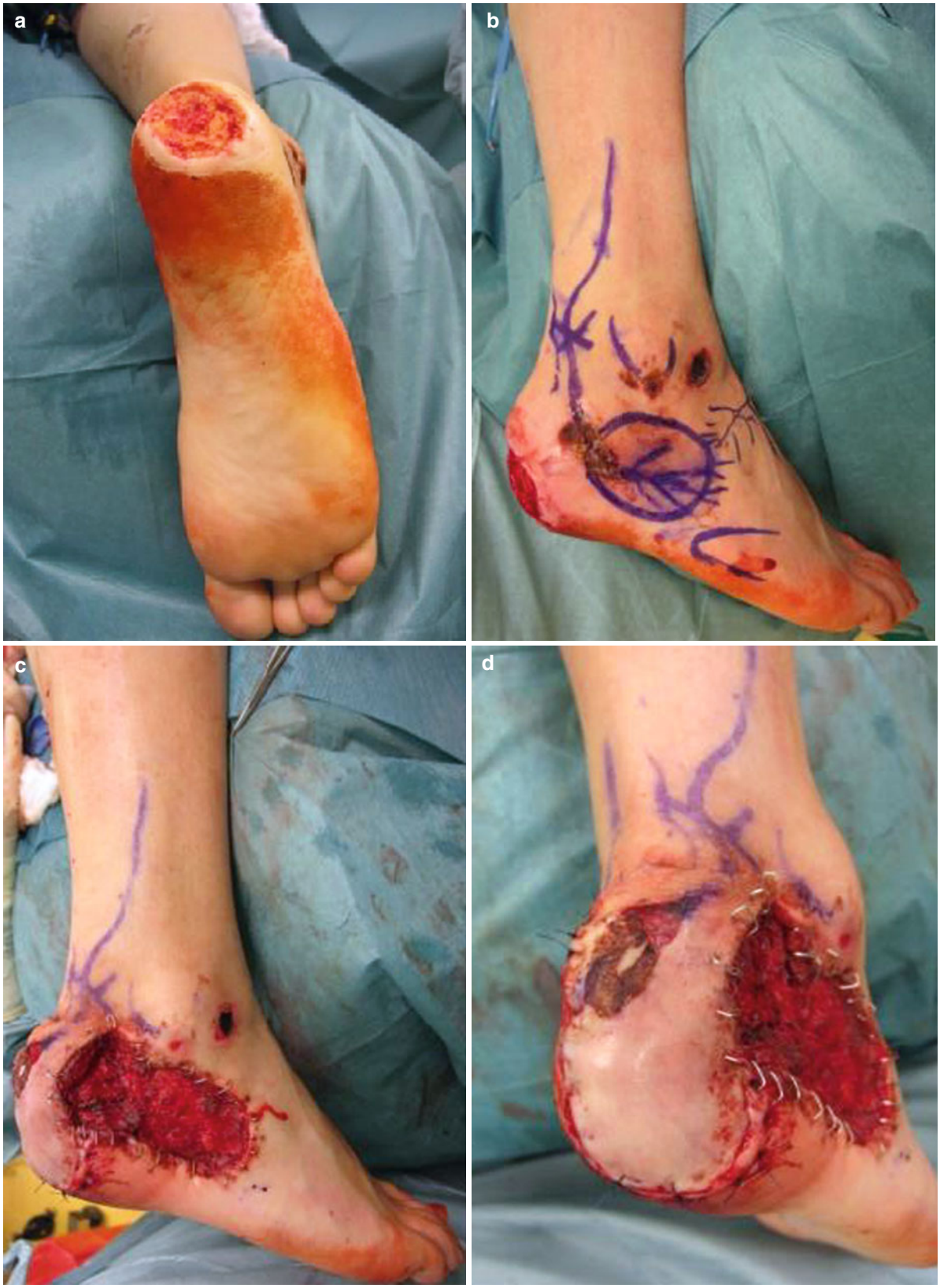

Fig. 12.10 (**a**) A 53-year-old man suffering from necrosis in the heel area following a severe car accident. (**b**) A lateral calcaneal flap was chosen to reconstruct and cover the defect. (**c**, **d**) The postoperative result with an additional split-thickness skin graft covering the host area

Conclusion

The treatment of complex soft-tissue injuries combined with severe closed or open fractures poses a clinical challenge for both orthopaedic and plastic surgeons. These injuries are often associated with significant clinical complications including wound infection, soft-tissue loss, compartment syndrome, non-union fractures, pain, stiffness, protracted course of treatment, joint contracture, osteomyelitis, chronic pain syndromes, and amputation of the respective extremity. For deciding on a treatment protocol, these complications as well as the correct timing of wound coverage, the adequate soft-tissue flap, the reasonable implant for primary osteosynthesis, the correct decision on limb salvage, and patient comorbidities should be considered. Moreover, there can be traumatic co-injuries that require a fast and solid reconstruction.

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Burn Injury

13

M.A. Altintas and P.M. Vogt

13.1 Introduction

Burns are devastating injuries to the skin and to the patient. The skin plays a key role in the regulation of temperature and fluid in the body and acts as a protective barrier against microorganisms. The anatomy of the skin can be divided into the *epidermis*, the outer layer of the skin; the *dermis*, comprising collagen-containing elastic fibers, nerves, blood vessels, sweat glands, and hair follicles; and the *subcutaneous tissue*, which contains fat and larger blood vessels and nerves. The severity of burns depends on the depth of destruction, location, and the involved body surface area. Inadequate treatment of burns can lead to increased visible (physical) and invisible (psychological) scars. Adequate and correct management of severe burns requires a skilled multidisciplinary approach that addresses all the challenges of burned patients. This chapter provides an overview of the most important aspects of burns.

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13.2 Causes of Burns

A burn is a type of injury to the skin caused by heat, chemicals, electricity, or radiation (i.e., sunburn). Scalding is a specific type of burning that is caused by hot fluids. Different causes can result in different effects on local microcirculation and histomorphology of burned tissue [1, 2]. Accordingly, superficial burn caused by ultraviolet radiation (sunburn) predominantly affects the deeper epidermal layers, whereas superficial burn induced by contact with heat leads to morphological alterations of superficial epidermal layers [2].

13.3 Epidemiology

According to the German Burn Association, in 2009 in Germany, about 1,900 patients had severe burns that warranted admittance into the intensive care unit for treatment in a specialized burn center. Of these, 1,312 (69.05 %) were male and 588 (30.95 %) were female. Most burns result from flame injuries (1,000 patients, 52.60 %). Burns resulting from scalds (487 patients, 25.60 %) are the next most common type, followed by explosion injuries (171 patients, 9.00 %). Contact burn occurred in 146 patients (7.70 %) and electrical trauma in 96 patients (5.00 %).

13.4 Burn Pathophysiology

Thermal overexposure can lead to destruction of the skin described as a burn wound of circumferential zones radiating from primarily burned tissues, as follows [3]:

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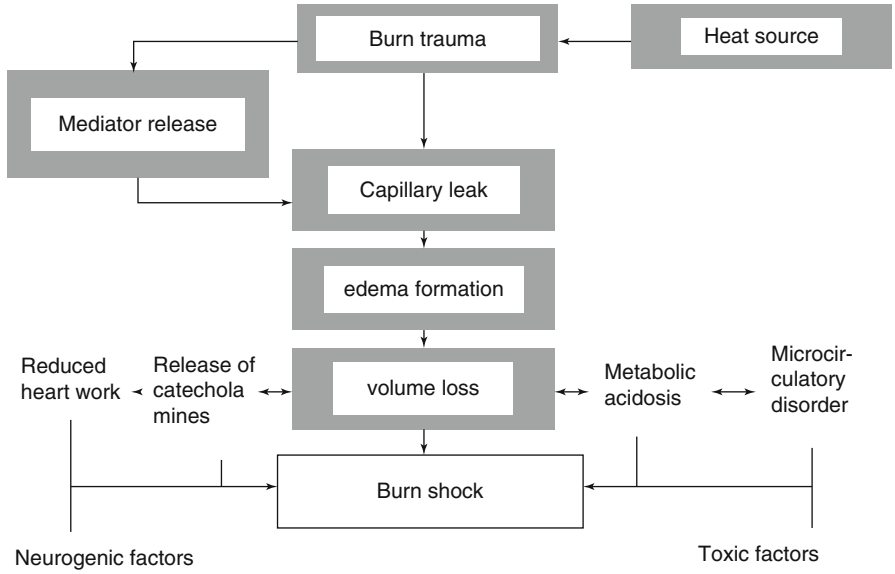


Fig. 13.1 Pathophysiology of burn shock

- *Zone of coagulation*—central area of the burn that has sustained the most intense contact with the thermal source; coagulation necrosis of the cells has occurred and the tissue is nonviable
- *Zone of ischemia or stasis*—tissues (both deep and peripheral) surrounding the coagulated zone; consists of potentially viable tissue; cells are ischemic because of clotting and vasoconstriction and die within 24–48 h after injury if not resuscitated properly
- *Zone of hyperemia*—peripheral tissues that undergo vasodilatory changes from neighboring inflammatory mediator release but are not injured thermally; tissues recover in 7–10 days if infection or profound shock does not develop

In cases of a severe burn, there is a local and systemic inflammatory response with appreciable loss of fluid, heat, electrolytes, and plasma proteins into the undamaged tissues. This is a result of mediator response of histamine, serotonin, prostaglandins, platelet products, complement components, and kinins leading to increased capillary permeability, extravascular osmotic activity, rapid edema formation, increased heart rate, and peripheral vascular resistance [4]. The continuous loss of intravascular fluid causes dehydration, increased haematocrit levels, and a rapid drop in plasma volume with decreased cardiac output, hypovolemia, and hypoperfusion. Burn shock develops if the fluid is not adequately restored. Additionally, the burn wound provides a vast area of entry for surface infection with a high risk of septic shock (Fig. 13.1).

13.5 Classifications of Burn Injuries

13.5.1 Burn Depth

Burns are classified by the depth of tissue affected. The depth of injury depends on the degree of temperature and duration of exposure to the offending source. The deeper the burn injury, the greater the number of skin layers that are damaged. Sweat glands and hair follicle roots are located in the deeper layers and will be destroyed with a deep burn. The burn depth is usually classified as superficial (first degree), superficial-partial and deep-partial thickness (second degree), and full-thickness (third degree). Oftentimes this classification is extended to a fourth degree burn.

Superficial burn is limited to the epidermis and causes erythema and edema without vesiculation. This type of burn is painful to touch, however, it will heal without scar formation.

Superficial partial-thickness burn involves the epidermis and papillary dermis. Blister formation is present. The wounds from this type of burn typically blanch with pressure; they are painful and will heal without scar formation.

Deep partial-thickness burn involves tissue destruction up to the reticular dermis. This type of burn

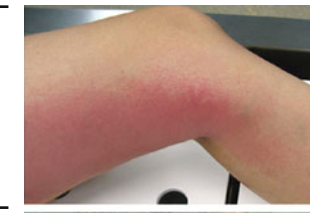
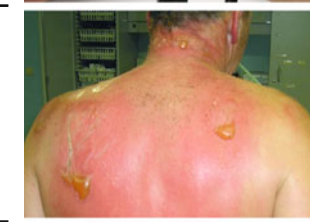
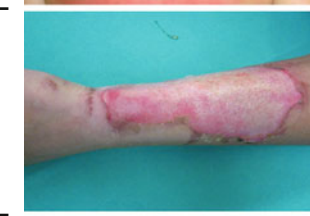
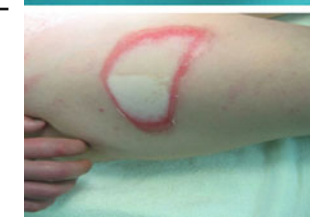
Nomenclature	Burn depth	Appearance	Healing	Example
Superficial-thickness burn	Epidermis	Erythema, minimal swelling, pain	7–14 days	
Superficial-partial-thickness burn	Papillar dermis	Wet, pink, blisters, moderate pain	2–4 weeks	
Deep-partial-thickness burn	Reticular dermis	Less wet, red, ± blisters, minimal pain	3–8 weeks with severe scar formation, need graft	
Full-thickness burn	Epidermis, Dermis, (Eschar formation)	Dry, white, insensate	Need graft	

Fig. 13.2 Characteristics of superficial thickness to full-thickness burns

appears poorly vascularized and is less painful. Healing of deep partial-thickness burns occurs with severe scarring.

Full-thickness burns involve destruction of the epidermis and all layers of the dermis. This type of burn appears waxy white in color, dry, leathery, and insensate because the skin nerve endings have been destroyed. Fourth degree burns extend deeply into the subcutaneous tissue and can involve the tendon, fascia, muscle, and bone. These areas can be charred black.

Figure 13.2 illustrates clinical examples and characteristics of the burn depth classification.

13.5.2 Burn Surface Area

Burns can also be classified in terms of total body surface area (TBSA). The Wallace "Rule of nines" is commonly used to determine the injured TBSA, although the measurement is adjusted for infants and children (Lund and Browder chart). The body is divided into anatomical regions that represent 9 % of the total body surface (Fig. 13.3). The outstretched palm and fingers equal 1 % of the TBSA ("Rule of palms"). Superficial burns should be excluded from the calculation.

13.5.3 Transfer Criteria to a Burn Center

In order to determine the need for referral to a specialized burn unit, the German Burn Association devised the following criteria:

http://www.verbrennungsmedizin.de/leitlinien_2.htm

- Burns involving specific anatomical zones (face, hands, axilla, feet, or perineum)

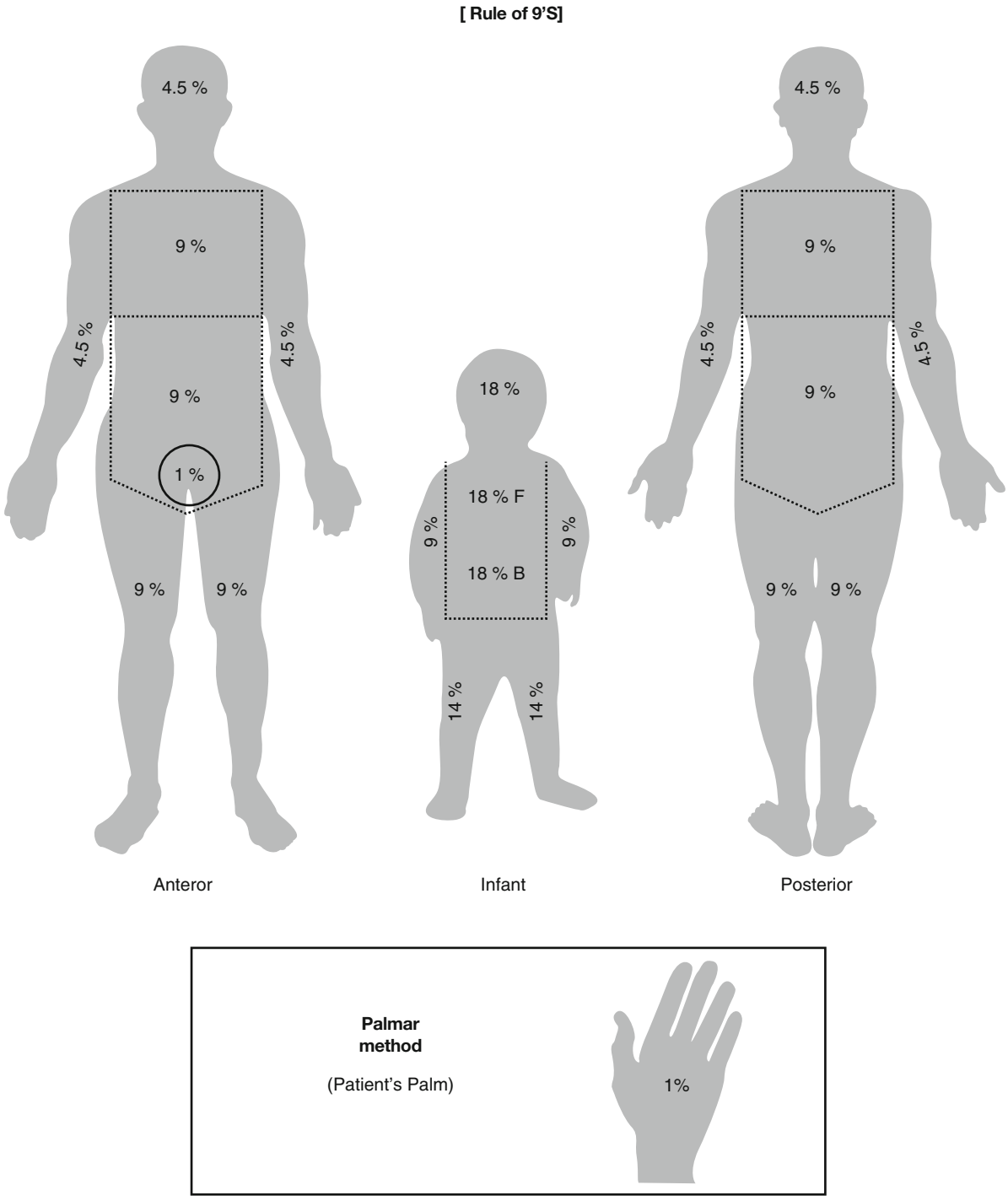


Fig. 13.3 Rules of nine to determine the body surface area

- Burns in infants (less than 8 years old) or the elderly (older than 60 years)
- Full-thickness burns over more than 10 % of the TBSA
- Partial-thickness burns over more than 15 % of the TBSA
- Circumferential burns to any extremity or complicated location
- Burns that cross major joints
- Burns associated with inhalational injury
- Burns associated with fractures or other trauma
- Electrical burns
- Additional pre-existing diseases

13.6 Management

Accurate estimation of burn wounds is essential in determining the type of first aid administered and the need for hospitalization. Burn treatment is in large part based on burn depth and the body surface area involved.

The following points should be considered regardless of the burn depth or cause

- Shock prevention
- Pain control
- Reduction of the risk of infection

13.6.1 Prehospital Care

- Stop the burn process
- Stabilize airway: consider early intubation as edema formation can later make endotracheal intubation difficult
- Large-caliber intravenous lines in peripheral veins
- Prevent hypothermia
- Ensure adequate analgesia
- Estimate the burn depth and TBSA burned
- Assess the presence of other injuries (inhalation injury, fractures, visceral injuries, and lacerations)
- Check transfer criteria to a burn center or other appropriate care center as indicated

13.6.2 Resuscitation

Initiation of increased fluid resuscitation in prehospital care is generally unnecessary. Clinical circulation therapy is goal-directed and takes into consideration the hemoglobin concentration, hematocrit, mean arterial pressure (MAP), diuresis, central venous pressure (CVP), and central venous sO_2 [5]. Fluid resuscitation is usually necessary in burns involving more than 20 % of the TBSA in adults and more than 10 % TBSA in pediatric patients. For initial volume replacement, balanced crystalloid solutions are preferred. Colloids, gelatine solution, and catecholamines should be avoided if possible [5].

The most widely used adult formulas are the Parkland (Baxter) formula and the modified Brooke formula.

The Parkland formula is used to guide fluid resuscitation during the first 24 h [6]:

$$4\ \text{cc of crystalloid solution} \cdot \text{kg} \cdot \%\text{TBSA} / 24\ \text{h}$$

Modified Brooke formula:

$$2\ \text{cc} \cdot \text{kg} \cdot \%\text{TBSA} / 24\ \text{h}$$

Half of the fluid should be administered over the first 8 h. All resuscitation formulas are meant to serve only as guides.

13.6.3 Aspects of Burn Care

Early necrosectomy, wound closure, prevention of septic complications, adequate nutrition, and control of the external environment are of utmost importance in the management of patients with severe thermal injuries. Immediate escharotomy is indicated in deep circumferential burns of the limbs, torso, or neck to avoid compartment syndrome, respiratory distress, or reduced circulation to the limbs as a result of constriction.

Accurate burn depth determination is important, particularly differentiation of superficial-partial thickness in contrast to deep-partial thickness burns because superficial-partial thickness burns can be treated conservatively, while deep-partial thickness burns need burn wound excision and skin grafting. Various methods have been applied to determine the depth of burns [7–12]. Currently, Confocal-laser-scanning microscopy is the most promising innovation for differentiating superficial-partial and deep-partial thickness burns on a histomorphological level [13, 14].

13.6.3.1 Burn Wound Care of Superficial and Superficial Partial-Thickness Burns

Superficial and superficial partial-thickness burns can be treated conservatively as follows:

The burned area should be cooled to reduce pain and swelling by conducting heat away from the skin surface. Hypothermia and cold injury should be avoided at all costs. Blisters should be deroofed under sterile conditions, and the wounds should be covered with an antiseptic solution and a nonadhesive wound dressing. A daily wound inspection and dressing change should be performed to prevent wound infection. Alternative dressing approaches for superficial partial-thickness burns are temporary synthetic skin substitutes that could stimulate and promote wound healing. These substitutes combine synthetic membranes and biological substances and prevent, at least, painful dressing changes [15, 16].

Superficial and superficial partial-thickness burns usually heal without additional treatment within 7–14 days. They may heal with pigment changes, and prophylactic systemic antibiotics are not indicated. If the burned area is large, or if the burn is on the face, hands, feet, groin or buttocks, or over a major joint, additional procedures (i.e., splint immobilization, hospitalization for pain control, rehydration) may be required.

13.6.3.2 Wound Care of Deep Partial-Thickness Burns

After initial cleaning and removal of dissolved tissue, deep partial-thickness burns can initially be treated as superficial partial-thickness burns, however, they will heal with massive scar formation, hence, wound excision and skin grafting is the preferred treatment.

Skin grafts can be divided into full-thickness and split-thickness, depending on the amount of dermis of the graft. The decision between full-thickness and split-thickness skin grafts depends on wound condition, size, location, and aesthetic considerations.

Split-thickness skin grafts are used by default to resurface burn wounds, particularly in patients with massive burn areas and/or for cosmetic alternatives to skin graft. Cultured epithelial autograft is available as cell spray or sheet and uses living skin cells from the burn patient to grow new skin cells in a laboratory setting resulting in excellent cosmetic outcomes compared with other methods [17].

Table 13.1 Classification of temporary and permanent skin replacement materials in terms of application and expected function

Material	Function	Application
Biobrane®, Suprathel®	Stimulate reepithelisation	Temporary
Allogenic skin Euroskin® Xenogenic skin Synthetic materials	Improve wound bed	Temporary
Cultured Epithelial Autograft (CEA) ReCell®	Epidermal regeneration	Permanent
AlloDerm® Integra® Matriderm®	Dermal reconstruction	Permanent
Autologous fibroblasts and keratinocytes cultured on collagen matrix	Epidermal and dermal reconstruction	Permanent

13.6.3.3 Wound Care of Full-Thickness Burns

Full-thickness burns should be subjected to early surgical excision and skin grafting. Split-thickness skin grafts are used by default. Prophylactic antibiotics are not indicated.

Collagen-elastin matrices, as dermal substitutes for deep partial and full-thickness burns, promise reduced wound contracture, enhanced elasticity, and pliability. This matrix represents an alternative to other types of defect coverage and should be considered in particularly delicate regions such as the joint regions. A one-stage procedure (Matriderm®) is regarded as a major advantage in comparison with a two-stage procedure (Integra®) [18]. Skin replacement materials are classified and summarized in Table 13.1.

13.6.4 Follow-Up Care

Subsequent to complete wound closure, follow-up care should involve assessing for evidence of hypertrophic scarring and contracture and should additionally consider ergotherapy, physiotherapy, splint immobilization, compression bandages, topical silicone gel sheets, sunblock, skin care, social and professional reintegration, and support groups

Fig. 13.4 Abbreviated burn severity risk index

• Male	0	% of burned skin			
• Female	1	10 %	1	81 – 90 %	9
• Age < 20 years	1	11 – 20 %	2	91 – 100 %	10
• 21 – 40	2	21 – 30 %	3		
• 41 – 60	3	31 – 40 %	4		
• 61 – 80	4	41 – 50 %	5		
• >80	5	51 – 60 %	6		
• Inhalation injury	1	61 – 70 %	7		
• Burns IIIrd degree	1	71 – 80 %	8		

Survival prognosis

2–3	99 %	10–11	20–40 %
4–5	90–99 %	12–13	<10 %
6–7	80–90 %	>13	<1 %
8–9	50–70 %		

13.7 Prognosis

Survival following burn injury has steadily increased over the past few decades; however, mortality from burn injuries rises with increasing burn depth, involved surface area, and age. Hence, the prediction of mortality from burn injury is a continuing subject of interest for burn surgeons. A fast and simple score for estimation of burn mortality is patient age in years plus the percentage of the burned body surface area (*Fisher score*) [19]. A value of up to 100 implies that survival is (still) possible whereas a value above 100 predicts a significant risk of mortality.

Fisher Score

Age + % TBSA=

0–80 Survival is likely

80–100 Survival is still likely

>100 Unfavorable prognosis

A more reliable score for the prediction of mortality from burns is the Abbreviated Burn Severity Risk Index (ABSI) Score (Fig. 13.4) [20]. However, mortality prediction by any scoring system is limited and decisions for individual patients should never be based solely on a statistically derived injury severity score.

13.8 Potential Complications

Once the epidermis is damaged and separated from the raw dermis, the body loses fluid and the ability to thermoregulate and block infection. The following complications should be considered: hypothermia; shift of proteins, fluids, and electrolytes; hypovolemia; shock; eschar; infection; systemic inflammatory response syndrome; sepsis; organ failure; pulmonary complications; respiratory failure; acute renal failure; stress ulcer; heart failure, hypertrophic scarring; and contracture.

13.9 Prevention

The fact that 90 % of burns are preventable has led to many attempts to decrease the number of risk factors that are statistically associated with burns. Hence, whether intended or accidental, most burn injuries can be prevented by identifying, removing, and reducing exposure to their causes.

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Thromboembolism

14

Michael Heinzelmann and Julia Fox

Abbreviations

AAOS	American Academy of Orthopaedic Surgeons
ACCP	American College of Chest Physicians
CTPH	Chronic thromboembolic pulmonary hypertension
CVC	Central venous catheter
DUS	Doppler ultrasonography
DVT	Deep vein thrombosis
FUT	Fibrinogen uptake test
GCS	Graduated compression stockings
HFS	Hip fracture surgery
HIT	Heparin-induced thrombocytopenia
INR	International normalized ratio
IPC	Intermittent pneumatic compression
IVC	Inferior vena cava
LDUH	Low-dose unfractionated heparin
LMWH	Low-molecular-weight heparin
PE	Pulmonary embolism
PT	Prothrombin time
PTS	Post-thrombotic syndrome
PTT	Partial thromboplastin time
SC	Subcutaneous
SCI	Spinal cord injury
THR	Total hip replacement
TKR	Total knee replacement
VFP	Venous foot pump
VKA	Vitamin K antagonist
VTE	Venous thromboembolism

14.1 Introduction

Venous thromboembolism (VTE) is a common and silent disease that disables, kills, and is expensive. In fact, VTE is the third leading cause of cardiovascular death in the United States, after myocardial infarction and stroke. Almost two million cases of deep venous thrombosis (DVT) occur every year. Post-thrombotic syndrome and pulmonary hypertension are severe sequelae that affect quality of life.

In orthopedic and trauma surgery, VTE is a well-known disease. Knudson et al. [1] queried the American College of Surgeons National Trauma Data Bank for episodes of DVT and/or pulmonary embolism (PE). They examined demographic data, VTE risk factors, outcomes, and VTE prophylaxis measures in patients admitted to the 131 contributing trauma centers. Of a total of 450,375 patients, 0.36 % had a VTE (998 had DVT, 522 had PE, 82 had both).

14.2 Risk Factors

The predisposing factors for VTE were initially described by the German pathologist Rudolf Virchow in 1856. Still relevant today, Virchow's triad of thromboembolic risk includes circulatory stasis, endothelial injury, and a hypercoagulable state. The role of trauma

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and other main risk factors are summarized in Table 14.1 [2]. The inciting event involves thrombus formation from local pro-coagulant events such as small endothelial disruptions at venous confluences and valve pockets or after injury. Platelets and neutrophils adhere to the thrombus and are activated to generate inflammatory and pro-coagulant mediators and thus amplify thrombus formation. It seems that the balance between pro-inflammatory and anti-inflammatory cytokines and chemokines determine the ultimate response at the venous wall. Additionally, tissue factor released from the vein also contributes to thrombosis when the vein is injured or when tissue factor becomes exposed to the flowing blood.

Table 14.1 Risk factors for VTE

Genetic factors	Environmental factors
Factor V Leiden	Surgery/trauma
Prothrombin gene mutation	Immobility
High factor VIII levels	Age
Hyperhomocysteinemia	Congestive heart failure/ myocardial infarction
Antithrombin deficiency	Hormone replacement therapy/oral contraception
Protein C deficiency	Cancer
Protein S deficiency	Pregnancy
Dysfibrinogenemia	Antiphospholipid antibodies
	Air travel

Adapated from [28]

The levels of thromboembolism risk are summarized in Table 14.2. Many procedures for trauma and orthopedic surgery have a high risk for VTE during and after the stay in the hospital. Importantly, the outpatient VTE rate is increased threefold when compared with inpatient VTE [3]. Almost half of the outpatients with VTE had been hospitalized in the recent past with a length of stay less than 4 days. Furthermore, less than half of the recently hospitalized patients had received appropriate VTE prophylaxis during their hospital stay [3], indicating a need for proper VTE prophylaxis in the surgical patient after hospitalization. Knudson et al. [1] found that in orthopedic and trauma surgery, 90 % of patients with VTE had one of the nine risk factors commonly associated with VTE. Six risk factors for VTE were found to be independently significant in multivariate logistic regression (Table 14.3).

A recent report sponsored by The Agency for Healthcare Research and Quality summarized a systematic review of 79 patient safety interventions based on the strength of the evidence: of the top ten safety practices, appropriate VTE for at-risk patients reached the highest rank. The others were perioperative beta-blockade, maximum sterile barriers for central venous catheter insertion, perioperative antibiotics to reduce

Table 14.2 Levels of thromboembolism risk and recommended thromboprophylaxis in hospital patients

Levels of risk (VTE risk without thromboprophylaxis, %)[a]	Suggested thromboprophylaxis options
Low risk: (up to 10 %)[a]	
Minor surgery in mobile patients	No specific thromboprophylaxis
Medical patients who are fully mobile	Early and "aggressive" ambulation
Moderate risk: (10–40 %)[a]	
Most general, open gynecologic or urologic surgery patients	LMWH (at recommended doses), LDUH bid or tid, fondaparinux
Medical patients, bed rest or sick	
Moderate VTE risk plus high bleeding risk (10–40 %)[a]	Mechanical thromboprophylaxis[b]
High risk: (40–80)	
Hip or knee arthroplasty, hip fracture surgery	LMWH (at recommended doses), fondaparinux, oral vitamin K antagonist (INR 2–3)
Major trauma, spinal cord injury	
High VTE risk plus high bleeding risk (40–80 %)[a]	Mechanical thromboprophylaxis[b]

Adapted from [28]
The descriptive terms are purposely left undefined to allow individual clinical interpretation
GCS graduated compression stockings, *INR* international normalized ratio, *IPC* intermittent pneumatic compression, *LDUH* low-dose unfractionated heparin, *LMWH* low-molecular-weight heparin, *VTE* venous thromboembolism
[a]Rates based on objective diagnostic screening for asymptomatic VTE in patients not receiving thromboprophylaxis
[b]Mechanical thromboprophylaxis includes IPS or VFP and/or GCS; consider switch to anticoagulant thromboprophylaxis when high bleeding risk decreases

Table 14.3 Risk factors associated with VTE in trauma patients

Risk factor (number with risk)	Odds ratio (95 % CI)
Age ≥40 years ($n=178,851$)[a]	2.29 (2.07–2.55)
Pelvic fracture ($n=2,707$)	2.93 (2.01–4.27)
Lower extremity fracture ($n=63,508$)[a]	3.16 (2.85–3.51)
Spinal cord injury with paralysis ($n=2,852$)	3.39 (2.41–4.77)
Head injury (AIS ≥3) ($n=52,197$)[a]	2.59 (2.31–2.90)
Ventilator days >3 ($n=13,037$)[a]	10.62 (9.32–12.11)
Venous injury ($n=1,450$)[a]	7.93 (5.83–10.78)
Shock on admission (BP <90 mmHg) ($n=18,510$)	1.95 (1.62–2.34)
Major surgical procedure ($n=73,974$)[a]	4.32 (3.91–4.77)

Adapted from [1]
Univariate analysis $p<0.0001$ for all factors
AIS abbreviated injury score, *BP* blood pressure, *CI* confidence interval, *VTE* venous thromboembolism
[a]Independent risk factors when using a multivariate analysis ($p<0.0001$ for all factors except head injury ($p=0.0125$))

postsurgical infections, patients restating/recalling what they have been told during informed consent, continuous aspiration of subglottic secretions to prevent ventilator-associated pneumonia, pressure-relieving bedding to prevent pressure ulcers, real-time ultrasonography to insert central venous catheters, self-management of warfarin, and nutritional support for postoperative and critically ill patients [4].

14.3 Prevalence

The prevalence of VTE in the absence of prophylaxis is shown in Table 14.4. Importantly, the incidence of VTE correlates with the number of risk factors [5].

In 1975, Kakkar et al. [6] published a prospective, randomized, multicenter study of the effect of low-dose unfractionated heparin on fatal postoperative PE. They investigated 4,121 patients older than 40 years undergoing a variety of elective major surgical procedures and found a significant reduction of patients with fatal PE treated with 5,000 IU heparin (subcutaneously 2 h preoperatively and 8 h thereafter for 7 days) compared with the control group without treatment (0.097 % and 0.77 %, respectively). However, bleeding complications also were increased; they were not significant for excessive blood loss but were significant for the occurrence of wound hematoma.

Table 14.4 Prevalence of venous thromboembolism in the absence of prophylaxis

Medical	10–20 %
General surgery	15–40 %
Major gynecologic surgery	15–40 %
Major urologic surgery	15–40 %
Total hip, knee or hip fracture	40–60 %
Neurosurgery	15–40 %
Major trauma	40–80 %
Acute spinal cord injury	60–80 %
Stroke	20–50 %
Critical care	10–80 %

Adapted from [28]

14.4 Long-Term Effects and Outcome After VTE

14.4.1 Post-Thrombotic Syndrome

Despite appropriate anticoagulant therapy, at least one of every two or three patients with DVT of the lower extremities will develop post-thrombotic sequelae [7]. Prandoni et al. [8] studied the long-term outcomes after a first DVT. In a prospective cohort follow-up study, they analyzed 528 consecutive patients with a first episode of venography-confirmed DVT. Criteria for the post-thrombotic syndrome (PTS) were recorded and scored. The criteria to assess PTS included presence of leg symptoms (pain, cramps, heaviness, pruritus, and paresthesia) and clinical signs (pretibial edema, induration of the skin, hyperpigmentation, new venous ectasia, redness and pain during calf compression, and ulceration of the skin). In this study, the cumulative incidence of recurrent VTE was 17 % after 2 years, 24 % after 5 years, and 30 % after 8 years [8]. Malignancy and impaired coagulation inhibition increased the risk of recurrent VTE. In contrast, surgery and recent trauma or fracture was associated with a diminished risk of recurrent VTE. The cumulative incidence of PTS was 25 % after 2 years, 30 % after 5 years, and 30 % after 8 years. Importantly, the PTS occurred in almost one third of patients and was strongly related to recurrent ipsilateral DVT.

The factors potentially related to the development of the PTS are older age, obesity, a history of previous ipsilateral DVT, iliac-femoral location of the current thrombosis, failure to promptly recover from

the acute symptoms, and insufficient quality of oral anticoagulant therapy. On the basis of recent findings, the lack of vein recanalization within the first 6 months after DVT seems to be an important predictor of PTS, while the role of venous reflux is controversial. According to the results of recent clinical studies, the prompt administration of adequate elastic compression stockings in patients with symptomatic DVT has the potential to reduce the frequency of PTS, and when carefully supervised and instructed to wear proper elastic stockings, more than 50 % of patients have the potential to either remain stable or improve during long-term follow-up. Nevertheless, because of limitations in current therapies, the management of PTS is demanding and often frustrating [7].

In a systematic review, Wille-Jørgensen et al. [9] studied the epidemiological association between asymptomatic postoperative DVT and the development of PTS. They found seven original publications (1984–2001) that addressed this question, mainly in abdominal surgery and hip and knee arthroplasty. The overall relative risk of developing PTS was 1.58 (95 % confidence interval, 1.24–2.02) in patients suffering from asymptomatic DVT compared to patients without DVT ($P < 0.0005$). They concluded that there is a significant association between postoperative asymptomatic DVT diagnosed with sensitive screening methods and occurrence of late PTS.

14.4.2 Pulmonary Hypertension

Pengo et al. [10] conducted a prospective, long-term follow-up study to assess the incidence of symptomatic chronic thromboembolic pulmonary hypertension (CTPH) in consecutive patients with an acute episode of PE but without prior venous thromboembolism. CTPH was considered to be present if systolic and mean pulmonary artery pressures exceeded 40 and 25 mmHg, respectively; pulmonary-capillary wedge pressure was normal; and there was angiographic evidence of disease. They found that symptomatic CTPH affects approximately 4 % of patients within 2 years after a first episode of symptomatic PE, with no subsequent increase in incidence. The following factors increased the risk of CTPH: a previous PE, younger age, a larger perfusion defect, and idiopathic PE at presentation.

14.4.3 Economic Burden

Although data on the exact cost attributed to VTE are lacking, a recent analysis of health care claims estimated that the total annual health care cost for VTE ranges from $7,594 to $16,644 per patient [11]. With estimates of 300,000–600,000 incident cases per year, this cost equates to a total annual cost of $2 to $10 billion attributable to VTE.

Dimick et al. [12] studied hospital costs associated with postoperative complications. The observational cohort study merged the National Surgical Quality Improvement Project private sector database to the hospital internal accounting data available in the University of Michigan Data Warehouse. The median total hospital costs (and the mean length of hospital stay) were $33,589 (20 days) for a patient with thromboembolic complications compared with $5,233 (5 days) for a patient without thromboembolic complication; $13,083 (9 days) for patients with infectious complications; $18,496 (4 days) for patients with cardiovascular complications; and $62,704 (19 days) for patients with respiratory complications.

An economic evaluation of VTE prophylaxis strategies in critically ill trauma patients at risk of bleeding has been published by Chiasson et al. [13]. They conclude that the attributable mortality resulting from PE in trauma patients with severe injuries is low relative to other causes of mortality. Prophylactic placement of a vena cava filter (VCF) in patients at high risk of VTE who cannot receive pharmacological prophylaxis is expensive and associated with an increased risk of DVT. Compared with the other strategies, serial Doppler ultrasound screening was associated with better clinical outcomes and lower costs [13].

14.5 Physiology of Plug Formation

Plug formation is a complex process that includes platelet aggregation and fibrin generation with the aim to generate a hemostatic clot. Platelet-plug formation at sites of injury occurs rapidly, within seconds of injury, and is of great importance to stop blood loss. The plasma coagulation system takes several minutes before this process is completed. The fibrin strands reinforce the platelet-induced plug. This reaction is particularly important in larger vessels to prevent recurrent bleeding hours or days after the initial injury. These two systems are closely linked. For example,

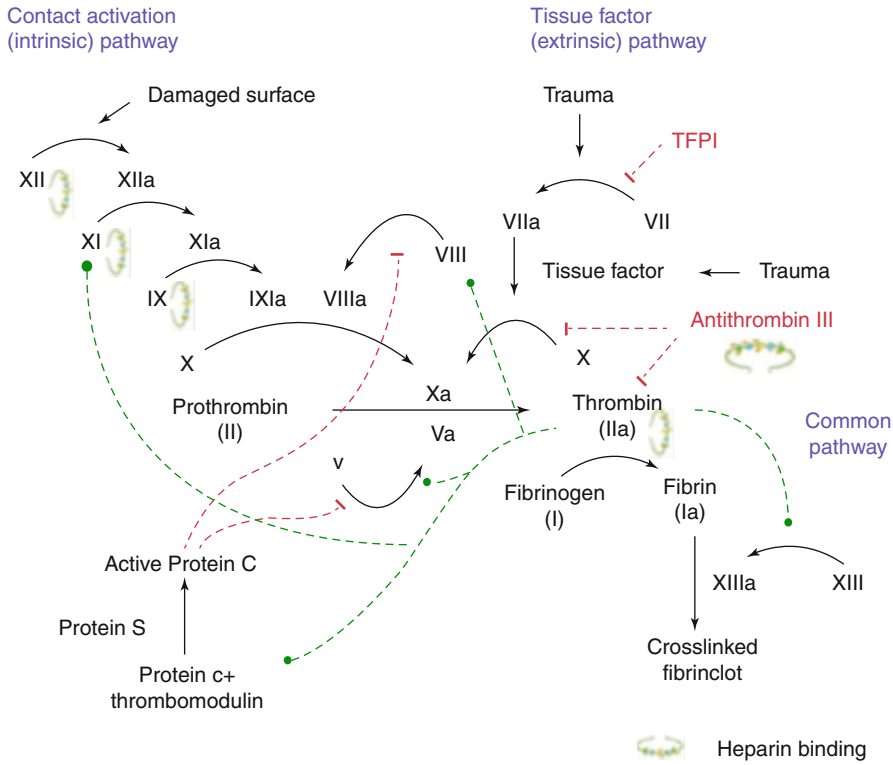

Fig. 14.1 Simplified model of the coagulation cascade. The extrinsic and intrinsic pathway merge in the activation of factor X, with further promotes the generation of thrombin and fibrin trough the common pathway. Heparin has unspecific binding to thrombin, IXa, XIa, and XIIa. The specific binding of heparin to antithrombin III eventually leads to binding of ATII to Xa with consecutive inactivation of Xa. Low molecular weight heparins and fonadaparinux also specifically bind to ATIII and thereby inactivate Xa. Activating effects are shown in dotted green lines, inhibiting effects are shown in dotted red lines. Abbreviations: Factors are abbreviated according to their number; *a* activated, *ATIII* antithrombin III, *TFPI* tissue factor pathway inhibiting factor (Adapted from [37])

activated platelets accelerate plasma coagulation and products of the plasma coagulation reaction, such as thrombin, stimulate platelet aggregation [14].

14.5.1 Coagulation

The coagulation pathways are a series of reactions in which inactive enzyme precursors and their co-factors are activated to become active components that then catalyze the next reaction in the cascade that ultimately results in cross-linked fibrin. Two pathways are known: (1) the contact activation (intrinsic) pathway, and (2) the tissue factor (extrinsic) pathway (Fig. 14.1).

The contact activation pathway begins at a damaged surface with formation of the primary complex on collagen by high-molecular-weight kininogen (HMWK), prekallikrein, and FXII (Hageman factor). Prekallikrein is converted to kallikrein and FXII becomes activated (FXIIa). The steps are demonstrated in Fig. 14.1. The minor role that the contact activation pathway has in initiating clot formation can be illustrated by the fact that patients with severe deficiencies of FXII, HMWK, and prekallikrein do not have a bleeding disorder.

The main role of the tissue factor pathway is to generate a "thrombin burst," a process by which thrombin, the most important constituent of the coagulation cascade, is released instantaneously. FVIIa circulates in higher amounts than any other activated coagulation factor.

The final common pathway starts with the generation of thrombin. Thrombin has different functions. Its primary role is the conversion of fibrinogen to fibrin with consequent formation of a hemostatic plug. In addition, thrombin activates Factors VIII and V and their inhibitor protein C (in the presence of thrombomodulin), and thrombin activates Factor XIII, which forms covalent bonds that crosslink the fibrin polymers.

Following activation by the contact factor or tissue factor pathways, the coagulation cascade is maintained in a prothrombotic state by the continued activation of FVIII and FIX to form the tenase complex, until it is down-regulated by the anticoagulant pathways.

14.6 Monitoring of the Coagulation Cascade

14.6.1 The Prothrombin Time

Prothrombin time (PT) was discovered by Dr. A. Quick and colleagues in 1935, and a second method was published by Dr P. Owren, also called the "p and p" or "prothrombin and proconvertin" method. It was used as a measure of activity for warfarin when used therapeutically.

- PT and its derived measures of prothrombin ratio and international normalized ratio (INR) are measures of the extrinsic pathway of coagulation (i.e., factors II, V, VII, X and fibrinogen).
- PT is used to determine the clotting tendency of blood in order to estimate warfarin dosage, liver damage, and vitamin K status.
- The reference range for prothrombin time is usually around 12–15 s.
- The INR, that is now widely accepted worldwide, was introduced in the early 1980s when it turned out that there was a large degree of variation between the various PT assays. This discrepancy was mainly a result of problems with the purity of the thromboplastin (tissue factor) concentrate.
- The normal range for the INR is 0.8–1.2.

14.6.2 Partial Thromboplastin Time

Partial thromboplastin time or activated partial thromboplastin time (aPTT) is a performance indicator that measures the efficacy of both the contact activation pathway and the common coagulation pathways. Apart from detecting abnormalities in blood clotting, it is also used to monitor the treatment effects with heparin.

14.6.3 Platelets

Platelets control bleeding when there is an injury to the blood vessel wall, and the endothelial cell layer is disrupted exposing the underlying extracellular matrix. Two adhesion receptors, glycoprotein (GP) Ib-IX–V that binds von Willebrand factor (vWF) and GPVI that binds collagen, are primarily responsible for regulating the initial platelet adhesion and activation in flowing blood. Following adhesion, rapid signal transduction leads to platelet activation, cytoskeletal changes associated with shape change, spreading and secretion, and inside–out activation of integrins that support adhesion and aggregation. The major platelet integrin GPIIb–IIIa binds vWF or fibrinogen and mediates platelet aggregation under shear conditions. Platelet activation that involves GPIb-IX–V or GPVI also leads to secretion of platelet agonists, such as adenosine diphosphate (ADP), which acts via the G protein-coupled receptors, P2Y1 and P2Y12, to reinforce platelet aggregation (Fig. 14.2). The activated platelet aggregates interact with the coagulation cascade and lead to stabilization of the clot by fibrin and GPIIb–IIIa-dependent mechanisms [15].

14.7 Mechanical Methods of Thromboprophylaxis

Early and frequent ambulation of hospitalized patients at risk for VTE is an important principle of patient care. However, many patients cannot be fully mobilized early after hospital admission or after surgery. In addition, mobilization alone does not provide adequate thromboprophylaxis for hospitalized patients and the majority of hospital-associated, symptomatic thromboembolic events occur after patients have started to ambulate.

Specific mechanical methods of thromboprophylaxis include graduated compression stockings (GCS), the venous foot pump (VFP), and intermittent pneumatic compression (IPC) devices. These methods increase venous outflow and/or reduce stasis within the leg veins and have important advantages and limitations (Table 14.5). The primary attraction of mechanical thromboprophylaxis is the lack of bleeding potential and the advantages for patients with high bleeding risks. While all three of the mechanical methods (GCS, VFP and IPC) reduce the risk of DVT in a number of patient groups, they have been studied less intensively than anticoagulant-based methods, and they are generally less efficacious when compared with anticoagulant thromboprophylaxis. Importantly, no mechanical thromboprophylaxis option has been

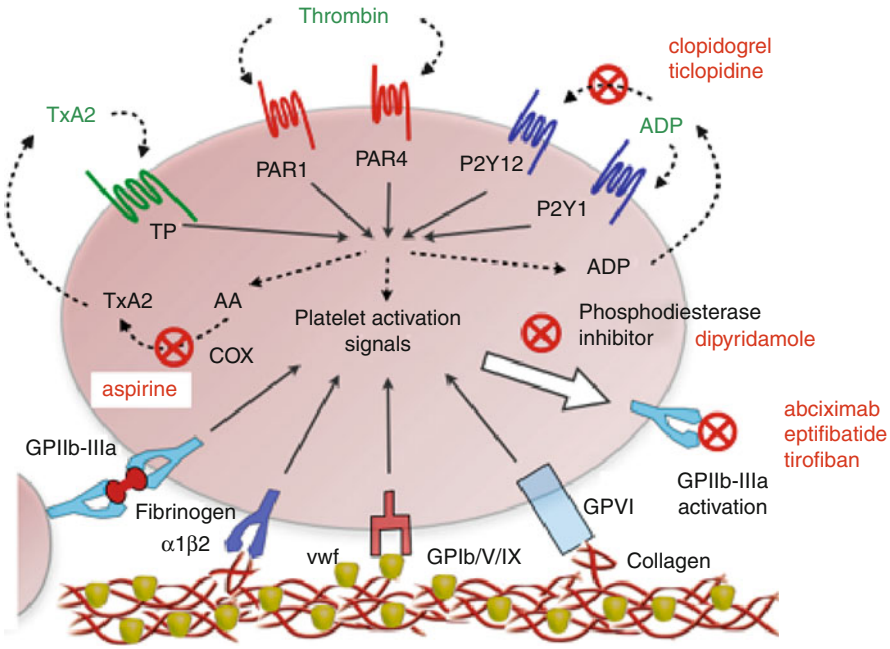

Fig. 14.2 Mechanisms of platelet activation and mode of action of current antiplatelet therapies. Platelets are initially activated by ligation of adhesion receptors by subendothelial proteins: glycoprotein (GP)VI and the integrin α2β1 bind collagens (*red strands*); GPIb/V/IX complex binds von Willebrand factor (vWf: *olive spheres*); and GPIIb–IIIa binds fibrinogen (*red dumbbell*). Propagation of platelet activation occurs by blood-soluble agonists: ADP released from activated platelets activates P2Y1 and P2Y12; and thromboxane A2 (TxA2) synthesised and released from activated platelets acts on thromboxane/prostanoid (TP) receptors; locally-generated thrombin activates protease-activated receptor (PAR)1 and PAR4. These inputs each signal the activation of GPIIb–IIIa, the key event in platelet aggregation. Antiplatelet agents inhibit the synthesis of TxA2 from arachidonic acid (AA) by the enzyme cyclooxygenase (COX) (aspirin), the binding of ADP to P2Y12 (clopidogrel and ticlopidine), the binding of ligands to activated GPIIb-IIIa (abciximab, eptifibatide and tirofiban), or the inhibition of intracellular signaling events mediated by phosphodiesterase (dipyridamole) (Adapted from [38, 39])

studied in a large enough sample to determine if there is a reduction in the risk of death or PE.

14.8 Pharmacology: Antithrombotic Agents

The ideal antithrombotic agent should include the following properties: a high efficacy to safety index, a predictable dose response, a parenteral and oral application, a rapid onset of action, the availability of a safe antidote, no side effects, and minimal interactions. To characterize and rate this potentially ideal agent, it is equally important to choose appropriate and clinically relevant endpoints such as fatal or nonfatal PE, proximal DVT, and PTS. On the other hand, factors that have an impact on cost or patient safety and comfort, (e.g., relevant side effects, need for laboratory monitoring, or oral administration of the compound) must be considered.

14.8.1 Vitamin-K Dependent Clotting Factors, Coumarins

The coumarins or vitamin K antagonists (VKAs) have been the mainstay of oral anticoagulant therapy for more than 65 years. Their effectiveness has been established by well-designed clinical trials for the primary and secondary prevention of VTE. VKAs are challenging to use in clinical practice for the following reasons:

- VKAs have a narrow therapeutic window.
- VKAs exhibit considerable variability in dose response among patients because of genetic and other factors.
- VKAs are subject to interactions with drugs and diet.
- Their laboratory control is difficult to standardize.
- Maintenance of a therapeutic level of anticoagulation requires a good understanding of the pharmacokinetics and pharmacodynamics of warfarin and good patient communication.

Table 14.5 Advantages and limitations of mechanical thromboprophylaxis modalities

Advantages
Can be used in patients at high bleeding risk
Risk of bleeding is not increased
Efficacy has been demonstrated in a number of patient groups
May enhance the effectiveness of anticoagulant thromboprophylaxis
May reduce leg swelling
Limitations
Not as intensively studied as pharmacologic thromboprophylaxis (fewer studies and smaller)
Almost all mechanical thromboprophylaxis trials were unblended and therefore have a potential for bias in high-risk groups are less effective than anticoagulant thromboprophylaxis
Many specific mechanical devices have never been assessed in any clinical trial
No established standards for size, pressure, or physiologic features
Greater effect in reducing calf DVT than proximal DVT
Effect on PE and death unknown
May reduce or delay the use of more effective anticoagulant thromboprophylaxis
Compliance by patients and staff often poor
Trials may overestimate the protection compared with routine use cost: associated with purchase, storage, dispensing, and cleaning of the devices, as well as ensuring optimal compliance

Adapted from [28]
DVT deep vein thrombosis, *PE* pulmonary embolism

Coumarins inhibit the vitamin K-dependent synthesis of biologically active forms of the calcium-dependent clotting factors II, VII, IX and X (Figs. 14.1 and 14.3), as well as the regulatory factors protein C, protein S, and protein Z. Other proteins not involved in blood clotting, such as osteocalcin, or matrix Gla protein, may also be affected.

The antithrombotic effect of VKAs has conventionally been attributed to their anticoagulant effect, which in turn is mediated by the reduction of four vitamin K-dependent coagulation factors (Fig. 14.3). Evidence suggests, however, that the anticoagulant and antithrombotic effects can be dissociated and that the reduction of prothrombin and possibly factor X are more important than the reduction of factors VII and IX for the antithrombotic effect.

14.8.2 Heparin

Heparin is one of the oldest drugs that is currently still in widespread clinical use. Heparin's discovery in 1916 can be attributed to the research activities of two men, Jay McLean and William Henry Howell. In the 1930s, Erik Jorpes discovered the structure of heparin. The first human trials of heparin began in 1935, and by 1937, heparin was considered to be a safe, easily available, and effective blood anticoagulant [16].

Heparin is a naturally occurring anticoagulant produced by basophils and mast cells. It was originally isolated from canine liver cells, hence its name (hepar is Greek for "liver"). Pharmaceutical grade heparin is derived from mucosal tissues of animals such as porcine intestine or bovine lung. Native heparin is a member of the glycosaminoglycan family of carbohydrates, which consists of variably sulfated repeating saccharide units. Interestingly, heparin has the highest negative charge density of any known biological molecule. Only one third of heparin molecules contain the high-affinity pentasaccharide required for anticoagulant activity.

Because of its negative charge, heparin binds in a **nonspecific** way to many proteins and other biological substances such as (1) receptors (steroids, growth factors receptors, ion channels); (2) enzymes (lipases, kinases, phosphatases); (3) cell matrix proteins (collagen, vitronectin, laminin); (4) nuclear proteins (histones, transcription factors); (5) lipoproteins (LDL, VLDL, apolipoproteins); (6) viral proteins (HIV, HSV, dengue); (7) prion protein, amyloid protein; (8) growth factors (FGF, VEGF); (9) heparin cofactor II; (10) thrombin, (11) enzymes Inhibitors (serpins), (12) Chemokines (PF4) (13) Heparin-binding protein HBP/CAP37 [17]. It is therefore not surprising that heparin, besides the desired anticoagulation effect, has many other biological effects that are related to size and nonspecific binding: thrombocytopenia (heparin-induced thrombocytopenia [HIT]), osteoporosis, endocrine and metabolic functions (glucose, lipid metabolism, calcium etc.), and modulation of inflammatory reactions [17, 18].

Specific binding of heparin to the enzyme inhibitor antithrombin III (ATIII) causes a conformational change that results in activation of ATIII. The activated ATIII then inactivates thrombin and other

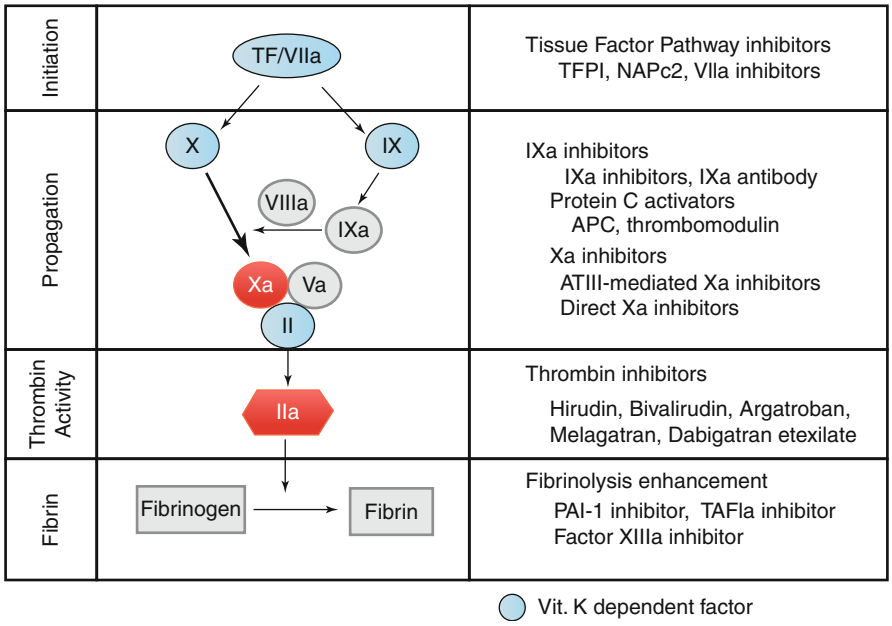

Fig. 14.3 Simplified model of the coagulation steps. Compared with coumarins that interfere with vitamin K dependent clotting factors new anticoagulant drugs have specific targets that interfere with the different steps of coagulation, modified according to [40, 41]. The important factors Xa and Thrombin are highlighted in red. The plasma half-life of the vitamin K dependent clotting factors (*blue*) are: VIIa 4–6 h, IX 24 h, X 48 h, and II 60 h. Abbreviations: *TF* tissue factor, *II* Prothrombin, *IIa* Thrombin, *Va* activated factor V, *VIIa* activated factor VII, *IX* factor IX, *X* factor X, *APC* activated protein C, *TFPI* tissue factor pathway inhibitor, *NAPc2* Nematode Anticoagulant Protein c2

proteases involved in blood clotting, most notably factor Xa (Fig. 14.1). The rate of inactivation of these proteases by ATIII can increase by up to 1000-fold due to the binding of heparin. ATIII binds to a specific pentasaccharide sulfation sequence contained within the heparin polymer (Fig. 14.4): GlcNAc/NS(6S)-GlcA-GlcNS(3S,6S)-IdoA(2S)-GlcNS(6S). However, for thrombin inhibition, thrombin must also bind to the heparin polymer at a site proximal to the pentasaccharide. The highly-negative charge density of heparin contributes to its very strong electrostatic interaction with thrombin and represents a physiologically important nonspecific binding of heparin. The formation of a ternary complex between ATIII, thrombin, and heparin results in the inactivation of thrombin. For this reason heparin's activity against thrombin is size-dependent, the ternary complex requires at least 18 saccharide units for efficient formation. In contrast, anti factor Xa activity only requires the specific pentasaccharide sequence for binding.

14.8.3 Low-Molecular-Weight Heparin

In order to reduce the size-related and nonspecific effects of heparin, various methods of heparin processing have been developed [19]. Hence, low-molecular-weight heparin (LMWH) consists of only shorter chains of polysaccharide (Fig. 14.4). As might be expected, products prepared by distinctly different processes have different physical, chemical, and biological properties. The main differences between LMWH and "unfractioned" heparin are:

- LMWH has a weaker effect on thrombin compared to heparin, but maintains the same effect on factor Xa.
- Average molecular weight of LMWH is about 4.5 kDa, of heparin about 15 kDa.
- Once-daily dosing by subcutaneous injection, rather than a continuous infusion of unfractionated heparin.
- No need for monitoring of the coagulation parameter aPTT.
- Possibly a smaller risk of bleeding.

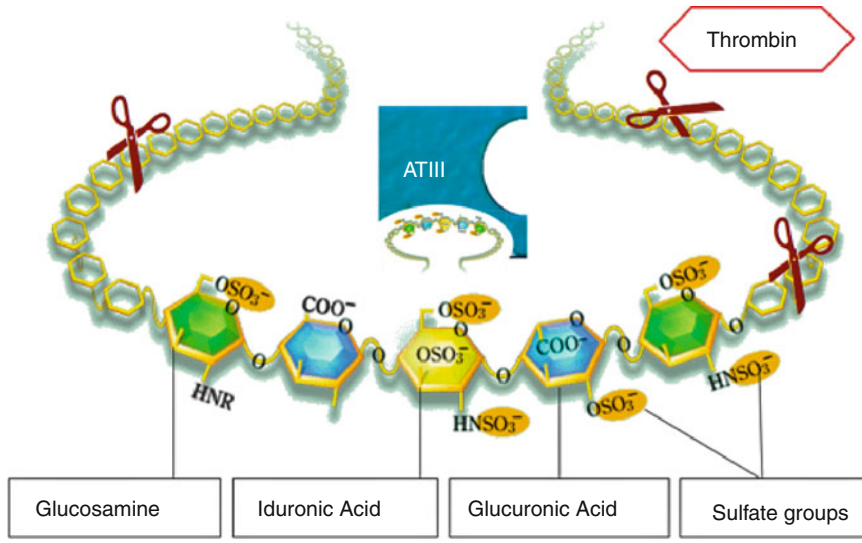

Fig. 14.4 Heparin. Heparin is a polysaccharide chain that consists of 18–70 monosaccharides. The scissors represent potential cutting sites during enzymatic or chemical processing of heparin to low molecular weight heparins (LMWH). The five monosaccharides GlcNAc/NS(6S)-GlcA-GlcNS(3S,6S)-IdoA(2S)-GlcNS(6S) provide the specific binding site to ATIII. New synthetic compounds such as fondaparinux consist of the specific ATIII binding sequence. For thrombin inhibition, however, thrombin must also bind to the heparin polymer at a site proximal to the pentasaccharide, this requires at least 18 saccharide units. This explains why LMWH have weaker and fondaparinux or no anti-thrombin activity. Abbreviations: *ATIII* antithrombin III (Adapted from [42])

- Smaller risk of nonspecific effects such as risk of heparin-induced thrombocytopenia or osteoporosis in long-term use.
- LMWH permits outpatient treatment of conditions such as DVT or PE that previously mandated inpatient hospitalization for unfractionated heparin administration, because LMWH can be given subcutaneously and does not require aPTT monitoring.

14.8.4 ATIII Mediated, Indirect Xa Inhibitors: Fondaparinux

In order to further reduce the size-related and nonspecific effects of heparin and LMWH, the group of Petitou, Herbert and colleagues [20] realized to synthesize the ATIII-binding sequence of heparin, the pentasaccharide fondaparinux. The main characteristics of fondaparinux are:

- It catalyzes the inhibition of factor Xa, but not thrombin, in an antithrombin-dependent fashion.
- It binds only to antithrombin; therefore, HIT and osteoporosis are unlikely to occur.
- It has excellent bioavailability when administered subcutaneously, has a longer half-life than LMWHs.
- It is administered once daily by subcutaneous injection in fixed doses, without anticoagulant monitoring.

In addition to the pharmacological anticoagulatory properties, the total chemical synthesis of fondaparinux also showed other advantages: (1) single chemical entity, (2) no risk of pathogen contamination, and (3) batch-to-batch consistency. Importantly, many clinical trials showed a significantly reduced VTE rate in major orthopedic surgery (total hip arthroplasty, total knee arthroplasty) and hip fracture surgery when compared with the LMWH enoxaparin [21].

14.8.5 Direct Xa Inhibitors

Direct factor Xa inhibitors include parenteral agents as well as several orally active drugs. All of the direct factor Xa inhibitors are small molecules that reversibly block the active site of factor Xa. The large number of new oral factor Xa inhibitors highlights the ongoing

focus on development of oral anticoagulants that may replace VKAs such as warfarin.

14.8.6 Inhibition of Thrombin Activity

In contrast to indirect anticoagulants, which require a plasma cofactor to exert their activity, direct thrombin inhibitors have intrinsic activity because they bind to thrombin and block its enzymatic activity. The currently approved direct thrombin inhibitors are hirudin, bivalirudin, argatroban [22], and dabigatran etexilate.

Hirudin is a 65-amino acid polypeptide originally isolated from the salivary glands of the medicinal leech, Hirudo medicinalis. Hirudin is now available in recombinant forms. Two recombinant forms of hirudin, known as lepirudin and desirudin, are currently approved for clinical use. Lepirudin is licensed for treatment of thrombosis complicating HIT, whereas desirudin is approved in Europe for postoperative thromboprophylaxis in patients undergoing elective hip arthroplasty.

Bivalirudin is a 20-amino acid synthetic polypeptide, an analog of hirudin. Bivalirudin is licensed as an alternative to heparin in patients with HIT (with or without thrombosis) who require percutaneous coronary interventions. In contrast to hirudin, bivalirudin is not immunogenic. However, antibodies against hirudin can cross react with bivalirudin in vitro. The clinical consequences of this cross-reactivity are uncertain.

Argatroban is a competitive inhibitor of thrombin and binds noncovalently to the active site of thrombin to form a reversible complex. The plasma half-life of argatroban is 45 min. It is metabolized in the liver via the cytochrome P450 3A4/5 enzyme system. Consequently, argatroban must be used with caution in patients with hepatic dysfunction. However, because it is not renally excreted, argatroban is particularly useful in patients with HIT with severe renal impairment.

Ximelagatran is an oral anticoagulant that acts by direct and reversible inhibition of thrombin and has (or had) the potential to replace warfarin [23]. In the US, the presentation of ximelagatran clinical program to the Food and Drug Administration Cardiovascular and Renal drugs Advisory Committee (CRAC) in September 2004 and the non-approval of the new drug application highlighted surprisingly divergent analyses of the benefits and risks associated with this drug [24]. Consequently, Ximelagatran was taken from the market. Ximelagatran has predictable pharmacokinetics and pharmacodynamics and was used with a fixed dose without coagulation monitoring. It is rapidly converted to its active form melagatran that directly inhibits thrombin. A regimen with melagatran intravenously (IV) followed by oral ximelagatran was registered and launched in Europe in 2004 for the short-term prevention of VTE in patients undergoing knee or hip replacement surgery. The database consisted of a total of 30,698 subjects and included five phase III pivotal studies. During the advisory panel debate, widely divergent analyses of the benefits and risks of ximelagatran were presented. Ximelagatran hepatic toxicity was a key feature leading the CRAC to conclude that the benefit risk ratio of ximelagtran was unfavorable for the proposed indications.

Dabigatran etexilate is a prodrug of dabigatran, a reversible inhibitor of the active site of thrombin. Dabigatran etexilate was approved for the prevention of VTE after total hip replacement (THR) or total knee replacement (TKR) in adult patients in the European Union and Canada in 2008. The 220 mg od dose is recommended for most patients, and the 150 mg od dose is reserved for elderly patients and those with moderate renal impairment (creatinine clearance of 30–50 ml/min). Treatment in patients with severe renal impairment (creatinine clearance <30 ml/min) is contraindicated [25].

14.8.7 Antiplatelet Drugs

The "old" antiplatelet drugs are summarized in Fig. 14.2.

14.8.7.1 Aspirin

The French chemist Charles Frederic Gerhardt was the first to prepare acetylsalicylic acid in 1853. The British pharmacologist John Robert Vane discovered the mechanism of aspirin in 1971 and received the Nobel prize in 1982. Aspirin is now known to inhibit arachidonate-induced platelet aggregation by irreversibly acetylating cyclooxygenase-1 and to reduce thromboxane A2 (TXA2) synthesis by >98 %. Importantly, some patients are resistant to usual doses of aspirin as manifested by incomplete inhibition of platelet aggregation and/or ongoing thromboxane A2 production and may therefore be more prone to recurrent cardiovascular events.

14.8.7.2 Thromboxane A2 Receptor Antagonists

TXA2 receptor antagonists inhibit platelet aggregation by the following mechanisms:

- TXA2 induces platelet aggregation by binding to the TXA2 receptor on platelets.
- The TXA2 receptor also binds prostanoids, such as prostaglandin F2a, which can promote platelet aggregation by causing vasoconstriction.
- TXA2 receptor antagonists block platelet aggregation in response to both TXA2 and prostanoids. In contrast, aspirin has no effect on prostanoid synthesis and incompletely inhibits TXA2 synthesis in some patients. Therefore, TXA2 receptor antagonists have the potential to be more effective than aspirin.

14.8.7.3 Thienopyridines

The thienopyridines irreversibly inhibit P2Y12, a major ADP receptor on the platelet surface. Currently available thienopyridines include ticlopidine and clopidogrel. Clopidogrel has largely replaced ticlopidine because the risk of hematological toxicity is lower and the drug can be given once daily. Clopidogrel has the following effects:

- When given in usual doses, clopidogrel incompletely inhibits ADP-induced platelet aggregation and produces a maximum of 70 % inhibition. The extent of inhibition varies between patients and some are resistant to clopidogrel.
- Clopidogrel has a delayed onset of action because it requires metabolic activation.
- Administration of loading doses of clopidogrel accelerates its antiplatelet effects, but maximum inhibition remains delayed for several hours.
- Clopidogrel does not only have a slow onset of action, but its offset of action is also delayed for at least 5 days because the active metabolites of clopidogrel irreversibly inhibit its target receptor. This causes problems for patients who require urgent surgery because clopidogrel increases the risk of bleeding.

14.8.7.4 Dipyridamole

Dipyridamole (trade name Persantine) has different effects that interfere with platelet function:

- It inhibits thromboxane synthase, lowers the levels of TXA2 and therefore stops the platelet aggregation effects of TXA2.
- It inhibits the cellular reuptake of adenosine into platelets, red blood cells, and endothelial cells leading to increased extracellular concentrations of adenosine.
- It inhibits the enzyme adenosine deaminase, which normally breaks down adenosine into inosine. This inhibition leads to further increased levels of extracellular adenosine.
- It inhibits the phosphodiesterase enzymes, which normally break down cAMP, and thereby increases cellular cAMP levels and blocks the platelet response to ADP.

14.8.8 New Drugs

A large number of new antithrombotic drugs, including new antiplatelet drugs and new oral anticoagulants, are being developed and tested in phase II and phase III trials. An extensive summary has been published in the 8th edition in the evidence-based clinical practice guidelines of the American College of Chest Physicians (ACCP) [26] and by Weitz [25]. The following sections will give a short overview.

14.8.8.1 New Antiplatelet Drugs

New antiplatelet drugs target different receptors on thrombocytes such as (Fig. 14.2):

- Thromboxane A2 receptor antagonist (e.g., S18886)
- ADP receptor (P2Y12) antagonists: Cangrelor (parenteral), Prasugrel, AZD6140 (oral)
- Thrombin receptor (PAR-1) antagonists: (e.g., SCH-530348, E5555)

The variable antiplatelet effects of fixed-doses of clopidogrel have led to the development of new drugs such as prasugrel, which produce more consistent inhibition of ADP-induced platelet aggregation. Direct acting P2Y12 inhibitors not only overcome the slow onset and offset of thienopyridines such as clopidogrel, but may also offer more potent ADP receptor blockade. The challenge with these new agents will be safety. Adding clopidogrel to aspirin increases the risk of major bleeding and the use of more potent P2Y12 inhibitors appears to further increase this risk.

PAR-1 antagonists represent a novel class of antiplatelet agents. These drugs are unique because unlike

Table 14.6 Comparison of upcoming oral anticoagulants

Drug	Apixaban	Rivaroxaban	Dabigatran etexilate
Effect	Direct FXa inhibitor	Direct FXa inhibitor	Direct thrombin inhibitor
Prodrug	No	No	Yes
Half life (h)	8–14	7–11	14–17
Renal elimination	25 %	2/3	80 %[a]
Bioavailability	~50 %	~80 %	6–7 %
Dosage	bid	od	od

Adapted from [25]
FXa activated Factor X, *bid* twice daily, *od* once daily
[a]1/3 unchanged, 1/3 as inactive metabolites

other antiplatelet drugs, they do not prolong bleeding time. Phase II results are promising and ongoing studies will determine the efficacy and safety of these drugs as adjuncts to current antiplatelet agents [26].

14.8.8.2 New Oral Anticoagulants

New anticoagulants can be classified according to their effect on the different coagulation steps (Fig. 14.3). One of the greatest needs in anticoagulation therapy is replacement of warfarin with an orally active agent that can be given in fixed doses without routine coagulation monitoring. Consequently, current attention is mainly focused on new oral anticoagulants. Those in the most advanced stages of development are the oral direct thrombin or factor Xa inhibitors. As the final effector in blood coagulation, thrombin is a logical target for new anticoagulants. Thrombin not only converts fibrinogen to fibrin, but also amplifies its own generation by feedback activation of factors V, VIII, and IX. Therefore, thrombin inhibition not only attenuates fibrin formation, but also reduces thrombin generation. In addition, thrombin also activates platelets [25].

Of the many substances tested, three drugs are in the most advanced stages of development (Table 14.6): the direct factor Xa inhibitors apixaban and rivaroxaban and the direct thrombin inhibitor dabigatran etexilate [25]. These substances will undergo extensive phase II and III evaluation for several indications, which include the prevention of VTE, VTE treatment, stroke prevention in patients with atrial fibrillation (AF), and the prevention of recurrent ischaemic events in acute coronary syndrome (ACS) patients. Table 14.7 summarizes the clinically relevant studies related to trauma and orthopedic surgery. Direct comparisons of the efficacy and safety of the various new oral anticoagulants cannot be made without head-to-head trials, particularly with regard to bleeding rates. Nevertheless, the superior efficacy of rivaroxaban over enoxaparin, the superior efficacy of dabigatran etexilate (150 mg bid), and the superior safety of the dabigatran etexilate (110 mg bid) over warfarin demonstrate the potential of these new agents as better anticoagulants [25].

It is noteworthy that the new anticoagulants have the disadvantage of their advantages: routine coagulation monitoring is not required with new agents such as rivaroxaban and dabigatran, but a simple test for monitoring would be useful in some circumstances, for example prior to surgery to ensure that these drugs no longer have any clinically relevant anticoagulant effect before the operation. Similarly, if patients take these new agents and present with a haemorrhagic or thrombotic event, appropriate testing would be useful to determine the anticoagulatory status of patients. Periodic coagulation testing may also be helpful to assess compliance.

Another potential drawback of the new oral anticoagulants is the lack of specific antidotes. Because the half-lives of these new agents is relatively short when compared with warfarin, the likelihood to need antidotes is relatively low. However, there will be instances when immediate reversal is needed [25].

14.9 ACCP Guidelines

14.9.1 Grading

In 2008, the ACCP has published the result of the 8th consensus conference on antithrombotic therapy. Their recommendations are based on published data

Table 14.7 Dabigatran etexilate and Rivaroxaban for thromboprophylaxis in major orthopedic surgery

Indication (patients)	Study arms[a]	Total VTE (%)	Major VTE (%)	Major bleeding (%)
Dabigatran etexilate				
THR (3494)	Enoxaparin 40 mg od	6.7	3.9	1.6
	Dabigatran etexilate 150 mg	8.6	4.3	1.3
	Dabigatran etexilate 220 mg	6.0	3.1	2.0
THR (2076)	Enoxaparin 40 mg od	37.7	3.5	1.3
	Dabigatran etexilate 150 mg	40.5	3.8	1.3
	Dabigatran etexilate 220 mg	36.4	2.6	1.5
TKR (2715)	Enoxaparin 30 mg bid	25.3	2.2	1.4
	Dabigatran etexilate 150 mg[b]	33.7	3.0	0.6
	Dabigatran etexilate 220 mg	31.1	3.4	0.6
Rivaroxaban				
THR (4541)	Enoxaparin 40 mg od	3.7	2.0	0.1
	Rivaroxaban 10 mg	1.1	0.2	0.3
THR (2509)	Enoxaparin 40 mg od	9.3	5.1	0.1
	Rivaroxaban 10 mg	2.0	0.6	0.1
TKR (2531)	Enoxaparin 40 mg od	18.9	2.6	0.5
	Rivaroxaban 10 mg	9.6	1.0	0.6
TKR (2300)	Enoxaparin 30 mg bid	10.1	2.0	0.7
	Rivaroxaban 10 mg	6.9	1.2	0.7

Adapted from [25, 43]
[a]All studies were double-blind, with independent outcomes adjudication committee
[b]Non-inferiority criterion not met
bid twice daily, *od* once daily, *THR* total hip replacement, *TKR* total knee replacement, *VTE* venous thromboembolism

and are graded according to benefit vs. risk, burden, and costs in two groups: group 1 indicates a clear benefit and group 2 indicates an unclear benefit (Table 14.8) [27]. The methodological quality of the study is reflected in letters A-C. The different chapters include: prevention of VTE, therapy of DVT and PE, HIT, antithrombotic drugs such as heparin, LMWH, VKAs, new drugs, different diseases such as stroke, myocardial infarction, valvular heart disease, trauma, children, and pregnancy. In this chapter we focus on recommendations related to general surgery, trauma surgery, and orthopedic surgery [28].

Table 14.8 ACCP guidelines: Grades of recommendation

Benefits vs. risks, burdens and costs
1. Clear benefit: strong recommendation
2. Unclear benefit: weaker recommendation
Methodological quality
A. RCT with consistent results
B. RCT, inconsistent results or methodological weakness
C. Observational studies
C+. Data overwhelmingly compelling

Adapted from [27]
The recommendations of the ACCP are based on published data and are graded in two groups. The methodological quality of the study is reflected in letters A–C
ACCP American College of Chest Physicians, *RCT* randomized controlled study

14.9.2 General Recommendations for the Prevention of DVT

The recommendation for the prevention of DVT are taken from the ACCP Evidence-Based Clinical Practice Guidelines (8th Edition) [28]:

14.9.2.1 Mechanical Methods of Thromboprophylaxis

- We recommend that mechanical methods of thromboprophylaxis be used primarily in patients with a high risk of bleeding (Grade 1A), or possibly as an

adjunct to anticoagulant-based thromboprophylaxis (Grade 2A).
- For patients receiving mechanical methods of thromboprophylaxis, we recommend that careful attention be directed toward ensuring the proper use of, and optimal adherence with, these methods (Grade 1A).

14.9.2.2 Aspirin
- We recommend against the use of aspirin alone as thromboprophylaxis against VTE for any patient group (Grade 1A).

14.9.2.3 Renal Impairment and Anticoagulant Dosing
- We recommend that renal function be considered when making decisions about the use and/or the dose of LMWH, fondaparinux, and other antithrombotic drugs that are cleared by the kidneys, particularly in elderly patients, patients with diabetes mellitus, and those at high risk for bleeding (Grade 1A). Depending on the circumstances, we recommend one of the following options in this situation: avoiding the use of an anticoagulant that bioaccumulates in the presence of renal impairment, using a lower dose of the agent, or monitoring the drug level or its anticoagulant effect (Grade 1B).

14.9.2.4 Neuraxial Anesthesia/Analgesia or Peripheral Nerve Blocks
- For all patients undergoing neuraxial anesthesia or analgesia, we recommend appropriate patient selection and caution when using anticoagulant thromboprophylaxis (Grade 1A).
- For patients receiving deep peripheral nerve blocks, we recommend that the same cautions considered for neuraxial techniques be applied when using anticoagulant thromboprophylaxis (Grade 1C).

14.10 General Surgery

- For low-risk general surgery patients who are undergoing minor procedures and have no additional thromboembolic risk factors, we recommend against the use of specific thromboprophylaxis other than early and frequent ambulation (Grade 1A).
- For moderate-risk general surgery patients who are undergoing a major procedure for benign disease, we recommend thromboprophylaxis with LMWH, low-dose unfractionated heparin (LDUH), or fondaparinux (each Grade 1A).
- For higher-risk general surgery patients who are undergoing a major procedure for cancer, we recommend thromboprophylaxis with LMWH, LDUH three times daily, or fondaparinux (each Grade 1A).
- For general surgery patients with multiple risk factors for VTE who are thought to be at particularly high risk, we recommend that a pharmacologic method (i.e., LMWH, LDUH three times daily, or fondaparinux) be combined with the optimal use of a mechanical method (i.e., GCS and/or IPC) (Grade 1C).
- For general surgery patients with a high risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis with properly fitted GCS or IPC (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).
- For patients undergoing major general surgical procedures, we recommend that thromboprophylaxis continue until discharge from hospital (Grade 1A). For selected high-risk general surgery patients, including some of those who have undergone major cancer surgery or have previously had VTE, we suggest that continuing thromboprophylaxis after hospital discharge with LMWH for up to 28 days be considered (Grade 2A).

14.11 Trauma and Orthopedic Surgery

14.11.1 Trauma

- For all major trauma patients, we recommend routine thromboprophylaxis if possible (Grade 1A).
- For major trauma patients in the absence of a major contraindication, we recommend that clinicians use LMWH thromboprophylaxis, starting as soon as it is considered safe to do so (Grade 1A). An acceptable alternative is the combination of LMWH and the optimal use of a mechanical method of thromboprophylaxis (Grade 1B).
- For major trauma patients, if LMWH thromboprophylaxis is contraindicated because of active bleeding or high risk for clinically important bleeding, we recommend that mechanical thromboprophylaxis with IPC, or possibly with GCS alone, be used

(Grade 1B). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).
- In trauma patients, we recommend against routine Doppler ultrasound (DUS) screening for asymptomatic DVT (Grade 1B). We do recommend DUS screening in patients who are at high risk for VTE (e.g., in the presence of a spinal cord injury [SCI], lower extremity or pelvic fracture, or major head injury), and who have received suboptimal thromboprophylaxis or no thromboprophylaxis (Grade 1C).
- For trauma patients, we recommend against the use of an inferior vena cava (IVC) filter as thromboprophylaxis (Grade 1C).
- For major trauma patients, we recommend the continuation of thromboprophylaxis until hospital discharge (Grade 1C). For trauma patients with impaired mobility who undergo inpatient rehabilitation, we suggest continuing thromboprophylaxis with LMWH or a VKA (target INR, 2.5; range, 2.0–3.0) (Grade 2C).

14.11.2 Acute Spinal Cord Injury

- For all patients with acute SCI, we recommend that routine thromboprophylaxis be provided (Grade 1A).
- For patients with acute SCI, we recommend thromboprophylaxis with LMWH, commenced once primary hemostasis is evident (Grade 1B). Alternatives include the combined use of IPC and either LDUH (Grade 1B) or LWMH (Grade 1C).
- For patients with acute SCI, we recommend the optimal use of IPC and/or GCS if anticoagulant thromboprophylaxis is contraindicated because of high bleeding risk early after injury (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).
- For patients with an incomplete SCI associated with evidence of a spinal hematoma on CT or MRI, we recommend the use of mechanical thromboprophylaxis instead of anticoagulant thromboprophylaxis at least for the first few days after injury (Grade 1C).
- Following acute SCI, we recommend against the use of LDUH alone (Grade 1A).
- For patients with SCI, we recommend against the use of an IVC filter as thromboprophylaxis (Grade 1C).
- For patients undergoing rehabilitation following acute SCI, we recommend the continuation of LMWH thromboprophylaxis or conversion to an oral VKA (INR target, 2.5; range, 2.0–3.0) (Grade 1C).

14.11.3 Burns

- For burn patients who have additional risk factors for VTE including one or more of the following: advanced age, morbid obesity, extensive or lower extremity burns, concomitant lower extremity trauma, use of a femoral venous catheter, and/or prolonged immobility, we recommend routine thromboprophylaxis if possible (Grade 1A).
- For burn patients who have additional risk factors for VTE, if there are no contraindications, we recommend the use of either LMWH or LDUH, starting as soon as it is considered safe to do so (Grade 1C).
- For burn patients who have a high bleeding risk, we recommend mechanical thromboprophylaxis with GCS and/or IPC until the bleeding risk decreases (Grade 1A).

14.11.4 Critical Care

- For patients admitted to a critical care unit, we recommend routine assessment for VTE risk and routine thromboprophylaxis in most (Grade 1A) cases.
- For critical care patients who are at moderate risk for VTE (e.g., medically ill or postoperative general surgery patients), we recommend using LMWH or LDUH thromboprophylaxis (Grade 1A).
- For critical care patients who are at higher risk (e.g., following major trauma or orthopedic surgery), we recommend LMWH thromboprophylaxis (Grade 1A).
- For critical care patients who are at high risk for bleeding, we recommend the optimal use of mechanical thromboprophylaxis with GCS and/or IPC at least until the bleeding risk decreases (Grade 1A). When the high bleeding risk decreases, we recommend

that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

14.11.5 Hip Fracture Surgery

- For patients undergoing hip fracture surgery (HFS), we recommend routine thromboprophylaxis using fondaparinux (Grade 1A), LMWH (Grade 1B), adjusted-dose VKA (INR target, 2.5; INR range, 2.0–3.0) [Grade 1B], or LDUH (Grade 1B).
- For patients undergoing HFS, we recommend against the use of aspirin alone (Grade 1A).
- For patients undergoing HFS in whom surgery is likely to be delayed, we recommend that thromboprophylaxis with LMWH or LDUH be initiated during the time between hospital admission and surgery (Grade 1C).
- For patients undergoing HFS who have a high risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

14.11.6 Elective Hip Replacement

- For patients undergoing elective THR, we recommend the routine use of one of the following anticoagulant options: (1) LMWH (at a usual high-risk dose, started 12 h before surgery or 12–24 h after surgery, or 4–6 h after surgery at half the usual high-risk dose and then increasing to the usual high-risk dose the following day); (2) fondaparinux (2.5 mg started 6–24 h after surgery); or (3) adjusted- dose VKA started preoperatively or the evening of the surgical day (INR target, 2.5; INR range, 2.0–3.0) (all Grade 1A).
- For patients undergoing THR, we recommend against the use of any of the following: aspirin, dextran, LDUH, GCS, or VFP as the sole method of thromboprophylaxis (all Grade 1A).
- For patients undergoing THR who have a high risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis with the VFP or IPC (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

14.11.7 Elective Knee Replacement

- For patients undergoing TKR, we recommend routine thromboprophylaxis using LMWH (at the usual high-risk dose), fondaparinux, or adjusted-dose VKA (INR target, 2.5; INR range, 2.0–3.0) (all Grade 1A).
- For patients undergoing TKR, the optimal use of IPC is an alternative option to anticoagulant thromboprophylaxis (Grade 1B).
- For patients undergoing TKR, we recommend against the use of any of the following as the only method of thromboprophylaxis: aspirin (Grade 1A), LDUH (Grade 1A), or VFP (Grade 1B).
- For patients undergoing TKR who have a high risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis with IPC (Grade 1A) or VFP (Grade 1B). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

14.11.8 Knee Arthroscopy

- For patients undergoing knee arthroscopy who do not have additional thromboembolic risk factors, we suggest that clinicians do not routinely use thromboprophylaxis other than early mobilization (Grade 2B).
- For patients undergoing arthroscopic knee surgery who have additional thromboembolic risk factors or following a complicated procedure, we recommend thromboprophylaxis with LMWH (Grade 1B).

14.12 Timing Duration of Prophylaxis

14.12.1 Commencement of Thromboprophylaxis

- For patients receiving LMWH as thromboprophylaxis in major orthopedic surgery, we recommend starting it either preoperatively or postoperatively (Grade 1A).
- For patients receiving fondaparinux as thromboprophylaxis in major orthopedic surgery, we

recommend starting either 6–8 h after surgery or the next day (Grade 1A).

14.12.2 Duration of Thromboprophylaxis

- For patients undergoing THR, TKR, or HFS, we recommend thromboprophylaxis with one of the recommended options for at least 10 days (Grade 1A).
- For patients undergoing THR, we recommend that thromboprophylaxis be extended beyond 10 days and up to 35 days after surgery (Grade 1A). The recommended options for extended thromboprophylaxis in THR include LMWH (Grade 1A), a VKA (Grade 1B), or fondaparinux (Grade 1C).
- For patients undergoing TKR, we suggest that thromboprophylaxis be extended beyond 10 days and up to 35 days after surgery (Grade 2B). The recommended options for extended thromboprophylaxis in TKR include LMWH (Grade 1C), a VKA (Grade 1C), or fondaparinux (Grade 1C).
- For patients undergoing HFS, we recommend that thromboprophylaxis be extended beyond 10 days and up to 35 days after surgery (Grade 1A). The recommended options for extended thromboprophylaxis in HFS include fondaparinux (Grade 1A), LMWH (Grade 1C), or a VKA (Grade 1C).

14.12.3 Vena Cava Filter

- For trauma patients, we recommend against the use of an IVC filter as thromboprophylaxis (Grade 1C) [28].
- In trauma patients, management of thromboprophylaxis may be problematical mainly because of concern about potential bleeding complications associated with anticoagulant treatment. For these reasons, the interest to use IVC filters for PE prophylaxis has grown considerably in the past few years [29]. Unfortunately, there are no randomized trials that demonstrate a clear benefit of IVC filter insertion in trauma patients [30]. Permanent filters have been shown to be effective, but have a number of long-term complications such as filter thrombosis or migration. Therefore, indications for placement of permanent filters should be accurately evaluated, especially in patients with a short period of contraindication to anticoagulation.
- In a large prospective study, 127 polytrauma patients underwent the prophylactic placement of retrievable IVC filters without any complications [31]. Sixty-six patients underwent uneventful retrieval of IVC filters after a mean of 71 days (5–116 days) from implantation, whereas in 45 patients, retrieval was not attempted (41 because of contraindication to anticoagulation and four because of trapped emboli within the filter). In addition, three small previously published studies reported a low rate of PE in patients with severe polytrauma who underwent prophylactic IVC filter insertion [30]. Large systematic reviews on the use of IVC filters in the primary and secondary prophylaxis of VTE have recently been published by Hann [32] and Imberti [30].

14.13 Antithrombotic Therapy of DVT

The recommendations for the treatment of DVT are taken from ACCP Evidence-Based Clinical Practice Guidelines (8th Edition) [33]:

14.13.1 Initial Anticoagulation of Acute DVT of the Leg

- For patients with objectively confirmed DVT, we recommend short-term treatment with SC LMWH (Grade 1A), IV unfractionated heparin (UFH) (Grade 1A), monitored SC UFH (Grade 1A), fixed-dose SC UFH (Grade 1A), or SC fondaparinux (Grade 1A) rather than no such short-term treatment.
- For patients with a high clinical suspicion of DVT, we recommend treatment with anticoagulants while awaiting the outcome of diagnostic tests (Grade 1C).
- In patients with acute DVT, we recommend initial treatment with LMWH, UFH, or fondaparinux for at least 5 days and until the INR is >2.0 for 24 h (Grade 1C).
- In patients with acute DVT, we recommend initiation of VKA together with LMWH, UFH, or

fondaparinux on the first treatment day rather than delayed initiation of VKA (Grade 1A).

14.13.2 IV UFH for the Initial Treatment of DVT

- In patients with acute DVT, if IV UFH is chosen, we recommend that after an initial IV bolus (80 U/kg or 5,000 U), it be administered by continuous infusion (initially at a dose of 18 U/kg/h or 1,300 U/h) with dose adjustment to achieve and maintain an activated partial thromboplastin time (aPTT) prolongation that corresponds to plasma heparin levels of 0.3–0.7 IU/mL anti-Xa activity by the amidolytic assay rather than administration as IV boluses throughout treatment, or administration without coagulation monitoring (Grade 1C).

14.13.3 SC UFH Compared with IV Heparin for the Initial Treatment of DVT

- In patients with acute DVT, if monitored SC UFH is chosen, we recommend an initial dose of 17,500 U, or a weight-adjusted dose of about 250 U/kg bid, with dose adjustment to achieve and maintain an aPTT prolongation that corresponds to plasma heparin levels of 0.3–0.7 IU/mL anti-Xa activity when measured 6 h after injection rather than starting with a smaller initial dose (Grade 1C).
- In patients with acute DVT, if fixed-dose, unmonitored SC UFH is chosen, we recommend an initial dose of 333 U/Kg followed by 250 U/kg bid rather than non–weight-based dosing (Grade 1C).

14.13.4 LMWH for the Initial Treatment of DVT

- In patients with acute DVT, we recommend initial treatment with LMWH SC once or twice daily, as an outpatient if possible (Grade 1C), or as an inpatient if necessary (Grade 1A), rather than treatment with IV UFH.
- In patients with acute DVT treated with LMWH, we recommend against routine monitoring with anti-factor Xa level measurements (Grade 1A).
- In patients with acute DVT and severe renal failure, we suggest UFH over LMWH (Grade 2C).

14.13.5 Catheter-Directed Thrombolysis for Acute DVT

- In selected patients with extensive acute proximal DVT (e.g., iliofemoral DVT, symptoms for <14 days, good functional status, life expectancy of >1 year) who have a low risk of bleeding, we suggest that catheter-directed thrombolysis (CDT) may be used to reduce acute symptoms and post-thrombotic morbidity if appropriate expertise and resources are available (Grade 2B).
- After successful CDT in patients with acute DVT, we suggest correction of underlying venous lesions using balloon angioplasty and stents (Grade 2C).
- We suggest pharmacomechanical thrombolysis (e.g., with inclusion of thrombus fragmentation and/or aspiration) in preference to CDT alone to shorten treatment time if appropriate expertise and resources are available (Grade 2C).
- After successful CDT in patients with acute DVT, we recommend the same intensity and duration of anticoagulant therapy as for comparable patients who do not undergo CDT (Grade 1C).

14.13.6 Systemic Thrombolytic Therapy for Acute DVT

- In selected patients with extensive proximal DVT (e.g., symptoms for <14 days, good functional status, life expectancy of >1 year) who have a low risk of bleeding, we suggest that systemic thrombolytic therapy be used to reduce acute symptoms and post-thrombotic morbidity if CDT is not available (Grade 2C).

14.13.7 Percutaneous Venous Thrombectomy

- In patients with acute DVT, we suggest that they should not be treated with percutaneous mechanical thrombectomy alone (Grade 2C).

14.13.8 Operative Venous Thrombectomy for Acute DVT

- In selected patients with acute iliofemoral DVT (e.g., symptoms for <7 days, good functional status, and life expectancy of >1 year), we suggest that operative venous thrombectomy be used to reduce acute symptoms and postthrombotic morbidity if appropriate expertise and resources are available (Grade 2B). If such patients do not have a high risk of bleeding, we suggest that catheter-directed thrombolysis is usually preferable to operative venous thrombectomy (Grade 2C).
- In patients who undergo operative venous thrombectomy, we recommend the same intensity and duration of anticoagulant therapy afterwards as for comparable patients who do not undergo venous thrombectomy (Grade 1C).

14.13.9 Vena Caval Filters for the Initial Treatment of DVT

- For patients with DVT, we recommend against the routine use of a vena cava filter in addition to anticoagulants (Grade 1A).
- For patients with acute proximal DVT, if anticoagulant therapy is not possible because of the risk of bleeding, we recommend placement of an IVC filter (Grade 1C).
- For patients with acute DVT who have an IVC filter inserted as an alternative to anticoagulation, we recommend that they should subsequently receive a conventional course of anticoagulant therapy if their risk of bleeding resolves (Grade 1C).

14.13.10 Immobilization for the Treatment of Acute DVT

- In patients with acute DVT, we recommend early ambulation in preference to initial bed rest when this is feasible (Grade 1A).

14.13.11 Duration of Anticoagulant Therapy

- For patients with DVT secondary to a transient (reversible) risk factor, we recommend treatment with a VKA for 3 months over treatment for shorter periods (Grade 1A).
- For patients with unprovoked DVT, we recommend treatment with a VKA for at least 3 months (Grade 1A). We recommend that after 3 months of anticoagulant therapy, all patients with unprovoked DVT should be evaluated for the risk-to-benefit ratio of long-term therapy (Grade 1C). For patients with a first unprovoked VTE that is a proximal DVT, and in whom risk factors for bleeding are absent and for whom good anticoagulant monitoring is achievable, we recommend long-term treatment (Grade 1A). Values and preferences: This recommendation attaches a relatively high value to prevention of recurrent VTE and a lower value to the burden of long-term anticoagulant therapy.
- For patients with a second episode of unprovoked VTE, we recommend long-term treatment (Grade 1A). For patients with a first isolated distal DVT that is unprovoked, we suggest that 3 months of anticoagulant therapy is sufficient rather than indefinite therapy (Grade 2B).
- For patients with DVT and cancer, we recommend LMWH for the first 3–6 months of long-term anticoagulant therapy (Grade 1A). For these patients, we recommend subsequent anticoagulant therapy with VKA or LMWH indefinitely or until the cancer is resolved (Grade 1C).
- In patients who receive long-term anticoagulant treatment, the risk-benefit ratio of continuing such treatment should be reassessed in the individual patient at periodic intervals (Grade 1C).

14.13.12 Intensity of Anticoagulant Effect

- In patients with DVT, we recommend that the dose of VKA be adjusted to maintain a target INR of 2.5 (range, 2.0–3.0) for all treatment durations (Grade 1A). For patients with unprovoked DVT who have a strong preference for less frequent INR testing to monitor their therapy, after the first 3 months of conventional-intensity anticoagulation (INR range, 2.0–3.0), we recommend low-intensity therapy (range, 1.5–1.9) with less frequent INR monitoring over stopping treatment (Grade 1A). We recommend against high-intensity VKA therapy (INR range, 3.1–4.0) compared to an INR range of 2.0–3.0 (Grade 1A).

14.13.13 Treatment of Asymptomatic DVT of the Leg

- In patients who are unexpectedly found to have asymptomatic DVT, we recommend the same initial and long-term anticoagulation as for comparable patients with symptomatic DVT (Grade 1C).

14.13.14 Elastic Stockings and Compression Bandages to Prevent PTS

- For a patient who has had a symptomatic proximal DVT, we recommend the use of an elastic compression stocking with an ankle pressure gradient of 30–40 mmHg if feasible (Grade 1A). Compression therapy, which may include use of bandages acutely, should be started as soon as feasible after starting anticoagulant therapy and should be continued for a minimum of 2 years, and longer if patients have symptoms of PTS. (Note: feasibility, both short and long term, refers to ability of patients and their caregivers to apply and remove stockings.) Values and preferences: this recommendation attaches a relatively high value to long-term prevention of the PTS and a low value to the burden (e.g., inconvenience or discomfort) associated with wearing stockings.

14.13.15 Physical Treatment of PTS Without Venous Leg Ulcers

- For patients with severe edema of the leg resulting from PTS, we suggest a course of IPC (Grade 2B).
- For patients with mild edema of the leg as a result of PTS, we suggest the use of elastic compression stockings (Grade 2C).

14.13.16 Physical Treatment of Venous Leg Ulcers

- In patients with venous ulcers resistant to healing with wound care and compression, we suggest the addition of IPC (Grade 2B).

14.13.17 Hyperbaric Oxygen and the Management of Patients with Venous Ulcers

- For patients with venous ulcers, we suggest that hyperbaric oxygen should not be used (Grade 2B).

14.13.18 Pentoxifylline

- In patients with venous leg ulcers, we suggest pentoxifylline, 400 mg po tid, in addition to local care and compression and/or IPC (Grade 2B).

14.13.19 Micronized Purified Flavonoid Fraction or Sulodexide for the Treatment of Venous Leg Ulcers

- In patients with persistent venous ulcers, we suggest that rutosides, in the form of micronized purified flavonoid fraction administered orally, or sulodexide administered intramuscularly and then orally, be added to local care and compression (Grade 2B).

14.14 IV or SC UFH, SC LMWH, SC Fondaparinux, and VKA for the Initial Treatment of PE

- For patients with objectively confirmed PE, we recommend short-term treatment with SC LMWH (Grade 1A), IV UFH (Grade 1A), monitored SC UFH (Grade 1A), fixed-dose SC UFH (Grade 1A), or SC fondaparinux (Grade 1A) rather than no such acute treatment. Patients with acute PE should also be routinely assessed for treatment with thrombolytic therapy.
- For patients in whom there is a high clinical suspicion of PE, we recommend treatment with anticoagulants while awaiting the outcome of diagnostic tests (Grade 1C).
- In patients with acute PE, we recommend initial treatment with LMWH, UFH, or fondaparinux for at least 5 days and until the INR is >2.0 for at least 24 h (Grade 1C).
- In patients with acute PE, we recommend initiation of VKA together with LMWH, UFH, or

fondaparinux on the first treatment day rather than delayed initiation of VKA (Grade 1A).

- In patients with acute PE, if IV UFH is chosen, we recommend that after an initial IV bolus (80 U/kg or 5,000 U), it should be administered by continuous infusion (initially at dose of 18 U/kg/h or 1,300 U/h) with dose adjustment to achieve and maintain an aPTT prolongation that corresponds to plasma heparin levels of 0.3–0.7 IU/mL anti-Xa activity by the amidolytic assay rather than administration as IV boluses throughout treatment, or administration without coagulation monitoring (Grade 1C).
- In patients with acute PE, if monitored SC UFH is chosen, we recommend an initial dose of 17,500 U, or a weight-adjusted dose of approximately 250 U/kg bid, with dose adjustment to achieve and maintain an aPTT prolongation that corresponds to plasma heparin levels of 0.3–0.7 IU/mL anti-Xa activity when measured 6 h after injection rather than starting with a smaller initial dose (Grade 1C).
- In patients with acute PE, if fixed-dose, unmonitored SC UFH is chosen, we recommend an initial dose of 333 U/Kg followed by a twice daily dose of 250 U/kg rather than non–weight-based dosing (Grade 1C).
- In patients with acute nonmassive PE, we recommend initial treatment with LMWH over IV UFH (Grade 1A). In patients with massive PE, in other situations where there is concern about SC absorption, or in patients for whom thrombolytic therapy is being considered or planned, we suggest IV UFH over SC LMWH, SC fondaparinux, or SC UFH (Grade 2C).
- In patients with acute PE treated with LMWH, we recommend against routine monitoring with anti-factor Xa level measurements (Grade 1A).
- In patients with acute PE and severe renal failure, we suggest UFH over LMWH (Grade 2C).

14.14.1 Systemically and Locally Administered Thrombolytic Therapy for PE

- All patients with PE should undergo rapid risk stratification (Grade 1C). For patients with evidence of hemodynamic compromise, we recommend use of thrombolytic therapy unless there are major contraindications owing to bleeding risk (Grade 1B). Thrombolysis in these patients should not be delayed because irreversible cardiogenic shock may ensue. In selected high-risk patients without hypotension who are judged to have a low risk of bleeding, we suggest administration of thrombolytic therapy (Grade 2B). The decision to use thrombolytic therapy depends on the clinician's assessment of PE severity, prognosis, and risk of bleeding. For the majority of patients with PE, we recommend against using thrombolytic therapy (Grade 1B).
- In patients with acute PE, when a thrombolytic agent is used, we recommend that treatment be administered via a peripheral vein rather than placing a pulmonary artery catheter to administer treatment (Grade 1B).
- In patients with acute PE, with administration of thrombolytic therapy, we recommend use of regimens with short infusion times (e.g., a 2-h infusion) over those with prolonged infusion times (e.g., a 24-h infusion) (Grade 1B).

14.14.2 Catheter Extraction or Fragmentation for the Initial Treatment of PE

- For most patients with PE, we recommend against use of interventional catheterization techniques (Grade 1C). In selected highly compromised patients who are unable to receive thrombolytic therapy because of bleeding risk, or whose critical status does not allow sufficient time for systemic thrombolytic therapy to be effective, we suggest use of interventional catheterization techniques if appropriate expertise is available (Grade 2C).

14.14.3 Pulmonary Embolectomy for the Initial Treatment of PE

- In selected patients who are highly compromised and who are unable to receive thrombolytic therapy because of bleeding risk, or whose critical status does not allow sufficient time for systemic thrombolytic therapy to be effective, we suggest that pulmonary embolectomy be used if appropriate expertise is available (Grade 2C).

14.14.4 Vena Caval Filters for the Initial Treatment of PE

- For most patients with PE, we recommend against the routine use of a vena caval filter in addition to anticoagulants (Grade 1A).
- In patients with acute PE, if anticoagulant therapy is not possible because of the risk of bleeding, we recommend placement of an IVC filter (Grade 1C).
- For patients with acute PE who have an IVC filter inserted as an alternative to anticoagulation, we recommend that they should subsequently receive a conventional course of anticoagulant therapy if their risk of bleeding resolves (Grade 1C).

14.14.5 Long-Term Treatment of Acute PE

- For patients with PE secondary to a transient (reversible) risk factor, we recommend treatment with a VKA for 3 months over treatment for shorter periods (Grade 1A).
- For patients with unprovoked PE, we recommend treatment with a VKA for at least 3 months (Grade 1A). We recommend that after 3 months of anticoagulant therapy, all patients with unprovoked PE should be evaluated for the risk-benefit ratio of long-term therapy (Grade 1C). For patients with a first unprovoked episode of VTE that is a PE, and in whom risk factors for bleeding are absent and for whom good anticoagulant monitoring is achievable, we recommend long-term treatment (Grade 1A). Values and preferences: This recommendation attaches a relatively high value to prevention of recurrent VTE and a lower value to the burden of long-term anticoagulant therapy. For patients with a second episode of unprovoked VTE, we recommend long-term treatment (Grade 1A).
- For patients with PE and cancer, we recommend LMWH for the first 3–6 months of long-term anticoagulant therapy (Grade 1A). For these patients, we recommend subsequent anticoagulant therapy with VKA or LMWH indefinitely or until the cancer is resolved (Grade 1C).
- In patients who receive long-term anticoagulant treatment, the risk-benefit ratio of continuing such treatment should be reassessed in the individual patient at periodic intervals (Grade 1C).
- In patients with PE, we recommend that the dose of VKA be adjusted to maintain a target INR of 2.5 (INR range, 2.0–3.0) for all treatment durations (Grade 1A). For patients with unprovoked PE who have a strong preference for less frequent INR testing to monitor their therapy, after the first 3 months of conventional-intensity anticoagulation (INR range, 2.0–3.0), we recommend low-intensity therapy (INR range, 1.5–1.9) with less frequent INR monitoring over stop- ping treatment (Grade 1A). We recommend against high-intensity VKA therapy (INR range, 3.1–4.0) compared with an INR range of 2.0–3.0 (Grade 1A).
- In patients who are unexpectedly found to have asymptomatic PE, we recommend the same initial and long-term anticoagulation as for comparable patients with symptomatic PE (Grade 1C).

14.14.6 Pulmonary Thromboendarterectomy, VKA, and Vena Caval Filter for the Treatment of Chronic Thromboembolic Pulmonary Hypertension

- In selected patients with CTPH such as those with central disease under the care of an experienced surgical/medical team, we recommend pulmonary thromboendarterectomy (Grade 1C).
- For all patients with CTPH, we recommend lifelong treatment with a VKA targeted to an INR of 2.0–3.0 (Grade 1C).
- For patients with CTPH undergoing pulmonary thromboendarterectomy, we suggest the placement of a permanent vena caval filter before or at the time of the procedure (Grade 2C).
- For patients with inoperable CTPH, we suggest referral to a center with expertise in pulmonary hypertension so that patients can be evaluated for alternative treatments, such as vasodilator therapy or balloon pulmonary angioplasty (Grade 2C).

14.14.7 Treatment of Superficial Vein Thrombosis

- For patients with spontaneous superficial vein thrombosis (SVT), we suggest prophylactic or intermediate doses of LMWH (Grade 2B) or

intermediate doses of UFH (Grade 2B) for at least 4 weeks. We suggest that as an alternative to 4 weeks of LMWH or UFH, VKA (target INR, 2.5; range, 2.0–3.0) can be overlapped with 5 days of UFH and LMWH and continued for 4 weeks (Grade 2C). We suggest that oral nonsteriodal antiinflammatory drugs should not be used in addition to anticoagulation (Grade 2B). We recommend medical treatment with anticoagulants over surgical treatment (Grade 1B). Remark: It is likely that less extensive SVT (i.e., where the affected venous segment is short in length or further from the saphenofemoral junction) does not require treatment with anticoagulants. It is reasonable to use oral or topical nonsteriodal anti-inflammatory drugs for symptom control in such cases.

14.15 Controversy: Guideline debate ACCP vs. AAOS?

The ACCP guidelines are widely used in North America and worldwide, and they have had a major impact on the use of thromboprophylaxis in patients undergoing total hip or knee arthroplasty. However, orthopedic surgeons have expressed concerns regarding the utility of and applicability to their practices of guidelines from ACCP for thromboprophylaxis in the settings of total hip and total knee arthroplasty [34]. These concerns include the acceptance of venographically assessed asymptomatic deep venous thrombosis by the ACCP as a meaningful clinical trial endpoint and a potential underestimation of the true risk of major bleeding and wound complication in unselected patient populations outside carefully controlled clinical trials. Because symptomatic PE is rare after THA and TKA, the American Academy of Orthopaedic Surgeons (AAOS) has developed a clinical practice guideline focused on preventing this complication while minimizing the risk of bleeding due to pharmacologic prophylaxis [34].

The most important disagreement between the ACCP and AAOS guidelines concerns the validity of DVT as a surrogate for PE. Both guidelines accept that the most important goal of thromboprophylaxis in patients undergoing hip or knee replacement is to prevent PE. The ACCP guidelines include asymptomatic (and symptomatic) DVT detected by venography as a measure of the efficacy of thromboprophylaxis, whereas the AAOS rejects DVT as a valid outcome because the panelists considered the link between DVT and PE to be unproven [35].

Eikelboom et al. [35] argue that the AAOS position is inconsistent with evidence (1) from imaging studies that link DVT with PE and (2) from clinical studies that demonstrate a parallel reduction of DVT and PE when antithrombotic agents are compared with placebo or untreated controls. According to Eikelboom, the AAOS panel ignored the randomized data demonstrating that thromboprophylaxis reduces both DVT and PE, and many of their recommendations are based on expert opinion and lack a scientific basis [35].

Conversely, Brown [36] criticizes the methodological flaws incorporated in the ACCP guidelines: (1) exclusion of randomized controlled trials without venographic outcome assessment; (2) incomplete outcome measures without inclusion criteria requiring measurement of symptomatic DVT, PE, fatal PE, major operative site bleeding complications, and major non-surgical site bleeding complications; (3) no quantitative analyses (meta-analysis or pooled analysis) of randomized controlled trials to estimate incidence of symptomatic DVTs, PEs, fatal PEs, major operative site bleeding complications, and major non-surgical site bleeding complications; and (4) potential conflicts of interest for multiple members of the guideline drafting committee [36].

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Muscle Injuries

15

Kuno Weise

15.1 Basics

The weight-bearing and locomotor system of the human body is basically composed of the skeletal muscles and of the systems that transfer the power of the muscles (i.e., the tendons and aponeuroses) in the torso, spine, and extremities. The construction and shape of individual muscles and their position in relation to the joints determine their function.

15.1.1 Anatomy

The microstructure of a muscle, with its individual mixture of different types of fiber, has a substantial effect on its physiological properties. While to a great extent the muscles can be trained, tendons and their origins in the skeleton cannot be strengthened in the same way, which explains their tendency toward ruptures and strain injuries. The copious blood supply to the musculature is the reason for its excellent capacity for regeneration, although increasingly severe damage to muscle fibers means that full recovery is no longer possible. In such cases fibrous scar tissue develops in the region of the rupture.

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15.1.2 Physiology and Pathophysiology

Muscle injuries can be subdivided according to their severity and thus their capacity for complete regeneration, or for a type of partial healing with scar formation, as follows:

- *Sore muscles* – microinjuries of the white, fast-twitch muscle fibers caused by overstrain. The tearing of parts of the muscle fibril accompanied by edema and the secretion of pain-inducing agents in the extracellular space are responsible for the symptoms. By reducing the intensity of the strain using stretching and mild dynamic-concentric contractions, complete recovery from sore muscle can be achieved.
- *Muscle stretching/overstretching* – the limit of the elasticity and stability of the muscle fibers is reached; complete recovery can generally be obtained. The distinction between overstretched and pulled muscle involving scarring and partial recovery is blurred.
- *Pulled muscle or muscle strain* – distinguished by the tearing of individual contractile elements. A complete return to the patient's former condition is impossible after this, the most frequent muscle injury. It is always repaired with scar tissue. Again, the distinction between muscle fiber rupture is blurred.
- *Tearing of muscle fibers* – defined as a more extensive lesion resulting from exceeding the limits of elasticity and stability of the muscle fiber bundles. It always results, to a greater or lesser degree, in partial repair with scar tissue.

From a pathophysiological point of view, sore muscles, pulled muscles, and the tearing of muscle fibers are considered to be similar lesions differing in severity.

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- *Myorrhexis or rupture of a muscle* – can give the impression of a partial or complete gap in the continuity of a muscle and represents a further increase in severity in injuries to the skeletal musculature. Depending on the extent of the lesion in relation to the total cross-section of the muscle belly, surgical treatment may be indicated under certain circumstances. There is always some degree of partial repair regardless of the treatment strategy.
- *Myocele or muscle herniation* – always results from blunt trauma, causing a rent in the fascia. As the muscle contracts, herniation occurs, causing much pain. Surgical closure of the rent in the fascia yields good results if the suturing is resilient.
- *Myositis ossificans* – also caused by blunt trauma, where the blunt injury to the musculature leads to metaplasia of cells from the hematoma, resulting in the formation of osteoblasts. These are responsible for dystopic ossification.
- *Rupture of a muscle at its origin* – can be partial or complete and, as a rule, is easy to diagnose. It is particularly frequent in young people and can manifest as bony lesions that are detectable on radiographs (e.g., rupture of the rectus femoris muscle at the pelvis) [1].

15.1.3 Specific Causes of Muscle Injuries

The causes of muscle injuries and damage range from acute or chronic overstrain, uncoordinated movement causing sudden changes in tension of the contractile elements, increased resistance or tension in the antagonistic muscles, to blunt trauma. The predisposing factors for muscle injuries or damage are as follows:

- Insufficient warm up/stretching before sport activities
- Inadequate blood supply to the musculature (cold)
- Inadequate training
- Poor technique, bad equipment
- Generalized disease

The disparity between the condition of the muscle and the demands made of it is the cause of indirect lesions. The individual forms and severity of muscle injuries are considered by most experts to be different manifestations of similar pathogeneses and mechanisms. Given the blurred distinctions between diverse muscle injuries, damage is considered to be either reversible (sore muscles, stretching, and overstretching) or irreversible (tearing of muscle fibers, rupture of a muscle). Pulled muscle involving a greater degree of pathologically and anatomically detectable overstretching, extending to rupture of individual contractile elements with subsequent scar tissue, represents the boundary between the two groups. In contrast, direct muscle trauma is a result of local damaging forces and involves a risk of compartment syndrome or myositis ossificans.

Most muscle injuries occur during rapid acceleration or takeoff during poorly coordinated sequences of movements and under unfavorable general conditions in the context of sport activity (e.g., track and field, ball and racket sports, and martial arts). Most direct lesions of the skeletal musculature occur in contact sports such as football or martial arts.

In accordance with the injury hypothesis, sore muscles are considered to be partial damage to the muscle fibrils in the sense of overstrain, accompanied by local edema, and are completely reversible [2].

15.1.4 Basic Principles of the Clinical Examination

The principle symptom in the diagnosis of muscle injuries is pain. The pain ranges from an unpleasant dragging pain on stretching the muscles, to the generally less severe pain accompanying a pulled muscle, and finally to the sudden burst of debilitating pain that occur when a muscle or muscle fiber is torn. In contrast, ruptures are generally less painful. The intensity of the pain is an indicator of the extent of the injury in the muscle. After documenting patient history, local inspection and palpation are the foundations of clinical diagnosis. Swelling, hematoma, changes in muscle relief, painful antalgic postures, and loss of function as well as a palpable gap in the continuity of the muscle belly (dimpling) are typical characteristics of acute muscle injury. Local pressure and indirect muscle tension pain are further diagnostic parameters.

15.1.5 Diagnosis by Imaging Procedures

The use of ultrasound to visualise the nature, localization, and extent of muscle injury plays an essential part in diagnosis as well as in the choice of therapeutic procedure. The size of the gap in muscle continuity, visualized in this way, as well as that of the accompanying hematoma, influence the choice of further procedures. In unclear cases, an additional magnetic

resonance imaging (MRI) scan can provide detailed information about the extent of injury. Radiographs, particularly of the adjacent joints, are sometimes indicated; they are obtained if myositis ossificans is suspected.

If compartment syndrome is suspected, measurement of the pressure in the compartment is indicated in addition to clinical diagnosis on the basis of pain and swelling and shiny skin.

Laboratory tests to determine muscle-specific enzymes are indicated only in the case of massive, extensive, muscle contusions in the context of high-speed or crush injuries. What is known as crush syndrome, with its life-threatening secondary phenomena (crush kidney), may be a consequence of these types of traumatic events. Electrodiagnostic testing such as electromyography is indicated only if there is accompanying nerve injury.

15.1.6 Organ-Specific Imaging

Apart from the ultrasound procedure described above as the standard procedure, no further imaging procedures are necessary except MRI, which is sometimes required, and radiography, which is ordered to exclude bone injuries.

15.2 Special Muscle Injuries and Damage to the Upper Extremity

- Deltoid muscle
- Biceps brachii muscle
- Triceps brachii muscle
- Compartment syndrome in the forearm

Muscle injuries in the region of the upper extremity generally give the impression of a strain or tear in the fiber, and less frequently of a partial rupture in the belly of the muscle. A compartment syndrome in the lower arm develops because of increased pressure in the fascial compartments as a result of edema and compression of the arterioles or venules. In general, injuries to the musculature of the upper extremity are rare. In contrast, acute lesions or damage induced by degeneration to their tendinous origins occur more frequently. Compartment syndromes in the forearm are concomitant phenomena of more severe, local, blunt force trauma. While indirect damage tends to occur in the context of sport activity (e.g., gymnastics, throwing sports, boxing), direct muscle traumas are observed predominantly in the context of industrial or road traffic accidents (e.g., trapping the forearm in a machine).

Typical symptoms include pain of varying severity, local swelling and hematoma, as well as impaired function. Ultrasound can be used to detect the gap in muscle continuity and edema and/or hematoma.

Characteristic symptoms of compartmental syndrome in the forearm are increasing pain that does not respond to pain relieving measures, extensive swelling with shiny skin, and the onset of decreased sensation with impaired muscle function at the periphery.

The development of myositis ossificans is generally a result of a local traumatization or a compartment syndrome, which is either undiagnosed and untreated or incorrectly diagnosed and treated. This could result in permanent impairment of function.

15.2.1 Diagnosis

15.2.1.1 Recommended Diagnostic Measures in Accordance with the European Standard

- Inspection: swelling, discoloration from hematoma, abnormal muscle contours, antalgic postures, indirect muscle tension pain
- Palpation: pain on pressure, palpable dimpling (gaps in continuity)

15.2.1.2 Additional Useful Diagnostic Procedures

- Ultrasound: imaging the localization and extent of the gap in continuity and accompanying edema/hematoma
- Radiographs to exclude bone injury
- MRI: indicated only in individual cases to confirm diagnosis or to select the therapeutic procedure
- Measurement of compartment pressure: when compartment syndrome is suspected

15.2.2 Treatment

15.2.2.1 Conservative Treatment

Recommended Therapeutic Measures in Accordance with the European Standard

Muscle injuries to the upper extremity are the domain of conservative treatment. As with all muscle injuries,

short-term immobilization (e.g., in a Desault or Gilchrist dressing) with local application of cold and concomitant anti-inflammatory treatment are indicated, followed by follow-up physiotherapy with muscular rehabilitation and manual therapy.

Additional Useful Therapy Options

The decision between conservative and surgical treatment for muscle tears can generally be made by taking the following criteria into account:

In favor of surgical care:

- Better assessment of the severity of the injury
- Potential evacuation of the hematoma
- Muscle length restoration through suturing
- Less scar tissue formation and thus better contractility
- Reduced rate of recurrent tears

15.2.2.2 Surgical Treatment

Recommended Therapeutic Measures in Accordance with the European Standard

The indication for a surgical procedure in the event of muscle tears to the upper extremity depends on the extent of the tear and its loss of function. Incomplete or complete muscle tears, especially in competitive athletes are considered indications for a surgical procedure, while partial tears, particularly in the deltoid muscle and triceps muscle need surgery only when a large hematoma has developed. In contrast, complete rupture of the biceps muscle at the tendon is an indication for surgical repair.

A manifest compartment syndrome is always an indication for surgery as this requires emergency surgery. The increased pressure in the muscle compartments should be diagnosed at the stage when it represents a threatening compartment syndrome and in certain cases prophylactic fasciotomy should be performed. The complete opening of all affected muscle compartments is an indispensable precondition for avoiding irreversible damage. Secondary closure after the swelling has regressed is achieved by direct suture or split-thickness skin graft [3].

Additional Useful Surgical Measures

An effusion of blood in the acute stage or non-absorption of the effusion can be an indication for evacuation and drainage of the hematoma and, in appropriate cases, can be combined with the intermittent application of a synthetic material such as Coldex® with drainage. Secondary restoration of continuity to the biceps or triceps brachii muscle is likely to be difficult because of possible shortening.

15.2.3 Differential Diagnosis

These infrequent muscle injuries to the upper extremity can be unequivocally diagnosed; difficulties in differential diagnosis are not to be expected.

15.2.4 Prognosis

Restoring continuity to the muscle and ensuring sufficient immobilization until the tear has been repaired with scar tissue are the conditions essential for a good result. The smaller the scar that develops after suturing the tear, and the more thorough and definitive the control of local hematoma, the smaller the risk of secondary loss of muscle tension or the development of myositis ossificans that can cause drastic deterioration in the functional result.

15.2.5 Examples of Surgical Procedures

15.2.5.1 Procedure 1

Complete muscle ruptures in the upper extremity are most likely to occur in the biceps or triceps brachii muscles. Reattachment of the muscle to the tendon is performed after complete evacuation of the hematoma using U-shaped sutures in absorbable suture material. Insertion of drainage is obligatory. The sutures must be protected by adequate immobilization (e.g., a Gilchrist dressing for 3–4 weeks).

Potential complications are the secondary divergence between the sutures in the region of the former rupture, generally caused by the stitches in the muscular portion tearing out. A further potential complication is the development of myositis ossificans.

15.2.5.2 Procedure 2

Forearm fasciotomy may prove necessary either in the flexor or extensor compartments and, if the injury is sufficiently severe, on both sides of the forearm. It is important that the incisions extend beyond the hand joint and include the carpal tunnel. The insertion of meander-shaped sutures for secondary suturing of the wound margins and conditioning of the

wound bed with skin substitute are standard therapeutic procedures. Secondary closure is performed using adaptive sutures and/or split-thickness skin graft or mesh graft.

Complications include seriously delayed splitting of the fascia with manifest compartment syndrome or what is known as rebound compartment syndrome. The latter is the recurrence of a manifest compartment syndrome after pressure relief, generally incomplete, of the muscle compartments. Both complications can lead to irreversible damage.

15.2.6 Special Remarks

Muscle injuries of the upper extremity are rare, generally observed in athletes (e.g., gymnasts, throwers etc.) and, on the whole, have good results after appropriate conservative or surgical therapy. Irrespective of wound repair with scar tissue, good functional results can be achieved after careful and gradual training.

15.3 Special Muscle Injuries and Damage to the Torso

- Back musculature
- Chest musculature
- Stomach wall musculature

Ruptures in the region of these muscle groups generally result from pulling or tearing the fibers during sport activity. In general, these injuries are infrequent and are caused by indirect mechanisms such as sudden and excessive muscle contractions. Direct traumas occur predominantly during ball and contact sports, but also after falls from great heights and from traffic accidents.

The principle symptom is the sudden onset of pain that may result in the assumption of an antalgic posture. Partial tears or ruptures of the musculature of the stomach wall are prone to lead to the development of large hematoma and therefore present a clinical picture of peritoneal irritation as a result of massive tension in the stomach wall. Movements of the torso are observed in cases of both tear injuries of the stomach wall and of the back musculature.

Complications of a significant nature are not expected in cases of muscle ruptures because of the indirect mechanisms, but may occur after direct trauma particularly to the stomach wall musculature with the accompanying risk of blunt injuries to the intraperitoneal organs.

15.3.1 Diagnosis

15.3.1.1 Recommended Diagnostic Measures in Accordance with the European Standard

- Inspection: swelling, discoloration from hematoma, asymmetry in the muscle contours in injuries to the stomach wall and back musculature, antalgic posture, impaired function.
- Palpation: pain on pressure, palpable gap in the course of the muscle, fluctuation during the formation of larger hematomas.

15.3.1.2 Additional Useful Diagnostic Procedures

- Ultrasound: presentation of a gap in the continuity of the affected muscle and the accompanying edema/hematoma. Abdominal ultrasound must be performed for injuries to the stomach muscles caused by direct trauma. A specific renal examination may be necessary in cases of blunt trauma in the region of the back musculature.
- MRI/Computed Tomography: required in individual cases only, particularly if there is suspicion of secondary intrathoracic or abdominal injury.
- Radiography: to exclude injury to the bones of the spine (e.g., fractures of the transverse processes of the lumbar spine).

15.3.2 Treatment

15.3.2.1 Conservative Treatment

Recommended Standardized Therapeutic Measures in Accordance with the European Standard

Muscle injuries to the torso are almost exclusively treated by conservative therapy. This consists of protection, local application of cold and concomitant analgesic therapy, and later in carefully building up the muscle under the guidance of a physiotherapist.

Additional Useful Therapeutic Options

Apart from the measures mentioned above, no additional treatment techniques are used.

15.3.2.2 Surgical Treatment

Recommended Standardized Therapeutic Measures in Accordance with the European Standard

Surgical treatment is considered in individual cases when, as a result of complete rupture, severe hematoma formation is detected. Whether it is expedient during revision surgery to insert sutures with adaptation of the tear in addition to evacuating the effusion of blood and inserting drainage is a decision to be made on an individual basis. Because of the reduced potential for immobilization, all suturing is exposed to a high risk of secondary dehiscence. Only complete rupture of the pectoral muscle at its transition with the tendon (which is very rare) would be an indication for surgical repair.

Additional Useful Surgical Measures

The care of secondary injuries to the chest and abdomen that may be required and that must be undertaken in accordance with the standard for the treatment of this kind of lesion are the only additional measures that can be suggested.

15.3.3 Differential Diagnosis

Only injury to the musculature of the stomach wall prompts differential diagnosis of an intra-abdominal injury/disease because the reflectory contraction of the muscles can simulate peritoneal irritation.

15.3.4 Prognosis

The prognosis of muscle injuries to the torso is basically good, but is influenced to a great extent by sound diagnosis and potential therapy of secondary injuries to the body cavities.

15.3.5 Examples of Surgical Procedures

15.3.5.1 Procedure 1

In the case of extensive hematoma caused by a muscle rupture in the region of the stomach wall, the effusion of blood is evacuated surgically after clinical and ultrasound diagnosis and exclusion of a concomitant intra-abdominal lesion. Careful control of hemorrhage follows and a drainage tube is inserted. Suturing is then performed for reattachment if the stitches can be anchored with a reasonable degree of firmness through the muscle fascia. As far as complications are concerned, recurrent hematoma can be associated with secondary suture insufficiency. If another hematoma develops, a broad-minded approach should be taken for further revision.

15.3.6 Special Remarks

Athletes who are predominantly affected by muscle injuries to the torso are competitors in track and field events, gymnasts, ball players, and those participating in martial arts. Preparing for the return to sport activity must consist of closely monitored intensive muscle training.

15.4 Special Muscle Injuries and Damage to the Pelvis and Lower Extremities

In addition to muscular lesions, rupture injuries to the bone have been observed, particularly to the pelvis, above all in children and adolescents and predominantly in the context of sport activity such as sprinting, high and long jump, etc. In contrast, muscle injuries to the lower extremity most frequently involve older patients and are based on degenerative changes, and are generally caused by abrupt passive joint movements with tensed muscles (e.g., the quadriceps muscles). Overall, tears to the tendinous portions of the traction apparatus (quadriceps tendon, ligamentum patellae) occur most frequently.

The principle symptom is pain associated with loss of function. Complications consist of the formation of large hematomas, the development of heterotopic ossifications or myositis ossificans, and reduced muscle strength on complete recovery [4].

15.4.1 Diagnosis

15.4.1.1 Recommended Diagnostic Measures in Accordance with the European Standard

- Inspection: swelling and hematoma, changed external contour, antalgic posture, indirect muscle tension pain
- Palpation: pain on pressure, palpable dimpling in the course of the muscle

15.4.1.2 Additional Useful Diagnostic Procedures

- Ultrasound: visualization of the localization and extent of the injury and the size of the secondary hematoma/edema
- Radiography: exclusion of bone injury, particularly to the pelvis, presentation of possible rupture injuries to the bone
- MRI: in individual cases as an additional diagnostic measure
- Measurement of compartment pressure: particularly in the lower leg, less frequently in the thigh if there is extensive bleeding under the skin and/or the development of edema or hematoma

15.4.2 Treatment

15.4.2.1 Conservative Treatment

Recommended Standardized Therapeutic Measures in Accordance with the European Standard

Muscle injuries to the pelvis and the lower extremity are subject to the general criteria for indicating conservative therapy (i.e., surgical treatment is indicated only in cases of more extensive types of rupture or large hematomas). All other muscle injuries can be treated conservatively. Temporary immobilization with concomitant analgesia and thromboembolic prophylaxis, followed by intensive physiotherapy to build up the muscles, as well as manual therapy are the foundations of the therapeutic concept.

Additional Useful Therapy Options

In the case of competitive and highly competitive athletes, the indication for surgical treatment is somewhat broader in order to, at the very least, reduce the formation of troublesome scar tissue or ossifications by evacuating the hematoma or suturing the musculature. In individual cases, if fresh hematoma occurs, puncture under sterile conditions can contribute to relief. Every effort should be made to obtain definitive wound closure as early as possible after splitting the compartment.

15.4.2.2 Surgical Treatment

Recommended Standardized Therapeutic Measures According to the European Standard

Extensive tears of the *gluteal and iliopsoas muscles* are an indication for surgical revision only when there is severe hematoma formation. This occurs only in exceptional cases; because this condition affects deep structures, the indication is proposed with reservations.

Tear injuries of the *adductors of the thigh* are treated surgically if large portions are affected. This applies particularly to competitive and highly competitive athletes. The same applies to muscle tears of the *hamstrings* or quadriceps muscle.

It is the *gastrocnemius muscles* in particular that are at risk from tears in the lower leg. Typical causes are racket and ball sports. The criteria given above, namely the extent of the injury, its localization, as well as hematoma formation are considered an indication for surgical treatment, as are the patient's expectations of subsequent sporting ability. The most important measure is the restoration of the continuity of the muscle using fine sutures following thorough evacuation of the hematoma. Surgical reconstruction is followed by temporary immobilization (e.g., in plaster); concomitant thromboembolic therapy is obligatory. Afterwards, intensive physiotherapy should lead to

gradual building up of the muscles and subsequently to muscle training specific to the type of sport in question.

If a threatening or manifest compartment syndrome occurs, emergency fasciotomy and delayed primary/early secondary closure should be performed. Evacuation of the hematoma alone requires sufficient drainage.

Additional Useful Surgical Measures

If intramuscular ossification occurs, which may contribute to deterioration in function, surgical removal of the foci of calcification may be indicated. A perioperative ossification prophylaxis is then indicated.

15.4.3 Differential Diagnosis

Muscle tears of appreciable size in the region of the lower extremities can be diagnosed without difficulty by clinical examination and ultrasound. This is different with the somewhat less frequent muscle tears in the region of the pelvis, hip joint, and thigh, which because of their deep localization, cannot be confirmed definitively by clinical examination, but only by ultrasound, and in cases of doubt, by MRI. Their diagnosis should be differentiated from other possibilities.

15.4.4 Prognosis

Prognosis depends above all on the extent of the injury. Incomplete or complete muscle tears in the region of the thigh and calf muscles stand out specifically in terms of incomplete healing or extensive scar tissue even after surgical reconstruction. However, loss of function or strength is generally only slight (e.g., tear in the rectus femoris muscle).

15.4.5 Examples of Surgical Procedures

15.4.5.1 Procedure 1

Extensive tears of the gluteal, iliopsoas, or adductor muscles are revised surgically if a large hematoma has developed. After evacuation and multiple rinsing, the temporary insertion of a synthetic sponge equipped with drainage (e.g., Vacuseal®) may be indicated and definitive wound closure is allowed only secondary to its removal.

15.4.5.2 Procedure 2

Partial or total tears of the thigh muscles (quadriceps muscle, hamstrings) or the gastrocnemius muscles are revised surgically. After evacuating the hematoma, the tear is resutured using fine, U-shaped sutures which should definitely not be tied under too great a tension. It is important to include the stable muscle fascia in the suture because they offer a better hold for the sutures inserted. What is problematic is the immobilization that is inherently necessary to protect the sutures and which, in the case of muscle tears to the thigh, is almost impossible to achieve.

15.4.6 Special Remarks

Muscle injuries to the lower extremity occur frequently in athletes and therefore a higher percentage than those to the upper extremity or torso are treated surgically. Despite repair with scar tissue after suturing, the affected muscle can still be trained and any loss of strength is generally only slight [5].

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Tendon Injuries

16

Kuno Weise

16.1 Basics

Fresh rupture or degenerative damage to large tendons is a clinical entity that is becoming increasingly common. This can be attributed to an increase in sport activity among older people in particular, and also to improved diagnosis and a greater degree of exposure to the systems that transfer muscle power to injury in professional life or in road traffic accidents. Substantial loss of function can result if the smaller tendons in the hand, for example, are severed as a result of direct blunt trauma or torn as a result of indirect injury mechanisms. Spontaneous tendon ruptures based on the indirect effects of force are often caused by more than one factor.

16.1.1 Anatomy

Tendons are made up of what is known as bradytrophic tissue (i.e., the blood supply is significantly lower compared to the muscles and ligaments). Nutrients are supplied to the tendon predominantly by small vessels from the peritendineum and to a lesser degree via the belly of the muscle attached to it. Tendons are made up of dense connective tissue that contains predominantly types I and III collagen fibers. Compared to the muscles, tendons are less receptive to training, which explains their tendency to strain injuries and spontaneous rupture.

16.1.2 Physiology and Pathophysiology

Tendons are part of the systems that transfer power (i.e., they transfer muscle contraction to the target organ, the bone, and its associated joints). They differ in length and configuration and show an appropriate adaptation in cross-section depending on strain and function. The reasons for gaps in the continuity of a tendon are direct trauma, such as cuts and stab wounds, and less frequently blunt trauma or spontaneous rupture resulting from indirect trauma. The latter is caused by a disparity between capacity and loading (e.g., when degenerative changes have occurred because of local circulatory disturbance and chronic overstrain). Local injections, metabolic disorders, and advanced age are further predisposing factors. Insufficient warm up and stretching, inadequate training, and unsatisfactory technique as well as poor conditions for sport activity are considered to be additional causes of these injuries.

16.1.3 Specific Causes of Tendon Injuries

Gaps in the continuity of the rotator cuff are predominantly the result of degenerative changes. The same applies to rupture of the long biceps tendon. Violent rupture of the rotator cuff requires special injury constellations that must involve a sudden change in length in excess of the resistance of the aponeurosis

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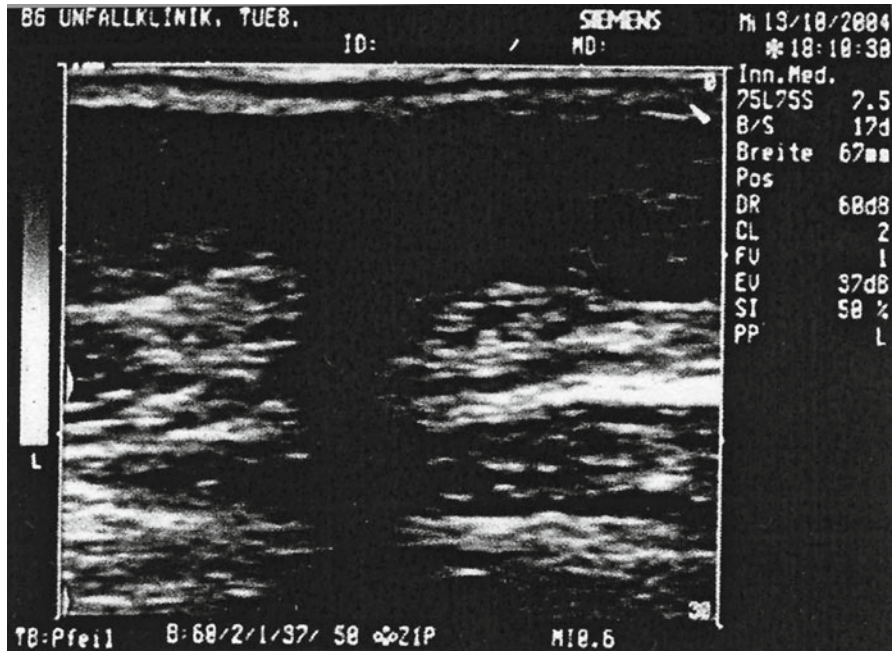


Fig. 16.1 Ultrasound image of a torn rotator cuff

(e.g., rupture of the supraspinatus tendon with anterior shoulder joint dislocation). Ruptures of the distal biceps tendon generally result from indirect trauma. The infrequent rupture of the triceps tendon is predominantly caused by direct injuries but can also occur after local cortisone injection. As a rule, tendon injuries to the forearm or hand are caused by direct trauma such as cuts.

At the lower extremity, in addition to the frequent spontaneous ruptures of the Achilles tendon ruptures of the tendons of the extensor system are the most common. The former frequently occurs in younger athletes, while ruptures of the quadriceps and patellar tendons are predominantly observed in older individuals. The remaining tendons of the lower extremity are less frequently involved. When the ankle and foot are affected it is generally because of straightforward severance.

16.1.4 Diagnosis

16.1.4.1 History and Clinical Examination

Swelling and hematoma, a palpable dimpling in the course of the tendon and impaired or reduced function, together with the patient's history, permit a tentative diagnosis.

16.1.5 Diagnosis by Imaging Procedures

16.1.5.1 Radiography

Native radiographs are used to exclude concomitant injury to the bone (e.g., a rupture injury to the tendon) or to demonstrate or exclude degenerative joint changes.

16.1.5.2 Ultrasound

Ultrasound imaging is the examination method of choice. It can supply accurate images of the gap in continuity and any concomitant edema or hematoma (Fig. 16.1).

16.1.6 Organ-Specific Imaging

16.1.6.1 Magnetic Resonance Imaging and Computed Tomography

In unclear cases it can be useful to obtain a magnetic resonance imaging (MRI) scan in order to reach a definitive diagnosis or for consideration of differential diagnosis (e.g., in cases of rotator cuff rupture). A distinction can be made between acute and chronic changes and an opinion formed on the issue of previous damage. Computed tomography (CT) for tendon injuries is the absolute exception.

16.2 Special Tendon Injuries and Damage to the Upper Extremity

- Rotator cuff
- Proximal/distal biceps tendon
- Triceps tendon
- Tendons in the muscles of forearm and hands

Tendon injuries to the upper extremity are relatively frequent and their cause becomes increasingly traumatic as we move in the proximal-distal direction. Tendon injuries in the forearm and hand region are generally caused by direct mechanisms, in particular by cuts. In contrast, the majority of the lesions of the rotator cuff and long biceps tendon results from degenerative changes caused by overstrain injuries (e.g., in individuals who undertake heavy, physical work).

Isolated traumatic ruptures to parts of the rotator cuff tend to be infrequent but can occur through mechanisms that suddenly increase the distance between the origin and insertion of the muscle belonging to it [1, 2]. This is feasible, for example, in anterior shoulder joint dislocation where a tear in the supraspinatus tendon or alternatively a bony rupture in the greater tubercle can occur. Rupture of the long biceps tendon, on the other hand, is caused almost exclusively by local wear with extensive degenerative changes in the region of the bicipital groove. In contrast, most ruptures of the distal biceps tendon are the result of indirect trauma. They regularly occur because of a violent force applied to the forearm when the elbow is bent and the biceps contracted. Rupture of the triceps tendon is rare (e.g., in power athletes and through indirect mechanisms after local cortisone injections or caused by direct blunt force trauma when the tendon is contracted).

Ruptures of the tendons in the forearm extensor and flexor muscles are caused either by local cuts, such as in the context of suicide attempts or, on occasions, by contusions with substantial soft-tissue damage or in the context of industrial or road traffic accidents. The latter typically involve different types of stab wounds or cuts to the hand. Rupture of the extensor tendon in the region of its insertion at the base of the distal phalanx of the middle finger and rupture of the extensor pollicis longus muscle in the thumb region are caused by degeneration.

The symptoms of tendon rupture at the upper extremity range from the typical signs of a fresh lesion with swelling, hematoma, pain, and loss of function to a complete absence of these characteristic signs of injury. This applies to the creeping occurrence of a rotator cuff rupture and to tears of the long biceps tendon, symptoms of which many patients initially perceive as a kind of strain. Rupture of the distal biceps tendon behaves differently. It is accompanied by swelling, pain, and deterioration of function or lack of strength when the elbow joint is bent. Direct gaps in the course of the tendon in the distal forearm or region of the hand and fingers as a rule inevitably lead to loss of function in the dependent target organ, but are often not recognized in the primary diagnosis. Before initiating any treatment, it is important therefore to test the function carefully for all cut injuries in which depth and extent are unclear.

The threatening complication of re-rupture should be taken into account in all tendon injuries, whether conservatively or surgically treated. Re-rupture is caused by the reduced ability of bradytrophic tissue to heal and by degenerative changes that may be present. In the case of open tendon injuries to the hand and fingers, inflammation of the tendon sheath can develop. Finally, loss of function occurs regardless of correct and complete tendon reconstruction because of local scar tissue formation or long immobilization.

16.2.1 Diagnosis

16.2.1.1 Recommended Diagnostic Measures in Accordance with the European Standard

- Inspection: swelling, hematoma, impaired function, change in muscle contours
- Palpation: pain on pressure, gap in the continuity of the tendon

16.2.1.2 Further Useful Diagnostic Procedures

- Ultrasound: imaging of the localization, extent, and type of tendon rupture (acute/chronic, transverse/multilevel, complete/incomplete) and extent of edema/hematoma.
- Radiographs: to exclude bone involvement (bone rupture). To assess any concomitant joint damage (e.g., rotator cuff lesion, rupture of the long biceps tendon).
- MRI: with an unclear ultrasound diagnosis. Reproducible, gives more detailed information.
- CT: only in exceptional cases (e.g., in cases of concomitant bone injury at the joints).

16.2.2 Treatment

16.2.2.1 Conservative Treatment

Recommended Therapeutic Measures in Accordance with the European Standard

The more acute and fresh the injury to a tendon in the upper extremity, the more pressing is the indication for surgical care. Ruptures of the rotator cuff are treated conservatively because of advanced wear phenomena, especially in elderly patients and particularly if the opposite side exhibits similar changes (ultrasound). Ruptures of the long biceps tendon are also the domain of conservative treatment in older patients. This also applies to proximal ruptures of the biceps tendon, which are chronic or diagnosed late. Various studies comparing conservative and surgical therapy with appraisals of the criteria of pain, strength, and mobility demonstrate only slight superiority on the part of surgical treatment [1–3].

Rupture of the extensor tendon at the distal phalanx is regularly treated conservatively and successfully. Special finger splints are used that hold the distal phalanx in overextension for 6–8 weeks [1].

With partial rupture of the superficial layers of the rotator cuff and degeneration-induced tears in elderly patients with a low degree of activity and where the lesion is no longer fresh, conservative, early, functional therapy can yield good results. Conservative management of ruptures to the long biceps tendon likewise involves early functional therapy during which strong exertion should be avoided in the initial weeks. A conservative therapy regime for injuries to the extensor tendons of the finger using synthetic splints for 6–8 weeks requires them to be worn continually; otherwise partial healing of the tendon can occur with a residual decrease in extensibility.

16.2.2.2 Surgical Treatment

Recommended Therapeutic Measures in Accordance with the European Standard

Fresh, traumatic rotator cuff rupture is a clear indication for surgical reconstruction. A basic distinction is made between technically demanding arthroscopic refixation of the affected part of the tendon and the open procedure, known as “mini open repair” via a “lateral deltoid split”. If there is any doubt, open repair to restore continuity should be preferred. The affected part of the rotator cuff can be re-anchored to the insertion site of the aponeurosis at the greater tubercle either by the transosseous refixation, which is considered reliable or by means of what are known as suture anchors, which are fixed in the bone at the insertion site or somewhat medially of the insertion site. In older or chronic ruptures, the retracted tendon stumps are treated in the same way after mobilization. Special suturing techniques are used. It is important to perform refixation without tension being too great; possibly with medialization of the insertion region. Various graft replacements are used with significant defects or degeneration-induced massive ruptures, such as those involving the deltoid or latissimus dorsi muscle [1, 2]. After completion of all reconstructive measures, temporary immobilization and a physiotherapy program involving a defined increase in mobility and building up of the muscles is necessary (Figs. 16.2 and 16.3).

Ruptures of the long biceps tendon are managed for the given indication by using the keyhole technique (Fig. 16.4). The distal end of the tendon is located and used to form a knot that is secured with a suture. Subsequently, with the elbow joint at 90°, a hole about 8 mm in diameter is drilled in the bone of the upper arm after the tendon/muscle has been sufficiently tensed. The drill hole is extended distally to form a slot. The knotted tendon is fitted into this “keyhole” [3, 4]. Concomitant and follow-up management includes early mobilizing physiotherapy. Alternatively, the tendon stump can also be connected to the short head of the biceps using Kessler-type sutures or can be anchored at the coracoid process. Concomitant and follow-up treatment includes early functional rehabilitation.

Anatomical reinsertion is performed at the radial tuberosity in distal biceps tendon rupture. Transosseous reinsertion via V-shaped drill holes is time-consuming, and recently, the tendon has been re-anchored using suture anchors that were inserted into the tuberosity [5, 6]. Because of potential lesions of the superficial and deep branches of the radial nerve and the occasional development of heterotopic ossification with subsequent reduction in joint function, the complication rate for these interventions is not negligible. Adjuvant and follow-up treatment can be performed as early functional procedures when the tendon has been reliably fixed (Figs. 16.5 and 16.6).

Cut injuries with tendon involvement in the distal forearm, wrist, or in the hand or finger region are frequent and are treated according to the rules of tendon surgery using special suture techniques and a

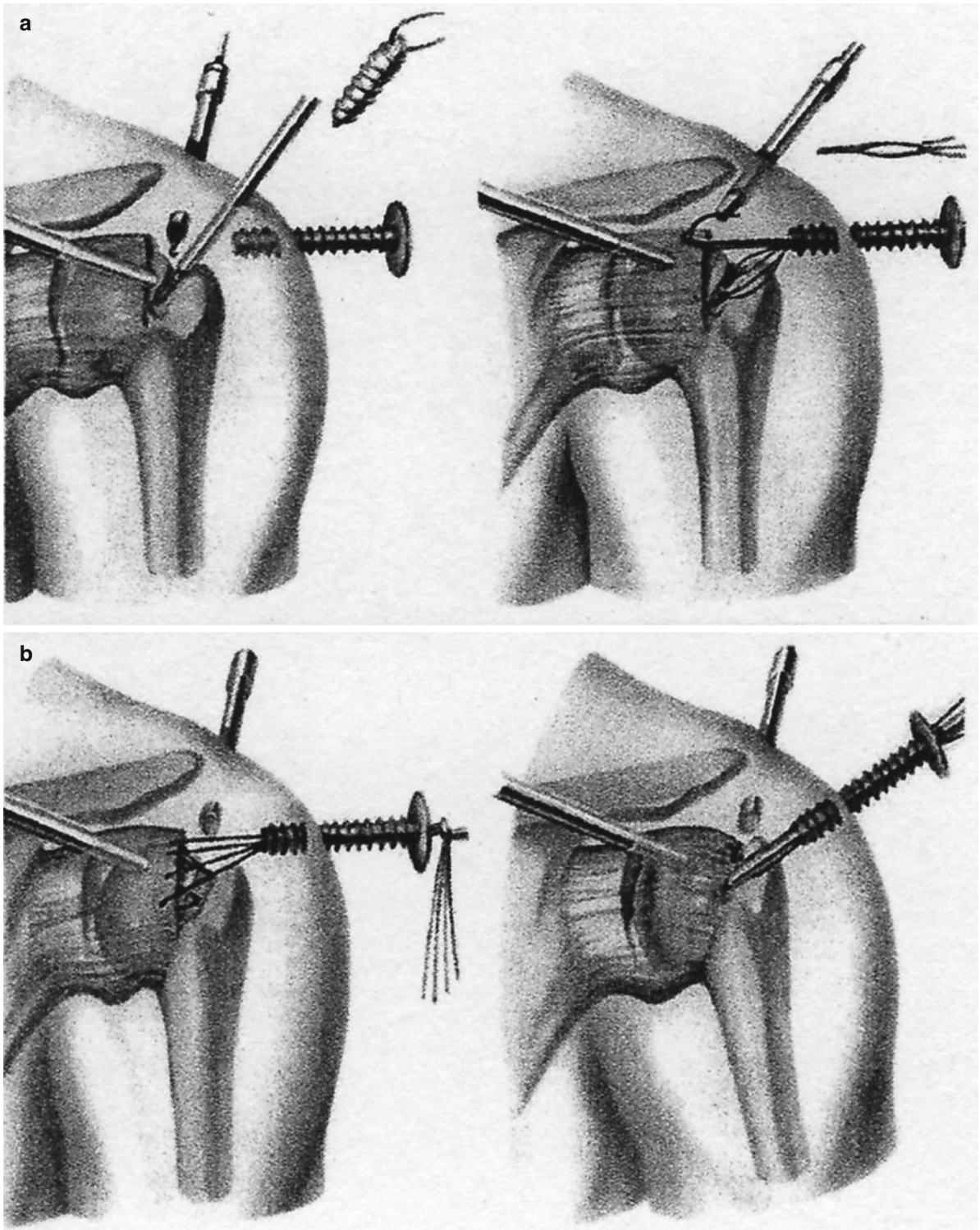


Fig. 16.2 (**a**, **b**) Arthroscopic technique of transosseous suture in rotator cuff tears

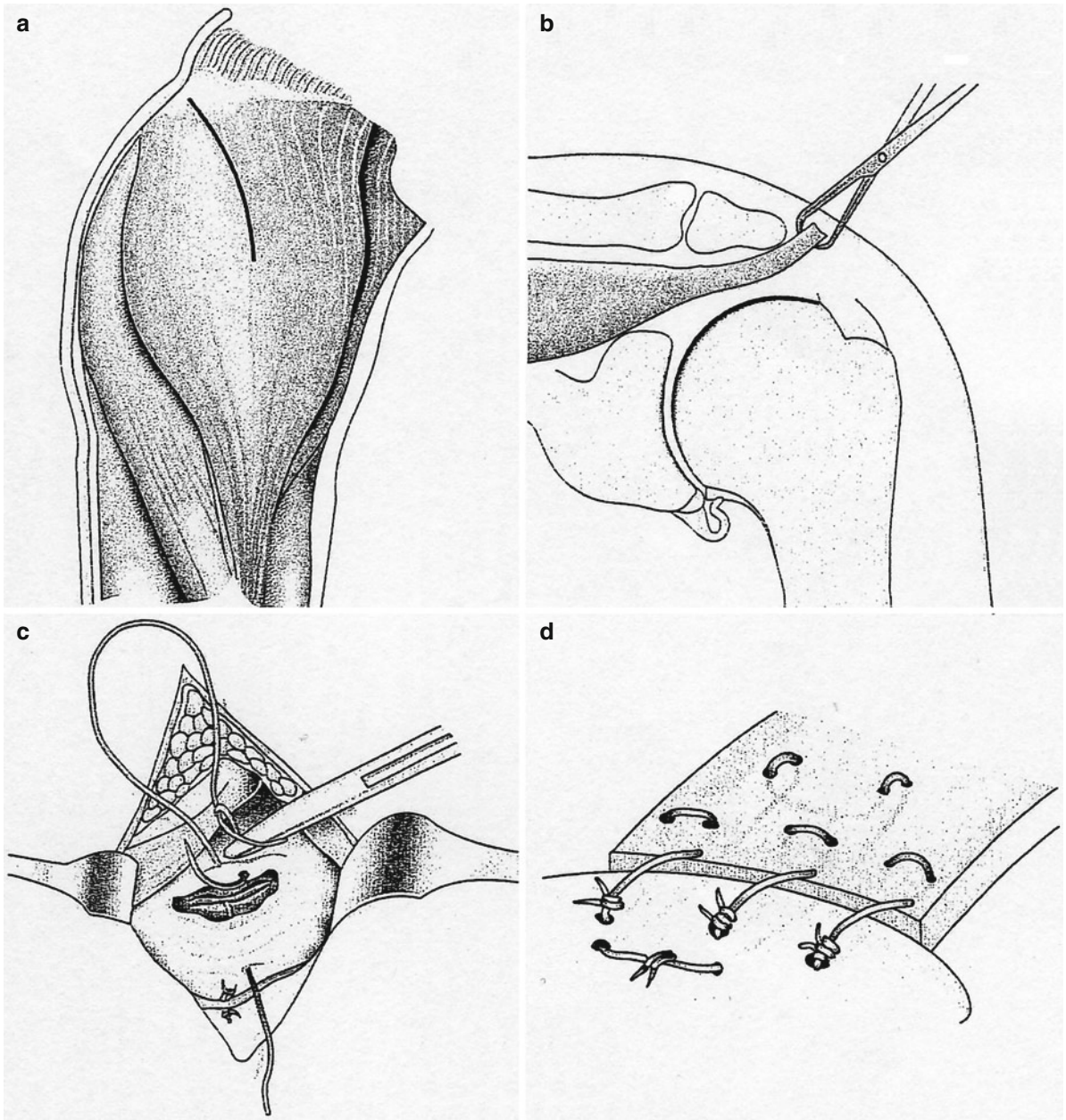


Fig. 16.3 Transosseous fixation of the torn rotator cuff at the site of the greater tubercle. (**a**) Incision. (**b**) Mobilization of the tendon. (**c**, **d**) Transosseous fixation

differentiated adjuvant and follow-up treatment using special functional splints. For loss of substance, tendon grafts or transfers are performed. Rupture injuries to the bone, such as to the extensor tendons, from a certain size and degree of dislocation are refixed using tension band fixation or small screws. Ruptures of the tendon of the extensor pollicis longus muscle, either on the basis of degenerative changes in chronic fractures or iatrogenic fractures of the distal radius occurring on reconstruction, are treated by using an extensor indicis proprius graft.

Additional Useful Surgical Measures

With degenerative-induced rotator cuff ruptures where the head of the upper arm has moved up and there are signs and symptoms of impingement, reconstruction of

the aponeurosis is combined with a subacromial decompression. Degenerative changes in the long biceps tendon are accompanied by biceps tendon tenodesis. The reconstruction of the relatively infrequent ruptures of the triceps tendon is performed surgically by end-to-end suture of the tendon stumps using U-shaped sutures. Functional adjuvant and follow-up treatment after refixation of the long and distal biceps tendon or triceps tendon can be undertaken after provision of splints with individually adjustable mobile joints.

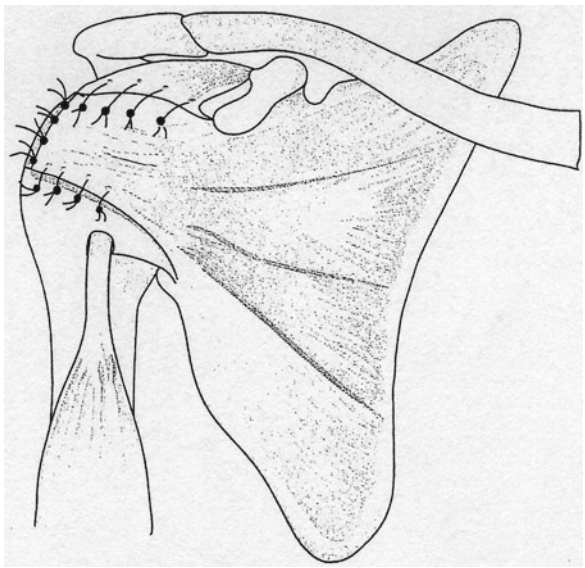


Fig. 16.4 Transfer of a m. subscapularis flap into the defect of the rotator cuff

16.2.3 Differential Diagnosis

Differentiating between traumatic rotator cuff ruptures and those induced by degenerative changes is significant, not least because of the need for expert opinions related to insurance claims. This differentiation also has an impact on the type and timing of treatment as well as on prognosis. Tears of the long biceps tendon as well as those of the distal biceps tendon are often overlooked initially because no change in the muscle contours can be seen on the flexor side of the upper arm. If there are grounds for suspecting cut injuries of the flexor and extensor tendons at the wrist, hand, and fingers, the precise functional tests, or under certain circumstances, surgical exploration are indicated in order to establish the actual extent of the injury.

16.2.4 Prognosis

In terms of prognosis, rotator cuff ruptures depend on the way they occurred, previous injury, the timing and quality of diagnosis and treatment, the extent of the defect, and last but by no means least, on an appropriate concomitant and follow-up treatment. The outcome after treatment of ruptures of the long biceps tendon is only marginally different under conservative or surgical regimes. Surgically treated ruptures of the distal biceps tendon are not infrequently accompanied by deterioration of elbow joint function and the rotatory movements of the forearm, particularly when heterotopic

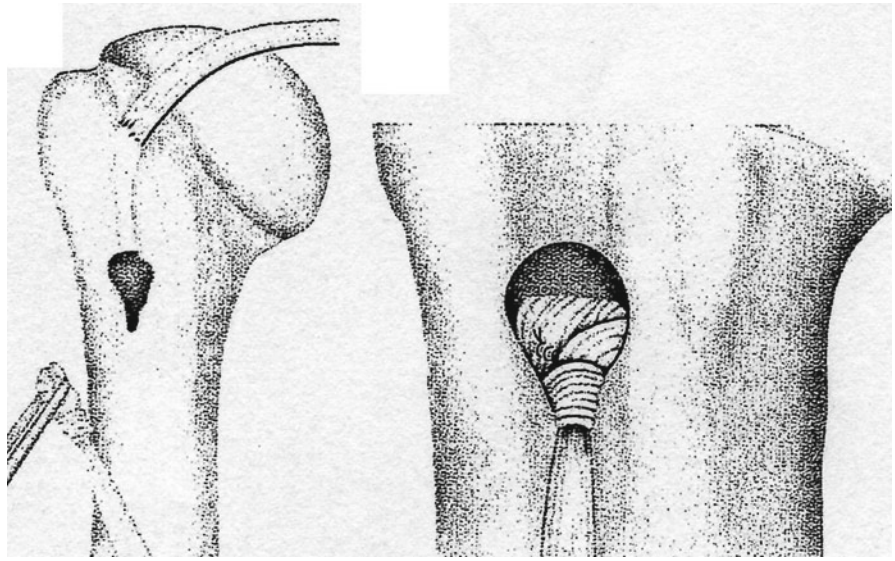


Fig. 16.5 Keyhole technique for re-fixation of the long biceps tendon

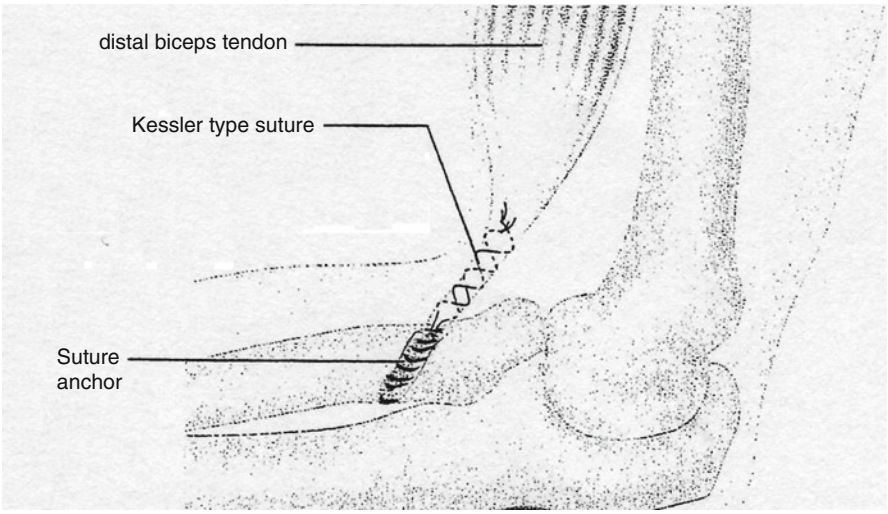


Fig. 16.6 Reinsertion of a distal biceps tendon rupture using suture anchors

ossification occurs. Lesions of the sensory and motor branch of the radial nerve leave a legacy of symptoms and marked abnormalities in function. The reconstruction of cut injuries of the flexor and extensor tendon or of tendon avulsion and ruptures in the hand can also be followed by residual impairment in function.

16.2.5 Examples of Surgical Procedures

16.2.5.1 Procedure 1

Recent traumatic rupture of the supraspinatus tendon in young, active patients is reconstructed surgically. The procedure can be performed using an open procedure or arthroscopically. The technique most frequently performed is open reinsertion via a lateral deltoid split with the patient in the beach chair position. After splitting the deltoid muscle, inserting a protective suture to protect the axillary nerve and carrying out subacromial decompression, the edges of the tendon are identified and débrided, as is the insertion site of the rotator cuff at the greater tubercle. After creating drill channels the tendon edges are reunited and tension-free and U-shaped absorbable sutures are inserted. Alternatively, suture anchors can be used.

16.2.5.2 Procedure 2

A rupture of the biceps tendon, for which there is clinical and ultrasound evidence, must be refixed surgically. An S-shaped, curved incision is made over the elbow, the radial nerve is identified and protected, and access is gained to deeper levels as far as the tuberosity of the radius. The ruptured tendon is located in the proximal region of the wound. With the elbow joint at 90°, 1–2 suture anchors are screwed into the tubercle, after which the tendon is sutured with Kessler-type sutures. These can be used to fasten the tendon stump to its insertion site. An alternative technique is transosseous refixation by means of a U-shaped drill hole at the tuberosity of the radius [5, 6].

16.2.6 Special Remarks

Tendon injuries and damage to the upper extremity occur frequently and are caused either by direct or traumatic external force or by advanced degenerative changes. A differentiation based on these etiological factors has direct impact on the appropriate therapy, adjuvant or follow-up treatment, as well as prognosis.

Most tendon injuries to the upper extremity result from sport activities or industrial accidents. Intensive preventative measures are needed to reduce the incidence of this kind of injury.

16.3 Tendon Injuries to the Pelvis and Lower Extremity

- Apophyseal avulsion fractures of the pelvis
- Tendon ruptures to the knee extensor system (quadriceps tendon, patellar ligament)
- Achilles tendon rupture
- Tendon injuries of the lower leg and foot muscles

In the case of tendon injuries to the lower extremity, it is clear that in numerical terms, Achilles tendon rupture dominates, followed by generally

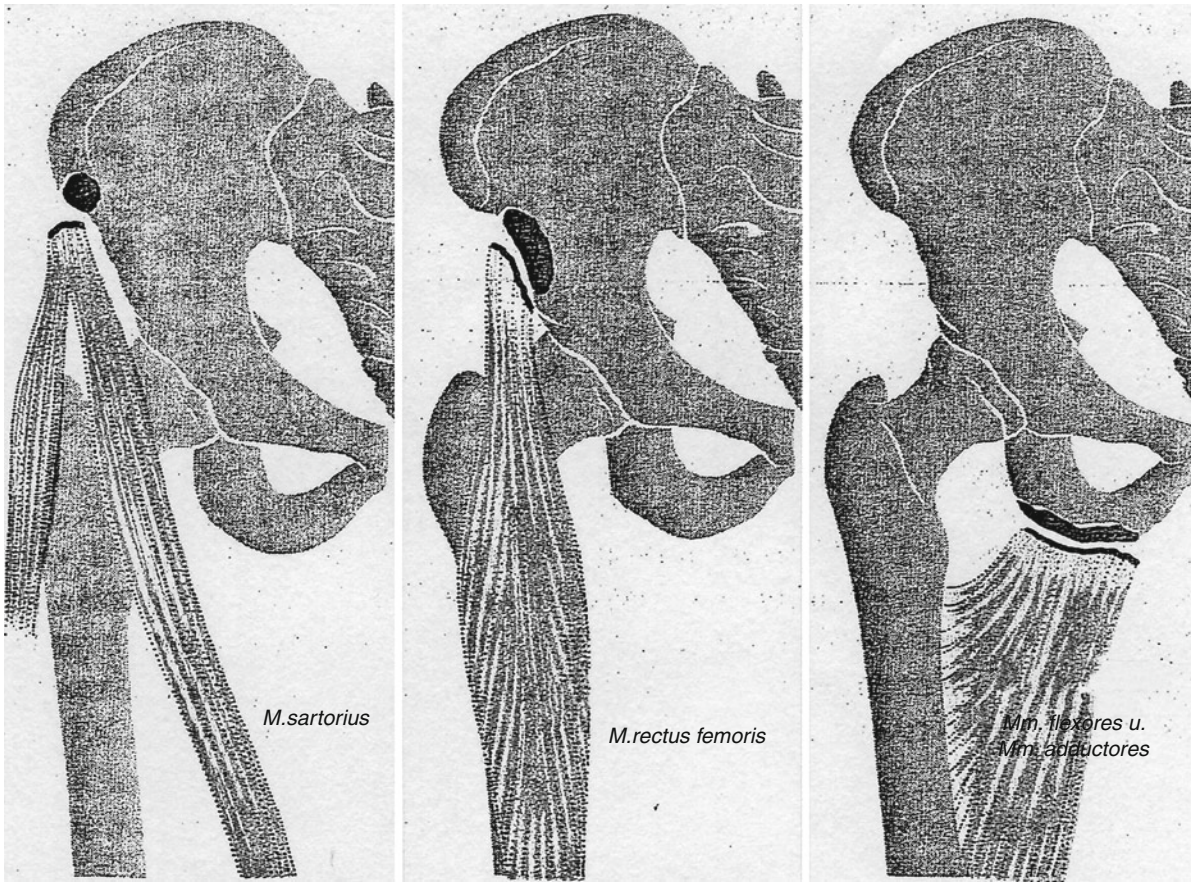


Fig. 16.7 Several types of epiphyseal avulsion fractures

degeneration-induced rupture injuries to the knee extensor system. While apophyseal avulsion fractures of the pelvis are generally seen in young people and result from sudden movements (e.g., starting, jumping), tendon injuries in the ankle and foot region tend to be caused by direct trauma (i.e., cuts, stab wounds) (Fig. 16.7).

The characteristic symptoms of tendon injuries to the lower extremity are substantial loss of function in the neighboring joints, such as loss of the knee extensor mechanism in ruptures of the quadriceps or patellar tendons, or patient inability to stand on their toes with Achilles tendon rupture. Apophyseal pelvic injuries have few symptoms; direct ruptures of ankle and foot tendons are accompanied by equivalent injuries and a dependent loss of function at the periphery.

The most serious and frequent complication of tendon injuries to the lower extremity is re-rupture, particularly where there are pronounced degenerative changes, an inadequate suturing technique, or premature loading.

16.3.1 Diagnosis

16.3.1.1 Recommended Diagnostic Measures in Accordance with the European Standard

- Inspection: possible swelling and hematoma at the pelvis as well as antalgic posture. In quadriceps or patellar tendon ruptures, changes in contours with swelling, hematoma, and loss of extensor mechanism. Open wounds in the case of cuts or stab injuries in the ankle or foot.
- Palpation: pain on pressure in the region of the pelvic apophyses and dimpling. Quadriceps/patellar

tendon, high-riding patella in patellar tendon rupture. In tendon ruptures to the ankle joint and foot the tendons are not palpable at typical localizations.

16.3.1.2 Further Useful Diagnostic Procedures

- Ultrasound: imaging technique of choice in all large tendon injuries, (e.g., knee extensor system, Achilles tendon, and the long tendons of the lower leg muscles).
- Radiography to confirm apophyseal avulsion fractures of the pelvis or to exclude concomitant bone lesions (e.g., rupture injuries to the bone at the patellar tendon/Achilles tendon, the tibial tuberosity, or calcaneal tuberosity).
- MRI/CT: MRI is used where findings are unclear and/or concomitant injury to adjacent joints is suspected, but is normally superfluous. The same applies to CT [1, 7].

16.3.2 Treatment

16.3.2.1 Conservative Treatment

Recommended Therapeutic Measures in Accordance with the European Standard

As a rule, apophyseal avulsion fractures of the pelvis in young people are treated conservatively. Only pronounced dislocations of larger fragments are an indication for surgical refixation in individual cases [1, 2].

Conservative measures in ruptures of the extensor system are considered only in infrequent cases of incomplete or partial ruptures. In the case of complete ruptures, without surgery, an extensor insufficiency will remain [8–10].

Achilles tendon rupture where ultrasound shows that the ends of the tendon are in contact when the foot is in plantar flexion can be successfully treated without surgery. A prerequisite for this is wearing a special boot continuously for about 8 weeks as plantar flexion is gradually reintroduced on full weight bearing. The shoe is used for about 1–2 weeks after the trauma following initial immobilization in plaster. Ultrasound follow-up assessments are recommended at regular intervals. After removing the shoe, a 2–2.5 cm raised heel must be worn for 4–6 weeks as part of the patient's ready-to-wear shoe [9, 11–13].

Acute ruptures of the ankle joint and foot tendons are not suitable for conservative treatment.

Additional Useful Therapy Options

Bed rest of 2–3 weeks duration with therapeutic positioning of the affected part is recommended for the treatment of apophyseal avulsions or pelvic rim fracture. In avulsion fractures at the ischial tuberosity, the patient is in the extended position; if these affect the anterior superior iliac spine then the hip joint is flexed. Conservative treatment of Achilles tendon rupture needs strict monitoring, on the one hand, and appropriate compliance on the part of the patient on the other. During treatment using the special boot, a defined physiotherapeutic adjuvant and follow-up treatment is necessary as well as regular ultrasound assessments. Rupture injuries to the Achilles tendon that are very distal and close to the insertion site or involve the bone are unsuitable for conservative therapy.

16.3.2.2 Operative Treatment

Recommended Therapeutic Measures in Accordance with the European Standard

Avulsion fractures of the large pelvic tendons are refixed in selected cases using screws or tension band fixation.

Ruptures of the tendons of the knee extensor system generally occur right at the tendon origin or insertion (i.e., at the upper or lower patellar pole or at the tibial tuberosity). Ruptures in the tendon that are caused by indirect trauma tend to be infrequent. They may result from direct blunt force trauma, such as through cut or stab wounds. Additional augmentation using cerclage wire or absorbable cord is required as well as suturing because of the poor healing ability. Tendon ruptures directly at the upper or lower patellar pole are fixed in a transosseous fashion, at best using U-shaped sutures through the tendon stump or longitudinal 2 mm channels drilled at the knee cap. Augmentation follows with the insertion of a framework of cerclage wire or a 2.00 mm Polydioxanon (PDS) cord positioned across the patella and proximal to the rupture site of the quadriceps tendon and through the latter. In the case of patellar injuries, they are placed through a horizontal drill hole at the level of the tibial tuberosity. After suture and augmentation the knee joint is moved through at least 60° of flexion in order to test whether the construct is reliable and to guarantee functional adjuvant and follow-up treatment [1, 2, 8, 10].

Surgical reconstruction of the Achilles tendon is indicated for athletic patients and if there is marked residual tendon diastasis, even with the foot in plantar

flexion. Recently, a percutaneous suture technique has prevailed that uses two 1.3 PDS cords inserted in opposite directions through stab incisions that are knotted, with the foot in plantar flexion, at the level of the rupture site medially and laterally of the tendon and through which adaptation of the tendon stumps is achieved. Alternatively, open suturing (e.g., the Kirchmayr technique, fibrin glue and suturing in combination with a primary turn-down flap) have been recommended. The latter is useful in pronounced degenerative changes and marked diastasis of the tendon stumps [11–15].

Transosseous fixation is used for fixation of tendon ruptures at the calcaneal tuberosity involving bone fragments and the suture is protected by augmentation.

Reconstruction of the course of the tendon after direct injury to the tendons of the lower leg and foot muscles is performed using the suture techniques usually used in tendon surgery, such as the Kirchmayr technique. The aim is reliable restoration of the continuity of the tendon, possibly accompanied by temporary tenodesis using Kirschner wire and subsequent immobilization (Fig. 16.8).

Additional Useful Surgical Measures

Chronic ruptures of the extensor tendons at the knee joint or secondary suture insufficiency require syndesmoplasty. Turn-up X-, Y-, or Z-shaped grafts can be used for the quadriceps tendon. Augmentation is always necessary to protect this grafting procedure. Immobilization lasts for 3–4 weeks.

Insufficiencies or chronic defects in the region of the Achilles tendon can be restored through re-adaption of the débrided tendon stumps, combined with a turn-up plasty, and in the case of defects that cannot be directly bridged, X- or Y-shaped grafts or plantaris tendon graft or grafts using the tendon of the peroneus brevis or the flexor hallucis longus muscle.

Revision is indicated in achillodynia and after unsuccessful conservative therapy. After oval excision of the thickened section of the tendon, bridging using a stitched turn-up graft is indicated.

16.3.3 Differential Diagnosis

Surprisingly, many ruptures of the extensor system, or more precisely of the Achilles tendon, are not primarily diagnosed despite the patient consulting a doctor (between 10 % and 20 % of cases according to publications in the literature). In cases of doubt, an MRI should be performed as a reproducible diagnostic procedure. Partial ruptures diagnosed clinically on both sides or by ultrasound are generally found to be complete ruptures during surgical revision.

16.3.4 Prognosis

Residual damage and symptoms should not be expected in young people after conservative treatment of apophyseal avulsions of the pelvis. Only larger dislocations and increased callus formation can cause regional mechanical problems.

On the other hand, the prognosis after surgical reconstruction of ruptures of the knee extensor system must be more tentative. Impairments of knee joint function as well as the risk of re-rupture are observed in a certain percentage of patients.

The outcome after conservative or surgical treatment of Achilles tendon rupture depends to a great extent on establishing the correct indication for the procedure in question, performing it correctly, undisturbed wound healing, and a gradual building up of strength while avoiding re-rupture. After complications occur, prognosis becomes appreciably less favorable. Residual impairments of function, loss of strength in the calf muscles, and impaired athletic ability can be long-term results. The reconstruction of severed tendons in the ankle and foot depends, as far as outcome is concerned, both on correct surgical technique and carefully monitored adjuvant and follow-up treatment.

16.3.5 Examples of Surgical Procedures

16.3.5.1 Procedure 1

Longitudinal parapatellar incisions extended proximally or distally are a suitable approach to reconstruction of ruptures of the knee extensor system. After identification and débridement of the tendon ends and biopsying for cellular examination, 2 mm channels are drilled, in accordance with the type of rupture, at the upper and lower patellar pole, through which the U-shaped sutures on the stump of the quadriceps or patellar tendon are directed and knotted at the end. A transverse hole drilled through the patella for augmentation and for passage proximally through the quadriceps tendon and distally, by means of a further drill hole, through the tibial tuberosity, makes it

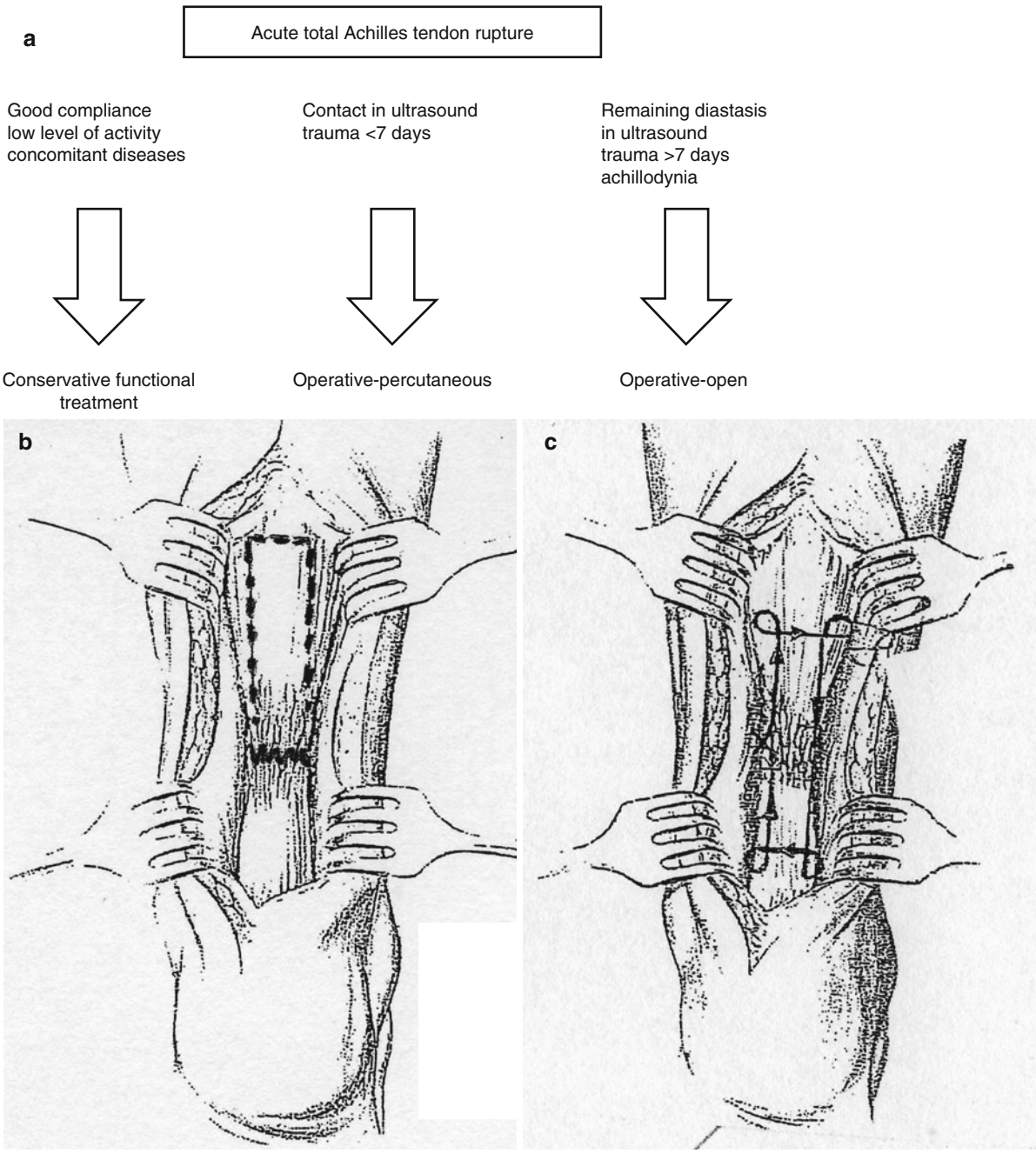
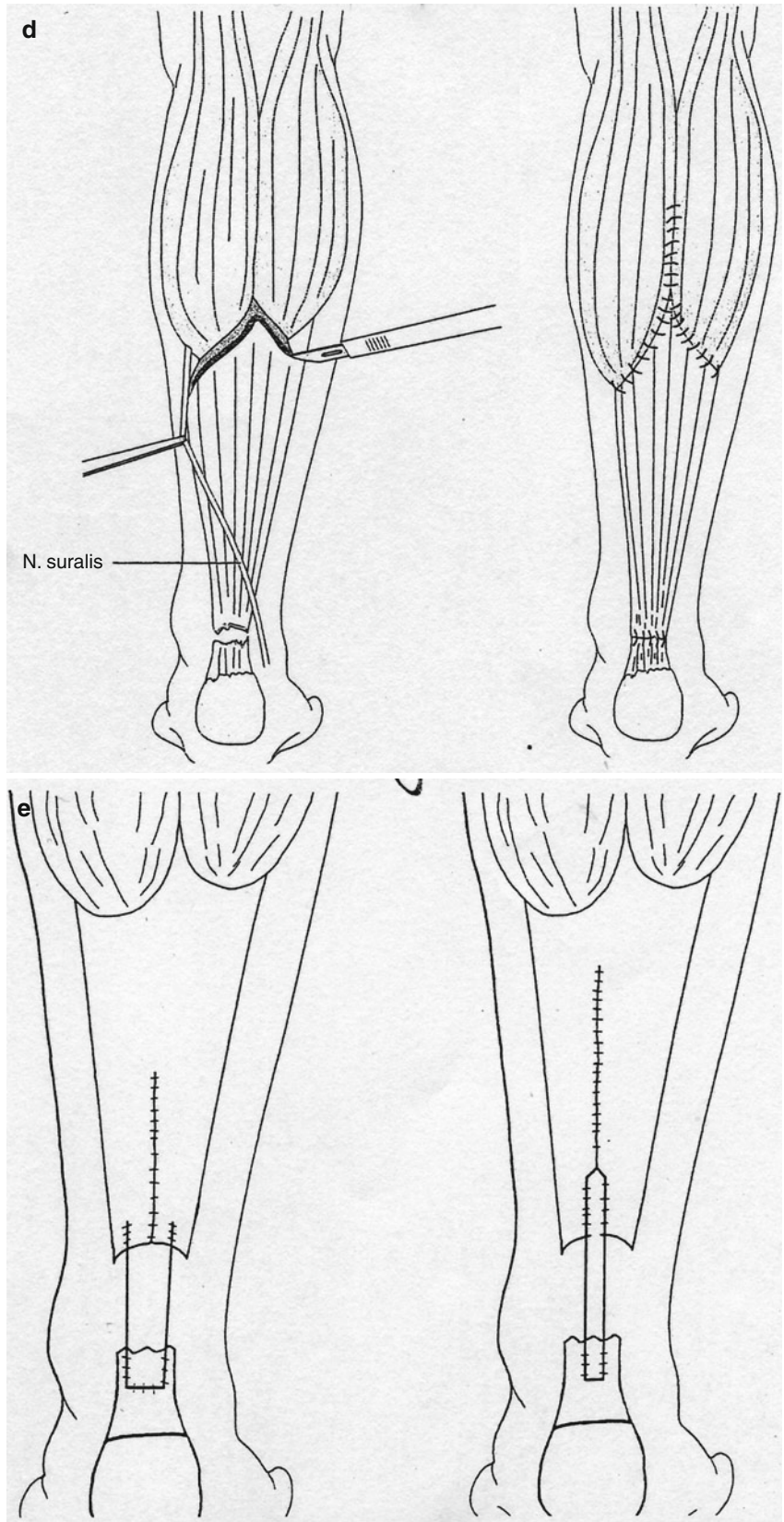


Fig. 16.8 (**a**) Kessler-Kirchmayr technique for suture in Achilles tendon rupture. (**b**) Augmentation for Achilles tendon rupture in Silverskjöld technique; preparation of the tendon flap. (**c**) Augmentation after bridging the rupture site by means of tendon flaps. (**d**) V-Y-plasty in Achilles tendon rupture with remaining defect. (**e**) Different types of Achilles tendon arthroplasties: Lindholm's arthroplasty, Lange's arthroplasty

Fig. 16.8 (continued)



possible to construct a frame-shaped augmentation using either tension band wire fixation or PDS cord to suit the type of rupture in question. PDS cord has the advantage of being biodegradable and does not, therefore, involve removal of implants. The disadvantage is the higher rate of irritation and inflammatory conditions. The correct height adjustment of the patella is highly significant, such as avoiding patella alta or baja through too tight adduction of the augmentation frame [8, 10]. Checks of the reconstructed tendon should be made intraoperatively to ensure the treatment carried out is stable up to at least 60° flexion of the knee joint (Fig. 16.9).

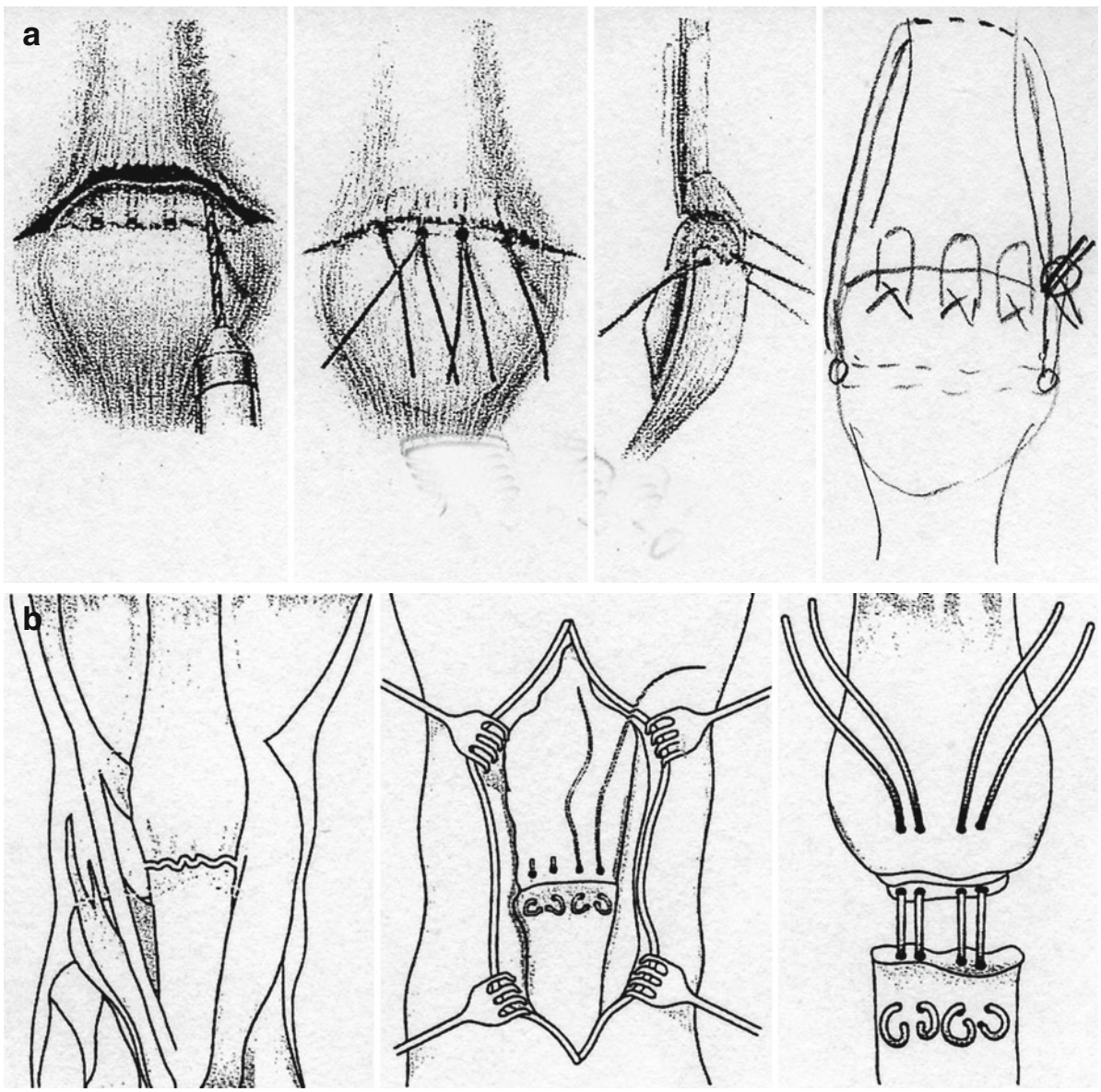


Fig. 16.9 (**a**) Transosseous re-fixation of a quadriceps tendon rupture. (**b**) Suture technique and transosseous re-fixation of a patellar tendon rupture. (**c**) Augmentation of the sutures by tension band wire of PDS cord

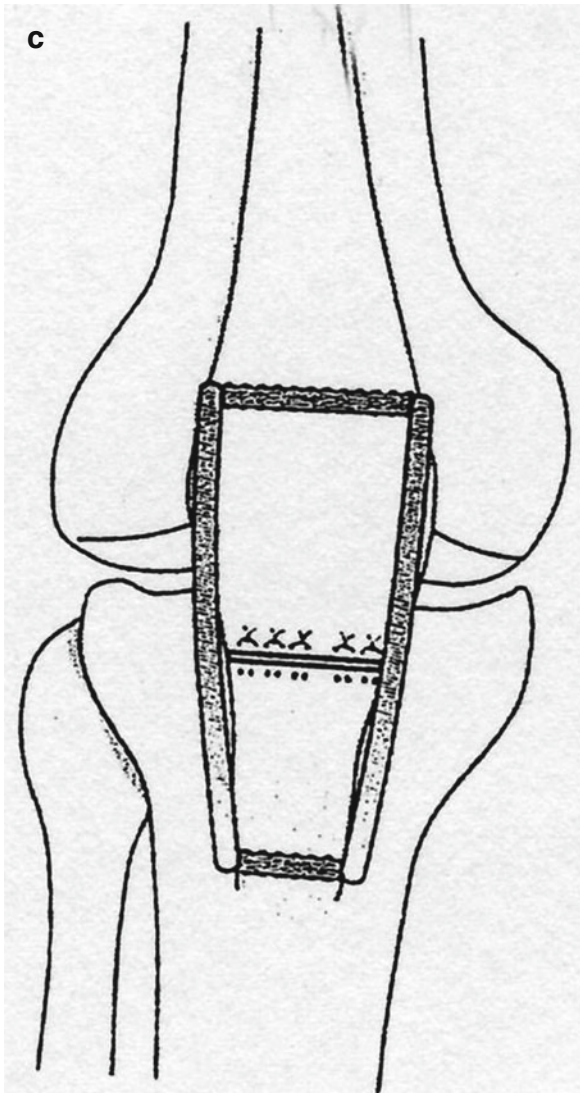


Fig. 16.9 (continued)

16.3.5.2 Procedure 2

Percutaneous suturing is suitable in Achilles tendon ruptures as an alternative to conservative therapy, which may be somewhat complicated, and will protect the contact between the tendon stumps when the foot is in plantar flexion. After ultrasound examination to exclude too great a diastasis between the tendon stumps, six stab incisions are marked in the prone position, which are made medially and laterally at the level of the rupture or 5 cm proximally or distally to it. It is essential to take the course of the sural lateral nerve into account. Using 1 × 1.3 mm PDS cord with reinforcement at both ends threaded through a straight needle, the tendon is perforated transversely proximally and distally, and the thread guided through the transverse point of exit via the stab incision at the level of the rupture (Fig. 16.10). Subsequently, knots are tied on both sides of the proximal and distal leg with the foot in plantar flexion and supplemented by a protective suture [11, 14]. Adjuvant and follow-up treatment is carried out with the patient wearing a special boot for 3 weeks in both plantar flexion and the neutral positions. Afterward, a raised heel of 2–2.5 cm is prescribed for 4–6 weeks.

16.3.6 Special Remarks

Tendon injuries to the lower extremity are frequent, caused to a great extent by previous degenerative damage. They generally require surgical reconstruction with temporary postoperative immobilization that should however, be kept as short as possible. Tendon injuries caused by direct traumatic external force resulting from cuts, stabs, or blows also need surgical repair to restore continuity. In such cases the patient needs to rest for a short time and then receive early functional follow-up treatment.

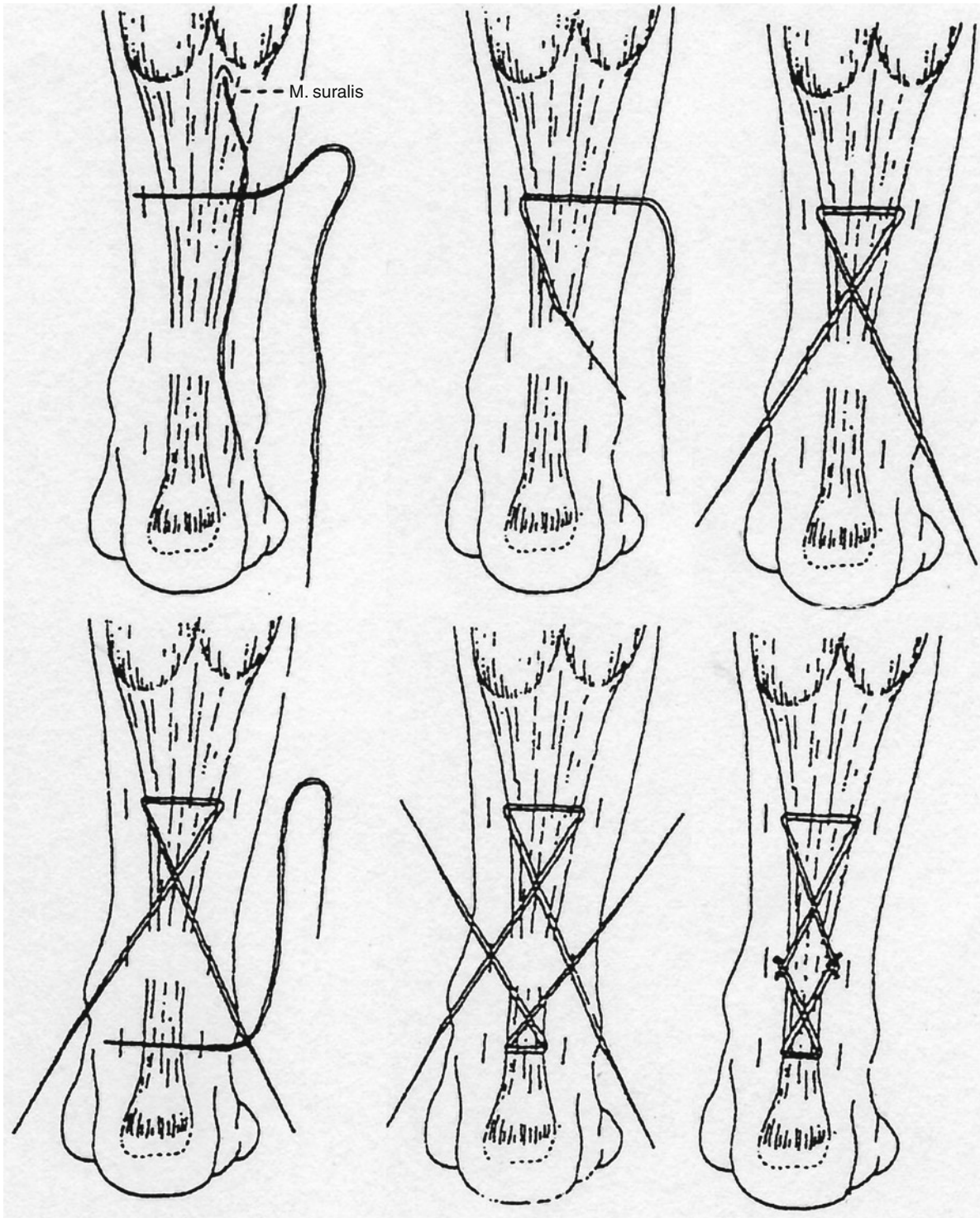


Fig. 16.10 Percutaneous suturing of Achilles tendon rupture

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Treatment Principles of Nonunion

17

Christian Hierholzer and Volker Bühren

17.1 Definitions

Historically, the definition of delayed union and nonunion have been based on time from the onset of injury. More recently, the exact time frames have been considered to be less important. Fracture healing is a dynamic progressive process, with intervention indicated for 3–5 months following injury if three consecutive monthly radiographic studies do not demonstrate progression of fracture healing [1].

17.1.1 Delayed Union

The term "delayed union" is used for a fracture that has not united within a period of time that would be considered adequate for bone healing. Delayed union suggests that union is slow but will eventually occur without additional surgical or nonsurgical intervention. The time frames are different for various fractures. Adequate fracture healing is dependent on localization, metaphyseal versus diaphyseal; fracture type, open versus closed, simple versus comminuted; fracture treatment, conservative versus operative; and patient age and condition, juvenile versus adult versus osteoporotic. Delayed union occurs if fracture healing does not progress in a timely fashion and is not completely healed within 6 months having taken all of these conditions into consideration.

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17.1.2 Nonunion

Various definitions of nonunion are used. Generally, failure of a fracture to heal within 6–8 months constitutes nonunion. In 1986, a Food and Drug Administration consensus conference defined nonunion as absence of fracture healing 9 months following injury without progressive radiological signs of bone healing on three consecutive radiographs taken at monthly intervals. Nonunion refers to a fracture that will not unite without additional surgical or nonsurgical intervention. Clinically, there motion and pain may present at the fracture site.

17.2 Classification

Nonunions are most commonly classified according to the Weber-Cech classification [2]. The classification is based on radiological appearance and correlates with fracture biology. Two basic types of nonunion, hypertrophic and atrophic, are recognized.

- Hypertrophic nonunions are hypervascular and are capable of biological reaction demonstrating increased vascularity and prolific callus formation. Hypertrophic nonunions have excellent healing potential and result from unstable fixation of the fracture.
- Atrophic nonunions are biologically inactive and inert with impaired osteogenesis, presumably caused by reduced activity of osteoblasts. Atrophic nonunions typically demonstrate little callus formation around a fibrous tissue-filled fracture gap. Bone ends may be tapered, osteopenic, and sclerotic. Healing potential is poor. However, vascularity may

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be preserved. Atrophic nonunions are regularly associated with unstable fracture fixation and axis deviation, predominantly varus axis deviation.

A specific subgroup of atrophic nonunions, synovial pseudarthrosis, is defined as nonunions with a fluid-filled cavity and a synovial-like membrane at the fracture site [3].

It is critical to determine if evidence of infection is present at the nonunion site for successful treatment. Noninfected and infected nonunions are distinguished.

17.3 Normal Fracture Healing

Fracture healing occurs in four distinct phases including recruitment, induction, modulation, and osteoconduction. Recruitment refers to taxis of systemic osteoprogenitor cells or inducible pro-osteoblasts to the fracture site. During induction, osteoblastic activity is increased followed by cell differentiation and proliferation of multipotential cells in the modulation phase. In the phase of osteoconduction, collagen and hydroxyapatite surfaces are transformed into a three-dimensional lattice leading to a biomechanically advantageous structure of bone formation [4].

17.4 Etiology

Although exact causes of delayed union and nonunion are unknown, both systemic and local factors contribute to impairment of fracture healing. Systemic and local factors affect two major determinants of nonunion development: pathological biology and pathological mechanics.

17.4.1 Systemic Factors Include

- General health, age, and activity level
- Osteoporosis
- Metabolic and nutritional status
- Use of steroids or anticoagulants
- Extensive use of anti-inflammatory and anti-depressant medication
- Use of tobacco and alcohol
- Polytraumatization

17.4.2 Local Factors

Local factors include condition and vascularity of bone, periosteum, and soft-tissue envelope

1. Open fracture
2. Segmental fracture, with impaired blood supply
3. Comminuted fracture
4. Excessive periosteal stripping and fragment denudation

Systemic and local factors may adversely affect bone healing by deteriorating *biology or mechanics*.

17.4.3 Pathological Biology

Pathological biology summarizes all conditions that impair osteogenesis predominantly by compromising vascularity, medullary activity, or by causing infection. In open fractures, high-energy impact with contusion and destruction of soft-tissue envelope and segmental or comminuted free fragments causes loss of blood supply to the fracture ends and damage to nutrient vessels [5]. Vascularity is impaired by surgical approach and open reduction of a fracture with excess stripping of the periosteum and damage to blood supply of bone and soft tissue during hardware insertion.

Medullary activity in the fracture hematoma is a key factor in bone consolidation, and can be impaired from excessive interfragmentary gap, infection, or large soft-tissue wounds. These conditions are capable of stimulating activation of macrophages and mediators that inhibit osteogenesis [6].

Infection contributes to nonunion because it predisposes the patient to nonunion by creating the same factors that cause nonunions of noninfected fractures: cortical bone death with subsequent formation of pus and sequestrum, creation of gaps by osteolytic infectious granulation tissue, and motion from loosening of implants.

17.4.4 Pathological Mechanics

Pathological mechanics summarize all conditions that result in instability and axis deviation.

1. Unstable fixation and interfragmentary instability
2. Fixed dehiscence and distraction
3. Angular deformity caused by inadequate reduction

4. Untimely weight bearing with inadequate immobilization

Excess motion is caused by inappropriate stabilization of the fracture by internal or external devices. A gap between fracture ends occurs secondary to distraction by internal fixation or traction, interposition of soft tissues, loss of bone, or malalignment. Interfragmentary motion stimulates secondary bone healing by exudation of morphogenetic substances and growth factors from the fractured bone ends and results in abundant callus formation [5, 6]. Rigid fixation minimizes the production of granulation tissue and external callus.

17.5 Examination

Physical examination of a patient with nonunion includes

- Past medical history
- Physical examination
- Assessment of the affected limb:
  - Condition of soft tissue, analysis of axis, and rotational deformities and length discrepancies. Vascular and neurological status.
  - Examination of the nonunion site: local tenderness and mobility
  - Functional assessment of adjacent joints: range of motion, condition of soft tissue, contractures.

17.6 Imaging Studies

Most often, basic radiographs in at least two planes will sufficiently outline the osseous problem and normally provide sufficient information on nonunion type and quality of bone. Based on radiographic findings, the distinction between atrophic or hypertrophic nonunion is possible. Occasionally, computed tomography (CT) scans are obtained in cases of complex nonunions or difficult interpretations of radiographs. CT reconstructions are beneficial in demonstrating the extent of nonunion and sequestrum.

In the lower extremity, assessment of the mechanical axis is performed using full length radiographs with weight bearing.

When infected nonunion is suspected, indium-labeled white cell scans may help to identify and localize infection.

- Magnetic resonance imaging (MRI) is very sensitive and specific in detecting osteomyelitis with an accuracy of over 90 %, and provides additional information on anatomy and location of infected bone, sinus track, and sequestrum. Interpretation of MRI scans is complicated by the presence of residual hardware. Technetium Tc-99m disphosphonate bone scanning has been used in an attempt to identify infections, but it is not specific for infection. However, in combination with Indium In-111–labeled leukocyte, imaging accuracy is increased to 82 % [7].

17.7 Other Tests

- Vascular studies are indicated if vascular injury is suspected or if free soft-tissue transfer or vascularized bone grafts are planned. In patients with peripheral vascular disease, arteriograms or Duplex studies are essential to determine the arterial status prior to revision surgery.

Histologic Findings: Histologic studies are helpful and demonstrate high sensitivity (87 %) and specificity (100 %) when assessing nonunion for the possibility of infection, particularly when microbiology findings are inconclusive [8].

17.8 Treatment Objectives

Treatment objectives follow the principle of improving biology and mechanics of the nonunion thereby optimizing conditions for bone healing.

17.8.1 Improvement of Impaired Biology

Improvement of impaired biology is achieved by biological activation of the nonunion site, bone substitution, graft augmentation, and irradication of infection. For biological activation of the nonunion site, limited reaming, extracorporeal shock waves (ESW), and local application of biological messengers are performed to stimulate osteogenesis. If pathological biology is the result of osseous defect, the nonunion is resected to increase fragment contact and buttress. Shortening of the extremity may be necessary. Osseous defects require bone graft augmentation or can be corrected

using distraction osteosynthesis. If infection is causative for nonunion, medical and surgical treatment should focus on irradicating the infection.

17.8.2 Improvement of Impaired Mechanics

Enhancement of impaired mechanics requires correction of axis deviation, elimination of interfragmentary instability, and nonunion gap. Axis and rotational deviation promote formation of nonunion. Instability caused by unstable osteosynthesis and nonunion gapping cause interfragmentary micromotion and prevent fracture healing. In these cases, revision surgery is indicated to correct axis deviation, remove nonunion dehiscence, and increase stability.

In addition, the goal of treatment is not only to restore continuity of the fracture site, but also to restore limb function including mobilization of adjacent joints and improvement of bone and soft-tissue condition.

17.9 Treatment Principles

17.9.1 Hypertrophic Nonunion

In hypertrophic nonunion, callus formation is a sign of instability and interfragmentary motion at a vascular nonunion. The interposed tissue is essentially fibrocartilage. Bony union is promoted by minimizing motion following application of stable internal fixation devices. Resection of nonunion tissue or bone ends is not necessary unless significant malalignment is present. Bone grafting is usually not required.

In hypertrophic diaphyseal nonunion of the lower extremity, correction of axis deviation may be achieved with a closed reduction technique and precise insertion of the intramedullary nail. Key to successful alignment is precise positioning of the guide wire into a central position at the distal tibial or femoral end followed by reaming of the intramedullary canal. Axis alignment and correction of deformity is performed when inserting the nail into the intramedullary cavity. The distal fragment will follow the seating-direction of the nail into correct axis alignment.

17.9.2 Atrophic Nonunion

Atrophic nonunions may occur as a result of open fractures or previous operative procedures in which the soft-tissue envelope has been separated from the bone, removed, or damaged; the bone remains avascular or is slowly revascularized. If alignment is good and there is no gap, decortication, stabilization under compression, and bone grafting will accelerate fracture healing. Malalignment and gap formation require resection of atrophic and fibrous scar tissue, shingling of sclerotic bone ends followed by open reduction, stable fixation, and bone graft augmentation.

In atrophic diaphyseal nonunion of the upper extremity, open reduction and resection of nonunion including shingling of sclerotic bone ends is recommended. In atrophic nonunion with bone defect, realignment may require square or oblique osteotomy to improve stability as well as cortex to cortex contact. Length discrepancies of a few centimeters are well tolerated in the humerus both functionally as well as cosmetically [9].

17.9.3 Alignment

Angulation contributes to nonunion because direction of transmitted forces create angular stress across the fracture site and increase deformity. Correction of malalignment results in improved axial load distribution with stimulation of bone healing. Realignment of angulation, rotation, or length discrepancy may be achieved in a single or staged procedure. Immediate realignment can be performed using closed reduction or open reduction techniques.

Progressive alignment is usually performed using circular external fixation devices. Correction of length discrepancies may be obtained with bone grafting, gradual callus distraction, or bone transportation techniques.

17.9.4 Stabilization of Fragments

Adequate stabilization of fragments is obtained by internal fixation using plating or intramedullary nailing techniques or by external fixation. Although absolute fixation is not required, shearing, rotation, and distracting forces must be neutralized after surgery. The choice of internal fixation depends on type of nonunion, condition of the soft tissues and bone, size and position of bone fragments, and extent of bony defect. Rigid fixation results in union by primary bone healing whereas more elastic or bridging fixation promotes secondary bone healing with callus formation.

17.9.4.1 Plate Fixation

Plate fixation requires a more extensive approach and opening of the nonunion site, potentially impairing blood supply to the fragments. Second, risk of secondary infection is increased. Stability relies on secured fixation of implants which is challenging in patients with poor bone quality as a result of osteoporosis or inactivity. Predominantly, plate fixation is utilized in atrophic metaphyseal nonunion and nonunion of the humerus and forearm [10].

17.9.4.2 Intramedullary Nailing

Intramedullary nailing, specifically interlocked nailing, is the treatment of choice in diaphyseal, hypertrophic nonunions of long bones such as the tibia and femur. Intramedullary nailing requires less exposure and preserves the soft-tissue envelope around the nonunion site. The procedure is regularly performed without opening of the nonunion site if alignment is acceptable or closed reduction is possible. When an open technique is required, limited exposure and dissection are performed.

The reaming procedure may be difficult in nonunion with obstruction of the medullary canal. Limited reaming is essential to avoid disruption of the endosteal blood supply and has been shown to elicit a periosteal vascular reaction [11]. Reamed nailing has the advantage of distributing intramedullary cancellous autograft to the nonunion site, which is a powerful stimulus for bone healing.

Therefore, external bone grafting is not required. Application of interlocking and compression nails allows for interfragmentary compression, dynamization, and early full weight bearing. The selection of the nail diameter is dictated by the size of the intramedullary canal and should be canal filling. Intramedullary nailing is not applicable for metaphyseal nonunion. Primary contraindication for intramedullary nailing is current or prior infection. In these cases, nailing may spread infection over the entire length of the medullar cavity [12].

17.9.4.3 External Fixation

External stabilization is a useful technique for correcting length discrepancy and deformities in a staged procedure, for managing bone gaps and defects, for treating metaphyseal fractures in close proximity to joints, and for temporal arthrodesis. More traditional pin external fixators using the Ilizarov principles are used in the management of nonunions, particularly when complicated by infection.

External fixation is relatively noninvasive, the soft-tissue envelope is preserved, and the nonunion site is not irritated by implants. An external fixation technique minimizes the risk of infection. Major problems include pin site infection, inhibition of range of motion because of transfixation of muscles and tendons, prolonged duration of application, patient dissatisfaction, and patient noncompliance. The external fixator requires continuous pin site care and frequent monitoring and follow up by trained medical personnel.

17.10 Stimulation and Augmentation of Bone Healing

Stimulation of osseous healing includes
- Bone graft augmentation
- Biological stimulation
- Vascular stimulation
- Mechanical stimulation
- Electrical stimulation
- Ultrasound

17.10.1 Bone Graft Augmentation

17.10.1.1 Functions of Bone Graft

Osteogenesis. Graft-dependent osteogenesis occurs independently of the host. Surface cells on cancellous and cortical grafts can survive and produce new bone. Because of its larger area, cancellous bone has more viable cells and therefore, more osteogenic potential [10].

Osteoinduction. Mesenchymal cells are recruited from surrounding tissues and differentiate into cartilage and bone forming cells. Graft bone morphogenic proteins (transforming growth factor-β [TGF-β], insulin-like growth factor [IGF]-I, IGF-II, fibroblast growth factor [FGF], platelet-derived growth factor [PDGF], interleukins, and granulocyte-stimulating factors) influence the differentiation of these mesenchymal cells [13].

Osteoconduction. Inert material cells act as scaffolding for living tissue, including connective tissue cells and blood vessels, to grow and form viable bone by gradual substitution. Osteoconduction follows a pattern determined by graft structure, vascular supply from surrounding tissue, and mechanical environment in where the graft is placed. The inert material is usually cancellous bone graft. However, various biological and non-biological materials are increasingly being utilized as alternatives.

Mechanical support. Bone graft is used to fill bone defects and provide structural support.

Bone Grafting as an Isolated Procedure. Indication for isolated bone grafting remains an exception and includes the Matti-Russe procedure for the treatment of scaphoid nonunion [14] and tibiofibular bone grafting for tibial nonunions with infection, segmental bone loss, or soft-tissue damage on the anterior aspect of the leg (intertibiofibular grafting) [3, 15].

17.10.1.2 Types of Bone Graft

Autografts
- Cancellous bone
- Cortical bone
- Nonvascularized and vascularized cortical bone

Allografts
- Cancellous bone
- Cortical bone
- Cortico-cancellous
- Demineralized bone matrix

Autografts

The gold standard for bone graft augmentation is application of autologous cancellous bone. The efficacy of autologous bone grafting has been confirmed for many orthopaedic procedures including delayed union and nonunion [16, 17]. Autograft histocompatibility and lack of immunogenicity [18, 19] compliment its osteoinductive (protein) and osteoconductive (matrix) properties [16, 20] and make it an ideal substance for nonstructural grafting. Furthermore, autologous grafting has no associated risk of transmitting occult diseases or infection [16, 21]. Autografts are osteogenic, easily revascularized, and quickly integrated into the recipient site. Osteogenesis is stimulated and early bone formation promoted resulting in stabilization of the nonunion site.

Cancellous autologous grafts are predominately obtained from the iliac crest or alternatively from the proximal tibia. The anatomy of the iliac crest provides reasonable surgical access and ample amount of graft material. Of concern has been the significant rate of morbidity associated with the autologous bone graft donor site. Donor site morbidity includes infection, severe pain, instability, insufficiency fracture, and secondary formation of heterotopic ossification, antalgic gait, persistent dysaesthesia, tenderness, and numbness.

Non-vascularized cortical bone grafts are osteogenic, provide initial structural support, and revascularize slowly. The major source is the fibula. As a result of osteoclast resorption, graft stability decreases following implantation and remains weaker for several months compared with normal bone [22].

Vascularized cortical graft can be harvested from the fibula, iliac crest, and ribs. These grafts demonstrate quick healing and integration because of high survival rate of osteocytes and absence of resorption relatively independent of the host bed.

Allografts

Cortical or cancellous bone allografts are used if the source of autogenous bone is either inadequate or inaccessible. Allografts promote osteoconduction and are composed of non-viable cells. Therefore, allografts lack osteogeneic and osteoinductive properties.

Demineralized bone matrix (DBM) is routinely used as bone graft augmentation and numerous indications exist including fracture and nonunion healing as well as filling of large bone defects [23, 24]. DBM is harvested from cadaveric donors, sterilized using irradiation, and is free of bacterial or viral load. DBM has both osteoconductive and osteoinductive capacity mediated by bone morphogenic proteins (BMPs), IGF-I, and TGF-β1 [25].

17.10.2 Mechanical Stimulation

Fracture healing is modulated by type of load distribution [26]:
- Low stress and strain leads to direct intramembranous bone formation
- Low tensile strain may stimulate intramembranous ossification
- Hydrostatic compressive stress is a stimulus for chondrogenesis
- High tensile strain is a stimulus for fibrous tissue production
- Poor vascularity can stimulate chondrogenesis in an osteogenic environment
  - Limited micromotion and cyclic loading result in secondary bone healing mediated by enchondral ossification of cartilage or fibrocartilage. Initial stability by bridging callus further facilitates enchondral ossification [26].

- In contrast, if stabilization of the fracture or nonunion site is insufficient, bending and torsional forces will create high strains in the regenerating tissue around the fracture gap, stimulating fibrous tissue formation.
- Continuous motion and consecutive vascular damage to new forming capillaries results in formation of cartilaginous caps at the bone ends with formation of nonunion.

The goal of stabilization of nonunion is to provide sufficient stability and to reduce mechanical shear stresses in order to optimize mesenchymal cell differentiation into bone-forming cells.

17.10.3 Vascular Stimulation

Angiogenesis with the formation of new blood vessels and stimulation of adjacent circulation are essential for fracture repair and osteogenesis. Angiogenic factors such as FGF and vascular endothelial growth factor contribute to fracture repair and bone healing [27, 28] specifically in conditions with impaired vascularity or angiogenesis.

17.10.4 Biological Stimulation

Several strategies have been suggested to promote bone healing through administration of biological messengers. Bone marrow aspirates with a dense population of osteoprogenitor cells are used to stimulate bone healing and bone formation [29]. Isolation techniques are performed to increase concentration of active mesenchymal stem cells. Currently, research focuses on enhancing bone healing by local injection or coating of implants using growth factors such as BMPs, TGF-β, IGF, and DGF with osteoinductive capacity [30, 31].

BMPs control key steps in the cascade of osteogenesis including chemotaxis, mitosis, and differentiation. Several BMP subtypes including BMP2, BMP4, and BMP7 have been shown to accelerate fracture and wound healing as well as promote healing of delayed and nonunion [32, 33].

Similarly, formation of fracture callus is increased following administration of TGF-β and IGF by stimulating cell proliferation and matrix synthesis of chondrocytes and osteoblasts [10, 34, 35].

17.10.5 Electrical Stimulation

Direct current stimulation may trigger mitosis and recruitment of osteogenic cells probably by induction of electrochemical reactions at the electrode/tissue interface [36]. Clinical experience has shown that electrical stimulation is effective in hypertrophic nonunions, but less so in atrophic nonunions and in the presence of a gap [37].

17.10.6 Ultrasound Stimulation

Low-intensity pulsed ultrasound has been used to accelerate healing of fractures of the upper and lower extremities [38]. Mechanisms include increase in blood flow, activation of metabolism of bone forming cells, such as increased ion influx, gene up-regulation, and induction of enzymatic processes [39].

17.10.7 High-Energy Extracorporeal Shock Waves

ESW treatment has shown to be effective in promoting healing of fractures or nonunion. ESW is capable of enhancing bone marrow stromal growth and differentiation and maturation of osteoprogenitors, presumably by induction of TGF-β [40].

17.11 Infected Nonunion

Infection is frequently a major etiological factor in nonunion. Both surgical and medical treatments are required to eradicate infection by excising necrotic tissue and removing infected implants sustaining the nonunion. Clinically, infected nonunion presents with atrophic appearance on radiologic imaging, poor fracture vascularization, inadequate soft-tissue coverage, and loose fixation devices.

Surgical treatment of infected nonunions consists of stabilization, débridement, local therapy, repair of defect to control infection, increase in stability of bone under load, and reconstitution of structural anatomy. Stabilization of the nonunion is critical both to allow for healing of the nonunion and for effectively treating infection.

Organism-specific antibiotics are delivered systemically, and locally with antibiotic-impregnated methylmethacrylate beads. Impaired soft tissue and bone are reconstructed with local or distant flaps and bone grafts.

Two phases of treatment are necessary to heal infected and draining nonunion: elimination of infection and healing of bone. The therapeutic strategy is carried out sequentially or concomitantly. Concomitant treatment is recommended for saving valuable time. If drainage has not occurred for 3 or more months and the wound is quiescent, infected nonunions can be treated as atrophic nonunions. Infection is usually associated with bone avascularity. Dead bone and necrotic areas are débrided to help eradicate infection. Bone ends are shingled and stabilized using internal or external fixation [4].

If swelling, tenderness, redness, or fever is present indicative of active infection or abscess formation, then open revision, vacuum sealing, and staged revision procedures are performed. Irradication of infection requires multiple revision surgery with radical and frequent débridement.

Frequently, secondary procedures are necessary to heal bone defects involving staged operations several weeks after initial debridement. Alternatively, lengthening or grafting may be performed at a site remote from the infected area.

17.12 Selected Localizations and Examples of Nonunion

In this section we will discuss selected localizations and examples of nonunions. More extensively, two specific entities, atrophic humeral shaft nonunion and hypertrophic tibial shaft nonunion, will be delineated.

Atrophic humeral shaft nonunions are a domain of open reduction, plate fixation, and bone graft augmentation. The treatment of choice is closed reduction for hypertrophic tibial shaft nonunion, internal bone grafting by intramedullary reaming material, and stabilization using compression nailing. These examples may serve as treatment guidelines for various nonunion localizations.

17.12.1 Nonunion of the Upper Extremity

17.12.1.1 Humerus

Humeral Shaft Nonunion

The incidence of humeral shaft nonunion as a complication of both conservative and surgical treatment has been reported from 8 to 12 % [41]. Risk factors for nonunion include injury-related factors such as unstable fracture patterns, segmental fractures, and open fractures and concomitant injuries. Preexisting shoulder or elbow stiffness transmit lever arm forces toward the fracture site and predispose patients to nonunion. Treatment-related factors include fracture gapping following traction cast or deficient nailing and plating techniques, loss of reduction, and hardware failure in osteoporotic bone.

Atrophic nonunions of the humerus shaft are treated with a standard protocol of open reduction, plate fixation, and bone graft augmentation [42]. In general, intramedullary nailing of atrophic humeral shaft nonunions following initial conservative fracture treatment can be performed but is not recommended because visualization of the radial nerve is not possible and the radial nerve is at risk during reduction and reaming procedure.

Approach

A triceps splitting approach is performed for midshaft or distal third nonunions. Dissection and neurolysis of the radial nerve is mandatory and requires surgical experience and often knowledge of microdissection techniques. Identification of the radial nerve can be complicated by secondary dislocation resulting from trauma, previous surgery, diastasis of nonunion fragments, as well as scar tissue formation. The ulnar nerve is best localized proximally in distal nonunions where it emerges beneath the triceps tendon. For humeral nonunion in the proximal third the deltopectoral approach is used.

Resection of Nonunion

Radical débridement is essential to remove all inert atrophic fibrous tissue. Gentle dissection is required to preserve soft-tissue attachments to bony fragments and residual blood supply. The medullary canal of both fragments is often sealed with fibrous tissue or a sclerotic bony end cap. Careful intrafocal débridement and evaluation of the nonunion is key to ensure optimal cortex to cortex stability that is required to allow for neovascularization and migration of osteogenic cells as well as to prepare the host environment for successful graft integration.

Open Reduction

Open reduction is performed following resection of atrophic tissue to correct rotational and angular deformity. Axis alignment is prerequisite for achieving

favorable interfragmentary contact and stable fixation following plate osteosynthesis.

Fixation

Preferentially, plate fixation is performed using locking plates. For midshaft nonunions, the plate is positioned on the dorsal side and in proximal nonunions, on the lateral aspect of the humerus. The length of each plate is determined by localization and pattern of the nonunion. Engagement of at least eight cortices is recommended on both sides of the nonunion. Bone loss can result in shortening of the arm. Humeral length discrepancies of a few centimeters are generally well tolerated both functionally, as well as cosmetically [9].

In diaphyseal humerus, nonunion that develops following fracture treatment with intramedullary nailing closed reduction and stabilization with exchange nailing is a surgical alternative. Hypertrophic nonunion caused by unstable intramedullary nailing benefit from exchange nailing with removal of implant, limited reaming, and internal bone grafting form reaming material, as well as insertion of a compression nail without opening of the nonunion site. Application of interfragmentary compression and insertion of interlocking screws provide sufficient cortex to cortex and rotational stability for osseous healing.

In contrast, intramedullary nailing of displaced diaphyseal nonunions following initial conservative fracture treatment exposes the patient to the risk of radial nerve entrapment during the reduction procedure, whereas exchange nailing of humeral nonunions does not endanger the radial nerve.

Distal Humeral Nonunion

Delayed unions and nonunions of distal humeral fractures are relatively rare. The prevalence of nonunion has been reported to range from 2 to 10 % [43]. Typically, the nonunion involves the supracondylar region, whereas the intercondylar region generally unites. Supracondylar nonunion are located proximal to, and low transcondylar nonunions distal to the proximal rim of the olecranon fossa.

Surgical treatment is performed using open reduction, stable fixation, and bone grafting at the nonunion site and also includes complete mobilization of the elbow joint [44]. Intra-articular adhesions, osseous incongruence, extra-articular fibrosis, as well as ligamentous and muscular contractures contribute to joint stiffness. Release of elbow contractures results in redistribution of normal forces across the elbow joint and decreases lever arm and bending forces at the nonunion site. Stability of the osteosynthesis is protected.

A treatment alternative to open reduction and internal fixation is elbow arthroplasty. Morrey and Adams recommended that total elbow arthroplasty be used as a salvage procedure when stable open reduction and internal fixation is not possible or the articular surface or joint anatomy is not salvageable [45].

In intraarticular or transcondylar nonunion, a chevron olecranon osteotomy offers ideal exposure of the nonunion site whereas in extraarticular-supracondylar nonunion a triceps-splitting can be sufficient [44]. The olecranon osteotomy is repaired using tension band fixation.

Reduction begins with reconstruction of the condylar block followed by fixation to the medial and lateral columns. For stable fixation, 3.5-mm pelvic reconstruction plates or locked compression plates are contoured to fit along the posterior aspect of the lateral column. The medial column is plated along its medial surface. Long screws starting from the medial or lateral epicondyles through the medial and lateral columns provide additional stability [44].

17.12.1.2 Nonunion of the Forearm

Nonunion of the Radial Neck

Nonunion of the radial neck is a rare complication of displaced radial neck fractures. Treatment options include salvage procedure with open reduction internal fixation and bone graft augmentation or excision of radial head and neck depending on pain, deformity, and functional restrictions.

Nonunion of Radius and Ulna

In nonunions of the proximal and midshaft radius and ulna, open reduction and plate fixation using a 3.5-mm dynamic compression plate or locking compression plate and bone graft augmentation are used for revision surgery. Preferentially, an eight- to nine-hole plate is applied. Distal radius nonunions are treated with locking T-plates as a buttress using a dorsal or palmar approach.

17.12.2 Nonunion of the Lower Extremity

17.12.2.1 Femur

Nonunion of the Femoral Neck

Following femoral neck fractures, several factors predispose a nonunion to occur including morphologic

features of the fracture, displacement and comminution, inadequate reduction, failure of fixation, and poor vascularity. However, mechanics and load distribution play a significant role in the pathogenesis of a nonunion.

Fracture anatomy is important. Pauwels demonstrated that shear forces created by high fracture angle of 70–90° (defined as Pauwels III) impair fracture healing and predispose to development of nonunion [46, 47]. In addition to fracture displacement, fracture comminution also contributes to nonunion [48, 49]. Nonunion is rare after nondisplaced femoral neck fractures whereas femoral neck fractures with more than 50 % displacement of the head fragment (Garden IV) demonstrate increased risk of nonunion. Posterior comminution adversely affects adequacy of reduction, fracture angle, and the ability to obtain stable fixation.

Several factors must be considered when treatment for nonunion is planned including patient's age, morphologic features of the fracture, femoral head viability, extent of femoral neck resorption, and bone quality. These factors help the surgeon to decide between the two major treatment options:

1. Salvage operation of the femoral head using revision fixation and bone grafting or intertrochanteric valgisating osteotomy.
2. Total joint replacement arthroplasty.

Salvage procedures are preferred in younger patients with viable femoral heads and a fixable fracture whereas arthroplasty is indicated for unfixable nonunions or elderly patients. The vitality of the femoral head is assessed using MRI even if hardware is present.

The purpose of intertrochanteric valgisating osteotomy is to decrease he Pauwels angle of the nonunion thereby converting shearing forces into compression forces. In addition, weight bearing line and hip load transmission are shifted medially. Rotational deformities are corrected. Conversion of the varus position of the proximal femur into valgus position results in lengthening of the extremity. As much as 2 cm of length can be gained. Bone grafting is not mandatory because of improved biomechanics [50].

Intertrochanteric osteotomy is preferable to a subtrochanteric osteotomy because presence of more cancellous bone in the intertrochanteric region ensures faster healing, better ability of obtaining correction, and easier conversion to arthroplasty if necessary.

Subtrochanteric Nonunion

Subtrochanteric nonunions are rare. Predisposing factors for acute fixation failure of subtrochanteric fractures include poor bone quality, unfavorable and unstable fracture patterns, or suboptimal position of fixation devices [51]. Treatment of nonunion or acute fixation failure of a subtrochanteric femur fracture is challenging because of fracture deformity, bone loss, comminution, and retained, often broken, hardware from previous surgeries.

Additionally, high tensile and compressive stresses across the subtrochanteric region require stable fixation of the proximal head and trochanteric fragment as well as the distal shaft fragment. New generation intramedullary nails with locked fixation of the femoral head screw are effective in achieving stable fixation of the proximal bone fragment. Revision internal fixation and bone graft augmentation for subtrochanteric nonunion consistently result in a high rate of fracture union and functional improvement [52].

Femoral Shaft Nonunion

Fractures of the femoral shaft are usually treated surgically. Surgical treatment encompasses intramedullary nailing, plating, and external fixation. The incidence of nonunion after nonsurgical treatment is 1–2 and 8 % after external fixation or plate fixation, respectively [53].

Intramedullary nailing, specifically interlocked nailing, is the treatment of choice in diaphyseal nonunions of the femur. If alignment is acceptable or closed reduction is possible, a closed nailing technique is performed without opening of the nonunion site. Transplantation of autologous bone grafting usually is not required but internal bone grafting by the reaming material is successfully used for stimulation of osteogenesis. If open reduction is necessary, limited exposure of the nonunion site and dissection should be performed. Similarly, nonunion after failed plating is treated by removal of plate, followed by bone grafting and intramedullary nailing. Early weight bearing is possible and the late effects of "stress shielding" do not occur. Primary contraindication for intramedullary nailing is current or prior infection.

Supracondylar Nonunion

Supracondylar nonunions can be treated with orthograde implantation of locked intramedullary nails. If the nonunion is displaced, open reduction and the use of locking plates or 95° dynamic condylar screw is an alternative. Intercondylar nonunions are best treated by open reduction and adequate exposure. A condylar buttress plate with six distal holes placed laterally is implanted. Occasionally, two plates are needed, one medially and one laterally.

17.12.2.2 Tibial Nonunion

Injury- and treatment-related factors contribute to the development of tibial nonunion.

Injury-Related Factors

Injury-related factors include severity of injury such as degree of fracture comminution and bone loss, open fracture, degree of soft-tissue injury, and fracture localization in the distal third. The subcutaneous position of the tibia renders the tibia susceptible for open fractures and provides less soft-tissue coverage. Subsequent complications such as infection or compartment syndrome adversely affect fracture healing [10, 54].

Treatment Related Factors

Treatment-related factors include delay in fracture treatment in open fractures, iatrogenic injury of the soft-tissue envelope such as excessive periosteal stripping, distraction across the fracture site, angular and rotational deformity, inadequate immobilization or fixation, and the splinting effect of an intact fibula.

Risk Factors

Use of nonsteroidal anti-inflammatory and antidepressant medications, cigarette smoking, the nutritional status of the patient, and noncompliance with the postoperative strategy place the patient at higher risk of delayed healing or nonunion [55].

Congenital Pseudoarthrosis

Congenital pseudoarthrosis of the tibia is a unique condition observed in children. Neurofibromatosis and fibrous dysplasia are predisposing factors, although some are idiopathic in nature. The pathology seems to lie in the periosteum [4].

Imaging Studies

- The goal of diagnostic imaging is assessment of fracture deformity. Plain radiography is typically the most helpful tool. Deformity is assessed in both anteroposterior and lateral planes, with resolution of the plane and degree of maximum deformity. Any rotational component must be assessed either clinically or with CT. Leg length discrepancies should be determined clinically or more accurately with CT-scanography or ultrasound. Finally, fracture stability is determined. Often, fracture nonunion is difficult to assess on plain radiography and fluoroscopy. CT may be helpful. Assessment of the fibula evaluates whether or not the splinting effect of an intact fibula is preventing tibial union.

Surgical Therapy

Treatment Principles

Treatment of tibial nonunion depends of classification, localization, and stability of the nonunion, alignment and axis deviation, soft-tissue injury including nerve deficits, presence of infection, possible concomitant injuries, and patient compliance.

Hypertrophic nonunions are vascular, demonstrate prolific callus formation, and have excellent healing potential. In general, hypertrophic tibial shaft nonunions are treated with rigid stabilization using intramedullary nailing with or without compression. Biologic stimulation is provided through intramedullary reaming material serving as internal bone grafting.

Atrophic nonunions are characterized by their absence of callus, deficient bone vascularity, and poor healing potential. Débridement of all necrotic tissue is mandatory with preservation of viable and vascular bone fragments. Biologic stimulation including bone grafting, soft-tissue coverage, or other forms of biologic stimulation such as BMPs is required to stimulate bone formation.

Surgical Treatment

- Fibular osteotomy
- Removal of ineffective, broken, or infected hardware
- Use of biologic bone stimulation, as described above
- Bone stabilization
- Eradication of infection

Whenever a splinting effect of an intact fibula blocks tibial dynamization or compression across the tibial nonunion site, oblique fibula osteotomy and resection of a 1–2 cm segment is performed followed by tension band fixation.

Removal of necrotic or infected bone is a prerequisite to ensure bone healing. This may involve the need for significant bone graft, shortening, or bone transport.

Bony alignment and stability is essential for successful treatment of tibial nonunion. The use of a reamed intramedullary nail is an excellent method for aseptic nonunions, particularly in the middle three fifths of the tibia [56]. Primary indication for reamed intramedullary nailing of tibial shaft nonunion is conversion from unreamed nailing or plating in closed and grades I or II open fractures with no evidence of infection. This technique has the advantage of early rehabilitation, maintenance of alignment, and early weight bearing. This technique is less effective for patients with very proximal or distal fractures.

Alternatively, compression plating can be performed to treat tibial nonunions. Wiss and colleagues plated 49 patients with tibial nonunion after initial external fixation [57]. The patients demonstrated a 92 % healing rate in a mean of 7 months with no further treatment. Compression plating with positioning of the plate under tension on the convex side of the tibia can assist in correction of any deformity and provides stable internal fixation. Plate fixation may impair wound healing and potentially devascularize bone segments. Therefore, soft-tissue preparation is performed atraumatically and dissection of fragments and periosteal stripping must be minimized. Plate fixation is less secure in patients with poor bone quality.

The use of external fixation, particularly small wire and hybrid external fixation, is an excellent option for the treatment of tibial nonunions, especially if the fracture is periarticular, if significant bone loss has occurred, if deformity including shortening is significant, or if infection is present. With application of an external fixator, multiple problems can be addressed concurrently. External fixation can provide stability of the fracture site, even in very proximal or distal fractures, with the use of fine wire fixation. Large infected bone segments can be removed and grafted and shortening can be performed.

Limb length equalization is achieved with bone transport or as an isolated procedure after union has occurred. Adjunct therapy, such as use of antibiotic bone cement or bone substitute beads, can easily be incorporated, and stabilization with external fixation usually provides access if soft-tissue grafts are needed. The use of external fixation is probably the best technique for patients with complex and significant angular deformities that cannot be corrected in a single procedure but require staged correction. Although highly versatile, pin site infections occur routinely, making subsequent conversion to an intramedullary nail difficult. Specialized training or experience in these techniques is important.

17.12.2.3 Metaphyseal Tibial Nonunion

Atrophic metaphyseal nonunions of the proximal and distal tibia are treated according to treatment principles using open reduction, resection of atrophic fibrous tissue, correction of angular and rotational deformity, stable plate fixation, and bone graft augmentation. Preferentially, locking plating techniques are used.

Nonunited pilon fractures of the lower tibia and fibula can be salvaged using intraarticular osteotomy and lag screw fixation with bone grafting. The reconstructed articular metaphyseal block is fixed to the lower shaft with a dynamic compression plate or a distal tibia locking compression plate. When the nonunion is supramalleolar and the joint is irrevocably arthritic, ankle fusion and stabilization of the nonunion is required using fixation anteriorly or laterally with one or more plates and liberal bone graft.

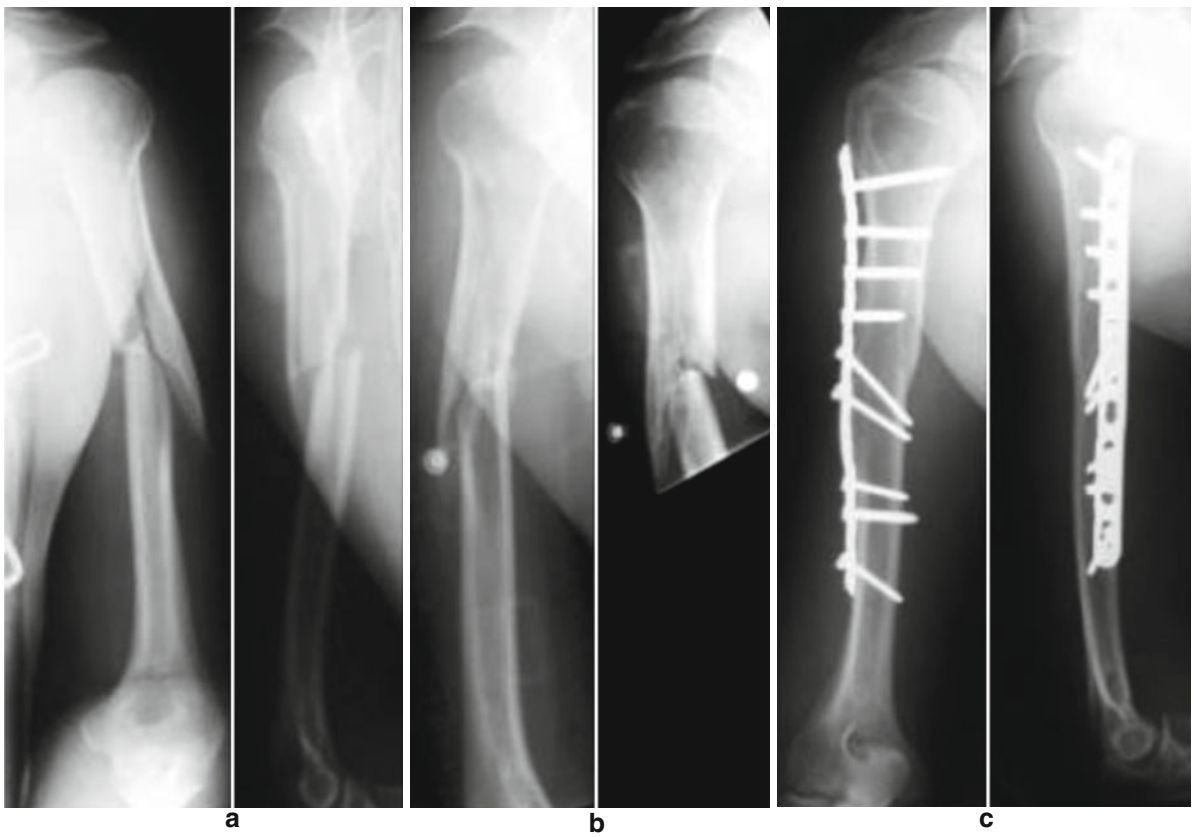
17.12.3 Examples

17.12.3.1 Case 1

An 85 year-old woman fell while walking and sustained a right-sided humeral fracture at the proximal metaphyseal/diaphyseal junction. She was treated conservatively using a course of multiple fracture braces and was referred to our institution 4 months following injury with a delayed union with gross painful motion

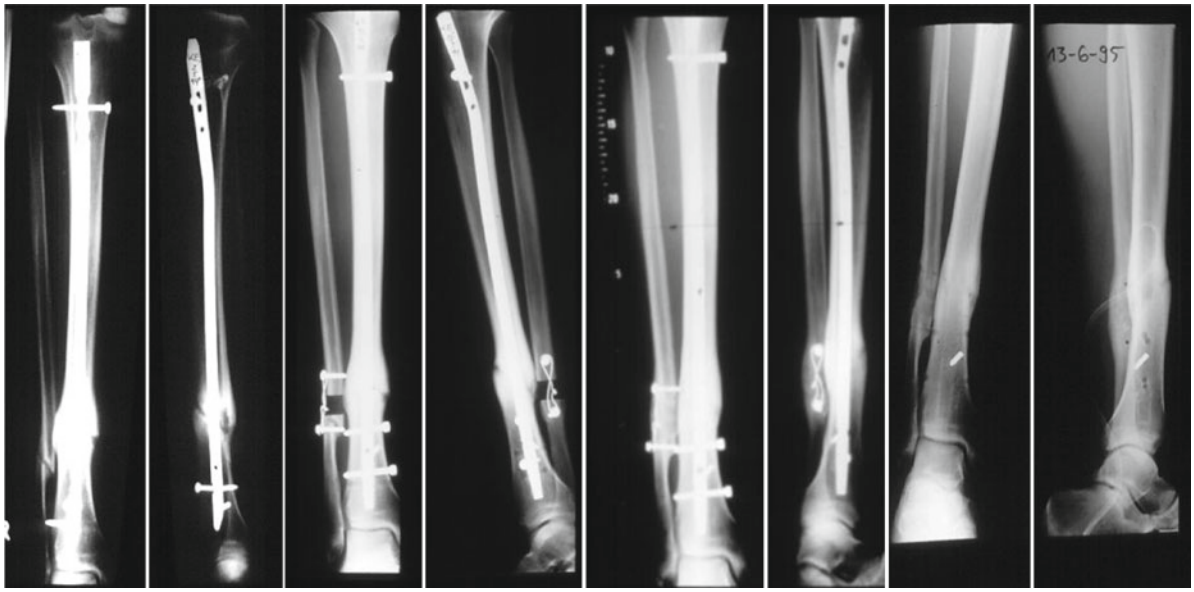
and crepitation at the fracture site. Open reduction and internal fixation was performed through a deltopectoral approach with placement of a 10-hole locking compression plate and screws and a lag screw with placement of supplemental demineralized bone matrix bone graft. 1 year after surgery the patient returned for follow-up with excellent clinical, functional, and radiological results including a return to her pre-injury activity status.

(a) Anteroposterior radiograph revealing a humeral fracture at the proximal metaphyseal/diaphyseal junction.
(b) Anteroposterior and lateral radiographs at 4 months showing a delayed union with minimal callous and obvious motion at the fracture site.
(c) Anteroposterior and lateral radiographs at 1 year following open reduction and internal fixation demonstrating bony union, adequate hardware positioning, and good alignment.



17.12.3.2 Case 2

A 47 year old man fell from his bike and sustained a distal tibia and fibula fracture. The patient was treated with unreamed intramedullary nailing and developed hypertrophic nonunion of the tibia. Seven months following initial revision, surgery was performed including removal of hardware, limited reaming, osteosynthesis with dynamically locked compression nail, fibula osteotomy, and tension band fixation. Hardware was removed following uneventful healing of nonunion.



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Osteitis

18

Matthias Militz and Volker Bühren

18.1 Basics

18.1.1 History

Since the antic the treatment of wound infections is known. With Lister, antiseptic procedures paved the way for a new era in surgery and wound management. Pasteur and Flemming transformed the treatment of septic surgery into an evolving era with the development of antibiotics. Furthermore, the rise in the number of complications shows a tendency of increasing operative fracture treatment. Even with the development of new implants, surgical techniques, and antibiotic drugs the problem of infections following trauma and orthopaedic surgery still remains. The economic aspect, in addition to the medical components, becomes and even more important factor. For prevention of infections in trauma and orthopaedic surgery and their effective treatment, knowledge of the pathophysiological pathways and experience in all established surgical procedures is necessary.

18.1.2 Anatomy

The incidence of osteitis depends on various factors and ranges between 1.5 % in cases of elective bone surgery up to 40 % in open fractures [1]. According to the occurrence of surgically treated fractures, the lower extremities are more often affected than the upper extremities [2]. Differentiation between cortical, spongiotic bone and joint infections is important for treatment. The interaction of soft-tissue covering, mechanical stability, joint movement, and preservation of neurological function is challenging in all types of treatment for osteitis.

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18.1.3 Pathophysiology

Every wound is associated with an invasion of bacteria in variable dimensions. The pathophysiological pathway of the "normal" inflammation reaction turns into infection under certain unfavorable conditions. Local, systemic, and outside influences determine further development.

Local factors are blood circulation, the concomitance of inflammatory substances, the number and type of bacteria, and the presence of implants. The critical number of bacteria was estimated using $2–8 \times 10^6$ [1]. Nevertheless, with the presence of implants the number decreases to less than 10^2 bacteria inducing an infection [3].

Furthermore, systemic factors also play a significant role in the development of infections. All systemic factors interfere with the local situation. The most important systemic factors in the alteration phase of switching from contamination to infection are older age, male gender, reduced general condition, diabetes, malignancy, immunodeficiency, adiposity, and malnutrition [3, 4].

The type and number of bacteria are the most important exogenous factors. The microbiological activity depends on the degree of contamination, the virulence, and the local conditions for growth. A certain number

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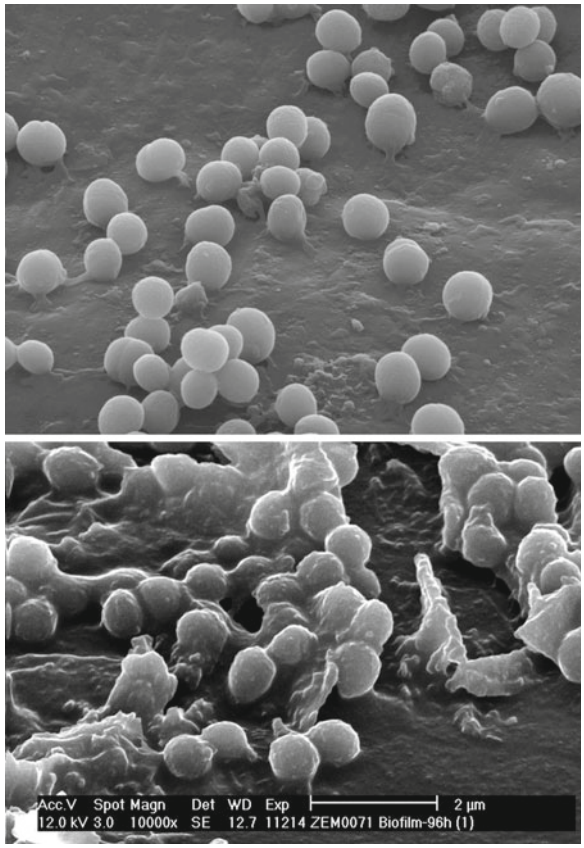

Fig. 18.1 Electromicroscopic slide of *Staphylococcus epidermidis*: Biofilm. *Upper figure*: *Staphylococcus aureus* from fluid culture; *lower figure*: *Staphylococcus aureus* in Biofilm (REM-slide from S. Sailer and I. Chatterjee, Homburg/Saar)

of bacteria are able to build up attaching themselves to artificial surfaces and generating a biofilm (Fig. 18.1). *Staphylococcus aureus, Staphylococcus epidermidis, Proteus mirabilis, Pseudomonas aeruginosa*, and other bacteria contain these characteristics. The biofilm can reach a thikness of 160 µm [1, 3, 5].

18.1.4 Prevention of Infections in Trauma and Orthopaedic Surgery

The treatment and healing process can be divided into three phases: preoperative, intraoperative, and postoperative.

In all three phases, the reduction of soft-tissue damage, the prevention of contamination, and the improvement of blood perfusion are necessary [6–8]. Therefore, the fracture should be reduced as early as possible, sufficient blood pressure should be reached, a examination of open fractures should be performed under sterile conditions in the operating room, and antibiotic drugs must be administered in the emergency room. The radical removal of dead tissue is required on open fractures. Additionally, the type of osteosynthesis and operative procedure chosen should prevent a decrease of local and systemic conditions for wound healing. In critical soft-tissue conditions, the method of choice is a temporary covering of the wound with a vacuum closure. Time plays a vital role in the third phase. By the time the surgeon reflects whether a revision procedure is necessary, the revision should be done.

The majority of severe infections and development of osteitis can be prevented with early and consequent management of complications in the third postoperative phase.

18.1.5 Principles of Clinical Examination

The usual principles for diagnosis of osteitis are valid.

In the clinical presentation of open fractures, operative fracture treatment, complications during wound healing, diabetes mellitus, and signs of general inflammation-like fever, swelling, and redness are indicative of osteitis.

Local signs of infection on clinical examination depend on the level of infection. The spectrum of local symptoms ranges from pain under stress to redness and swelling, up through the existence of fistula with purulent secretion, and in severe cases, systemic sepsis.

18.1.6 Laboratory Diagnostics

A specific laboratory parameter for detecting osteitis does still not exist.

In clinical practice, C-reactive protein (CRP) seems to be reliable parameter for evaluation of the activity of an inflammatory process [9, 10].

18.1.7 Imaging Methods

There are different imaging methods for diagnosing acute postoperative and the chronic osteitis. For the diagnosis of acute osteitis, the imaging methods are less helpful [9, 11].

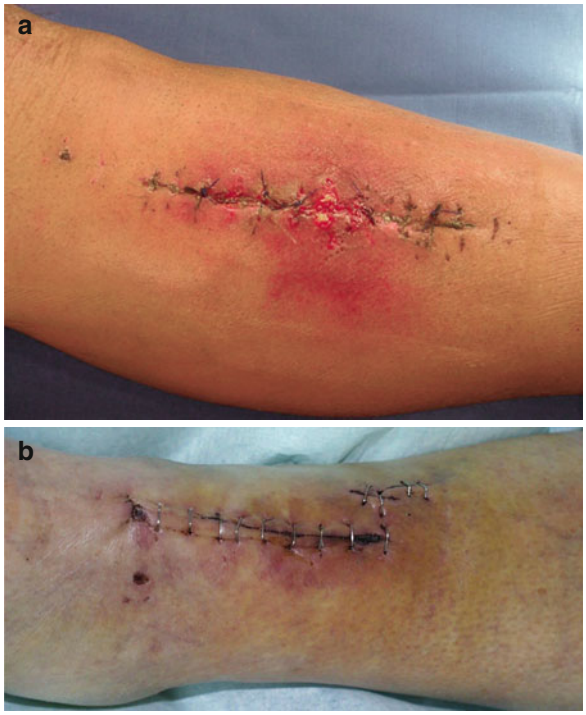

Fig. 18.2 (**a**, **b**) Acute osteitis: clinical aspect

For chronic osteitis, plain radiographs, computed tomography (CT), and magnetic resonance imaging (MRI) are methods of diagnosis. Thus, enclosed gas in a bone formation seen on CT scans is a strong argument for chronic osteitis. The uptake of contrast medium in the adjacency of a bone sequester is deemed to be strong evidence of chronic osteitis.

Ultrasound imaging is not appropriate for the diagnosis of osteitis because it is not highly specific. In recent years, results using fluorodeoxyglucose positron emission tomography (FDG-PET) have shown to be a valid method for the diagnosis of osteitis. Available studies report sensitivity with an of average 96 % and specificity of 91 % compared with bone scintigraphy (82 %/25 %), leukocyte scintigraphy (61 %/77 %), and MRI (84 %/60 %) [12]. Using FDG-PET CT should show an improvement of expressiveness (Fig. 18.2).

18.1.8 Bacteriology

A positive microbiological culture shows the highest evidence for the diagnosis of osteitis. The bacterial probes must be taken from the intraoperative situs. The tests must be representative for aerobe and anaerobe bacteria. The time between extraction of the material and the beginning of processing the microbiological investigation is important for the significance of the probes. If incubation of the probes begins too late, a false negative result can present for noninfected tissue. The same is essential for the extraction of the probes from the wound. Using gloves and instruments for avoiding contamination from the skin and other tissue areas is indispensable. In clinical cases with a high suspicion of infection without a positive microbiological result, specific infections must be excluded (e.g., tuberculosis, Lues).

18.2 Acute Osteitis

18.2.1 Synonyms

Acute posttraumatic osteitis

18.2.2 Definition

The definition of acute posttraumatic osteitis (APO) is the bacterial infection of bone and soft tissue adjacent to a fracture, and implants within 6 weeks after fracture treatment or joint replacement.

18.2.3 Epidemiology/Etiology

Depending on the type of fracture and the operative procedure the incidence of APO ranges between 0.5 % in elective orthopaedic surgery up to 40 % in acute trauma surgery of open factures [13, 14].

The level of soft-tissue damage, type and amount of bacterial contamination, presence of implants, and the general conditions of the patient are the most important parameters.

In addition to these factors, postoperative wound management plays an important role. The wound hematoma presents the bacteria with ideal conditions for growth. With the early removal of postoperative hematoma, effective prevention of the development of APO is possible.

The occurrence of APO is connected to an increase of number of days in hospital to an average of 13–24. As a result, additional costs for one case of APO are estimated to rise up to 14,000 € [6].

18.2.4 Symptoms

Clinical symptoms of APO are redness, swelling, fever, increasing CRP level, pain, and treatment of fracture within the previous 6 weeks (Fig. 18.2a, b).

18.2.5 Complications

The most important complication is absent and failed treatment of APO and has the potential consequence of turning into chronic osteitis. During the treatment of APO, dependant on localization, general conditions, type of bacteria, and type of previous treatment, surgical complications may occur. Because treatment of APO immobilization of the affected region requires, the risk of thromboembolism is high. The use of a cast imcontains the risk of pressure ulcer to prevent pes equinus. The risk for thromboembilism and pressure ulcer rise in the presence of bad general conditions and other factors (e.g., diabetes mellitus, arteriosclerosis).

18.2.6 Diagnostics

18.2.6.1 Recommended European Standard for Diagnostic Investigation

The diagnostic of APO is based on:

- Medical history
  - Operative treatment, open fracture, complications after primary surgery,
  - Bad general conditions
- Clinical investigation
  - Pain, redness, swelling, fever, decreased function
- Laboratory findings
  - Increasing CRP, positive microbiological blood culture
- Imaging
  - Radiographs for detecting loosening of the implant, CT for detecting gas in necrotic bone
- Microbiological culture
  - Positive microbiological culture from the affected tissue (aerobe and anaerobe testing).

18.2.6.2 Useful Additional Examinations

In preparation for surgical revision of a joint replacement, the puncture is helpful in detecting bacteria. The indication for the puncture must be handled carefully because contamination of the joint by the puncture is also possible.

18.2.7 Conservative Treatment

18.2.7.1 Recommended European Treatment Procedures

In consideration of the pathophysiological features a conservative treatment of APO is not reasonable.

18.2.7.2 Useful Additional Therapeutic Strategies

Additional systemic administration of antibiotics

18.2.8 Surgical Treatment

18.2.8.1 Recommended Surgical European Standard

Early revision of the affected wound, if necessary under emergency conditions

Revision of all parts of the wound

Removal of tissue probes for urgent bacteriological investigation

Change of the sterile covering, gloves and instruments after wound irrigation and before vacuum closure

Local antibiotics

Closure of the wound after revision surgery with vacuum technique

Immobilization (cast, external fixator)

Systemic antibiotic drugs (cephalosporin of the third generation or analogue)

Repetition of the revision procedure after 2–3 days

Administration of the antibiotic drugs according to the result of the first microbiological probes

Removal of the implant, if after repeated revision procedures a negative bacteriological result can not be achieved

18.2.8.2 Useful Additional Surgical Treatment

The low pressure jet lavage of long bone marrow hole is helpful, but not mandatory. For the lavage of soft tissue jet lavage is not favorable, because mechanical alteration occurs with decrease of tissue nutrition and possible impaction of residual bacteria into tissue.

18.2.9 Differential Diagnosis

The abacterial postoperative wound haematoma is the most important differential diagnosis, clarified always as the result of a surgical revision procedure.

18.2.10 Prognosis

Healing of APO is accomplished in the majority of cases if a consequent surgical revision concept is applied. In 40 % of cases, the removal of the implant cannot be avoided [15–17].

Nevertheless, therapy for APO is not successful in all cases, with 10–30 % progressing to chronic osteitis.

18.2.11 Surgical Procedure

18.2.11.1 Septic Operative Management

There is no question about the consequent realisation of the principles of aseptics and antiseptics during septic surgery in the operating room to prevent further contamination and osteitis [15, 16, 18, 19].

The goal of surgical therapy is the complete removal of necrotic tissue and therefore the decrease of the number of bacteria in the wound.

In addition to parameters such as general conditions, blood perfusion, soft-tissue covering, and antibiotic drug therapy, the amount of bacteria in the wound is a deciding factor for the emergence of osteitis (s. Sect. 18.1.3). Decreasing of quantity of bacteria in septic surgical procedures can be achieved by changing gloves, instruments, and sterile coverings after débridement of the necrotic tissue and lavage of the wound [20–22]. During the process of changing these items, an antiseptic solution can be used. The same handling is essential in cases of exchanging implants. A decrease of positive bacterial culture of 70 % was observed in laboratory investigations.

The first revision procedure is aimed at identifying the surgical problem, taking microbiological samples, and performing a sufficient vacuum closure. Whereas the first look must be done as an emergency procedure, the planned second and following procedures are elective. In preparation of revision procedures in long bones and joint replacements a major blood loss must be calculated. Usage of a cell saver or a self blood donation is not feasible.

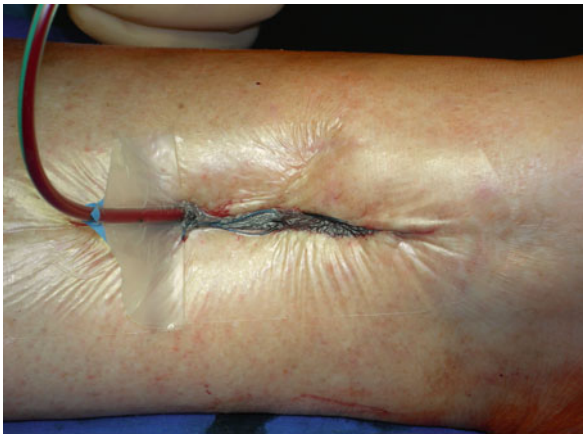

Fig. 18.3 Vacuum closure of the wound

At the beginning of revision procedure the closure of the wound must be taken into consideration because the soft-tissue covering is the basis for all further surgery. Under the revision concept, the edge of the wound has a tendency of retracting. With the vacuum closure of the wound the approximation of the edges of the wound *with* a continuous intracutane suture should be used (Fig. 18.3). Immobilization of the affected region is required during the revision procedure.

Proceeding with additional revision procedures is determined by the results of the microbiological samples.

18.2.11.2 Wound Revision

Technique

Removal of skin sutures, revision of all parts of the wound and necrotic tissue, excision of the affected wound edge, and taking tissue samples for microbiological testing must be done under sterile conditions.

Possible Complications

Possible complications include bleeding, wound closure inability, additional damage to bone and functional structures.

18.2.11.3 Removal of Implants

Technique

Removal of implants should be approached through existing scars if possible and with positioning of the patient on the table with possibility for intraoperative imaging. Removal of all implants should be achieved without additional soft-tissue damage. Planning should be undertaken the wound closure and bone stabilization after revision procedure, as well as preparation of casts for lower leg immobilization during the salvage procedure.

Possible Complications

Possible complications during removal of implants include injury of functional structures, implant breakage, incomplete removal, or instability after removal of implant.

18.2.11.4 Nail Exchange

Technique

Planning for availability of instruments and implants.

Reaming of the medullary canal after removal of the nail.

Positioning of the patient on the table with a possibility for reosteosynthesis.

Prevention of additional bone destruction.

Possible Complications

Possible complications include loosening of the locking bolts, shortening, torsional displacement, and additional fracture of the affected bone.

18.2.11.5 External Fixator

Technique

Placement of the pins should be in the center of the cortical bone with drilling before positioning the pins. Bicortical fixation. Adequate soft-tissue incision regarding to joint movement.

Possible Complications

Displacement of the pins, injury of functional structures, soft-tissue impairment, pin track infection.

18.3 Chronic Osteitis

18.3.1 Synonyms

Osteomyelitis

18.3.2 Definition

Bacterial infection of bone and implants over a period of 6 weeks or longer after treatment of fracture or joint replacement.

18.3.3 Epidemiology/Etiology

In trauma and orthopaedic surgery, the presentation of chronic osteitis is a major complication following primary surgery [16, 23]. Chronic osteitis is characterized as bacterially infected bone after a period of longer than 6 weeks following primary surgery. Chronic osteitis is a challenge for the patient, the patient's family, as well as the surgeon.

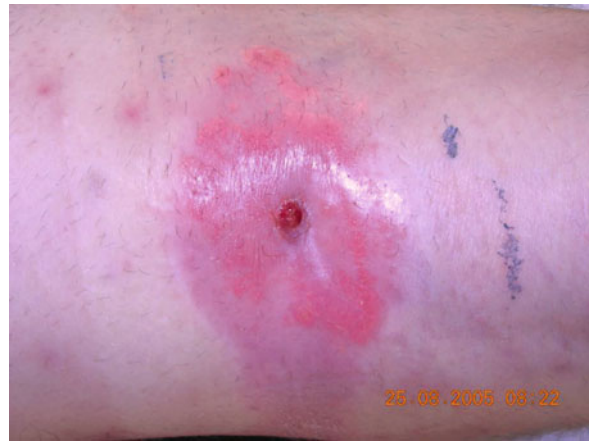

Fig. 18.4 Chronic osteitis: fistula in the hollow of the knee

In Germany, a change in condition from acute osteitis to chronic osteitis is estimated to occur in 10–30 % of all cases [24–26] (s. Sect. 18.2). The change to chronic osteitis as a result of inconsequent surgical management of acute osteitis, open fractures, and extensive soft-tissue damage.

Most detected bacteria are *Staphylococcus aureus*, *Pseudomonas*, *Proteus*, *Streptococcus*, and other types that include mixed flora bacteria [1, 27]. The causes for chronic osteitis are necrotic and avital tissue parts and implants colonized by bacteria.

Depending on the virulence of the bacteria, the local soft-tissue situation, and the immunological competence of the patient, different levels of infection can evolve. The clinical appearance can change from pseudarthrosis without signs of infection, to local infection with fistula, to septic shock.

The lower limbs, particularly the shank, are most affected with chronic osteitis because the soft-tissue covering in this region is inadequate.

18.3.4 Symptoms

Local and general signs of infection differ depending on the level of infection and localization (s. Sect. 18.3.3)

In low-grade infections, symptoms present with a clinical impression of pseudarthrosis with pain, marginal swelling, and redness. Existing fistula near the fracture region will sometimes demonstrate chronic osteitis (Fig. 18.4).

Classic signs of inflammation are seen in acute recrudescing chronic osteitis and with infection of joint replacements in the aforementioned interval. In cases of unknown fever, inflammation, and a positive medical history, an infection of the bone and joint replacement must be excluded.

18.3.5 Complications

Chronic osteitis that is left untreated can lead to septic shock and additional problems. If treatment is unsuccessful, amputation or exarticulation can result. Addicted to the type of method for salvage (eradikation) the chronic osteitis deformities of affected limbs and decreased function are feasible.

18.3.6 Diagnosis

A positive medical history of open fracture, additional infection, and indices for immunodeficiency are indices for chronic osteitis. Laboratory findings are not specific, but depending on the grade of infection, the signs of inflammation are typically positive. Progression of CRP indicates chronic osteitis.

Plain radiographs are mandatory, but not argumentative. An irregular periosteum will sometimes demonstrate a chronic inflammatory reaction and in advanced cases, sequestering of bone can be found. CT is required for detecting necrotic bone (Fig. 18.5a, b). Uptake of contrast medium adjacent to sequestering as well as gas formation in the bone are deemed as evidence for chronic osteitis (s. Sect. 18.1.7)

MRI can be helpful for viewing soft tissue, but it is not specific enough (Fig. 18.6a–c).

Various methods of scintigraphy will show regions of increased bone metabolism, but are not specific enough for proof of an infection.

PET scans can show pathologic glucose metabolism in the bone with highly specific information in connection with chronic osteitis (Fig. 18.7). Additional information about the localization of the infected focus is available. Microbiological samples from a suspect bone with a positive result typically verify chronic osteitis. False-positive results must be prevented.

The synopsis of clinical, anamnestic, laboratory, imaging, and microbiological findings can indicate chronic osteitis. Angiography may be required for the evaluation of perfusion in the perspective of a contingently microvascular surgical treatment.

18.3.6.1 Recommended European Standard for Diagnostic Investigation

Medical history, plain radiographs in two planes, CT, PET, microbiological probes, CRP

18.3.6.2 Useful Additional Examinations

MRI

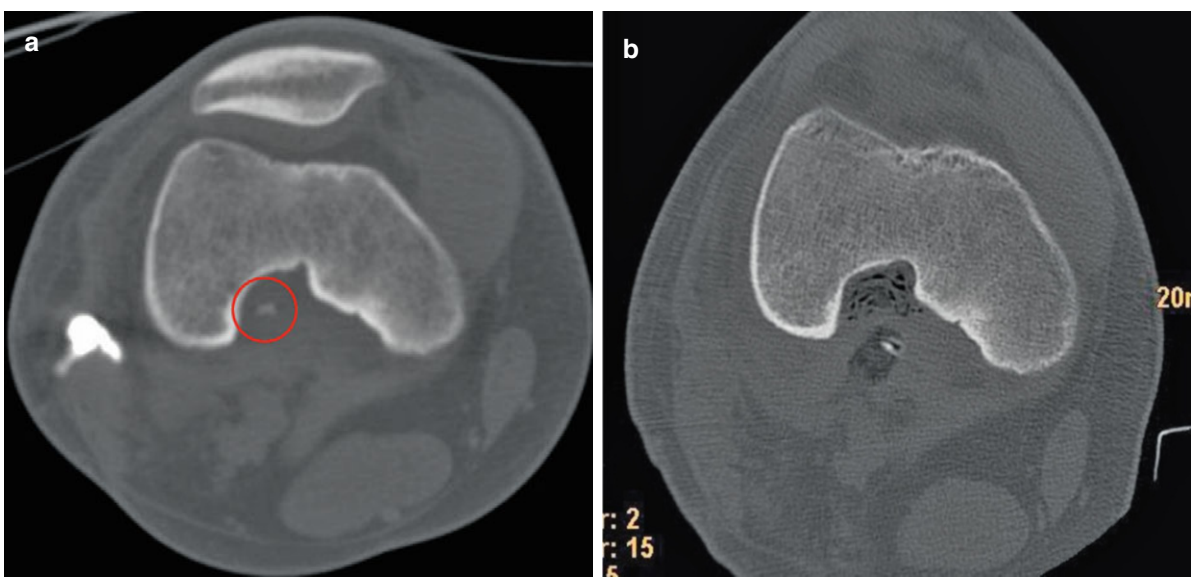

Fig. 18.5 (**a**, **b**) Chronic osteitis: bone sequester in the popliteal fossa before and after removal. In the center of the *red circle* a small piece of bone was detected as a sequester which was the cause for chronic infection (**a**). After removal of this piece of necrotic bone the infection was healed

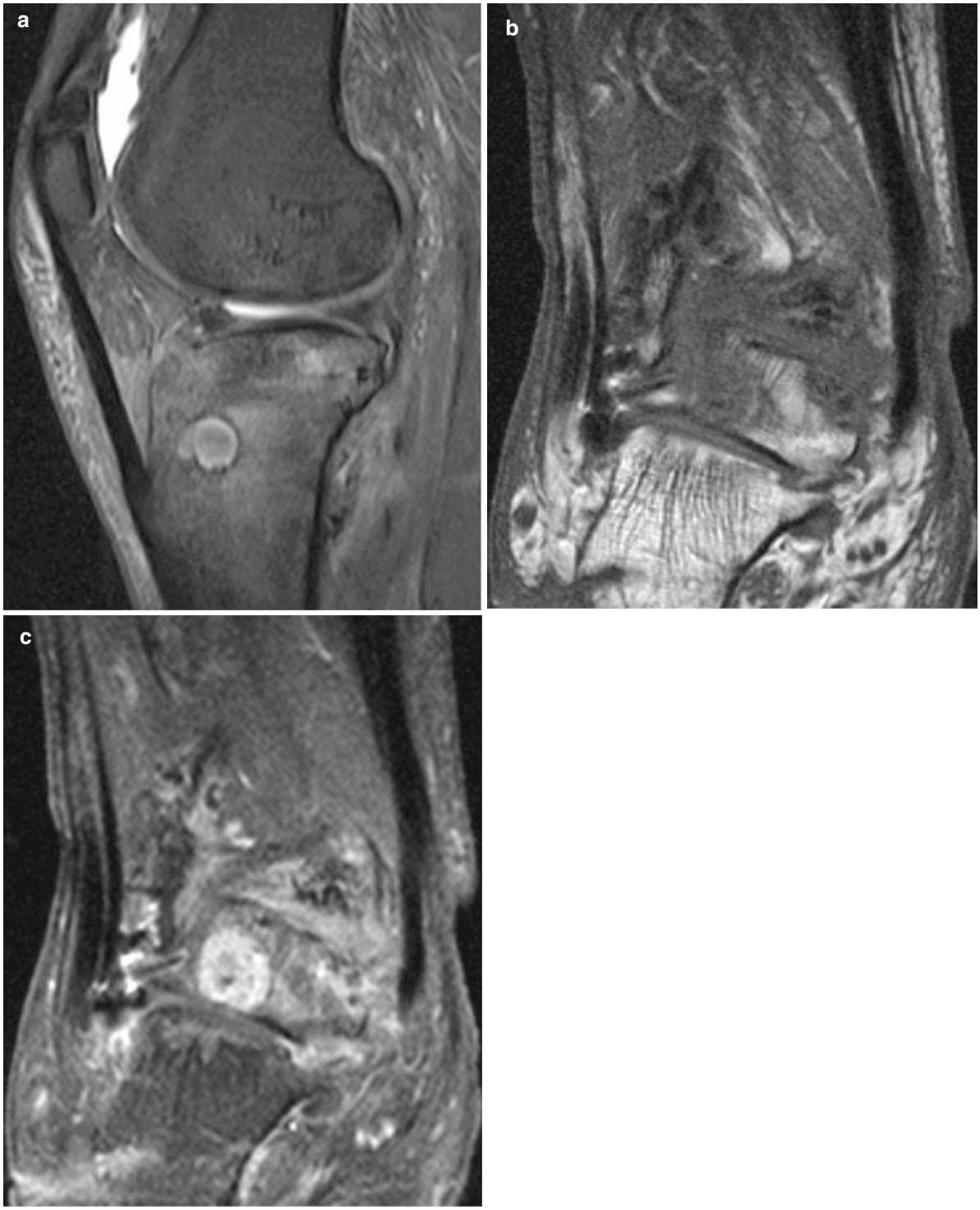

Fig. 18.6 (**a**) Chronic osteitis: increased signal on MRI. (**b**, **c**) Chronic osteitis: increased signal in MRI and uptake of contrast medium in T1 sequences

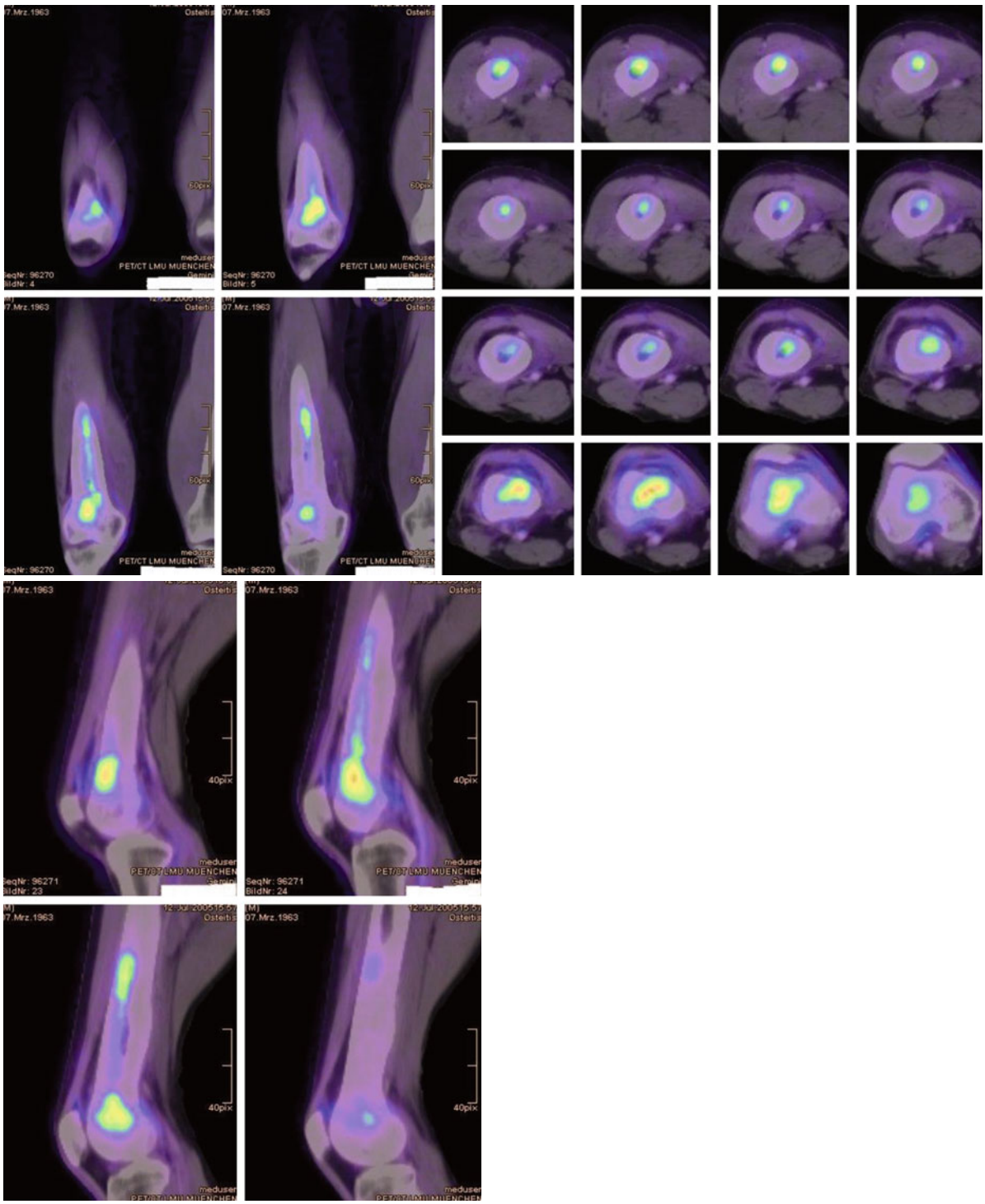

Fig. 18.7 Chronic osteitis: image of right femur with FDG PET CT

18.3.7 Therapy

In contrast to the therapy for acute posttraumatic osteitis, three steps for therapy of chronic osteitis can be taken.

Focus on the first step of therapy is the priority with eradication of the infection. The second step is characterized by reconstruction of the soft-tissue covering. Bone reconstruction can be performed after successful completion of steps one and two. During the salvage procedure, a combination of step two and three can be helpful.

18.3.7.1 Conservative Therapy

Recommended European Standard of Therapy

The issue of chronic osteitis can be resolved with conservative treatment. Conservative treatment of chronic osteitis is possible even with the long and uncertain period of therapy as well as procedures that are not accepted by the patient, particularly in elderly patients.

Useful Additional Conservative Treatment

Cast

18.3.7.2 Surgical Treatment

Surgical therapy must be planned in order to solve the chronic osteitis in dependence from local and general conditions. The duration of therapy must be discussed with the patient to gain acceptance for further procedures. In preparation for surgical treatment, predictable instability must be prevented through the use of a customized cast.

The first step is characterized through evaluation of the situs, extraction of microbiological samples, resection of infected bone, and vacuum closure of the wound after placement of a spacer. The bone cut should be done by using a saw. Heating of the bone must be prevented by lavage and resection should be straight and parallel, which will make the reconstruction of the bone easier. Following the salvage procedure, replacement of instruments, covers, and gloves is required.

Sufficient vacuum closure without leakage, dead space, and unneeded covering of intact skin is essential for the success of the salvage procedure.

Following the successful completion of step one, the reconstruction of the bone is determined using various methods, depending on the size and localization of the defect. In a defect in the long bones of more than 3 cm, callus distraction is a safe and successful method in chronic osteitis. Callus distraction with internal stabilization using a nail is comfortable, but demands sufficient fixation of the nail, and an additional transport mechanism outside of the skin by an external fixator or cable traction (Fig. 18.8a–c). Segment transportation begins 7 days following surgery with a speed of 0.5 mm/day in the lower leg and 1 mm/day for femur distraction. Using plain radiographs, periodic measurement during transportation once a week is necessary. The fixation of the transported segment with a small plate after completion of the distraction is advised. Callus formation can be advanced using low-intensity ultrasound stimulation. One month per centimeter of distraction must be calculated for callus duration [28, 29].

Recommended European Standard of Surgical Therapy

A complete resection of the infected bone, the complete removal of implants, a vacuum closure of the wound, an external temporary stabilization (external fixation or cast), antibiotic drugs administered in accordance with microbiological findings, repeating the revision procedure until negative bacteriological probes can be extracted, sufficient soft-tissue coverage, and reconstruction of bone defects respectively to the dimension of the bone loss if necessary for plastic surgery procedures.

Useful Additional Surgical Treatment

Administration of hyper bar oxygen therapy is optional, however, firm data regarding the treatment are not available.

18.3.8 Differential Diagnosis

Pseudarthrosis (s. Chap. 17)

18.3.9 Prognosis

Depending on the grade of infection, type of therapy, general conditions of the patient, and patient compliance, a successful treatment can be achieved between 60 and 80 % of cases.

18.3.10 Surgical Procedures

18.3.10.1 Removal of Implants

Instrument check before removal, blood supply; approach of choice using existing scars if possible; complete

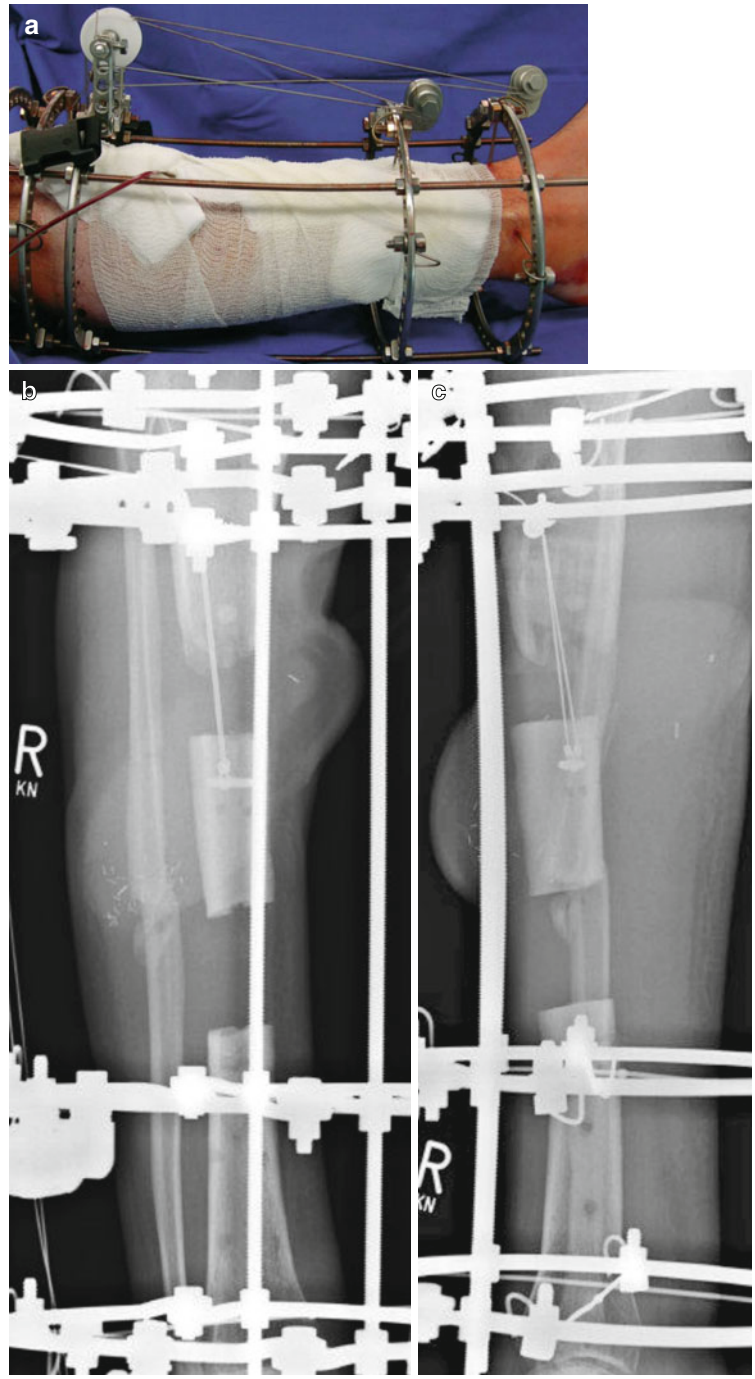

Fig. 18.8 (**a**–**c**) Chronic osteitis: segment transportation with cable system

removal of implants and cement as well as broken screws; control of complete removal using image intensifier; refill of defects using sterilized metal or cemented spacer

Technique

The technique will depend on the existing condition; prevention of additional trauma and soft-tissue damage

Possible Complication

Additional bone loss; bleeding by injuring vessels; opening of adjacent joint

18.3.10.2 Segment Resection

Technique

Detection of infected bone through microbiological probes; determination of cutting level; assessment of resection length; shortening of bone, if necessary; planning further method of stabilization and segment transportation

Possible Complication

Injury of adjacent functional structures depending on the localization

18.3.10.3 External Fixator

Technique

Checking of available instruments and implants; plain radiographs obtained in two views; positioning of region of interest on the operating table for a possibility of intraoperative imaging; skin incision and soft-tissue protection with drill sleeve under sterile conditions; bicortical and central positioning of pins; fixing of clamps with adequate distance to soft-tissue surface; reconstruction of length and torsion by connecting distal and proximal clamps with rods

Possible Complication

Injury of function structures (vessels, nerves, tendon, joint); soft-tissue impairment; pin track infection; additional fracture of bone

18.3.11 Special Remarks

In consideration of the the complex issue influenced by local and general conditions of the patient, hygenic and antimicrobial aspects and surgical challange the treatment of such patients should be done in specialised and experienced departments.

Despite clear basic treatment guidelines the therapy options mostly have to adapted individually.

18.4 Special Forms

18.4.1 Joint Infection

18.4.1.1 Synonyms

Empyema

18.4.1.2 Definition

A bacterial infection of the joint with an inflammatory reaction

18.4.1.3 Epidemiology/Etiology

Joint infections are specific affects of trauma and orthopaedic surgery with the contamination and infection of preexisting space. Furthermore, during the treatment of joint infections, the function of the joint plays an important role for further guarantee of mobility.

Immediate arthroscopic salvage procedures have priority in joint infection treatment. Arthroscopic revision should be performed after 48 h with the removal of necrotic tissue and hematoma. Additional antibiotic drugs, drainage, and immobilization are obligatory. An adjustment in the administration of systemic antibiotics according to the results of the microbiological testing is strongly recommended. In the majority of cases, *Staphylococcus aureus* and *Staphylococcus epidermidis* are detectable [29, 30].

Arthrotomy and open synovectomy are necessary if within the course of three revision procedures no negative microbiological result is achieved.

A preexisting degeneration can prevent salvage of the infection making removal of the cartilage surface essential in the preparation for further joint replacement.

Depending on general conditions such as age and mobility after the successful treatment of the joint infection, further surgical therapy must be adjusted. A joint replacement procedure can be planned only following a time period of 6–8 weeks without any infection.

18.4.1.4 Symptoms

Fever, pain, decreased function, swelling, flowing, redness, hyperthermia

18.4.1.5 Diagnosis

Plain radiographs; puncture with microbiological probes (under sterile conditions!!!); arthroscopy; CRP; inflammatory parameters; positive microbiological culture

18.4.1.6 Therapy

Immediate arthroscopic lavage; immobilization; antibiotics; planned arthroscopic; revision after 48 h

18.4.1.7 Complication

Joint destruction; stiffening of joint mobility; amputation

18.4.2 Infection of Joint Replacement

18.4.2.1 Synonyms

Periprosthetic infection

18.4.2.2 Definition

Bacterial infection of implanted artificial joints and adjacent bone and soft tissue

18.4.2.3 Epidemiology/Etiology

Infections of the endoprothesis are problematic in joint infection.

In addition to cartilage, soft tissue, and bone, implants can be affected by bacterial contamination.

The incidence of a surgical site infection after joint replacement ranges between 0.5 and 5 % [31–34]. Early and late infections can be distinguished by the moment of incidence 29].

An early infection of the joint prosthesis requires a similar procedure as in acute osteitis.

Sensitive implant surfaces must be protected against damage. Removal and temporary substitution of moving parts are also essential. Consequent and radical surgical management can save an infected endoprosthesis. If the salvage procedure is not successful, a change into a chronic infection with infected loosening is nearly inevitable. Successful treatment of revision joint replacement can be achieved in 60–80 % depending on multifactorial influences and time [35, 36].

18.4.2.4 Diagnosis

Plain radiographs, inflammatory laboratory parameters, arthroscopic, (better) open revision with microbiological probes, PET, scintigraphy, puncture of joint.

Low-grade infections present with the difficulty of differentiation for aseptic loosening because results from imaging the marginal pathologic and joint puncture can be negative in normal nutrition mediums. Common inflammatory signs such as mild fever, night sweats, and local signs of an infection are indicative of infection. An existing fistula is evidence of an infection.

The sensitivity and specificity with PET is reported in approximately 88 and 78 %, respectively[37, 38].

Bone scintigraphy and leukocyte scintigraphy have an accuracy of approximately 50–80 % for detecting a joint infection [39].

18.4.2.5 Imaging

Ultrasound is not useful because only zones of poor echo will demonstrate a fluid conglomeration.

Plain radiographs are mandatory for the diagnosis of an infected endoprosthesis. A loosening edge and hyperostosis are indicators.

CT and MRI are not helpful because of implant disturbance.

Scintigraphy is suitable for detecting regions of increased bone metabolism, but because of its low specificity, it is not possible to use it as a quantitative measurement for the differentiation of aseptic loosening.

A semi-quantitative determination of the infection in the endoprosthesis is possible using PET, additionally, a three-dimensional display is helpful. The puncture of a suspect artificial joint can generate informative bacterial probes, but includes the risk of an iatrogenic contamination of non-infected joints. False-positive results resulting from skin contamination are also possible.

18.4.2.6 Therapy

(a) Conservative

Conservative treatment of infected artificial joints cannot be recommended because the diagnosis is only certain in cases of an existing fistula and without the removal of infected vital material, salvaging of an infection using antibiotics cannot be expected.

(b) Operative Therapy

The operative treatment of an infected endoprosthesis can be performed with and without the preservation of the prosthesis.

Salvaging of the prosthesis is the goal in an acute postoperative infection. Because of an implanted prosthesis, not all regions of joint space can be reached. Mobile parts of the implant must be removed, particularly polyethylene.

Careful management for the protection of sensitive surfaces is required during the revision procedure; as a

result of this, arthroscopic revision is limited, and orientation is mainly given through reflecting surfaces. In addition, polyethylene revision is not possible arthroscopically, therefore, early open revision is preferable.

The condition for successfully finishing the salvage procedure is three consecutive negative bacterial tissue probes.

18.4.2.7 Revision with Removal of Implant

An early decision for the removal of all implants, including cement, is needed in cases without negative bacterial probes after three revisions. The removal must be performed carefully in expectation of further reimplantation of the endoprosthesis. Additional bone and soft-tissue damage must be avoided. Temporary stabilization, using a conventional or self-made spacer, is helpful and reduces pain and shortening.

Vacuum wound closure is the method of choice. After a successful salvage procedure, the decision regarding further treatment must be made. According to general patient conditions, age, bone situation, and claim of the patient, further endoprosthesis or arthrodesis can be planned. If a salvage of the infection is not achievable, amputation is an acceptable alternative with a good function and rapid recurrence to work and familiar ambiance.

18.4.2.8 Symptoms

Pain, especially on weight bearing, inflammatory local and general reaction, decreased function, fistula

18.4.2.9 Diagnosis

Plain radiographs, CRP, scintigraphy, PET, puncture

18.4.2.10 Therapy

Open revision procedure, early removal of implants, and salvage procedure until verification of negative bacterial probes.

Additional administration of antibiotics until wound healing completion.

18.4.2.11 Complications

Thromboembolism, injury of function structures (vessels, nerve, tendon, joint)

Bone loss and destruction, shortening, general infection, septic shock syndrome, bleeding

18.4.3 Spondylodiscitis

18.4.3.1 Synonyms

Spondylodiscitis, discitis

18.4.3.2 Definition

Bacterial infection of vertebral body and discs

18.4.3.3 Epidemiology/Etiology

The incidence of all bacterial bone infections is less than 5 % [40]), in 1–50 % of the cases they are caused hematogenously [41, 42], occurs after invasive procedures at the spine postoperatively with an incidence of 3–12 % [43]. The spectrum of bacteria depends on the origin of contamination which is mostly *Staphylococcus aureus*, and in rare cases tuberculosis. Elderly people are predominantly affected.

18.4.3.4 Symptoms

Most cases are characterized with light inflammatory clinical and laboratory signs, pain, and neurological failure, but severe septic progression is also possible.

18.4.3.5 Diagnostic

Plain radiographs of the affected spine area, neurological investigation, laboratory parameters (CRP), scintigraphy, MRI, CT with guided puncture

18.4.3.6 Therapy

The conservative treatment is through immobilization and administration of systemic antibiotic drugs over a period of 6–8 weeks.

Operative treatment entails the removal of the infected tissue, refill with spongy bone, stabilization of affected segments, and administration of antibiotic drugs. Early postoperative mobilization and elimination of the infected area are relevant advantages. The indication for surgery can be prevented by a rapid diagnosis so that spondylitis can be successfully treated through consequent immobilization in a plaster bed and administration of appropriate antibiotics [44, 45]

18.4.3.7 Complications

A neurological palsy can arise in cases of an increasing abscess with the spinal cord and adjacent vertebral bodies being affected, development of psoas abscess, and septicemia. Recurrence of spondylodiscitis is a

deficiency of primary therapy and improper elimination of the area of infection.

18.4.4 Infected Pseudoarthrosis

18.4.4.1 Synonyms
Infected nonunion

18.4.4.2 Definition
Bacterial infection of a non-healed fracture at least 6 months after injury

18.4.4.3 Epidemiology/Etiology
The incidence correlates with the number of open or surgically treated fractures and ranges between 0.5 and 1 % after surgical fracture treatment [46]. The spectrum of bacteria depends on the origin of the injury or operation, mostly *Staphylococcus aureus, Staphylococcus epidermidis,* and bacteria such as those presenting in osteitis.

18.4.4.4 Symptoms
Pain, particularly with weight bearing; local signs of inflammation; fever, taps pain

18.4.4.5 Diagnosis
Plain radiographs, CT, scintigraphy, PET, light to severe increase of infection parameters (CRP)

18.4.4.6 Therapy
A salvage procedure for the eradication of an infection (s. Sect. 18.3) after three negative bacterial probes and sufficient soft-tissue covering re-osteosynthesis according to the present situation.

18.4.4.7 Complications
S. Sect. 18.3.

18.4.5 Hematogenous Osteomyelitis

18.4.5.1 Synonyms
Juvenile osteomyelitis, myelitis, periostitis

18.4.5.2 Definition
A purulent infection of the bone marrow mostly in the childhood, caused by hematogenous spreading from the infected area to other locations (tonsillitis, otitis media, and pyodermia)

18.4.5.3 Epidemiology/Etiology
The incidence ranges between 2 and 4 arthritides in relationship to 10,000 children under the age of 16 years in industrialized countries [31, 49, 50]; more than 50 % are under the age of 5 years. The ratio between girls and boys is 1:2. More than 80 % of the isolated bacteria are *Staphylococcus aureus*. The pathogenetic pathway seems to be a mismatch between the virulence of bacteria, the age at vascularization, and the microcirculation of the bone and local/general conditions of immune deficiency. Predominantly, the long bones are affected after bacteremia of other infected areas. Osteomyelitis is rare in adults and occurs mostly under poor general immunologic conditions.

18.4.5.4 Symptoms
Local and general signs for infection presenting in different grades. There is no correlation between the level of clinical signs and the dimension of infection. Severe septic courses are possible during childhood. Local pain appears in the affected region.

18.4.5.5 Diagnosis
Bacterial blood culture, puncture of bone marrow for bacteriological investigation in children, plain radiographs, scintigraphy, or MRI (highest specificity and sensitivity) for the differentiation of neoplasm. Ultrasound is convenient for detecting soft-tissue edema and abscess formation in early childhood. A guided puncture is possible.

Increasing CRP disguised by antibiotic therapy shows the progression of the infection.

18.4.5.6 Therapy
Therapy is based on the administration of the antibiotic drug cephalosporine of the third generation for at least 3 weeks, if necessary a correction according to the antibiogram arises. Immobilization is mandatory. Surgical intervention is necessary for opening of abscesses, revision of fistula, and removal of sequester corresponding to salvage procedures in acute osteitis (s. Sect. 18.2).

18.4.5.7 Complications
During childhood, the most important complication is the destruction of the epiphyseal gap. A change to chronic osteitis occurs in 10 % of the cases.

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Pathologic Fractures

19

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19.1 Definition

A pathologic fracture is defined as a fracture occurring in a pathologically altered bone whose normal integrity and strength have been compromised by an invasive disease or destructive process. Usually a low mechanical force, one which would have left a normal bone intact, is sufficient to fracture the bone altered by a local or systemic disease process. Pathologic fractures usually lack significant soft tissue injury unlike traumatic fractures [1].

19.2 Epidemiology

The incidence of pathologic fractures is difficult to estimate because of the underreporting and inaccuracies of diagnosis. Osteoporosis, the most common cause of pathologic fractures in the elderly population, affects approximately seven million people in Germany alone. As the population ages, the number of people affected by osteoporosis will rise. The affected population has a 32 % risk of sustaining spine fractures, 16 % risk for distal forearm fractures, and 15 % risk for proximal femoral fractures. It is estimated that between 50 and 70 % of all patients with carcinoma develop skeletal metastases during the course of their disease, as do 85 % of women with breast cancer [2, 3].

19.3 Mechanism of Injury

Pathologic fractures typically occur following trivial injury during the normal activities of daily life. However, they can also occur high-energy trauma affecting a region of the bone affected by the pathological process [3].

19.4 Structural Integrity of Bone

The bony skeleton has an important role as the body's framework. Different conditions can negatively affect this structural integrity and strength of the bone leading to the occurrence of pathologic fractures. It must be kept in mind that bone is a dynamic tissue, and that not only destructive lesions affecting it, but also disturbances in its metabolic activity can have significant consequences on its structural integrity and strength [4].

19.5 Etiology of Pathological Fractures

Broadly speaking, the etiologies of pathological fractures include metabolic bone diseases, metastatic bone disease, infection, disuse, primary bone tumors, iatrogenic causes (e.g., bone defect following excision of a osteoid osteoma), and areas of bone necrosis [5].

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19.6 Classification of the Pathologic Process

Pathologic fractures can be caused by either systemic skeletal diseases or local diseases. Local diseases can be classified as benign, primary malignant, metastatic, and other miscellaneous conditions [5]

19.6.1 Systemic Causes

These are a group of diseases causing the bones to weaken predisposing them to fractures. In most cases, however, the healing potential following fractures may be normal. They include osteoporosis, osteomalacia, hyperparathyroidism, renal osteodystrophy, osteogenesis imperfecta, polyostotic fibrous dysplasia, osteopetrosis, Paget disease, rheumatoid arthritis, and Gaucher disease [5].

19.6.1.1 Osteoporosis

Osteoporosis is the most common cause of pathologic fractures in the elderly population. Osteoporosis has been defined by the National Institutes of Health as an age-related systemic disorder characterized by decreased bone mass and increased fracture risk. The main risk factors for osteoporosis include low body weight, postmenopausal states, female gender, white, and north western European descent. Sedentary life style, low calcium intake, alcohol use, smoking, various endocrinal disorders (e.g., hyperparathyroidism and Cushing's disease), various drugs (including steroids and heparin), and some neoplastic disorders (e.g., multiple myeloma) play an important role in increasing the risk of osteoporosis [5, 1].

Two different types of loss of bone mass have been described with osteoporosis. Type I is a rapid postmenopausal type affecting women between 51 and 65 years of age, and affecting mainly areas of trabecular bone. It is characterized by vertebral and wrist fractures.

Type II or senile osteoporosis causes bone loss of both cortical and trabecular bone and classically affects both men and women older than 75 years. It is characterized by fractures of the hip, pelvis, and humerus.

Fractures in patients with osteoporosis are associated with increased morbidity and mortality. Hip fractures are the most common cause of morbidity and mortality in patients suffering from osteoporosis [5].

19.6.1.2 Disorders of Mineral and Collagen Metabolism

These include rickets and osteomalacia, renal osteodystrophy, hyperparathyroidism, Paget disease, and osteogenesis imperfecta.

19.6.1.3 Rickets and Osteomalacia

Rickets and osteomalacia represent failures of bone mineralization as a result of disorders in vitamin D metabolism occurring in children and adults, respectively. They carry an increased risk of pathologic fractures. Patients may show characteristic deformities. The adult patient with osteomalacia may have localized bone pain and muscle weakness. They are responsive to treatment once the diagnosis is correctly made and, with appropriate medical treatment, the fractures typically heal well [5, 1].

19.6.1.4 Renal Osteodystrophy

In patients with renal disease, hypocalcemia and hyperphosphatemia result. The resulting hyperphosphatemia is an important factor in the development of secondary hyperparathyroidism and is a feature of the high turnover form of renal osteodystrophy. The low turnover form of the disease is similar to rickets and osteomalacia. Bone pain, especially in the lower back, hips and legs, together with muscle wasting are features of renal osteodystrophy. Bony deformities are a major clinical feature of the disease in children. They are more prone to pathologic fractures, and fracture healing is delayed in these patients [5].

19.6.1.5 Hyperparathyroidism

Hyperparathyroidism can be primary or secondary, usually from chronic renal insufficiency. The patient may complain of chronic bony pains from the resulting osteopenia, a swelling as a result of the superficial brown tumor, or a pathologic fracture. Tooth loosening, renal stones, and depression are other complaints.

The clinical history usually reveals polydypsia, polyuria, psychic and muscular weakness, and constipation.

19.6.1.6 Osteogenesis Imperfecta

These are a group of genetically transmitted dysplasias in which the bones are extremely fragile predisposing the patient to multiple fractures [5].

Clinically, the disease can appear with a wide spectrum of manifestations according to the severity of the

condition. This can range from stillborn babies with numerous fractures to active adolescents with a history of several fractures occurring at various times during childhood and possible resulting deformities [5].

19.6.1.7 Paget Disease

Paget disease is a disorder characterized by a disturbance in the rate of bone turnover. Initially, there is increased bone resorption that is followed by excessive and pathologic bone formation. The excess bone formed is "brittle" and therefore susceptible to pathologic fractures. Nonunions are common, particularly with femoral neck and subtrochanteric fractures [5].

Paget disease is seen mostly in patients older than 50 years, and is most common in men. It commonly affects the pelvis, tibia, and femur. Patients complain of bone pain, neurologic deficits sometimes occur, and there might be increased warmth of the bone and overlying skin resulting from the increased vascularity.

19.6.2 Local Causes

19.6.2.1 Benign Local Disease

These include non-ossifying fibroma, unicameral bone cyst, aneurysmal bone cyst, enchondroma, chondromyxoid fibroma, monostotic fibrous dysplasia, giant cell tumor, osteoblastoma, and chondroblastoma

19.6.2.2 Non-ossifying Fibroma

Most occur in children between the ages of 10 and 20 years, and are found predominantly in the femur or tibia. They are histologically similar to fibrous cortical defects but larger in size. They may present with pain or with a pathologic fracture.

19.6.2.3 Unicameral Bone Cyst

These are common lesions seen mainly between the ages of 5 and 15 years. Most (60 %) are seen in the proximal humerus, followed by the proximal femur. They are usually painless and asymptomatic, until a pathologic fracture occurs. They are usually diagnosed as a chance radiographic finding or after a pathologic fracture occurs [6].

19.6.2.4 Aneurysmal Bone Cyst

These are osteolytic, hyperplastic, hyperemic-hemorrhagic lesions. Eighty percent present before the age of 20 years. The most common sites are, in decreasing order, the long bones of the lower limb, the long bones of the upper limb, the spine, and the pelvis. They are usually metaphyseal in location.

Pain and swelling are the main symptoms. Swelling may be severe due to the blow-out tendency of the lesion. In vertebral lesions, signs of neurologic deficits may appear [6].

19.6.2.5 Fibrous Dysplasia

Fibrous dysplasia is a dysplastic lesion occurring intramedullary in bone, consisting of fibroosseous tissue. It may be monostotic or polyostotic. It usually begins prior to puberty, but can be discovered at any age. Sites of predilection include the femur (particularly proximal), the tibia, craniofacial bones, the ribs. These are followed by the humerus, the forearm, and the pelvis (especially ilium) [7]. Some lesions are asymptomatic whereas others may present with bone pain. Swelling may be noted in superficial bones (e.g., ribs). They may present as a pathologic fracture. A severe polyostotic type may present with deformities and limb-length inequality. Additionally, *Cafe au lait spots* may be seen [7, 8].

19.6.2.6 Enchondroma

Enchondroma occur mostly in the second, third, and fourth decades of life. The small tubular bones of the hands and feet are most often involved. They are the most frequent tumor of bone in the hand. They are typically found after a pathologic fracture. However, they may present with pain if the tumor is growing [5, 9].

19.6.2.7 Giant Cell Tumor

Giant cell tumors typically occur in patients between the ages of 20 and 40 years and are most frequently seen in the distal femur, proximal tibia, followed by the distal radius. They can be very aggressive and less than 5 % can be malignant.

Most patients present with pain that is initially related to activity but progresses to become evident at rest. About 10–30 % present with a pathologic fracture [5, 9].

19.6.2.8 Primary Malignant Bone Lesions

These include Ewing sarcoma, multiple myeloma, non-Hodgkin lymphoma, osteosarcoma, chondrosarcoma, fibrosarcoma, and malignant fibrous histiocytoma

Multiple Myeloma

This is the most common primary malignancy of bone in adults with peak incidence in the fifth through the

seventh decades and with male predominance. Bone pain is the most common complaint. Other systemic problems including weakness, anemia, weight loss, thrombocytopenia, peripheral neuropathy, hypercalcemia, and renal failure are frequently present at the time of presentation. Pathologic fractures are relatively common. The spine is the most common location followed by the ribs and pelvis. The diagnosis can be confirmed by serum immunoelectrophoresis demonstrating a monoclonal gammopathy [5].

Osteosarcoma

This is the second most common primary malignant bone tumor, and the most common in adolescents. The majority of the patients are in the second decade of life (it may occur in the sixth decade if on top of Paget disease). Osteosarcoma has a predeliction for the appendicular skeleton, and more than 50 % of cases are around the knee. It is usually metaphyseal in location, and is mostly aggressive in behavior [10].

Most patients present with pain and swelling. The pain is progressive and is increased at night. However, they can also present with a pathologic fracture. The majority of hematogenous spread from the tumor is to the lungs which are affected in up to 50 % of the cases [10, 11].

Ewing's Sarcoma

This is the second most common bone malignancy in children following osteosarcoma. It typically affects children in the first and second decades of life, and more than 90 % occur before the age of 30 years. It can affect any bone in the body, in any location, but is mostly diaphyseal. The pelvic girdle and lower extremities are affected in greater than 60 % of cases [12, 13].

They present clinically with pain and swelling, and sometimes they present with local signs suggestive of infection with swelling, tenderness, and warmth. More confusingly, the laboratory results will show leucocytosis, anemia, and an elevated erythrocyte sedimentation rate [12, 13].

19.6.2.9 Metastatic Bony lesions

It is the most common bony malignancy encountered in the adult patient. Bony lesions in any patient with a known malignancy, even in the past, are most likely metastatic. Most carcinomas metastatic to bone are from the breast and prostate, followed by the lung, kidney, thyroid, and gastrointestinal tract in decreasing order of frequency. Patients usually present with bony pain or a pathologic fracture. In advanced stages they may present with a soft-tissue mass or neurologic deficit in vertebral lesions. The primary carcinoma may be found from the clinical history or examination. Anemia, weight loss, or lymphadenopathy may also be encountered. An aggressive bone lesion in an adult with no known malignancy is also most probably metastatic or as a result of myeloma. After all the essential work up (discussed later), a biopsy will verify the diagnosis for patients with no known malignancy or for patients with known malignancy but a solitary bone lesion, which should not always be assumed in such case to be a metastasis [14, 15, 16].

19.6.2.10 Bone Infection

Fractures in bone affected by chronic osteomyelitis are a challenging problem. The patient usually has a history of chronic osteomyelitis with pain, occasional swelling, local warmth, and discharging sinuses. The source of infection is typically postoperative following an open fracture, or hematogenous. Some patients may have undergone débridement resulting in bony defects weakening the bone, and subjecting it to a pathologic fracture [5].

19.6.2.11 Miscellaneous Causes

These include irradiated bone and localized structural defects.

19.7 Clinical Evaluation

19.7.1 History

Certain aspects in the history may draw attention to the possibility of a pathological fracture. These include:

- Trivial causative trauma.
- History of pain at the site of the fracture preceding the trauma.
- Swelling or warmth at the site of the fracture preceding the trauma.
- Patients with history of previous multiple fractures.
- Patients with characteristic bony deformities also affecting the contralateral intact limb.
- Patients known to suffer from certain metabolic diseases.
- History of exposure to radiotherapy.
- Patients with known malignancies.

- Patients known to suffer from chronic osteitis at the site of the fracture.
- Patients with known risk factors such as steroid treatment, smoking, exposure to carcinogens, certain blood diseases, or excessive alcohol use [5, 9].

19.7.2 Physical Examination

The standard physical examination of the encountered fracture is performed as usual. In addition, some other aspects must included in the physical examination:

- Examination for a possible soft-tissue mass at the fracture site.
- Evidence of local chronic infection (e.g., skin sinuses).
- Characteristic bone deformities suggestive of metabolic bone diseases (e.g., back deformity and bow legs of Paget's disease), skeletal deformities (e.g., genu valgum) associated with renal osteodystrophy, exaggerated dorsal kyphosis in osteoporosis, characteristic deformities of rickets, or crumpled limbs of osteogenesis imperfecta.
- Examination with the purpose of locating the primary site in cases of suspected metastatic disease (e.g., examination for breast masses, prostatic nodules, thyroid masses, rectal masses, or lymphadenopathy) [5, 14].
- Noting other physical findings related to other organs but suggestive of a certain pathologic process (e.g., evidence of primary or metastatic malignancy, earthy look of uremic patients, blue sclera of osteogenesis imperfecta, hearing loss in Paget disease, or features of hyperthyroidism).
- Proper examination of all other painful sites to rule out other impending fractures [9, 14].

19.8 Laboratory Investigations

The laboratory investigations for suspected pathological fractures should include:

- Full blood count with differential count and a peripheral smear. Anemia will be associated with different types of malignancies and generalized organ diseases. Leucocytosis may be seen in cases of infection. Leukemias can be diagnosed from a characteristically high leucocytic count, anemia, and immature peripheral cells.
- Erythrocyte sedimentation rate will be high in cases of malignancy, collagen diseases, and infections.
- Blood chemistry with *electrolytes* (e.g., hyperkalemia in renal disease), *serum calcium* (elevated in metastatic malignancy, multiple myeloma, hyperparathyroidism and occasionally in Paget disease; hypocalcemia occurs in renal disease), *serum phosphate* (hyperphosphatemia in renal disease, and hypophosphatemia in hyperparathyroidism), *alkaline phophatase* (raised in diseases with high bone turnover as rickets and osteomalacia, also raised in some bone malignancies), *serum albumin and globulin*.

  Specific laboratory investigations include:
- Acid phosphatase: For males with unkown primary tumor.
- Prostatic specific antigen: Males with suspected prostatic carcinoma.
- Parathyroid hormone: For cases with suspected hyperparathyroidism.
- Bence Jones protein in urine for suspected multiple myeloma.
- Protein electrophoresis for suspected multiple myeloma.
- Stool guaiac: In cases with suspected colonic carcinoma.
- 24 h urine hydroxyproline: For suspected Paget disease.
- Thyroid function tests.
- Certain tumor markers (e.g., carcinoembryoinc antigen) [5, 9, 14].

19.9 Radiographic Evaluation

19.9.1 Plain Radiographs

As for any other type of fracture, plain radiographs including the joint above and the joint below are obtained. Much information can be obtained from the plain radiographs, not only regarding the diagnosis of a pathologic fracture, but also regarding its definite cause. It should be realized that at least 30 % of the bone must be involved in the osteolytic process before any changes are seen on a plain radiograph. It should be noted that compared with any other test, conventional radiography provides the most useful information for evaluation of bone lesions [9, 14]. Often, the patient's age and plain radiologic findings are sufficient to arrive at a specific diagnosis. Radiographic appearances of some of the important causes of pathological fractures include:

Osteoporosis: Plain radiographs are of little use in measuring bone mass. However, estimating the bicortical to whole-bone width ratio for long bones, and the decrease or loss of transverse trabeculae in spine radiographs suggests osteopenia. More accurate radiologic diagnosis requires the use of dual energy x-ray absorptiometry or quantitative computed tomography (CT) scanning [5].

Osteomalacia: Shows evidence of osteopenia as in osteoporosis, and can also show "Looser's zones" especially in the pelvis and femoral neck which should not be confused with a fracture, and may show a "rugger jersey spine" appearance [5].

Paget Disease: Pagetic bone may show transverse pseudofractures typically on the convex side of the bone. The bone (especially pelvis, tibia, and femur) is expanded and the cortices are thickened. There is bowing of the femur and the tibia [5].

Osteogenesis Imperfecta: The findings vary according to the severity of the disease. There may be multiple fractures in different stages of healing throughout the skeleton. The skull shows a "wormian bone" appearance. The long bones are thin and osteopenic. The femur may look crumpled as a result of multiple fractures [5].

Osteopetrosis: There is increased density in the bone of the entire skeleton with complete absence of the medullary canal in addition to metaphyseal widening. The pelvis, vertebrae, hands, and feet may show a "bone within a bone" appearance [17].

Hyperparathyroidism: There is a variable degree of osteopenia according to disease severity. Unlike osteoporosis, it also affects the cranium and the hard lamina of the teeth. The diaphyses and the hands are also affected. In more intense cases of the disease, the osteopenia may present with a "moth eaten" appearance.

Subperiosteal bone resorption in typically seen in the hands with resorption of the tufts of the terminal phalanges. It can also be seen in the metaphyses of long bones. Subchondral resorption is frequent at the acromial end of the clavicle.

Brown tumors, either solitary or multiple, may be seen. They are osteolytic lesions, ranging from small to huge in size. They can be central or eccentric. The cortex may be attenuated or even expanded and there is no periosteal reaction. Occasionally, the osteolysis may be veiled by a ground glass radiodensity [5].

Fibrous Dysplasia: It presents as an osteolytic lesion with margins that are well defined. It can occur in the epiphysis, metaphysis, or diaphysis. Radiolucency is typically veiled by a "ground glass" opacity as a result of the delicate trabeculae of woven bone. The cortex may be thinned and moderately expanded. Curvature of long bones may be seen. The most often presentation noted is the "shepherd crook" deformity of the proximal femur (Fig. 19.1) [7].

Chronic Osteitis: There are usually obvious bony changes with cavitation, sequestrum, and involucrum formation [5].

Non Ossifying Fibroma: Presents between the ages of 10 and 20 years. They are metaphyseal lesions mainly in the femur or tibia. They present as osteolytic eccentric lesions, generally oval in shape. Multilocular appearance or ridges in the bony wall may be seen (Fig. 19.2) [9].

Unicameral Bone Cyst: Usually presents between the ages of 5 and 15 years. It is usually seen in the proximal metaphysis of the humerus or the femur. It presents as a central osteolytic lesion extended to the whole cross section of the bone. It may slightly expand the cortex. The cortex remains well defined and with no periosteal reaction. Pathologic fractures through the cyst may show the "falling leaf" sign (Fig. 19.3) [6].

Aneurysmal Bone Cyst: Most cases are seen before the age of 20 years. The lesion is purely osteolytic, metaphyseal in long bones, and usually eccentric. The cortex is attenuated or completely destroyed. The periosteum is often elevated in a blow-out image with no apparent demarcation with the soft tissues [6].

Enchondroma: They are found mostly in the tubular bones of the hand, but can be seen in other long bones such as the femur. They are seen as osteolytic, round or lobulated lesions, with well-defined edges. They are usually central and metaphyseal. They sometimes contain opacities producing a "popcorn" appearance [5, 9].

Chondoblastoma: It is usually epiphyseal, occurring in adolescents. The proximal humerus is the most common site. It shows as an osteolytic lesion centered in the epiphysis with the physeal plate open or just closed. The osteolysis is usually rounded and well-defined by a thin rim of osteosclerosis. It may be spotted by granules of fading radiodensity. The cortex may be expanded, and the metaphysis invaded [9].

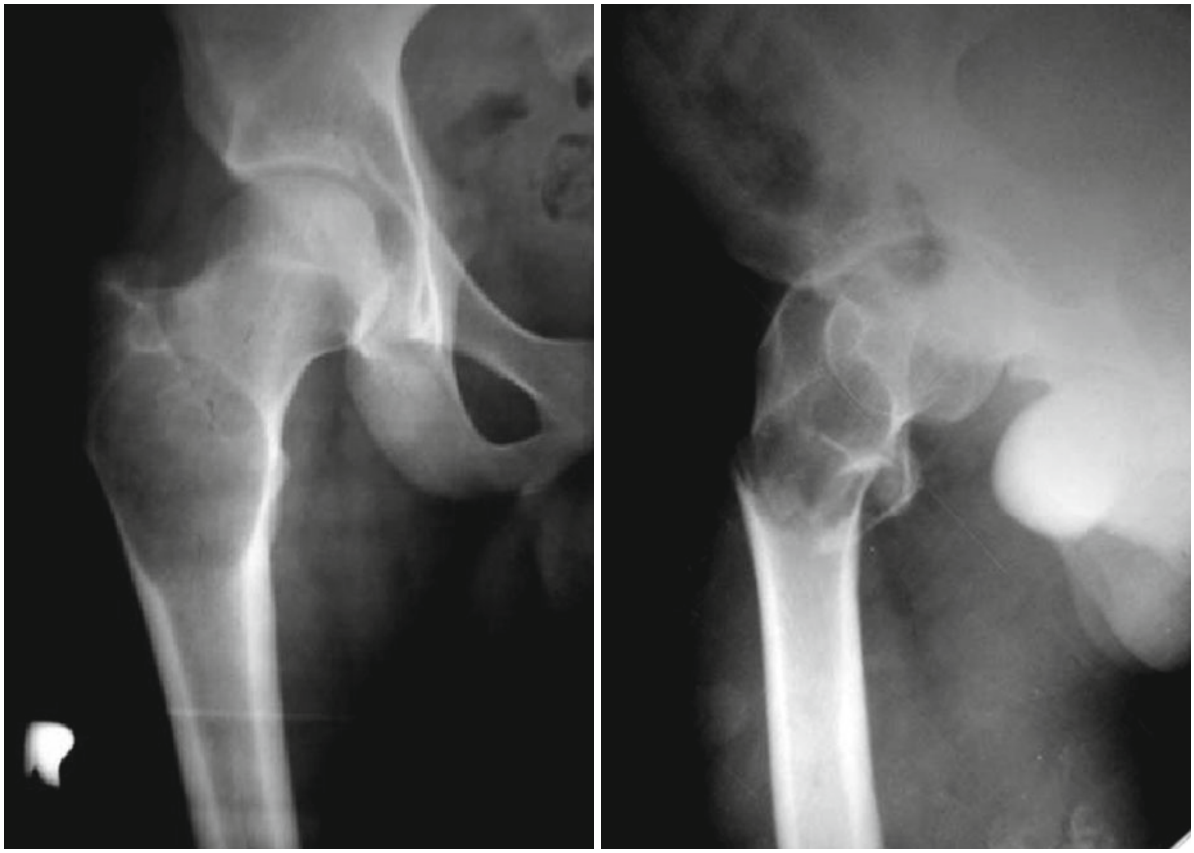


Fig. 19.1 A case of fibrous dysplasia of the proximal femur causing a pathologic fracture

Giant Cell Tumor: Found usually at the ends of long bones and 50 % are found around the knee. They involve both the epiphysis and the metaphysis. The lesion is intramedullary and purely osteolytic. The cortex is generally moderately expanded and constituted by a thin shell of reactive bone [5, 9].

Ewing's Sarcoma: Appears roentgenographically as a destructive lesion in the diaphysis of long bones. Patients are typically under the age of 15 years. The lesions show characteristic "onion skin" appearance. It is not uncommon for a large portion of the bone to be involved [13].

Osteosarcoma: Classic osteosarcoma is metaphyseal, usually around the knee or in the proximal humerus. The lesion is intramedullary with a combination of radiolucency and osseous radiodensity. It may breach the cortex and expand towards the soft tissues. The soft-tissue extension may show stripes of radiodensity perpendicular to the cortex "sun-ray appearance" [5, 9, 11].

Multiple Myeloma: Appears roentgenographically as multiple "punched-out", sharply demarcated, purely lytic lesions without any surrounding reactive sclerosis. There is usually obvious osteopenia [5, 9].

Lymphoma: Typically appears as an ill-defined area of bone destruction, usually diaphyseal, and often with a permeative appearance. Periosteal reaction is rarely seen and frequently a large portion of the bone may be involved [5, 9].

Bone Metastases: The roentgenographic appearance of metastatic carcinoma is variable. However, the appearance is usually aggressive, suggestive of malignancy. It should be remembered that in any patient over the age of 40 years, even without a history of malignancy, an aggressive-appearing bone lesion is most likely metastatic or a result of multiple myeloma. The lesions can be lytic, blastic, or mixed. Most metastases are purely or predominantly lytic, as are those from the kidney, lung, breast, thyroid, gastrointestinal tract, and melanoma. Carcinomas

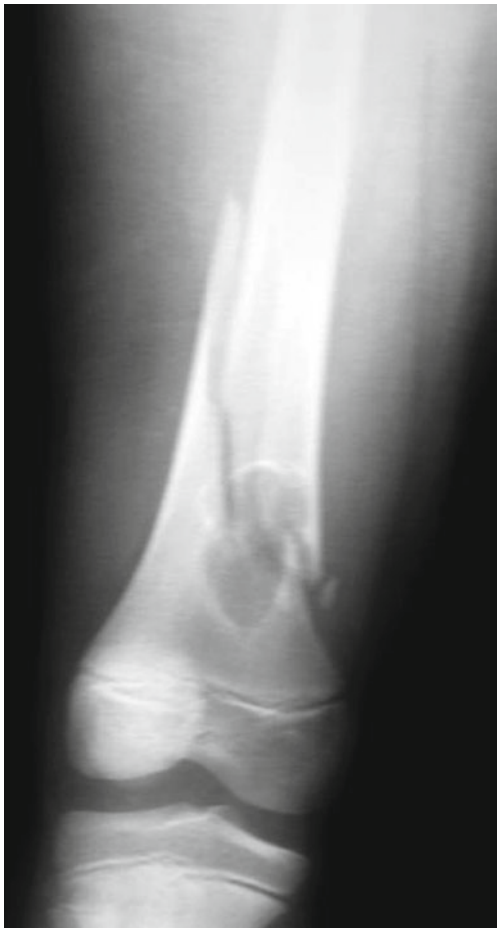


Fig. 19.2 Non-ossifying fibroma of the distal femur with a pathologic fracture

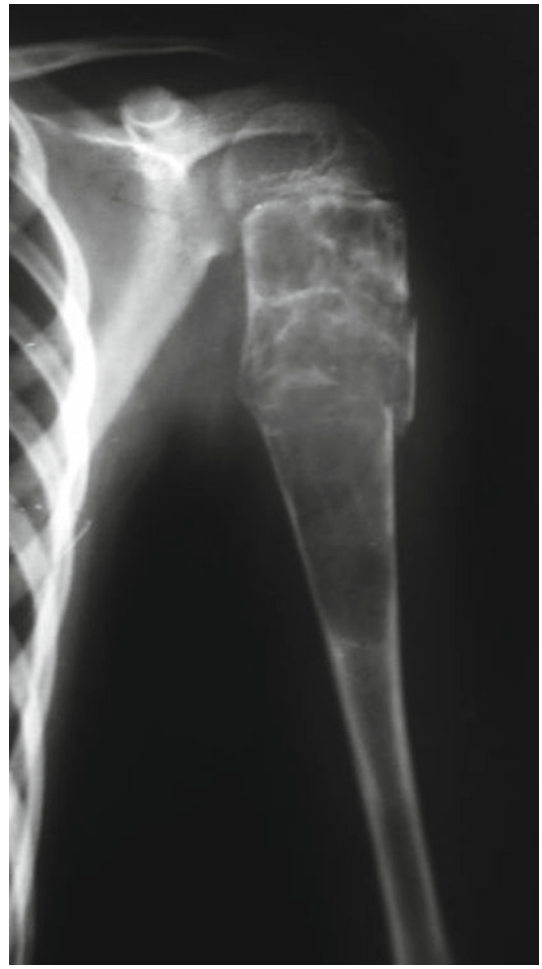


Fig. 19.3 Simple bone cyst with secondary aneurysmal changes and a pathologic fracture of proximal humerus

of the kidney or thyroid are usually associated with pure osteolysis and a blow-out appearance of the bone. Blastic metastases are those mainly from prostate cancer. Mixed blastic and lytic metastases are particularly frequent in breast and lung carcinoma, but can also be seen in carcinomas of the gastrointestinal tract. Metastases distal to the knee or elbow are rare, and in such cases, lung cancer is the most likely cause. The most common locations for bony metastases are the spine, ribs, pelvis, femur, and humerus [9, 14].

– Localization also depends on the primary carcinoma. Breast and thyroid metastases prefer the locations of the trunk, proximal humerus, proximal femur, and skull. Prostate, rectum, uterus metastases frequently occur in the lumbar spine, sacrum, pelvis, and proximal femur. The intracortical or subperiosteal metastases of the shafts are typical of lung carcinoma, as are the rare metastases to the hand, while the metastases to the foot are usually because of carcinomas of subdiaphragmatic organs.

Metastases from the breast and prostate tend to become widely disseminated, while those from the kidney and thyroid may remain solitary for an extended period of time [14, 16, 18].

– *CT and magnetic resonance imaging (MRI) of the affected bone*: CT is superior in delineating osseous details and destruction. MRI is particularly important for showing marrow changes and extent of soft-tissue spread. It is highly important in the staging of some primary malignant bone tumors. The amount of soft-tissue extension and

the number of muscle compartments invaded as shown by MRI can have great relevance as to the decision of management of primary malignant bone lesions. It is to be emphasized that all local radiologic examinations must be fulfilled before a biopsy is performed as this will distort the local anatomy, and usually gives an impression that the tumor is larger than it actually is [15, 19].

– *Angiography*: May be needed as part of the preoperative planning in some fractures. It helps to assess the proximity, and possible invasion, of the vascular bundle which holds importance in the decision of limb salvage versus amputation regarding some malignant bone tumors, and in properly planning the surgery. Preoperative embolization may also be needed in some highly vascular lesions (e.g., metastases from kidney and thyroid) [2, 9, 14].
– *PET*: Positron emission tomography (PET) images glucose metabolism, and therefore gives a non-invasive reliable method of assessing the grade of malignancy of bone tumors. It is to be noted, however, that although metabolic activity is usually correlated with the degree of malignancy, some benign tumors may show marked metabolic activity (e.g., giant cell tumor). Post-treatment reduction in glucose metabolism by the tumor is useful in assessing the response to chemotherapy, and radiotherapy. PET is also a useful tool in the detection of bone metastases [5, 9, 14].
– *Bone scan*: Is highly sensitive in picking up multiple bone lesions (e.g., metastases or skip lesions). Bone scans should be obtained in all cases with bone malignancy. Hot areas seen on the scan are then correlated with plain radiography. It should be remembered that some lesions (e.g., myeloma) present as cold areas [5, 9].
– *Chest radiograph*: Are obtained in all cases as a part of preoperative assessment, to rule out primary lung tumors, or lung metastases.
– *CT chest* is important before the definitive management of some primary malignant bone tumors known to metastasize early to the lung (e.g., osteosarcoma). It may also show a primary lung carcinoma in metastatic disease.
– *CT abdomen and pelvis* are important in locating the primary source of malignancy, and in the staging of some tumors (e.g., lymphoma).

Other tests used in evaluating a patient with a suspected pathologic fracture of unknown etiology include:

- Mammography.
- Upper and lower gastrointestinal series.
- Endoscopy.
- Liver, spleen, and thyroid scans.
- Intravenous pyelogram and renal ultrasound.

It should be noted that despite fulfilling all the mentioned examinations, the primary source will not be found in approximately 15 % of patients with suspected metastatic bone disease [5, 9].

19.10 Management and Preoperative Planning of Pathologic Fractures

Before proceeding with management of any patient with pathologic fracture, careful preoperative planning must be undertaken to evaluate the case, confirm the diagnosis, and assess the general condition. This includes clinical evaluation, laboratory investigations, radiologic examination, and finally biopsy in certain cases. The goal is to confirm the diagnosis, assess the severity and extent of the bone lesion, document the stage in primary malignant conditions, and assess the general condition of the patient. It is to be emphasized that a team approach to the preoperative planning in the management of pathologic fractures caused by malignancy should include not only the surgeon, but also the oncologist, pathologist, radiologist, internal medicine physician, and radiation therapist [2, 3, 5].

19.10.1 Bone Biopsy

Before proceeding to the management of a bone lesion with impending fracture, or with a pathologic fracture, every effort must be made to clarify the nature of the lesion including clinical, laboratory, radiologic investigations, and finally, the use of bone biopsy. This is not required in patients with known malignancy and multiple metatstases.

General Biopsy rules:

- A biopsy should be planned as carefully as the definitive procedure. It should only be done after all the clinical, laboratory, and roentgenographic examinations are fulfilled. It is preferably done in the same center where the definitive surgery will

take place. It has its unique role in diagnosis of primary bone lesions, and other bone lesions of unknown aetiology. Solitary metastasis in a patient with known malignancy should also be biopsied.

- A biopsy can be done using fine-needle aspiration, core needle biopsy, or an open incisional procedure. Incisional biopsy is associated with complications, but is least likely to be associated with a sampling error and provides enough tissue for additional diagnostic studies. Core needle biopsy is the preferred technique at our facility. It should be remembered that whether a needle or incisional biopsy is done, the biopsy track should be considered contaminated with tumor cells [5, 20].

The general rules for biopsy include:

- The biopsy track should be in line with the incision of the definitive surgery as it must be completely excised in the definitive surgery.
- We do not favor the use of tourniquets, however, if a tourniquet is used, then the limb may be elevated but should not be exsanguinated by compression.
- Transverse incisions should be avoided, and in an extremity, the incision should be as distal as possible.
- The incision should move directly toward the tumor passing through a single muscle rather than in an intermuscular plane.
- If the tumor has a soft-tissue component, then this is best biopsied.
- If a hole must be drilled in the bone (not in cases presenting with a pathologic fracture) then it must be oval or round and not act as a stress riser and should be sealed by the least amount of bone cement to not push the tumor up or down.
- The periphery of the lesion is the most viable tissue to be biopsied as the center usually yields necrotic tissue.
- Complete hemostasis should be achieved by the end of the procedure.
- If a drain is used, it should exit in line with the incision so that its track can be excised with the definitive surgery [20, 21].

The definitive procedure can be carried out immediately depending on the results of a frozen section only if it confirms the clinical and radiological diagnosis. Otherwise, the definitive procedure should be delayed until a definite diagnosis is reached.

Regarding small lesions, or lesions in difficult sites where the accuracy of the conventional intraoperative C-arm can be limited, we have found a great value for the use of CT-based 3D navigation system or 3D C-arm imaging to accurately localize those lesions intraoperatively [22].

19.11 Treatment of Pathologic Fractures

Treatment of pathologic fractures is not necessarily surgical and depends on the definite pathology and on the fracture site and geometry among other parameters. It is to be noted that bones affected by a local pathology do have the ability to heal after a fracture although the healing time is usually slower than normal bone, particularly after radiation therapy or chemotherapy.

Initially, all patients with pathologic fractures should be offered the usual fracture care with immobilization and reduction. Optimization of the medical condition in elderly or fragile patients should start. Evaluation of the underlying pathologic process is a must with a full clinical work up (as formerly stated), laboratory investigations, radiology, and finally biopsy for unknown or locally destructive lesions [5].

19.11.1 Non-surgical Treatment

Fractures through certain benign bone lesions that can be reduced and maintained conservatively can be managed non-surgically. Examples include certain fractures associated with rickets, unicameral bone cyst, osteoporosis, or osteopetrosis [5, 6].

Radiotherapy is considered the mainstay of treatment of metastatic disease to the spine from a radiosensitive tumor unless there is gross instability or if neurologic deficit occurs [23].

19.11.2 Surgical Treatment

Surgical stabilization of pathologic fractures allows the patient to conduct activities of daily living, alleviates pain, and prevents complications of recumbency and disuse atrophy.

Fixation of pathologic fractures is accomplished with internal fixation with or without the use of bone cement to fill cavities or augment fixation. Loss of fixation as a result of poor bone quality is a common problem with some pathologic fractures. When feasible, intramedullary nails are preferred because they allow early weight bearing and protect the entire bone. In fractures in proximity to joints, or where internal

fixation will not be rigid enough to allow weight bearing, prosthetic replacement is used [15, 19].

Contraindications to the surgical management of pathologic fractures include:

- Poor general condition that is inadequate to tolerate anesthesia and the surgical procedure.
- Patients with deteriorated level of consciousness that precludes the need for pain relieving measures.
- Life expectancy of less than 1 month (controversial) [2, 5].

19.12 Treatment of Specific Pathologic Fractures

19.12.1 Osteoporosis

Fractures caused by osteoporosis are always associated with increased morbidity and mortality. They are typically multifragment fractures with metaphyseal bony defects. They affect mainly the spine, proximal femur, distal radius, and distal femur. It is worth noting that patients with osteoporosis normally go through the early stages of fracture healing by endochondral repair. It is the last stage of remodeling that is slowed in those patients.

The surgical procedure chosen should allow stable fracture fixation with early weight bearing and return of function. Prolonged recumbency can have very serious and fatal consequences in such elderly patients. Therefore, they are best served by a rapid definitive treatment. Because these patients are usually on their best health on the day of injury, surgical intervention should not be delayed unless there is a good medical reason.

It is to be noted that those patients not only have weak bones, but the whole softtissue envelope is rather atrophic. The operative management chosen should ideally be done in a short time and with minimal blood loss in such fragile patients [1].

Because early mobilization is needed in these patients, intramedullary fixation techniques, whenever suitable, are superior to plate fixation. Indirect closed reduction and nailing should be the goal (Fig. 19.4).

In cases of intra-articular and para-articular fractures where anatomical reduction is required with plate fixation, the problem is always the poor purchase of the plate to the weak bone with subsequent loosening and loss of fixation. The generous exposure sometimes needed is also too much of a burden of these patients.

The use of internal fixators is most appropriate in these patients. It allows a minimally invasive approach in addition to the stability of the construct to the bone because of the self-locking property of the screws to the plate.

The use of a computer-based navigation system in osteoporotic fractures particularly of the spine and the pelvis offers the advantage of indirect reduction and minimally invasive accurate surgery [22].

Vertebral fractures without neurologic deficit and with minimal pain may be managed conservatively. However, if after a period of conservative management they continue to be painful, then kyphoplasty or simply vertebroplasty, can be a good pain-relieving measure in patients with old painful fractures [22].

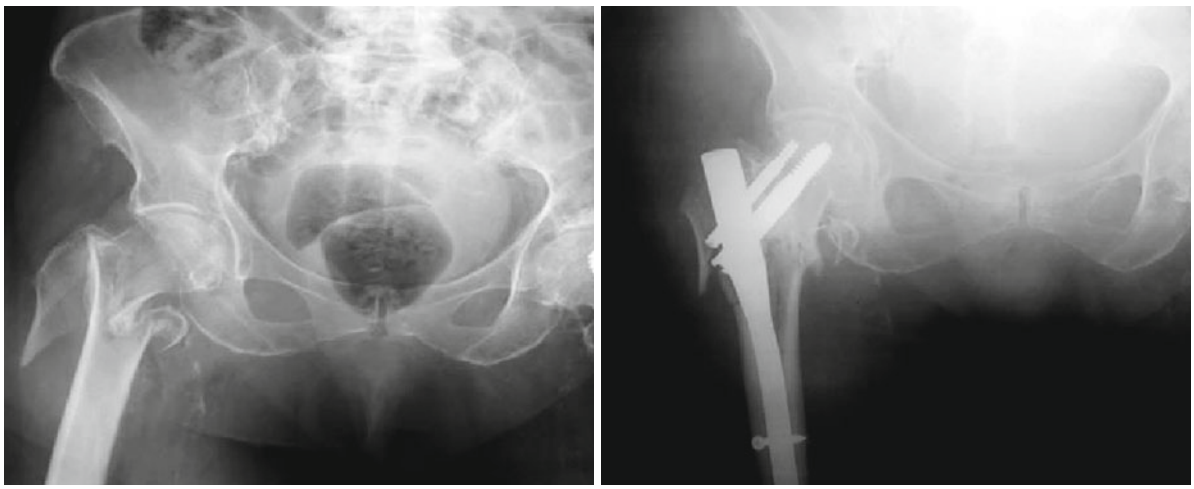


Fig. 19.4 Intertrochanteric fracture of the proximal femur in an osteoporotic case corrected using a proximal femoral nail

Prophylaxis against future fractures should be prescribed with vitamin D, calcium, and bisphosphonates. Proper mobilization is crucial.

Femoral neck fractures in elderly patients are best treated with a hemiarthroplasty (bipolar prostheses). Regarding intertrochanteric fractures, we recommend the use of the dynamic hip screw only in stable fractures, otherwise the use of intramedullary fixation (e.g., proximal femoral nail) shows greater stability and allows earlier weight bearing, which should always be the goal.

19.12.2 Unicameral Bone Cyst

Treatment can be conservatively undertaken in many fractures apart from displaced lower limb fractures. Contrary to popular belief, the cysts rarely regress after fracture healing, and follow-up with subsequent management as for any ordinary bone cyst (according to site, size, and activity) is required. Displaced lower limb cysts may need internal fixation. In the same instance curettage of the lesion with bone grafting is done [6].

19.12.3 Aneurysmal Bone Cyst

Treatment is essentially surgical. Excessive blood loss should be anticipated in those patients. Complete curettage with extraperiosteal excision of the lesion, along with bone grafting/bone cement, and internal fixation are usually required. Strut grafts may be needed. Marginal en block resection may be needed in some cases. In cases involving the spine or pelvis, preoperative arterial embolization can be helpful [6].

19.12.4 Fibrous Dysplasia

In patients with fibrous dysplasia, the cortex is usually thinned and the shaft expanded. It is difficult to totally eradicate the disease in the absence of complete excision. Therefore, the goal of intervention is to alleviate the symptoms and offer bone stability and integrity, and not complete cure. The options include splinting, internal fixation and/or curettage and bone grafting, and wide excision (Fig. 19.6). Closed management may suffice for upper extremity fractures, but in the lower extremities it is rarely successful. Intramedullary nailing is usually used for the femur and tibia and/or osteotomies to restore alignment if grossly deformed. The surgeon should anticipate difficulties during closed nailing procedures as well as excessive blood loss because the medulla in those patients is typically vascular and not very distinct [7, 8].

19.12.5 Osteogenesis Imperfecta

Intramedullary rods are generally used in patients with fragile bones because they offer the biomechanical advantage of load sharing. Multiple osteotomies may be needed to straighten a bone crumpled by previous multiple fractures to allow insertion of the rods, and straightening of the bone. Telescoping rods, although technically more difficult to insert, are preferred because they grow with the child, and hence lessen the chances of subsequent fractures as the child grows. Various designs are available [24].

19.12.6 Osteopetrosis

Diaphyseal bone in patients with osteopetrosis is hard and chalky. It is difficult to drill, and hence when appropriate, non surgical closed treatment is the best option. Intramedullary nailing is almost impossible because of the actual lack of a medullary canal in those patients. Drills used in the process of internal fixation must be sharp and constantly cooled by sterile saline to avoid thermal necrosis. Presence of a plate on the shaft of a long bone is a significant stress riser leading to subsequent fractures at the ends of the plate. If rigid fixation is needed, then external fixation can be the wisest option [17].

19.12.7 Chronic Osteomyelitis

The management of fractures in bone affected by chronic osteomyelitis is beyond the scope of this chapter. However, the main guidelines are:

- Débride all infected tissue including soft tissue and bone.
- Stabilize the fracture (usually using an external fixator or ring fixator).
- Do not perform cancellous bone grafting unless there is a clean granulating base.
- Tissue transfers may be needed for coverage in cases with extensive soft-tissue loss.

19.12.8 Primary Malignant Bone Tumors

Lesions such as osteosarcoma, chondrosarcoma, fibrosarcoma, and malignant fibrous histiocytoma are usually symptomatic and the patient typically seeks medical care and advice resulting from the pain before a pathologic fracture occurs. Therefore, it is uncommon for pathologic fractures to be the first presentation in those patients. They may, however, occur during the course of treatment.

With the progress of adjuvant chemotherapy, and radiotherapy, many of these lesions can be treated by limb slavage techniques [21, 25].

A pathologic fracture, although it increases the contamination with malignant cells and converts an intracompartmental tumor into an extracompartmental tumor, in addition to seeding of muscle compartments not previously affected, is not a contraindication to limb salvage under certain measures. The modern advances in chemotherapy and radiotherapy have promising expectations regarding limb salvage in patients with pathologic fractures [21, 25].

The alternative to limb salvage in patients with pathologic fractures resulting from primary malignant bone lesions will be an amputation or an intercalary amputation (rotationplasty) in children.

Before proceeding to the treatment of such pathologic fractures, a complete work up, as formerly stated, including clinical and laboratory work, should be done:

- Plain radiology of the affected bone.
- Plain radiography and CT of the chest to detect metastases.
- MRI of the affected bone to assess the amount of intramedullary spread, skip lesions, and to assess the extracompartmental spread with the number and extent of compartments affected. This is crucial for the staging (usually according to Enneking's system).
- Bone scan to detect other lesions and skip lesions.
- Angiography to assess the relation to the major vascular bundle may be needed in some locations as around the knee, and some pelvic tumors.
- A biopsy is performed to confirm the diagnosis and assess the grading of the tumor and its response to chemotherapy (if the fracture occurred during the course of treatment) [21, 25].
- There are certain contraindications to limb salvage in patients with primary malignant bone lesions including:
  - Infilteration of the major neurovascular bundle. However, resection and grafting of the vascular bundle can be done. As for the nerve, resection of the perineurium with the tumor leaving the nerve (if not included in the tumor margins) can be performed, additionally, nerve resection with cable grafting can be tried.
  - Infection (e.g., from previous incisional biopsy) leads to wide contamination and highly compromises the results of any salvage surgery. Inappropriate placement of the biopsy incision is also a relative contraindication as the track *must* be removed en bloc with the tumor.
  - Disseminated metastases with short life expectancy (controversial). Limited pulmonary metastasis should be surgically, and even repeatedly, resected by wedge pulmonary resections. Also, limited extrapulmonary metastases are surgically resected with wide margins.
  - Children younger than 12 years (highly controversial especially with the advent of expandable prostheses).

Preoperative (neoadjuvant) and postoperative chemotherapy has a major and crucial role in management [5, 10]. As a general rule, the surgical resection should aim at wide non contaminated margins with the biopsy track included, and all excised en bloc. Resection is usually intraarticular for the distal femur and proximal tibia, whereas it is usually extraarticular for the proximal femur and proximal humerus.

The techniques used for reconstruction after resection depend on the location of the tumor and the resulting limb function expected by the patient. The alternatives after resection of all or part of a major joint include custom prosthesis, osteochondral allograft, allograft prosthetic composite, or an arthrodesis. As for segmental bony resection, a vascularized fibular graft or segment transfer using the Ilizarov technique can be performed. The same Ilizarov technique with segment transfer can be used in cases managed by resection and arthrodesis [5, 10, 21, 26].

19.12.9 Multiple Myeloma

Primary treatment of multiple myeloma is chemotherapy. Painful bony lesions respond well to radiotherapy. Surgical intervention is needed for pathologic fractures and impending fractures of the spine, proximal femur, acetabulum, and the proximal humerus. Most patients

have a short life expectancy and a rigid fixation allowing weight bearing should be offered. Bone cement can be used to augment the fixation or fill the cavities. If this is not possible, then cemented total joint or hemiarthroplasty should be considered [5].

19.12.10 Bony Metastases

Metastatic carcinoma is the most common bony malignancy encountered. The basic workup of such fractures includes history, physical examination, laboratory tests (aimed at showing anemia, hypercalcemia, specific carcinoma markers, and excluding monoclonal gammopathy typical of myeloma), radiology including radiographs of the entire bone affected, chest radiograph, as well as CT scans of the chest, abdomen, and pelvis. A bone scan to detect other sites of bony affection is also required. CT or MRI of the affected bone is needed. A biopsy (according to the general rules as for a primary malignant bone tumor) is performed to ascertain the diagnosis and define the primary if possible. It is performed if the patient has no history of malignancy or if this is the first site of the bone being affected in a patient with known malignancy. For patients with known malignancy and multiple metastases, it can be assumed that the local pathology is a result of metastases from the known primary tumor [2, 3].

It must be emphasized that treatment of carcinoma metastatic to bone is multimodal, and that different specialties share in it. It includes (in addition to fracture management) use of systemic cytotoxic drugs, radiotherapy, and hormone manipulation in some malignancies such as prostate and breast. The different specialties should cooperate in planning the treatment. Treatment of pathologic fractures as a result of metastases is predominantly operative.

The treatment of metastatic disease, apart from exceptional cases with a single metastasis and completely excisable primary, is not aimed at curing the patient, but relieving symptoms and offering a better quality of life. The management should not be too aggressive or too lenient. It should not only address the pathologic fractures, but also prophylactic fixation of impending fractures according to certain rules that will be discussed later.

The goal of operative treatment in such fractures is to achieve rigid fixation allowing immediate full weight bearing. Unlike the bone healing in non-pathologic fractures, bone healing may or may not occur in pathologic fractures because of the tumor itself or the adjuvant chemotherapy or radiotherapy. Also, the unpredictability of survival makes proper surgical care more challenging. The fixation should be stable enough to allow immediate weight bearing, but it should also ideally be durable enough to last for many years if the patient should survive [15, 27].

Regarding extremity fractures, internal fixation devices (intramedullary nails and plates), and prosthetic devices are most commonly used (Figs. 19.5 and 19.6). Whenever possible, the entire bone is protected with intramedullary fixation

Closed nailing can be done in patients with multiple metastases. Conversely, if open fixation is done, the tumor should be debulked and the cavity can be filled with methylmethacrylate to augment the fixation. It is to be remembered that the fixation will eventually fail if there is no bony union. We recommend bone grafting (cancellous or cortico-cancellous) on the opposite side of the plate in cases with plate fixation and bone cement to give a chance for bony union to happen. When the bone stock has been substantially destroyed near a joint, or when internal fixation is not expected to be stable enough to offer immediate weight bearing, segmental bone resection and prosthetic replacement is indicated. This occurs most frequently in the proximal femur, or the proximal humerus. Preoperative arterial embolization may be helpful in hypervascular lesions (metastases from kidney and thyroid). Radiotherapy as an adjuvant treatment is usually needed and begun 3 weeks after surgery. Amputation is indicated when there is massive expansion of the metastases with skin ulceration and bleeding [15, 16].

Regarding impending extremity fractures, it can be stated that the amount of cortical bone destruction is the most useful criterion to predict a pathologic fracture. Other factors include the type of metastases, and their location. The advantages of prophylactic fixation include an elective operation that can be properly timed between the courses of chemotherapy, less blood loss, technically easier, and avoidance of the pain of a pathologic fracture. The decision is best individualized for each patient according to condition and expected survival. Whenever possible, intramedullary nails are used to support the entire bone [3, 28].

Mirels developed a scoring system based on the degree of bone destruction, presence of lytic or blastic lesions, location of the lesion, and type of bone pain. Patients with a score of 9 or greater are prone to fractures and are candidates for prophylactic fixation.

Variable	1	2	3
Site	Upper limb	Lower limb	Peritrochanteric
Pain	Mild	Moderate	Severe
Size	<1/3	1/3–2/3	>2/3
Lesion	Blastic	Mixed	Lytic

From Mirels H, *Clin Orthop* 249:258, 1989 [28]

Spinal metastases are common among patients with adenocarcinoma. Because of the preponderance of metastatic disease, spinal lesions in the adult are most likely to result from metastases, myeloma, or lymphoma. Metastases tend to appear in the verterbral bodies affecting one or both pedicles [22, 27, 29].

Not all patients with spinal metastases require surgery. Radiotherapy remains the most appropriate treatment for most patients with spinal column metatases. Radiotherapy (for a known radiosensitive primary prostatic cancer, breast cancer, or myeloma), or chemotherapy (for a known chemosensitive primary thyroid

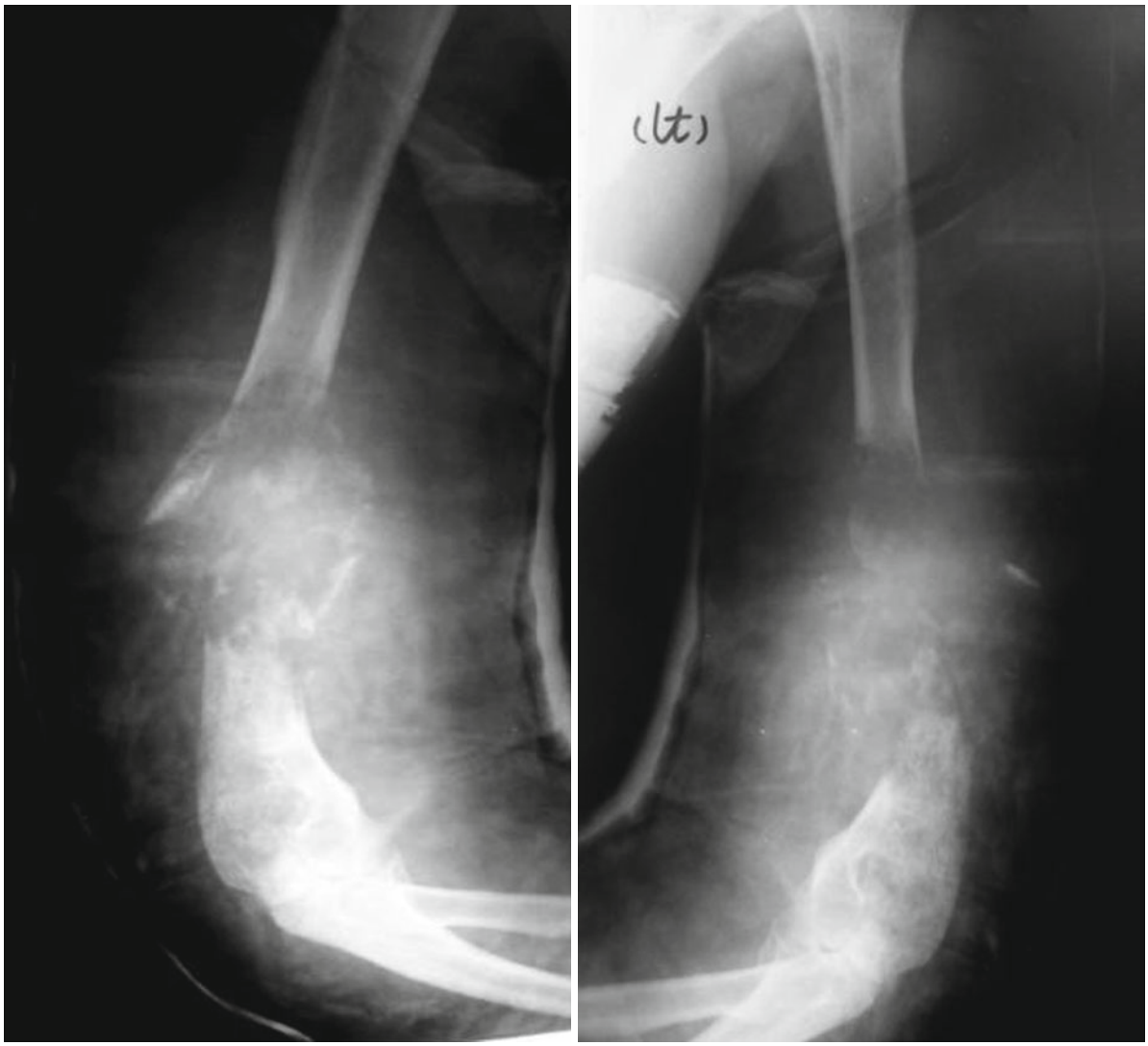
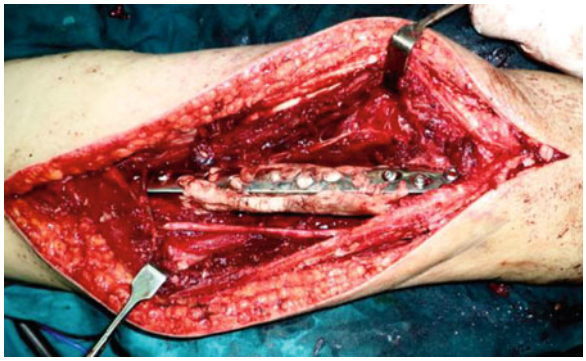


Fig. 19.5 Pathologic humerus fracture in a case with metastatic colonic carcinoma corrected by plating augmented with methylmethacrylate



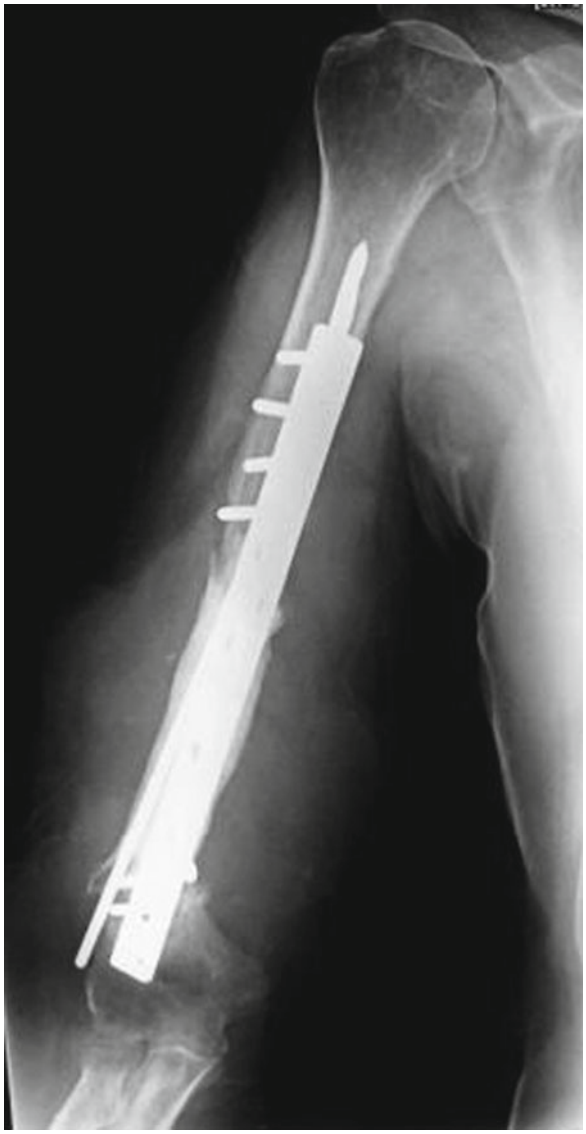


Fig. 19.5 (continued)

cancer; usually with radiotherapy) may be all that is required. Pathologic fractures without marked mechanical instability, neurologic deficit, or severe pain can also be managed by radiotherapy, particularly in patients with advanced disease [23].

The main indications for surgical treatment in spinal metastases include:

- Neurologic compression from pathologic fracture.
- Mechanical instability with severe pain or impending neurologic deficit.
- Resectable solitary metastasis in a patient with expected long-term survival.
- Known radioresistant tumor.
- Tumor progression and severe pain despite radiotherapy [23, 29].

Decompression and instrumentation are usually required to restore stability in patients with spinal metastases associated with neurologic compression and/or mechanical instability. Anterior surgical approaches with anterior column reconstruction are associated with a high incidence of complications in fragile patients including wound dehiscence, infection, and pulmonary complications. Pedicle screw fixation, with direct or indirect decompression, is particularly helpful. Use of a computer-aided navigation system allows for precise and rapid surgery. It should be noted that if there is severe destruction of the anterior column and it is not reconstructed, screw failure can be expected, but will depend on the life expectancy of the patient [22, 23].

Anterior column reconstruction may be needed in patients with advanced anterior column destruction or in patients where anterior decompression was needed as a result of the tumor mass. Use of minimally invasive endoscopy can be useful in such lesions and decreases the surgical load in such fragile patients. Thoracoscopy can be used to approach levels T5-L1, thoracoscopy and endoscopy via diaphragm splitting for L2, and retroperitoneal endoscopy for L3/4 lesions. If vertebrectomy was performed (in cases of a primary malignant bone tumor or large compressing metastases) then reconstruction of the anterior column is mandatory. A variety of prosthetic implants (expandable cages); allograft fibula, rib, or tricortical graft; or methymathacrylate with Steinmann pins can be used to anchor the space [23, 27, 29].

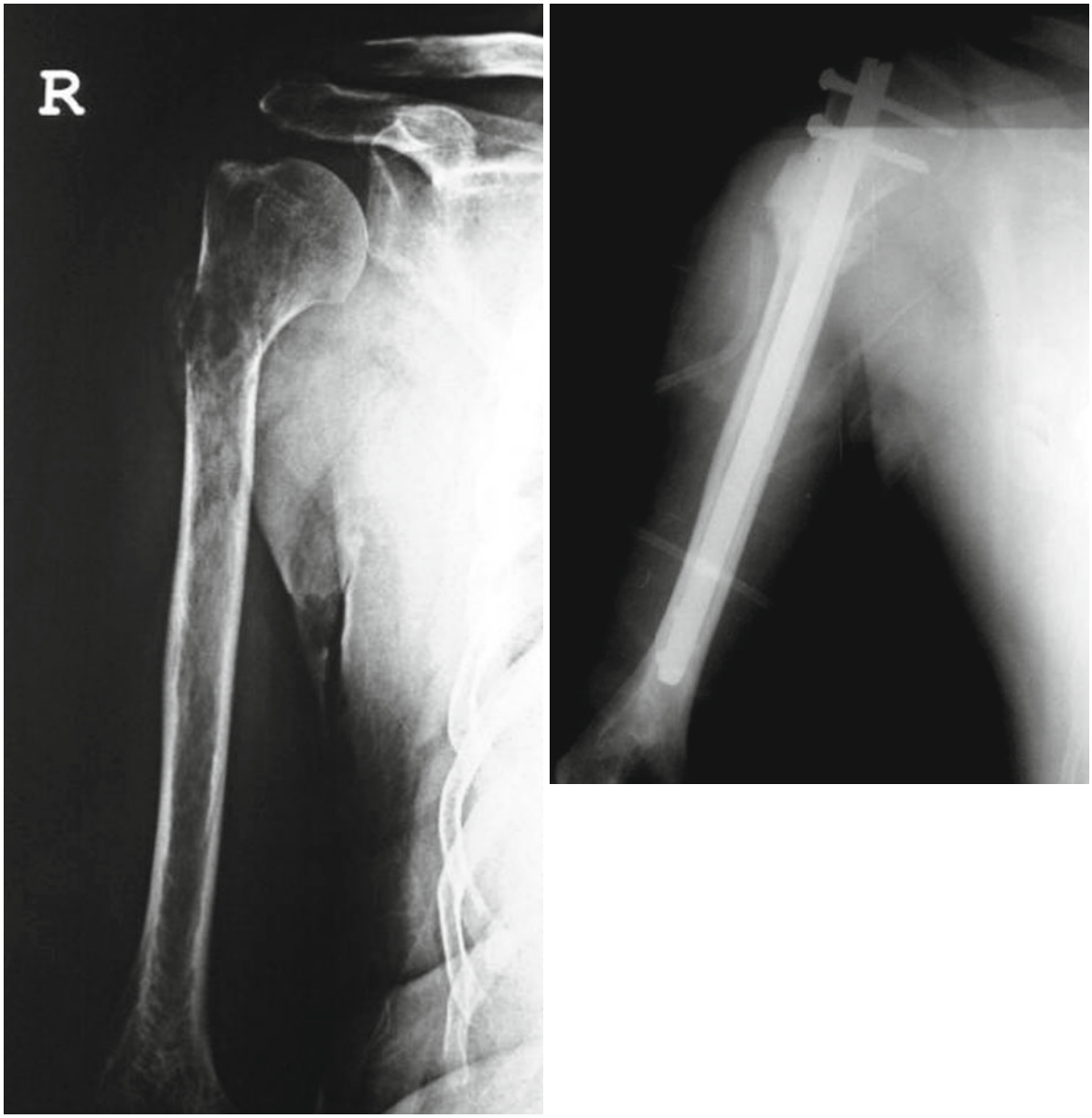


Fig. 19.6 Pathologic fracture of the proximal humerus in a case with hepatome metastases corrected by intramedullary nail augmented with bone cement

19.12.11 Adjuvant Therapy

19.12.11.1 Radiation Therapy and Chemotherapy

Radiation therapy and chemotherapy are useful adjunctive therapies in the management of certain pathologic fractures and are considered the mainstays of treatment in certain metastatic bone diseases known to originate from a radiosensitive primary (e.g., prostate cancer or breast cancer) or chemosensitive primary malignant tumor (e.g., thyroid cancer) [5, 15].

Both are useful in decreasing the size of the lesion, stopping its progression, and decreasing patient symptoms. Radiation and chemotherapy delay soft-tissue healing and may lead to wound complications

postoperatively. Therefore, they should not be commenced until 2–3 weeks postoperatively.

Finally, we would like to reemphasize the fact that the management of pathologic fractures occurring as a result of bone malignancy requires a team approach including the trauma surgeon, radiologist, pathologist, oncologist, internal medicine physician, and radiation therapist.

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