Chapter 2
Nonmechanical Falls

2.1 Introduction

The World Health Organization (SOURCE: **www.who.int**) states that falls are the second leading cause of unintentional traumatic death, causing 684,000 deaths per year. Among those who fall, 37.3 million require medical attention. To understand who is at risk to fall, and why people fall, it is important to distinguish between those falls that are nonmechanical and those that are mechanical.

Nonmechanical falls occur in persons who are vulnerable and have underlying medical conditions that precipitate the fall. Mechanical falls happen when a person who is usually vulnerable, but sometimes perfectly healthy, slips, loses balance, trips, or stumbles. Regardless of the cause, much can be done to both decrease the chance of falling and reduce the risk of significant injury. We are on a continuum of improving and collectively learning from mishaps that precede us. Yet, despite the best efforts of family, healthcare providers, and those who are trying to create a safe environment, falls do occur.

As a nephrologist, a doctor who cares for patients with kidney disease, I have a particular interest in falls because it consistently jeopardizes the well-being of my patients. Many of my patients require a procedure known as dialysis. This is because their kidneys have failed, and the dialysis procedure replaces many of the functions that the kidneys do automatically. A dialysis population is a perfect group in which to study falls, and much of the knowledge we gain from this group of patients translates to the general population, particularly those who are aged. In this index population, age was the primary factor associated with falls, but age alone is not the culprit. In fact, falls are less common in those with preserved cognitive function. Falls are associated with a previous history of falling, frailty, poor nutrition, poor cognitive function, the number and type of medications, several diseases or comorbidities, and decreased walking ability. That is a lot to unpack but it constitutes the main reason that nonmechanical falls occur. We will explain and expand on each of these concepts.

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Falls are less common in those with preserved cognitive function, healthy levels of vitamin D, and a normal serum albumin level. The serum albumin is an index of chronic disease. Keep reading for the explanation.

2.2 Nonmechanical Falls: A Deep Dive

For purposes of simplifying and understanding nonmechanical falls, we divide them into three categories. There is overlap; that is, the borders between these three categories are quite fuzzy. The categories are (1) frailty, cognitive decline, and neurological deficit, (2) overmedicated persons, and (3) those with systemic diseases who have trouble with balance, walking, muscle weakness, or eyesight.

2.2.1 Category 1: Frailty, Cognitive Decline, Neurologic Deficit

Frailty

Frailty [1] is the condition of degradation that generally accompanies chronic illness and or aging. It is the result of diminished physiological reserve. Aging and deconditioning vary for many reasons but invariably end in frailty. We intuitively recognize frailty in our friends, loved ones, or patients. It is characterized by poor appetite and weight loss without dieting, fatigue or lack of energy, a loss of strength and muscle weakness, a slowed gait when walking, and decreased physical activity.

Frailty can be rapidly triggered by an acute lung infection, gastrointestinal tract disorder, or worsening kidney function. It also accompanies the end stages of diabetes and heart disease. In hospitalized patients or central venous catheter-dependent dialysis patients who must receive their treatments through a plastic tube, an infected intravenous line can trigger frailty. Frailty can be triggered by an episode of shingles—and we recommend that elderly people, in general, have a shingles vaccine. Influenza and COVID-19 are also malicious culprits that lead to frailty. A fall can trigger frailty, particularly if it results in a fracture or immobilization. Likewise, frailty can result in increased falls. Frailty may follow a cardiac event such as congestive heart failure; a heart attack or myocardial infarction; the sudden onset of a rapid, irregular heartbeat such as atrial fibrillation; or a heart valve disorder. A surgical operation on an elderly person can often diminish body reserves and can also trigger the manifestation of frailty.

In certain diseases, one disorder is complexed with several others. For instance, kidney disease results when the kidneys fail and cannot eliminate body wastes or control blood pressure. The maladaptive responses associated with kidney disease and hypertension damage blood vessels. Diabetes also damages the blood vessels supplying oxygen and nutrients to target tissues and organs. All cells need oxygen

and nutrients like amino acids, fats, sugar molecules, cofactors, hormones, and minerals. Over time, when the cells cannot get oxygen or nutrients or cannot pass back the carbon dioxide and wastes that they generate, they simply cannot do their jobs and slow down. Thus, the tissues and organs and the entire body weaken. When blood vessels are damaged by years of a chronic disease like high blood pressure, diabetes, atherosclerosis, or immunological disorders like lupus, they slowly compromise the delivery of oxygen and nutrients to the cell, tissue, and organ failure. This takes its toll. Since this happens over a very long time, training our youngsters to develop good lifestyle habits can preserve blood vessels, leading to healthier and longer lives.

The Maladaptive Responses in Kidney Disease and Diabetes

Kidney disease occurs in one out of seven people in the USA, and 90% do not even know they have it. 11.3% of the population is diabetic (SOURCE:CDC). The National Institute of Health estimates that one out of three people in the USA are obese. The maladaptive responses of these conditions accelerate aging through various mechanisms, including inflammation. Inflammation is how the body responds to an "attack" and initiates repair. Although its major intent is to protect the body from infection, it is also a response to many other conditions. It can be acute or can be slow and insidious. Its consequences can be widespread, affecting the kidney, liver, pancreas, heart, brain, and muscles. In inflammation, disease states turn on or signal specific hormones known as cytokines. These cytokines recruit inflammatory cells that function like a militia. They are programmed to protect against viruses and bacteria, mainly by oxidation, but when they are too reactive, they also cause collateral damage. An aggressive acute inflammatory response was seen during the COVID-19 pandemic and was responsible for many deaths.

Oxygen is essential for life because it vigorously attracts the atomic particles known as electrons. Electrons are essential for driving the biochemical reactions inside the cells that store energy. This process is done in the energy engines known as mitochondria. When oxygen and electrons do not match up perfectly, then oxygen will try to attract electrons from innocent tissues, damaging them. We speak of oxidative stress as damaging and antioxidants as ways of tying up and calming down the oxidative stress response. Oxidative stress can occur when the necessary process of making energy is impacted or when there is inflammation.

The insidious inflammatory response associated with kidney disease stimulates scar tissue formation or fibrosis. Inflammation damages not only the kidneys but the blood vessels. To understand this better, we must recognize that blood vessels are the networks that allow the movement of oxygen and nutrients from the lungs to the body tissues and carry carbon dioxide back to the lungs. Oxygen and nutrient supply to the energy cells must have to keep functioning.

The kidneys rid the body of excess acid, and with kidney disease, these acids must steal calcium from the bone to act as a buffer. This can lead to excess calcium deposits in the outside rim of the blood vessels, making them hard and stiff. The heart, having to pump against stiff blood vessels, also weakens. Hardened arteries become stiff when calcium is deposited in the outside rim, making the heart work very hard. Eventually, the heart tissues wear out and become replaced by scar tissue. This results in cardiac rhythm disorders and in a decreased pumping ability.

Diabetes happens when either the pancreas does not produce insulin at all (type 1) or produces it too late to do the job of moving sugar into a cell (type 2). The second type is associated with insulin resistance. Patients with type 1 diabetes must have insulin injections, while those with type 2 can control their diabetes with either diet or medications, at least initially. While insulin sensitivity helps the cells to utilize glucose better, resistance does the opposite. The resistance has many causes, one of which occurs in cells when the receptors that carry the insulin signal are blocked. Over time, factors that block either insulin release from pancreatic beta cells or that block its receptor activity result in excess sugar remaining in the bloodstream. The excess sugar directly damages the pancreas, and after a while, type 2 patients require insulin administration for survival. The abundance of sugar excites the cytokines that muster an inflammatory condition. This inflammation also occurs in blood vessels and is known as endothelial dysfunction. Diabetes and kidney disease are linked to hypertension, a condition that raises the pressure inside blood vessels. Hypertension is present in about one of three people on the planet, and this too leads to blood vessel damage. Damaged blood vessels either restrict or block nutrients and oxygen from reaching end organs, eliciting damage. Diabetes and kidney disease ultimately affect virtually every tissue and organ in the body. This damage results in frailty.

Obesity is an energy imbalance that is the result of eating more energy forming calories than the body can use. It is measured by the relation between the weight and the height (kilograms/meter squared or kg/m^2), known as the body mass index or BMI. A BMI of greater than 30 kg/m^2 signifies obesity. Excessive fat intake signals fat cells to reduce a hormone known as adiponectin. Adiponectin is a protein that helps promote insulin sensitivity. Adiponectin also blocks fat cells under the skin from over-absorbing fatty acids, and they instead deposit in the viscera—leading to the "pot" belly. The fat cells not only store fat, but they also play a role in promoting inflammation. Without adiponectin, inflammation worsens.

Sometimes calcium forms plaques or scales inside the blood vessel wall, narrowing the vessels and impeding their flow. They can also form clots and totally block the flow to a vital organ like the heart itself or the brain. They can also block the blood flow to the feet. These are acute and serious problems. Recovery from any such event will likely lead to enough debility to result in frailty.

No one lives forever, and we all age. DNA inside the genes of the cells works like a computer code. They code all proteins that form either the structures, enzymes, or the organelles (organs inside the cells) we require for everyday biochemical processes. These strong carbon- and nitrogen-containing substances provide the necessities for cellular housekeeping. DNA codes the enzymes and structures that maintain the mitochondria—little energy engines that drive all the cell's chemical reactions. An intact and functioning cell is necessary for the electrons that create the cellular energy to behave. Errant electrons or dysfunctional oxygen molecules rapidly destroy cells. They work like bleach. They are known as oxidative stress and also shorten telomeres.

Nucleic acids—DNA and RNA—carry the codes that keep us alive. DNA is so essential that if it becomes defective, the body has a way of removing it. Each DNA strand contains long regions of repetitive sequences known as telomeres. These telomeres protect DNA from being destroyed but become shorter as the DNA divides, and as we age, they become so short that the capping proteins that protect the productive portion of the DNA can bind to them. The exposed DNA that is no longer capped triggers the removal of that DNA strand from service; it is destroyed. In aging, the necessary proteins to sustain the cell can no longer be made if too much DNA has been damaged and destroyed.

Telomere shortening is accelerated by the oxidative stress that is associated with errant electrons and dysfunctional oxygen. There is relatively little we can do to definitively stop aging, but we can slow it somewhat. Antioxidants may help protect telomeres [2]. Chronic kidney disease, diabetes, and chronic heart disease all produce inflammation and oxidative stresses that accelerate aging, even if insidiously. Frailty is the response of the body to this aging process and is worsened by chronic diseases, lifestyle indiscretion, and just plain time.

Recognizing Frailty

Frailty may be seen over time in a person because the temples become hollower, the blood pressure may be lower, and the person seems less sharp and aware. It is harder for the frail person to walk, and preferentially, a frail individual may remain in bed. Indifference to life events worsens. When one tries to walk, the muscles may not support them, or they may lose the muscle memory that once controlled the sense of balance. This inability to walk, or even stand, results in falls.

In 2001, Linda Fried and colleagues classified frailty into clinical indicators. She demonstrated the role frailty played as a risk factor for falls. Falls in the frail culminate in a low quality of life and are an intermediate phase between independence and ultimate death. A more recent study established in 2008 classified frailty according to three criteria, a weight loss of over 5% in the past year, the inability to do the

sit-to-stand test more than five times, and answering "no" to the question, "Do you feel full of energy?" The sit-to-stand test is demonstrated in this book and involves rising from the sitting to the standing position from a chair without using one's arms.

Fried's classification uses five criteria, grip strength, the speed of walking, the presence of exhaustion, the amount of physical activity, and whether there has been unintentional weight loss. Those exhibiting no criteria are considered robust, while those who exhibit one or two of the five conditions are classified as prefrail. Frailty is defined as having three or more of the five criteria [3].

The Surprise Question

Frailty is associated with a concept known as the surprise question (SQ), where one would not be surprised if an individual dies in the next 6–12 months. The concept has been validated and has resulted in the development of a mathematical equation used today [4, 5]. The SQ is used as a screening tool to determine if a patient is nearing the end of life and will be appropriate for palliative care. In a large-scale study of 21,109 patients with an average age of 62.8 years, 12.4% had a positive response of "no, it would not surprise me if the patient passed away within 12 months." The question was asked by trained nurses. It demonstrated that the accuracy of the SQ in predicting death was 68% [6]. The SQ has been studied in various settings—kidney disease, cancer, inpatient settings, emergency departments, nursing homes, and even pediatrics [7]. Surprisingly, a systemic review showed that the predictive value of a "yes" response is even greater than the "no" response—93% vs. 37%, respectively [8]. The SQ is actually more valuable at predicting if patients will live greater than a year.

Immobility and Frailty

Frailty is the cousin to immobility. This relates to gravity and its impact on vertebrate paleontology. Fish swim in a gravity-free aqueous environment and have small, delicate bones. 365 million years ago, a group of fish opted for land, and at once, these terrestrial tetrapods became subject to gravitation forces on a molecular scale. Among the many adjustments these first tetrapods and all other land species had to make, bone development was one of the most dramatic. The tiny amounts of tension created by mechanical loading led to calcification that followed a lattice-type structure. This structure is mimicked by engineers who design bridges and is a natural response to physical force. Gravity also turned off products that destroyed the muscle so that it could gain strength and support the bones.

The impact of gravity on the bone can be demonstrated in astronauts. During spaceflight, bone resorption increases, and maintaining healthy bones is a challenge space travelers must overcome. Gravity also potentiated the formation of red blood cells. "Space anemia" occurs after just 5.4 days in space [9]. Like healthy astronauts, returning to the bedridden state of immobility leads to losing bone and

muscle mass and red blood cell production [10]. While immobility alone does not define the state of frailty, it appears among those with the highest levels of frailty.

Frailty and Falls

Falls are a major health problem worldwide. They are associated with frailty. In a study of 1397 falls, signs of frailty such as reduced handgrip strength and exhaustion both significantly occurred [11]. In China, for instance, they are the leading cause of injury-related death in the elderly and the second leading cause of death in the middle-aged population. To study this, a group of researchers in China used a 40 deficit frailty scoring system to compare the incidence of falls among middle-aged (45–59 years old) or elderly patients who were frail (≥ 60 years old). The study included 13,877 subjects. The fall incidence was 16.6%. Among robust individuals who were not classified as frail, the risk was 13.3% but rose to 21.1% in prefrail patients. In the frail population, the fall rate was 31.8%. The frail patients had a 97% higher risk of falling than those who were robust, and not frail [12].

Stroke

Strokes result from a blood vessel in the brain either becoming blocked (ischemic stroke), cutting off the supply of nutrients and oxygen to this vital organ, or leaking, resulting in hemorrhaging into the brain. An ischemic stroke is twice as common as hemorrhagic stroke, but overall, it is a global problem and the second leading cause of death after ischemic heart disease. Although the mortality rate from stroke has decreased over the past quarter century, the incidence has risen, particularly in those younger than 70 years of age. In 2019, there were 12.2 million incident strokes. Additionally, the incidence of stroke is 3.6 times higher in low-income than in high-income countries.

It is estimated that between 85 and 90% of strokes result from risk factors that are potentially modifiable. The biggest risk factor for stroke is the body mass index—an index of obesity. If this risk factor were minimized, the incidence of stroke would fall 24.3%. Other risk factors are high blood pressure, chronic kidney disease, elevated lipids, uncontrolled diabetes, smoking, lack of physical activity, and an unhealthy diet. An unhealthy diet is considered high in sodium or red meat and low in vegetables, fruits, or whole grains. Alcohol consumption and tobacco use are also modifiable risk factors [13].

Strokes can be either related to emboli, organic plugs that are either calcified plaques, blood clots, or even infectious clumps, that originate in another part of the body and travel to the brain. The emboli block the blood supply to a specific brain area, resulting in ischemia (poor blood supply). This can result in paralysis. A second major cause of stroke is hemorrhage or bleeding into the brain. This can be very destructive and is often lethal. Common reasons for a stroke are atrial fibrillation—caused when the top chambers of the heart (atria) do not pump blood properly into

the lower chambers of the heart. There is a stasis or slowing down of blood allowing clot formations to occur. These embolic clots can be pumped through the arteries feeding the brain, causing an ischemic stroke. Calcified plaques that form inside the blood vessels that feed the brain can break off and travel into the brain, locally stopping its blood supply. As with atrial fibrillation, these emboli can likewise cause paralysis. In hypertension, the high-pressure head damages the delicate blood vessels inside the brain, weakening them. They can leak or hemorrhage slowly, leading to insidious damage that may be mistaken for chronic cognitive decline. Alternatively, they can rapidly leak, causing widespread damage to the brain. A subarachnoid hemorrhage can occur when a weak section of the blood vessel wall between the brain surface and its inner cover ruptures. This weakened wall is known as an aneurysm. Trauma can also cause a subarachnoid hemorrhage.

Falls after a stroke are common and have multifactorial explanations. The immobility, paralysis, or weakness caused by the stroke impairs balance and gait. Strokes lead to depression and are also associated with other risk factors like cardiovascular disease, diabetes, hypertension, and genitourinary disorders (including kidneys). The brain is divided into two hemispheres, and they control movement on opposite sides of the body. In other words, a right-handed person with a stroke in the right hemisphere will have left-sided weakness or paralysis. Strokes that occur in the right hemisphere result in twice the incidence of a fall as victims tend to neglect the left, nondominant side [14]. Stroke victims generally fall in the direction of their impairment. This is known as hemineglect.

The percentage of persons who fall following a stroke is variable, ranging between 14 and 65% [15]. It is estimated that 7% of falls occurred within the first week of the stroke [16], 37% within the first 6 months, and 73% have fallen at one year [17].

In a hospital stroke care center in Toronto, the incidence of falls was 24%. Among those who fell, their hospital stay was extended by 11 days. Twenty-three percent of the patients who fell experienced an injury, the majority of which were minor. Thirty-four percent of the falls occurred when transferring; 19% while reaching, bending, or turning; and 9% while walking. The majority occurred either in the patient's room or the bathroom/tub area [18]. Falls generally occur in the midmorning or late afternoon periods and are often the result of losing balance or the inability to sense a cluttered obstacle. This happens because of the gait and balance disorders that accompany strokes.

The risk of a fall after a stroke continues. It is most common in the first 2 months after hospital discharge. But, even a year later, around one-third of patients experience a fall [15].

The most likely candidate for a stroke-related fall is a patient with moderate debility. Those who are too immobile to participate in any activity have a lower opportunity of falling [19]. Caregivers must be trained to handle the immobile patient, however, to avoid mishaps. Falls related to strokes present challenges to caregivers and family members. Opportunities for mitigating the risk of a stroke will be discussed in a later chapter.

Dementia

Dementia occurs with functions that are involved with thought starting to decline. These generally involve recognition, memory, thinking, planning, problem-solving, and reasoning. While it can start with forgetfulness and misplacing items, it progresses to the point that the patient can no longer recognize family members, becomes confused in familiar places, becomes socially isolated, and eventually is no longer capable of performing the usual activities of daily living. The World Health Organization estimated that there are 55 million people worldwide who have dementia, 60% of whom live in low-income countries.

The most common and well-known disease associated with dementia is Alzheimer's disease, accounting for 65% of cases. Alzheimer's disease is associated with a type of protein—Tau protein—depositing in the cells that support the nerves of the brain and with aggregates of protein-containing plaques known as amyloid plaques. While this constitutes most cases of dementia, the syndrome can also be associated with the abnormal deposition of proteins inside brain cells, known as Lewy body dementia. This also is associated with a Parkinson's tremor. Frontotemporal dementia is associated with the deterioration of areas of the brain that are associated with behavior control, speaking, and understanding speech. Dementia can also occur as a result of long-standing hypertension, COVID-19, and alcohol. A particular type of dementia—chronic traumatic encephalopathy—is associated with traumatic sports injuries. This list is not all-inclusive, as there are many other diseases and conditions that can result in dementia. At the present time, there is no cure for any of the forms of dementia.

Alzheimer's disease is associated with cognitive decline, and around two-thirds of cases occur in persons who are over 65 years of age. There may be a genetic component to it—it can be inherited. But, its incidence is increasing, suggesting that environmental factors also play a role. It is characterized by plaques composed of a protein known as amyloid that forms plaques. It can also form tangles of proteins known as tau proteins. These help support the brain's housekeeping functions. Risks include the presence of the APOE e4alle on genetic testing, smoking, brain trauma, depression, social isolation, and a family history of dementia. Although there is no treatment, activities that stimulate the brain, a healthy diet, and exercise may reduce the risks [20]. It is more common in women than men, but estrogen therapy has not been helpful in treating it. It is a subject for active research, and many theoretical remedies have been postulated, but the therapy of this disorder still lies in the future.

Lewy body dementia (LBD) is associated with Lewy body deposition and progresses over a 2-year period. It is characterized by the deposition of eponymous Lewy bodies, aggregate fibrils containing the protein alpha-synuclein, in the brain stem, cortex, and basal ganglia. The cortex of the brain is involved with cognitive function. The basal ganglia are involved with coordination and thus are affected in diseases like Parkinson's disease. LBD is characterized by cognitive, functional, and nutritional deterioration and a tremor that is characteristic of Parkinson's disease [21].

Frontotemporal dementia (FTD) is at first characterized by emotional problems and difficulty communicating—including understanding speech and reading, but also speaking. The disease is characterized by deterioration in areas of the brain that control speech and personality. Its course is variable, as are its symptoms. Over time, it is difficult to control movement. In contrast to Alzheimer's disease, 60% of patients are between 45 and 64 years of age. Patients with FTD cannot control their impulsive behavior. Supranuclear palsy (SNP) is a form that is associated with unexplained falls and difficulty with speech, walking, and balance. It is also characterized by body stiffness and abnormal facial expression. It can also be associated with the nerves that affect muscle movement, Lou Gehrig's disease, or amyotrophic lateral sclerosis (ALS), and with Parkinson's disease. The cause of FTD is not known, and there is no treatment [22].

Vascular dementia After Alzheimer's disease, is the most common cause of cognitive decline, accounting for 15–20% of cases. Increased blood pressure is associated with cognitive defects, especially in younger persons. Even whitecoat hypertension and borderline hypertension are associated with cognitive changes [23]. This suggests that we must consider treating elevated blood pressure earlier and more aggressively, as it may be a valid marker for changes in the brain's architecture. There is concern that if the chronically managed blood pressure is too low, it can also affect cognition in the elderly. A large clinical trial sponsored by the NIH enrolled 9361 participants with hypertension. This was the Systolic Blood Pressure Intervention Trial (SPRINT). One of the populations studied was 3250 persons ≥75 years of age. The aim of the 4-year study was to determine if aggressive blood pressure control (< 120 mm Hg) would reduce the incidence of death, heart disease, and stroke. The study was actually stopped early because the results were very good—a 25% reduction in the primary composite outcome of heart disease or stroke and a 27% decrease in death. Although intensively treated patients did have a higher incidence of fainting [24], this large study did not show that cognitive function changed for better or for worse over the 4-year period of intensive control [25].

Vascular dementia can result from various mechanisms. White and gray matter changes occur. Both thickening and fibrotic (scarred) changes occur with long-standing, poorly treated high blood pressure. The high pressures inside blood vessels everywhere in the body trigger mechanisms that cause them to react by forming scar tissues. This decreases brain reserves. Changes in the brains of persons with chronic hypertension can be seen on magnetic resonance imaging (MRI). Since the brain uses a great deal of energy to store and manage the neurological processes that control every aspect of how our body moves, thinks, and breathes, there must be an abundant supply of blood vessels. Some of these vessels are sharply angled to adequately penetrate brain tissues. This angulation makes it difficult for them to handle high pressures. The impact of pressure weakens the walls of individual brain blood vessels by causing microaneurysms or pouching. When these walls rupture, they cause tiny lakes of blood that interrupt some of the brain's circuitry. These are called lacunar infarcts. Over time, this becomes extensive enough to affect cognition [15, 26]. They can result in falls, as has been reported in type 2 diabetics [27].

Chronic traumatic encephalopathy [28] Mike Webster (1952–2002), a member of the Pro Football Hall of Fame, was a center on two National Football League teams—15 seasons with the Pittsburgh Steelers and then with the Kansas City Chiefs. He was nicknamed "Iron Mike," won four Super Bowl rings, and was ranked among the top football players ever by The Sporting News. In his later years, he struggled with mental illness and a personality change, and although he died at age 50 of a heart attack, he was diagnosed to be the first NFL player to have chronic traumatic encephalopathy (CTE) [29]. CTE has since been linked to repeated blunt head trauma and is seen in American football, soccer, boxing, and other contact activities. It develops over an 8 to 10-year period and is initially associated with dizziness, confusion, headaches, and disorientation, progressing to cognitive dysfunction and social instability. It terminates in tremors, speech disorders, and dementia. Patients with CTE can be unsteady when walking and have difficulty with balance. They can easily fall. Webster's autopsy revealed a pathological picture that became typical of CTE, degenerative changes that included diffuse plaques, and nerve fiber tangles, with tau proteins in the thinking half of the brain. PET scans can now identify tau protein deposition and can aid in the diagnosis. There is no cure, and preventive measures are being studied by the various athletic associations.

2.2.2 Medications

As you read this section, please remember that each person is different and that this section is not presented as medical advice. It is for your edification, but the author fully expects you to consult with your doctor or healthcare provider. They know your case far better and can give you the guidance you require and deserve.

Multiple medication use is common. Some are prescribed by a physician, while others are purchased "over the counter" (OTC) or online. The combinations of medications, whether prescribed or otherwise, may appear harmless but, in some situations, can result in the accumulation of toxic breakdown products that can have an injurious effect on the body.

No doubt, the convenience of OTC medications has created value to the public and to many patients. OTC medications are commonly purchased for pain relief (acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs)), upper respiratory infection relief (cough or cold remedies), indigestion and reflux (Pepcid, Tagamet), constipation or diarrhea (stool softeners, laxatives, antidiarrheal agents like Imodium or Pepto-Bismol), hay fever or itching (antihistamines), fungal infections (Nizoral), vitamin supplements, and sleep aids (melatonin). "Baby aspirin" has been considered useful in preventing heart attacks and strokes, but it is highly dangerous to use in children. This is ironic since the name "baby aspirin" stems from an era when ASA was commonly used to treat flu and fever symptoms in young people. Acetaminophen is another commonly used pain reliever. Alcohol interferes with its metabolism, creating an intermediate product that can damage the liver. NSAIDs decrease blood flow and reduce the effects of prostaglandins. While prostaglandins are important signals for triggering a febrile response, they also are

critical for kidney function and thus NSAIDS may cause kidney damage, sometimes irreversible. In some cases, these medications may be formulated as gummy bears. While these are delicious and chewable, they are drugs and not candy. Even too many gummies can have a cumulative, toxic effect.

The use of OTC medications therefore comes with caution—first, try to be familiar with the label and common side effects, and, secondly, share with your healthcare provider or pharmacist what prescribed and OTC medications you take. They can research any drug interactions that might create a problem.

Multiple medication use is a modifiable risk factor for a fall injury. The use of multiple medications is known as polypharmacy. The use of more than five medications is associated with over twice the chance of having a fall. Some medications are associated with the risk of falling. They even have their own abbreviation—FRIDs—which stands for fall risk-increasing drugs.

For convenience and ease of understanding, we divide FRIDs into three major categories. The first are drugs prescribed for sleep, sedation, or pain relief. These include prescription sleeping pills, sedatives, and narcotic pain relievers. Opioids are included in this category, as are medications used for mental health disorders. Sedation and pain relief may create a state of drowsiness that makes it highly dangerous to ambulate. Not just the hazard of collapsing, but of tripping over stairs or obstacles, or being hit by a car, creates additional dangers. The second group of FRIDs is used to control hypertension or high blood pressure. If the blood pressure is too low, oxygen and glucose cannot supply the brain, causing a loss of consciousness. A sudden loss of consciousness can cause one to uncontrollably fall. The final and third FRID category is the medication used to treat diabetes. This entails bringing the serum glucose levels into a normal range. If the blood sugar falls below a critical point because of therapy, the brain cannot receive enough glucose to power its energy needs. This low blood sugar or hypoglycemia leads to a loss of consciousness and is a fall hazard.

Older people who are on multiple medications have a high risk of falling, particularly when one of the medications used is a FRID. Among 1764 people in the age group of 70–79 who were followed for 5 to 11 years, 36% took six or more prescription medications every day. They had a higher fall rate—nearly one-third fell. When FRIDs were part of their medication regime, the hazard of falling increased 22%. Reviewing medication lists and using fewer FRIDs may help reduce falls. But deprescribing medications may not be enough. Other risks for a fall need to be considered [30–32].

Sedatives and falls A review of articles published in medical journals showed that most people (65–93%) who had a fall-related injury were using sleeping pills or antidepressant drugs. Opioid use varied from 4.4 to 21%. There is 1.6 times a chance of falling in patients taking opioids. In the observational studies, when there was a change in the use of a FRID after a fall, the fall rate decreased. In the elderly, stopping medications associated with falling may not be sufficient to stop falls from occurring and must be combined with other interventions [32]. Although pain itself is a risk factor for falling, pain management with opioids and other sedatives may

induce drowsiness. The risk of using opioids is fivefold higher in the elderly and increases further after an injury from a fall. When opioids are used, they should only be used to treat acute pain, and not as the first choice.

Aside from cancer-related pain, arthritis is a common reason for taking prescription medications to control pain. Pain commonly interferes with daily activities but is often not optimally managed. There are many non-pharmacological interventions that can help alleviate arthritis pain. Cognitive behavior therapy (CBT) may be effective. Physical therapy can be a worthwhile adjunct. Optimal management also means managing the medications with the severity of the pain. In many instances, alternative medications should be used for at least 2 weeks before using opioids.

Certain diseases that commonly affect patients can cause nerve pain. When in the lower limbs, this can be particularly disturbing. Peripheral neuropathy is a well-recognized type of nerve pain, and the benefit of opioids for its treatment has been questioned. Drugs such as selective anti-SSRI depressants or gabapentin-like drugs Lyrica (pregabalin) or Neurontin (gabapentin) may be more beneficial and safer. SSRI stands for serotonin-norepinephrine reuptake inhibitors and includes medications like Lexapro (escitalopram), Celexa (citalopram), paroxetine (Paxil), sertraline (Zoloft), and Prozac (fluoxetine). These drugs enhance serotonin, the chemical that carries signals across nerve endings. Low serotonin levels may cause anxiety and depression. They can also worsen neuropathy. The opioid, tramadol, not only helps block the nerve transmission of pain but also helps interferes with medications used to treat depression and generally is not used with these classes of drugs.

When opioids are used in pain management, one must recognize that their metabolism, or breakdown, slows in patients who are elderly. Patients with chronic liver disease such as cirrhosis may also have impaired drug metabolism. Opioids are broken down by liver enzymes known as CYPs (cytochrome P450). In many instances, these breakdown products are then enzymatically changed or conjugated to become water-soluble and excreted by the kidney.

Opioids share breakdown pathways with other prescribed medications, and the use of several drugs that have the same pathways can create the equivalent of a metabolic traffic jam. Some medications block the metabolic pathways of other drugs, creating the equivalent of a road closure. The use of several medications that are metabolized by common pathways can have varied and often deleterious effects depending on the particular drug. Potentially harmful effects can occur with the use of a drug that accumulates when the patient is on many other prescribed medications. Some opioids, like codeine and oxycodone, have active metabolites. Translated, this means that after they have been broken down in the liver and have been conjugated so that they can be excreted by the kidneys, they can still cause sedation and thus falls if kidney function is impaired.

Patients who must take one of the newer antidepressants such as Spravato (esketamine) should be highly cautious of the potential for falls. This nasal spray medication is based on the pain medication and the general anesthetic, ketamine. Its side effects include significant sedation, lethargy, dizziness, and numbness, and it is used for patients with severe depression that has not responded to other therapy.

One of the main reasons why people using opioids fall is that they become drowsy, less alert, and not as attentive to their surroundings. They are more likely to trip over an obstacle left on the floor or to lose their balance on the staircase. Confusion is also likely with the use of opioids. Sedatives like opioids can cause blood pressure to become unstable. Usually, when one stands, the blood pressure self-regulates to prevent dizziness. With several diseases and medications, this regulation does not happen, and the low blood pressure causes a feeling of wooziness or even fainting. This can lead to falls [33].

Diuretics and blood pressure medications Diuretics are also associated with falls. The use of diuretics was associated with nearly a threefold increase in the risk of falls. The reason for this is that diuretics cause the kidneys to eliminate salt and lower blood pressure. The downside of this is that if the blood pressure is too low, fainting may occur. It is imperative to stand or sit slowly and let the body adjust when on blood pressure-lowering medications. As referenced above, the blood pressure self-regulates when one changes positions. Like opioids, diuretics and other blood pressure medications can either reduce the volume necessary to sustain the blood pressure or interfere with the regulatory pathway [34].

Although associated with hypotension and hypokalemia, a comprehensive review of 58 major clinical trials published in medical journals did not show that medications used to control blood pressure increased the chance of falling. The 28,638 participants were followed for 2–4 years. Although there was an increased rate of fainting episodes, treatment with blood pressure medications reduced the rates of death and stroke. The treatment of high blood pressure has more benefits than risks [35]. In this sampling, antihypertensives were not associated with falls in patients (adjusted odds ratio (OR) 0.473 95% CI 0.319–0.700) [34]. In a national cohort study of discharged elderly patients (mean age 77; n = 4056), intensifying blood pressure therapy resulted in an increased risk of readmissions within 30 days, with a hazard ratio (HR) of 1.23 (95% CI, 1.07–1.42). The HR for serious adverse events was 1.41 (95% CI, 1.06–1.88) [36]. The performance and mobility assessment for this population was not decreased. Yet the risk of falling increases when patients have multiple chronic conditions. The risk of falling worsens with excessive antihypertensive therapy because of an exacerbation of adverse events such as postural hypotension, balance and gait impairment, and dizziness. A Medicare claims review of 4,961 patients demonstrated that antihypertensive medications were associated with an 11.6% fall incidence in patients on moderate-intensity antihypertensive therapy and a 10.9% fall incidence on high-intensity therapy. In patients who were not on antihypertensive medications, the fall risk was 9.0%. In a 1-year subgroup analysis of patients who had a previous fall, antihypertensive therapy doubled the risk of another fall compared to patients who were not on antihypertensive therapy [37]. As we will see below, the real reasons why antihypertensive therapy is associated with falls is not due to the medication, but to the population studied. When controlled for frailty, hypertensive treatment is not the culprit for falls. In fact, blood pressure control benefits persons who have a fall risk.

Diabetic therapy A systemic review and meta-analysis of falls demonstrated that falls are more common in people with diabetes (risk ratio (RR) 1.64 95% CI 1.27–2.11). The RR of falling was 1.94 (95% CI 1.42–2.63) in those managed with insulin compared to an RR of 1.27 (95% CI 1.06–1.52) in those not treated with insulin [38]. This could be because patients who require insulin are generally sicker and have more of the complications that are associated with advancing diabetes. Hypoglycemia means a low blood sugar. The brain requires a continuous supply of sugar and energy. Without it, the brain shuts down and stops working. When the blood sugar first starts to fall, patients become hungry, start sweating, and feel very poorly. These are warning signs that the brain needs sugar immediately.

In overzealous treatment, there are risks that the blood sugar will fall too low. This can occur when there is a mismatch of insulin and either dietary intake or activity. Continuous glucose monitoring has tremendously aided this dilemma. An opportunity for low blood sugar to occur is the diabetic patient who was scheduled for surgery in the morning and fasted all night. The surgeon had an emergency and bumped the case to the afternoon. Another chance for a serious fall in blood sugar is the patient who is suddenly active. Increased motor activity uses glucose without insulin. Thus, athletes who are not monitoring their insulin and glucose management during strenuous activity can have a drop in blood sugar.

A third cause of hypoglycemia can occur when the patient is treated with antidiabetic therapy without realizing that medications that are broken down by the kidney may accumulate if kidney disease worsens. The kidney plays a role in clearing insulin and increasing sugar's biochemical manufacturing. Coupling this with the altered metabolism of antidiabetic agents or parenteral insulin is a setup for hypoglycemia.

There is controversy over how strictly one should control diabetes in CKD. The HbA1C is a reliable marker for how well diabetes is controlled. Using continuous glucose monitoring, one can estimate the AIC, the estimated AIC (eAIC). This is now termed the glucose management indicator (GMI) based on clinical trials and has a new formula [39].

The KDIGO guidelines that nephrologists rely on recommend measuring the HbA1C as often as four times a year to monitor glycemic control in diabetic patients with CKD. The targets range from <6.5% for patients with mild CKD. This population has very few complications associated with diabetes and is highly functional. Were they to develop unexpected drops in blood sugar, they would have the resources to quickly seek help. Since intensive glucose control is associated with a long life expectancy, it is reasonable that they aim for lower HbA1c or GMI.

In patients with advanced diabetes with many complicating disorders and a shorter life expectancy, there is a greater risk of having low blood sugar with an adverse event than of actually benefitting from intensive diabetes control. Persons in this population may be elderly, live alone, and may not have the ability to seek immediate help if their blood sugar drops. For these reasons, in this group of patients, the HbAIC should be kept at <8.0% in CKD [40].

In patients with advanced CKD, including dialysis, the HbA1C may not be as accurate in estimating diabetic control [41]. Dialysis patients do better with adequate diabetes control ($p = 0.024$) [42]. However, they have many complications and other diseases that make them fall into a high risk for hypoglycemia. Doctors need to individualize the care in this special population. Continuous glucose monitoring is finding increased favor in the dialysis population [43].

Comment Polypharmacy—using too many medications—may be complicated when patients have mildly decreased cognitive function. Deprescribing initiatives have successfully reduced excessive medication use [44]. Nevertheless, in patients who have many complications, deprescribing alone may not be sufficient to reduce the risk of a fall.

2.2.3 Chronic Illnesses and Disorders

The third category of falls is made of the many underlying diseases and conditions that predispose one to fall. These range from factors that cannot be modified, such as age or a chronic underlying disease. They also include conditions that are treatable. In addition to age, kidney disease, diabetes, chronic disorders that affect the heart and cause lung disease, or cancer, chronic disorders such as arthritis and neuropathy are associated with falls. Living alone, impaired vision, gait and mobility disorders, muscle weakness, and volume-related disorders are also risk factors contributing to a fall.

Age

The older we get, the higher the chance of falling. Approximately one-third of persons aged 65 and older fall at least once a year. Falls account for 70% of accidental deaths in persons 75 years of age and older. They are responsible for an estimated three million emergency room visits and nearly one million hospitalizations annually in the USA. The aging process is universal, natural, and ultimately fatal. Our efforts to slow it are challenging because we are going against the course of nature.

This deserves an explanation because it is a major focus of this book and, no doubt, on all of our minds. Our cells are each controlled by genes. These are made up of strands of DNA, combinations of proteins and sugars that have existed for billions of years and carry the codes to assemble all living organisms. The simplest yeast cells, roundworms, salamanders, and us humans share this basic commonality. This code is intertwined in a long helix. Each of our cells contains around 6 feet of DNA, and given that each of us is a community of ten trillion cells, we contain 60 trillion feet of DNA. This translates to 11.36 billion miles. Think of the DNA like a shoelace with a little plastic cap on the end. These caps, which we refer to as telomeres, can be repaired several times, but after so many years, their numbers wear

out, and the DNA frays. The body has a mechanism to remove frayed DNA. Sadly with the loss of each strand of code, we lose some functionality. Eventually, the cells are no longer sustainable, become senile, and die. The greatest enemies we have are inflammation, DNA damage, and cancer.

As our cells die, several events cause us to eventually lose our ability to move and function. Aging can be worsened by inflammation. Also, damaged DNA cells can convert to cancer. Cells and their DNA have the capacity to last far longer than they do in humans. In 1850, the famous scientist, Charles Darwin, visited the Galapagos Islands. What was amazing was that some of the baby tortoises that he encountered were still alive 150 years later. These giant creatures live well—they have little stress because they have no predators, they are vegetarian, they are hardly ever in a hurry, and they take their time breeding. In addition, they have some features that we simply lack. The tortoises that inhabited the Seychelles Islands (Aldabra atoll) were cousins of the Galapagos tortoises that greeted Darwin. A Seychelles Island inhabitant, the famous Aldabra giant tortoise, Lonesome George, died in 2012. In an article published in *Nature Ecology & Evolution*, scientists found that George had genes that handled glucose better. This helped reduce insulin resistance—a cause of type 2 diabetes. He also had duplicate genes that handled cancer suppression and oxidative stress. He also had duplication of the genes that repaired DNA that became damaged by oxidative stress. He also had variant genes that decreased telomere attrition [45].

Since we lack the magic genetic composition that tortoises apparently possess to delay aging, we need to focus on modifiable risk factors to mitigate aging and minimize the chance of a serious fall. Not only are falls a marker of poor health in the elderly, but those whose health is declining fear falling and consequently limit their activities. The body is very efficient and senses whether the muscles are being used or not. Those muscles and bones not in use weaken—that is, their proteins are reabsorbed and recycled. The lack of exercise further increases the chances of a fall. It is no wonder that 90% of hip fractures can be traced to a fall, generally in a person over 70 years old. Many other factors are also modifiable. This means that by understanding an intervention, we can reduce both the dangers and damages associated with falls in the elderly [46–48].

2.2.4 Kidney Disease

The Kidney's Jobs

As we age, our kidney function declines. Most people think of the kidney as an organ that cleans the blood and makes urine. They are correct, but only partly so. The kidney has acquired many responsibilities as it evolved. Freshwater fish always faced the danger of over-dilution and could eliminate large amounts of water. But 96% of fish live in salt water and developed organs to conserve water and eliminate salt. Animals that moved to land developed kidneys that specialized in conserving

both salt and water. They needed mechanisms to control their blood pressure. With millions of years of experience, the kidney became a master regulator of blood pressure.

Not just the salinity but acidity in the community of mammalian cells needs to be carefully controlled. The biochemical reactions that govern our tissue's functioning well work only when the acid levels, known as the pH, are set at around 7.4. Too much acid in the body is known as acidosis. Controlling acidosis became the responsibility of the kidney, which eliminated or conserved bicarbonate—an important determinant of acidosis. The kidney also used an ammonia-trapping mechanism to rid the body of acids that were derived from the diet and metabolism. Acidosis is harmful; it turns on mechanisms that break down muscles.

Another job of the kidney is to prevent anemia. As an organ that has a million filtering units and corresponding blood vessels through which large numbers of red blood cells flow, it is no surprise it acquired the responsibility to regulate the synthesis of red blood cells determined by the altitude and the presence of oxygen in the air. Another kidney job is to regulate minerals that help make and rebuild bones. Calcium plays a role in bone formation and in regulating the pH.

2.2.5 The Kidney and Bones

With marine life, tissue support is evenly distributed. But on land, gravity created a challenge—*Elginerpeton* were four-legged amphibian animals that emerged from the sea around 378 million years ago (see Fig. 2.1).

Their ancestors, including us, evolved strong bones for support. Just compare the leftover bones from a recent fish dinner with those of the 11- to 15,000-pound *Tyrannosaurus rex* (see Fig. 2.2)—an animal that terrorized the Earth from 90 to 66 million years ago.

How does the kidney fit in? Since birth, bones must be disassembled and reassembled to grow to adulthood. Gravity creates stresses on bones that enable calcium to deposit with phosphorus into the proteins we know as bone. Areas of the bone with little or no gravitational stress are torn down, so their minerals can be recycled. This requires a complex regulatory mechanism that the bone cell figures out long before amphibians and reptiles roamed the Earth. Bones require several hormones for assistance and control. One is vitamin D [49]—which helps to build bones—and the other, parathyroid hormone, is synthesized by glands in the neck when calcium levels are sensed to be too low. The parathyroid hormone breaks down the bone to liberate calcium.

When kidneys start to fail, they release hormones that eliminate phosphorus. Phosphorus is an important mineral, and despite this effort, it ultimately builds up when kidney function worsens. The failing kidney also cannot activate vitamin D, the helpful hormone that builds the bone and helps the intestines absorb calcium. To liberate calcium, the body maladapts by releasing the parathyroid hormone that breaks apart bone. Since kidney function is poor, excess calcium displaced from the

Fig. 2.1 Once the *Elginerpeton* ventured to land, they had to conform to the stresses of gravity. One major change was the emergence of bones that served as major support structures. Photo by Stephen Fadem—from Houston Museum of Natural Science

bone is now free to combine with phosphorus to calcify the blood vessels. The bones become weak as they lose calcium.

2.2.6 Kidney Disease, Weak Bones, and Falls and Fractures

Many patients with chronic kidney disease (CKD) thus have weakened bones and muscles, anemia, calcified blood vessels, and acidosis. Thus, the patient with kidney disease is at high risk for a fall. The incidence of falls in CKD increases by up to 60% with age. Falls lead to a twofold cause of death and hospitalization in kidney patients. The risk of falling is higher when patients have associated diseases like pneumonia, gastrointestinal disease, depression, dementia, or diabetes [50].

Kidney disease often requires a therapy known as dialysis. In an analysis of patients of all ages who fell after dialysis, 28.4% of participants reported a fall, and 71% required hospitalization [51]. One would predict that the combination of a high fall rate and weakened bones would increase the risk of bone fractures in kidney patients. This is exactly what we see. Skeletal fractures are relatively common in kidney patients, around three times as high as in the general population. They are a major challenge [52–54].

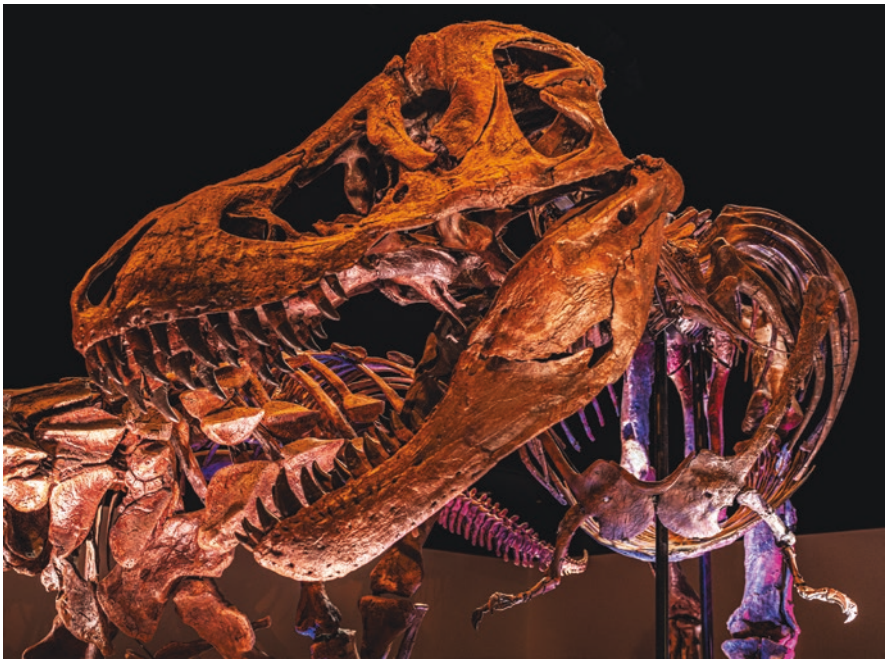

Fig. 2.2 Massive bones support the 11,000- to 15,000-pound *T. rex*. Photo by Stephen Fadem—from Houston Museum of Natural Science

Hypertension

The heart steadily pumps blood through the blood vessel network. This beating action creates pressure. In between the pumping cycles, when the heart is resting and filling with blood, the blood that is in the system still creates pressure against the walls of the blood vessels. If the walls are stiff, the heart has to work harder. Since stiff vessels are also narrowed, they are more resistant to flow, and the resting pressure is also higher. The pumping motion is termed systolic, and the resting motion is diastolic. Blood pressure is measured with a special cuff that is either wrapped around the arm or the wrist. Blood pressure measurements can be obtained at home or in the doctor's clinic. The pressure is read as systolic/diastolic in millimeters of mercury (mm/hg). Normal blood pressure is less than 120/80 mm/hg, and hypertension is defined as a systolic blood pressure of greater than 130/80. These numbers are based on the American College of Cardiology and American Heart Association guidelines. The CDC reports that 116 million adults (nearly half) have hypertension. Many patients are not being treated. Given the risk to patients of heart disease and stroke, this is a major health challenge.

Hypertension is also among the diseases that increase the risk of a fall [55]. This is a modifiable risk factor because hypertension treatment can lower the risk of falls. As clarified above, treating blood pressure with medications is not associated with

falling. The medical community agrees that treating blood pressure to recommended guideline levels is beneficial and does not cause fall-related injury.

Sever clinical studies have been performed to look at falls and blood pressure. There are several factors to consider: For patients who are studied in a clinical center, and who must travel, the results will be better than studies where patients are studied at home. This is because the rigor of traveling, parking, and ambulating to a doctor's office self-selects out those who are too frail to leave their homes.

When evaluating the treatment of hypertension in the elderly, it is important not to conflate frailty. As discussed above, frailty is an independent risk factor for falls and fall-related injuries. Yet, a study of 6,595 persons with an average age of 91 revealed a 24.2% history of falls. There was a 20% higher odds of a fall with blood pressures ≥140 mm Hg. When frail persons were compared with those who were robust, the odds of falling were 39% [56]. In another study that looked at 5,236 persons who were ≥ 65 years old, neither systolic or diastolic blood pressure nor the number of blood pressure medications was associated with falls. This was a well-sampled population of patients and looked at Medicare claims. Since the patients did not have to leave their homes for the study, the bias of excluding a sicker and more frail population was eliminated. The study was balanced to assure that racial, educational, and economic disparities were accounted for. The study evaluated frailty, body mass index, history of falls, and quality of life. This confirmed the epic SPRINT (Systolic Blood Pressure Intervention Trial) that demonstrated the value of treating blood pressures to a systolic level of 120 mm Hg [57].

Diabetes

Diabetes mellitus is characterized by an abnormality in sugar metabolism. Its clinical picture has been known for 3,000 years [58]. Invariably, it involves a disorder in the pancreas's ß-cells' ability to either make insulin or to secrete insulin appropriately. It is diagnosed by an elevated fasting blood sugar of 126 mg/dL. A blood sugar between 100 and 126 mg/dL indicates that diabetes is on the border of occurring. Type 1 or juvenile diabetes is characterized by a complete absence of insulin secretion. These patients require supplemental insulin or a pancreas transplant. With insulin pumps and continuous glucose monitoring (CGM), the prognosis has substantially improved. Type 2 is more common and is often referred to as adult-onset diabetes. It is characterized by insulin secretion that is delayed. Since the timing is off, the blood sugars are elevated and potentiate tissue damage. The insulin release may be delayed to the point that it actually causes a low blood sugar level, stimulating the appetite. Type 2 is both potentiated by obesity and leads to obesity. In fact, strict dietary control can reduce the blood sugar and control the disease in many patients. In others, medications can either potentiate the timely release of insulin or block the kidney's reabsorption of glucose. The management of diabetes is a complex subject worthy of an entire discussion that lies beyond the scope of this book. The major message is that diabetes can be controlled, but when it is not, the sugars

that linger in the blood and tissues damage blood vessels, nerves, and end organs. Diabetes is associated with vascular disease that blocks the circulation to the legs, kidney failure, diminished eyesight, heart failure, coronary artery disease, disorders of the nervous system that affect blood pressure control, delay emptying of the stomach and bladder, as well as a loss of feeling in the lower extremities, hypertension, strokes, infections, and dementia. Strict diabetes control has been associated with slowing the progression of the disease.

When diabetes is poorly controlled, the risk of falls increases. In studies that evaluated 14,685 people, the number of falls in diabetics was 25% and in nondiabetics was 18.2% [38]. Not just falls but increased numbers of fractures are associated with diabetes. There are several reasons: increased bone fragility, muscle atrophy or weakness, obesity, blood pressure drops when standing, neuropathy, walking problems, poor balance control, and heart disease. The bone turnover is decreased and bone structures are altered. This can be related to the circulation in the bone and the effect sugar plays on allowing collagen to particulate in the bone-forming process. With diabetes, fat cells decrease their production of hormones known as adipokines. These adipokines are important for insulin sensitivity. They also decrease fat entry into peripheral fat cells, and thus, it accumulates in the belly, stimulating inflammation and atherosclerosis [59]. Fracture risk reduction and improved skeletal health in diabetes may be modifiable by dietary control and lifestyle intervention [60].

It follows that patients who are treated with insulin have the highest risk of falling because they have the most serious disease. Hypoglycemia may play a role in falls, and thus the care that people with diabetes receive must be closely tailored to the patient's environment and clinical status—the number of complicated conditions that accompany the diabetes and the ability to respond to a diabetic emergency. Insulin and antidiabetic medications in the oral sulfonylureas class are more likely associated with falls than metformin or some of the newer agents.

The following are newer agents for diabetes control (glucagon-like peptide (GLP-1), sodium-glucose cotransporter-2 (SGLT-2) inhibitors):

GLP-1: These are a class of diabetic agents that also lead to weight loss. The most commonly used are dulaglutide (Trulicity), exenatide (Byetta), semaglutide (Ozempic), and liraglutide (Victoza). These medications are active after a meal, stimulating insulin. They also curb hunger. They have been shown to improve heart and kidney disease. The risk of causing a low blood sugar is small if they are used as single agents [61].

SGLT-2 inhibitors: These drugs block a protein that transports glucose across the kidney tubule, blocking its excretion into the urine. Blockage of this protein helps manage diabetes. It also helps eliminate sodium and can control a feedback mechanism that increases hyperfiltration. Hyperfiltration can damage delicate kidney filters, and hence this class of drugs may also help delay the progression of kidney disease. They also decrease cardiovascular complications. As single agents, they are less likely to cause hypoglycemia. The two well-known SGLT2 inhibitors are empagliflozin (Jardiance) and dapagliflozin (Farxiga) [62].

Chronic Heart Disease

The risk of falls in patients with heart disease is around 60% when analyzing hospitalized patients with heart failure, a myocardial infarction, or atrial fibrillation. The reasons are multifactorial, related to blood pressure drops when standing, abnormal heart conduction, and structural heart disease being most likely to cause falls.

2.2.7 Congestive Heart Failure

Structural heart disease may include a weak cardiac muscle, known as a cardiomyopathy, or an abnormally functioning heart valve. Since the heart must constantly move blood between chambers to ensure it is well oxygenated in the lungs and delivered to all tissues, valves are necessary to ensure that blood is not pumped back into either the upper chambers when the ventricle contracts or the ventricle itself, when it relaxes and fills. The valves ensure that blood will always move forward but may leak. Heart failure increases the odds of falling by 14% in the elderly, and those with a heart failure diagnosis have a fourfold increased risk of fracturing a hip or limb compared with those of other heart disease. The American Heart Association (AHA) has developed a consensus statement that encompasses falls. They suggest that an interdisciplinary approach is needed to decrease these risks.

2.2.8 Atrial Fibrillation

Atrial fibrillation is a condition where the upper chambers of the heart pump erratically and do not send regular signals to the lower chambers of the heart. Therefore, the pumping action of the heart is sporadic and irregular. Not only does this lead to a decreased cardiac output of blood containing essential nutrients and oxygen, but the slowed blood flow in the upper chambers leads to blood clots that can pass through the heart and into the brain, causing a stroke [63].

Atrial fibrillation doubles the risk of falling. It is common in the elderly but also occurs in younger people who have intrinsic conduction disorders. The heart systematically sends signals from the sinus node to the atrioventricular (AV) node and then distributes them through the His-Purkinje system throughout the heart. A block in the AV node is associated with an increased risk of atrial fibrillation and ventricular arrhythmia. This is actually a misnomer. There is not a true block in the AV node but a delay. This delay may be related to fibrosis, medications, or reversible disorders such as thyroid disease. A first-degree AV block is considered benign, but is a predictor of severe arrhythmias, and associated with a higher placement of pacemakers and implantable defibrillators. It is associated with a higher mortality rate [64, 65].

Atrial fibrillation can also be associated with acute disorders like COVID-19 [66]. It has multiple etiologies and thus is linked to illnesses like chronic kidney disease. The accumulation of uremic toxins can cause oxidative injury and damage the structure of the AV node. Anemia increases the workload of the heart. Inflammation can lead to damage to the AV node's structure and can cause fibrosis. Kidney disease is associated with derangements of minerals that the kidney is responsible for eliminating, particularly those involved with electrical conduction such as potassium and calcium and with magnesium which is essential for energy since it is bound to ATP. Since the conduction system relies on the conversion of chemicals to electricity, it is very sensitive to changes to all of these minerals.

The initial blood thinning agent used to prevent atrial clot formation and strokes was difficult to control and has been replaced by newer agents that target different clotting factors and are safer to use. Medications can be used to control the heart rate, but the best therapies are either an ablation of some of the excitatory areas that are causing the irregular heartbeat or the Watchman implant. The ablation therapy, while successful, still requires that the majority of patients continue taking a blood thinner.

2.2.9 Postural Hypotension

When changing from a lying to a sitting or sitting to standing position, one may become dizzy. This may be related to a decrease in blood pressure. Orthostatic and postural hypotension are terms used to describe this condition. It is characterized by a 20 mm Hg or more drop in blood pressure with position changes. It may be related to the nerve damage that is associated with diabetes or could be secondary to diuretics used to treat congestive heart failure or hypertension. Patients who are unable to safely stand are at a high risk for a fall. Managing the underlying causes starts with adjusting medications, wearing compression garments, and avoiding environments that can potentiate the problem. Occasionally, medications are used to control postural hypotension.

2.2.10 Cardiac Biomarkers

Biomarkers are molecules that can be detected after some biological event. They are leftover reminders that something happened. As science advances, we discover more and more biomarkers that help us with early and accurate disease detection. One such biomarker is troponin. Troponin is part of the heart muscle contraction system and helps to tie the two muscle filaments, actin and myosin, together when the heart is stimulated to contract. Troponin levels can be elevated for various

reasons, including endurance exercise and chronic kidney disease. They are frequently associated with acute myocardial infarction. In a population of patients with an average age of 75 who fell, 22.5% of men had an elevated troponin level, suggesting that it might have value in predicting the potential for a fall in older men [67].

Chronic Lung Diseases

Chronic obstructive pulmonary disease (COPD) is most commonly called emphysema. It is most common in persons who have smoked cigarettes. A review of what is known in the medical literature demonstrated that the fall rate in COPD was 30%. Twenty-four percent fell frequently. Age, smoking, a previous history of falls, coronary artery disease, using supplemental oxygen, impaired balance, and the number of medications and coexisting medical problems all contributed to the risks of falls. Females with lung disease fell more frequently than men [68].

In addition to intrinsic lung deterioration, patients with lung disease have chronic inflammation, muscle weakness, and alterations in how their nerves interact with muscles. Using biomechanics, scientists have studied the posture of patients with COPD. Although swaying is normal when standing, COPD patients have greater amounts of sway. This is more intense when patients close their eyes or stand on an unstable surface like foam. This may respond to therapy. The speed of one's gait is a predictor of falling. COPD patients have a slower gait as their disease progresses. These changes are supplemental to gait disturbances and poor utilization of oxygen [69].

Sleep Disorders and Falls

It is common for older people to have trouble both falling asleep and sleeping throughout the night. This may be related to other medical problems like heart disease, medications, and lifestyle changes such as a lack of exercise. Also, our body has a 24-hour cycle biological clock that is controlled by the brain and synchronized to the hour of the day and levels of an internal sleep hormone known as melatonin. Our melatonin levels decrease as we age. In some people, the circadian rhythm may be altered to the extent that people are sleepless at night and sleep excessively during the day. Older women are more likely to experience sleep disorders. Sleep disorders can cause a risk of falling [70]. Excessive daytime sleeping is independently associated with falls in women, and these falls are more likely to occur outside [71].

Cognitive behavioral therapy may help persons with sleep disorders, but spending excessive time in bed and not having a regular sleep schedule can aggravate a sleep disorder. Persons are advised to get out of bed when unable to fall asleep. Napping and lack of exercise, spending less time outdoors, avoiding sunshine, and drinking caffeine or alcohol in the evening are well known to affect sleep [72].

Cancer and Chronic Conditions

Many patients have trouble with walking, balance, muscle strength, or eyesight due to the complications of a chronic disease that they endure. It is well established that they are at risk for a fall. Add aging and disability to chronic disease, and the risk of a fall worsens. A study of 79 consecutive admissions to intermediate care facilities was performed in 1986. It showed that 25 patients fell recurrently. Fall risks were characterized by the ability to walk, bear weight, hear, and see adequately. One's morale and mental status contribute to the risk. Back disorders, drops in blood pressure when standing, and the number of medications one was taking also played a role. Falls were also related to the ability to perform daily, routine activities. The risks added up. In those patients who had seven or more factors, the chance of falling was 100%. Around a third of the patients who had four to six risk factors fall. The fall risk was not identified in persons with less than three risk factors. Tests that demonstrated walking ability were the best predictor of recurrent falling [73].

Surviving a serious illness such as cancer is a major challenge. It is emotionally wrenching—a roller coaster of emotional highs and lows. It often entails surgical procedures, chemotherapy, radiation therapy, pain management, and rehabilitation or reconstruction. Many cancer survivors have physical limitations resulting from removing vital tissue or therapy to a diseased organ or limb. Persons adapt to having experienced an illness like cancer based on individual traits and features, but nearly all persons who sustain a serious malignancy are left with emotional remembrances that affect their lives. If we are fortunate, we can gain from the painful experiences of being ill and develop a stronger sense of compassion for fellow human beings [74].

The site of a tumor and how advanced it became when arrested determines the residual defects, if any. Many very serious cancers are successfully treated and do not physically impair the patient. Others who are less fortunate are left with impairments that can result in a fall. In fact, many cancer survivors have a high risk of a fall. The risk of falling is related to the ability to perform daily activities. Persons who fall once are likely to fall a second time. This fall risk is not necessarily related to age and can occur in any age group. Evidence to support the risks of a fall trended recurrently through several quality medical journal articles. These included medication type, the ability to walk or balance, and cognitive and physical ability [75].

Arthritis and Peripheral Neuropathy

The odds of falling increase with osteoarthritis, depending on the number of joints involved. A longitudinal study of men and women over 45 years old in rural North Carolina determined that the odds of falling when one joint is involved are 53%, 74 with two joints, and 85% with three to four joints. Arthritis involving the knee or hip is associated with increased odds of falling [76].

Living Alone

The English Longitudinal Study of Aging is a national study of people over the age of 50 living in private households in England. A review of fall incidences from self-reports and hospitalizations revealed that 52% of people self-reported having fallen. Fewer than 10% had a fall-related hospitalization. There was a 17% risk of falls among individuals who lived alone. In the hospital group, the risk of falling was 29% [77]. This study did not distinguish which patients had CKD.

Vision Disorders

The risk of falling in 251 persons with a visual impairment aged 65–92 years was examined. There were nearly 600 falls during a year period. Smoking, awakening at night, and having glaucoma or retinal degeneration increased the risk of falls [78]. In addition to visual acuity, the inability to accurately judge depth perception, or having an impairment, also increased the fall risk [79].

Gait, Balance, and Mobility Disorders

Balance is controlled by vision, sensations from the inner part of the ear, and how we perceive our position using our joints and muscles. Falls result from underlying diseases and conditions affecting balance, gait, and mobility. Kidney disease is an example a fall risk that may affect balance, gait, and mobility. Advancing age and living alone without social support increase the risk of falling and subsequently injuring oneself. Impaired vision may increase the susceptibility to falling. An acute inner ear disorder can also affect balance and lead to falls. Clinical fall conditions include hypertension, diabetes, cardiovascular disease, and arthritis. Primary or secondary disorders affecting the nerves can be related to diabetes, medications, or a disorder known as amyloidosis. These can cause falls. Acute conditions that relate to volume depletion, such as dehydration secondary to poor fluid intake, over-diuresis, vomiting, or diarrhea, may result in postural hypotension. This list of disease states highlights conditions that can precede a fall but are not inclusive.

Normally we sway slightly when standing. However, in those who are elderly or at risk of falling, this sway is exaggerated [80].

Gait disorders stem from various clinical disorders and, in the aging population, are associated with higher fall risks. The assessment of gait is part of the standard neurological evaluation. Inspection of walking patterns may reveal a neurological disorder (stroke, Parkinson's disease, ataxia, spasticity, and frontal gait) or a non-neurological disturbance related to arthritis or peripheral vascular disease. Ataxic gaits are generally wide-based and unsteady. They are associated with poor balance. Gait disorders may be associated with neuropathy and loss of sensation, foot drop, and decreased reflexes. Patients with a frontal gait have a wide base, take short strips, and have difficulty lifting their feet. The patient with a Parkinsonian gait may

take small, shuffling, jerky steps and festinate with a quick, short stride. They may not swing their arms when walking. Spasticity may be associated with scissoring, crossing one leg in front of another when walking. A proximal myopathy may be associated with a waddling gait [81]. In a study of 632 elderly patients with gait disorders, the fall rate was 39% (244 subjects). The average age of participants was 80.6 years of age. Neurologic gait disorders were more frequently associated with a slower gait velocity. Falls were associated with moderately severe neurological gaits [82].

Studies of the gait of older adults who fall reveal that they have a more constrained, less adaptable trunk movement compared to younger people and that the walking pattern is different from those who do not fall [83]. Other studies have demonstrated that while a decreased walking speed was not associated with falls, a decreased stride length was associated with falls in men over 74 years of age [84].

Muscle Weakness

Muscle breakdown and production should always be in balance. When breakdown exceeds production, the muscles weaken. This is known as sarcopenia. CKD is among the disorders that potentiate the breakdown of muscle. Other disorders include a lack of activity, space travel, inflammatory diseases such as cancer or HIV, severe infections, starvation, and metabolic acidosis. Sarcopenia is also associated with advancing age and diabetes [85, 86]. Vitamin D deficiency and the inability to properly utilize insulin also accelerate muscle loss. Sarcopenia is a major risk for falls. A review of clinical studies in medical journals included 52,838 persons who were either 65 years of age or older. Almost half of the studies reported a significantly higher risk of falls and fractures in persons with sarcopenia [87]. Sarcopenia also appears to play a role in frailty [88].

Bone Loss

As mentioned above, our bones are the response to living in a gravity-driven environment. Bone develops when calcium deposits in connective tissue. The bones support the body and are essential for locomotion. Therefore, they must have the ability to adapt their structure to environmental stresses. This adaptation is known as bone remodeling. The bone that is not used for support is resorbed by a group of cells known as osteoclasts. Osteoclasts also play a role in disease states like osteoporosis and cancer.

A bone cell that makes bone is called an osteoblast. The osteoblast begins its life as a stem cell. Bone-making proteins are better known as bone morphogenic proteins (BMPs). They induce the stem cells to become osteoblasts. BMPs are turned on by gravity through compression. This action turns on a master gene to make a protein with a very catchy name—Runx2. Runx2 sends signals that tell DNA to turn on a specific patch of RNA to make the matrix that will become bone. Runx2 is a transcription factor [89]. Genes work when their DNA is signaled by transcription factors like Runx2 to incorporate RNA to send code to the areas of the cells that produce proteins [90]. The

Fig. 2.3 Calcified organisms from millions of years ago taught us the basics of depositing calcium into collagen to create shells and then teeth and bones. Photography by Stephen Fadem. From the Houston Museum of Natural Science

proteins produced are all essential for capturing calcium, work in complex unison, and developed this mechanism 541 million years ago (see Fig. 2.3). The major protein is collagen, and along with neighboring proteins, it creates the collagen-containing matrix within which calcium resides. Among the hormones that control bone formation, parathyroid hormone is chiefly responsible for bone breakdown or resorption. Bone formation and mineralization are complex, and a reflection on health and well-being.

Osteoporosis is the imbalance between bone formation and breakdown. The breakdown of bone is associated with an inflammatory molecule nuclear factor-κß (NF-κß). Osteoporosis is measured by the bone mineral density (BMD) test which indexes the amount of dense mineral in the bone. It is a global health issue. The lifetime probability of sustaining a fracture related to osteoporosis in postmenopausal European woman has been estimated at 40% [91]. It is worsened by the use of corticosteroids and improved with the use of estrogens. Smoking and alcohol consumption, a family history, advancing age especially being postmenopause for women, a lack of exercise, and poor nutrition are closely associated with decreased mineralization of the bone. It is seen in several chronic disorders, including kidney and liver disease, inflammatory bowel disease, celiac disease, anorexia nervosa, rheumatoid arthritis, and type 1 diabetes [92]. Vitamin D is integral to bone development and growth, even as we age. Estrogens are also critical for bone maintenance. As women age past menopause, lower estrogen levels are a major reason for osteoporosis [93, 94].

A side effect of falls associated with osteoporosis is a fractured hip. Hip fractures have a high mortality rate. In a Norwegian study of 146,132 people, 24.3% died within the first year. But, within the first 30 days, the fall causing the fracture was the underlying cause in over half the cases [95].

It is a well-known fact that space travel causes bone loss and that gravity is essential for bone formation. Muscles are also essential. As babies learn to crawl, their core muscles are not strong enough for them to walk upright. After a few months, they are able to do so. As they continue to walk, the bones that bear the pressure of walking grow along stress lines. As we age we lose muscles, and the core muscles that support our upright posture become weak. The lack of mobility also contributes to weakened bones. Osteosarcopenia is the combined syndrome of decreased

muscle protein synthesis and of new bone formation. It is characteristic of aging, making persons prone to falls. In addition, falls in patients with osteosarcopenia are more likely to result in a fracture.

Volume-Related Disorders

When one does not consume enough fluid, the blood pressure can fall, the skin becomes dry, and one becomes thirsty. Dehydration can result from inadequate water intake, lack of access to water, vomiting, or diarrhea. Exercising, running, or hiking without replenishing the water losses associated with exercise and the hot sun can lead to severe dehydration and even heat exhaustion. The kidney tries to retain water and salt—and this is reflected in the blood tests—the blood urea nitrogen (BUN), a kidney test, rises as does the serum sodium level. A study of health records from the University of Wisconsin identified 11,622 dehydrated patients. Among these, the odds ratio of a fall statistically rose with dehydration. Dehydration was also associated with antipsychotic medications and loop diuretics [96].

The dialysis procedure that is used to clean the blood of patients with advanced kidney disease may cause a drop in the blood pressure and stress on the heart. This stress can be related to a sudden lowering in body fluids, low oxygen levels, an irregular heartbeat, and electrolyte abnormalities [97]. In addition to the adverse consequences of stress related to dialysis treatments, some dialysis patients may have sudden drops in blood pressure when standing. This is called orthostatic hypotension and is particularly true in diabetes because the autonomic or involuntary nervous system cannot regulate blood pressure when one stands. Standing and then walking unassisted when orthostatic hypotension is present may result in a post-dialysis fall. It was reported that while 34.8% of patients may have orthostatic hypotension predialysis, 69.6% have orthostatic hypotension after treatment. The underlying cardiac stress of dialysis, the use of blood pressure-lowering medications, autonomic insufficiency, and excessive amounts of fluid gained between dialysis treatments predispose patients to postural hypotension and the risk of falling [98].

2.3 Conclusion

Nonmechanical falls are associated with medical illnesses. They can be categorized into falls related to cognitive disorders or strokes, falls secondary to medication, and falls that are associated with other clinical conditions like diabetes, heart and kidney disease, or disorders of gait or balance. Patients should discuss the risk of falling with their doctors and take the necessary measures to decrease the chances of a fall or injury. In the next chapter, we will discuss the different types of mechanical falls.

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