INTRODUCTION

Aging is a fundamental process that affects all of our systems and tissues. The rate and magnitude of change in each system may differ person to person, but total body decline is an inevitable part of life for everyone. Ironically, we spend about 75% of our entire life span undergoing the process of decline.

Although there are hundreds of theories on why we age there is no one unifying theory that satisfactorily accounts for all the changes the body undergoes. Indeed, the study of aging is still in its infancy. Although enormous strides have been made in our understanding of the aging process, there is still much to discover about the science of age-related decline. A recent advancement is the recognition that whole-body inflammation is an important contributor to aging-related decline: a significant shift from concepts such as wear and tear and the biological clock based on genetic programming. Also it has only recently been realized that approximately half of the decline with age has a genetic basis.1-5 The remainder of age-related change is the consequence of lifestyle, primarily physical inactivity that can account for the other half of the decline with age. Coupling sedentary lifestyle with inadequate nutrient intake, excess body weight (which puts stresses on tissues, increases inflammation, predisposes toward disease), and variables such as smoking and excessive alcohol intake, the biological decline is more precipitous and greater in magnitude.6-8

Even though age-related decline may result in the loss of lung capacity, renal clearance, or aerobic endurance, we have enough tissue reserve in each of our systems to get through 80 to 90 years without infirmity. Indeed, those who surgically donate a kidney or lung, which obviously results in the loss of half of the tissue function, still have a normal life span. As examples of normal aging there are 90-year-olds who can run marathons, do finger-tip push-ups, and dance vigorously.

Because so much of the decline with aging is lifestyle related, physical therapists have ample opportunity to intervene along the way, with successful results likely at any age. Indeed, there is a growing body of evidence indicating that exercise is a powerful modifier of inactivity-related decline, even for sarcopenia, the age-related wasting of muscle.9-13 Loss of skeletal muscle mass and force is inevitable with aging and can be further exacerbated by a host of variables, such as nutrition and disease. However, sedentary lifestyle is likely to take the greatest toll.2,3,7,14-16 By and large, men and women who include physical activity in their daily routine should have sufficient muscle mass and force to achieve all of the fundamental activities of daily living for 90 to 100 years. Sarcopenia is distinct from another muscle wasting condition, cachexia. Cachexia is rapid and relentless muscle wasting that frequently occurs before death. Cachexia occurs with terminal disease such as cancer. Physical therapy is highly successful for the modification of sarcopenia; however, physical therapist intervention cannot remediate cachexia, as will be discussed below.

Aging is manifested by cellular and subcellular changes within all tissues. The intent of this chapter is to describe what occurs in selected systems for the purpose of understanding the functional consequences of aging as they present to the physical therapist clinically. For example, the natural decline in bone mineral content may predispose patients to osteoporosis. It is not uncommon for those with osteoporosis to manifest postural changes that affect balance, diminish lung capacity, and shorten step and stride length. Once cellular changes are described, other inactivity- and lifestyle-related events that further contribute to systemic decline will be addressed. Thus, physical therapists must consider all the sequelae of health disorders.

There is not a single tissue or system that does not undergo age-related changes. However, only those
systems that physical therapists treat directly or affect the ability to render optimal care will be discussed in this chapter. Gastrointestinal or genitourinary systems, for example, will not be discussed in detail, except with respect to the issue of drug clearance through the kidney. Skeletal muscle is also excluded, as it will be covered in a separate chapter. Finally, some attention will be given to age-related issues that are amenable to change with exercise: sleep, sexual function, depression, gastroesophageal reflux disease (GERD), gastric motility, and constipation.

AGING: A DECLINE IN HOMEOSTASIS

Homeostasis is a critical concept that summarizes all of aging from a functional standpoint. Homeostasis refers to the physiological processes that maintain a stable internal environment of the body. The extent to which the body can adapt to physiological stressors and maintain homeostasis will influence susceptibility to illness and injury. As we age the capacity to tolerate stressors decreases but remains partially modifiable with lifestyle adaptations. The physical stress theory (PST) proposed by Mueller and Maluf captures the essence of homeostasis. The physical stress theory (PST) proposed by Mueller and Maluf17 captures the essence of homeostasis. The ability to improve tolerance for physiological stress and, thus, provide a wider homeostasis window is possible using principles incorporated in the PST. Tolerance range increases in response to exercise, and decreases with the addition of chronic disease and greater inactivity. The older individual with very low tolerance to physiological stressors is highly susceptible to illness and has low capacity to combat the effects of the illness: a bout of influenza may kill.

When a person is in homeostasis, exercise results in robust positive change with systemic adaptation. Strength and balance can increase as can aerobic and muscle endurance. When the inactive older adult with stable chronic diseases engages in exercise, positive change also occurs, albeit more slowly and of smaller magnitude. Under both sets of circumstances, a widening of the window of homeostasis occurs, providing greater tolerance to physiological stress, thus reducing the possibility of moving out of homeostasis into cachexia and death. The wider the window of homeostasis, the greater the chance of survival and of maintaining independence in physical function. Furthermore, the wider the window, the greater the physical reserve as well as the capacity of the body to draw on a “well” of immune function, strength, and endurance among other resources in order to meet the demands of another day.

The natural corollary of homeostasis is survival. Those who maintain homeostasis will continue to thrive, whereas men and women unable to maintain homeostasis against even small stressors may become cachexic, or succumb to a devastating illness such as pneumonia. One of the biggest challenges of current practice is to promote wellness and enhance survival through the maintenance of a large physiological reserve that maintains homeostasis even in the presence of large stressors. It is necessary to define several terms that characterize many older adults. Cachexia typically refers to an inexorable decline in muscle (and body) wasting that cannot be arrested nutritionally.18-20 Cachexia is associated with end-stage cancer, AIDS, tuberculosis, and certain infectious diseases and is a response to one or more pathologies that overwhelm the body. Although some young adults with more “reserve” may recover from a cachectic state, most people do not, and rarely do older adults recover from cachexia. The cachexia of old age typically precedes death and is the final stage of chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), and other terminal pathologies. Although the cause of cachexia is not well defined, it is believed to be the consequence of a massive increase in inflammatory cytokines, which will be discussed later in this chapter.18-21

The other term that must be defined is sarcopenia, which is the muscle wasting of old age.19 Sarcopenia is present if muscle mass as determined by dual-energy x-ray absorptiometry is two or more standard deviations below values obtained for young adults.22-26 Approximately 22% of all men and women older than age 70 years have sarcopenia; for those older than age 80 years the number of sarcopenic individuals approaches 50%, with a higher percentage for men than women.27
The major distinction between the muscle wasting of sarcopenia versus cachexia is that sarcopenia is amenable to change. Indeed, sarcopenic muscle is completely capable of responding to strength-training exercise, with significant increases in muscle mass and strength.\(^{10,12,28}\) In contrast, cachexic muscle will not respond to exercise, and physical therapy treatment to improve strength at this phase of old age is generally unwarranted.

In the United States and around the world, the fastest growing segment of the population are those adults who are age 85 years and older. Although longevity continues to increase, quality of life frequently does not. Indeed, approximately half of all individuals in the 85+ years age group are physically dependent on others for basic essentials such as shopping, cooking, housekeeping, medication management, walking, and bathing. Some of the decline in functional ability is secondary to sarcopenia; for others, accumulated declines in strength, balance, and endurance—often the consequence of inactivity—have resulted in frailty. Sarcopenia is frequently the hallmark of frailty and the number of men and women with frailty is growing exponentially.\(^19\) The increasing incidence of sarcopenia and frailty provides limitless opportunities for positive impact through physical therapy. Further discussion of sarcopenia is included in the chapter on impaired muscle performance.

Physical decline occurs in all systems. The age-related changes in the systems most applicable to physical therapy are presented in the following sections. The potential for enhanced tissue and organ function through physical therapy is also discussed.

**Skeletal Tissue**

Skeletal tissue is remarkably susceptible to change in response to day-to-day nutrient intake, inactivity, weight bearing, hormones, and medications.\(^{29-34}\) These day-to-day changes occur in addition to the ongoing decline in bone mineral that begins in the 3rd decade and continues on through life (Figure 3-3). It is well known that women have a faster rate of bone mass loss during the menopause, where the typical yearly decrease of 0.5% to 1% doubles to about 2% per year.
for the 5-year peri- and menopausal era. Given the smaller bone size of women compared to men, women are much more susceptible to developing osteopenia with menopause. The current estimated risk for osteoporosis in the postmenopausal woman is a staggering 50% (International Osteoporosis Foundation).

Bone is composed of three cell types: the osteoclast, which breaks down bone; the osteoblast, which produces and increases bone mineral; and the osteocyte, which maintains bone. These three cell types form the basic metabolic unit (BMU) of bone as suggested by Frost.\(^{35}\) Under normal circumstances, there is a balance between osteoblastic and osteoclastic activity such that the loss/gain ratio each day is one-to-one. With aging, there is a shift, believed to have a hormonal basis, that causes either a higher bone breakdown rate or reduced bone accretion rate, which is what causes age-related bone decline.\(^{29,31}\) Thus, with advancing age, the BMU favors bone catabolism rather than bone anabolism which, of course, is what occurs during growth.

Factors other than aging may affect the health and well-being of men and women throughout the life span and account for more decline in bone mass than aging alone. Some of these factors are nonmodifiable, but many factors affecting bone mass are modifiable with lifestyle. Factors that are modifiable with lifestyle and those that are not modifiable are summarized in Box 3-1.

It is important to realize that estrogen is critical for the maintenance of bone mass in both men and women. Recently, it has become evident that testosterone and estrogen are independent mediators of bone health in men.\(^{26}\) Thus, any condition affecting sex hormones (e.g., prostate cancer, breast cancer) automatically affects skeletal health in both sexes.

The fact that tomorrow’s osteoporotic women are being created among the youth of today gravely concerns the Centers for Disease Control and Prevention (CDC).\(^{36}\) Young women are not drinking milk, are highly sedentary, are not using their muscles, are not going outside routinely for sun exposure, and are eating nutritionally poor foods without adequate calcium, protein, and vitamin D. Each day spent without the building blocks of bone robs the skeletal system of more mineral. During the teenage years, bone mass increases tremendously and it is during the ages of 12 to 18 that the ultimate skeletal profile is determined. Thus, if a teenager drinks no milk, eats pizza and burgers most days of the week, and gets no exercise outside, chances increase that these adolescents will emerge from their teens with a skeletal profile of a 60-year-old. At the other end of the age spectrum is the older women in a nursing home who spends 23.5 hours per day lying in bed or sitting inside.\(^{31,34}\) These women, who already are at unusually high risk for fracture, are becoming more osteoporotic and frail, and more predisposed to falling and bone breakage with each passing day.\(^{37,38}\)

Exercise is critical to the health and well-being of skeletal tissue. The natural pull of contracting muscles is what maintains bone mineral density; inactivity robs bone of a critical stimulus for osteoblastic activity. A classic example is the remarkable amount of bone loss that occurs when someone is immobilized in a cast or goes into space. The loss of bone in space has been estimated at 0.5% to 1.0% per day because muscle contractions are not producing any demand on bone.\(^{39}\)

Several studies have indicated that exercise or hormone replacement therapy (dehydroepiandrosterone [DHEA], testosterone, estrogen, or estrogen/progesterone combined), either alone or in combination, can add bone mineral density to the osteopenic framework of older men and women. Dalsky,\(^{40}\) for example, used loading exercise as the stimulus in 60- to 70-year-old women during a 1-year study and observed a 3% to 6% increase in bone mineral content.\(^{38,41}\) Kohrt and colleagues found that older women who were already on hormone replacement therapy (HRT) gained additional bone mineral density (BMD) in the spine and hip with loading exercise. Activities consisted of weight training and wearing a weighted vest while ascending stairs.\(^{52}\) Furthermore, Villareal demonstrated that frail older women (older than age 75 years) on HRT also had significant increases of approximately 3.5% in lumbar spine BMD with 9 months of resistance and aerobic exercise training.\(^{43,44}\)
Thus, the evidence suggests that bone in women of all ages is able to respond to HRT and to exercise with additive effects. In one of the few studies that included men, DHEA was given for 2 years to subjects of both sexes aged 65 to 75 years. Women on DHEA increased spine BMD 1.7% the first year and by 3.6% after 2 years of supplementation. No increases in bone were observed for men. Given the current trend of increasing osteoporosis in men, successful therapies are needed. Natural alternatives such as genistein and other food additives are being investigated in both sexes. It is also still unclear whether exercise coupled with selective estrogen receptor modulators (SERMs) such as tamoxifen or raloxifene affect bone in a synergistic and additive fashion.

Body Composition
Throughout the decades there is a gradual shift in body composition such that lean mass decreases and fat mass proportionately increases (Figure 3-4). To provide a typical example, it is not uncommon for a man in his 20s to have a lean body mass/fat mass ratio of 85/15. Even if this same man maintains body weight for the next 50 years he is likely to have a lean/fat ratio of 70/30. For women, it is not uncommon to observe a fat mass of 50% at age 80 years even though the individual appears to be no more than “pleasingly plump.” Of considerable significance is the fact that most of the fat increase occurs inside the peritoneum,7,46-51 which is now believed to be a significant contributor to the increased inflammation that occurs with age. The increase in intra-abdominal fat is also believed to predispose older individuals, particularly women, to elevated lipids and prediabetes.51,52 Fat is an extraordinarily active metabolic tissue, and its contribution to age-related decline and disease is just beginning to be understood.

The more intra-abdominal fat the greater the risk for heart disease, metabolic syndrome, diabetes, and cancer. Women are particularly vulnerable to these diseases after menopause as the protective effects of estrogen are gone and women have more fat than men at all ages.50 Exercise plays an important role in controlling intra-abdominal fat.49,52,53 Every mile walked is about 100 calories burned. When the heart rate goes up in response to exercise and muscles are engaged, metabolic rate increases and fat is burned as fuel. Men and women of all ages who are consistently active do not add intra-abdominal fat to the same extent as those who are sedentary.52 Consequently, active men and women have less whole-body inflammation and less disease.43

Collagenous Tissues
Collagen is probably the most ubiquitous tissue type in the body, comprising the skin, tendons, ligaments, fascia, and a host of lesser entities. Essentially, collagenous tissues hold us together while still permitting freedom of movement in all directions. Over the decades, subtle change occurs in all collagenous tissues, but only three of these changes will be discussed here: loss of water from matrix, increase in crosslinks, and loss of elastic fibers.54-57

Collagenous tissues are composed of collagen, which provides substantial tensile strength, and a surrounding semifluid matrix that binds water and permits collagen fibers to easily glide past one another. Matrix composition changes over the years such that water content decreases considerably. The most obvious consequence of the water loss is body shrinking or height loss primarily because of water loss from the intervertebral discs. Articular cartilage also loses water and becomes more susceptible to breakdown (osteoarthritis). Clinically, the loss of water manifests itself in two ways: reduced range of motion and loss of “bounce,” that is, the ability to absorb shock. From an exercise standpoint, working toward end range becomes more and more important with advancing age to prevent range losses from limiting function. Exercises too should be shifted away from activities that are jarring such as jumping from high surfaces. Although plyometric exercises are recommended as an excellent stimulus to increase bone mass, care should be taken to choose exercises that act as a stimulus to bone without being too stressful on an older body less able to absorb the impact.

Because the number of collagen crosslinks also increases with age, two observable clinical changes become manifest: a decreased range of motion and an increase in stiffness. Even though end range is diminished with advancing years, range should still be sufficient to accomplish all activities of daily living, including
reaching into high cupboards and down to the floor. Range loss should not preclude accomplishing any basic activities—it merely reduces the potential for extremes. Stiffness, on the other hand, has several clinical implications. From a biomechanical perspective, stiffness implies a lack of “give” that translates, for example, to a greater likelihood of tendon avulsion rather than rupture.\textsuperscript{58,59} Stiffness also means that the passive tension within tissues is increased. Phrased another way, the proportion of total tension (i.e., total muscle tension as the sum of active and passive tension) that can be attributed to passive stiffness is increased with age. Couple the increase in passive “drag” with the decline in muscle force that occurs with aging, the consequence is greater muscular effort required for less output. Increased tissue stiffness is one factor contributing to less muscle endurance with age.

Box 3-2 summarizes the three major age-related changes in collagenous tissues: decreased water content from the matrix, increase in number of collagen crosslinks, and loss of elastic properties. Loss of elasticity is abundantly evident in aging skin which no longer has its turgor and tends to hang. Tendons, ligaments, and muscles also lose their elasticity, further contributing to change in function. As inconceivable as it is to regard a 35-year-old baseball or basketball player as “too old” for the sport, age-related change in connective tissue is one of the major contributors to “losing one’s edge” in athletics. In addition to tendons and muscles, internal organs are no longer held in place as well as they were, and age-related changes in connective tissues contribute to the tendency for uterine prolapse, bladder issues, constipation, and hernia with advancing years.

**Cardiovascular Tissues**

Fundamental changes in vascular tissues that occur with aging, summarized in Box 3-3, have a profound effect on function. Probably the most notable and clinically important change is the decline in maximum heart rate.\textsuperscript{60-62} The typical formula of 220 minus age provides a relative guideline for an expected change in maximum heart rate. Thus, an 80-year-old individual is likely to have a maximum heart rate (HRmax) of 140 bpm which obviously limits the extent of cardiovascular challenge that can be endured for any duration. One of the primary reasons for the slowing of aerobic performance with age is the reduction in maximum heart rate. Even though 90-year-olds are still capable of completing the New York City marathon, their times are typically 7 to 8 hours, which is analogous in speed to a 3-mph walk.

Box 3-2 Major Age-Related Changes in Collagenous Tissues and Associated Clinical Consequences

<table>
<thead>
<tr>
<th>Anatomic/Physiological Change with Age</th>
<th>Clinical Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decline in maximum heart rate</td>
<td>Smaller aerobic workload possible</td>
</tr>
<tr>
<td>Decline in VO\textsubscript{2}max</td>
<td>Smaller aerobic workload possible</td>
</tr>
<tr>
<td>Stiffer, less compliant vascular tissues</td>
<td>Higher blood pressures</td>
</tr>
<tr>
<td></td>
<td>Slower ventricle filling time with reduced cardiac output</td>
</tr>
<tr>
<td>Loss of cells from the SA node</td>
<td>Slower heart rate</td>
</tr>
<tr>
<td>Reduced contractility of the vascular walls</td>
<td>Lower HRmax</td>
</tr>
<tr>
<td></td>
<td>Lower VO\textsubscript{2}max</td>
</tr>
<tr>
<td></td>
<td>Smaller aerobic workload possible</td>
</tr>
<tr>
<td>Thickened basement membrane in capillary</td>
<td>Reduced arteriovenous (O_2) uptake</td>
</tr>
</tbody>
</table>
has a maximum HR of 140 and a $\text{VO}_{2}\text{max}$ of $\sim 20$ to $25$ mL $\text{O}_2/\text{kg/min}$. The presence of vascular and cardiovascular disease, however, can decrease the maximum by another 50% to values as low as 10% or 15%.

There is also a correlation between muscle mass and $\text{VO}_{2}\text{max}$, which is the primary reason men have higher max values than women. The higher the lean mass at any age, the higher the maximal aerobic capacity. Those who are sarcopenic have very low aerobic capacity. Hypothetically, adding muscle mass to the sarcopenic individual will enhance adaptation to aerobic exercise—a compelling reason for frail older adults with sarcopenia to participate in resistance training.

Physical therapists regularly treat older adults who have a long history of inactivity and periodic bouts of disease- or illness-related bed rest. These patients are likely to have gained weight over the years and live in a society that poses little to no physical challenges. Thus, it is quite common for patients older than age 60 years to have $\text{VO}_{2}\text{max}$ values in the 13 to 18 mL $\text{O}_2/\text{kg/min}$ range, which translates to inability to climb a flight of stairs without resting and inability to walk a quarter of a mile. Nearly all physical therapists have faced the challenge of the deconditioned older adult who is hospitalized, further imposing inactivity-related decline on a system that has nearly run out of cardiovascular capacity, and who reaches an unacceptably high HR just getting from bed to the bathroom. This scenario, reflecting enormous loss in cardiovascular reserve, is one major contributor to loss in homeostasis as well as loss of independence.

Because of the fundamental changes in connective tissues, increased crosslinking of collagen, altered matrix composition, and loss of elastin, the entire vascular system, including the heart and peripheral vessels, is stiffer and less compliant. Most noticeable is the increase in blood pressure that occurs with age, the consequence of stiffer connective tissues within the vascular walls. Contractility of the left ventricle is compromised as well, which results in a reduction of cardiac output, one of the major components of $\text{VO}_{2}\text{max}$. In the author’s clinical experience, most (approximately 65%) of the clients older than age 70 years are medicated for hypertension. Rarely has the patient’s medication dosage been examined beyond a fundamental baseline blood pressure ascertained while the patient was sitting in the physician’s office. It is not uncommon to see patients overwhelm their hypertension medications during exercise. Consequently, from the standpoint of exercise safety, the physical therapist must watch for blood pressure increases that are unacceptably high. It is imperative that older adults perform warm-ups prior to aerobic exercise to accommodate for the slower arteriovenous oxygen exchange, stiffer vascular tissues, reduction in sympathetic nervous system output, and lower aerobic capacity associated with older age.

Perhaps as a consequence of connective tissue changes, or other factors, the basement membrane in the capillary wall thickens with age. Thus, the exchange of oxygen and nutrients from the vasculature to working tissues occurs more slowly. Because tissue perfusion occurs more slowly, the “burn” in working muscles takes longer to subside during the initial phases of exercise, necessitating a warm-up longer than the usual requisite 3 minutes prior to more rigorous work. Thickening of the basement wall occurs in sedentary people but not in master athletes, which suggests that this aspect of “age-related” decline is actually a lifestyle modification. Indeed, an aerobic exercise training study of older (age 60 to 70 years), previously sedentary men and women revealed that basement membrane thickening was no longer present after 3 months of training at 70% or more of $\text{VO}_{2}\text{max}$. Whether basement membrane thickening occurs at older ages in men and women with a lifetime history of exercise is not known. Diseases of the peripheral vasculature such as diabetes and peripheral vascular disease (PVD) further increase basement membrane thickness, which can result in sufficient lack of oxygen perfusion to skin tissues for breakdown and nonhealing of ulcers. Lack of perfusion to skeletal muscle results in additional loss of fibers, and lack of perfusion to nerves leads to neuropathy.

There is controversy in the literature as to whether the goal in the management of age-related increases in blood pressure is to achieve a blood pressure in the 120/80 range. Because of the increase in connective tissue stiffness within the vascular tree, there is currently a question if blood pressures of 140/80 should be considered as more “normal.” This should not be interpreted to suggest that increased blood pressure is not problematic. There is a substantial body of literature indicating that blood pressures that are too high can lead to stroke, and treating this condition increases life span. From a physical therapy perspective, the more important question is whether a patient is safe in our care. In a patient who is overmedicated, hypotension can result in dizziness and heightened risk for falling. Changes in medication are likely indicated. If patients have exercise pressures that are exceptionally high, medication modification is probably needed here as well. More clarity on what constitutes “normal” blood pressure for an 80-year-old versus that of a 60-year-old and a centenarian is needed.

What are acceptable and safe blood pressures for sleeping, waking, exercising, and postprandial conditions for patients with heart disease is not known. Also unknown is whether age affects the effectiveness of treatments for hypertension.

Peripheral to the discussion of age-related decline in the cardiovascular system is an issue of enormous importance to physical therapy: anesthesia. Men and women of all ages are affected by inhalation anesthesia, but the effects are most noticeable in older adults who have already lost a significant amount of cardiovascular
Although the mechanism is unknown, inhalation anesthesia obliterates mitochondria and, thus, the ability to deliver ATP during exercise is severely compromised.78 Thus, in our patients, after surgery with inhalation anesthesia, muscular and cardiovascular endurance is severely compromised.78 Physical therapists often see patients the day after total joint replacement surgery, often the day after fractured hip and, inevitably, these men and women become exhausted with minimal effort. It is no surprise that spontaneous improvement begins to manifest 2 months after the initial surgery or insult, long after physical therapy has come to an end. The initial phase of physical therapy following hip fracture is effective for teaching patients the essentials: transfers, walker use, home exercise, proper gait pattern, and mobility strategies. Evidence strongly suggests that therapy aimed at strengthening and endurance adaptations given to patients in the days immediately following surgery for hip fracture is ineffectual.79 The enormous devastation to the energy delivery system, coupled with bed rest, the trauma of surgery, and inactivity indicate that perhaps physical therapy intervention would be more effective 2 to 3 months after hospital discharge. As a profession, physical therapists need to reevaluate intervention effectiveness under these treatment conditions.

One aspect of aging needs to be emphasized. Even though maximum heart rates and aerobic capacity are reduced, there is no reason that exercise in healthy older adults should be restricted to a low-intensity level for fear of a heart attack or stroke. The aging heart is fully capable of reaching HR zones of 70% to 80% of maximum.61,62,65,66,69 The Cooper Institute and other cardiac programs around the country have recorded tens of thousands of hours of strenuous exercise for older adults of all ages and for patients with blatant cardiovascular disease.80,81 To enhance cardiovascular endurance, exercise programs must challenge older adults. Walking a patient in the hallway 100 feet does not constitute an acceptable aerobic challenge for most people, unless heart rate is within a training zone of 60% to 80% of the HRmax estimated. For training to occur, elevated HRs have to be sustained for 20 minutes or more, which many older adults cannot achieve. Nonetheless, it is not unreasonable to accumulate 20 minutes of aerobic challenge throughout the course of a daily treatment. Five minutes of exercise bike followed by a rest followed by 5 minutes of alternating normal/brisk gait is an example of accumulating aerobic exercise.72 The heart, like any other muscle, must be challenged to grow stronger. Treating older adults like fragile objects is inadequate treatment.

**Nervous System**

There are fundamental changes within the central and peripheral nervous systems that have significant import for function. Slowing of the nervous system is an inherent aspect of aging. Nerve conduction studies of young and older adults confirm anatomic observations. Many years ago, Norris and colleagues stimulated the ulnar nerve 5 cm below the axilla, at the elbow, and at the wrist; and recorded the latency response at the hypothenar eminence. Response times were on average about 10 ms slower in men in the oldest age group (80 to 90 years) compared to 20- to 30-year-olds. Gradual change was apparent with each successive decade.82

Slowing of movement speed is one of the major clinical manifestations of a slowing nervous system. Examples abound but two will be given here. Alexander and colleagues identified the fact that even men and women in the young-old category (65 to 74 years) are already at heightened risk for falling as response time to an induced fall was too slow for recovery.83 In this instance, subjects were leaning forward into a harness that was preventing them from falling forward. Next, however, the harness was released and subjects were allowed to stumble and fall (an overhead suspension system prevented anyone from actually striking the ground). Their study found that most of the young-old healthy adults studied could not get their legs back underneath the body quickly enough and step appropriately to prevent a fall. Other studies from the same lab have indicated that response times to external perturbations to balance are slowed, which may explain the noticeable increase in number of falls per year in those older than age 60 years.84 In the author’s lab, reaction times have been assessed in hundreds of young and old healthy individuals. The task involved simulated driving, where the person being tested must respond as quickly as possible to a red light by moving the foot from the gas pedal to the brake pedal. The clock begins the instant the light changes from green to red and stops as soon as the brake pedal is depressed. Times for young adults ranged between 150 and 250 ms, which is well within the 500 ms cut-off time imposed by many Motor Vehicle departments for the same task. Reaction times for the approximately 150 healthy older adults (ranging 70 to 85 years old) tested ranged from 350 to 1200 ms.

Exercise has a modest effect on speed of reaction but the increase in speed is not likely to attain sufficient magnitude to make an impact on function.85,86 Toe tap times, for example, increased after exercise from 27 to 30 in 10 seconds, which is still a long way from the 47 taps in 10 seconds expected of younger adults. Several investigators have demonstrated a slight exercise-induced increase in peg board times in that the number of pegs that could be moved in 30 seconds increased. Most of the slowing occurs centrally, but sloughing of myelin has been demonstrated anatomicall in peripheral nerves, which will certainly slow conduction velocity. It should be borne in mind that most studies on changes in movement speed were performed on healthy individuals, not those with disease that would also affect movement speed further. Studies done to date have also not considered the potential blunting effects of many drugs.
Although the aging of muscle is covered thoroughly in another chapter, it should be mentioned here that another facet of age-related decline is a fallout or loss of neurons.\(^87,88\) Roughly half of the decline in muscle mass is the consequence of neuronal, specifically, axonal loss.\(^87\) Indeed, muscle is not the only tissue that experiences loss of innervation; innervation declines in all tissues, with far-reaching outcomes that affect the sympathetic, parasympathetic, sensory, and motor systems.

Before age-related decline begins, the yin–yang of the parasympathetic and sympathetic nervous systems is delicately balanced and poised to participate in flight or fight. With age, the balance of the parasympathetic and sympathetic nervous system output is altered (although poorly defined) and likely related to the slowing of gastric motility, possible issues with bladder control, hyper- and hypotension, and deficits in control of blood flow to and from the periphery.\(^89\) The failure of the sympathetic nervous system to adequately respond to heat and cold is responsible for the deaths of many seniors each summer and winter as they failed to perceive the need to cool down or warm up.

One of the most complex and poorly understood phenomena with aging is altered somatic sensory input.\(^89,90\) It is common for vague symptoms of pain in one area of the body to represent a totally unrelated event. It is a tremendous challenge for physical therapists to discern if and when something is wrong with an older patient based on vague somatic complaints. Abdominal pain could reflect a host of possible issues ranging from simple indigestion to pancreatitis, cancer, intestinal obstruction, peritonitis, impending heart attack, or inguinal hernia. Back pain could reflect a simple muscle or joint irritation but could also reflect an abdominal aorta aneurysm, appendicitis, bladder infection, and cancer. Carefully noting these complaints is important, particularly if complaints are coupled with sudden change in function, sensorium, the emergence of fever, or an increase or sharpening of symptoms.

Peripheral sensation gradually diminishes in older adults, even those individuals without vascular diseases or neuropathy secondary to diabetes. To illustrate, Semmes-Weinstein testing on 125 older adults without diabetes revealed the absence of normal sensation (6.13-g monofilament) in all persons tested (M. Brown, unpublished data). Protective sensation was still present in these individuals (5.07-g monofilament), but fine discrimination was lacking. The blunting of peripheral sensation undoubtedly contributes to the inability to perceive excessive heat or cold. Box 3-4 summarizes physiological changes of the nervous system and impact on function.

### BOX 3-4 Major age-related Changes in the Nervous System and Associated Clinical Consequences

<table>
<thead>
<tr>
<th>Anatomic/Physiological changes</th>
<th>Clinical Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sloughing/loss of myelin</td>
<td>Slowed nerve conduction</td>
</tr>
<tr>
<td>Axonal loss</td>
<td>Fewer muscle fibers</td>
</tr>
<tr>
<td>Autonomic nervous system</td>
<td>Slower systemic function</td>
</tr>
<tr>
<td>dysfunction</td>
<td>(e.g., C-V, GI) with altered</td>
</tr>
<tr>
<td></td>
<td>sensory input</td>
</tr>
<tr>
<td>Loss of sensory neurons</td>
<td>Reduced ability to discern</td>
</tr>
<tr>
<td></td>
<td>hot/cold, pain</td>
</tr>
<tr>
<td>Slowed response time (speed</td>
<td>Increased risk of falls</td>
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<td>of reaction)</td>
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The Immune System

There are literally hundreds of theories on why we age, ranging from accumulated wear and tear to programmed apoptosis to the accumulation in errors during translation of messages from the DNA. Although many of the current theories are likely to have some veracity, few of the current theories have import for physical therapy. Recently, however, one aspect of age-related decline has emerged as a major contributor to the loss of muscle and organ reserve that has considerable import for physical therapy. It is now evident that with advancing age, there is an increase in systemic inflammation because of changes in the immune system. Major increases in proinflammatory cytokines such as interleukin 1 and 10 (IL-1, IL-10), C-reactive protein (CRP), and tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) occur with advancing age, which is significantly associated with muscle wasting and loss of physical function.\(^6,7,14,46,72,91,92\)

The increase in systemic inflammation is also an underlying factor in the development of age-related diseases such as Alzheimer’s disease, atherosclerosis, cancer, and diabetes.\(^91,93\) Thus, it is hypothesized that controlling inflammatory status may allow for more successful aging.\(^8,94,95\)

Four approaches to the management of total-body inflammation have been considered: anti-inflammatory drugs, use of antioxidants, caloric restriction, and exercise.\(^6,94-96\) Of the three, exercise is far superior to the minimal impact noted from anti-inflammatory drugs and antioxidants.\(^21,27,48,53\) One exercise bout results in a significant reduction in markers of inflammation such as IL-1 and TNF-\(\alpha\).\(^48,50,92,93\) Cumulative exercise sessions further reduce inflammation, which should enable chronic exercisers to resist fatal infections and aggressive pathogens.\(^57\) Men and women who are habitually physically active have less systemic inflammation than those who are sedentary, which may be the major reason for the enhanced well-being of exercisers, who also have a wider window of homeostasis. These current findings suggest that physical therapy can play an important role in the management of systemic inflammation, enhancing systemic “reserve,” reducing risk for disease, and delaying functional decline through the use of exercise. An example of the power of exercise is that many fewer men and women who consistently exercise have Alzheimer’s disease than those who are sedentary.\(^91,93\)
One of the probable contributors to the rise in inflammation is the shift in fat mass from the periphery to the abdomen coupled with the general increase in total intra-abdominal fat with advancing years.\textsuperscript{27,51} Abdominal fat is metabolically active and is an inflammatory organ. Not only do inflammatory cytokines result in muscle wasting, they diminish the function of other organ systems as well, which reduces reserve and shrinks the window of homeostasis. The increase in inflammatory cytokines is also associated with metabolic syndrome.\textsuperscript{98}

The Hormonal Axis

One of the realities of aging is a loss of hormones, a loss in responsiveness of hormone target tissues, or both.\textsuperscript{27-31,99} It is not uncommon for older adults to develop “senile” diabetes because insulin sensitivity, particularly in skeletal muscle, is reduced.\textsuperscript{99} Women after menopause have little estrogen, and men lose testosterone throughout the course of a lifetime, such that the majority of men in the 8th decade are hypogonadal.\textsuperscript{99,100} Recently, the loss of sex hormones has been determined to be a contributor to the reduction in muscle mass and, in particular, muscle strength.\textsuperscript{100,101} Indeed, older hypogonadal men given testosterone replacement gain a significant amount of lean mass although data suggest that the increase in mass is not accompanied by much strength change unless resistance exercise and testosterone are given together.\textsuperscript{99}

Loss of estrogen has only recently received interest. A meta-analysis concluded that estrogen is an anabolic steroid that is associated with an increase in strength and lean mass in postmenopausal women.\textsuperscript{102} Taaffe and co-workers conducted a double-blind study of 80 women (50 to 57 years) who were randomly assigned to one of four groups: control, hormone replacement therapy (HRT), exercise, or HRT plus exercise. Subjects were in the research study for 1 year and exercised two to three times a week. Prior to and following the year enrollment, lean mass of quadriceps and hamstrings, strength, vertical jump height, and running speed were assessed. Those in the HRT and exercise plus HRT groups (not the exercise only group) had significant increases in running speed, muscle mass in both compartments and vertical jump height compared to controls. No strength measures were reported. A recent study of postmenopausal twins, one of whom was on HRT whereas the other was not, has further substantiated estrogen effectiveness.\textsuperscript{101} The women taking HRT were between 5 and 15 years postmenopause. Vertical jump height, fast gait, and grip strength were higher in the twin taking hormones. Curiously, knee extension strength was not greater. Other studies of older postmenopausal women suggest the same important outcome: more muscle mass and strength with HRT.\textsuperscript{103}

One of the most interesting findings in muscle deprived of estrogen was reported in several studies of rats. When ovaries were removed, simulating menopause, specific muscle force (force/unit of muscle mass) almost immediately declined by about 15%.\textsuperscript{104} When estrogen was returned to the system, specific force normalized back to baseline values.\textsuperscript{105} It is not uncommon to hear complaints of weakness from women who have undergone ovariohysterectomy. Perhaps these findings from rats provide an explanation for these complaints. Findings also suggest that strength training for postmenopausal women at any age is particularly important.

From a rehabilitation perspective, several important findings have been reported on estrogen-deficient muscle from rodents. When muscle atrophy is induced in rats (simulated bed rest), recovery of muscle mass and strength fails to occur or occurs more slowly in estrogen-deficit rats.\textsuperscript{106-108} These findings may provide an explanation for why women do not progress as well as men with spinal injury, severe trauma, or head injury, all conditions that cause estrogen values to plummet to undetectable ranges. Rodent studies also indicate that estrogen-deficient muscle is more susceptible to injury, which may be another factor influencing recovery of muscle mass and strength in women who are estrogen-deficient.\textsuperscript{109-112}

Replacement of one hormone may not be sufficient to overcome a specific deficit as hormones tend to work in concert with one another. For example, testosterone has been shown to increase insulin-like growth factor-I (IGF-I), which stimulates protein synthesis in muscle.\textsuperscript{100} However, if IGF-I levels are already low, then perhaps the utility of testosterone is limited. One scientist has recommended hormone replacement, particularly for men as they lose muscle mass at a more rapid rate than women. His conclusion was that perhaps in future studies multiple hormones should be administered simultaneously as low values in one hormone are likely to reflect deficiencies in other hormones.\textsuperscript{113} Hormone supplementation is in its infancy and should bring considerable change. An enhanced understanding of how hormones can influence health and well-being is to be expected in the years ahead.

EXERCISE FOR REVERSING DECLINE AND PREVENTING DISEASE

It is becoming evident that a lifestyle that includes routine exercise can be extremely influential in preventing physical decline and disease. Those who exercise routinely (at any age) have less cardiovascular disease, osteoarthritis, diabetes, vascular disease, metabolic syndrome, pain, and Alzheimer’s disease, to name a few. Studies of Masters athletes and habitual exercisers indicate that physical activity promotes optimal well-being and enhanced self-efficacy.\textsuperscript{114,115} Physical therapists have more potential to promote healthy aging than any health care professional, and it should be the profession’s mission to do so.
Is there a threshold for physical activity that is protective? The answer to this question is unclear but evidence suggests a dose–response aspect of benefit. For example, it is possible to gain strength with a stimulus that is 50% of 1-repetition maximum (1 RM). However, more strength will be gained if the demand is higher. The same holds true for cardiovascular conditioning; additional reserve will be gained with higher intensity training but any stimulus over and above what is encountered on a day-to-day basis will result in positive change. Several interesting findings have emerged from the research of Paffenbarger and Blair that may influence decision making on this issue. In their studies, subjects were divided into three categories of “fitness” based upon number of minutes spent in physical activity per week. In addition, subjects were divided into three categories based upon body mass index. As expected, those with the highest body mass had the highest rate of disease (e.g., cardiovascular) and mortality and those who were the most physically active had the least. What was not expected was that the incidences of disease and mortality were not that different for those in the moderate and vigorously active categories. Moreover, those with high BMIs were protected from disease and premature mortality if they were moderately or vigorously active. In all likelihood, there is a threshold of activity that is protective but it differs from individual to individual based upon natural endowment of muscle mass and cardiovascular capability, genetic predisposition to disease based upon family history, self-efficacy, soft-tissue integrity, and a host of other factors. Thus, discussing an identifiable level of physical activity for the older individual is premature, but the evidence in favor of a physically active lifestyle is overwhelming.

**SUMMARY**

Aging is an inevitable process and decline occurs in all tissues and systems. Nonetheless, with a thoughtful lifestyle approach, it is possible to prevent or attenuate the severity of some diseases, and delay (possibly avoid) the condition of frailty.

Indeed, physical activity is the most potent tool of physical therapists to optimize function throughout the entire life span. Inactivity should be considered as much a contributor to impairments and loss of function as pathology or disease. Physical therapists can utilize the principles espoused in the physical stress theory to help guide the modulation of exercise for older adults to the appropriate level to achieve positive gains in tissue functioning and homeostasis; while avoiding, both the tissue damages of excessively high stress and the physiological decline of inadequately low stress.

It is appropriate for physical therapists to consider the impact of age-related changes on the rehabilitation and wellness plan for their older adult patients. However, physical therapists must take care not to underutilize active rehabilitation; rather, they need to adjust the rehabilitation to meet the unique needs of the older patient. Physical therapists should use their understanding of age- and disease-related changes in tissue functioning to focus a rehabilitation and wellness plan. This plan should be based on a careful examination of the specific impairments, tasks, and activities affecting function; an integration of all evaluation data (including patient goals and preferences) to inform prognosis; then careful targeting of the structures and tasks that can provide greatest functional gain; and finally determination of the intensity of the intervention to optimize positive adaptation to stress.

**REFERENCES**

To enhance this text and add value for the reader, all references are included on the companion Evolve site that accompanies this text book. The reader can view the reference source and access it online whenever possible. There are a total of 119 cited references and other general references for this chapter.
REFERENCES


