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488 Biology of Aging

Rafael de Cabo, David G. Le Couteur

Biology of Aging The increase in older people over the past few decades is one of the most significant changes in human history. For the first time, people over the age of 65 years now exceed children under the age of 5 years (Fig. 488-1). Aging is associated with an exponential increase in the incidence of many chronic diseases (Fig. 488-2). This has significant implications for the delivery of health services and aged care in all nations. Older people are living even longer due to advances in medical care but at the cost of longer periods of frailty and disability and of iatrogenic burdens associated with intensive medical care of multiple diseases, such as polypharmacy. Establishing the relationship between aging and dis ease, particularly noncommunicable disease, is one of the most impor tant goals for biomedical research. Studies in animal models confirm that aging is malleable. The “longevity dividend” refers to the concept whereby an intervention that slows the aging process is likely to delay the onset of a wide range of age-related diseases and syndromes, as well as potentially increasing years of healthy lifespan (“health span”). DEFINITIONS OF AGING Aging is a progressive process associated with deterioration in struc ture and function, leading to increased susceptibility to disease and mortality, and often associated with impaired reproductive capacity. There are statistical, biological, and phenotypic components to most definitions of aging (Fig. 488-3). THEORIES OF AGING ■ ■MUTATION ACCUMULATION AND

ANTAGONISTIC PLEIOTROPY Evolutionary theories of aging attempt to explain why aging, which impairs health and survival, has evolved, and why there is so much variability in lifespan across taxa. Aging is generally considered to be nonadaptive. This means aging has not been shaped by evolution or genetically programmed. However, many genes influence the aging process, and the initiating process of aging is most likely to involve sto chastic, nonprogrammed changes in nuclear maintenance that influ ence gene expression and repair. Many theories of aging are based on the concept that, in the wild, mortality is secondary to extrinsic causes, such as predation, injury, and infection, and evolutionary selection

65 years and older Percentage of world population

Less than 5 years

Year FIGURE 488-1 Globally, people over the age of 65 years now exceed children under the age of 5 years.

Aging PART 18 pressure is generated by early life survival and reproductive success. There is minimal selection pressure to maintain health and extend life beyond early reproductive years and inevitable death from extrinsic causes. In fact, traits may evolve that are beneficial in early life and for reproduction but become harmful if the animal lives to an older age. These theories were set out by the classic “mutation accumulation” (John B.S. Haldane) and “antagonistic pleiotropy” (George C. Williams) theories of aging. ■ ■DISPOSABLE SOMA THEORY There is often a trade-off between aging and reproduction. Animals with high extrinsic mortality tend to have short lives, small bodies, and greater reproductive output, while animals with low extrinsic mortality, such as humans and other primates, tend to have longer lives, larger bodies, and fewer offspring. The disposable soma theory of aging (Thomas Kirkwood) explicitly hypothesizes that evolution selects strategies that prioritize utilization of finite resources to main tain germ cells necessary for reproduction rather than for maintenance of the soma (nongerm cells), hence leading to age-related accumulation of damage to the soma. ■ ■INFORMATION THEORY OF AGING This theory has its foundations in studies of aging biology and the role of DNA methylation in aging and as an “aging clock.” With aging, there are marked changes in the epigenome (an analog information system), which have profound effects of gene expression (an informa tion retrieval system). By contrast, the DNA code (a digital information system) is relatively stable with aging. COMPARATIVE AGING ACROSS SPECIES ■ ■NEGLIGIBLE SENESCENCE AND

PROGRAMMED AGING There are some animals that undergo “negligible senescence,” mean ing that there are no obvious biological changes of aging and the rate of mortality does not increase with time. These include some strains and species of clams, sharks, hydra, and worms. The longest living vertebrate is the Greenland shark, which may live up to nearly 400 years of age. On the other hand, there are a few animals that undergo programmed aging and death. These are the semelparous animals such as Pacific salmon and marsupial mice (Fig. 488-4). ■ ■GRANDMOTHER EFFECT There are species, including humans, where evolution could influence late-life survival through what is called the grandmother effect. In these species, survival of offspring depends on the care provided by their long-lived grandmothers. This also explains the development of extended postreproductive survival in humans. BIOLOGICAL HALLMARKS OF AGING Aging is associated with a range of molecular processes that are remarkably similar between species. These “hallmarks of aging” are the mechanistic pathways that cause aging. The processes are highly interconnected, and impairment of one process will impact the others. The hallmarks include those that act at the various biological strata and together erode various pillars of health (Fig. 488-5). Interventions that alter the behavior of each of these pathways (via genetic manipulation, pharmacologic treatments, or nutritional inter ventions) influence aging and lifespan of laboratory animals such as mice, fruit flies (Drosophila melanogaster) or worms (Caenorhabditis elegans). Each of the hallmarks is a potential target for pharmacothera pies that might delay aging and the onset of age-related morbidity and increase both health span and lifespan. ■ ■GENOMIC INSTABILITY The integrity of DNA is vulnerable to many exogenous (e.g., irradia tion, chemicals, transposons) and endogenous (e.g., oxidative stress)

Alzheimer’s dementia Chronic obstructive pulmonary disease Stroke

Incidence

Ischemic heart disease Non-Hodgkin lymphoma

FIGURE 488-2 Many noncommunicable diseases have an exponential increase in incidence with age. Aging biology is likely to be an integral part of the mechanisms for these diseases. stresses that generate largely random DNA lesions such as point muta tions, translocations, and chromosomal anomalies. Mitochondrial DNA is especially susceptible to damage with aging because of its proximity to free radicals produced during oxidative phosphorylation and lack of histones and repair mechanisms. Genetic manipulation of nuclear and mitochondrial DNA repair mechanisms shortens lifespan in mice, while human premature aging syndromes are associated with deficiencies in genes necessary for nuclear maintenance. For example, Werner's syndrome is caused by mutations in a recQ helicase gene (WRN) required for repair of double-stranded breaks, and HutchinsonGuildford progeria syndrome is caused by mutations in the lamin A gene (LMNA) required for structural support of the nucleus. ■ ■TELOMERE ATTRITION Telomeres are repeat sequences at the ends of linear chromosomes that counter the inability of DNA polymerase to replicate the tips of chromosomes. In humans, telomeres consist of a redundant TTAGGG sequence repeated several thousand times. Some cells (e.g., germ cells, tumor cells) contain telomerase, which can reform telomeres that are shortened during replication. In most cells, after multiple divisions, the telomeres are truncated to a point where cell division cannot con tinue. In cell culture, this number of divisions is called the Hayflick limit, and cells that cannot undergo further division are said to have Dementia Cataracts Delirium Cancer Incontinence Sarcopenia C B A Age

FIGURE 488-3 Definitions of aging often include (A) a biological component encapsulated by the 12 hallmarks of aging, (B) a phenotypic component that includes many chronic diseases and syndromes of aging, and (C) a statistical component that in most species involves an exponential (Gompertz) increase in the risk of mortality with age.

Colon and rectum cancer

Age entered a phase of "replicative cellular senescence." Some studies in humans have found that telomere length in blood cells decreases with age, while mice that have been genetically manipulated to have short or long telomeres have decreased and increased lifespans, respectively. In humans, telomerase deficiency is associated with pulmonary fibrosis and aplastic anemia. ■ ■EPIGENETIC ALTERATIONS Gene expression is regulated by DNA methylation, histone modifica tion, chromatin remodeling, and noncoding RNAs. These all change with age, leading to altered transcription of genes, especially those involved with inflammation, mitochondrial function, and autophagy pathways. There are consistent age-related changes in the pattern of DNA methylation in human blood samples that have been called "epigenetic clocks" (e.g., "Horvath epigenetic clock") because they reflect chronologic age. Histones are proteins that package DNA into nucleosomes, thus influencing DNA available for transcription. The sirtuins are a family of NAD-dependent proteins that regulate histones through deacetylation and have significant effects on aging and lifes pan. For example, overexpression of sirtuins and activation by drugs such as resveratrol increase lifespan in model organisms. De-repression of retrotransposons has been implicated in aging, and nonreverse tran scriptase inhibitors decrease this and delay aging in mice. 1.0 1.0 Risk of death Survival 0.8 0.8 Risk of death 0.6 0.6 Vascular disease Survival Falls 0.4 0.4 Osteoporosis 0.2 0.2 Frailty 0.0 0.0

Ocean quahog clam Greenland shark Negligible senescence Antechinus Pacific salmon Semelparous animals Asian elephant Humans Grandmother effect FIGURE 488-4 Some animals undergo negligible senescence, while others such as the semelparous animals undergo programmed aging and death. In some longlived species, including humans, there is a prolonged postreproductive period that can evolve because of the beneficial effects of grandmothers on survival of infants. ■ ■LOSS OF PROTEOSTASIS Damaged proteins in cells are removed by the autophagy-lysosomal system and ubiquitin-proteosome system. These processes are impaired with aging, which can lead to intracellular and extracellular aggregates of damaged proteins and other cellular components such as lipofuscin, Lewy bodies, neurofibrillary tangles, and amylin (Fig. 488-6). ■ ■DISABLED MACROAUTOPHAGY Autophagy refers to the sequestration and digestion of proteins (i.e., proteostasis), nonprotein macromolecules (e.g., glycogen), and organ elles (e.g., mitochondria, “mitophagy”). Autophagy and the expression of autophagy-related genes decline with old age. Autophagy is activated by caloric restriction (CR), spermidine, and inhibition of mechanistic target of rapamycin (mTOR) that all are associated with delayed aging. Loss of function of genes that are associated with autophagy in humans is associated with increased susceptibility to a range of age-related diseases. ■ ■DEREGULATED NUTRIENT SENSING Nutrition has a profound effect on aging in all species. One of the most important nutritional interventions that influences aging is CR. CR involves providing animals with less food (usually ~30–50% less than eaten by ad libitum fed controls). When this is maintained over a lifetime, lifespan is increased, and many age-related pathologies and diseases are delayed. There are several interconnected pathways that mediate the effects of nutrition and CR on aging and age-related health through a wide range of downstream effects (Fig. 488-7). Drugs that act on these pathways to replicate CR are called CR-mimetics

and increase lifespan regardless of calorie intake. These key pathways include the following:

1. Insulin and insulin-like growth factor (IGF)-1 signaling pathway (IIS), including growth hormone (GH). Animals with genetic downregulation of this pathway have longer lifespans, including the very long-living Methuselah mice with knock out of the receptor for GH. Humans with GH receptor deficiency (Laron syndrome) have less incidence of cancer and diabetes. Many of the downstream effects on aging pathways are mediated by FOXO (forkhead box O) transcription factors. Genetic variation in some FOXO genes is associated with longevity in humans.
2. mTOR pathway. This pathway is activated by amino acids via tRNA and the IIS and therefore can be manipulated by dietary protein intake. Inactivation of mTOR by dietary restriction or rapamycin is associated with reduced protein synthesis and increased autophagy, leading to increased lifespan.
3. Sirtuins. The sirtuins are a class of seven proteins that respond to CHAPTER 488 dietary energy via the cofactor NAD. Sirtuins regulate gene expres sion via deacetylation of histone and nonhistone proteins and have been shown to impact many processes related to aging, including apoptosis, inflammation, DNA damage/repair, and mitochondrial biogenesis. Increased sirtuin activity induced by genetic manipula tion, resveratrol, or NAD supplementation has been associated with increased lifespan.
4. AMP-activated protein kinase (AMPK) responds to dietary energy Biology of Aging restriction via cellular levels of AMP. Activation of AMPK with metformin increases lifespan in animals, and observational studies in humans suggest that metformin impacts age-

related conditions. Human clinical trials of metformin are underway to determine its effects on aging.

5. Fibroblast growth factor 21 (FGF21) responds to dietary protein, with protein restriction leading to increased production and release into the blood. FGF21 promotes AMPK signaling and insulin sensi tivity, and overexpression in mice increases lifespan. ■ ■MITOCHONDRIAL DYSFUNCTION Age-related changes in mitochondria include increased electron leak age and decreased ATP production, primarily due to impaired complex IV activity. Mitochondrial DNA damage accumulates with age, and mitochondria may become swollen with disrupted cristae. Impaired mitochondrial function leads to increased generation of superoxide radicals and hydrogen peroxide, which are potent oxidants. Conse quently, aging is associated with the accumulation of oxidative damage to fat, proteins, and DNA. This forms the basis of the free radical the ory of aging. Antioxidants have been investigated as a method to delay age-related oxidative stress but have been ineffective in delaying aging. On the other hand, many of the nutritional and pharmacologic inter ventions that delay aging are associated with increased mitochondrial biogenesis, usually via their effect on the PGC1α transcription factor. ■ ■CELLULAR SENESCENCE Senescent cells have stopped dividing because of either telomere short ening or other damage mediated by the INK4/ARF system. Senescent cells (sometimes called zombie cells) accumulate in various tissues with increasing age. They produce a range of inflammatory cytokines including interleukin 6 (IL-6) and tumor necrosis factor α (TNF-α), collectively called the senescence-associated secretory phenotype (SASP), which contributes to systemic inflammation. Elimination of senescent cells that express INK4 and several drugs that eradicate senescent cells called senolytics (e.g., dasatinib, quercetin, fisetin) delay the progression of age-related pathologies. ■ ■STEM CELL EXHAUSTION The numbers of stem cells decline with aging, probably secondary to replicative senescence and telomere shortening. Transplantation of plu ripotent stem cells from young donors to old recipients extends lifespan in mice and may improve frailty in humans. Another strategy involves induction of genes that regulate stem cells (Yamanaka OSKM factors:

GENE Genomic instability Epigenetic alterations Telomere attrition METAORGANISM MAINTENANCE OF HOMEOSTASIS Dysbiosis Integrity of cellular barriers Recycling and turnover Circadian rhythm PART 18 Aging Hormesis Cellular resilience Repair and regeneration SYSTEM Inflammation CELL Altered cellular communication Cellular senescence Deregulated nutrient sensing pathways Stem cell depletion FIGURE 488-5 The hallmarks of aging include 12 processes that form the foundations of the biological changes of aging and age-related diseases and syndromes. OCT4, SOX2, KLF4, MYC), which delays aging in progeria mouse models. After bone marrow transplantation, no evidence suggests that the recipient runs out of donor stem cells even though the stem cell population could be compromised numerically and due to the age of the donor. Can the stem cells renew themselves in the new host? Lipofuscin Lewy bodies Neurofibrillary tangles Amylin FIGURE 488-6 Impaired proteostasis with old age contributes to the accumulation of aggregates often associated with disease (lipofuscin in the liver, Lewy bodies in the substantia nigra, neurofibrillary tangles in neurons, and amylin in pancreatic islets).

■ ■ALTERED INTRACELLULAR COMMUNICATION Many signaling pathways undergo changes with old age including insulin/IGF-1, dopaminer gic, sex hormones, growth differentiation factor 11 (GDF11), and the renin-angiotensin system. These and other bloodborne factors might explain

some of the antiaging effects of blood transfusions. Age-related changes are also noted in the extracellular matrix, including increased fibrosis, that impact cell-to-cell communication. ORGANELLE ■ ■CHRONIC INFLAMMATION Aging is associated with low-grade activation of the innate immune system, leading to elevated levels of IL-6 and TNF-α and often elevated C-reactive protein and erythrocyte sedimentation rate (ESR) with a lower lymphocyte-to-neutrophil

ratio. This has been called “inflammaging.” This may be secondary to several factors including the SASP, chronic infection with cytomegalovirus, obesity, leaky gut, and activation of the nuclear factor κB (NF-κB) pathway. Inflammation is a key factor in the pathogenesis of many chronic diseases and, in particular, frailty. Mitochondrial dysfunction Disabled macroautophagy Loss of proteostasis ■ ■DYSBIOSIS Complex changes occur in the gut microbiome with old age in humans. The degree of microbial heterogeneity declines, and changes are seen in some species and phyla (e.g., Bacteroidetes, Akkermansia). Fecal microbiome transplantation and various probiotics have some effects on aging in mice. GEROSCIENCE Old age is the major risk factor for many chronic diseases. The nature of the relationship has been the source of debate for millennia. On one hand, it has been argued that aging is similar to any other disease and, therefore, is amenable to therapeutic interventions. On the other hand, it has been argued that aging is an inevitable and untreatable process that increases the risk for other diseases. Regardless, there is a marked and often exponential increase in the prevalence and incidence of most chronic diseases with age (Fig. 488-2), and there are several conditions that are generally considered to be primarily age-related disorders, including dementia, sarcopenia, frailty, and osteoporosis. These conditions are very rare below the age of 50 years. Geroscience refers to the study of the relationship between aging biology and disease. Aging leads to impairment of many physiologic systems that will increase susceptibility to disease. For example, aging is associated with marked changes in immune function. Immunose nescence refers to age-related deterioration of the responsiveness of the immune system to infection and other antigenic challenges, caused by thymic involution with reduced naïve T cells and impaired memory T cells, a reduction in hematopoietic stem cells, and impaired antigenpresenting cell function. Aging is associated with many endocrine changes, most notably a reduction in sex steroids and GH, which contributes to sarcopenia and osteoporosis. Vascular changes includ ing increased arterial stiffness leading to high peripheral vascular resistance and microvascular pathology have an obvious link with cardiovascular disease, but also probably contribute to other conditions such as dementia, osteoarthritis, and sarcopenia. Although the usual dogma is that aging is a process that increases susceptibility to diseases, the relationship between chronic disease and aging may be much more fundamental. The pathogenesis of most chronic diseases includes one or more of the hallmarks of aging, and differences between disease and normal aging are defined by a quantitative difference in the expression of these hallmarks and the tissues that are affected. Likewise, the difference between aging and

Dietary energy Dietary calories Nutrient-sensing pathways AMPK SIRT1 mTOR Insulin/IGF-1 FGF21 Key downstream proteins ATG FOXO PGC1A S6K Fundamental cellular functions influenced by diet and aging Autophagosome autophagy proteostasis Nucleus regulation transcription FIGURE 488-7 Nutrient sensing pathways. The main molecular switches that respond to changes in dietary intake (blue boxes: insulin/IGF-1, mTOR, AMPK, SIRT1, FGF21) influence a range of downstream intermediaries (some of these are shown in the gray boxes). These regulate key cellular processes (white boxes) including metabolism, autophagy, mitochondria, and protein synthesis. disease in terms of the clinical features is often based on quantitative differences. Therefore, there is a

continuum between aging and many chronic diseases. These are often separated by so-called “prediseases” or “subclinical diseases,” which are evidence for this continuum. Then, chronic disease can be considered a manifestation of aging that is predominant in a particular tissue. The presence of several chronic dis eases, termed multimorbidity, represents aging changes that are more advanced in several tissues. Frailty can be defined as a multisystem aging syndrome where aging changes are present in most tissues, lead ing to multiple deficits and impaired function. STRATEGIES THANT INCREASE HEALTH SPAN AND DELAY AGING Aging is an intrinsic feature of human life whose manipulation has fas cinated humans ever since becoming conscious of their existence. Sev eral long-term experimental interventions (e.g., resveratrol, rapamycin, spermidine, and metformin) may open doors for pharmacologic strate gies. Surprisingly, most of the effective aging interventions proposed to date converge on only a few molecular pathways: nutrient signaling, mitochondrial proteostasis, and the autophagic machinery. Lifespan is inevitably accompanied by a gradual functional decline, steady increase of several chronic diseases, and ultimately death. For millennia, it has been a dream of mankind to prolong both lifespan and health span. Developed countries have profited from advances in medical care and technology, improvements in their public health care systems, and better living conditions derived from their socioeconomic power—to achieve remarkable increases in life expectancy during the past century. In the United States, the percentage of the population aged ≥65 is projected to increase from 13% in 2010 to 19.3% in 2030. However, old age remains the leading risk factor for major life-threatening disorders. The number of people suffering from age-related diseases is anticipated to almost double over the next two decades. The prevalence of age-related pathologies represents a major threat and an economic burden that urgently needs effective interventions. Molecules, drugs, and other interventions that might decelerate aging processes continue to be a major focus among the general public and scientists of all biological and medical fields. Over the past three decades, this interest has taken root because many of the molecular mechanisms underlying aging are interconnected and linked with pathways that cause diseases, including cancer and cardiovascular and neurodegenerative disorders. Unfortunately, results often lack reproducibility because of the unavoidable problem of the time needed to assess the effectiveness of antiaging interventions in mammals. Experiments lasting the lifetime of animal models are prone to develop

CHAPTER 488 Endoplasmic reticulum protein synthesis Cytoplasm metabolism of fats and carbohydrates Mitochondria ATP synthesis Biology of Aging artifacts, increasing the possibilities and time windows for experimen tal discrepancies. Some inconsistencies in the field arise from over interpreting the results of animal models with shortened lifespan and scenarios of accelerated aging. Molecules, drugs, and other interventions have been proposed to have antiaging properties throughout history and into the present. In the following sections, interventions will be restricted to those that meet the following highly selective criteria: (1) promotion of lifespan and/or health span, (2) validation in at least three model organisms, and (3) confirmation by at least three different laboratories. These include CR and intermittent fasting regimens, some pharmacotherapies (resve ratrol, rapamycin, spermidine, and metformin), and exercise. ■ ■CALORIC RESTRICTION One of the most important and robust interventions that delays aging is CR. This outcome has been recorded in rodents, dogs, worms, flies, yeasts, monkeys, and prokaryotes. CR is defined as a reduction in the total caloric intake, usually of ~30%, and without malnutrition. CR reduces the nutrient-mediated release of growth factors, such as GH, insulin, and IGF-1, which have been shown to accelerate aging and enhance the probability for mortality in many organisms. Yet, the effects of CR on aging were first discovered by McCay in 1935, long before the discovery of these

hormones and growth factors and sig naling properties. Some of the pathways that mediate this remarkable response of CR have been elucidated in experimental models. These include the nutrient-sensing pathways (mTOR, AMPK, insulin/IGF-1, and sirtuins) and the family of FOXO transcription factors (orthologs are found in D. melanogaster and C. elegans). The transcription factor Nrf2 appears to confer most of the anticancer properties of CR in mice, even though it is dispensable for lifespan extension. The effects of CR in monkeys have been assessed in two studies with different outcomes: one study observed prolonged life, while the other did not. In these monkey studies, there were key differences in the onset of the intervention, diet composition, feeding protocols, and genetic background that may explain this discordance. However, both studies confirmed that CR increases health span by reducing the risk for diabetes, cardiovascular disease, and cancer. In humans, CR is associated with extended lifespan and increased health span. This is most convincingly demonstrated in Okinawa, Japan, where one of the most long-lived human populations resides. In comparison to the rest of the Japanese population, Okinawan people usually com bine an above-average amount of daily exercise with a below-average food intake. However, when Okinawan families moved to Brazil, they adopted a Western lifestyle that affected both exercise and nutrition,

causing a rise in weight and a reduction in life expectancy by nearly two decades. In the Biosphere II project, volunteers lived together for 24 months undergoing an unforeseen severe CR that led to improve ments in insulin, blood sugar, glycated hemoglobin, cholesterol levels, and blood pressure—all outcomes that would be expected to benefit lifespan. CR changes many aspects of human aging that might influ ence lifespan such as the transcriptome, hormonal status (especially IGF-1 and thyroid hormones), oxidative stress, inflammation, mito chondrial function, glucose homeostasis, and cardiometabolic risk fac tors. Epigenetic modifications are also an emerging target for CR. The first clinical trial of CR in people at average weight (a body mass index between 20 and 25) started in 2007. The Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) included 143 adults between the ages of 21 and 50 years intending to reduce their caloric intake by 25% of their typical intake for 2 years; also included was a group of 75 people who remained on their normal diets and caloric intake. CALERIE has provided evidence for improvements to the quality of life, immune health, cardiometabolic integrity, liver function, and skeletal muscle quality, even though the participants only reached a moderate level of CR (11.9 ± 0.7%) over the 2-year span. CR in this clinical trial also led to a reduction in the rate of biological aging measured by a series of common clinical biomarkers of preservation of physiologic and functional integrity (e.g., liver enzymes, albumin, fast ing blood glucose, insulin, and blood pressure). At the molecular level, gene expression analyses in a subset of CALERIE participants indicate that CR induces the regulation of core longevity pathways linked to the preservation of mitochondrial function and stability, lowering chronic inflammation and reducing oxidative stress.

PART 18 Aging ■ ■PERIODIC FASTING It must be noted that maintaining CR while avoiding malnutrition over a long period of time is not only arduous in humans but also linked with substantial side effects. For instance, prolonged reduction of calorie intake may decrease fertility and libido, impair wound heal ing, reduce the potential to combat infections, and lead to amenorrhea and osteoporosis. How can CR be translated to humans in a socially and medically acceptable way? A whole series of periodic fasting regi mens are asserting themselves as suitable strategies, among them (1) the alternate-day fasting diet, (2) the “5:2” intermittent fasting diet, (3) a 48-h fast once or twice each month, and (4) daily time-restricted feeding (TRF). Periodic fasting is

psychologically more viable, lacks some of the negative side effects of CR, and is only accompanied by minimal weight loss. All these dietary interventions involve a substan tial reduction of caloric intake for a defined period and typically lead to an elevation of circulating ketone bodies during those low-calorie intake periods, illustrating the metabolic switch from the utilization of glucose as a fuel source to the use of fatty acids and ketone bodies. This metabolic shift results in a reduction in the respiratory exchange ratio (the ratio of carbon dioxide produced to oxygen consumed), indicating greater metabolic flexibility and energy production efficiency from use of fatty acids and ketone bodies. It is striking that many cultures implement periodic fasting rituals, for example, some Buddhists, Christians, Hindus, Jews, Muslims, and practitioners of African animistic religions. It could be speculated that a selective advantage of fasting versus nonfasting populations is con ferred by health-promoting attributes of religious routines that peri odically limit caloric intake. Indeed, several lines of evidence indicate that intermittent fasting regimens exert antiaging effects. For example, improved morbidity and longevity were observed among Spanish nursing home residents who underwent alternate-day fasting. Rats subjected to alternate-day fasting live up to 83% longer than control animals fed ad libitum, and even one 24-h fasting period every 4 days is sufficient to generate lifespan extension. Repeated fasting and eating cycles may circumvent the negative side effects of sustained CR. This strategy may even yield health ben efits despite overeating behavior during the nonfasting periods. In a landmark experiment, mice fed a high-fat diet in a time-restricted manner, i.e., with regular fasting breaks, showed reduced inflamma tion markers, did not develop fatty liver, and were slim in comparison

to mice fed ad libitum despite equivalent total calories consumed. From an evolutionary point of view, this kind of feeding pattern may reflect mammalian adaptation to food availability: overeating in times of nutrient availability (e.g., after a hunting success) and starvation in times of food scarcity. This is how some indigenous peoples who have avoided Western lifestyles live today; those who have been investigated show limited signs of age-induced diseases such as cancer, neurodegen eration, diabetes, cardiovascular disease, and hypertension. Fasting exerts beneficial effects on health span by minimizing the risk of developing age-related diseases, including hypertension, neu rodegeneration, cancer, and cardiovascular disease. The most effective and rapid repercussion of fasting is a reduction in hypertension. Two weeks of water-only fasting resulted in blood pressure <120/80 mmHg in 82% of subjects with borderline hypertension. Ten days of fasting cured all hypertensive patients who had been taking antihypertensive medication previously. Periodic fasting also dampens the consequences of many age-related neurodegenerative diseases in mouse models of Alzheimer’s disease, Parkinson’s disease, Huntington’s disease, and frontotemporal dementia, but not amyotrophic lateral sclerosis. Fasting cycles are as effective as chemotherapy against certain tumors in mice. When combined with chemotherapy, fasting protects mice against the negative side effects of chemotherapeutic drugs, while enhancing effi cacy against tumors. Combining fasting and chemotherapy rendered 20–60% mice cancer-free when inoculated with highly aggressive tumors like glioblastoma or pancreatic tumors, which have 100% mor tality even with chemotherapy. ■ ■PHARMACOLOGIC INTERVENTIONS TO

DELAY AGING AND INCREASE LIFESPAN Virtually all obese people know that stable weight reduction will lower their risk of cardiometabolic disease and enhance their overall survival, and yet only 20% of overweight individuals are able to lose 10% weight for a period of at least 1 year. Even in the most motivated people (e.g., the “Cronies” who deliberately attempt long-term CR to extend their

lives), long-term CR is extremely difficult to adhere to. Thus, much focus has been directed at the possibility of developing medicines that replicate the beneficial effects of CR but without the need for reducing food intake (“CR-mimetics,” Fig. 488-8). • Resveratrol. Resveratrol, an agonist of SIRT1, is a polyphenol that is found in grapes and red wine. The potential of resveratrol to pro mote lifespan was first identified in yeast, and it has gathered fame since, at least in part, because it has been suggested to be responsible for the so-called French paradox whereby wine reduces some of the cardiometabolic risks of a high-fat diet. Resveratrol has been reported to increase lifespan in many lower-order species such as yeast, fruit flies, worms, and fish, as well as mice on high-fat diets. In monkeys fed a diet high in sugar and fat, resveratrol had beneficial HO OH O HO O O OH N O O O O HO O O O OH Rapamycin Resveratrol NH NH H N NH2 NH2 H2N N H N Metformin Spermidine FIGURE 488-8 Chemical structure of four agents (resveratrol, rapamycin, spermidine, and metformin) that have been shown to delay aging in experimental animal models.

outcomes related to inflammation and cardiometabolic parameters. Some studies in humans have also shown improvements in car diometabolic function, while others have not. Studies in animals and humans reveal that resveratrol mimics some of the metabolic and gene expression changes of CR. In most experimental models, resveratrol induces beneficial health effects by suppressing inflam mation, oxidative damage, tumorigenesis, and immunomodulatory activities. Resveratrol also leads to improvements in mitochondrial function and protection against obesity, cancer, and cardiovascular dysfunction. • Rapamycin. Rapamycin, an inhibitor of mTOR, was originally dis covered on Easter Island (Rapa Nui, hence its name) as a bacterial secretion with antibiotic properties. Before its emergence in the antiaging arena, rapamycin was known as an immunosuppres sant and cancer chemotherapeutic in humans. Rapamycin extends lifespan in all organisms tested so far, including yeast, flies, worms, and mice. However, the potential utility of rapamycin in lifespan extension in humans is likely to be limited by adverse effects related to immunosuppression, impaired wound healing, proteinuria, and hypercholesterolemia, among others. An alternative strategy may be the implementation of intermittent rapamycin treatment, which was found to increase mouse lifespan. • Spermidine. Spermidine is a physiologic polyamine that induces autophagy-mediated lifespan extension in yeast, flies, and worms. Endogenous spermidine levels decrease during life in virtually all organisms including humans, with the remarkable exception of centenarians. Oral administration of spermidine or upregulation of bacterial polyamine production in the gut leads to lifespan extension in short-lived mouse models. The lifespan effects of spermidine are mediated through the inhibition of histone acetylases and the activa tion of autophagy genes, such as atg7, atg11, and atg15 (Morselli et al., 2009). Spermidine has also been found to have beneficial effects on neurodegeneration and cardioprotection through activa tion of autophagy. Spermidine supplementation is safe in humans and has been associated with positive effects on cognitive function of older adults and on blood pressure maintenance. • Metformin. Metformin, a biguanide first isolated from the French lilac, is widely used for the treatment of type 2 diabetes. Metformin decreases hepatic gluconeogenesis and increases insulin sensitiv ity. Other actions of metformin include AMPK activation, leading to mTOR inhibition and lower mitochondrial complex I activity, and activation of the transcription factor SKN-1/Nrf2. Metformin increases lifespan in different mouse strains including female mice predisposed to high incidence of mammary tumors. At a biochemi cal level, metformin supplementation is associated with reduced oxidative damage and inflammation and mimics some of the gene expression changes seen with CR. Based on experimental data on the positive outcomes in model organisms and the evidence emerging from epidemiologic studies, a clinical

trial known as TAME (Tar geting Aging with Metformin) has been initiated to assess whether metformin can delay the onset of age-related diseases beyond its effects on glucose metabolism. TAME is planning to enroll 3000 subjects, ages 65–79, in a multicenter trial in the United States. ■ ■EXERCISE AND PHYSICAL ACTIVITY In humans and animals, regular exercise reduces the risk of morbidity and mortality. Given the marked increase in cardiovascular disease in the elderly, the effects of exercise on human health may be even stronger than those seen in laboratory mice, as mice do not develop atherosclerosis and have a far lower incidence of age-related cardiovas cular disease. An increase in aerobic exercise capacity, which declines during aging, is associated with favorable effects on blood pressure, lipids, glucose tolerance, bone density, and depression in older people. Likewise, exercise training protects against aging disorders such as cardiovascular disease, diabetes mellitus, and osteoporosis. Exercise

is the only intervention that can prevent or even reverse sarcopenia (age-related muscle wasting). Even moderate or low levels of exercise (30-min walking per day) have significant protective effects in obese subjects. In older people, regular physical activity has been found to increase the length of stay in independent living.

While clearly promoting health and quality of life, regular exercise does not extend lifespan. Furthermore, the combination of exercise with CR has no additive effect on maximal lifespan in rodents. How ever, alternate-day fasting with exercise is more beneficial for muscle mass than either treatment alone. In nonobese humans, exercise com bined with CR has synergistic effects on insulin sensitivity and inflam mation. From an evolutionary perspective, the responses to hunger and exercise are linked: when food is scarce, increased activity is required to hunt and gather. ■ ■HORMESIS Paradoxically, the term hormesis describes the protective effects conferred by the exposure to low doses of stressors or toxins (or as Nietzsche stated, “What does not kill me makes me stronger”). Adap tive stress responses elicited by noxious agents (chemical, thermal, or radioactive) precondition an organism, rendering it resistant to subse quent higher and otherwise lethal doses of the same trigger. Hormetic stressors have been found to influence aging and lifespan, presumably by increasing cellular resilience to factors that might contribute to aging such as oxidative stress. CHAPTER 488 Biology of Aging Yeast cells that have been exposed to low doses oxidative stress exhibit a marked anti-stress-like response that inhibits death following exposure to lethal doses of oxidants. During ischemic preconditioning in humans, short periods of ischemia protect the brain and the heart against a more severe deprivation of oxygen and subsequent reper fusion-induced oxidative stress. Similarly, the lifelong and periodic exposure to various stressors can inhibit or retard the aging process. Consistent with this concept, heat or mild doses of oxidative stress can lead to lifespan extension in C. elegans. CR can also be considered as a type of hormetic stress that results in the activation of antistress transcription factors (e.g., Rim15, Gis1, and Msn2/Msn4 in yeast, Nrf2 and FOXO in mammals) that enhance the expression of free radical–scavenging factors and heat shock proteins. CONCLUSIONS Clinicians need to understand aging biology to better manage and care for the elderly. Moreover, strategies based on aging biology are needed that delay aging, reduce the onset of age-related disorders, and increase health span for future generations. Dietary interventions and drugs that act on nutrient-sensing pathways are being developed and, in some cases, are already being tested in humans. Well-controlled human clinical trials have started to recapitulate the preclinical evidence of intermittent fasting on obesity, diabetes mellitus, cardiovascular dis ease, cancers, and neurologic disorders. While most animal studies show that intermittent fasting improves health throughout the lifespan, most human

studies are focused on relatively short-term interventions over a few days or months. While intriguing, it remains to be seen whether people will be willing to maintain strict intermittent fasting regimens over long periods of time or if short-term clinical benefits can be obtained in combination with other therapeutic approaches. ■ ■FURTHER READING Ferrucci L et al: Measuring biological aging in humans: A quest. Aging Cell 19:e13080, 2020. Le Couteur DG, Thillainadesan J: What is an aging-related dis ease? An epidemiological perspective. J Gerontol A Biol Sci Med Sci 77:2168, 2022. López-Otín C et al: Hallmarks of aging: An expanding universe. Cell 186:243278, 2023. Morselli L et al: Autophagy mediates pharmacological life extension of spermidine and resveratrol. Aging 1:961, 2009.

02 - 489 Caring for the Geriatric Patient

489 Caring for the Geriatric Patient

Joseph G. Ouslander, Bernardo Reyes

Caring for the

Geriatric Patient DEMOGRAPHICS OF AGING AND

ITS IMPLICATIONS FOR CARE

OF OLDER ADULTS The United States and other countries will continue to experience a rapid increase in the number of older adults who seek health care. The most rapidly growing segment of the population in the United States and many other developed countries is those older than 80 (Fig. 489-1). According to the United Nations 2022 Aging Report, 1 in 6 people worldwide will be 65 years old or older by the year 2050. The sex and gender composition of the aging population around the world is also expected to change. Although females outlive males, an improvement in the survival of the oldest-old males could result in a more balanced gender distribution in the geriatric population in the future. PART 18 Aging In high-income countries, consumption of health care resources will be most affected by the shift in the age distribution of the population over the next several decades. The World Health Organization continues to work actively to raise awareness of the changes necessary in current health care systems beyond increments in their budgets. As life span increases, efforts should continue to focus on promoting healthy aging to reduce the burden of disability in health care systems all over the world. The geriatric population requires different approaches to care for several reasons. The wide variations seen in aging make it difficult to develop age-related guidelines for diagnosis and treatment. For example, acute illnesses are most often not treated in isolation but in the context of multiple comorbidities. Close to half of those older than 80 have three chronic conditions, and about one-third have four or more chronic conditions (Fig. 489-2). Functional disabilities are preva lent (Fig. 489-3), which require careful attention in the evaluation of the older patient, along with assessment of social support available for assistance when needed for independent and safe living. Effectively caring for the geriatric population requires consideration of several key principles:

1. Aging is not a disease; normal aging changes generally do not cause symptoms but do increase susceptibility to many diseases and con ditions due to diminished physiologic reserve.

Japan Italy United Kingdom United States China Mexico

Percentage of population 80+ years old

Years FIGURE 489-1 Percentage of the population age >80 years from 1950 to 2050 in representative nations. (Updated data available at: https://esa.un.org/unpd/wpp/Graphs/DemographicProfiles/. Accessed December 30, 2016.)

2. Medical conditions are commonly multiple (“multimorbidity”) and multifactorial in origin, requiring a comprehensive approach to evaluation and management.
3. Many potentially reversible and treatable conditions are underdi agnosed and underevaluated in this population, such as fall risk, urinary incontinence, and elder abuse and neglect; simple screen ing tools can help detect them.
4. Cognitive and affective disorders (e.g., mild cognitive impairment, dementia, depression, anxiety) are common and may be undiag nosed in early stages; simple screening tools can help detect them.
5. Iatrogenic illnesses are common, especially related to adverse drug reactions, immobility, and related deconditioning, as well as other complications.
6. Focus on functional ability and quality of life, as opposed to cure, are key goals of care.
7. Social history, social support, and patient preferences are critical to treating older people in a safe and person-centered manner.
8. Effective geriatric care requires multidisciplinary collaboration among many different disciplines.
9. Geriatric care is provided most commonly outside the hospital (e.g., outpatient clinics and offices, at home, in skilled nursing and assisted living settings), and attention to care transitions between settings is essential for effective care.
10. Ethical issues, palliative care, and end-of-life care are critical aspects of caring for the geriatric population. Another way to summarize key concepts of caring for older adults is using the “5M’s of geriatrics” (mentation, medication, mobility, multi complexity, and matters most) This framework organizes care of older adults in a person-centered manner instead of a disease-driven para digm. The intention of the 5M’s is to optimize the utilization of existing resources during the hospitalization of older adults, as well as to focus on key geriatric issues in all settings of care. At the core of the 5M’s is what matters most to the patient in terms of goals of care and everyday living (Fig. 489-4). Mobility is critical to individual function, quality of life, and fall risk, and ranges from the ability to move around the com munity to walking and transferring from a chair. Because mild cogni tive impairment, dementia, delirium, and depression are all common in older adults, mentation is a core area for geriatric assessment. Poly pharmacy and prescription of potentially inappropriate and harmful medications remain common; thus, careful medication reconciliation and consideration of deprescribing are core aspects of care for all older adults. Many older adults have complex clinical issues in more than one of the four M’s just discussed, as well as geriatric syndromes (e.g., falls, incontinence), thus focusing attention on multiple comorbidities and multicomplexity. In addition to these 5M’s, social determinants of health play a critical role in providing comprehensive care to older people. In this chapter, these key principles serve as the background for the clinical recommendations for managing older adults. The reader is referred to textbooks of

geriatric medicine for more details on each of the principles and the management of common diseases and condi tions in this population. FUNDAMENTALS OF GERIATRIC CARE ■ ■PERSON-CENTERED CARE Person-centered care is a critical concept in caring for older people because of the complexity of their medical, functional, and psychoso cial problems and, in many instances, the lack of rigorous data on the most effective strategies for caring for specific conditions in patients with multimorbidity. For almost any condition, from common disor ders such as hypertension and diabetes to geriatric syndromes such as fall risk and urinary incontinence, the answer to how best to treat medical conditions in an older patient is “it depends.” It depends not only on evidence-based medicine but also on careful weighing of many factors that can be important to individual older people. The American Geriatrics Society (AGS) identifies the following elements as key to person-centered care: (1) an individualized, goaloriented care plan based on the person’s preferences; (2) ongoing review of the person’s goals and care plan; (3) information sharing and

100% 90% Percentage in comorbidity groups 80% 70% 60% 50% 40% 30% 20% 10% 0% 65–69 70–74 75–79 80–84 85+ Age group (years) FIGURE 489-2 Prevalence of comorbidity by age group in persons ≥65 years old living in the United States and enrolled in Medicare Parts A and B in 1999. (From JL Wolff et al: Arch Intern Med 162:2269, 2002.) integrated communication; (4) education and training for providers and, when appropriate, the person and those important to the person; and (5) performance measurement and quality improvement using feedback from the person and caregivers. In everyday practice with complex older patients, it is essential to have a comprehensive approach that addresses medical conditions, geriatric syndromes, improving or maintaining function and independence, quality of life, comfort, and dignity. Several tools are available to assist in implementing evidence-based and person-centered care, including estimation of prognosis (e.g., “ePrognosis”) and “Choosing Wisely” recommendations from the AGS and AMDA—The Society for Post-Acute and Long-Term Care Medicine. Examples of these recommendations that are relevant to internal medicine practice are illustrated in Table 489-1. ■ ■COMPREHENSIVE GERIATRIC ASSESSMENT General Principles of Geriatric Assessment Comprehensive geriatric assessment addresses all of the components required for Medicare’s annual wellness visit and more. In addition to management of common medical conditions and syndromes in older people (see below), a series of screening questions can be useful as a “geriatric review of systems” in clinical practice because of the importance and high prevalence of functional impairments and disabilities, limited social support to assist with functional limitations, cognitive and affec tive disorders, and geriatric conditions that may go undetected and cause patient safety issues and complications (Table 489-2). Positive responses to one or more of the screening questions for each item should prompt consideration of further assessments, many of which can be accomplished using standard and validated tools available on the Internet, such as activities of daily living scales, depression scales, sleep questionnaires, and mental status examinations. One very useful component of the geriatric assessment is the foot exam. Improper footwear and foot deformities, especially painful ones, Independent living difficulty

Self-care difficulty

Ambulatory difficulty

Cognitive difficulty

Vision difficulty

Hearing difficulty

Any disability

FIGURE 489-3 Percentage of people age 65+ with various disabilities. (Source: U.S. Census Bureau, American Community Survey, 2013. Available at https://aoa.acl.gov/Aging_Statistics/Profile/2014/index.aspx. Accessed December 30, 2016.)

are a major cause of falling (see below). If a person is not wearing socks, this may be an indication they have difficulty putting them on due to hip arthritis or another condition. Inspection between the toes is important to detect poor hygiene and ulcers, especially in diabetics. Poorly trimmed and/or fungalinfected toenails suggest that the individual cannot trim their toenails, has no one to help them do it, and does not have access to a podiatrist or regular pedicures. Other unique aspects of comprehensive geriatric assessment are described below. Evaluation of Medical Decision-Making Capacity Key aspects of decision-making in older adults are illustrated in Fig. 489-5. Including the patient in the consent process for any treatment is the foundation of patient autonomy and person-centered care. Because aging is associated with an increasing potential to develop cognitive impairment, the determination of decision-making capacity is impor tant not only to protect the patients against potential abuse but also to preserve autonomy when possible and, when it is not, to ensure an appropriate surrogate decision-making process is followed. Assess ing for capacity is usually triggered by specific circumstances (e.g., the need for invasive diagnostic testing or surgery). Determination of decision-making capacity limited to medical circumstances should be differentiated from declaring a patient “incompetent” to make all decisions. Declaring someone incompetent is a legal definition and usually is reserved for court settings. Another caveat about evaluating decision-making capacity is distinguishing lack of capacity from poorly presented information, sensory impairment, language barriers, and/ or low level of literacy. Diversity in values and beliefs can influence the perception of capacity for different cultures. Moreover, clinicians should be aware of the possibility of undue influence where caregivers might have secondary gain (financial or other) from taking control over decision-making on behalf of an older adult. The clinician should corroborate that the patient has received all the necessary information, comprehends the information provided, and has no major auditory or visual impairments. For geriatric patients, it is important to determine if the patient uses hearing aids or prescription glasses and ensure they are available for their use. Processing speed can slow with age and should be considered while completing a capacity assessment. Lastly, an important determinant of capacity is the presence of acute illness that could produce a transient alteration of cognition. Therefore, if the decision-making is deferred to a surrogate, this should be limited to procedures and treatments that are needed urgently.

Number of chronic diseases Four or more Three Two One None Standard tests of cognitive function correlate poorly with the capacity to consent for specific interventions. Several standardized tools have been validated to determine decision-making capacity. The MacArthur Competence Assessment Tool–Treatment (MacCAT-T) is one of the

several resources for determining decision-making capac ity. It is a structured tool that has been validated, but it is lengthy and can be difficult to administer in some patients. The Capacity to Consent to Treatment Instrument (CCTI) is another tool that has been validated in patients with mild to moderate Alzheimer's disease. Evaluation of the Older Driver For many older adults in the United States, driving is essential for maintaining independence, and driving cessation is associated with nega tive outcomes including social isolation and depression. On the other hand, older adults are at higher risk of being involved in fatal crashes than younger counterparts, with up to a ninefold higher risk for those ≥85 years old. Older people should be routinely assessed for their driving status and whether they have been involved in motor vehicle crashes in addition to assessment for sensory, functional, and cognitive impairments that can make driving unsafe (Table 489-3). In

Mobility Mentation Matters Multicomplexity Medications FIGURE 489-4 The 5M's of geriatrics. addition to common geriatric conditions, several different types of drugs can impair various aspects of driving performance and should be carefully considered in older people who continue to drive, including antianxiety agents, narcotic analgesics, antipsychotics, anticonvulsants, and drugs with strong anticholinergic properties. PART 18 Aging Suspected driving impairment can be a source of conflict between the patient (who wants to maintain independence), the family (who may want their relative to continue driving due to lack of other trans portation, or may be concerned about their safety, or both), and the physician (who is concerned about all who are at risk from a car crash). These decisions involve liability since local governments might not require driving retesting for all older drivers, but in some states, physi cians are required to report older people who they believe are unsafe drivers. Evaluation of driving should be aimed to correct any reversible cause of losing driving skills, such as vision and hearing impairment. Although tests of executive function such as the Trails B have been associated with poor driving performance, no single screening test predicts unsafe driving. A combination of neuropsychological testing by a psychologist and on-road testing by a trained occupational therapist can provide the physician with essential input in making the difficult decision on driving cessation. The AGS and the U.S. Depart ment of Transportation's National Highway Traffic Safety Administra tion have updated the "Physician's Guide to Assessing and Counseling TABLE 489-1 Examples of Choosing Wisely Recommendations Helpful in Implementing Person-Centered Care in Complex Geriatric Patients • Don't recommend percutaneous feeding tubes in patients with advanced dementia; instead, offer oral assisted feeding. • Don't use antipsychotics as the first choice to treat behavioral and psychological symptoms of dementia. • Avoid using medications other than metformin to achieve hemoglobin A1c <7.5% in most older adults; moderate control is generally better. • Don't use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation, or delirium. • Don't use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present. • Don't prescribe cholinesterase inhibitors for dementia without periodic assessment for perceived cognitive benefits and adverse gastrointestinal effects. • Don't recommend screening for breast, colorectal, prostate, or lung cancer without considering life expectancy and the risks of testing, overdiagnosis, and overtreatment. • Don't routinely prescribe lipid-lowering medications in individuals with a limited life expectancy. • Don't obtain a Clostridioides difficile toxin test to confirm "cure" if symptoms have resolved. • Don't recommend aggressive or hospital-level care for a frail elder without a clear understanding of the individual's goals of care and the possible benefits and burdens. Source: Adapted from http://www.choosingwisely.org/societies/americangeriatrics-society/ and http://www.choosingwisely.org/societies/amda-the-societyfor-post-acute-and-long-

term-care-medicine/amda-choosing-wisely-list/. Accessed June 1, 2021.

Older Drivers," which can be helpful to practicing clinicians and is available on the AGS website. Interpretation of Diagnostic Tests Physiologic changes associ ated with aging can affect the results of some common diagnostic tests. The large variation of many physiologic measures that are associated with normal aging makes establishing what is "normal" for many tests challenging. For this reason, the results of several diagnostic tests must be interpreted cautiously. Ambulatory cardiac monitoring may identify a variety of arrhythmias in older adults. Such arrhythmias must be linked to symptoms or adverse outcomes if left untreated before considering the use of potentially toxic medications or invasive procedures. Advanced imaging also could demonstrate incidental abnormalities. Although a significant portion of these findings are benign, the rate of malignancy among incidental findings in the colon and extracolonic structures, as well as ovarian and thyroid gland, is ~20%. Musculoskel etal imaging, such as magnetic resonance imaging (MRI) of the spine, may reveal multiple abnormalities that may or may not be related to symptoms. Unless further evaluation would not lead to a change in the goals of care and treatment plan, abnormal diagnostic tests require further evaluation in older patients. Examples include low hemoglobin levels, abnormal thyroid function tests, age-/sex-/weight-adjusted creatinine clearance, and elevated liver function tests. None of these abnormal findings are the result of normal aging and generally indicate the pres ence of a disorder that may or may not be reversible. ■ ■PREVENTION IN OLDER ADULTS Age-Appropriate Screening Screening tests for specific diseases, as opposed to screening for geriatric conditions, require a careful person-centered approach. The focus of preventive medicine depends heavily on the ability to identify those who are at risk for specific conditions, as well as the time to benefit from interventions when considering the individual's life expectancy (Chap. 6). Several profes sional societies have provided guidance regarding specific tests in older adults (Table 489-3). An important caveat about screening to prevent disease in older patients (e.g., colonoscopy for colon cancer, Pap smears, prostate-specific antigen testing) is that abnormal results may lead to subsequent testing and treatment among individuals who will not suffer morbidity or mortality from the disease because of limited life expectancy. Thus, geriatric patients pose a significant challenge in deciding what screening tests could offer a reasonable ratio of benefit and risk as well as being cost-effective. As an example, the U.S. Preven tive Services Task Force recommends colorectal cancer screening up to the age of 75 years. Due to the limited net benefit, for those between 76 and 85 years old, the recommendation is to only consider colonoscopy if they have never been screened and are healthy enough to undergo treatment if colon cancer is detected. Vaccinations The use of vaccines in older adults is aimed at creat ing immunity against common infections that could lead to serious complications and rebuilding previously obtained immunity. The U.S. Centers for Disease Control and Prevention (CDC) recommends routine vaccination against influenza, pneumococcus, and shingles as they are prevalent in this age group. CDC's recommendations on vac cination for COVID-19 and its variants, as well as respiratory syncytial virus, should be reviewed regularly because of frequent updates. Other countries in Europe and Asia have similar trends in vaccinations with small variances. Sexually Transmitted Diseases Although most sexually trans mitted diseases (STDs) occur in younger people (Chap. 141), some older adults do have high-risk sexual behavior. Most Americans remain sexually active in their 60s and 70s, and up to a quarter of individuals in their 80s consider themselves sexually active. Sexually active older adults may have a lower awareness of the need for safe sexual prac tices, such as the risks of multiple sexual partners and condom use. The incidence of STDs in older people is still relatively low. Nonethe less, patients presenting with

symptoms compatible with syphilis or

TABLE 489-2 Examples of Screening Questions and Tools and Strategies for Further Evaluation of Social Support, Functional Status, Geriatric Syndromes, and Cognition and Affect GERIATRIC ASSESSMENT DOMAINS RECOMMENDED SCREENS FURTHER ASSESSMENT FOR POSITIVE SCREEN Social Support Do you live alone? Do you have a caregiver? Are you a caregiver? Elder Neglect/Abuse Do you ever feel unsafe where you live? Has anyone ever threatened or hurt you? Has anyone been taking your money without your permission? SOCIAL Advance Directives Would you like information or forms for a power of attorney for health care? Would you like information on a living will? Functional Status Do you need assistance with shopping or finances? Do you need assistance with bathing or taking a shower? Driving Do you still drive? If yes: While driving, have you had an accident in the past

6 months? Driving concerns by family member? FUNCTIONAL Vision Do you have trouble seeing, reading, or watching TV? (with glasses, if used) Hearing Do you have difficulty hearing conversation in a quiet room? Unable to hear whisper test 6 inches away? Medications Do you take five or more routine medications? Do you understand the reason for each of your medications? Fall Risk Have you fallen in the past year? Are you afraid of falling? Do you have trouble climbing stairs or rising from chairs? GERIATRIC SYNDROMES Continence Do you have any trouble with your bladder? Do you lose urine or stool when you do not want to? Do you wear pads or adult diapers? Weight Loss Weight <100 pounds or Unintentional weight loss ≥10 pounds over 6 months? Sleep Do you often feel sleepy during the day? Do you have difficulty falling asleep at night? Pain Are you experiencing pain or discomfort? • Pain assessment Alcohol Abuse Do you drink >2 drinks/day? • AUDIT-C Depression Do you often feel sad or depressed? Have you lost pleasure in doing things over the past few months? COGNITION AND AFFECT Cognition Self-reported memory loss? Cognitive screen positive? (three-item recall and Clock Draw test “Mini-Cog”) Confusion Assessment (CAM) for delirium Abbreviations: 3IQ, Three Incontinence Questions; AUA, American Urological Association; AUDIT-C, Alcohol Use Disorders Identification Test; MOLST, Medical Orders for Life-Sustaining Treatment; PHQ, Patient Health Questionnaire; POST, Physician Orders for Scope of Treatment. Source: Adapted from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2017. gonococcal infection (cervicitis, urethritis, proctitis, epididymitis) should be screened for high-risk sexual behavior and educated if necessary. Clinical symptoms of herpes simplex infection and the pos sibility of becoming contagious also decrease with age. As ulcerative lesions are less frequent, herpes simplex virus 2–specific serologic testing should be considered for patients with recurrent nonspecific genital symptoms. Therapy should not be started unless the patients are symptomatic. In the United States alone, 450 per 100,000 persons above the age of 55 are infected with HIV. Since the introduction of highly active antiretroviral therapy, the life expectancy of patients with HIV has increased, resulting in a significant increase in the number of older adults living with the disease. De novo infections have also contributed

• Consider referral to a social worker • Refer to area agency on aging • Consider referral to a social worker and/or adult protective services • Discussion on advance directives • Physician Orders for Life-Sustaining Treatment (POLST) (or MOLST or POST) • Instrumental Activities of Daily Living (ADL) Scale • Basic ADL Scale CHAPTER 489 • Vision testing • Consider occupational therapy and/or formal driving evaluation • Vision testing • Consider referral for eye exam Caring for the Geriatric Patient • Check for cerumen in ear canals and remove if impacted • Hearing Handicap

Inventory • Consider audiology referral • Match medications with diagnoses • Consider reducing doses, stopping drugs, adherence aides, and/or consultation with a pharmacist • “Get Up and Go” test • Consider full fall assessment • Consider physical therapy evaluation • Consider home safety assessment • Consider full continence assessment • 3IQ Questionnaire (women) • AUA 7 symptom inventory (men) • Assess for common risk factors for malnutrition • Consider referral to dietician for nutritional evaluation • Epworth Sleepiness Scale or Pittsburgh Sleep Index • Consider referral for sleep evaluation • PHQ-9 or Geriatric Depression Scale • Screen for suicide risk • Montreal Cognitive Assessment or Mini Mental State Examination • If diagnosis is unclear, consider neuropsychological testing to the rising number of HIV cases in older adults. See Chap. 208 for details on HIV infection. TREATMENT OF COMMON DISEASES

IN THE GERIATRIC POPULATION ■ ■HYPERTENSION In the United States, 70% of older adults have hypertension. Several clinical trials have demonstrated the benefits of hypertension treatment on risk reduction of cardiovascular events in older people. Nonetheless, blood pressure targets remain controversial. The balance between the cardiovascular protective benefits versus the risk of treatment-related adverse events must be considered in individual patients based on their

Structure – Accessibility, setting – Availability, quality of relevant support services (interpreter, social work) – Decision support and resources available, at appropriate health literacy level Process – Characteristics of provider- patient relationship, interaction – Continuity of care – Provider decision-making style, communication methods, skills – Provider experience, education, cross-cultural training, sensitivity – Patient prior experiences with health care, decision making Provider Trustworthiness PART 18 Aging Patient/surrogate Competence Communication with Patients and Families External variables – Illness characteristics – Access to care – Insurance coverage, reimbursement – Patient beliefs, approach to decision-making – Family structure, social support – Patient motivation, self- efficacy – Provider specialty, setting – Provider and patient knowledge, expectations FIGURE 489-5 Key aspects of decision-making in older adults. (Reproduced with permission from SM Dy, TS Purnell: Key concepts relevant to quality of complex and shared decision-making in health care: A literature review. Soc Sci Med 74:582, 2012.) comorbidities and level of function. For example, hypotension and postural hypotension related to antihypertensive therapy are common causes of syncope, falls, and related injuries in the geriatric population, especially those with multimorbidity. In addition to cardiovascular disease prevention, control of systolic blood pressure (SBP) may reduce the burden of white matter changes in the brain, which are associated with gait abnormalities and cognitive decline. A secondary analysis of the SPRINT trial (see below) suggests that intensive treatment of sys tolic blood pressure might reduce the risk of dementia and mild cogni tive impairment (MCI) among those at higher risk for such conditions. The European Society of Cardiology/European Society of Hyperten sion guidelines recommend pharmacologic treatment for individuals 80 years old or older if SBP is 160 mmHg or higher. In contrast, the American College of Physicians recommends starting treatment if SBP is 150 mmHg or higher. Two large studies (HYVET and SPRINT) have shed some light on these issues. HYVET was a multicenter study conducted in sev eral countries involving ~3800 patients ≥80 years old. The study demonstrated that active treatment of hypertension with a target of

≤150 mmHg significantly reduced not only the risk of stroke and heart failure but also the mortality risk. As with other large hypertension studies like ALLHAT, a linear association was noted between blood pressure and stroke reduction. Nonetheless, in the HYVET study,

Concepts Provider Competence Outcomes – Appropriate, informed, timely decision-making – Treatment adherence – Health status – Satisfaction and values-based health outcomes Cultural Competence Information Quality Roles and Involvement this association was less prominent as age increased. SPRINT was another large randomized trial targeting lowering SBP to targets of <140 versus 120 mmHg (measured with an automated device) with a subgroup analysis in those aged 75 and older. Significant reductions were documented in the primary endpoint, which was a composite of cardiovascular disease events (including myocardial infarction, acute coronary syndrome, heart failure, stroke, or death from cardiovascular causes). However, it is critical to recognize that patients with diabetes, a history of stroke or heart failure, SBP <110 mmHg after 1 min of stand ing, as well as people with several other comorbidities, were excluded from the SPRINT trial, and aggressive treatment in the setting of these comorbidities may incur more risk of adverse effects. In addition, the reduction in adverse outcomes detected during the study was not observed long term. Overall, these data strongly suggest a person-centered approach to hypertension in the heterogeneous older population. For older patients with minimal comorbidity, no postural hypotension, and low risk of falls and volume depletion, the benefit-risk ratio favors lower targets for SBP (<130 mmHg measured by a hand sphygmomanom eter). Aggressive targets also may be more beneficial for patients with concomitant nonvalvular atrial fibrillation or coronary artery disease. However, for those with diabetes, heart failure, or postural hypotension, treatment of hypertension with higher SBP targets (e.g., <150 mmHg)

TABLE 489-3 Recommendations for Primary Prevention Screening for Specific Diseases in Older Adults from Different Professional Societies TYPE OF SCREENING TEST FREQUENCY USPSTFa ACSb ACPc Colorectal Fecal occult blood test or fecal immunochemical test (FIT) or Sigmoidoscopy or Colonoscopy Annual Every 5 y Every 10 y Screen all adults age 50–75; prognosis may support screening individuals of age 76–85 if never screened; not recommended for adults over age 85 Breast Mammography Every 1–2 y Biennial screening of all women age 50–74; evidence of benefits and harms is insufficient for women age >75 Cervical Pap smear HPV test Pap only, every 3 y HPV + Pap, every 5 y Screen women age 21–65; discontinue at age 65 if adequate prior screening Lung Low-dose CT scan Annual Screen age 55–80 current and former smokers with a 30+ pack-year smoking history; discontinue screening once a person has not smoked for 15 years or develops a health problem that limits their ability or willingness to have curative surgery Prostate Prostate-specific antigen (PSA) 1–2 y Do not screen men for prostate cancer with PSA if age 70 y or older Osteoporosis Dual-energy x-ray absorptiometry (DEXA) Measure height, preferably with a wallmounted stadiometer Perform bone mineral density testing

1–2 y after initiating medical therapy for osteoporosis and every 2 y annually thereafter USPSTFa NOFg Screen women age 65; the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men Carotid disease Carotid ultrasound Once SOCIETY OF VASCULAR SURGERY Age over 65, coronary artery disease, need for coronary bypass, symptomatic lower extremity arterial occlusive disease, history of tobacco use, and high cholesterol would be appropriate risk factors to prompt ultrasound in patients with a bruit Coronary artery disease (CAD) Coronary calcium score (CCS) Once SCCTh AHA/ACCi Do not use CCS for patients with known CAD Abdominal aortic aneurysm Abdominal ultrasound Once USPSTFa AAFPj The USPSTF recommends one-time screening for abdominal aortic aneurysm with ultrasonography in men aged 65–75 y who have ever smoked; there is insufficient evidence to recommend screening for women even if they have ever smoked Diabetes Fasting

blood glucose, glucose tolerance test, or hemoglobin A1c Annually USPSTFa ADAk No evidence to screen for diabetes after the age of 70; recommendation being reviewed at the time of this publication aU.S. Prevention Services Task Force. bAmerican Cancer Society. cAmerican College of Physicians. dEastern Cooperative Oncology Group. eAmerican College of Chest Physicians. fAmerican Urology Association. gNational Osteoporosis Foundation. hSociety of Computed Tomography. iAmerican Heart Association/American College of Cardiology. jAmerican Academy of Family Physicians. kAmerican Diabetes Association. Abbreviation: CT, computed tomography.

PROFESSIONAL SOCIETY ISSUING RECOMMENDATIONS Screen all adults age >50; discontinuing screening is reasonable in people with severe comorbidity that would preclude treatment Screen all adults age 50–75 People with life expectancy <10 y should not be screened Annual screening starting at age 40; continue while in good health ECOGd Annual screening starting at age 40 y Screen women age 21–65; discontinue at age 65; discontinue at age 65 if regular screening normal Screening should stop at age 65 if evidence of negative adequate prior screening CHAPTER 489 Screen 55–74-y-old current and former smokers in good health with a 30+ pack-year smoking history ACCPe In settings that can deliver the comprehensive care provided to National Lung Screening Trial participants, offer screening to people age 55–74 who are current and former smokers with 30+ pack-year smoking history Caring for the Geriatric Patient Screen men age 50 and over with a life expectancy >10 y after discussion about the risks, benefits, and uncertainties of PSA screening Follow-up screening should occur annually if PSA >2.5 ng/mL or biennially if PSA

<2.5 ng/mL AUAf Biennial PSA screening in men age 55–69 y with life expectancy >10–15 y, after shared decision-making discussions accounting for values and preferences Screen women age 65 and older and men age 70 and older; postmenopausal women and men age 50–69, based on risk factor profile; postmenopausal women and men age 50 and older who have had an adult-age fracture CCS of 0 may have a strong negative predictive value for coronary events in older adults Recommended for men aged 65–75 y who have ever smoked Screen people 45 y and older

is probably a safer approach. In addition to diet, exercise, and sodium restriction, specific pharmacologic approaches most often depend on co-occurring conditions, such as coronary artery disease, heart failure, and atrial fibrillation (see Chap. 288).

■ ■DIABETES The prevalence of type 2 diabetes in the older adult population is now

> “ 25% and is expected to increase due to adverse lifestyle changes and an increased incidence of obesity. In addition, advances in the care for type 1 diabetes have increased the number of individuals living beyond the age of 64 with this chronic illness. Those between the ages of 65 and 74 have the highest rates of com plications associated with diabetes. However, older diabetic patients are at significant risk of hypoglycemia because of potential medication errors, progressive renal insufficiency, and inconsistent oral intake. Diabetic patients age 75 or older have twice the risk of visiting the emergency department due to hypoglycemia. Hypoglycemic episodes are associated with progressive cognitive decline in older adults, espe cially those with existing

cognitive impairment. On the other hand, chronically uncontrolled diabetes is associated with an increased risk of all-cause dementia. PART 18 Aging Data from randomized clinical trials suggest that intensive glycemic control does not reduce major macrovascular events in older adults. Thus, the AGS guideline on diabetes in older adults (see “Further Readings”) and the Choosing Wisely recommendations (Table 489-1) suggest that, in most older adults, the harms associated with a hemo globin A1c (HbA1c) target <7.5% are likely to outweigh the benefits. These recommendations are consistent with the American Diabetes Association guidelines from 2023 that recommend an HbA1c target of 7 or 7.5% for older adults with intact cognition and functional capacity and few comorbidities. The goals of treating diabetes in the geriatric population should be tailored to the patient’s functional status, coexist ing geriatric syndromes, social support, personal goals, perception of risk, and life expectancy. Insulin should be avoided when possible, and in particular, long-term use of sliding-scale insulin should be avoided because of the relatively high incidence of hypoglycemia, the challenges and discomforts of repeated glucose measurements, and the high bur den it can place on caregivers. For those who do requires insulin, the use of continuous glucose monitoring may be useful. For specifics of treatment options, see Table 489-4 and Chap. 416. Regardless of the therapeutic goals for HbA1c, older diabetic patients should be regularly examined for neuropathy and retinopathy. Neuropathy can lead to unhealing foot lesions and other podiatric conditions. Retinopathy can lead to vision loss and require ophthalmo logic intervention. In addition, lifestyle management is an important component of the plan of care. Diabetic older adults should exercise regularly to the extent possible and should have an adequate protein intake to try to maintain muscle mass. ■ ■HYPERLIPIDEMIA While good evidence exists regarding the benefits of statins for second ary prevention among those ≥75 years old, the use of these medications for primary prevention has been controversial. The use of statins in those older than 75 or 80 for primary prevention of cardiovascular events and mortality is the subject of ongoing debate in the geriatric literature. Secondary analyses of large clinical trials have demonstrated primary prevention and disability-free survival benefits with statin use among selected subgroups of older adults. Two other factors make the use of statins in older adults controversial. First, the major benefits have been demonstrated over long-term use; thus, life expectancy is a limiting factor for meaningful change in outcomes. Second, although many older adults on statins complain of muscle pain, the risk of myo sitis and rhabdomyolysis is increased mostly with the coexistence of other risk factors. On the other hand, statins are safe to use in older adults, especially at moderate to low doses. Adverse effects of statins on cognitive func tion appear to be uncommon. Relatively healthy adults older than 75 with a life expectancy of >10 years may benefit from statin use, and the approach to hyperlipidemia should be person-centered in

TABLE 489-4 Recommendations and Considerations for Pharmacologic Therapy of Diabetes in Older Adults MEDICATION RECOMMENDATIONS AND CONSIDERATIONS Metformin • Metformin is the first-line agent for older adults with type 2 diabetes • Low risk of hypoglycemia • Recent studies suggest it may be used safely in patients with estimated glomerular filtration rate ≥30 mL/min/1.73 m2 • Use with caution in patients with advanced renal insufficiency or significant heart failure • Can cause gastrointestinal symptoms with lower appetite Sodium-glucose cotransporter 2 (SGLT-2) inhibitors • Offer an oral route, which may be convenient for older adults • Low risk of hypoglycemia and hypotension • Strong evidence for renal protection and improved outcomes among patients with congestive heart failure • Caution when combined with other therapies such as diuretics Thiazolidinediones • If used at all, should be used very cautiously in those with, or at risk for, congestive heart failure and those at risk for falls or fractures Sulfonylureas • Associated with hypoglycemia and should be used with caution • Shorter-duration sulfonylureas such as glipizide are preferred • Leads to severe and persistent hypoglycemia in the settings of acute kidney injury • Glyburide is longer duration and contraindicated in older adults Dipeptidyl peptidase 4 (DPP-4) inhibitors • Few side effects and minimal hypoglycemia, but costs may be a barrier • No evidence of increase in major adverse cardiovascular events Glucagon-like peptide 1 (GLP-1) agonist • GLP-1 receptor agonists are injectable, which requires visual, motor, and cognitive skills • Associated with nausea, vomiting, diarrhea, and weight loss, which may not be desirable in some older patients, particularly those with cachexia Insulin therapy • Use oral medications whenever possible • Administration requires that patients or their caregivers have good visual and motor skills and cognitive ability • Insulin doses should be titrated to meet individualized glycemic targets and to avoid hypoglycemia • Once-daily basal insulin injection therapy is associated with minimal side effects and may be a reasonable option in many older patients • Multiple daily injections of insulin may be too complex for the older patient with advanced diabetes complications, life-limiting comorbid illnesses, or limited functional status • Avoid sliding scale in postacute and long-term care facilities except during periods of instability associated with acute illness; risk of hypoglycemia is high; glucose checks, insulin administration, and documentation require excessive staff time, and most patients do not like frequent fingersticks Source: Based on recommendations from the American Diabetes Association 2020 and JS Custódio et al: Drugs Aging 37:399, 2020. this population, as discussed for both hypertension and diabetes. In addition, current scientific evidence supports the use of moderate- to high-dose statins in older adults after an acute cardiovascular event (myocardial infarction, stroke) to prevent a recurrence. Even among cognitively and functionally impaired adults, another event could cause further impairment that interferes with function and quality of life. This is not true, however, for individuals at the end of life. A substantial proportion of older people (close to a third) are maintained on statins at the end of life. In a pragmatic clinical trial including older adults

with a life expectancy of up to 1 year taking statin discontinuation was associated with improved quality of life and reduction of polypharmacy burden without increased risk of cardiovascular complications. Thus, discontinuation of statins in this situation is strongly recommended. ■ ■OSTEOARTHRITIS AND CHRONIC PAIN By far, the most common cause of chronic pain in older people is osteoarthritis (OA). The approach to the management of symptomatic OA in older people differs from the approach in younger patients (Chaps. 382 and 383) because of the substantial toxicity of nonsteroi dal anti-inflammatory drugs (NSAIDs) in this population. Nonphar macologic interventions, briefly discussed below, should be the first line of treatment. While some patients older than 65 can tolerate NSAID use with concomitant protection from gastrointestinal (GI)

bleeding with a proton pump inhibitor (PPI), this regimen exposes patients to two drugs with numerous potential adverse drug effects. NSAIDs are well known to be associated not only with GI bleeding but also with wors ening renal function as well as fluid retention, hypertension, and exac erbation congestive heart failure. In addition, a substantial number of older patients are on anticoagulants or platelet aggregation inhibitors, which could further increase the risk of bleeding from NSAIDs. PPIs are associated with a higher incidence of pneumonia, osteoporosis, and Clostridioides difficile–associated diarrhea, and they may be associated with a higher risk of dementia. Thus, in older patients with multimorbidity who have painful OA, the risks of NSAIDs most often outweigh the benefits, and older patients should be discouraged from taking nonprescription NSAIDs without consulting their primary care clinician. Topical NSAIDs are better tolerated, and 4 or 5% lidocaine patches and other nonpre scription analgesic creams (e.g., 1% diclofenac) may also be effective. Acetaminophen in doses of 1 g 2–3 times daily should be the basis of pharmacologic treatment. Failure to respond could be followed up with careful trials of tramadol or a narcotic agent (started in a short-acting preparation) with appropriate attention to avoiding narcotic-induced constipation. Tramadol has less addiction potential and side effects than more potent narcotics and can be very effective for some older people. However, it is contraindicated in patients with seizure disorders and must be used cautiously with selective serotonin reuptake inhibi tor and serotonin-norepinephrine reuptake inhibitor drugs to prevent serotonergic toxicity. Another pharmacologic option that can be very useful in older people with primary or secondary muscular pain due to an arthritic condition, especially those with dysphoria or depres sion (common in people with chronic pain), is a trial of duloxetine. Duloxetine is approved for the treatment of depression as well as pain, but it must be started in low doses (e.g., 20 mg) and titrated up to a maximum of 60 mg, if needed, over several weeks. Although the prescription of narcotics is getting increasingly cum bersome because of high rates of abuse, this should not deter the pre scription of these agents to relieve pain and disability in older patients, especially postsurgical pain. If opioids are prescribed, a bowel regimen consisting of adequate fluid, a bulk-forming agent, and use a stimulant such as senna or polyethylene glycol is highly recommended for people who have not had a movement to avoid severe constipation. Note that although docusate is often prescribed, its efficacy is highly variable. In addition, as in any other population, there should be close monitoring of issues such as diversion and abuse or addiction. Many older patients respond well to various nonpharmacologic interventions, including stretching, strengthening, timely and appro priate use of heat and ice, massage (including the use of “massage guns”), swimming and whirlpool therapy, bracing, acupuncture, and therapeutic electrical stimulation These interventions are best carried out under the supervision of physical therapists or other professionals with appropriate expertise to avoid injury. Although now frequently offered by telehealth, they will not be optimally effective unless a trained therapist teaches the technique and assesses its proper use periodically in person. Surgical interventions, including replacement of major joints, have improved over the past several years, and even older patients with multimorbidity may benefit in terms of function and quality of life. Total knee replacement, for example, is effective in

generally healthy older patients and should be considered in selected higher-risk patients. “Pre-habilitation,” with targeted strengthening and endurance exercises, and willingness to go through several weeks of postoperative physical therapy should be prerequisites for referring older patients for joint replacement.

■ ■CANCER More than half of new cases of cancer and mortality associated with it occur after the age of 65. Data regarding older adults with multiple comorbid conditions and their response to cancer treatment are lim ited. While only ~10% of clinical trials have had age-stratification analyses, the available evidence suggests that age alone is not a predic tor of harm. Nonetheless, making treatment decisions is challenging due to both shorter life expectancy in older adults and the cumulative effect of multiple comorbidities. Thus, a person-centered approach that integrates the principles of geriatric and palliative care is essential. Older adults generally experience decreases in functional status after receiving chemotherapy. Most of this negative effect appears to be related to comorbidity and baseline functional status, rather than due to age alone. For this reason, specialists in geriatric oncology have proposed using comprehensive geriatric assessment, covering many of the issues addressed in Table 489-3, as a strategy to better predict which older adults will tolerate and benefit most from cancer treatment. Tools such as the Chemotherapy Risk Assessment Scale for High-Age Patients have been validated to estimate the risk of chemotoxicity. Lack of social support has been associated with poor outcomes after radia tion and chemotherapy, especially in older women. Other important issues in cancer treatment planning include the availability of transpor tation for treatments, economic and insurance status, the patient’s abil ity to follow treatment plans, and family and social support available during therapy, when adverse effects and functional decline may occur. CHAPTER 489 Caring for the Geriatric Patient Newer treatment options such as immunotherapy have shown promising results in the general population with lung and bladder cancer as well as lymphomas. Unfortunately, older adults are under represented in clinical trials using these agents, and there is a lack of robust evidence regarding tolerability and efficacy. ■ ■ANEMIA Low hemoglobin or hematocrit is common in older adults but is not a normal age-related change. All anemic older adults should have a basic evaluation including a complete blood count, examination of a periph eral red blood cell smear, reticulocyte count, and measurement of iron, iron-binding capacity, and transferrin saturation. A serum ferritin level can help distinguish iron deficiency anemia from the anemia of chronic disease, two common forms of anemia in older adults. Iron deficiency is the most common cause of anemia in the older population, with other nutritional anemias (e.g., B12 deficiency) and myelodysplasia each accounting for a smaller percentage. Anemia of chronic disease is common in older people who have several chronic illnesses. The etiol ogy of the anemia in older adults cannot be specifically explained in more than a third of the cases, and this unexplained anemia is generally normocytic, mild in degree, with a low reticulocyte count, and associ ated with normal or low erythropoietin levels in the face of inadequate production of new red cells. Anemia is frequently asymptomatic, but severe cases could present with symptoms such as generalized weak ness and functional decline, shortness of breath, chest pain, or syncope. The unexplained anemia of aging appears to be responsive to erythro poietin, but it is unclear whether correction of the anemia improves outcomes. Thresholds for transfusion of packed red cells among older adults should be based on symptoms and associated conditions. For example, for geriatric patients suffering acute blood loss anemia after an orthopedic procedure, transfusion is indicated when hemoglobin is <8 mg/dL (instead of 7 mg/dL). Similarly, older patients with active cardiovascular disease, such as angina or heart failure, may need to be transfused at levels <8 or 9 mg/dL. For details of the general evaluation and management of anemia, please refer to Chap. 66. ■ ■HEART FAILURE Although the incidence of heart failure (HF) has decreased over the years, the prevalence has seen an uptrend. This paradoxical

epidemiologic trend is explained by longer survival. As many as 20% of individuals ≥80 years old carry a diagnosis of HF, with two-thirds of those having preserved ejection fraction. The management of HF is discussed in detail in Chaps. 264 and 265. The treatment of HF in frail older adults depends on cardiac ejection fraction (preserved vs reduced) and is limited by tolerability of low-sodium diets, fluid restriction, and adverse effects of medication. Medications such as diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers may be poorly tolerated due to hypotension, electrolyte imbalances, volume depletion, and orthostatic hypotension. Newer therapies such as angiotensin receptor–neprilysin inhibitors, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter 2 inhibitors (SGLT2i) have been shown to improve out comes in older adults with specific types of HF. Thus, echocardiogra phy to check ejection fraction is essential in the management of older people with HF. In contrast with other chronic disease processes, older adults have been well represented in clinical trials with these newer agents, allowing multiple subanalyses that have proven efficacy.

PART 18 Aging GERIATRIC SYNDROMES AND CONDITIONS In this section, selected geriatric syndromes and conditions likely to be encountered by internists in hospitals, clinics, and postacute and longterm care (LTC) settings are discussed. For a more thorough discussion of these and other syndromes and conditions, the reader is referred to textbooks that focus specifically on geriatrics and gerontology (see “Further Reading”). ■ ■FALLS Epidemiology and Impact Among all geriatric syndromes, falls are probably the most common that internists will encounter. Falls are responsible for potentially devastating consequences for function and quality of life, as well as mortality. About one in three older communitydwelling and one in two older LTC facility residents fall annually, with many more at risk for falls. The consequences of falls include fear of falling with adverse effects on quality of life, painful injuries includ ing hip and wrist fractures, subdural hematomas, and death. Falls are associated with loss of function and death within the year after a fall. With the increasing prescription of anticoagulants, falling presents a frequent conundrum in balancing the risks and benefits of anticoagula tion. For these reasons, internists should regularly screen older people for falling using questions such as, “Have you fallen in the past year?” “Are you afraid of falling?” “Do you have trouble climbing stairs or ris ing from chairs?” (Table 489-2). Evaluation The risks and causes of falls are multifactorial. Most older people at risk for a fall or who have suffered a fall have more than one potential underlying risk factor or cause. Many falls are labeled as “mechanical” and attributed to simply tripping or slipping. It is essential to recognize, however, that older people who trip or slip may have a variety of underlying reversible conditions that could have contributed to the event. Thus, a thorough evaluation of all falls is war ranted. In addition to evaluating the patient who has fallen for injury, it is critical to determine, to the extent possible, whether the patient had a syncopal episode or a seizure, which dictates a very different approach to evaluation and management. As many as half of “unexplained falls” in older people with dementia (e.g., found on the floor) may be due to near-syncope or syncope related to postural hypotension. Figure 489-6 illustrates an overview of the approach to an older person who reports a history of one or more falls in the past 6 months, and Table 489-5 provides more detail on the immediate evaluation of an older person who has fallen. Chap. 28 provides more detail on the evaluation of gait and balance disorders. Management Table 489-6 illustrates approaches to the manage ment of falls. Immediately after a fall, injuries and underlying acute illnesses should be identified and treated. It is common practice for older patients who come to an emergency department with a history of a fall to have a brain imaging study. While this is understandable from a potential liability standpoint, it is also reasonable to avoid such

studies if no history or signs of head trauma, neurologic symptoms or signs, or anticoagulation is noted and to monitor the patient carefully over the next 48–72 h for the development of specific indications for a brain imaging study. Because the causes of and risk factors for falls are often multifacto rial, management commonly requires multiple interventions in the same patient. Among the most common and effective interventions are physical therapy for strengthening and balance; Tai Chi has also been shown to be effective in multiple trials. Although many older people who fall are vitamin D deficient, the role of vitamin D replacement in preventing falls or preventing injuries from falls when combined with interventions such as strength and balance training remains unclear. The risk/benefit ratio probably favors vitamin D replacement with at least 800 IU per day, but high-dose vitamin D (60,000 IU in one oral dose monthly) has been associated with an increase in the risk of falls. Patients who suffer a fracture after a fall should be investigated and treated for osteoporosis. Patients at high risk for recurrent falls and injuries should be encouraged to use a fall alert system; selected patients may benefit from hip protectors. All older patients at fall risk should have an environmental evalu ation for potential hazards and home improvements and a fall-alert system that can help prevent lying on the floor for many hours with the risk of rhabdomyolysis. In older people at high fall risk and with atrial fibrillation or flutter, the risk of life-threatening bleeding associated with anticoagulants is substantially lower than the risk of stroke. Because of the devastating effects a stroke can have on function and quality of life, anticoagula tion is generally preferred. Patients with this combination should also strongly consider insertion of a left atrial appendage closure device. ■ ■POLYPHARMACY Epidemiology and Impact Polypharmacy is defined as the pre scription of multiple medications using various thresholds (gener ally ranging from five up to nine simultaneous drugs) and has been identified as a major challenge in the geriatric population for decades. About 40% of the U.S. population age 65 and older take five to nine medications, and close to 20% take 10 or more. Polypharmacy is an increasingly complex challenge because of the rising prevalence of multimorbidity, a plethora of clinical practice guidelines, the prolif eration of medications that can effectively treat common geriatric conditions, and rising patient and family demand for medications due in part to television advertising and information available on the Inter net. For example, based on several condition-specific clinical practice guidelines (which do not account for multimorbidity), an 80-year-old person with multimorbidity including diabetes, chronic obstructive lung disease, hypertension, osteoporosis, and degenerative joint dis ease might be prescribed an extremely complicated nonpharmacologic regimen and over a dozen medications with the potential for multiple drug-drug and drug-disease interactions and high out-of-pocket costs. Polypharmacy increases the risks associated with age-related changes in the pharmacology of many drugs and the risk of adverse drug events. Such events cause >100,000 hospitalizations per year; the main culprits are warfarin and other antiplatelet agents as well as insulin and other hypoglycemic agents. Other categories of drugs are also involved, including cardiovascular drugs that can cause electrolyte and volume disturbances and hypotension, falls, and syncope; central nervous system drugs associated with altered mental status and falls; and antimicrobials, which cause allergic reactions, diarrhea, and other adverse drug effects. Evaluation Because many older patients see multiple specialists, internists should perform careful medication reconciliation at each office or clinic visit and especially at the time of care transitions, includ ing acute hospitalization, hospital discharge, admission to a long-term care facility or home health program, and discharge from a postacute care facility to home. At each transition, all medications should be considered in terms of unclear diagnosis or indication, uncertain dose or route of administration, stop date, hold parameters, lab tests needed for monitoring, dosages different than the last care setting, medication

Ask all patients about falls in the past year Report >1 fall, or difficulty with gait or balance, or seeking medical attention because of fall Gait or balance problem Multifactorial fall risk assessment History of falls Medications Gait and balance Cognition Visual acuity Lower limb joint function Neurological impairment Muscle strength HR and rhythm Postural hypotension Feet and footwear Environmental hazards FIGURE 489-6 Algorithm depicting assessment and management of falls in older patients. HR, heart rate. (Reproduced with permission of American Geriatrics Society. American Geriatrics Society and British Geriatrics Society: Clinical Practice Guideline for the Prevention of Falls in Older Persons. New York, American Geriatrics Society, 2010.) duplication, medications that should be restarted, and the potential for drug-drug and drug-disease interactions. Possible adverse drug effects, effectiveness of drug therapy, and adherence should be evaluated. Management Internists should serve as the “quarterback” for all prescribing to help ensure adherence and minimize the potential for adverse drug effects. Table 489-7 lists several general recommenda tions for geriatric prescribing that should help make drug therapy more effective and safer in older patients, especially those with multimorbid ity, and Fig. 489-7 illustrates a stepwise approach to optimizing medi cation management. Clinical pharmacists can be extremely helpful in achieving these recommendations and goals. Chap. 71 also provides information on the general principles of clinical pharmacology. While undertreatment of certain conditions may occur in older people (e.g., osteoporosis, depression, and overactive bladder), more attention is now being paid to “deprescribing.” Deprescribing must be done carefully, especially at the time of care transitions, when indica tions for specific drugs and patient preferences may not be clear. The AGS’s updated Beers criteria include a comprehensive list of drugs that may be inappropriate in older people and the rationale for this rating. The Screening Tool of Older Persons’ Prescriptions (STOPP) criteria are also useful in identifying drugs that should be reconsidered in older people. Several commonly prescribed drugs should be considered for depre scribing efforts, including (1) diuretics and hypotensive agents when patients have systolic hypotension or postural hypotension that can precipitate near-syncope and falls; (2) overreliance on antianxiety and hypnotic medications, especially benzodiazepines; (3) psychotropic

Recommend fall prevention, education and exercise program that includes balance, gait and coordination training and strength training No falls One fall past 6 months No problem CHAPTER 489 Check for gait or balance problems Caring for the Geriatric Patient Intervene with identified risks Modify medications Prescribe individualized exercise program Treat vision impairment Manage postural hypotension Manage HR and rhythm abnormalities Supplement vitamin D Address foot/shoe problems Reduce environmental hazards Education/training in self-management and behavioral changes Reassess periodically and other drugs with anticholinergic activity that can cause dry mouth and constipation and increase the long-term risk of cognitive impair ment; (4) PPIs with unclear indications because of numerous reported potential adverse drug effects, including increased risk of pneumonia, osteoporosis, and dementia; (5) cholinesterase inhibitors and meman tine in patients with severe cognitive impairment who have been on them for years; (6) hypoglycemic agents in patients with multimorbid ity who should not have tightly controlled blood sugar with increased risk of hypoglycemia; and (7) statins and prophylactic aspirin in patients with severe chronic illness who are near the end of life. Careful deprescribing is a critical aspect of person-centered care in the geriatric population. Several general principles, including those in Table 489-7 and Figure 489-7, may assist with deprescribing efforts. The AGS’s comprehensive Deprescribing Toolkit and the deprescribing. org website can be very helpful these efforts. ■

■COGNITIVE IMPAIRMENT: DELIRIUM

AND DEMENTIA The reader is referred to other chapters in this text (Chaps. 442–445) on cognitive impairment. Because these conditions are so prevalent in the older population, selected aspects highly relevant to geriatrics are briefly discussed here. Epidemiology and Impact Delirium occurs in up to 40% of hospitalized older patients and is associated with increased morbid ity, length of hospital stays, need for institutional care, health care utilization, and mortality in this population. An even higher incidence of delirium can be seen in older patients with underlying cognitive

PART 18 Aging TABLE 489-5 Evaluating the Older Person Who Falls—Immediate Postfall Evaluation History • Circumstances surrounding the fall • Relationship to changes in posture, turning of head, after a meal or medication intake, rushing to the toilet, nocturia, straining to urinate or defecate • Accidental trip or slip (note that many correctable factors can contribute to a reported "mechanical" fall—see text) • Hazards in the living environment (loose rugs, cords, unsafe steps, slippery floors, etc.) • Premonitory or associated symptoms • Dizziness (lightheadedness vs vertigo); cardiovascular (postural lightheadedness, palpitations, chest pain, shortness of breath); focal neurologic symptoms suggestive of stroke or transient ischemic attack (weakness, sensory disturbance, dysarthria, ataxia, aphasia); symptoms of a seizure (witnessed clinic movements, incontinence of urine or stool, tongue biting) • Symptoms over the previous few days that may have led to volume depletion (poor food/fluid intake, nausea/vomiting, diarrhea, urinary frequency/polyuria) • Exclude loss of consciousness or seizure (may be difficult without a witness) • Medications—chronic and within the few hours before the fall • Diuretics and other antihypertensive drugs • Nitrates • Drugs that cause bradycardia—beta blockers; cholinesterase inhibitors • Psychotropics—antipsychotics, hypnotics, sedatives, antidepressants • Antiparkinsonian drugs • Hypoglycemic drugs • Excessive alcohol intake Physical Examination • Exclude physical injury • Head trauma, hip range of motion, pubic bone tenderness, wrist pain, other signs of trauma • Bruising in patients on anticoagulants/platelet inhibitors • Exclude acute illness • Vital signs • Postural vital signs (if feasible/safe) • Fingerstick glucose in diabetics • Poor skin turgor suggesting volume depletion (over chest; other areas unreliable) • Signs of an acute respiratory, cardiovascular, or abdominal condition • Focal neurologic signs suggestive of stroke • Signs of conditions that increase risk for falls • Poor visual acuity; use of bifocals • Limited range of motion of neck (to detect possible cervical arthritis/disk disease) • Cardiovascular—arrhythmias, carotid bruits, aortic stenosis, mitral insufficiency, heart failure • Degenerative joint disease in lower extremities causing pain, limited range of motion, and/or deformity • Podiatric conditions (calluses; bunions; ulcerations; poorly fitted, inappropriate, or unsafe shoes) • Neurologic signs—lower extremity muscle weakness; peripheral neuropathy; tremor, rigidity, and/or bradykinesia suggestive of undiagnosed Parkinson's disease; cerebellar signs (abnormal heel to shin or heel tapping); abnormal reflexes that could reflect upper motor neuron disorder such as spinal cord compression or subdural hematoma; cognitive deficits that can result in poor judgement • Observation of gait and balance—simple Get Up and Go test (see text) with observation for short steps, poor foot elevation, wide-based gait, multiple steps to turn 180 degrees; other abnormalities that might suggest normal pressure hydrocephalus (especially in combination with symptoms of incontinence and/or cognitive impairment) Laboratory and/or Imaging Studies • Should be guided by history and physical examination—common examples include: • Complete blood count, basic metabolic panel to exclude/verify acute illness • Urinalysis (only when additional symptoms of urinary tract infection present) • Electrocardiogram (in patients suspected of acute coronary syndrome or with significant known cardiovascular disease) • X-rays to exclude fractures • Brain imaging if signs present to exclude subdural hematoma, stroke •

Cardiac monitoring in patients with history suggestive of syncope or near-syncope • Electroencephalography in patients with history suggestive of seizure Source: Adapted from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2018. impairment after surgery or while in the intensive care unit. While most episodes of delirium clear within a few days if the underlying cause(s) is identified and treated, delirium may persist for weeks or, in a few cases, for months after an acute hospitalization. Normal aging does not cause impairment of cognitive function of sufficient severity to render an individual dysfunctional, which is the hallmark of dementia syndrome. Slowed thinking and reaction time, mild recent memory loss, and impaired executive function can occur with increasing age and may or may not progress to dementia. Figure 489-8 illustrates the prevalence of memory impairment with increasing age. Just over 20% of people over age 70 in the United States have cognitive impairment without dementia, generally referred to as MCI. Up to 15–20% of those diagnosed with MCI will progress to dementia over a year; thus, most people with MCI will progress to dementia within 5 years. Therapeutic implications of MCI are subjects of intensive research. No nonpharmacologic or pharmacologic intervention has been shown to prevent the progression of dementia. The definitions of Alzheimer's disease and related dementias have been updated by the American Psychiatric Association. The prevalence of dementia increases with age; by age 85, between 30 and 40% of

TABLE 489-6 Examples of Management for Underlying Causes of Falls in Older Patients CAUSES EXAMPLES OF TREATMENT Cardiovascular Arrhythmias Antiarrhythmic medication, ablation, pacemaker (depending on nature of arrhythmia) Aortic stenosis with syncope or near syncope Valve surgery (transcatheter procedure if appropriate) Postural hypotension Reduce or eliminate hypotensive drugs Hydration, support stockings Medication (Proamatine [midodrine], fludrocortisone, droxidopa) Adaptive behaviors (e.g., pausing and getting up slowly) Hypertension Manage carefully to avoid hypotension and near syncope; control may be important in patients with periventricular white matter changes in preventing further gait disturbance Neurologic Autonomic dysfunction with postural hypotension As above Cervical spondylosis (with spinal cord compression) Neck brace; physical therapy; consider surgery Parkinson's disease Antiparkinsonian drugs Visual impairment Ophthalmologic/optometric evaluation and specific treatment Seizure disorder Anticonvulsants Normal-pressure hydrocephalus Surgery (ventricular-peritoneal shunt) Dementia Supervised activities Hazard-free environment Benign positional vertigo Habituation exercises Anti-vertiginous medication Others Foot disorders Podiatric evaluation and treatment Gait and balance disorders Properly fitted shoes Physical therapy Exercise with balance training (including Tai Chi where available) Muscle weakness, deconditioning Lower extremity strength training Drug adverse effects (e.g., sedatives, alcohol, other psychotropic drugs, antihypertensive) Elimination of drug(s) when feasible Vitamin D deficiency Vitamin D supplementation Recurrent falls Fall alert system for those who live alone; hip protectors in selected patients Source: Reproduced with permission from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2018. patients have a dementia syndrome. Alzheimer's disease and vascular dementia, which often occur together based on pathologic studies, account for most dementias in older people. Dementia with Lewy bodies accounts for up to 25% of dementia and is characterized by parkinsonian features early in the disease (as opposed to dementia in Parkinson's disease, which generally occurs years after the onset of Parkinson's), personality changes, alterations in alertness and atten tion, and visual hallucinations that can cause paranoia. Although most dementia syndromes are slowly progressive over several years, dementia is a terminal illness among patients who do not succumb to other comorbidities and results in a devastating loss of

cognition and function in the later stages. Evaluation Regardless of setting, the new onset of delirium should be treated as a medical emergency because it can be the manifestation

TABLE 489-7 General Recommendations for Geriatric Prescribing

1. Evaluate geriatric patients thoroughly to identify all conditions that could (a) benefit from drug treatment; (b) be adversely affected by drug treatment; and (c) influence the efficacy of drug treatment.
2. Manage medical conditions without drugs as often as possible.
3. Know the pharmacology of the drug(s) being prescribed.
4. Consider how the clinical status (e.g., renal function, hydration) of each patient could influence the pharmacology of the drug(s).
5. Avoid potentially serious adverse drug-drug interactions.
6. For drugs or their active metabolites eliminated predominantly by the kidney, use a formula to approximate age-related changes in renal function and adjust dosages accordingly; the Cockcroft-Gault formula (below) is probably safer as it tends to underestimate creatinine clearance. − × × × Creatinine clearance= (140 age) body weight (kg) 72 serum creatinine level (0.85 for women) CHAPTER 489
7. If there is a question about drug dosage, start with smaller doses and increase gradually until the drug is effective or intolerable side effects are observed.
8. Drug blood concentrations can be helpful in monitoring several potentially toxic drugs used in the geriatric population.
9. Help to ensure adherence by: Caring for the Geriatric Patient a. Making drug regimens and instructions as simple as possible b. Using the same dosage schedule for all drugs whenever feasible (e.g., once or twice per day) c. Timing the doses in conjunction with a daily routine d. Paying attention to impaired cognitive function, diminished hearing, and poor vision when instructing patients and labeling prescriptions e. Instructing relatives and caregivers on the drug regimen f. Enlisting other health professionals (e.g., home health aides, pharmacists) to help ensure compliance g. Making sure the older patient can get to a pharmacist (or vice versa), can afford the prescriptions, and can open the container h. Using aids (e.g., special pillboxes and drug calendars) whenever appropriate i. Performing careful medication adjudication and patient/family education at the time of every hospital discharge j. Keeping updated medication records and review them at each visit k. Reviewing knowledge of and adherence with drug regimens regularly
10. Monitor older patients frequently for adherence, drug effectiveness, and adverse effects, and adjust drug therapy accordingly. Source: Reproduced with permission from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2017. of an underlying critical illness. The first step in the evaluation is to identify predisposing and precipitating factors such as hearing or visual impairment, symptoms of depression, laboratory abnormalities, uncontrolled pain, infections, exacerbation of chronic illnesses, and history of alcohol or other substances use. The most validated evalua tion for delirium is the Confusion Assessment Method, which requires an acute onset and fluctuating course and inattention and disorganized thinking or altered level of consciousness. Because the causes and risk factors for delirium are multifactorial, evaluation requires a careful history, physical examination, and selected laboratory studies based on the findings. The benefits of screening older community-dwelling adults for cog nitive

impairment are controversial, but many interventions may ben efit patients and families early in the course of the disease (see below). Older patients in outpatient settings with complaints (or family reports) of early signs of cognitive impairment benefit from neuropsychological testing, which can help differentiate between MCI and dementia and identify concomitant factors such as depression and anxiety. The MiniCog is a sensitive screening tool for cognitive impairment and consists of a three-item recall test and clock drawing. Further evaluation of dementia includes a comprehensive history and physical examination, functional status assessment (since the diagnosis depends on impaired function), a brain imaging study, and selected laboratory tests, includ ing a complete blood count, comprehensive metabolic panel, thyroid

General Approach to Optimizing Medication Management and Deprescribing in Older Adults Link each medication to at least one condition Yes Conditions being treated with more than one medication? No Drug-disease or drug-drug interactions? Bothersome or harmful adverse effects? No PART 18 Aging Medications used to treat side effects of another medication? (i.e., a prescribing cascade**)? Time to benefit from medications used for prevention of complications of chronic illness longer than life expectancy?*** No Continue medication using minimum effective dosing Consider gradual dose reduction if and when appropriate *Many types of drugs should be tapered to avoid withdrawal with sudden discontinuation, e.g., antidepressants, sedatives, hypnotics, analgesics. **A common example of a prescribing cascade is treating edema associated with amlodipine with a diuretic. ***Common examples are continuing statins and inappropriate goals resulting in overtreatment of hypertension and diabetes causing hypotension and hypoglycemia in people with very limited life expectancy. FIGURE 489-7 General approach to optimizing medication management and deprescribing in older adults. This algorithm illustrates a stepwise approach to optimizing medication management. function tests, vitamin B12 level, and, if suspected, tests for syphilis and human immunodeficiency virus antibodies. Management Table 489-8 lists pharmacologic and nonpharma cologic management strategies for various underlying risk factors and causes of delirium. Every attempt should be made to avoid or discontinue any medication that may be worsening cognitive func tion in a delirious geriatric patient. This may not be possible, and in some patients, psychotropic drugs may be needed to treat delirium

Prevalence (%)

Men

Women

70–74

75–79 Age 80–84 85–89 FIGURE 489-8 Prevalence of mild cognitive impairment by age and sex in Olmsted County, Minnesota. (Reproduced with permission from RC Petersen et al: Prevalence of mild cognitive impairment is higher in men. The Mayo Clinic Study of Aging. Neurology 75:889, 2010.)

If an appropriate indication cannot be identified, consider tapering*/discontinuing the medication No Yes Consider consolidating therapy Consider tapering*/discontinuing the medication Yes

Consider tapering*/discontinuing the medication Yes if the patient is a danger to themselves or others and/or if delusions and hallucinations are present. Low-dose risperidone (0.25–0.5 mg) or quetiapine (12.5–50 mg at night to take advantage of sedation) may be effective; more sedating antipsychotics and benzodiazepines should be avoided unless the goal is to put the patient to sleep for a short time. If a benzodiazepine is used, it should be short-acting (e.g., lorazepam) and in a low dose; alprazolam should be avoided as many patients become dependent on it long-term. Overall, multifactorial-proactive interven tions and geriatric consultation have been associated with decreased incidence and duration of delirium in the hospital setting. Many nonpharmacologic interventions for older people with dementia, their families, and other caregivers may be beneficial (Table 489-9). Four basic approaches to the pharmacologic treatment of dementia are employed: (1) avoidance of drugs that can worsen cog nitive function, mainly those with strong anticholinergic activity; (2) use of agents that enhance cognition and function; (3) drug treatment of coexisting depression, which is common throughout dementia; and (4) pharmacologic treatment of complications such as paranoia, delu sions, psychosis, and behavioral symptoms such as agitation (verbal and physical). The use of antipsychotics to treat the neuropsychiatric symptoms of dementia is controversial. Most experts and guide lines recommend avoiding these drugs and using nonpharmacologic strategies unless patients are a danger to themselves and others or if nonpharmacologic interventions have failed. Patients with new or worsening behavioral symptoms associated with dementia should have a medical evaluation to identify potentially treatable precipitating conditions. Pain may be especially hard to detect, and if suspected, a therapeutic trial of acetaminophen should be considered. The effectiveness of cholinesterase inhibitors and memantine in improving function and quality of life in patients with various types

TABLE 489-8 Evaluation and Management of Delirium CONTRIBUTING FACTORS APPROACHES TO EVALUATION AND MANAGEMENT Drugs Consider the etiologic role of newly initiated drugs, increased doses, interactions, over-the-counter drugs, and alcohol; consider especially the role of high-risk drugs: lower the dose, discontinue the drug, or substitute a less psychoactive medication. Consider withdraw from chronic medications. Pay special attention to psychotropic medications. Electrolyte disturbances Assess for and treat, especially, dehydration, hyponatremia and hypernatremia, and hypothyroidism Infection Urinary tract infections, pneumonia, soft tissue infection Visual/hearing impairment Encourage the use of glasses and hearing aids if available Urinary and fecal disorders Treat urinary retention and fecal impaction Pulmonary disorders Correct hypoxemia Prevent or Manage Complications Urinary incontinence Scheduled toileting Immobility and falls Encourage early mobilization to maintain baseline mobility Pressure ulcers Mobility and repositioning, nutrition Sleep disturbances Sleep hygiene, avoid sedatives, avoid unnecessary awakenings Feeding disorders Feeding assistance if necessary, aspiration precautions, liberalize diet if possible Maintain Patient Comfort and Safety Behavioral interventions Staff education regarding de-escalation techniques for treatment of hyperactive delirium; facilitate family visitation if possible Pharmacologic interventions Only if patients become a threat to themselves or others and other interventions have failed Restore Function Hospital environment Adequate lighting, reduce noise Cognitive reconditioning Reorient patient frequently Physical reconditioning Physical and occupational therapy Discharge planning Assess new needs based on predischarge functional status, evaluate social support, coordinate transitions of care, medication reconciliation Source: Adapted from ER Marcantonio: Delirium in hospitalized older adults. N Engl J Med 378:96, 2018. of dementia is controversial, and the potential benefits of these drugs versus their risks and costs must be weighed carefully to provide opti mal person-centered care. The best evidence for the

effectiveness of cholinesterase inhibitors is in delaying the progression of Alzheimer's disease and increasing the time before institutional placement is needed. GI side effects can be problematic and include nausea, vomit ing, and diarrhea; nightmares can be bothersome as well. In addition to these bothersome side effects, cholinesterase inhibitors can cause bradycardia and have been associated with syncope, injurious falls, and pacemaker placement. Memantine can cause dizziness, headache, confusion, and constipation. In one study, vitamin E was more effec tive than memantine in preventing functional decline in patients with Alzheimer's disease. The diagnosis and management Alzheimer's disease and related disorders is changing rapidly because of the recent availability of more accurate biomarker testing and antiamyloid antibody therapy. Plasma p-tau 217 has been shown to be reasonably accurate in identifying amyloid-β and predicting cognitive decline in people with Alzheimer's disease. Antiamyloid antibodies have been approved by the U.S. Food and Drug Administration and can clear amyloid on positron emission tomography scan imaging. However, none have been shown to have major impacts on cognition as of the end of 2024. In addition, they

TABLE 489-9 Key Principles in the Management of Dementia Optimize the patient's physical and mental function through physical activity and mind plasticity principles and activities Treatment underlying medical and other conditions (e.g., hypertension, Parkinson's disease, depression) Avoid use of drugs with central nervous system side effects (unless required for management of psychological or behavioral disturbances—see Chap. 31) Assess the environment and suggest alterations, if necessary Encourage physical and mental activity Avoid situations stressing intellectual capabilities; use memory aids whenever possible Prepare the patient for changes in location Emphasize good nutrition Identify and manage behavioral symptoms and complications Driving (consider a formal driving evaluation) Wandering Dangerous driving Behavioral disorders Depression Agitation or aggressiveness Psychosis (delusions, hallucinations) Malnutrition Incontinence Provide ongoing care Reassessment of cognitive and physical function Treatment of medical conditions Provide information to patient and family Nature of the disease Extent of impairment Prognosis Provide social service information to patient and family Local Alzheimer's association Community health care resources (day centers, homemakers, home health CHAPTER 489 Caring for the Geriatric Patient aides) Legal and financial counseling Use of advance directives Provide family counseling for: Setting realistic goals and expectations Identification and resolution of family conflicts Handling anger and guilt Decisions on respite or institutional care Legal concerns Ethical concerns Consideration of palliative and hospice care Protect the caregiver from effects of caregiver stress Source: Reproduced with permission from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2018. have side effects, including intracerebral hemorrhage, and a high outof-pocket cost (see Chap. 442). ■ ■URINARY INCONTINENCE AND

OVERACTIVE BLADDER Epidemiology and Impact Urinary incontinence is curable or controllable in many older patients, especially those who have adequate mobility and mental functioning. Even when it is not curable, incon tinence can be managed in a manner that keeps people comfortable, makes life easier for caregivers, and minimizes the costs of caring for the condition and its complications. Approximately one in three women and 15–20% of men older than age 65 years have some degree of uri nary incontinence. Between 5 and 10% of community-dwelling older adults have incontinence more often than weekly and/or use a pad for protection from urinary accidents. The prevalence is as high as 60–80% in many nursing homes, where residents often have both urinary and stool incontinence. Many older people (~40%) suffer from "overactive

PART 18 Aging bladder” (OAB), which may or may not include symptoms of incon tinence. Symptoms of OAB include urinary urgency (with or without incontinence), urinary frequency (voiding every 2 h or more often), and nocturia (awakening at night to void). If nocturia alone is the pre dominant symptom, the patient should be asked about sleep disorders (see next section). The pathophysiology, evaluation, and management of OAB are essentially the same as for urge urinary incontinence. Incontinence and OAB are associated with social isolation and depression and can be a precipitating factor in the decision to seek nursing home care when it cannot be managed in a manner that main tains hygiene and safety. In addition to predisposing to skin irritation and pressure ulcers, the most important potential complications of urinary incontinence and OAB are falls and resultant injuries related to rushing to get to a toilet. Older people with gait disorders, espe cially those with OAB and multiple episodes of nocturia or nocturnal incontinence, are at especially high risk for falls and related injuries. In addition to the bother of the condition to the older person or a caregiver, fall risk is a compelling reason for undertaking a diagnostic evaluation and specific treatment for incontinence and OAB in the geriatric population. Evaluation Internists should ask older people about symptoms of urinary incontinence because these symptoms are often hidden out of embarrassment or fear. Simple questions can help identify incontinent patients, such as “Do you have trouble with your bladder?” “Do you ever lose urine when you don’t want to?” “Do you ever wear padding to protect yourself in case you lose urine?” (Table 489-2). A substantial number of older people will respond “no” to the first two questions but “yes” to the third one. Several points are worth noting for the practicing internist. The his tory and physical examination should focus on identifying potentially reversible causes and contributing factors (Table 489-10) and identify ing the specific lower urinary tract symptoms. A simple, three-item validated questionnaire can assist in distinguishing between the most common types of incontinence (Fig. 489-9). Key aspects of the his tory and physical exam are outlined in Table 489-11. Among older women, the most common symptoms are a mixture of urge and stress incontinence (Fig. 489-10); the urge is usually the more bothersome. Stress incontinence can often be objectively observed during a physi cal examination with a comfortably full bladder by having the patient cough in the standing position; leakage of urine simultaneously with TABLE 489-10 Reversible Conditions That Cause or Contribute to Urinary Incontinence and Overactive Bladder Symptoms in Older People CONDITION MANAGEMENT Lower urinary tract conditions Urinary tract infection (symptomatic with frequency, urgency, dysuria, etc.) Antimicrobial therapy Atrophic vaginitis/urethritis Topical estrogen (not a primary treatment for incontinence but may help prevent recurrent infections and ameliorate symptoms of overactive bladder; oral estrogens can cause or worsen incontinence) Stool impaction with irritation of bladder/urethral innervation and/or partial bladder outlet obstruction Disimpaction; appropriate use of stool softeners, bulk-forming agents, and laxatives if necessary; implement bowel regimen Increased urine production Metabolic (hyperglycemia, hypercalcemia) Better control of diabetes mellitus Therapy for hypercalcemia depends on underlying cause Excess caffeine or fluid intake Reduction in intake of caffeinated beverages; reduction in fluid intake (most older people with incontinence or overactive bladder self-restrict fluid intake) Volume overload with increased urine production at night Support stockings Venous insufficiency with edema Leg elevation Sodium restriction Diuretic therapy (late afternoon dose may be effective) Congestive heart failure Medical therapy Impaired ability or willingness to reach a toilet Delirium Diagnosis and treatment of underlying cause(s) Chronic illness, injury, or restraint that interferes with mobility Regular toileting Use of toilet substitutes Environmental alterations (e.g., bedside commode, urinal) Remove restraints if possible Psychological (depression, anxiety) Appropriate nonpharmacologic and/or pharmacologic treatment

Drug side effects Remove offending drug(s) if feasible; modification of dose, frequency, or timing may also reduce symptoms for some drugs: Diuretics (polyuria, frequency, urgency) Anticholinergics (constipation, incomplete bladder emptying) Psychotropic drugs Tricyclic antidepressants (anticholinergic effects) Antipsychotics (immobility, sedation) Sedative-hypnotics (immobility, sedation) Narcotic analgesics (constipation, incomplete bladder emptying) α-Adrenergic blockers (urethral relaxation) α-Adrenergic agonists (urethral contraction and potential incomplete bladder emptying) Cholinesterase inhibitors (urinary frequency, urgency) Angiotensin-converting enzyme inhibitors (cough precipitating stress incontinence) Calcium channel blockers, gabapentin, pregabalin, glitazones (edema with nocturia) Alcohol (polyuria, frequency, urgency, sedation, delirium, immobility) Caffeine (polyuria, bladder irritation) Source: Reproduced with permission from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2018.

The 3IQ is a patient questionaire that helps your doctor distinguish urge incontinence from stress incontinence. It should take no more than a couple of minutes. Complete the quiz and bring it to your next appointment. (if this response is marked, the 3IQ test is complete)

1. During the last 3 months, have you leaked urine (even a small amount)? Yes No
2. During the last 3 months, did you leak urine (check all that apply): When you were performing some physical activity, such as coughing, sneezing, litting, or exercising? When you had the urge or the feeling that you needed to empty your bladder, but you could not get to the toilet fast enough? Without physical activity and without sense of urgency?
3. During the last 3 months, did you leak urine most often (check only one): When you were performing some physical activity, such as coughing, sneezing, litting, or exercising? When you had the urge or the feeling that you needed to empty your bladder, but you could not get to the toilet fast enough? Without physical activity and without sense of urgency? About equally as often with physical activity as with a sense of urgency? Definitions of type of urinary incontinence are based on responses to question 3. Response to Question 3 Type of incontinence Most often with physical activity Stress only or stress predominant Most often with the urge to empty the bladder Urge only or urge predominant Without physical activity or sense of urgency Other cause only or other cause predominant About equally with physical activity and sense of urgency FIGURE 489-9 The 3 Incontinence Questions (3IQ) Assessment Tool. (From Annals of Internal Medicine, JS Brown et al: The sensitivity and specificity of a simple test to distinguish between urge and stress urinary incontinence. 144 (10):715, 2006. Copyright © 2006 American College of Physicians. All Rights Reserved. Reprinted with the permission of American College of Physicians, Inc.) coughing indicates that stress incontinence is present. Older men com monly have symptoms associated with OAB and/or symptoms of void ing difficulty (hesitancy, poor or intermittent urinary stream, postvoid dribbling); the OAB symptoms are usually more bothersome. These symptoms overlap with those of both benign and malignant disorders of the prostate, and many internists may choose to consult a urologist for further management (Chap. 92) because a urinary flow rate and postvoid residual determination, and further evaluation if malignancy is suspected, help determine therapy. Most older patients with symptoms of incontinence or OAB should have a postvoid residual determination, especially men, diabetics, those with neurologic

disorders, and those with symptoms of voiding difficulty because incomplete bladder emptying is common in older patients and is difficult to detect by history and physical examination alone. There is no specific cutoff for an abnormal postvoid residual; the test must be done with a full bladder, and straining during the test can alter the results. In older patients, a postvoid residual between 0 and 100 mL is normal, a residual between 100 and 200 mL must be interpreted based on symptoms, and a value >200 mL is abnormal and usually influences treatment. Incomplete bladder emptying is a com mon contributing factor in urinary frequency and nocturia if bladder sensory function is intact or hypersensitive. Management Some patients should be referred for further urologic, gynecologic, and/or urodynamic evaluation. Examples include a history of lower urinary tract surgery or radiation or recurrent symptomatic urinary tract infections, marked pelvic prolapse on physical examination of a woman, suspected prostate cancer, and sterile hematuria.

CHAPTER 489 Caring for the Geriatric Patient Mixed Potentially reversible conditions should be addressed, including the many types of medications that can affect bladder function, which should be eliminated if possible (Table 489-10). Table 489-12 lists treatments for different types of incontinence. Many patients respond well to properly taught and adhered to behavioral interventions. Physi cal therapists and nurses who specialize in treating lower urinary tract symptoms can be very helpful and should be consulted if available. Pharmacologic treatment of incontinence and OAB is dictated by the innervation of the lower urinary tract. α-Adrenergic stimulation increases tone in the smooth muscle of the urethra; thus, α-agonists have been used to treat stress incontinence in women (although none are approved by the U.S. Food and Drug Administration for this indi cation), and α-blockers are used to decrease urethral tone in men with OAB associated with prostate enlargement. Anticholinergic/antimus carinic agents and β3-agonists inhibit bladder contraction and are used for OAB and urge incontinence. The latter do not have the bothersome anticholinergic effects of antimuscarinic drugs. In men with OAB and normal postvoid residual who do not respond to an α-blocker (with or without a 5α-reductase inhibitor), adding an antimuscarinic or β3adrenergic agent may improve symptoms with a very low risk of caus ing urinary retention. Patients with severe cognitive impairment and/ or immobility can often be managed effectively by prompted voiding (during the daytime) and/or incontinence undergarments, as long as comfort, dignity, and safety are maintained. Older people with incontinence or OAB who have gait disorders or a history of falling should be encouraged to use a urinal, bedside com mode, or external catheter. If they insist on walking to the bathroom, they should have a clearly lit and uncluttered path to do so.

PART 18 Aging TABLE 489-11 Key Aspects of the History and Physical Examination of an Older Patient with Symptoms of Urinary Incontinence and Overactive Bladder History Active medical conditions, especially neurologic disorders, diabetes mellitus, congestive heart failure, venous insufficiency Medication review for drugs that can contribute (see Table 489-10) Fluid intake pattern Type and amount of fluid (especially caffeine and fluids before bedtime) Past genitourinary history, especially childbirth, surgery, dilatations, urinary retention, recurrent urinary tract infections Symptoms of incontinence Onset and duration Type—stress vs urge vs mixed vs other (see Fig. 489-10) Frequency, timing, and amount of incontinence episodes and of continent voids (a voiding diary may be useful) Other lower urinary tract symptoms Irritative—dysuria, frequency, urgency, nocturia Voiding difficulty—hesitancy, slow or interrupted stream, straining, incomplete

emptying Other—hematuria, suprapubic discomfort Other symptoms Neurologic (indicative of stroke, dementia, parkinsonism, normal-pressure hydrocephalus, spinal cord compression, multiple sclerosis) Psychological (depression) Bowel (constipation, stool incontinence) Symptoms suggestive of volume-expanded state (e.g., lower extremity edema, shortness of breath while horizontal or with exertion) Environmental factors Location of bathroom Availability of toilet substitutes (e.g., urinal, bedside commode) Perceptions of incontinence Patient's concerns or ideas about underlying cause(s) Most bothersome symptom(s) Interference with daily life Severity (e.g., "Is it enough of a problem for you to consider surgery?") Physical Examination Mobility and dexterity Functional status compatible with ability to self-toilet Gait disturbance (e.g., that may suggest parkinsonism, normal-pressure hydrocephalus) Mental status Cognitive function compatible with ability to self-toilet Motivation Mood and effect Neurologic Focal signs (especially in lower extremities) that could suggest a central nervous system condition Signs of parkinsonism Sacral arc reflexes (e.g., loss of perianal sensation or an anal wink in response to perianal stimulation) Abdominal Bladder distensiona Suprapubic tenderness Lower abdominal mass Rectal Perianal sensation Sphincter tone (resting and active) Impaction Masses Size and contour of prostate (neither is diagnostic of urethral obstruction) Pelvic Perineal skin condition Perineal sensation Atrophic vaginitis (friability, inflammation, bleeding) Pelvic prolapse or mass Other Lower extremity edema or signs of congestive heart failure (if nocturia is a prominent complaint) aClinically significant degrees of urinary retention may be difficult to detect on physical examination; many incontinent patients should have a postvoid residual determination done by ultrasound (see text). Source: Reproduced with permission from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2018.

Prevalence of pituitary incontinence

30–39 40–49 50–59 60–69 70–79 80+

Age group FIGURE 489-10 Rates of urge, stress, and mixed incontinence, by age group, in a sample of 3552 women. *Based on a sample of 3553 participants. (Adapted from JL Melville, W Katon, K Delaney, K Newton: Urinary incontinence in US women: A population-based study. Arch Intern Med 165:537, 2005.) ■ ■SLEEP DISORDERS Sleep disorders are discussed in more detail for the general adult popu lation in Chap. 33. Because they are so common and have some unique features in older patients, they are discussed briefly here. Epidemiology and Impact Aging is associated with multiple changes in sleep architecture as well as multiple diseases and disorders that can disrupt sleep. Thus, complaints of sleep difficulty are common in older adults. Consequences of sleep difficulty include lower health-related TABLE 489-12 Primary Treatments for Different Types of Geriatric Urinary Incontinence TYPE OF INCONTINENCE PRIMARY TREATMENTS Stress Pelvic muscle (Kegel) exercises Other behavioral interventions including timed voiding and double voiding to avoid residual urine α-Adrenergic agonist (none are approved by the U.S. Food and Drug Administration for this purpose) Topical estrogen to strengthen periurethral tissue (not effective alone; oral estrogens contraindicated) Periurethral injections to provide bulking and support Surgical bladder neck suspension or sling for severe incontinence, based on patient preference Urge and overactive bladder symptoms Pelvic muscle (Kegel) exercises Other behavioral interventions: timed voiding and double voiding to avoid residual urine Antimuscarinic and β-3-adrenergic drugs Incontinence with incomplete bladder emptying α-Adrenergic antagonists in men with a 5α-reductase inhibitor if the prostate is enlarged); an antimuscarinic or β-3-adrenergic drug

can be added if unresponsive to the α-adrenergic agonist Bladder training, double voiding Intermittent catheterization Indwelling catheterization in selected patients in whom risks and discomforts of urinary retention outweigh risks of a chronic indwelling catheter Incontinence with impaired physical and/ or cognitive function Behavioral interventions (prompted voiding, habit training) Environmental manipulation including use of urinal or bedside commode, safe lit path to bathroom) Incontinence undergarments and pads Source: Reproduced with permission from RL Kane et al (eds): Essentials of Clinical Geriatrics, 8th ed. New York, McGraw-Hill, 2018.

quality of life, increased medication use, more cognitive decline, and greater health care utiliza tion. Four types of primary sleep disorders are common in the geriatric population: insomnia, sleep-disordered breathing due to obstructive sleep apnea (OSA), restless leg syndrome (RLS), and periodic leg movements in sleep (PLMS). Complaints of bothersome insomnia—the inability to fall asleep or stay asleep despite a conducive environment—increase with age and occur in close to 30% of people older than 65. Insomnia is commonly associated with depres sion, anxiety, alcohol intake, and ingestion of caffeinated beverages later in the day. OSA occurs in ~10% of older adults but is prob ably underreported and underdiagnosed. It is associated with medical comorbidities, such as obesity and congestive heart failure. RLS occurs in 5–10% of adults, and its prevalence increases in those older than 70. It is almost twice as common in women than in men. Fam ily history, iron deficiency, and intake of anti histamines and most antidepressants are risk factors. PLMS can be found in up to 45% of older people but is often of unknown clinical consequence and remains undiagnosed.

Urge Stress Mixed CHAPTER 489 Caring for the Geriatric Patient Evaluation Older people should be screened for sleep difficulty with questions such as, “Do you often feel sleepy during the day?” and “Do you have difficulty falling asleep at night?” Further evaluation of the nature and impact of the complaints can be accomplished with standardized questionnaires (Table 489-3). Patients with significant sleep complaints should be asked about conditions that can interrupt sleep, such as nocturia, gastroesophageal reflux, cough due to reflux, chronic sinusitis with postnasal drip, chronic pain, and caffeine or alcohol intake. Specific questions characterizing the complaints should include inquiring about loud snoring (for OSA), the urge to move legs associated with uncomfortable sensations (RLS), and leg movements during sleep (PLMS; which may result in kicking a bed partner). Management Patients suspected of having OSA, RLS, or PLMS should be referred for formal sleep evaluation. While hypnotics are among the most commonly prescribed drugs in the geriatric popula tion, nonpharmacologic management of sleep should be the initial and primary approach, as many patients can benefit from properly taught and adhered to sleep hygiene interventions (Table 489-13). Benzodi azepine hypnotics should be avoided whenever feasible because they are associated with next-day hangover effects, which may manifest as cognitive impairment and can precipitate falls and car crashes and rebound insomnia. Patients with sleep-onset insomnia may respond to melatonin or low-dose trazadone, both of which are safer than using a benzodiazepine chronically. ■ ■FRAILTY Definition, Epidemiology, and Impact The term frail is often used to describe older adults. However, over the past several years, frailty has been defined as a specific syndrome, and the word frail is more appropriately used to describe people who meet frailty criteria. Frailty is a state of increased vulnerability characterized by a decline in physiologic reserve and function across multiple systems. Many dif ferent definitions and tools to define frailty exist. Fried criteria based on the Cardiovascular Health Study (see below) and the Frailty Index (a list of several specific diagnoses developed by Rockwood and col leagues) have

been used to screen for frailty in clinical settings. The importance of screening for frailty is to mitigate disability and adverse health outcomes as well as for the assessment of benefits and risks of treatment decisions. The prevalence of frailty is higher among women and increases with age. The overall prevalence of frailty in communitydwelling adults aged 65 and older varies considerably but, on average, is 10–14% depending on the definition. The prevalence of frailty

TABLE 489-13 Nonpharmacologic Management of Insomnia in Older Adults Sleep Hygiene Rules Check effect of medication on sleep and wakefulness Avoid caffeine, alcohol, and cigarettes after lunch Limit liquids in the evening Keep a regular bedtime-waketime schedule Avoid naps or limit to 1 nap a day, no longer than 30 min Spend time outdoors (without sunglasses), particularly in the late afternoon or early evening Exercise—but limit exercise immediately before bedtime Instructions for Stimulus-Control Therapy Only go to bed when tired or sleepy If unable to fall asleep within 20 min, get out of bed (and bedroom if possible); while out of bed, do something quiet and relaxing PART 18 Aging Only return to bed when sleepy If unable to fall asleep within 20 min, again get out of bed Repeat these behaviors until able to fall asleep within a few minutes Get up at the same time each morning (even if only a few hours of sleep) Avoid naps Source: Adapted from JB Halter et al (eds): Hazzard’s Geriatric Medicine and Gerontology, 8th ed. New York, McGraw-Hill, 2022. increases with age, reaching close to 16% in individuals age 80–84 and 26% in those aged 85 or older. In older hospitalized patients and insti tutionalized older people, the frailty prevalence varies from about 27% to up to 80%. Irrespective of the definition, the prevalence of frailty shows a U-shaped relationship with body mass index (BMI), with higher levels of frailty in individuals with both low and very high BMI. Pathophysiology Frailty is a three-dimensional process that involves changes at the cellular, physiologic, and phenotypical levels. At the cellular level, frailty manifests as changes in mitochondrial func tion, the development of oxidative stress and DNA damage, telomere shortening, and stem cell exhaustion. These changes at the cellular level result in physiologic alterations including inflammation, cell mediator dysfunction such as low production of nitric oxide by the endothelium, sarcopenia, and energy unbalance. Fried and colleagues conceptualize frailty as a vicious circle of declining energetics and reserve, whose elements represent both the diagnostic criteria for the syndrome iden tification and the core elements of its pathophysiology. The process manifests phenotypically as an overall decline in physical function and cognitive impairment. In particular, the phenotype of frailty has been defined by Fried and colleagues by the five following characteristics: unintentional weight loss, weakness, exhaustion, slowness, and low activity (with specific operational definitions of each). Management Although there is conflicting evidence regarding the effectiveness of specific interventions to treat or prevent frailty, personcentered physical activity programs and nutritional supplementation appear to improve components of frailty such as muscle strength, gait speed, and overall mobility. In addition, optimizing the management of chronic conditions, medication management including mitigation of polypharmacy, and identifying the individual’s priorities could lead to reversing or slowing the progression of frailty. The growing field of “geroscience” is actively studying drugs including metformin and a variety of senolytic agents for their potential effects on preventing or mitigating frailty. ■ ■ELDER ABUSE AND NEGLECT Epidemiology and Impact The incidences of elder abuse neglect and self-neglect are unknown because they are often unrecognized. The best data suggest that the incidence over 12 months is at least 8–10%. Abuse and neglect can result in physical injuries and related pain, worsening of chronic medical conditions, dehydration and pres sure ulcers, emotional distress, and loss of income and savings.

Evaluation Because abuse and neglect are underreported, are unsuspected, and have such devastating consequences, older adults should be screened (without the presence of caregivers) with questions such as, “Do you ever feel unsafe where you live?” “Has anyone ever threatened or hurt you?” “Has anyone been taking your money without your permission?” (Table 489-2). Table 489-14 outlines the definitions, symptoms and signs, and key aspects of evaluating suspected abuse and neglect. Management In addition to treating the physical, medical, and emotional consequences, patients suspected of elder abuse or neglect should be reported to the appropriate local or state agency to investigate and ensure the patient’s safety. The reader is referred to two reviews of this topic for further information on specific aspects of management. ■ ■COVID-19 The COVID-19 pandemic disproportionately affected the older popu lation, especially those residing in nursing homes and assisted living facilities. Compared with those between the ages of 18 and 29 years old, older adults are at greater risk for adverse outcomes after infection with COVID-19, especially those with multiple comorbidities. Internists should regularly refer to the CDC guidelines on vaccination as they are frequently updated. (See Chap. 205 for more details on managing COVID-19). The COVID-19 epidemic had devastating and persistent effects on nursing home staffing and heightened awareness of changes that are essential for long-term care quality in the United States (see National Academies of Sciences, Engineering, and Medicine report in “Further Reading”). END-OF-LIFE AND PALLIATIVE CARE End-of-life and palliative care are critical aspects of caring for the geriatric population and require a comprehensive, person-centered approach; they are addressed in detail in Chap. 13, and pain manage ment is addressed in Chap. 14. For older patients, limited life expec tancy is a critical factor to consider when making end-of-life care decisions. General principles of decision-making are especially relevant when considering palliative and/or end-of-life care in older patients (Fig. 489-5). Decision-making becomes complicated, however, among older patients with multimorbidity. Without a clear terminal diagnosis, when to start palliative care/end-of-life care could be challenging. While it is sometimes clear when an older patient has a terminal condi tion, such as end-stage congestive heart failure or chronic obstructive pulmonary disease, many older patients with multimorbidity have combinations of conditions of varying severity. Moreover, neuro generative disorders, including most forms of dementia, Parkinson’s disease, and patients with multiple strokes, commonly have a gradu ally progressive course, and it can be challenging to determine when discussions about palliative and end-of-life care should be initiated. Dementia, however, should be considered a terminal illness in the advanced stages. Internists should play a pivotal role in making the decision when to initiate these discussions and should be proactive in encourag ing patients and their families to execute advance directives before a health care crisis occurs. There are good data that bear on some of the decisions. For example, the survivability of cardiopulmonary resuscita tion (CPR) in hospitalized patients age 65 and older is <20%; among the old-old with multimorbidity, it is much lower. The survivability of CPR in nursing home residents is almost zero, making it a futile intervention for most in this setting. Data and recommendations from major organizations suggest that enteral feeding tubes should not be placed in patients with end-stage dementia (Table 489-1). Tools for the estimation of prognosis such as ePrognosis.com, for holding conversa tions with older people and their families about advance care planning, and for documentation of advance directives (e.g., living will, durable power of attorney for health care, Physician Orders for Life-Sustaining Treatments [POLST], and other order sets) will assist internists in pay ing careful attention to factors that contribute to person-centered care and in dealing with these challenging issues in end-of-life geriatric care.

TABLE 489-14 Elder Abuse and Neglect CATEGORY DEFINITION AND EXAMPLES SYMPTOMS AND SIGNS KEY ASPECTS OF EVALUATION Physical abuse Acts of violence that may result in pain, injury, or impairment • Pushing, slapping, hitting, Abrasions Lacerations Bruises Fractures Use of restraints Burns Pain Depression Delirium or onset or worsening of dementia-related behavioral symptoms force-feeding • Improper positioning or use of restraints • Improper use of medications Psychological or verbal abuse Conduct that causes mental or emotional distress • Verbal harassment or Direct observation of verbal abuse Subtle signs of intimidation, such as deferring questions to a caregiver or potential abuser Evidence of isolation Depression, anxiety, or both intimidation • Threats of punishment or deprivation • Isolation Financial abuse Misuse of the person's income or resources for the financial or personal gain of a caregiver or advisor • Stealing money or Inability to pay for medicine, medical care, food, rent, or other necessities Failure to renew prescriptions, adhere to medication regimens or other treatments, or keep medical appointments Malnutrition, weight loss, or both, without an obvious medical cause Evidence of poor financial decision-making Firing of home care or other service providers by abuser Unpaid utility bills Initiation of eviction proceedings possessions • Denying a home • Coercing to sign contracts or spend money Sexual abuse Sexual coercion or assault Bruising, abrasions, lacerations in the genital or anal areas or abdomen Newly acquired sexually transmitted diseases, especially in nursing home Urinary tract infection Neglect (by caregiver or self-neglect) Failure to provide the materials, supplies, food and drink, or services necessary for optimal functioning or to avoid harm Malnutrition Dehydration Poor hygiene Pressure ulcers Nonadherence to medication regimen or other treatments Worsening of dementia-related behavioral symptoms MODELS OF GERIATRIC CARE Several innovative models of care have been developed over the past three decades designed to provide high-quality and effective care for the burgeoning geriatric population with multimorbidity, functional and cognitive impairment, and challenges with social support. These include outpatient comprehensive geriatric assessment programs, inpatient acute care for the elderly (ACE) units, consultation and co-management services, and home-based programs. These models of care are assuming greater importance in the emerging era of valuebased health care services. ■ ■CARE TRANSITION INTERVENTIONS Improving transitions of care between settings has become a major focus of governments, health systems, hospitals, postacute care (PAC) and LTC organizations and programs, physicians, and other health care

The interview should be conducted alone with the patient; it may reveal discordant histories or findings inconsistent with the history provided by the caregiver. Ankles and wrists should be examined for abrasions suggestive of the use of restraints. Findings that are discordant with the mechanism of injury reported or multiple injuries in various stages of healing should raise the suspicion of abuse. Injuries to the head, neck, and upper arms occur in victims of physical elder abuse but must be distinguished from accidental injuries. Jaw and zygomatic fractures are more likely to be sustained from a punch than from a fall, which more typically result in fractures to orbital and nasal bones. Assess the size and quality of the patient's social network (beyond the suspected abuser). Conduct standardized assessments of depression, anxiety, and cognition, directly or through referral. Ask specifically about verbal or psychological abuse with questions such as, "Does your relative/caregiver ever yell or curse at you?"; "Have you been threatened with being put into a nursing home?"; or "Are you ever prevented from seeing friends and family members whom you wish to see?" CHAPTER 489 Caring for the Geriatric Patient Ask about financial exploitation with questions such as, "Has money or property been taken from you without your consent?"; "Have your credit cards or automated teller machine card been used without your

consent?”; and “At the end of the month, do you have enough money left for food and other necessities?” Abrupt changes in financial circumstances of the caregiver in either direction may herald an increased risk of financial exploitation or exploitation already under way. Abuse of the power of attorney; if the person with power of attorney or health care proxy is suspected of not acting in the best interest of the patient, documents necessary to ensure that the assumption of fiduciary responsibilities is authorized. Inquire directly about sexual assault or coercion. For patients with dementia, direct queries to caregivers about hypersexual behavior as part of a larger history regarding dementiarelated behaviors and assess patient’s capacity for decision-making about sexual activity. If indicated, refer to an emergency department for assessment for sexual assault and collection of specimens (forensic evidence should be collected by experienced professionals, such as nurses who have undergone Sexual Assault Nurse Examiners [SANE] training). Interview primary caregiver about their understanding of the nature of the patient’s care needs and how well care is being rendered. Neglect by a caregiver may be intentional or unintentional. Assess hygiene, cleanliness, and appropriateness of dress. Examine the skin for pressure ulcers, infections, and infestations. Assess nutrition and hydration, including measuring body mass index and blood urea nitrogen and creatinine to assess hydration. professionals. Geriatric patients are especially vulnerable to complica tions at the time of discharge from an acute medical or psychiatric hospi tal, as well as at the time of discharge from a PAC facility (skilled nursing facility [SNF], acute rehabilitation or long-term hospital) or home care program. With the increasing role of hospitalists, and others who specialize in SNF care, medical care for geriatric patients has become fragmented at the time of transitions, creating opportunities for commu nication problems and medical errors. Changes in reimbursement and financial penalties for high rates of hospital readmissions have driven the development of many care transition interventions (Table 489-15). ■ ■INTERPROFESSIONAL TEAMS AND

CO-MANAGED CARE The complexity of caring for the aging population is more evident during hospitalizations due to a new acute illness or exacerbation of

TABLE 489-15 Examples Care Transitions Interventions INTERVENTION WEBSITE CORE INTERVENTIONS Re-Engineered Discharge

(Project RED) (Jack et al: 2009) https://www.bu.edu/fammed/ projectred/ “Discharge advocate” performs the following: • Facilitates patient education and understanding • Performs medication reconciliation • Coordinates postdischarge appointments and communication with primary care provider (PCP) • Calls patient 2–3 days after discharge Transitional Care Model (Naylor et al: 2004; Naylor et al: 1999) https://www.nursing. upenn.edu/ncth/ transitional-care-model/ Advanced practice nurse performs the following: • Coordinates patient care before and after discharge • Assesses each patient’s needs; engages and activates the patient and family • Facilitates communication among patient, family, and health care providers • Conducts regular home visits and telephone support after discharge Care Transitions Program® (Coleman et al: 2004) http://www.caretransitions. org “Transition coach” performs the following: • Facilitates improved self-management skills including medication management and how to respond to warning signs/symptoms • Makes postdischarge home visits and phone calls PART 18 Aging Better Outcomes for Older Adults through Safe Transitions (BOOST) (Hansen et al: 2013) https://www. hospitalmedicine.org/ clinical-topics/ care-transitions/ Includes toolkit facilitating the following: • Comprehensive identification and assessment of high-risk patients • Patient/caregiver education •

Enhanced communication with posthospitalization care providers • Follow-up phone call with patient after discharge Interventions to Reduce Acute Care Transfers (INTERACT) (Ouslander et al: 2013) http://www.interact-pathway. com Includes tools for skilled nursing, assisted living, and home health care, including: • Quality improvement • Communication • Decision support • Advance care planning preexisting chronic conditions. Interprofessional teams integrate dif ferent areas of expertise to provide patient-centered care. Physicians should understand and respect the roles of nurses; physical, occupa tional, and speech therapists; nutritionists; pharmacists; psychologists; social workers; clergy; and other direct care staff. The evolution of interprofessional teams has resulted in a comprehensive approach to care by opening channels of communication between health profes sionals from different disciplines. Co-managed medicine is an example of how enhanced communica tion between different providers improves outcomes, avoids common complications, and saves resources. In the era of person-centered and value-based care, effective co-managed medicine appears to deliver consistently high-quality care at a lower cost. Collaborations between internists and geriatricians are examples of this strategy. Hip fracture and trauma co-management programs also have been developed in many academic and community hospitals and are demonstrating some success in reducing complications and length of stay in older trauma patients. ■ ■AGE-FRIENDLY HEALTH SYSTEMS A new framework for providing comprehensive, integrated, and per son-centered care across settings of care has been developed called “age-friendly health systems.” Health systems participating in the devel opment of age-friendly programs focus on the 5M’s discussed previously (Fig. 489-4) as a strategy to achieve high-quality care across the system. Strategies are implemented to educate and facilitate all system health care providers to focus on the 5M’s of geriatrics under the leadership and mentorship of specially trained geriatrics health professionals. ■ ■FURTHER READING 2019 American Geriatrics Society Beers Criteria Update Expert Panel: American Geriatrics Society 2019 Updated AGS Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 67:674, 2019.

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