INTRODUCTION

The elderly population in the United States is growing at a remarkable rate, with considerable implications for delivery of intensive care to those in the later years of life. The numbers tell the story: in the 2000 US census, those 62 years of age and older represented 14.7% of the population. Between 2000 and 2010, the population 65 years and older increased at a faster rate (15.1%) than the total US population (9.7%). In fact, the 85- to 94-year-old group experienced the fastest growth between 2000 and 2010, increasing in size by 29.9%, from 3.9 to 5.1 million (1). As of 2013, remaining life expectancy for 65-year-old men was 18 more years, and for 65-year-old women, it was over 20 years (2).

At the dawn of the 20th century, the elderly population of the United States was a small percentage of its total, 3.1 million people (4% of the population); presently, the corresponding value is 35 million people (11.3%). Based on revolutionary advances in public health and the development of medications and techniques of acute medical care provided to those born in the 20 years after World War II, 70,000,000 individuals will find themselves in the population subgroup known as “elderly” by 2030 (3). At that time, those 65 years and older are forecast to compose 26% of the population of Florida, which recently passed New York to become the third most populous state behind California and Texas (4). By virtue of the diseases and natural organ aging and deterioration that accompany 65—and more—years of living and working, those who advance into this age range become increasingly voracious consumers of medical care resources, including the specialized capabilities of the intensive care unit (ICU).

In 2013, spending by Medicare for those older than 65 years totaled approximately $420 billion of the $2.9 trillion spent nationwide for health care (5). The US Census Bureau predicts that, by 2025, of the nearly 75,000,000 individuals of 65 years or older living in the United States, about 119,000 will be centenarians (6). Intensive care consumes 4% of national health care expenditures (7). During the last 6 months of their lives, 11% of Medicare recipients spend 8 or more days in the ICU; various studies documenting ICU occupancy by those older than 65 years note that this use consumes from one-quarter to one-half of available ICU beds (8,9). The financial implications of these statistics are significant, as a portion of this care will be provided in the ICU; in 2011, the mean cost of hospitalization that included ICU care was 2.5 times as expensive as that which did not include the ICU: $61,800 versus $25,200 (10). The level of these expenditures, projected to continue their slow but exponential growth, has resulted in the argument being made that, in the context of increasing demand for limited health care resources—an economically unsustainable situation—blanket cost-cutting actions such as limiting scarce ICU availability to those who would “most benefit” society and themselves in later life should be instituted. The geriatric population, in the minds of some, does not qualify for this category of expenditure. The logic of this position, however, belies reality. Although functionality diminishes with advancing age in a bell-curve like manner, many individuals continue to perform both complex physical and intellectual tasks well into their eighth or ninth decades of life, bringing to bear resources of experience and problem solving not yet acquired by their descendants. The tactic of cost savings through measures that “cut out the expensive waste” in the ICU care of the elderly is both misleading and inaccurate (11–13). Furthermore, at least in the United States, while increasingly alarmed by the financial implications of medical care costs associated with an aging population, we continue to postpone in-depth reckoning with the consequences and management of this information, just as we continue to postpone end-of-life (EOL) discussions. Until we are ready to deal with these issues, one must maximize use of the resources available, while being mindful of the individual patient's expectations and likelihood of recovery.

The response of the human body to physiologic insult evolves with age. A parallel with outdoor activity is useful in understanding this evolution. Imagine that a man is placed on a long ridgetop that is quite wide and smooth, and that man is told to walk down the middle of the ridge with his eyes closed. Unknown to him, as he walks, the ridge slowly becomes strewn with larger and larger rocks and other impediments to ambulation, and narrows inexorably as he approaches the end. Initially, the man walks quickly, with little risk of tripping or nearing the edge. As he advances further, however, his drifting excursions off the centerline each take him closer to the treacherous rocky edge, increasing the risk of a fall. If he is careful and walks slowly, he hears the wind blowing near the cliff and is able to redirect himself away from the danger. Eventually, however, the narrowed ridgetop is completely covered with loose rocks to the very edges, and no step is possible without catastrophe. By analogy, one can think of the human body as possessing a certain amount of physiologic reserve that sustains it through times of stress brought on by disease or injury, with the maximum amount of reserve being present in young adulthood. With age, baseline organ function declines at a generally predictable rate, leaving the aging person with progressively less and less capacity to respond fully and expeditiously to stressful demands. Furthermore, there is the accumulation of permanent detrimental consequences of lifestyle decisions, such as tobacco use and lack of exercise, and of only partially controllable genetic influences, such as familial hypercholesterolemia or essential hypertension, with which the aging individual must contend, thereby increasing the likelihood of succumbing to a stressful physiologic insult. This progressive loss of physiologic reserve has come to be termed frailty, a syndrome of vulnerability involving domains of functional status, deficit accumulation, and biologic indices, separate from direct effects of age, comorbidity, and disability (14) and generally increasing the likelihood of poorer...
outcome from physiologically stressful events (15). The progressive impairment of physiologic vigor is exemplified by the exponential increase in the death rate from sepsis with age, although the incidence of sepsis increases only linearly (16), reflecting the compromised physiologic vigor accessible to the critically ill elder. Quantification of frailty to assist in assessment and management of elderly patients that have sustained traumatic injuries is an area of investigation among acute care surgeons (17,18).

CARDIOVASCULAR DISEASE IN THE ELDERLY

Approximately 35% of all deaths in the United States are attributable to one of several manifestations of cardiovascular (CV) pathophysiology, namely coronary artery disease and other conditions that involve the myocardium, hypertension, and arteriosclerosis of the central and peripheral arterial tree and cerebral vascular system, with three-fourths of these deaths directly attributable to a cardiac cause (19). This proportion is higher in the elderly population, with CV disease manifesting itself as a complicating cofactor in the management of any older person’s serious illness. For example, although only 6% of the US population is 75 years of age or older, individuals in this age group account for 30% of all myocardial infarctions and 60% of the infarction-related deaths (20).

Aging and the CV System

Studying the effect of the natural aging process on CV physiology is quite complex. From the epidemiologic standpoint, it is difficult to differentiate the basis of decline in CV function of the well-conditioned octogenarian who exercises aggressively from that of his sedentary twin who has led a life of excess, because some features and consequences of natural aging resemble those seen with disease. Although degenerative CV processes are most often looked on as “what happens as you grow old,” these have been demonstrated not to be the obligatory sequence of events in human aging (21,22). The common causative elements within modern civilized existence, such as diet, minimal demands for aerobic exercise, and recurrent and ubiquitous emotional and physical stress are so intimately associated with mere existence that they may be looked on as inevitable and unchangeable. The clinical consequences to these apparently unalterable processes may be perceived by the clinician or investigator as the natural process of CV aging, but the accuracy of this perception may be compromised. The rapidity of deterioration seen in aging is increased by both a sedentary lifestyle and by the CV disease processes that are epidemic in western society’s geriatric populations.

A degenerative process that occurs in most elderly individuals is that of stiffening of the central arterial tree. Although the consequences of this process do not manifest in acute ways that are within the direct purview of the intensivist, they induce chronic progressive conditions that complicate critical illness in the elderly. Oxygen- and nutrient-bearing blood is carried to organs via the arterial tree. In doing so, distensible large arteries perform transport and cushioning functions, transforming pulsatile flow into a steady stream of blood to the periphery (23). Release of the potential energy stored with each heartbeat within the stretched arterial wall elastin fibers propels the column of blood smoothly toward the muscular arterioles and capillary bed (23). With age—likely related to both replacement of deteriorating, nonregenerating structural elastin fibers with nondistensible collagen, and to the progressive calcification of wall structural components (24)—vascular remodeling causes the progressive slow dilatation and stiffening of the arterial wall, transforming the robust, plant central vasculature typical of youth to that commonly seen in the elderly, more akin to a thick-walled, stiff, nondistensible garden hose (25,26). Augmented tensile and shear stresses, related to the nonlaminar flow characteristic of fluid flow through vessels with impaired compliance contribute to progressive occlusive disease (27), typically found at turbulent areas of narrowing, bending, and bifurcation (28). The prominent manifestation of this progressive central arterial stiffening is that of the so-called systolic hypertension syndrome—the gradual increase in systolic blood pressure with simultaneous diastolic decline or maintenance at the same level (29). In years past, the transmission velocity of the cardiac-generated pressure impulse was discovered to change with patient age and to vary as a function of central arterial stiffness (30–33). With increased central arterial elastance—stiffness—comes an increased velocity of impulse transmission in both the forward and backward (i.e., reflected) directions. In the young, with distensible central arteries, the arrival of the reflected wave coincides with diastole, thereby augmenting coronary perfusion and modulating the magnitude of the disease-inducing tensile shear forces on the vasculature. Youthful vessels have little disease, and thus seldom display the wide pulse pressure (PP) that is the hallmark of central thickening. Aging and stiff central arteries transmit the cardiac impulse outward more rapidly and turbulently such that its reflected return arrives at the end or even the height of systole (33). In those with such vessels—the elderly—isolated systolic hypertension is noted. Although this term seems to imply a benignity that was previously thought to be true, with opinion further generalized that sustained diastolic pressure elevation was the lethal culprit (34); this is no longer thought to be the case. The insidiously destructive nature of the augmentation index—the reflected augmentation of systolic pressure at the expense of diastolic coronary perfusion, yielding an easily observed increased PP (35)—has been recognized as the true contribution of central vascular stiffness to the morbidity and mortality among the elderly. Indeed, the speed with which the cardiac impulse is propelled outward, known as pulse wave velocity (PWW), and PP are recognized as factors strongly associated with all forms of CV disease:

$$PP = SBP - DBP$$

where SBP is systolic blood pressure and DBP is diastolic blood pressure. These measurements, when elevated over time, strongly predict mortality and are indicative of vascular and cardiac pathology, even if the patient’s blood pressure measurements and examination findings at a given moment appear benign (27,34,36,37).

Other specific processes within the CV system change with age, even in healthy elderly. With myocardial aging, there is a predictable loss of myocytes, possibly from apoptosis (38,39). Because cardiac myocytes are unable to regenerate, functional “replacement” of these contractile cells occurs by hypertrophy of the remaining myocytes, with only slight overall loss of myocardial mass. As cardiac fibroblast synthetic function is...
maintained, cardiac tissue becomes infiltrated with an increasing proportion of noncompliant connective tissue, causing the gradual thickening and stiffening of the ventricular wall and impairment of left ventricular diastolic relaxation and filling. This appears similar to the fibrosis seen in pathologic left ventricular hypertrophy leading to congestive heart failure (HF) (40). Diastolic relaxation is an energy-requiring process, consuming ATP to recover calcium back into the sarcoplasmic reticulum after its release during systole (41). Development of impaired diastolic relaxation with age, resulting from age-related malfunction of the calcium-sequestering mechanism involving a dysfunctional SERCA (smooth endoplasmic reticulum calcium) pump, is partially responsible for the increased percentage of geriatric HF who display lusitropic dysfunction (42). Consequently, the filling process is delayed, with a smoother—though steeper—slope of passive diastolic ventricular filling (43) into a more slowly relaxing ventricle that ends diastole with lower volume. The ventricle thereby becomes more dependent on the contribution of atrial contraction to ventricular filling for optimum systolic function. In other words, as the aging ventricle becomes progressively more and more lusitropically impaired, it fills progressively less well by virtue of thickening from age-related myocardial depletion and incomplete relaxation from SERCA pump dysfunction. The resulting dependence on volume repletion, control of heart rate, and the robust synchrony of atrial contribution to ventricle filling assume increasing importance in managing geriatric cardiac issues. In the critically ill elderly patient in whom there is a very high chance of harboring occult diastolic dysfunction if not overt congestive HF, the strictest attention must be paid to maintenance of both sinus rhythm and volume repletion within a narrow range. Furthermore, preserved ejection fraction viewed on echocardiogram may be deceptive, because systolic function is preserved in the normal healthy geriatric heart (44) and can be maintained at greater than 50% in a very high proportion of those whose cardiac status has deteriorated to the point of being symptomatic from lusitropically deficient congestive HF (45,46).

Equally important is recognition of the progressive decrease in the responsiveness of myocardial and vascular tissue to adrenergic stimulation (47–49). This phenomenon manifests itself as an age-associated lowering of exercise-induced maximal heart rate, with a gradual shift to augmented ventricular filling to meet exercise-related demands. The stressed or exercising younger adult musters additional cardiac output by increasing contractility and heart rate and by vasodilation in the areas of maximum demand—in the case of exercise, the skeletal muscles—in response to increased levels of norepinephrine and epinephrine, with unchanged or reduced end systolic volume as output is ejected into a dilated vascular tree. The elderly, by comparison, with reduced myocardial and vasodilatory responsiveness to exercise-induced beta-1 and beta-2 stimulus (49) have increased reliance on ventricular filling (the Frank–Starling mechanism) to achieve augmented cardiac output (50,51).

Optimal care requires clinical awareness of age-related CV differences such as diastolic dysfunction. The clinician must contend with the challenge of managing the stiff, hypertrophied ventricle perfusing a nondistensible vascular tree. With the fraction of elderly patients who harbor CV disease being as large as it is in western society, clinical manifestations of this condition may complicate the management of virtually every older patient. Because the elderly may not display the “usual, common” symptoms of HF, one must maintain a level of suspicion to recognize the more subtle presentations of age-related lusitropic pathophysiology. The phenomenon of lusitropic insufficiency that is termed diastolic dysfunction has recently been recognized as part of a constellation of cardiac and systemic symptoms and pathology, associated with advancing age, that is more accurately named heart failure with preserved ejection fraction (HFrEF), and it is exceedingly sensitive to the impact of common elderly comorbidities on cardiac function (52). Accurate diagnosis of HFrEF by the most common noninvasive modality, echocardiography, can be a difficult and complex task to accomplish (53).

Acute Coronary Syndrome in the Elderly

Acute coronary syndrome (ACS) presents a particular challenge from the standpoints of recognition and management. Optimal management of myocardial ischemia and infarction in the elderly population is less well defined than in younger populations, because those older than 75 years are less commonly included in ischemia-related studies (54). Further, elderly patients are, unfortunately, less likely to be managed according to evidence-based guidelines (55), or to be admitted under the care of a cardiologist (56). The ACS mortality rate of the elderly exceeds that found in younger individuals (57) but the former benefit most in mortality reduction from intervention (58). In the young, acute ischemic processes are often associated with onset of classic angina or one of its common equivalents; in the elderly, symptoms may be much more subtle and nondistiguishing, but the condition is more likely to be fatal (59). Therefore, proper identification of myocardial ischemia and infarction must occur in a timely manner, as aggressive management is warranted. The diagnostic picture can be further complicated by the postoperative sedated state, when hypotension or arrhythmias may easily be attributed to hydration or electrolyte disturbances rather than to coronary insufficiency. ICU patients often have contraindications to intervention, and the risks of reperfusion therapy must be weighed thoughtfully against the benefits; the intensivist must remember that only a small percentage of elderly patients warranting reperfusion therapy actually receive it (60), even when no absolute contraindication exists. This is attributable to two misperceptions: the magnitude of risk to the geriatric patient, and the likelihood of benefit (58). The cardiology literature contains studies covering enormous numbers of patients evaluating the strategies of treatment to optimize the restoration of coronary blood flow, and in-depth discussion is beyond the scope of this chapter. Nonetheless, a few generalities focusing on the management of the elderly patient can be made.

As mentioned above, few elderly individuals have been included in many of the large trials (61), especially considering the prevalence of coronary disease in this group; for this reason, optimal management strategies may not be as well defined as those that address ACS within a younger population. ACS must be identified correctly, nonetheless, because treatment strategies of the patient subgroups within this very large category differ (62). One of the underpinnings of any strategy is that of expeditious implementation, in that the more quickly the intervention is begun, the greater the mass of myocardial tissue preserved and the greater number of lives saved (63). Rapid restoration of coronary blood flow is the major goal of the treatment for STEMI (ST-segment elevation
myocardial infarction). A decrease in mortality of 25% with reperfusion therapy has been demonstrated (64). From identification of STEMI, it is recommended that the infusion of thrombolytics begin within 30 minutes, or that the dilating balloon be inflated within 90 minutes (65). In general, percutaneous coronary intervention (PCI) is the preferred mode of treatment for STEMI, as long as the time constraints are met (66). Again, extrapolation of this analysis to the elderly population is done with some trepidation, because only small numbers of elderly patients were included in the studies covered by this meta-analysis (66). Nevertheless, it appears that elderly patients in the situation of evolving myocardial infarction, in which the risk of death is particularly high by virtue of the risk factors associated with advanced age (67) and by the emergent nature of the situation, are best served by PCI (57,68). PCI yielded lower mortality in the elderly population than did thrombolysis, with more benefit found as age progressively advanced, although possibly at the risk of a slightly increased rate of major bleeding events.

In non-STEMI, early invasive strategy with catheterization and revascularization (when warranted) significantly benefits those older than 65 years of age (69); early invasive strategy, however, led to a significant increase in in-hospital major bleeding (16.6% vs. 6.5%; p = 0.009) and blood transfusion (20.9% vs. 7.9%; p = 0.002) in the patients older than 75 years of age. There were no significant increases in minor bleeding orstroke in any study group. The potential benefits of PCI in the elderly patient in the elective and emergent arenas must be weighed closely against the risks incurred by this group of individuals in the form of increased bleeding and vascular complications (70). Over the past decade, the use of PCI in the management of ACS in the elderly has been increasing (71).

Cardiomyopathy

In the United States, 5,000,000 persons suffer from HF, with more than 50,000 new cases diagnosed yearly; over 80% of the individuals with HF are older than 65 years of age (72–74). Symptomatic HF by itself carries a dismal prognosis, with a median survival of 1.7 years for men and 3.2 years for women (75). Critical illness superimposed on decompensated HF is challenging for even the most adept clinician. Common causes for HF in the elderly include coronary artery disease and hypertension, followed by diabetes mellitus, valvular disease (especially aortic stenosis and mitral regurgitation) and cardiomyopathies other than ischemic (76). The incidence of HF increases with age; Framingham Study data reveal a doubling in incidence with each decade after 45 to 54 years of age (77). Factors in the critical care arena that may precipitate HF decompensation abound; these include ischemia and infarction, which is more often “silent” and subly manifest in the elderly (78), dysrhythmias and extremes of heart rate, fever and infection, medication side effects, and rapid fluid shifts such as with bleeding and aggressive fluid resuscitation. Suspicion of CV decompensation warrants aggressive, timely investigation. Marginal coronary reserve should be presumed and investigated with measurement of cardiac enzymes and documentation of electrocardiogram (ECG) patterns. An echocardiogram is usually readily available and may be useful in separating those suffering from lusitropic dysfunction from those with inotropic insufficiency. Particular points of interest to be investigated include systolic ejection fraction, lusitropic state (i.e., diastolic “relaxability” between contractions, reflecting preload), valvular integrity, and wall motion abnormalities. Over the last several years, it has been recognized that an increasing predominance of instances of HF in the elderly are those with preserved ejection fraction (HFpEF), especially in women and increasing in prevalence with progressively older individuals (52). HFpEF, which can be challenging to manage successfully (79) seems to be a manifestation of a systemic global disorder of associated with aging and multiple comorbidities seen in older patients. The initial diagnosis of HF is clinical; early clarification of ventricular function can be provided by echocardiogram which may reveal a nearly normal ejection fraction despite the patient’s clinical decompensation. The intensivist should maintain a low threshold to advance to invasive monitoring to clarify an uncertain hemodynamic state and guide infusion of vasactive medications. In the elderly patient with HF, an eroded reserve may not allow more than a trivial aberration beyond the margins of physiologic compensation.

Dysrhythmias

Dysrhythmias are frequent in the elderly patient (80,81), including those who manifest no other overt CV abnormailties, although 20% to 45% of those with atrial fibrillation (AF) harbor coronary artery disease (82). With advancing age, sinus node and conduction system integrity deteriorate, with gradual replacement of cardiac pacemaker cells by collagen and elastic tissue (83–87). Such triggering events as autonomic tone disruption (88,89), ischemia or infarction (which portends worse outcome) (90,91), anatomic alterations such as fluid overload or cardiac surgery (92,93), and a host of other cardiac conditions (including strong correlation with the presence of diastolic dysfunction) (94,95) may initiate potentially injurious tachydysrhythmic events, the most common of which is AF.

The occurrence of AF increases with age (96), carrying an increased risk of stroke and death (97) in those older than 60 years, even in the absence of other cardiac abnormalities. Several issues remain unsettled in the optimal management of AF (98). Of these, the two that receive the most attention are rate control versus rhythm control, and management of anticoagulation. The AFFIRM investigators (99) found no clear survival advantage to either rate or rhythm control in AF, but the rate control strategy did appear to manifest some advantages in the area of medication side effects. All choices for chemical control of rate and rhythm in the elderly population must be made within the skewed context of the high percentage of these patients who harbor comorbid conditions, especially HF; as choices for immediate rate control include beta-blockers and calcium channel blockers, the clinician must remain mindful of their impact on the state of HF compensation. Amiodarone or digoxin may be used in those with HF in the absence of an accessory pathway. Digoxin is not recommended in such patients, as it may precipitate profound tachycardia via the accessory pathway, with heart rate nearing 300 beats per minute (bpm), leading to CV collapse. In the case of acute hemodynamic instability, recovery of sinus rhythm with biphasic DC cardioversion after sedation is appropriate. Digoxin or amiodarone can provide rate control, but the former is not recommended for chemical cardioversion, and several medications primarily used by cardiologists surpass the latter in class of recommendation for this purpose (100).
There is no “one size fits all” solution to the question of anticoagulation in AF, although it has been well demonstrated (101) to reduce the incidence of AF-related stroke, a major avoidable comorbidity in the elderly. Equally well demonstrated (102,103) is the extent to which anticoagulation is underused in the elderly, presumably because of concern for bleeding risk in this accident- and fall-prone population, and inadequate awareness of the extent to which AF warrants anticoagulation to minimize the risk of AF-associated stroke. Oral anticoagulation therapy (OAC) is warranted in those with AF to decrease embolic stroke, reducing its instance in nonvalvular AF by 60% when warfarin is utilized (104). A variety of non-vitamin K antagonist oral anticoagulants (NOACs) have come to market recently, offering the benefit of reduced testing frequency—as is required with warfarin therapy—at the expense of very limited reversibility. Target international normalized ratio (INR) of 2.0 to 3.0 is recommended for those receiving vitamin K antagonists (105). The final anticoagulant medication decision must take into account bleeding risk, presence of CAD, renal and hepatic function, the frailty of the patient, other medications, and the patient’s risk of an embolic event (106). Clearly, maintenance of long-term anticoagulant regimens has limited applicability to the patient who suffers a critical injury or illness, and rapid normalization of INR may be warranted. Quickly reversible heparin may be a better choice in such a situation if continued anticoagulation is, in any event, warranted. AF that persists beyond 48 hours mandates anticoagulation for 2 weeks (100,105) or transesophageal echocardiogram evaluation by a cardiologist—with particular attention to the left atrium and its appendage—for the presence of clot prior to conversion to sinus rhythm. The most complete and recent American College of Cardiology/American Heart Association guidelines for the management of all issues relating to AF appear in the references to this chapter (107).

Complex ventricular dysrhythmias and ventricular tachycardia (VT) present a difficult management problem in the elderly. Sudden cardiac death (SCD) is, to a large extent, a product of untreated VT degenerating into ventricular fibrillation (VF), followed by asystole (108,109). In the elderly population as a whole, ambulatory monitoring reveals a very high incidence of ventricular dysrhythmias, including VT (110,111). Therefore, there is a high likelihood that any given elderly ICU patient will have worrisome ventricular ectopy, with a significant number displaying VT (112–114). Despite the high prevalence of ventricular ectopy in this population, only those patients with underlying heart disease have a poorer long-term prognosis by virtue of the ectopy (115). Underlying HF and left ventricular hypertrophy (116) associated with increased ectopy are prognostic of an increased likelihood of subsequent adverse cardiac events, including myocardial infarction and sudden death (117). Pulseless cardiac arrest due to VF or VT warrants management following current advanced cardiac life support (ACLS) guidelines, using cardiopulmonary resuscitation (CPR) with chest compressions and immediate defibrillation (118). The timely recognition of these lethal dysrhythmias and initiation of most recent ACLS protocols is crucial for patient welfare, because survival is a direct function of the immediacy of electrical resynchronization therapy (119); defibrillation for VF provides the optimal chance of survival if provided within 3 minutes (120). The frequency of ventricular ectopy is increased in the geriatric ICU population where several factors, including ischemia, sepsis, extremes of heart rate, hypoxia, electrolyte imbalance, and autonomic disruption associated with recent surgery, can aggravate cardiac irritability and induce lethal dysrhythmias in a marginally compensated individual. These inciting factors should be readily recognized and reversed in the constantly vigilant ICU environment. Empiric treatment of ventricular ectopy per se, however, has been demonstrated to be more prodyshrythmic than beneficial (121,122), often increasing mortality and/or inducing drug-related side effects. Nonetheless, certain medications warrant closer attention; beta-blockers after myocardial infarction have been demonstrated to reduce subsequent total mortality and SCD (123). After initial enthusiasm, amiodarone has not, in a recent study of cardiacmyopathy patients, proven to be beneficial in reducing SCD when given prophylactically to patients with ejection fraction ≤35% and New York Heart Association (NYHA) class II or III HF, as compared to that achieved with a single-lead automatic implantable cardiac defibrillator (AICD) (124). With the emergence of AICD technology, there has been a gradual reduction in mortality from SCD in elderly patients, in whom there is a higher incidence than in the general population of coronary artery disease. In this situation, the AICD appears superior to medications in preventing SCD (125). Elderly individuals accrue an equal or greater benefit from AICD placement compared to younger individuals, with minimal risk involved in the actual placement of the device (126). The indications for AICD placement continue to evolve (127–130). Clearly, the expertise of a cardiac electrophysiologist is indicated when medications or AICD placement are considered in the management of a patient at risk for or who has survived SCD.

With advancing age comes a parallel increase in conduction system disease, often mandating permanent pacemaker (PPM) placement. In 1990, the implantation rate for cardiac pacemakers was 329 devices per million patients; by 2002, the rate had risen to 612 per million (131); the mean age of implanted patients was 75.1 years (131), and the commonest reason for implantation of a pacemaker is sick sinus syndrome (SSS), a cardiac rhythm irregularity that affects 1 in 600 patients over the age of 65 (132). Such statistics make it likely that an elderly person with a PPM will at some time arrive in the ICU for a noncardiac ailment. Furthermore, advances in engineering and microcircuitry have allowed the development of single devices that incorporate PPM and AICD capability. Although management of issues directly referable to these increasingly complex machines is more within the purview of the cardiologist, certain data can be gathered quickly that will expedite investigation of such a device’s performance, as is well detailed in the recent literature (133–135). Considerable guidance can be formulated from information on the PPM manufacturer’s card that is carried by the patient, from a chest radiograph showing lead position and integrity, and from an ECG with rhythm strip. Details of electrical patterns should be apparent from the rhythm strip and interrogation findings. Any ICD discharge should be investigated with interrogation.

In the instance of withdrawal or termination of unwanted medical care from a terminally ill patient, the intervention of a normally functioning ICD or PPM is directly contrary to the natural process of dying, analogous to instituting CPR when “Do Not Resuscitate” orders exist. In such an instance, deactivation is indicated (136).
PULMONARY DISEASE

Human pulmonary function deteriorates with age, yet quantification of this age-induced deterioration is quite difficult. Measurement solely of the effects of aging on the respiratory system would require exclusion of all factors that influence respiratory function other than those relating directly to breathing and gas exchange, namely chest wall mechanics, lung histologic structure, and neural/muscular respiratory control. The list of such influencing factors includes environmental pollution and tobacco smoke exposure, occult disease, and effects of previous nutritional deficiencies. Furthermore, these factors complicate contemporaneous comparison between different generations because of the variability of their impacts on these generations. The alternative is the longitudinal study of a rigorously screened cohort of subjects, which has been performed in a few cases (137,138). Analytic difficulties notwithstanding, it is possible, in some instances, to identify the predictable alterations in respiratory physiology that occur with age, so as to prepare the intensivist to contend with a common form of critical illness pathophysiology in the elderly—that of profound respiratory insufficiency.

Microscopic examination of tissue samples from young and older individuals reveals the basis of age-related changes in pulmonary physiology. One sees alveoli from older patients to be less fully surrounded by the elastin/collagen network (139,140), each less robustly tethered open by one another—less radial traction—yielding an increasingly compliant lung with diminished recoil (141). Loss of cartilaginous supporting tissue in the small airways further contributes to loss of lung elasticity. The concepts of first, airway collapse, worsened in the patient with advanced emphysema, and second, the progressive stiffening of the chest wall with age allow one to forecast and better understand the evolution of geriatric respiratory function: alterations in lung volume due to gas trapping at higher residual volumes and deterioration of gas exchange. In addition, neural factors alter responsiveness to changes in PaCO2 and PaO2 (142,143); the magnitude of these changes varies from person to person.

Geriatric flow–volume curves reveal “scoping” of the expiratory limb, implying early closure of airways, and increased residual volume as seen in obstruction from airway collapse in emphysema, a similar phenomenon (144,145). Furthermore, chest wall compliance decreases from calcification of the cartilaginous rib and thoracic spine joints, with kyphotic changes stiffening the thoracic spine itself (146). Compromised compliance results in a substantial increase in the work of breathing, to be provided by deconditioned, aging muscles, likely in the face of low cardiac output and poor nutrition. Such factors yield the respiratory pattern displayed by a significant percentage of the elderly: rapid, shallow breathing at rest, with little exertional reserve. A diagram of lung volumes versus age reveals a slight increase in functional residual capacity (FRC) and residual volume, with a steep rise in closing capacity, the volume at which airway collapse takes place in the dependent airways. Thus, airway closure occurs in the upright person without pulmonary disease at a lung volume that exceeds FRC (147). In other words, airway collapse can take place in the upright healthy elderly lung even during quiet resting tidal volume during spontaneous breathing, with ventilation/perfusion (V/Q) mismatch increasing shunt fraction and alveolar–arterial partial pressure of oxygen (PO2) gradient, with relative hypoxemia for a given inspired fraction of oxygen (FiO2). Subjecting the supine elderly patient with compromised FRC to controlled positive pressure ventilation demands that meticulous attention must be paid to ventilator management to correct V/Q mismatch. The complex details of mechanical ventilation are addressed elsewhere in this textbook (see Chapter 103). In general, one must use PEEP (positive end-expiratory pressure) while administering the lowest FiO2 possible, avoiding overdistention of the better inflated (more superior, nondependent) alveoli, and providing sufficient expiratory time to avoid auto-PEEP and breath stacking, as well as sufficient tidal volume into the restricted thoracic cage without exceeding peak pressure limits.

It is commonly held that healthy elderly individuals have a significantly lower PaO2 for a given FiO2, compared to equally healthy younger counterparts. Traditional teaching has proposed the following formulae (148,149):

\[
\text{PaO}_2 = 104.2 - (0.27 \times \text{age})
\]

\[
\text{PaO}_2 = 100.1 - 0.325 \times \text{age (years)}
\]

\[
\text{PaO}_2 = 109 - 0.43 \times \text{age (age)}
\]

More recent studies have yielded varying results (150,151), certainly not confirmatory of a pronounced “predestined” decline in oxygenation with age, and questioning the hypothesis that progressive disruption of the matching of ventilation and perfusion in the elderly is actually the cause of whatever decline actually occurs (152). The related questions of rise in (A–a) gradient with age, and “normal” age-related decline in PaO2 are, similarly, quantified by different investigators (148,149,153,154).

NUTRITIONAL ISSUES

Malnutrition, also known as undernutrition, is a common companion of elderly individuals and frequently a complicating factor in the efficient and successful management of an elderly ICU patient. The natural decline in energy expenditure with age begins at about age 30 and accompanies the age-related increase in body fat-to-protein ratio (155–157). The evolution of nutritional intake with age is one of decline that exceeds the decrease in energy expenditure (158,159) for various reasons. Thus, even the healthy individual will eat less and lose weight with time, and will be at risk for malnutrition if illness occurs or social support wanes. For example, in elderly nursing home patients, a population in whom initially minor medical problems can quickly blossom into life-threatening conditions, the incidence of undernutrition can approach 85% (160,161). Malnutrition at the onset of critical illness portends poor outcome, as does insufficient nutritional support during the course of the illness (162,163). Mortality is considerably higher in the malnourished elderly patient, compared to those who are nutritionally replete (162). Undernutrition has several common causes: (i) functional decline and social isolation from family and other support systems, (ii) anorexia associated with older age—the so-called anorexia of aging—or chronic illness, (iii) anatomic or gustatory impediments to mastication or swallowing, (iv) abuse or neglect, and (v) insufficient financial resources (164–167). Therefore, the prevalence of undernutrition in hospitalized, geriatric patients is relatively high (168,169) and is often unrecognized unless sought specifically (170).
Identification of malnutrition in the elderly patient (170) may be facilitated by the routine employment of easily used physical examination and laboratory screening tools as part of an organized, proactive nutrition screening program (171). There is little literature addressing nutrition in the geriatric ICU patient per se, and the principles set forth below are generally applicable to any ill elderly patient.

Undernutrition imposes a considerable burden on the marginally compensated geriatric patient. The conditions known as protein–energy malnutrition (PEM) and micronutrient deficiency complicate the treatment of several conditions seen in the ICU. These include the contribution of gastrointestinal (GI) tract nonintegrity to multiorgan system failure (172,173), and other common CV (174,175), pulmonary (176–178), and infectious issues (179). Wound healing is impeded by a poor nutritional state (180–182); in particular, development of decubitus ulcers is more common in malnourished elderly individuals, and successful management is decidedly more difficult (181). Patients with PEM are at increased risk for serious complications while in the hospital (182), with slower recovery (183), poorer functional status at discharge, and higher rates of mortality after discharge (184–187).

Malnutrition is a disorder of body composition in which macronutrient and/or micronutrient deficiencies occur when nutrient intake is insufficient, resulting in reduced organ function, abnormal blood chemistry studies, and suboptimal clinical outcomes (188). Nutritional deficiency is found in 35% to 65% of elderly hospitalized patients (189). Of the available screening techniques reflecting nutritional status, one of the most revealing is the dietary and weight loss history, as found in such structured nutritional questionnaires as the Mini Nutritional Assessment (MNA) and other tools (190,191) and nutrition evaluation steps taken on admission (192). Although probably more applicable to the long-term outpatient setting, certain pieces of information gathered from the patient or family via the MNA are helpful in providing a “snapshot” of the patient’s nutritional status as the initial steps in the continued assessment of overall nutritional condition (193). Obtaining the patient’s weight immediately on admission is an obvious step in assessing nutritional integrity (194).

The Department of Health and Human Services defines normal BMI as being within the range of 18 to 24.9, with those with BMIs less than 18 being underweight, the overweight range being 25 to 29.5, and those displaying a BMI above 30 being obese (195). These data, however, cover—in the United States—the adult population as a whole. The picture in a unique subset such as the elderly is more complex. In the geriatric population, BMI less than 20 is predictive of nearly 50% 1-year mortality (196), a stronger predictor of death than is diagnosis; similar results were found among critically ill adults with a BMI less than or equal to the 15th percentile (197). Such data lead researchers to suggest that the optimal BMI lies higher in the elderly than in the general population (198); this supposition has been supported by a large study demonstrating that the detrimental effect on mortality of excess body weight declines with age (199). Furthermore, the BMI calculation does not differentiate between differences in body morphology; obese, malnourished individuals whose BMIs fall within the normal range may go unidentified using this formula (200). Because an age-associated loss of height can be significant in the geriatric population, especially in kyphotic individuals, substitution of arm span as the denominator of the BMI calculation has been suggested to give a more accurate comparison of an individual patient’s BMI to the standards that were originally established in younger persons (201,202). Arm span is identical to height in younger years; although height may decline with age, arm span remains unchanged, providing more accuracy within the previously determined younger age frame of BMI reference. Knee height, as measured from plantar surface to top of patella with the ankle at 90 degrees, is another measurement (203) that can be substituted in corrected BMI calculations in those with diminished stature who are unsuitable for arm span measurement. Triceps skin fold thickness and mid-arm circumference can also provide an idea of body fat content (204).

In general, however, use of the BMI in the elderly is suspect, regardless of the height measurement used, as there are few normal BMI data that specifically describe those older than 65 years. The ages of geriatric patients included in nutrition studies vary, anthropometric characteristics vary in different advanced decades, and incidence of weight-changing diseases and conditions—such as cancer or the anorexia of aging—increases with age (205). These factors make the formulation of accurate statements and recommendations addressing ideal weight and BMI in the elderly difficult to formulate (156). Although the percentage of older Americans falling into the definition of obese continues to climb (206), one should not make the assumption of nutritional integrity. Age-related redistribution of caloric stores may disguise the overweight elderly patient with severe PEM (200) as one who is obese in the mind of the unwary clinician who is not familiar with the metabolism of geriatric patients and the pathophysiologic implications of these changes (207). Misguided hypocaloric feeding, directed at mobilizing excess fat stores in the obese, but malnourished, elderly patient may worsen the situation by leaving the ongoing catabolic protein breakdown associated with critical illness uncorrected (208). Several easily measured laboratory parameters are reflective of nutritional status on admission, and some can be followed periodically to assess the success of nutritional support. Albumin is a product of hepatic metabolism, synthesized ultimately from ingested or infused nitrogenous precursors in the presence of adequate caloric support. Although it is held that the serum albumin level is reflective of the nutritional state, various factors influencing serum albumin levels make it only vaguely reflective of overall nutritional status (209), with an ROC (receiver operating characteristic) curve rating of 0.58 compared to the clinical subjective global assessment tool. Serum albumin level does decline somewhat with age—0.8 g/L per decade for individuals older than 60 years of age—but generally remains within the numerical normal range. Significantly reduced albumin concentration, therefore, should be attributed to disease processes (210,211) and be aggressively investigated. A substantial decline in serum albumin concentration is accurately predictive of mortality and worse outcome among the elderly, both in the setting of apparent health and illness (212–216), possibly reflective of the presence of chronic disease- or inflammation-induced mediators that simultaneously suppress...
albumin gene expression (217). The half-life of albumin, 18 to 19 days (218–220), makes its use less than optimal in monitoring metabolic and synthetic functions, in which rapid change is significant. The reliability of previously favorite nutritional indicators such as prealbumin and retinol-binding protein in demonstrating the adequacy of nutritional support in critically ill patients has recently been called into question (221).

As critical illness induces substantial catabolism (220,222,223), resting energy expenditure (REE) rises during the first 2 weeks of this state, with mobilization of nitrogen stores as a component of the associated inflammatory response to physiologic insult. Total energy expenditure (TEE) may rise dramatically in critically ill, septic, or trauma patients, repletion of which is most difficult without correcting the underlying inciting process (224,225). In the elderly individual with marginal nutritional reserve at the onset of critical illness, early provision of caloric and protein support is warranted. Catabolic processes characteristic of critical illness are not reversible by nutrient supplementation alone; they are incited by inflammatory mediators rather than by pre-existing deficiency or inadequate repletion and are thus not forestalled by aggressive nutritional support. Traditional guidance recommends 25 kcal/kg/day of nutritional support, with an additional protein supply of 1.2 to 1.5 g/kg/day (188,226) based on actual body weight. Obese individuals, defined as above (227,228), warrant feeding based on ideal, rather than actual, body weight (IBW):

- **Men**: IBW (kg) = 50 + 2.3 kg per inch over 5 ft
- **Women**: IBW (kg) = 45.5 + 2.3 kg per inch over 5 ft

Greater accuracy can be achieved using one of several formulas to calculate REE (229) the Harris–Benedict equation is commonly used (230):

- **Men**: REE = 66.5 + (13.75 × weight in kg) + (5.003 × height in cm) – (6.775 × age in years)
- **Women**: REE = 655.1 + (9.563 × weight in kg) + (1.850 × height in cm) – (4.676 × age in years)

This may be insufficient in the critically ill geriatric patient in the throes of the inflammatory response, unless the higher stress and activity factor is used (231). Resting metabolic rate may be nearly double in the critically ill or injured individual (224) compared to the healthy uninjured person. Protein supplementation for the most critically ill ranges from 1.2–1.5 g/kg to 2.0–2.5 g/kg (232–234) although, in the initial stages of such a condition, the rate of catabolism may just not be ameliorable despite aggressive support in appropriate quantities (235). Initial empiric dosages should subsequently be adjusted based on indirect calorimetry and nitrogen balance studies if there is suspicion of inadequate nutritional support (236–240). Enthusiastic overprovision of macronutrients in a misguided and vain attempt to thwart and correct inflammatory catabolism, on the other hand, leads to a host of complications and considerable morbidity (241) for which the geriatric patient may be unable to compensate. Most recently, it appears that the optimal outcome attributable to nutritional support is achieved only when both the energy (as determined by indirect calorimetry) and protein requirements are reached within 1 to 2 days (242); the wisdom of “permissive underfeeding” of predicted energy requirements has recently also been documented (243). The confounding factor of obesity sometimes seen in the nutritionally deficient geriatric patient makes the recipe that provides optimal nutritional support frustratingly difficult to determine. In such situations, measurements of energy expenditure performed at frequent intervals are even more strongly advisable, because energy requirements fluctuate with time and medical condition, and vary significantly from those of younger patients on whose metabolism nutritional recommendations are often based. In general, most, although not all, studies show that enteral nutrition is preferred because of the purported preservative effects on intestinal mucosal integrity, cost issues, and a lesser degree of risk exposure to the patient, both infectious and mechanical, associated with placement of flexible nasointestinal feeding tube versus central line for parenteral nutrition (188,244–249). This statement, however, is the source of endless controversy and the basis of considerable investigation (249–251). The optimal site of delivery of the enteral solution, gastric versus postpyloric, surprisingly, remains controversial (252,253) as does the importance of gastric residual volume (GRV) measurement and its impact on outcome (254,255). The risks and benefits of the common routes of nutritional support have been reviewed in considerable detail (256,257).

One additional point that is critical to remember is that of the possibility of development of potentially fatal refeeding syndrome in a critically ill patient who is already nutritionally deficient, as many elderly people are. Meticulous attention to the introduction of nutrients in those at risk, with frequent monitoring and generous replenishment of electrolytes, is very important to avoid this morbid complication (258).

**Renal Considerations**

Deterioration of renal function in a critically ill patient has a dramatic impact on survival. Despite this, it is often not recognized in a timely manner, is managed poorly or incompletely, and is often preventable or able to be ameliorated by suitable intervention (259). Acute kidney injury (AKI, the name given to what was previously known as acute renal failure [ARF]) carries a mortality of nearly 30% in a general ICU population; a decline of renal function of even lesser severity also impacts mortality significantly (260), more so in the geriatric population. An elderly patient with compromised renal function will often succumb to the added insult of renal failure after a complex surgical intervention or traumatic injury. The chance for at least partial renal functional recovery after critical illness-related AKI is greater than 90% among those alive a year after their illness (261). Presently there is little available for treatment of renal insufficiency or failure other than identification of the etiology with certainly so as to administer the correct therapeutic medications when warranted (e.g. steroids, imuran, etc.), optimization of hemodynamics, prevention of further renal damage by removal of any nephrotoxic medications or processes, aggressive management of complications such as hyperkalemia, and initiation of renal replacement therapy if indicated and deemed appropriate within the patient’s wishes. The intensivist holds a pivotal role in the understanding of renal physiology and the principles of renal protection to minimize the impact of critical illness on renal function and its influence on outcome.

Just as in other physiologic systems, there is a gradual deterioration of renal function with age, beginning at age 30 years
It is well described that renal blood flow declines after the fourth decade (264,265). When the sixth decade is reached, this deterioration generally continues, although with a very wide bell curve of distribution (266). There is loss of renal—primarily cortical—mass (267) and the onset of glomerular sclerosis and involution, causing a decrease in the number of functional glomeruli (268), in turn causing a decrease in glomerular filtration rate (GFR) of 30% to 40% by the age of 80 years (262,269). Deterioration of tubular function parallels that of the glomerulus (270). In the elderly patient, factors other than age-related deterioration may complicate renal function, including pre-existing renovascular disease, hypertensive nephrosclerosis, or hypotension associated with trauma or neglect. Laboratory measurement of serum blood urea nitrogen (BUN) and creatinine (Scr), used individually or in a ratio, act as surrogates of renal function; they are, however, less accurately reflective of renal function in the elderly than in a younger person. BUN rises slightly with age over 60 years, paralleling the gradual decline in renal function; Scr reflects muscle mass and, while completely filtered (and only minimally secreted) into the tubule and therefore generally reflective of GFR, may not climb as expected despite age-related falling renal filtration (271). The age-related muscle mass diminution, frequently paralleling deterioration of renal function, generates less creatine (and thus, creatinine), leading to what may erroneously be looked upon as a normal baseline Scr. Assessment of GFR should be individualized by using the Cockcroft–Gault formula (272) to generate a more accurate estimate of function based on weight, age, and serum creatinine:

\[
\text{Creatinine clearance} = [(140 - \text{age}) \times \text{weight in kg}] \div (72 \times \text{Scr})
\]

(arithmetic result \times 0.85 = clearance for female patients)

This formula provides a “snapshot” of function at a given time and is most useful if calculated on ICU arrival and daily thereafter. Other laboratory surrogates of GFR have been devised, such as the measurement of cystatin C (273–275) and MDRD (modification of diet in renal disease) equations (276), but the ease with which the Cockcroft–Gault calculation is performed, especially when performed daily to “trend” the result rather than depend on one individual number, makes its routine replacement unlikely. The CKD–EPI formula (277) has been found to be more accurate in some circumstances. One must be mindful that any assessment of renal function utilizing Scr to infer creatinine clearance as reflective of GFR is limited by the nonlinear rise in Scr, as renal function declines (278,279) in that a small change in a close-to-normal value Scr represents an insignificant change in GFR, while a similar numerical change in an already-elevated Scr likely represents further compromise of already impaired renal function. If GFR remains uncertain, urine collection for measurement of creatinine clearance can be done with fair accuracy using at least an 8-hour urine collection period (280,281); 24-hour collection is preferred in critically ill patients and is easily done in patients with indwelling urinary catheters. A variety of methods exist to assess renal function, both by measurement and by estimation (282,283).

Fluid and electrolyte handling is altered in the aging kidney, related to tubular dysfunction which is proportional to the GFR decline. Although baseline electrolyte values and fluid status are likely within normal range in the previously healthy geriatric patient, age-related tubular dysfunction narrows the limits of correction of water and sodium aberrations that the elderly kidney can readily accomplish. Sodium excretion and reabsorption declines in efficiency, with those older than 60 years requiring considerably more time to achieve homeostasis in the face of sodium overload or deprivation (284). Similarly, the range of specific gravity and osmolality achievable in the face of water excess or deficit is narrowed in comparison to that of a younger individual (285); rectification of acid–base perturbations is similarly deficient (286). The stresses of critical illness or injury typical of the elderly ICU patient intensify the effects of these functional deficiencies, and must be foreseen and addressed aggressively to forestall the profound effects of deterioration of renal function on morbidity and mortality. These stresses include volume depletion from GI bleeding, severe dehydration, diarrhea, aggressive diuresis, insensible losses in burn patients or those with drainage from wounds or fistulas, and disruption of renal blood flow from sepsis, shock, or surgical causes such as complex renovascular surgery. Management of deteriorating renal function requires accurate diagnosis of the inciting cause, while addressing complicating or resultant metabolic derangements and preventing further insult. The details of the diagnosis of renal pathology are not specific to the geriatric patient and are addressed elsewhere in this text (see Chapter 132).

It is important to recognize that AKI occurs in as many as 67% of ICU admissions (260), as identified by RIFLE (risk, injury, failure, loss, end-stage) criteria (287), and that the effect of renal deterioration is quite detrimental to the elderly individual. Initial evaluation must include performance of a physical examination that may reveal an occluded urinary catheter causing an enlarged bladder; bladder scanning can be performed on those in whom an enlarged bladder might not be palpable. Hypovolemia, both absolute, as in severe dehydration, and relative, as in sepsis, must be aggressively corrected with appropriate fluid and blood products; invasive monitoring is warranted in this population of patients with limited reserve. Dosage adjustment of potentially nephrotoxic medications is mandatory, using assessment of GFR as a guide. Antimicrobials such as cephalosporins and aminoglycosides, nonsteroidal anti-inflammatory medications, certain chemotherapeutic medications, and angiotensin-converting enzyme inhibitors are common offenders (288). The use of “protective” medications such as N-acetylcysteine, dopamine, mannitol, or loop diuretics to minimize the detrimental impact of contrast material on renal function has generally been demonstrated to be ineffective (289,290). On the other hand, pre-procedure isotonic fluid loading, mindful of the possibility of occult HF in elderly patients, is the strategy most likely to benefit post-contrast renal function (291). The use of isotonic bicarbonate solution, while possibly decreasing the incidence of CIN compared to isotonic saline, does not decrease the subsequent incidence of dialysis or in-hospital mortality (292,293).

Beyond awareness of medications that impact renal function, there is the effect of age-related diminished renal function on drug metabolism and excretion (294). Recall again that common indicators of renal function, BUN and Scr, although appearing normal in the elderly, may mask a compromised GFR, risking medication-induced complications if this fact is overlooked, and mandating more specific assessment of GFR (see above) if question arises. Early nephrology consultation is encouraged when RIFLE criteria suggest compromised renal function; similarly, a critical care pharmacologist can assist.
in clarifying renal-active medication issues in these complex patients.

ASSESSMENT AND MANAGEMENT OF TRAUMATIC INJURIES

Elderly individuals suffer a significant number of severe and often lethal traumatic injuries, the analysis and management of which can be frustratingly complex (295). In the 55- to 64-year-old age group, unintentional injury was the THIRD leading cause of death in 2013; in those older than 65 years of age, 45,942 deaths were attributed to trauma (296) compared with 35,000 in 2003 (297). Most serious injuries are caused by falls, the occurrence rising dramatically as age advances into the 60s and beyond (298). This predominance continued to be seen through 2015 (299). Falls from a standing or even sitting position, imparting an apparently trivial amount of kinetic energy to frail tissue, may result in fatal injury, accounting for half the trauma-related deaths as compared to those of younger people (300). Most remaining significant traumatic injuries to the elderly involve motor vehicles, either as vehicle occupants or as pedestrians (301), while there is a small but persistent incidence of injury and death from penetrating trauma in the geriatric population, declining to less than 1% in those older than 75 years (299,302,303).

Evaluation and management of the injured elderly requires familiarity with characteristic injury patterns and knowledge of comorbid diseases and particulars of geriatric physiology that impact treatment (304). Practice management guidelines for geriatric trauma (305) are helpful in this situation. Triage of injured geriatric patients to more experienced trauma centers improves outcomes, to such an extent that some practitioners in the field of trauma management advocate the hyperspecialization of some centers to be the location of management of seriously injured elders (306).

Immediate assessment of the resuscitation status of any patient arriving in the ICU, whether from the operating room, emergency department, or elsewhere in the hospital, is imperative. The paucity of overt physical findings of intravascular fluid deficiency seen in the elderly patient adds additional urgency to its accurate analysis, while the lusitropic compromise that typifies the geriatric patient mandates avoidance of overgenerous fluid repletion. Although standard protocols may serve as a guide to ensure that all systems are evaluated, one must remain mindful that standard and acceptable initial hemodynamic measurements may actually conceal unsuspected injury or bleeding in the confused elderly trauma patient who may be taking medications that affect vital signs. Airway management in the elderly carries its own set of difficulties. Age-associated arthritic spinal, mandibular, and arytenoid deformities, and an increased incidence of occult cervical spinal injuries (307–309) may be seen; marginal respiratory drive and compromised airway reflexes may warrant securing the airway preemptively, avoiding a later “crash” difficult airway emergency. A thorough and detailed physical examination is fundamental. Timely sequential measurement of routine hematology tests, even in the stable geriatric patient, may reveal unsuspected hemorrhage. Arterial blood gas analysis is a convenient tool because it is quickly performed and allows frequent measurement of hemoglobin, base deficit, and lactate.

The latter two values are powerful indicators of resuscitation status and, when elevated, predict increased mortality in the elderly population (310,311). In one study of elderly trauma patients, mortality was decreased from 54% to 34% ($p < 0.003$) by institution of a protocol of trauma team activation and early noninvasive and subsequently invasive monitoring for resuscitation of all patients older than age 70 years with an injury severity score (ISS) greater than 15, even for those with nonworrisome initial vital signs and fairly minor injuries (311). This supports the precept that achieving adequate tissue perfusion early, while often difficult to accomplish, is fundamental to successful trauma management. One must be mindful, furthermore, that while invasive monitoring carries its own risks, judicious use of these tools can improve outcome and survival in the elderly trauma patient (312–314).

Certain patterns of injury are found in geriatric patients. Traumatic brain injury (TBI) affects the elderly with extraordinary severity. High mortality leaves fewer survivors, most of whom suffer debilitating sequelae (315). A large meta-analysis revealed an overall mortality of 38.3% in patients 60 years and older with moderate and severe TBI (316). In 2003, there were 90,000 emergency department visits involving TBI in those older than 63 years, of whom 38.4% died (317); some series document mortality rates for severe TBI in those older than 55 years of age as high as 80% (318). Initial neurologic examination of an elderly with significant intracranial injury may be deceptively normal (319); the reliability of the Glasgow Coma Scale in identifying elders with severe TBI is not as great as in younger individuals (320). A high index of suspicion for the presence of an occult central nervous system (CNS) injury must be maintained if such individuals arrive in the ICU without radiologic evaluation having been performed, warranting frequent, sequential neurologic evaluations by the same examiner and a conservative approach to ordering a cranial CT scan. Those elderly whose cause of TBI is a fall—nearly 50%, from 1988 to 1998—are likely to have three or more significant comorbid conditions complicating ICU management (321,322). Outcome after TBI is optimized by using meticulous clinical assessment, timely radiologic re-evaluation, and aggressive invasive monitoring to facilitate immediate recognition of worsening status, such as that due to recurrent intracranial hemorrhage, while minimizing secondary injury. Elderly patients taking anticoagulant medications and antiplatelet (ACAP) agents experience higher TBI-related inhospitality mortality (323). Secondary injury may occur when even transient episodes of hypoxia or hypotension affect cerebral perfusion pressure (CPP) (324) and, in the setting of elevated intracranial pressure (325), with hyperglycemia (326), hyperthermia (327), or aggressive hyperventilation (328,329). Infusion of hypertonic saline (330) may supplemen the management of elevated intracranial pressure that resists control by the usual initial measures. The cornerstone of TBI treatment is the maintenance of cerebral oxygenation by ensuring adequate oxygen content and CPP, guided by data derived via invasive intracranial monitoring devices that are inserted based on specific indications (331). Little, however, has been written specifically addressing geriatric CPP requirements. Although $60 \text{ mmHg}$ is considered the threshold below which the CPP should not be allowed to drop (332), this has not been rigorously studied specifically in the geriatric population. Cerebral autoregulation in the elderly is subject to the same influences as those that affect the younger individual. In this population,
the abundance of comorbidities, such as untreated hypertension, may have acclimated the cerebral vasculature to a new baseline, making invasive cerebral monitoring even more critical in ensuring adequate perfusion for the aging brain. The profound influence of even mild TBI (316,332–335) on short- and long-term outcome in the elderly patient mandates aggressive monitoring, optimization of cerebral perfusion, and meticulous attention to hemodynamic parameters. The impact on long-term survival of severe head-injured elderly trauma patients, compared to other multi-trauma patients without TBI is considerable (336).

Cervical spine injury is common in the geriatric trauma patient (337); plain radiographs (307,338) may be unrevealing of fracture or difficult to interpret because of age-related boney changes obscuring acute pathology (308). Fracture of the upper cervical spine is more common in the elderly than in younger individuals, especially in those who have fallen (309), and is more likely to be unstable (339). There is a very high incidence of odontoid fracture in the very elderly, with significant associated mortality (340,341). Helical CT is superior to plain radiographs to identify cervical spine injury in this population (338,339,342,343). Cervical spine pathology may exist in totally asymptomatic individuals with unremarkable examination findings, only to be discovered by a diligent clinician who takes extra steps to search for such an injury (344,345). In the geriatric patient with a cervical injury, the likelihood of coincident painful injury—a distracting injury in which the pain from another injury distracts the patient's attention from the perception of neck pain or a condition such as altered mental status—that would affect the examiner's decision to forgo radiographic evaluation is so high as to make such an evaluation imperative in nearly all cases. Again, one must be mindful of the greater likelihood that cervical injuries in the elderly often occur in the arthritis-prone superior vertebrae, which are notoriously difficult to depict on plain films (346), and consider CT evaluation of virtually all geriatric trauma patients in whom even subtle symptoms, history, or mechanism of injury suggest cervical injury, regardless of the initial examination findings or any comforting results of a protocol-based decision-assisting algorithm that suggest the safety of less aggressive investigation.

Traumatic rib fractures impose substantial morbidity; those older than 45 years with more than four fractures are particularly affected (347). In a study of patients traditionally defined as elderly—those older than 64 years—rib fractures profoundly affected morbidity and mortality, with longer length of stay (LOS) in the ICU, more frequent pneumonia, and overall mortality rate of 22% compared to 10% (p < 0.001) in those less seriously injured (348). Of note in this study was that rates of mortality and pneumonia both increased with each additional rib fracture. Epidural analgesia would appear to be the ideal technique to alleviate the pain associated with rib fractures to optimize pulmonary status and, indeed, has been found to be successful in nongeriatric adults (349,350). In one recent study, however, the opposite has been demonstrated in an elderly population when compared to parenteral analgesia (351).

The management of abdominal trauma follows pathways similar to those for younger patients, with certain caveats: findings on physical examination indicating serious abdominal pathology can be subtle, especially when complicated by distracting orthopedic or mild head injury. Liberal use of CT scanning is strongly recommended if mechanism of injury, external abdominal findings such as a seat belt mark, or laboratory evidence of hypoperfusion (elevated base deficit or serum lactate) suggest visceral injury. Nonoperative management of certain radiologically well-characterized injuries of solid organs—namely the spleen, the liver, and the pancreas—in the hemodynamically stable elderly patient is becoming increasingly accepted as evidence of the success of this approach accumulates (352–354).

Serious orthopedic injuries frequently befall older victims of polytrauma, and portend a substantial risk of mortality (355). Decrease in bone mineral density (BMD) in patients older than about 30 years heightens the risk of fracture in general; this phenomenon is observed in varying degrees in both genders and all races, but is particularly severe in postmenopausal Caucasian women (356,357). Pelvic fracture in the aged is associated with a greater likelihood of significant blood volume transfusion and mortality (p < 0.005) (358). Open pelvic fracture often has substantial associated bleeding, which is seldom treatable, with the exception of arterial bleeding, in any way other than with early stabilization, aggressive transfusion, and correction of coagulopathy in hopes of eventual tamponade of the retroperitoneal bleeding source. Arterial bleeding from lacerated pelvic vessels warrants embolization (359). The more typical scenario, however, is that of diffuse venous oozing, which, nonetheless, may render the elderly patient hemodynamically unstable, requiring large-volume transfusion of blood products as a temporizing measure until anatomic stabilization can be achieved (359,360). The presence of an open pelvic fracture, with frequent associated visceral injuries (361,362), further worsens outcome (358). Hemodynamic consequences of large-volume transfusion and frequent septic complications can drive the mortality in both younger and older adults to nearly 80% (363). Long-bone fractures, in general, warrant early immobilization and stabilization to minimize ongoing hemorrhage and generation of fat emboli; such fixation improves mortality significantly (364). Optimal timing of surgical stabilization of these quite morbid fractures, however, is a complex issue to resolve when they occur in the larger setting of the patient with severe head, chest, or abdominal injuries (365). Although postponing the operative stabilization of a femur or complex pelvic fracture to allow time to achieve hemodynamic stability in a traumatized patient bears benefit, it is also not without risks (366,367). Prolonged immobilization of the elderly patient with such a fracture prior to stabilization results in compromised respiratory status, likely exposing the patient to extended intubation, pulmonary thromboembolism, and infection.

Studies of elderly trauma patients have consistently documented the increase in mortality in this population (302,313,367,368). The mortality rate begins to climb for those in their sixth decade, even for less severe injuries (369) when compared to younger individuals. For those with moderate injuries, the mortality curves steepen beginning in the fifth decade, with another even steeper turn in the seventh. With advancing age, trauma-related mortality rates for those in the seventh decade and above range as high as 47% for those with an ISS more than 30, compared to those 45 years old or younger (20.1%) (370). Identification of parameters which might predict mortality in the individual patient is an important area of study (371). Within the context to which allusion
was earlier made—that of future payoff in return for resource use—the complexity and enormity of the issue grows as health care costs rise, and as the percentage of the population represented by the elderly increases. As these rising numbers of individuals cease working, and, thereby, are no longer able to generate an income that can be taxed to finance public health care funding programs such as Medicare, or be used to pay for personal private health insurance to cover costs of traumatic injuries, the costs of providing that trauma—and, indeed, all—care will have to be borne by a source other than the patients themselves. It is clear that focusing the resources of the modern ICU on the management of elderly trauma patients improves outcome (372), so the skills associated with successful management of elderly trauma patients are improving with experience. Based on the size of these costs and the likelihood of marginally or poorly acceptable outcomes among a substantial minority of geriatric trauma patients (3,370–375), investigations have tried to answer two important trauma outcome-related questions. These are as follows: (1) is it possible to identify an elderly trauma patient who will certainly die later, even if the patient survives the initial period of resuscitation, surgery, and further stabilization, and (2) to what level of functioning will the elderly survivor of trauma-related intensive care return on discharge? For many elderly individuals, the prospect of lingering in the netherworld of prolonged posttrauma multi-organ system failure with the certainty of death pushed back “only as long as the machines keep me running,” or existing debilitated in a non-home environment where even bowel function and bathing are at the behest of another, is worse than death itself, not really living at all, and is the basis of much concern among the elderly.

There are, however, grounds for hope. In one study of victims of penetrating trauma more than 60 years old, 91% were discharged home, most without assistance (303). The postdischarge level of functioning in elderly patients surviving blunt trauma varies widely, as would be expected in a population whose baseline physiologic attributes are so diverse. Clearly, even the healthiest octogenarian is not the physiologic equal of a two-sets-of-tennis 65-year-old and will have a significantly decreased likelihood of returning to premorbid functionality, although both individuals may be described as elderly. Nonetheless, even after significant traumatic injuries, a substantial percentage of recovering geriatric patients, even the very old, will be able to live relatively independently, albeit for some patients, in a protected environment with assistance. Many will be able to return home with or without periodic professional assistance (373–378). In one retrospective study of 38,707 elderly trauma patients with a mean ISS of 11.7 ± 0.05 (standard error of mean), in which 10.3% died in hospital, 52.2% of the survivors went home. The percentage of patients returning home after serious traumatic injuries, many requiring prolonged intensive care, varied considerably with age, from 66.7% of those 65 to 74 years to 30.5% of those 85 years of age or older (378). With aggressive rehabilitation, improvement in function and independence can continue for substantial periods of time after discharge, including in those who have suffered TBI (379,380). In another study, recovery of elderly trauma patients was improved by early involvement of physicians from a geriatric trauma consult service, who assisted in recognition and treatment of medical issues, and in advanced care and disposition planning (381). Additionally, determining the optimal destination for posthospitalization rehabilitation can be facilitated by employment of assessment tools that include such parameters as the 15-item Trauma Specific Frailty Index, the Barthel Index, and others (382).

Life expectancy in the United States is presently 78.8 years (383), and while it is greater at any given age now than it was even 15 years ago, objective evaluation must be made of the appropriateness—and likelihood of successful outcome—of aggressive critical care medical services provided to geriatric patients. Presently, geriatric patients represent between 25% and 50% of all ICU admissions (9,11). In 2000, ICU costs represented 13.3% of hospital costs, 4.2% of health care expenditures, and 0.56% of the US gross domestic product (384). By 2005, the latter value had increased to 0.66%, with Critical Care expenditures representing 13.4% (∼$82 billion) of hospital expenditures (385). As of this writing in 2016, expenditure for CCM services represents approximately 1% of the US GDP. The enormous expense associated with ICU care has prompted some analysts to raise the subject of limits on expenditures for the elderly (386,387), because, for example, an 80-year-old who is supported through a 3-week bout of sepsis is not likely to return to the revenue-generating work force. Indeed, the literature dealing with geriatric medical issues is liberally populated with articles addressing ageism in the context of delivery of services to the elderly (388–390), raising the concept of providing less aggressive or intensive levels of acute care to an elderly person on the basis of age, the inference being that such care provides a less robust postillness benefit to the patient and to society as a whole. Meaningful discussions addressing the more philosophical issues of critical care such as the correct level of aggressiveness of care and appropriateness of withdrawal of care, to say nothing of the financial issues, simply cannot be addressed in any rational way without an accurate picture of what critical care accomplishes in these elderly patients.

A successful ICU admission is certainly defined within cultural and social, as well as personal, contexts. Although the family member’s “do everything for Granddad” dictum is familiar, it often represents an unrealistic appraisal of the possible benefit from certain modalities of care that can be, but possibly should not be, carried out. Although the ICU is designed as a temporary environment that allows support of body functions during recovery, the complicated technology and meticulous attention to detail that characterize that environment are not the basis for such “magical” accomplishments as saving the life of a patient who has a lethal...
condition, despite the expectations and exhortations of some. Indeed, death can often skillfully be forestalled with polished and professional ICU care to such a degree that it may occur immediately after a de-escalation of such care, or later while the patient is on the general ward, in a step-down unit or rehabilitation facility, or after returning home (either early or late) (391). Meaningful discussions with elderly patients and their families, whether prior to complex morbid surgical procedures or as an ICU stay extends past the first few days, must include accurate outcome data, so as to facilitate informed decisions regarding the specifics and suitability of continued care. Studies addressing outcome in the critically ill geriatric population have produced various results that vary with the metric employed, the duration over which the outcome is monitored and broad intrapopulation patient variability. The latter category highlights differences in age, premorbid physical status, statements of preference regarding aggressiveness of long-term medical care, and patient and family declarations addressing such subjective concepts as posthospitalization quality of life (QOL). As the numbers of geriatric patients admitted to ICUs increased with the growing geriatric population, some more meaningful data identifying which elderly patients are likely to survive and return to meaningful posthospitalization lives is becoming available (392). In one recent study from Canada, 25% of elderly ICU patients 80 years of age and older survived and had returned to their premorbid levels of functioning by 1 year later (393).

The term geriatric population encompasses a quite heterogeneous group of individuals from the standpoint of age, premorbid general medical health as a reflection of functional status, the severity of the event justifying ICU admission, and cultural mores as they impact interaction with the modern health care structure of the country in question. Studies assessing the results of care delivered to the elderly may or may not reflect this diversity (394), making interpretation of individual study conclusions and their application to individual clinical situations suspect. Furthermore, the term outcome must be specifically defined as to the depth of support required by the post-ICU elder and its correspondence with that autonomous person’s preferences which, again, may vary widely based on cultural, religious, national, and other parameters. Although many elders prefer a less aggressive care regimen designed around EOL comfort at the expense of duration of remaining life, some may desire life extension in the face of critical illness by use of complex technology despite a vanishingly small or nonexistent expectation of recovery (9,395,396). Furthermore, the clinician’s perceptions of the patient’s desires may not be accurate, and thus may lead to withdrawal of care or withholding of a modality of treatment in a manner that would not be considered in the care of a younger patient (395). It is important to remember that while age may be associated with worse outcome from critical illness, numerous investigations have demonstrated that age, in and of itself, is less a factor than is the severity of the specific condition that warrants intensive care or the general medical condition (i.e., frailty) (397) of the patient prior to the institution of intensive care (398–403). Despite being subjected to procedures that are potentially morbid, the otherwise healthy elderly patient may fare quite as well as a younger individual (400,404). In one study of outcome after intensive care in octogenarians, postdischarge survival was more accurately forecast by care dependency at the time of discharge, as a reflection of pre-morbid condition and severity of illness, rather than solely by LOS (405). The subjective term Quality of Life in the post-ICU elder does not necessarily imply inferiority to that of younger individuals (406); indeed, overall QOL has been demonstrated to be similarly good across age groups ranging from middle aged to very old (above 80 years) (407,408). It must be remembered, however, when evaluating outcome data in elderly ICU patients, that while ICU survival is less a function of age than of premorbid condition or severity of illness (36,405,406,409,410), when the aggressive ICU support is de-escalated with recovery, physiologic reserve may no longer suffice to forestall death in the few months after discharge, and thus may not be reflected in ICU outcome statistics. With the wide variability of desires for aggressiveness of care displayed by the elderly and the inaccuracy with which they are analyzed by many physicians (411), the most important function of the geriatric intensivist may be that of conducting a thorough discussion at the outset of care with the patient and involved family members so as to tailor intensiveness of care to the patient’s educated and informed preferences. Fluency in initiating and conducting EOL discussions with patient and family is important for intensivists to possess, and can be learned with clear guidance and polished with experience (412). Depending on the intensivist’s point of view and experience, some modalities of available ICU treatment may be viewed as “futile”—or possibly more objectively spoken as “medically inappropri-ate.” Although this may lead to strong differences of opinion regarding the depth of and extent to which intensive care plans are formulated and should be executed (413,414), it is incumbent upon the ICU practitioner to expend all possible effort to resolve the differences equitably and objectively; the assistance of Ethics Consultative services may be beneficial (415).

**DRUG DOSING IN THE ELDERLY**

As more patients live longer and are placed on a larger number of medications, it is necessary for health care providers to understand the risks, benefits, and consequences of drug therapy in older patients. Several important pharmacologic and nonpharmacologic issues influence the safety and effectiveness of drug therapy in this population. Pharmacokinetics, the study of the action of a drug in the body over a period of time, changes with age. The physiologic changes accompanying aging affect the pharmacologic processes of absorption, distribution, metabolism, and excretion (Table 70.1). The effects of these age-related changes are variable and difficult to predict; some changes are related solely to aging, whereas others are most likely due to the combined effects of age, disease, and the environment. Although increasing age is often accompanied by decreased physiologic reserve in many organ systems independent of the effects of disease, this change is not uniform. The alterations in pharmacokinetics and pharmacodynamics that occur with increasing age suggest a pharmacologic basis for concern about the vulnerability of the elderly to the effects of medications. Unfortunately, the results of epidemiologic studies that explore these relationships are unclear, in part due, in this area of medical investigation as in many others (416), to the small number of older people included in premarketing studies relative to the patient population most likely to be exposed to the drug. The oldest—those aged 80 years or older—have not generally been included in clinical
trials of investigational drugs, and those older subjects who do participate in such trials tend to be healthy “young-old” people. Thus, the results of these trials and the side effects reported often have limited application to the older patient with multiple illnesses, taking several medications. In general, consideration of the individual patient, his or her physiologic status—hydration, nutrition, and cardiac output, and how this status affects the pharmacology of a particular drug—are more important in prescribing that drug than any specific age-related changes.

Absorption of drugs, which occurs mainly by passive diffusion, changes little with advancing age; the changes listed in Table 70.1 could potentially affect drug absorption. More important changes result from concurrent administration of several medications. For example, antacids decrease the oral absorption of cimetidine, and alcohol accelerates the absorption of chloral hydrate.

Unlike absorption, drug distribution is affected by age in clinically meaningful ways. In older persons, the relative increase in body fat and the decrease in lean body mass alter drug distribution so that fat-soluble drugs are distributed more widely and water-soluble drugs less so (Table 70.2) (417). The increased distribution of fat-soluble drugs can delay elimination and may result in prolonged duration of action of a single dose. This effect is especially important for drugs such as hypnotics and analgesics, which may be given in single doses on an intermittent basis. For example, the volume of distribution of diazepam is increased almost twofold in older patients, and the elimination half-life is prolonged from 24 hours in young patients to approximately 90 hours in the elderly. By way of contrast, the volume of distribution of water-soluble compounds, such as digoxin, is decreased in older patients, and thus the dose required to reach a target plasma concentration is decreased. Likewise, due to the decreased volume of distribution, the loading dose of aminoglycosides is decreased in older patients.

For drugs that bind to serum proteins, equilibrium exists between the bound or ineffective portion and the unbound (free), or effective, portion. For acidic drugs that are highly bound to albumin, the free plasma concentration may correlate best with pharmacologic effect. Although albumin concentration decreases only slightly with age, it may decrease dramatically during periods of critical illnesses; this can result in elevated levels of unbound acidic drugs in older persons during episodes of illnesses, and thus in an increased potential for toxicity. These changes can be significant for drugs such as thyroid hormone, digoxin, warfarin, and phenytoin. On the other hand, some basic drugs, such as lidocaine and propranolol, bind mainly to alpha-1 acid glycoprotein, an acute phase–reactant protein; the concentration of this protein tends to rise as a person ages and is elevated following myocardial infarction and in chronic inflammatory diseases and malignant conditions (418). The plasma binding of these drugs is increased in older patients, but because these age-related changes are not great, their exact clinical relevance is uncertain.

Overall, changes in protein binding are an important consideration initially when a drug is being started, when the dosage is changed, when serum protein levels change, or when a newly administered drug displaces another protein-bound agent. Because the free portion of the drug is generally smaller than the bound portion, the normal mechanisms of
metabolism and excretion ultimately eliminate the free drug. If either hepatic or renal function is impaired due to age or disease, this elimination may be slowed.

Although in vitro studies of drug-metabolizing enzyme activity from human liver biopsy samples have not demonstrated any changes with aging, some investigators speculate that the decline in liver size with age may result in decreased metabolic capacity. A significant decline in hepatic blood flow occurs with age, reductions of 25% to 47% being reported in persons between the ages of 25 and 90 years. This decrease in hepatic blood flow is clinically important because hepatic metabolism is the rate-limiting step that determines the clearance of most metabolized drugs. This change is especially relevant for drugs that undergo rapid hepatic metabolism (e.g., propranolol); drugs that undergo extensive first-pass metabolism are likely to reach higher blood levels if hepatic blood flow is decreased.

The liver metabolizes drugs through two distinct systems: phase I metabolism, involving drug oxidation, reduction and hydrolysis; and phase II metabolism, involving glucononidation, sulfation, acetylation, and methylation. Phase I metabolism is catalyzed primarily by the cytochrome P-450 system in the smooth endoplasmic reticulum of hepatocytes; this enzyme system is a superfamily of microsomal drug-metabolizing enzymes important in the biosynthesis and degradation of endogenous compounds such as steroids, lipids, and vitamins, as well as the metabolism of most commonly used drugs (419). Phase I metabolism activity decreases substantially with age, so drugs that are metabolized through phase I enzymatic activity have prolonged half-lives. Examples of some drugs whose metabolism is slowed because of these age-related changes in hepatic metabolism include meperidine, phenytoin, diazepam, propranolol, theophylline, labetalol, lidocaine, and quinidine. Age-related changes in phase I metabolism, coupled with the use of multiple medications, place older patients at increased risk for adverse drug reactions; these occur due either to inhibition or induction of cytochrome P-450 enzymes, especially CYP3A, which is thought to be involved in the metabolism of more than half of the currently prescribed drugs (420). Clinical outcomes are determined by the potency of the CYP3A inhibitor (moderate vs. potent), the availability of alternative pathways, and the seriousness of the symptoms. A drug is considered a potent CYP3A inhibitor if it causes more than a five-fold increase in the plasma concentration of another drug that is primarily dependent on CYP3A for its metabolism (421). Thus, clinicians should be cognizant of potential drug interactions when they prescribe drugs from classes that include potent or moderate inhibitors of CYP3A. If a potent CYP3A inhibitor or inducer and substrate must be taken together, dosage adjustment and close clinical monitoring are warranted to avoid adverse reactions.

Phase II hepatic metabolism involves the conjugation of drugs or their metabolites to organic substrates. The elimination of drugs that undergo phase II metabolism by conjugation is generally altered less with age. Thus, drugs that require only phase II metabolism for excretion (e.g., triazolam) do not have a prolonged half-life in older people. These drugs contrast with agents such as diazepam that undergo both phases of metabolism and have active intermediate metabolites. Although the effect of aging on hepatic drug metabolism is variable, phase I metabolism is the process that is most likely to decrease in older persons. The apparent variable effect of age on drug metabolism is probably due to the fact that age is only one of many factors that affect drug metabolism. For example, cigarette smoking, alcohol intake, dietary modification, drugs, viral illness, caffeine intake, and other unknown factors also affect the rate of drug metabolism. Induction of drug metabolism can occur in older persons. The rate of elimination of theophylline is increased by smoking and by phenytoin in both young and older persons (422). Not all metabolizing isoenzymes are induced equally in the young and the old. For example, antipyrine elimination is increased after pretreatment with dichloralphenazone in younger patients but not in older patients.

An important pharmacokinetic change that occurs in persons of advanced age is that of reduced renal elimination of drugs. This change results from the age-related decline in both GFR and tubular function. Drugs that depend on glomerular function (e.g., gentamicin) and/or on tubular secretion (e.g., penicillin) for elimination both exhibit reduced elimination in older patients. Because drug elimination is correlated with creatinine clearance, measurement of creatinine clearance is helpful in determining the maintenance dose. As noted earlier, the average creatinine clearance declines by 50% from age 25 to 85 despite a serum creatinine level that remains unchanged at approximately 1.0 mg/dL. The Cockcroft-Gault formula (see above) is useful in the accurate assessment of renal function when planning administration of medications excreted by the kidneys. Although helpful in adjusting for age, weight, and the measured serum creatinine level, it does not account for individual variation.

Altered renal clearance leads to two clinically relevant consequences: the half-lives of renally excreted drugs are prolonged, and the serum levels of these drugs are increased. For drugs with large therapeutic indices (e.g., penicillin), this is of little clinical importance, but for drugs with a narrower therapeutic index (e.g., digoxin, cimetidine, aminoglycosides), side effects may occur in older patients if dose reductions are not made. Thus, it is not surprising that digoxin is the drug that most often causes side effects in the elderly, especially if the dose exceeds 0.125 mg daily (423). To define dose requirements further, therapeutic drug monitoring should be performed for drugs with a low therapeutic index.

In addition to the factors that determine the drug concentration at the site of action—the pharmacokinetics—the effect of a drug also depends on the sensitivity of the target organ to the drug. The biochemical and physiologic effects of drugs and their mechanisms of action—pharmacodynamics—and the effects of aging are not clearly known. Pharmacodynamics has been even less extensively studied in older patients than has pharmacokinetics. Accurate generalizations are very difficult to make, and the effect of age on sensitivity to drugs varies with the drug studied and the response measured. These differences in sensitivity occur in the absence of marked reductions in the metabolism of the drug and its related compounds. Thus, sensitivity to drug effects may either increase or decrease with increasing age. For example, older patients seem to be more sensitive to the sedative effects of given blood levels of benzodiazepine drugs (e.g., diazepam) but less sensitive to the effects of drugs mediated by beta-adrenergic receptors (e.g., isoproterenol, propranolol). Although an age-related decline in hormone receptor affinity or number (e.g., in beta-adrenergic receptors) is suspected, definitive data demonstrating such an alteration are sparse. Other possible explanations offered for
these differences are alterations in second-messenger function and alterations in cellular and nuclear responses.

Because the response of older patients to any given medication is variable and cannot be foreseen, all drugs should be used judiciously in older patients. The physician should resist the temptation to apply protocol-based strategies to administration of medicines in the elderly. In general, knowledge of the pharmacology of the drugs prescribed, limits on the number used, determination of the preparation and dosage based on the patient’s general condition and ability to handle the drug, combined with downward adjustment of the dose in the presence of known hepatic or renal impairment in concert with surveillance for untoward effects, will minimize the risks of medication use in elderly patients.

**SPECIFIC ISSUES**

**Neurologic Disorders**

Neurologic problems common among older adults in the critical care setting include delirium, stroke, and sleep disorders.

**Delirium**

**Background and Risk Factors**

Delirium is an acute mental disorder common among elderly patients; a recent review noted that 29% to 64% of the hospitalized elderly develop delirium (424) increasing the 6-month mortality rate among these patients to 10% to 26% (425,426). Recognition is difficult, with only 25% of cases being diagnosed using standard screening tools (427,428). Delirium-associated morbidity complicates the hospitalization of 2.3 million older people annually, adding 17.5 million inpatient days and $4 billion to Medicare expenditures to cover increased lengths of stay and greater need for postdischarge institutionalization, rehabilitation, and home care (429–432). Of note, delirium is associated with increased in-hospital mortality even after correction for severity of disease, as documented in a meta-analysis of 42 studies covering 16,395 patients (433,434). Older adults with multiple comorbidities, particularly pre-existing cognitive deficits, are predisposed to delirium (434–436), with a prevalence rate surpassing 50% during intensive care; symptoms persist in nearly that number after ICU departure (437). Particularly at risk are those with a history of hypertension, smoking, elevated bilirubin level, recent epidural analgesia, and recent administration of morphine (435,436,438). Other predictors of delirium include respiratory disease, infection, fever, hypotension, hypocalcemia, and hyperamylasemia (439). Invasive devices, sensory alteration, and inadequate or overaggressive pain control likely aggravate delirium-inducing medication effects in the critically ill patient (434–436), with a prevalence rate surpassing 50% during intensive care; symptoms persist in nearly that number after ICU departure (437). Particularly at risk are those with a history of hypertension, smoking, elevated bilirubin level, recent epidural analgesia, and recent administration of morphine (435,436,438). Other predictors of delirium include respiratory disease, infection, fever, hypotension, hypocalcemia, and hyperamylasemia (439). Invasive devices, sensory alteration, and inadequate or overaggressive pain control likely aggravate delirium-inducing medication effects in the critically ill patient (434–436). Among the many other factors, some particularly predictive factors include smoking more than 10 cigarettes per day, consuming three or more alcoholic drinks per day, or living alone; these all substantially increase the odds ratio of developing delirium during hospitalization (441). Most studies show that among the most critically ill, comatose patients, those with high APACHE II scores, “poly-trauma” patients that undergo emergency surgery, and those with metabolic acidosis are additionally at risk for falling into a delirious state (442).

**Pathophysiology**

Specific pathophysiologic mechanisms are not well understood. The phenomenon can be viewed as a final pathway of various causes of acute brain dysfunction. These include the following: (a) direct brain injury from trauma, cerebrovascular disease (443), or CNS infection; (b) systemic disturbances such as hypoxemia, hypotension, renal failure, hepatic failure, sepsis, and endocrine dysfunction; (c) effects of toxic or pharmacologic agents such as anticholinergics, narcotics, and sedative-hypnotics; and (d) the consequences of withdrawal of substances to which the brain has developed tolerance (e.g., alcohol or benzodiazepines). Delirium is more likely to occur when these factors coexist in patients with pre-existing comorbidities (444–456). Those elderly patients that enter the delirious state with pre-existing dementia, a condition commonly found in older patients, have less chance of full recovery of mental faculties and greater chance of dying than those without pre-existing dementia (457). Current theory proposes alteration of CNS neurotransmitter levels and metabolism by age, medication, or illness as paramount in producing the mental status that characterizes delirium, particularly the acetylecholine and dopamine pathways, serotonin, GABA, histamine, glutamine, and norepinephrine systems (458–461); rapid advances in neuroimaging may allow additional insight into microanatomic bases of delirium (462).

**Diagnosis**

Criteria defining delirium are detailed in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) of the American Psychiatric Association, specifically: (a) a disturbance in attention and awareness; (b) the disturbance develops over a short period of time, represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day; (c) there is an additional disturbance in cognition; (d) the disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma; and (e) there is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies (463). Additional features include alteration of sleep/wake cycle and psychomotor activities. Various screening tools and protocols have been developed that allow accurate and timely diagnosis using these criteria (436,464–468) when the diagnosis is specifically sought. Patterns of psychomotor symptoms are termed hyperactive and hypoactive (469–471). Patients occasionally display features of both types, termed mixed. Hyperactive patients are agitated and combative, with loud, inappropriately boisterous outbursts and motor activity that can be harmful to self or caregiver. Those termed hypoactive alternate between calm, possibly appropriate behavior and a minimally interactive, withdrawn state with flat affect, making this variant easy to overlook. Mixed delirious patients’ symptoms fluctuate between agitated and apathetic (472); more than half of the delirious patients older than 65 years display the mixed subtype (473). Delirium may erroneously be attributed to such conditions as dementia or depression—the three may coexist—or simply not be recognized (474), delaying the
diagnosis. Delays may be explained by the following: (a) the fluctuating nature of the signs and symptoms; (b) inadequate or insufficiently detailed scheduled neurologic and cognitive assessments of patients at risk for delirium; (c) avoidance of interactions with patients displaying altered mental status; or (d) misperception of mental status changes “expected” in critically ill patients (475,476). Altered mental status in any patient suggests delirium; an organized approach to its investigation (477) that focuses on known risk factors is paramount to avoid overlooking the condition. Of particular interest to the intensivist who manages elderly patients are alterations of mental status temporally related to a surgical procedure, specifically delirium developing within the immediate (minutes to days) postoperative period, and the more indolent neurocognitive decline that may appear days to weeks to months later, termed postoperative cognitive dysfunction (POCD); the uniqueness of these conditions lies in their association with the postoperative period. Emergence delirium, the transitory restlessness and disorientation often apparent in the postanesthesia care unit or an ICU that receives patients directly from the operating room, is seen in up to 30% of adults after operation, most often manifests with hypoxic signs of delirium, may portend worse outcome in the postoperative period but generally clears without sequelae (478). More worrisome is interval delirium, appearing 2 to 7 days after operation, the patient manifesting disorientation and agitation, and being at risk for postoperative complications and suboptimal outcome (including increased mortality) (479) by virtue of its appearance. Risk factors for postoperative delirium are additive to those menacing the nonoperative elderly patient such as pre-existing mental compromise, age over 70 years, consumption of substances such as tobacco, alcohol, and sedatives, and renal compromise (480). Procedure-related factors include perioperative hypoxemia and hypotension, exposure to anesthesia-related medications—anticholinergics such as atropine, volatile inhalational anesthetics, neuromuscular blocking agents, and potent opioids—and high-volume blood transfusion and rapid fluid shifts associated with surgery. Procedures using cardiopulmonary bypass raise the possibility of microscopic atheromatous or air emboli as contributors, although investigators have found that the incidence of postoperative cognitive dysfunction at the 6-year milestone is similar for on- and off-pump coronary artery bypass graft (CABG) (481). The incidence of postoperative delirium may not even be related to the anesthetic technique employed (482). The incidence of postoperative delirium ranges from 0% to 74%, varying with age group, surgical procedure, variability of diagnostic criteria, and pre- and postoperative cognitive status (483).

POCD was first identified in 1955 (484), characterized by the appearance weeks to months after a surgical procedure of impairment of memory, concentration, comprehension of language, and social integration (485). Although seldom charged with management of POCD, the intensivist is instrumental in its recognition in that delirium in the early postoperative period may forecast its later reappearance (486). One well-designed investigation of elderly patients undergoing noncardiac surgery reported the incidence of delirium to be 25% at 1 week after operation, with symptoms of POCD being present in 9.9% of patients at 3 months, significantly worse than controls at both intervals (485), and revealing advancing age as the only factor significantly predictive of POCD. More recently, it has been recognized that, in the postsurgical patient, in addition to age over 60, those with previous CVA (even without residua), lower level of education, and POCD at the time of discharge are all predictive of much longer duration of cognitive dysfunction, and of a higher likelihood of dying within 3 months of major noncardiac surgery (487). Similarly, abundant literature (488–491) exists addressing this syndrome in cardiac surgery patients following both on- and off-pump procedures, most of whom were older than 60 years. Although most cardiac surgery patients suffer various concurrent confounding medical conditions that make the specific effects solely of cardiac surgery on subsequent mental status difficult to isolate, meticulous attention to statistical and study control issues allows identification of a substantial incidence (53%) of CABG patients (average age, 60.9 ± 10.6 years) showing cognitive deterioration consistent with POCD at the time of discharge, and 42% at 5 years (491), with age being a univariate predictor of decline. The specific cause of POCD is obscure; suggested causes are those noted above as well as more abstract considerations such as brain inflammation, genetic factors, cerebral edema, and blood–brain barrier dysfunction (492–496), and possibly direct toxic effects of some general anesthetics, and effects of disordered postoperative sleep patterns on brain chemistry (495). Timely recognition of the onset of delirium is required for optimal treatment, facilitating rapid identification of reversible precipitating factors. Beyond that, treatment is supportive, with aggressive treatment of symptoms and protection of the patient from the sequelae of their delirious state. Prevention is central, requiring a multicomponent approach that includes modification of environmental factors and provision of supportive measures, as demonstrated in a prospective—although nonrandomized—study of 832 patients over 70 years old admitted to a general medicine service in which a multicomponent delirium prevention strategy achieved a one-third reduction in the incidence of delirium, compared to those who received standard care (429). Although this study included patients in a general ward, one may extrapolate the findings to profoundly at-risk ICU patients. A skilled geriatrician can help decrease the incidence of postoperative delirium (POD) by assisting in utilizing delirium intervention programs (496). Symptomatic treatment uses both pharmacologic and nonpharmacologic strategies. Instrumental are the use of repeated reorientation, cognitive stimulating activities, promotion of adequate sleep on a normal sleep/wake cycle, physical therapy and mobilization, early removal of catheters and physical restraints, and provision of eyeglasses and hearing aids, combined with the judicious use of medications particularly targeted at calming agitation. All potentially neuroactive medications such as benzodiazepines, opioids, or those with anticholinergic effects that are not absolutely fundamental to the patient’s treatment plan and improvement should be discontinued (436,438,439). Beware, however, of withholding benzodiazepine medications from delirious patients in situations in which they are appropriate such as alcohol withdrawal (497). Nonbenzodiazepine medications are recommended for intubated patients requiring sedation, after sufficient analgesia is achieved (498). It appears that dexmedetomidine, the centrally acting alpha-agonist, has a lower associated incidence of delirium than benzodiazepines when sedation is needed (499). Additionally, this medication allows smoother arousal from the sedated state and earlier extubation in some patients, but at the expense of a greater instance of bradycardia and hypotension (500). The butyrophenone haloperidol is often used in the management of delirium-induced
agitation, having few active metabolites and minimal anti-cholinergic, sedative, and hypotensive effects (501). A recent retrospective analysis suggested that haloperidol use was independently associated with lower mortality in 989 critically ill patients (502). More recently, the so-called atypical antipsychotic medications have been utilized in the treatment of delirium in the elderly, with varying results (503). For POCID, there is no management other than prevention; no therapy has been identified that is curative once the syndrome had developed. In all cases, contributing problems must be identified and corrected and the patient protected. Support must also be provided to family members, who likely will be affected by their loved one's distressing symptoms and by the prospect of additional responsibilities for caring for that person.

**Stroke**

**Incidence and Risk Factors**

Stroke is the third leading cause of death and the leading cause of disability in the elderly. Compared to the 40 to 59 age group, the prevalence of stroke quadruples between 60 and 79 years of age, and nearly doubles again above 80 years of age (504). The stroke incidence similarly increases dramatically with age > 55 years, especially in women (504). Each year, nearly 800,000 individuals suffer strokes in the United States, corresponding to one event every 45 seconds and leading to one death every 3 minutes. Among those ≥ 55 years old, the incidence of stroke doubles with each additional decade of life (504), despite a decline in the United States, Canada, and Western Europe through the later part of the 20th century to the present, attributable to improved management of modifiable risk factors. Among these factors, hypertension is by far the most powerful; aggressive blood pressure control can reduce the risk of stroke by 40% (504). Coronary atherosclerosis, left ventricular hypertrophy, and AF contribute to stroke risk; diabetes mellitus may increase likelihood of stroke by a factor of two to four, but tight glucose control significantly reduces this risk, and may postpone such vascular complications as retinopathy and nephropathy (505,506). Modifiable factors also include cigarette smoking, hyperlipidemia, lack of physical activity, and excessive alcohol consumption (507).

**Classification**

Stroke classification can be based on location, cause, and time course. Prior to routine availability of CT, history and clinical findings provided the sole method of neurologic lesion identification. Today, rapid CT localization supplemented by the time-sensitive history and clinical examination findings allow much more rapid formulation of a treatment plan. Although the details of stroke syndromes are addressed elsewhere in this textbook (see Chapter 124), discussion of some issues as they affect the elderly are warranted.

**Location**

The most common location in which a stroke occurs, representing approximately two-thirds of ischemic strokes (508), is in the distribution of the middle cerebral artery (MCA). Findings include contralateral hemiplegia and hemianesthesia. Proximal MCA occlusion produces profound symptoms: contralateral homonymous hemianopsia with deviation of the head and eyes toward the side of the lesion. Involvement of the dominant MCA distribution may cause aphasia, either expressive, receptive, or both. Dominant hemisphere MCA lesions may induce depression in the elderly, whereas those in the nondominant hemisphere produce visuospatial deficits, unilateral neglect, and emotional lability that can mimic depression, sometimes delaying correct diagnosis. Anterior cerebral artery (ACA) stroke, the least common variety accounting for about 2% of ischemic infarcts (508), most profoundly affects the contralateral leg and foot, generally with lesser impact on the arm and little involvement of the face. Very proximal ACA occlusion, however, may affect the entire contralateral side. Abundant collateral flow in ACA territory yields various symptoms associated with anterior circulation stroke. One may observe frontal lobe features such as emotional lability, mood impairment, personality changes, and intellectual deficits; aphasia is uncommon. Stroke-related paraplegia and incontinence may leave the elderly victim wheelchair-bound and unable to control critical body functions, greatly complicating rehabilitation and subsequent independent living. Strokes in the distribution of the posterior cerebral artery (PCA) manifest a diversity of findings due to the variability of anatomic origin, namely partial or complete origin from the basilar artery or internal carotid arteries. Neurologic consequences of PCA stroke include contralateral hemianesthesia and hemianopsia with sparing of central macular vision, difficulty with reading and calculations, and hemiballismus from subthalamic involvement (508). With vertebrobasilar atherothrombotic disease, cerebellar dysfunction predominates. Common symptoms include vomiting, dizziness, ataxia, nystagmus, and double vision. Vertigo can be profound, causing an already tenuously balanced elderly person to sustain a fatal fall. Other symptoms include weakness of the face and the contralateral body, with dysarthria or dysphasia; facial numbness may occur. Brain stem involvement may be revealed by altered mental status or quadriplegia (508). Lacunar stroke, caused by occlusions of the small penetrating and subcortical arteries, tend to occur in the basal ganglia, internal capsule, thalamus, or pons. Depending on the specific sites of lesions, a wide variety of presentation may occur, including pure motor or sensory findings, symptoms that appear parkinsonian, or a mixture of presenting abnormalities.

**Cause**

Strokes are either ischemic or hemorrhagic, the distribution being approximately 87% and 13%, respectively. Ischemic events involve occlusion of the cerebral vessel by embolus or thrombosis; the remaining include hemorrhage into the brain parenchyma (10%) or its surrounding spaces (subarachnoid hemorrhage, 3%) (504). Rapid identification of the specific cause of the stroke is fundamental to its management, because modalities of treatment vary with cause. Embolic phenomena most often originate from the heart, commonly associated with atrial fibrillation, which is frequent in the elderly population. Atherosclerotic disease of the aortic arch is emerging as an increasingly important and recognized risk factor for recurrent stroke when the wall thickness exceeds 4 mm (509). Atheroma-associated clot formation may produce neurologic syndromes known as thrombotic stroke. Subintimal vascular disease is the ultimate inciting event, inducing arterial narrowing with ulcerated plaque formation in areas of more turbulent flow, such as...
the carotid bifurcation, leading ultimately to symptoms ranging from a temporary deficit (i.e., a transient ischemic attack [TIA]) to complete arterial occlusion caused by clot formation.

**Time Course**

Stroke phases are termed acute, subacute, and chronic, each with its unique needs and goals of care. Time spans are generally said to extend from symptom onset to 48 hours, 48 hours to 3 months, and past 3 months, respectively. The intensivist is little involved in direct management of stroke-related symptoms after the first few days, although elderly patients who fall within the later stages of recovery may certainly require intensive care for recurrent stroke, a stroke-related complication, or other critical illness.

**Acute Phase of Stroke (Admission to 48 hours).** Management of the acute phase involves, first and foremost, ensuring airway and hemodynamic stability. Thereafter, the goals of care are (a) identification of the stroke as ischemic or hemorrhagic; (b) initiation of thrombolytic therapy when indicated; and (c) recognition and treatment of medical or neurologic complications. The first goal is most easily achieved by obtaining a non-contrast-enhanced CT scan of the brain as quickly as possible when stroke is suspected; hemorrhage is usually obvious on this scan. Early in the course of ischemic stroke there may be no visible abnormality. Early CT may reveal one of the many mimics of stroke: subdural hematoma, neoplasm, or hydrocephalus; contrast enhancement may improve yield if tumor or infection are likely. Recall that comorbid conditions abound in the elderly; cardiac dysrhythmias or infarction may provoke or result from a cerebrovascular event, mandating 12-lead ECG and continuous cardiac monitoring in all stroke patients. Questions of the numerous other causes of altered mental status in the geriatric patient must be investigated and settled quickly. For those in whom, with the assistance of expert consultation, it is decided that ischemic stroke is present, the risks and benefits of thrombolytic therapy must be weighed. Current recommendations for management include initiation of intravenous thrombolytic therapy with recombinant tissue plasminogen activator (rt-PA) as soon as possible, within 180 minutes of onset of stroke, in the absence of contraindications (510). Thrombolysis between 3 and 4.5 hours is associated with improved 90-day outcome, but with a higher risk of intracranial hemorrhage (511). Intrarartorial thrombolysis may be an option for those with occlusion of the MCA. Of note is that rt-PA is approved by the Food and Drug Administration (FDA) for intravenous administration, but not for intra-arterial use. None-the-less, the use of rt-PA improves outcome from stroke at 3 months (512).

There is a relative paucity of data documenting treatment of older stroke patients compared to those in younger age groups (a situation similar to those studies addressing thrombolysis in myocardial infarction), although there is presently an ongoing study in Italy investigating the use of rt-PA in patients older than 80 years (513). It does appear, however, that while there may be poorer outcome from stroke in the elderly population in general, there is no increased likelihood of rt-PA–induced severe intracranial hemorrhage (514–517). This was more recently confirmed in a publication from Australia in a study of 206 patients over 80 years to whom rt-PA was administered for acute stroke, and in which there was no increase in the instance of hemorrhagic transformation after thrombolysis (518). A number of stroke scales, including the National Institutes of Health Stroke Scale (NIHSS), have been devised to assist in quantification of severity of stroke-related symptoms as a guide to optimal management. Important issues such as blood pressure management and anticoagulation are best addressed in concert with expert consultation (510,511,519).

**Subacute and Chronic Phases of Stroke Management.** The acute events and aggressive treatment related to stroke often stabilize within 48 hours; thereafter, close attention to complications or neurologic decompensation is warranted. With meticulous attention to the return of intact airway reflexes and sufficient recovery of mental status, early extubation of the trachea is advisable. Otherwise, early tracheostomy for airway protection allows withdrawal of sedation, early mobilization, and more robust participation in physical and occupational therapy, with the long-term goal of rehabilitation to maximal recovery. During the period from 2 to 5 days after the stroke, the risk of acute complications continues, including such events as hemorrhagic transformation, the onset of catastrophic cerebral edema warranting aggressive monitoring and management, deep venous thrombosis, hyperglycemia, and elevated temperature, all of which must be recognized and treated aggressively to optimize outcome (520). The common complications associated with compromised mental status, namely pulmonary aspiration, skin breakdown, infections, and limitation of extremity range of movement, can be ameliorated by aggressive rehabilitation efforts. Early nutritional support via feeding tube is sometimes overlooked in the flurry of initial management activity but must be initiated as early as possible. Formal rehabilitation programs may be organized in the setting of the acute inpatient rehabilitation unit, or in long-term rehabilitation hospitals, skilled nursing facilities, outpatient rehabilitation centers, or home. Optimal programs incorporate comprehensive assessment and treatment by a multidisciplinary team that includes physical, occupational, and speech therapists, and a geriatrician, physiatrist, psychologist, nurse, and social worker in the first few months during which most neurologic recovery occurs. A pre-existing state of debilitation, however, may limit the 3-hour period of active participation traditional to inpatient environments, mandating alternate plans. General goals of rehabilitation include restoration of motor and sensory function, and strengthening of intact functions to facilitate compensation for residual deficits. Beyond the first few months, while neurologic function likely plateaus, functional recovery continues when encouraged and supported by family presence, social interaction, and adequate nutrition. The stroke recurrence rate of 30% within 10 years warrants continued attention to chronic medical conditions. The Framingham Study data document survival in stroke victims of 50% in 5 years (521–523). Preservation of functional gains, avoidance of complications, and aggressive management of contributing comorbid conditions may well forestall the decline that often follows a stroke in an elderly patient.

**Sleep Disorders**

**Background**

Insomnia plagues the elderly, afflicting nearly 50% of older adults (524). The genders are generally equally affected,
although sleepless men predominate after 85 years of age. Prevalence increases in the elderly with the number of coincident medical conditions (525,526). Common sleep complaints among the community-dwelling elderly are difficulty in initiation of sleep, and nighttime and early morning awakening (527). Sequelae of insomnia include physical and mental fatigue, anxiety, and irritability, which worsen as bedtime approaches and personal worries re-emerge without the protective diversion of normal daytime activities (528). Chronic dysfunctional sleep induces a state of endless fatigue, affecting memory and concentration (525,529). The elderly are particularly affected, with steepened cognitive decline and risk of falls, with associated morbidity and mortality (530–532). Hospitalization amplifies the morbidity of sleep disturbances; ICU admission likely subverts any semblance of a normal sleep pattern. Sedation to facilitate mechanical ventilation subdues consciousness but disrupts normal variation in sleep stages, preventing rest. Circadian rhythms are disrupted, with dysynchrony in anticipated light/dark time cycles and inadequate daily morning exposure to sufficient bright light (533,534). Many elderly patients become disoriented at night. Exhaustion and confusion from constant alarms, noises, dressing changes, and unscheduled diagnostic procedures, and the impact of acute severe illness may all produce delirium in nearly two-thirds of elderly ICU patients. Dementia contributes to this problem.

Identification and Management of Sleep Disorders

The sleep/wake cycle is regulated by a complex neurochemical interaction subserved by the brainstem, hypothalamus, pons, and preoptic areas of the brain (534). Aberrations of sleep patterns produce dysfunctional sleep (535), disrupting daytime functioning. Sleep architecture is determined for an individual by performance of a sleep study displayed on a hypnogram. Normal sleep architecture displays three segments: light sleep (stages one and two); deep (delta or slow wave) sleep (stages three and four), which is the most restorative segment; and rapid eye movement, or REM, sleep (stages one and four) (536). In nonelderly adults, typical cycle time between REM and non-REM sleep is 90 to 120 minutes (537). Advanced age alters sleep by shortening sleep latency and total sleep time, preserving REM sleep, decreasing the delta segment, and advancing the natural onset of sleepiness to an earlier time in the evening (527). Nocturnal sleep fragmentation worsens with age, with daytime somnolence and frequent napping being commonplace, sometimes causing reversal of the sleep/wake cycle. Acute insomnia in the geriatric patient may be precipitated by a host of issues, including the critical illness itself. Metabolic derangements related to sepsis or trauma, recent exposure to potent anesthetic agents, and the unfamiliar ICU environment filled with off-schedule and frequent disruptions effectively prevent restful sleep. Although not generally within the purview of the intensivist, investigation of the cause of insomnia may be initiated for the ICU patient by meticulous history gathering, discussion with family members, use of sleep-related questionnaires such as the Multiple Sleep Latency Test (535) and the Epworth sleepiness scale screening too (537), and observation of the patient for evidence of any of the primary sleep disorders that respond to specific treatment modalities. These include a spectrum of conditions collectively termed sleep-disordered breathing (SDB), periodic limb movements in sleep/restless legs syndrome, and REM sleep behavior disorder. Some causes of SDB (obstructive sleep apnea, specifically) respond to continuous positive airway pressure (CPAP) (538), and the latter two respond to medications (539,540). Secondary causes of disordered sleep are legion, including medications, sleep-disruptive behavioral habits (such as prolonged bedtime naps, sedentary lifestyle, overindulgence in tobacco or alcohol, late evening meals), numerous medical conditions (HF with orthopnea, incomplete bladder emptying with nocturia, gastric reflux, dementia), or environmental deficiencies (insufficient daytime sunlight exposure, inadequate climate control) (536).

In the ICU, it is unlikely that a patient will experience a normal sleep cycle, and the consequences of disrupted sleep may be consequential. In the adult ICU patient, sleep architecture is typically disrupted, with decrease in REM sleep and redistribution of bouts of fragmented sleep into unusual patterns of time distribution (541). Examination of schedules of care during the 12-hour “night shift” time period has revealed that the typical ICU patient likely experiences an astounding number of potential sleep interruptions—42 in 12 hours, or 3.5 per hour (542); is it any wonder that our patients are at risk for delirium while in our ICUs? Circadian rhythm patterns are altered in the critically ill, associated with disrupted melatonin and cortisol secretion, and altered 24-hour cyclic temperature and other vital sign patterns (543,544), all of which contribute to aberrant sleep patterns. In those with age-related Circadian Rhythm compromise (545), the impact of sleep disruption on the onset of delirium and associated worsening of outcome can be profound; effective treatment obviously requires accurate diagnosis. Evidence of primary causes should be relayed to the patient, family members, and the physician responsible for long-term management of the patient after transfer. All possible accommodations should be made to minimize interruption of the older patient’s restful nighttime sleep periods, minimizing noise, procedures, and cycling of lights on and off. Daily exposure to bright sunlight through nearby windows is beneficial (546,547). Pharmacologic treatments are best addressed on an individual basis, and within certain guidelines (548). Various medications are available (536); each, however, may provoke delirium in elderly patients. The use of benzodiazepines and opioids to promote sleep in the elderly, with their impact on the occurrence of delirium, is discouraged (549). In-depth guidelines for the evaluation and treatment of sleep disorders are available (529,550–556).

REHABILITATION AFTER ACUTE ILLNESS

The impact of critical illness on the lives of elderly patients is profound. Beyond the associated death rates, level of functioning is compromised in a substantial percentage of survivors (557), and increasing vulnerability to long-term dependence increases with age (558). Medical intervention in the critically ill or injured patient has evolved to a level of sophistication and capability that allows a previously unsalvageable patient to survive. Thoughtful and comprehensive discharge planning,
initiated at the time of admission, can shorten LOS (559) and provide the springboard for return to a reasonable, though often compromised, level of functional autonomy (560). Many of these elderly individuals, after considerable improvement, may nevertheless linger for a prolonged period, requiring a single isolated critical intervention such as mechanical ventilation, and thus further risking the decline of inactivity, and subsequently find themselves after hospital discharge confined to a non-home location (561). The deleterious effects of such a prolonged hospital confinement can be ameliorated by early use of the expertise of rehabilitation professionals. Additionally, optimal recovery from common medical occurrences and conditions simply is not possible without active patient participation, which can be assisted and promoted by the physical medicine team. It is being increasingly recognized that early institution of rehabilitation planning and execution by such a team of specialists can reduce health care costs, LOS, and severity of disability after discharge (562). Shortening of hospitalization decreases the exposure of the marginally compensated patient to its debilitating risks (563). Avoidance of postillness disability is of paramount importance in that it is associated with higher mortality and greater dependence on family and other caregivers (564,565) (see Chapter 12).

Rehabilitation, as a general concept, encompasses several basic tenets that meld smoothly with the critical care frame of reference (566). Fundamental to any rehabilitation plan is stabilization and treatment of the primary inciting disorder; such a precept is the essence of the practice of critical care medicine, and thus is accomplished by virtue of the provision of critical care services. The unique jeopardy in which the elderly exist by virtue of their frailty and vulnerability to complications warrants the most meticulous attention to routine ICU precautions, which must be recognized by the intensivist (567). These include frequent turning, early nutrition, appropriate deep venous thrombosis (DVT) prophylaxis, semi-recumbent positioning, and maintenance of day–night cycle of auditory and visual stimulation. Early evaluation by a multidisciplinary team of specialists facilitates identification of evolving and anticipated functional deficits that are amenable to treatment, whether preventive or corrective. Integrated rehabilitation treatment and planning should occur in both the immediate and long-term settings by involvement of the physiatry team. Attention by the intensivist to ICU occurrences that are predictors of disability after critical illness—delirium and immobility—can assist in minimizing subsequent disability that would warrant institutionalization (568). Admission of a frail elder to a specialized unit designed around and attentive to specific features of geriatric pathophysiology has been demonstrated to improve functional outcomes (569). A number of evaluation tools have been devised to assess an individual’s frailty that may be used in rehabilitation planning after illness; they appear to be useful primarily in excluding rather than identifying frailty (570).

The fundamental tool available to the geriatrician with which to organize the management and treatment of medical issues, including problems warranting formal rehabilitation, is the Comprehensive Geriatric Assessment (CGA) (571). The integrated, patient-centered concept of treatment implicit in CGA is often accomplished in specialized hospital units or within the framework of treatment considerations peculiar to the elderly, managed by a devoted multidisciplinary team. Such units include the geriatric evaluation and management (GEM) unit, as is found in some Veterans Administration hospitals, a specifically formulated management plan termed Acute Care for Elders (ACE) (572), or a construct of aggressive hospital-wide screening and treatment for at-risk patients by specialists and volunteers in an organization such as the Hospital Elder Life Program (HELP) (573). An alternative for the intensivist, whose patients are clearly unavailable for transfer to such a location remote from the ICU, is consultation by an in-patient geriatric consultation service team including individuals knowledgeable in rehabilitation issues (574). To date, the success of CGA in improving functionality and decreasing disability in the elderly after discharge seems clear (569,575), and has been validated as an effective tool to decrease morbidity and mortality in acutely ill elderly patients (576).

Several specific medical issues mandating ICU admission require active rehabilitation measures to achieve successful treatment. These include cardiac events related both to ACS and cardiac surgery, stroke, serious traumatic injury, various debilitating musculoskeletal conditions, and such morbid orthopedic procedures as lower extremity amputation and hip fracture repair. Large studies and reviews (577) document the success of aggressive rehabilitation after acute myocardial infarction and cardiac surgery in reducing cardiac mortality; over recent years, the benefit of this treatment is beginning to be documented (578) in the elderly population as well. It appears that an aggressive program of cardiac rehabilitation conducted for elderly patients, although often limited by arthritis or coexistent peripheral vascular or pulmonary disease, is safe, able to improve aerobic capacity, and favorably affects body fat percentage, lipid profiles, and physical function scores (579–581). A variety of issues may explain lower participation among elderly cardiac patients, especially women, compared to younger people (582–585).

Recovery from acute stroke presents a complex challenge to victim and physician alike. Whereas the cardiac patient may see improvement after surgery that continues during rehabilitation, the stroke patient often must endure impaired mental status and motor/sensory capabilities from the initial insult, often yielding a debilitated depressed individual (586) with little motivational reserve to assist recovery, an occurrence that impacts mortality after discharge (587). Survival beyond the first few days likely mandates prolonged assistance that may be required for months to achieve optimal improvement. Stroke rehabilitation targets improvement of impaired movement and function to minimize disability and optimize recovery to the premorbid state (588); this rehabilitation process hopefully will be initiated while the patient is still confined to the ICU. The extent of improvement hinges on several issues. These include age (589), the nature and severity of the initial deficit (590,591), presence of intracranial hemorrhage-related, rather than infarction-related, stroke as a with the former improves more than one with the latter for a given initial severity (592), and early initiation of the rehabilitation activities, preferably within 7 days (593), this period possibly including the ICU period. The plasticity of injured and unaffected normal brain tissue may allow gradual improvement over the subsequent several months (594). Specific stroke-related rehabilitation issues include the following: (a) optimal location for therapy; (b) speech and swallowing; (c) recovery of upper extremity function scores (579–581). A variety of issues may explain lower participation among elderly cardiac patients, especially women, compared to younger people (582–585).
function; (d) balance and walking; and (e) strengthening exercises (590). Evaluation tools such as the Barthel Index and the Stroke Impact Scale (595) are used to quantify a stroke patient’s recovery, which may continue for as long as 6 months of recovery in the absence of another complication (596, 597). Success of recovery from stroke varies over a large population (598) based on aforementioned variables and, to some extent, social status (599).

Rehabilitation of an injured elderly patient often involves continued long-term supportive therapy of conditions from which a younger individual may well recover quickly, namely mild TBI and/or extremity fracture. Indeed, continuity of specialized geriatrician involvement may facilitate continued attention to several issues during a prolonged trauma-ICU admission. These include comorbid problems, functional abilities and family support, formulation and continuous assessment of an itemized management plan toward realistic goals, and early initiation of planning for discharge and follow-up care (600, 601). Of particular concern to intensivists managing elderly patients is hip fracture, of which more than 250,000 occur annually (602), with most patients being older than 50 years of age. Such fractures increase mortality—compared to that of similar patients without fracture—in those older than 65 years of age by 12% to 36% (603), as well as the likelihood of subsequent institutionalization (604) and functional dependence (605, 606). A patient with pre-existing cognitive dysfunction or delirium will likely fare worse (604, 606). Successful management requires identification and correction/stabilization of comorbid conditions, appropriate surgical treatment, and early initiation of important precepts of rehabilitation (602, 607). These include early mobilization, initially to chair, followed by standing and walking with weight bearing; prolonged bed rest fosters deconditioning and is to be avoided. The intensivist who manages a particularly ill elder must address the potential for thromboembolic complications by encouraging early mobilization to minimize venous stasis, and by using prophylactic anticoagulant medication; regimens differ according to the exact situation (608–611). Functionality can be profoundly affected after hip fracture (612, 613) and is further impacted by a high level of comorbidity (614). Although more men than women die initially after hip fracture, those who survive after the first year experience comparable functional recovery equally (615). Very advanced age is not necessarily a contraindication to hip fracture surgery in the absence of another complication (596, 597). The health care needs of elderly patients represent enormous challenges to all members of the medical profession. The aspirations and personal convictions of such individuals are as fundamental to the well-being and fruitfulness of their lives as are those of any other segment of the population. Although years of living bring elderly patients with the most complex illnesses and morbid conditions to the hospital and ICU, it is to be remembered that the elderly often recover fully, or almost so, from profoundly serious illness despite numerous worrisome impediments that would discourage all but the most optimistic clinician. In general, vigilance and dispatch in investigations and treatment of critically ill geriatric patients, using the guidelines listed in this chapter, will facilitate recognition of the subtleties of such conditions. Although a substantial percentage of the elderly cannot be brought back to an independent level of functioning, every effort should be expended to achieve accurate diagnosis and expeditious treatment, providing full intensive support to conditions that are correctable and recognition when reasonable limits have been reached.

**SUMMARY**

The health care needs of elderly patients represent enormous challenges to all members of the medical profession. The aspirations and personal convictions of such individuals are as fundamental to the well-being and fruitfulness of their lives as are those of any other segment of the population. Although years of living bring elderly patients with the most complex illnesses and morbid conditions to the hospital and ICU, it is to be remembered that the elderly often recover fully, or almost so, from profoundly serious illness despite numerous worrisome impediments that would discourage all but the most optimistic clinician. In general, vigilance and dispatch in investigations and treatment of critically ill geriatric patients, using the guidelines listed in this chapter, will facilitate recognition of the subtleties of such conditions. Although a substantial percentage of the elderly cannot be brought back to an independent level of functioning, every effort should be expended to achieve accurate diagnosis and expeditious treatment, providing full intensive support to conditions that are correctable and recognition when reasonable limits have been reached.
Key Points

- The number of elderly individuals is increasing, both in actual numbers and as a percentage of the population, with important implications in the management of critical care resources over the next 20 to 40 years.
- Physiologic reserve diminishes inexorably with age as part of aging, independent of the impact of comorbidities common in the elderly, with significant importance in managing the medical conditions in the elderly.
- The desire to continue aggressive critical medical care in the face of likely marginal chance of recovery varies widely in the elderly population, so it is critically important to generate an accurate plan of care early in the course of treatment in the elderly critically ill.
- CV compromise, often occult, affects most elderly individuals, just from the effects of less compliant vasculature and restructuring of myocardial architecture associated with age; addition of comorbidities of HFpEF, hypertension, and coronary disease explain the high morbidity and mortality from cardiac events in the elderly.
- Virtually all other body systems in the elderly, such as the pulmonary, neurologic, and renal systems, are at risk for sudden pathologic deterioration, similar to that seen in the CV system, when a disease process is imposed upon a system that is less robust by virtue of aging.
- Acute interventions involving intravascular interventions, both chemical and mechanical, to relieve vascular occlusion in the elderly should not be bypassed solely on the basis of age, because the elderly often benefit greatly from such interventions.
- Drug administration must be scrutinized closely in the elderly because of altered medication kinetics seen in geriatric physiology.

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**Chapter 70 The Geriatric Patient**

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