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Exercise and aging

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The interaction of physical activity, exercise, and physical fitness with health and biologic aging is complex and multifaceted, but there is general acknowledgment of its importance to major public health outcomes [1–12]. Although many questions remain about mechanisms of effect and dose-response curves [13], a synthesis of the literature indicates many potentially positive effects of participation in physical activity on the aging process. To understand the potential role of exercise in aging and incorporate it into clinical practice, health care professionals should understand the rationale for various modalities and doses of exercise in relation to specific health-related goals and optimization of biologic aging.

This rationale for the use of exercise to optimize aging can be divided into five broad topics, each of which is discussed briefly in the sections that follow. Regular participation in physical activity or planned exercise has been shown to

1. minimize the physiologic changes associated with typical aging;
2. contribute to psychologic health and well-being;
3. increase longevity and decrease the risk of several of the most common chronic diseases of industrialized societies;
4. be useful as primary or adjunctive treatment for certain chronic diseases and counteract specific side effects of standard medical care; and
5. assist in the prevention and treatment of disability.

Taken together, this broad spectrum of potential benefits of a physically active lifestyle warrants incorporation of an exercise prescription into mainstream medical practice for adults of all ages, if the dual goals of health promotion and disease prevention are to be embraced fully.

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Minimizing the biologic changes of aging

There is a great overlap between the physiologic changes that are attributable to disuse and those that typically have been observed in aging populations [14]. These effects span a wide range of organ systems and functional capacities potentially relevant to health status in older adults. In most physiologic systems, the normal aging processes do not result in significant impairment or dysfunction in the absence of pathologic conditions or under resting conditions. In response to a stress or significant disuse, however, the age-related reduction in physiologic reserves causes a loss of homeostatic balance or an inability to complete a task requiring near-maximal effort. Some of the most notable changes common to disuse and aging include the following:

- Decreased muscle mass, strength, power, endurance, contraction velocity, mitochondrial function, and oxidative enzyme capacity
- Decreased maximal and submaximal aerobic capacity, cardiac contractility, maximal heart rate, stroke volume and cardiac output, impaired endothelial relaxation, and reduced heart rate variability (autonomic dysfunction)
- Increased arterial and myocardial stiffness and systolic and diastolic blood pressure
- Decreased nerve conduction velocity, impaired proprioception and balance, slowed gait velocity, and reduced gait stability
- Reduced insulin sensitivity and glucose tolerance
- Increased visceral fat mass, total body fat, and intramuscular lipid accumulation
- Impaired immune function
- Decreased tissue elasticity, thinning of cartilage, cross-linkage of collagen, and shortening and weakening of tendons
- Decreased bone mass, strength, and density

Recognition of this overlap between the syndromes of disuse and aging has led to numerous investigations attempting to separate ''immutable'' biologic changes from those that are modifiable with specific patterns and modalities of exercise. Some of the areas most relevant to clinical health and function with age are reviewed in the paragraphs that follow.

Maintenance of exercise capacity

Many studies suggest that chronic adaptation to physical activity can attenuate markedly the decrements in exercise capacity and physiologic morphology and function that would otherwise occur with aging, with the notable exception of maximal heart rate (owing to declining sensitivity to β-adrenergic stimulation in the aging heart [15]). Although the peak exercise workload achievable therefore is always lower in aged individuals, the cardiovascular

and musculoskeletal adaptations to chronic aerobic exercise [16–21] enable the trained individual to sustain higher submaximal workloads with less of a cardiorespiratory response (heart rate, blood pressure, and dyspnea) and less overall and musculoskeletal fatigue. Apart from peak athletic performance, the adaptations to cardiovascular training can overcome much of the day-to-day functional limitations that might otherwise be imposed by the physiologic changes of aging and disuse [22].

Musculoskeletal function (strength, power, and muscle endurance) is dictated largely by the size of the muscle mass that is contracting, and to a lesser extent, by changes in surrounding connective tissue in the joint (cartilage, tendons, and ligaments) and neural recruitment, conduction velocities, and fatigue patterns. Sedentary individuals lose large amounts of muscle mass during the course of adult life (20%–40%), and this loss plays a major role in the similarly large losses in muscle strength observed in cross-sectional and longitudinal studies [23–26]. Unlike many other changes that affect exercise capacity, muscle mass usually cannot be maintained into old age even with regular aerobic activities in either general populations [27] or master athletes [28]. Only overloading of muscle with weight-lifting exercise (resistance training) may prevent losses of muscle mass (and also strength) in older individuals [29]. Appropriate progressive resistance training programs of 3 to 6 months or more in duration can be shown to increase muscle strength by an average of 40% to 150%, depending on the subject characteristics and intensity of the program, and to increase total body lean mass by 1 to 3 kg or muscle fiber area by 10% to 30% [30–38]. Similarly, there is evidence that balance training [39–42] and flexibility training [1,43] induce positive adaptations in these domains of exercise capacity in both young and old adults.

Optimizing body composition

The typical patterns of change in body compartments seen in ‘‘usual aging’’ include decreased muscle mass, decreased bone mass, and increased total and visceral fat mass. The extent to which these changes occur in an individual depends on a combination of genetic, lifestyle, and disease-related factors that are all interrelated [44,45]. All of these body composition changes may affect metabolic, cardiovascular, and musculoskeletal function negatively [46–48], even in the absence of overt disease, so it is important to optimize lifestyle choices and other treatments that can counteract the negative effects of aging or disease on body composition.

At all ages, an exercise prescription is important for the prevention and treatment of osteoporosis. Osteogenic adaptation seems optimal with application of forces that are rapid in onset, diverse in direction, intermittent, and progressive over time. A combination of lifestyle choices, organized sports, unstructured play, and household and occupational tasks can contribute to a desirable exposure to physical activity that will be lifelong and robust enough to counteract age- and disease-related losses of bone. An initial emphasis on weight-bearing aerobic

and high-impact activities in youth, shifting toward resistive loading and balance-enhancing exercises in old age, seems to optimally address the needs and capacities of the musculoskeletal system throughout the life span. There is substantial randomized, controlled trial evidence that a stabilization or increase in bone mass in premenopausal and postmenopausal women is achievable by either resistive [49–53] or weight-bearing aerobic exercise [54–59]. High-impact loading such as jumping [52,60] has been shown to be effective only in premenopausal women at this time, for unclear reasons. Exercise-induced effects on bone density (differences of 1%–2% per year compared with control subjects) may be important for prevention and treatment of osteoporosis and related fractures and disability, as reviewed in several recent meta-analyses [61–65]. Even if exercise alone is an insufficient stimulus to maintain bone density at youthful levels, the combination of exercise effects on bone geometry and strength, muscle mass, muscle strength, and balance should lower the risk of injurious falls substantially in physically active individuals.

Decreases in total adipose tissue accumulation and its abdominal (visceral) deposition are achievable by aerobic [66–68] and resistive training [69–71]. Significant changes in total body fat usually are seen only in conjunction with an energy-restricted diet [72–74] or high volumes of energy expenditure in exercise (5–7 hours per week of high-intensity activity). Preferential visceral fat mobilization often is seen in response to exercise and dietary interventions [75–78], however, which means that small amounts of total body weight or fat mass (5%) may be associated with substantial changes in visceral fat ($\geq$20%). This selectivity has important metabolic implications for the prevention or treatment of the insulin resistance syndrome [74,79], a precursor to atherosclerosis and type 2 diabetes. Such targeting of excess adiposity is both protective and therapeutic for many common chronic diseases, offering significant risk reduction in the case of osteoarthritis; cardiovascular disease; gall bladder disease; type 2 diabetes; breast, colon, and endometrial cancer; hypertension; stroke; and vascular impotence, for example [8,80–84]. Although generalized obesity is associated with excess mortality, cardiovascular disease, osteoarthritis, depression, mobility impairment, and disability, it is predominantly excess visceral fat that is associated with sleep apnea; dyslipidemia; elevated fibrinogen, cortisol, and cytokines; hyperinsulinemia; glucose intolerance or diabetes; endothelial cell dysfunction; hypertension; and cardiovascular disease.

An increase in muscle mass, in contrast to changes in fat and bone, is achievable to a significant degree only with progressive resistance training or generalized weight gain from extra energy and protein consumption [31,34,35,85,86] and has a potential role in prevention for diabetes [87–90], functional dependency [91–94], and falls and fractures [95–100], as well as being important in the treatment of chronic diseases and disabilities [101] that are accompanied by disuse, catabolism, and sarcopenia. For some diseases, such as type 2 diabetes mellitus, there are potential advantages to minimizing fat tissue and maximizing muscle tissue because these compartments have opposite and likely independent effects on insulin resistance in the elderly [74].

Promotion of psychologic well-being

Psychologic well-being is vital to optimal aging, and it is dependent on a host of factors, including genetic traits, social support systems, personality types, and the presence of positive and negative psychologic constructs such as happiness, optimism, morale, depression, anxiety, self-esteem, self-efficacy, and vigor. Depression will be the leading cause of early death or disability among adults in the developed world in this century, according to the World Health Organization, and it is of vital importance as a target for health promotion efforts. Physical activity participation has been shown to be associated with more positive psychologic attributes and a lower prevalence and incidence of depressive symptoms in many cross-sectional and prospective epidemiologic studies [102,103] and experimental trials [104,105]. The randomized, controlled trial evidence for exercise as an isolated intervention for the treatment of clinical depression in younger and older cohorts is robust and consistent. In 14 randomized, controlled trials in adults aged 18 to 91 with clinical depression, both aerobic [106–117] and resistance-training [109,110,118,119] exercise produced clinically meaningful improvements in depression, with response rates ranging from 31% to 88%.

No study has shown standard treatment to be superior to exercise for the relief of depression. Blumenthal et al [114] directly compared high-intensity aerobic exercise to antidepressant medications in older adults with major depression and found the two approaches equipotent (60%–69% recovery), with no added benefit of combined exercise and medication. In the studies that have addressed the issue of exercise modality, resistance training was found to be equivalent to aerobic training in young adults with depression [109], and yoga was found to be as effective as aerobic exercise.

A summary of the literature on exercise and depression suggests that it is effective in young and old, it is approximately as effective as antidepressants in clinical cohorts, that aerobic and resistance modalities seem equally beneficial, and that optimal responses are seen with higher intensities. It is notable that effects are most significant in those with comorbid illness, such as cardiovascular or pulmonary disease [120] or major depression [114], attesting to the clinical relevance of this exercise adaptation.

How exercise works to prevent or treat affective illness is not clear. Numerous studies provide evidence of impaired neuroplasticity in the hippocampal region in particular, associated with mood disorders [121], and there is some evidence that antidepressants exert their effects in part through signaling pathways responsible for enhancing structural neuroplasticity and cell survival [122]. Degeneration of hippocampal volume (a proxy of impaired neurogenesis) is associated with cognitive dysfunction, in particular memory loss [123], and is believed to play a critical role in the pathogenesis of depression [121]. Some data suggest that relief of depression with either drugs or exercise is accompanied by reversal of these hippocampal volume losses associated with depression [122]. Further studies are required to elucidate the role of physical activity in neuro-

plasticity, as related to prevention and treatment of affective and cognitive changes of aging.

Increasing longevity and prevention of common chronic diseases

The effects of exercise on total mortality are unlikely to ever be substantiated by randomized, controlled clinical trials, given the impracticality of random assignment to various physical activity regimens during the course of a lifetime. There is clear evidence, however, of an inverse, linear dose-response relationship between the volume of physical activity reported in epidemiologic studies (with sample sizes ranging from <500 to >2.5 million individuals) and all-cause mortality rates [124–127]. These relationships are demonstrable for men and women and for older (>60 years of age) and younger cohorts [128–133]. Volumes of energy expenditure during exercise of at least 1000 kcal/wk reduce mortality by approximately 30%, whereas reductions of 50% or more are seen with volumes closer to 2000 kcal/wk [124]. Despite the consistency of the data from well-designed observational studies, many questions still remain regarding the minimum threshold for efficacy; the effect of exercise intensity, duration, and frequency (apart from contributions to overall volume); the effect of nonaerobic modalities of exercise; and the mechanism of benefit.

Physical activity patterns may be influenced by aging and genotype, and physical activity in turn may influence physiologic capacity, psychologic health, dietary intake, other adverse behaviors, or risk factors for chronic disease. All of these factors are potential pathways by which exercise ultimately could influence the prevalence of chronic disease in a population. Other than genetic factors and environmental insults (ie, pollution, asbestos, heavy metals, infectious agents, and so forth), most of the major contributors to the development or severity of chronic diseases are in some way related to habitual levels of physical activity. Examples include cardiovascular disease [130,134], stroke [135], type 2 diabetes [90,136], obesity [137,138], hypertension [139–141], osteoarthritis [142], depression [114,143–145], and osteoporosis [4,146–150]. Notable exceptions to these patterns are some diseases of the central nervous system (eg, Parkinson's disease and other degenerative neurologic diseases) that have not been linked substantively with exercise or physical activity. Animal studies recently have documented the potential for exercise to augment neuroplasticity by way of enhancement of neural growth factor activity in the hippocampus. Such hippocampal adaptation or protection ultimately may explain associations among exercise, depression, and dementia that have been noted in several large, prospective epidemiologic studies.

The relationship between exercise and risk factors for chronic disease (eg, obesity and hypertension) is clearly bidirectional. Although appropriate levels of physical activity may optimize such risk factor profiles, the presence of risk factors may lead to reduced physical activity and thus, heightened risk

for disease. For example, inactivity may lead to sarcopenia, followed by muscle weakness and further restriction in activity levels, subsequently contributing to the development of osteopenia and gait abnormalities, and finally, hip fracture.

Most of the evidence linking exercise to chronic disease prevention is drawn from the epidemiologic literature, as might be expected, given the long latency period required for the development of most of these diseases. Examples include a reduced risk of cardiovascular disease, type 2 diabetes, osteoporosis, stroke, breast cancer, colon cancer, depression, and disability itself [151–156] in more physically active or fit individuals as compared with inactive or less-fit individuals. In the best studies, this protective effect persists even after adjustment for other known risk factors for the disease in question. Because exercise likely works in part by reducing the presence or severity of some of these risk factors (such as visceral obesity, fibrinogen levels, hypertension, hyperlipidemia, and so forth) the *true* protective effect of exercise may be far greater than that represented by its ''independent'' effect on disease incidence.

Longitudinal cohort studies generally have confirmed the cross-sectional data linking exercise to reduced disease risk. Of particular interest are studies such as those by Blair et al [129], in which middle-aged sedentary adults with low fitness levels have become fit at follow-up and markedly have reduced cardiovascular mortality compared with those remaining unfit or inactive. These findings suggest that preventive exercise prescriptions instituted in middle age or beyond may be as important as those initiated at younger ages.

Randomized clinical trials are better able to eliminate the bias inherent in observational studies, in which physical activity levels are self-selected. Such data are now available for prevention of some disease states (cardiovascular disease, diabetes mellitus, and falls) but not yet available for others (stroke, osteoporotic fracture, and depression). For example, The Diabetes Prevention Program Research Group (a randomized, controlled trial of 3234 middle-aged and older overweight individuals with impaired glucose tolerance) [157] found that participants randomly assigned to the intensive lifestyle intervention of diet and aerobic exercise reduced their risk of incident type 2 diabetes by 58% in 3 years. Of particular interest is the finding that those individuals who were older than 60 responded best, with a 71% reduction in the development of diabetes. In another example of secondary prevention, Posner et al [158] reported a reduced incidence of recurrent cardiovascular events in older adults participating in long-term outpatient aerobic exercise compared with sedentary control subjects. Campbell et al [159–161] reported a series of randomized controlled trials of fall prevention in women older than 80, for whom balance and strength training and home-based walking programs reduced falls incidence over 2 years by 30% to 40%. Similarly, Rubenstein et al [162] reported that a low- to moderate-intensity program emphasizing strength, endurance, balance, and mobility increased physical activity levels while reducing activity level–adjusted fall rates after 3 months in elderly men at risk.

The role of exercise in the treatment of chronic disease

There are many ways to conceptualize the integration of exercise into the treatment of established disease. Traditional medical interventions typically do not address disuse syndromes accompanying chronic disease that may be responsible for much of the patient's associated disability. Exercise is particularly good at targeting syndromes of disuse and may affect disability significantly without necessarily altering the underlying disease itself in any primary way. Examples include Parkinson's disease [163,164], chronic obstructive pulmonary disease [165,166], intermittent claudication [167], and chronic renal failure. Exercise also may lower the risk for recurrences of a disease, such as secondary events in patients with cardiovascular disease [8,158] or prevention of recurrent injurious falls in an individual after a hip fracture. Sometimes an underlying pathologic condition that is central to a disease may be addressed specifically by exercise, whereas standard care does not affect this factor. For example, losses of visceral fat achieved through resistive or aerobic training improve insulin resistance and complement dietary and pharmacologic management of type 2 diabetes in the older adult with central obesity [138,168]. Exercises designed to stimulate skeletal muscle hypertrophy in congestive heart failure [31,169,170] provide benefits that counteract the catabolic effects of circulating cytokines in this disease [171] and are not achievable with cardiac medications alone. Functional improvements in individuals with arthritis [142,172,173] who are given quadriceps exercises improve joint stability and may add to the benefits of anti-inflammatory and analgesic medication [174]. Exercise may counteract undesirable side effects of standard medical care, a use of exercise that now is emerging in the literature. Such use of exercise includes instituting resistance training for patients receiving corticosteroid treatment to counteract the associated proximal myopathy and osteopenia [175–177] and neutralizing the adverse effects of energy-restricted diets in obesity [71,178] or protein-restricted diets in chronic renal failure [30], for example.

Exercise and the prevention and treatment of disability

There are many ways in which physical activity may influence the development and expression of disability in old age. These theoretic relationships are now borne out in many epidemiologic investigations and provide the rationale for the experimental studies and exercise recommendations that are found in many recent reviews of this topic [151,179–182]. There is a great deal of overlap between the identifiable risk factors for disability and the consequences or correlates of habitual inactivity [14,101,153,183,184]. At the most basic level, shared demographic characteristics between those individuals at risk for disability and those individuals who are more likely to exhibit sedentary behavior include advanced age, female gender, nonwhite ethnicity, and lower educational level and income. Psychosocial features common to both cohorts include social isolation,

low self-esteem, low self-efficacy, depressive symptoms, and anxiety. Lifestyle choices more prevalent in disabled or inactive adults include smoking and excess alcohol consumption. Body composition changes associated with both functional decline and inactivity include sarcopenia, obesity, visceral obesity, and osteopenia. Exercise capacity typically is reduced in both conditions in all domains, including aerobic capacity, muscle strength, endurance and power, flexibility, and balance. Gait instability and slowness, as well as impaired lower extremity function and mobility, characterize both disabled and inactive populations. In addition to the associations of inactivity and risk factors for disability, chronic diseases associated with inactivity, such as osteoarthritis, cardiovascular disease, stroke, osteoporosis, type 2 diabetes, hypertension, and depression are all risk factors for disability as well.

The theoretic model that describes the potential role of physical activity in the development of disability is complex and not completely understood. It is likely that exercise exerts it effects through multiple pathways simultaneously, and it is not clear that a single mechanism of action is dominant, even within a given disease paradigm. It is clearly not as simple as impairments leading to functional limitations, and ultimately, disability. For example, impairments in strength explain less than 20% of the variance in lower extremity physical performance in the Women's Health and Aging Study [185]. Depressed individuals may be disabled without any impairment in physical capacity. Conversely, the use of adaptive devices such as motorized wheelchairs and environmental modifications may allow completely paralyzed individuals to function without disability.

Few studies have examined a variety of physiologic factors and activity in the same cohort, so it has been difficult to attribute differential risk to various impairments in exercise capacity. For example, Laukkanen et al [186] reported that in 291 80-year-olds residing in the community in Finland, difficulty with activities of daily living (ADL) functioning was explained in part by muscle strength, balance, and upper extremity flexibility, but not by aerobic capacity. Cross-sectional data from the ongoing Women's Health and Aging Study [187] indicate that in 1002 disabled community-dwelling women older than 65, there is an inverse relationship between disability and physical activity levels, knee extension, and handgrip strength at baseline, and these factors contribute independently to the severity of the disability. These authors have proposed a spiraling deterioration process, in which motor disability, contributed to by age, chronic disease, and knee pain, leads to a reduction in physical activity, which in turn causes muscle strength to decrease and further disability to emerge. Foldvari et al [188] measured muscle strength, endurance, power, and aerobic capacity, physical activity level, psychologic status, and health conditions in 80 disabled community-dwelling women. Although upper and lower body strength and power, aerobic capacity, and physical activity level were related to functional dependency in univariate analyses (as well as self-efficacy, depression, and burden of disease), only leg extension power and physical activity level were independently predictive of disability in a multiple-regression model, explaining fully 40% of the variance. Given the fact that muscle power declines more

severely than muscle strength with aging [189] and such emerging relationships of muscle power to functional status and fall risk, exercise programs targeting increased muscle power are recommended increasingly [190].

Longitudinal studies are better able to determine the putative causal role of sedentariness and impairments to disability. An extensive systematic review of the literature in community-dwelling elderly was reported by Stuck et al in 1999 [191]. In the 78 longitudinal studies included, low levels of physical activity and impairments of upper and lower body strength or function were rated as among the strongest predictors of future disability in these cohorts. Recent longitudinal studies have strengthened the hypothesized causal relationship between sedentariness, functional limitations, and disability in older adults. Miller et al [152] reported results from 5151 participants in the Longitudinal Study of Aging and showed that physical activity results in a slower progression of functional limitations, and thereby slower progression to ADL or instrumental ADL disability. Specifically, older adults who walked a mile at least once per week were significantly less likely to progress to functional limitations or disability than their sedentary counterparts over the 6 years of follow-up.

Few investigators have examined primary prevention of disability itself by way of exercise in controlled trials of initially healthy adults. Kerschan et al [192] reported results from 124 initially nondisabled postmenopausal women who were nonrandomly assigned to home-based exercise or control groups during a visit to an outpatient medical clinic. After 7.7 years of follow-up, there were no differences between the groups in any measures of physiology or disability. The exercise program, which included elements of balance, flexibility, strengthening, postural control, and walking prescribed 3 days per week, was performed by only 36% of the exercise group at follow-up and was likely not robust enough to induce physiologic or functional changes.

Secondary prevention of disability in adults with pre-existing impairments or functional limitations has been studied somewhat more extensively, but with mixed results. In a sample of 215 community-dwelling older adults with self-reported functional limitations, 6 months of home-based strength training with elastic bands modestly increased strength, gait stability, and measures of social role functioning (but not physical functioning) compared with untreated control subjects [193]. These changes were preserved at 6 months of follow-up after the intervention ended. In the largest reported randomized, controlled trial of exercise and disability to date, the author and colleagues [194] randomly allocated residents of nine nursing homes (sample of 1235 residents) into resistive exercise (using dumbbells and ankle weights), nursing rehabilitation, or usual care control conditions. After 17 months of follow-up, residents who underwent resistance training and those who were in nursing rehabilitation homes had significantly less decline in ADL function and walking endurance compared with those who were in usual care homes. There was a dose-response relationship between the amount of weight lifted and the functional benefits observed. This study suggests the potential for exercise to benefit even those at the extremes of frailty and advanced age. A review of studies targeting disability in disease-specific populations such

as depression, cardiovascular disease, stroke, chronic lung disease, and arthritis is beyond the scope of this article, but there is evidence that exercise is beneficial in all of these conditions as a primary or ancillary treatment. The largest body of data exists for older adults with osteoarthritis, which is the most common condition related to disability in the elderly [172]. Five of the 11 randomized, controlled trials reported up to 1999 demonstrated improvements in disability scores relative to control subjects in trials from 4 weeks to 18 months in duration. Weight-bearing functional exercises, walking, and resistance training were used in various combinations in these studies, and there is no clear indication of the superiority of one modality to another in the reduction of pain and disability from osteoarthritis. The largest trial, by Ettinger et al [142] in 1997, found that 439 patients randomly assigned to aerobic exercise or resistance training for 18 months had less pain and disability at follow-up compared with control patients, who declined functionally during this period. Physiologic improvements in strength or aerobic capacity were not observed in this trial, and compliance was only 50% at 18 months, suggesting that other mechanisms (such as observed interactions of knee and ankle strength, gait, and balance in osteoarthritis [174]) may have been operative in the benefits observed. It is likely that the disability reductions in arthritis are due to the impact of exercise on a variety of factors, including muscle strength, gait and balance, body weight, pain, comorbid disease expression, self-efficacy, and depressive symptoms, among others.

Assessing the risks and benefits of exercise in the elderly

The contraindications to exercise in the older adult are not different from those applicable to younger, healthier adults [195]. In general, frailty or extreme age is not a contraindication to exercise, although the specific modalities may be altered to accommodate individual disabilities [196]. Acute illnesses, particularly febrile illnesses, undiagnosed or unstable chest pain, uncontrolled diabetes, hypertension, asthma, congestive heart failure, or new or undiagnosed musculoskeletal pain, weight loss, or falling episodes warrant investigation, regardless of exercise status, but certainly before a new regimen is begun. Temporary avoidance of certain kinds of exercise is required during treatment of hernias, foot ulcers, cataracts, retinopathy, or joint injuries, for example. A small number of untreatable or serious conditions are more permanent exclusions for vigorous exercise, including an inoperable enlarging aortic aneurysm, known cerebral aneurysm, malignant ventricular arrhythmia, critical aortic stenosis, end-stage congestive heart failure or other rapidly terminal illness, or severe behavioral agitation in response to participation in exercise secondary to dementia, alcoholism, or neuropsychologic illness.

The literature on exercise training in the frail elderly in nursing homes, between the ages of 80 and 100, includes no reports to date of serious cardiovascular incidents, sudden death, myocardial infarction, exacerbation of metabolic control of diabetes, or hypertension [38,194,196–212]. A considerable body of

data now exists to demonstrate the safety of initiating exercise in these settings in cohorts with multiple comorbidities and pre-existing functional impairment and disability.

Summary

There is increasing evidence that the black box we have referred to as "biologic aging" is composed of genetic factors and many types of environmental exposures. Some of the most potentially modifiable elements of this syndrome are those attributable to disuse or insufficient exposure to certain kinds or intensities of physical stressors during the course of the life span. Beneficial adaptations to exercise once thought restricted to genetically endowed master athletes now are seen to occur just as predictably in frail elders with chronic disease, opening the door to vastly improved physical function and associated health benefits. Knowledge of the benefits of physical activity, however well substantiated, may be necessary, but it is not sufficient to change either physician-prescribing habits or the likelihood of adoption and long-term adherence to exercise on the part of patients. Ultimately, the penetration of an exercise prescription to optimize aging into the most inactive cohorts in the community, who have the most to gain from increases in levels of physical activity and fitness [129,213], will depend on a combination of clear evidence-based guidelines coupled with health professional training and behavioral programs tailored to age-specific barriers and motivational factors [214–216].

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