Changes in the peripheral nervous system produce a major impact on safety and quality of life in the elderly. The challenges of aging reflect alteration of both neuromuscular and sensory function. Of particular concern are motor and proprioceptive deficits increasing the risk of falls. In addition, changes in sensory pathways may predispose the elderly to neuropathic pain. This review will focus on aspects of aging in muscle and nerve relevant to these issues.

Sarcopenia

Sarcopenia refers to the degenerative loss of muscle mass and strength with increasing age. It begins in mid-life and accelerates significantly in the seventh and eighth decades. Both active and sedentary individuals suffer sarcopenia, though it is worsened by inactivity. Muscle mass decreases earlier in women but men experience greater overall loss, averaging 30-40% of their muscle mass by age 80.1

The causes of sarcopenia are multiple. They include loss of muscle cells as well as hormonal changes that influence the growth and regeneration of different cells within muscles. In addition, degeneration of spinal motor neurons has a profound effect on the muscles they innervate.2, 3

Satellite cells are essentially stem cells residing in muscle. In response to physical trauma or even vigorous exercise, satellite cells proliferate to form new muscle fibers or fuse with damaged fibers to repair them. Most studies have shown reduction in the number of satellite cells with aging. This, along with changes in growth factor and hormone levels, decreases the regenerative capacity of muscle over time.3

Testosterone (T), growth hormone (GH) and insulin-like growth factor (IGF) all regulate protein synthesis within muscle. IGF appears to increase synthesis of actin and myosin (the principal contractile proteins in muscle), while GH and T promote protein stability. Decreasing levels for all three of these hormones in mid to late life presumably contribute to sarcopenia. The role of estrogen is less well established, though its sharp perimenopausal fall may help explain the relatively early onset of muscle loss in women.1, 2

The interaction of nerve and muscle can be described in terms of "motor units". One motor unit consists of a single spinal motor neuron and the muscle fibers it supplies through the branches of its axon. A motor unit in hand muscles typically includes about 100 muscle fibers, whereas calf and thigh muscle motor units include 1000-2000.4 In addition to transmitting electrical excitation, each motor neuron provides trophic support to the muscle fibers in its motor unit. Once a muscle fiber loses its nerve input, it undergoes atrophy unless connection with another nerve terminal can be restored.

Growth hormone supplementation has not demonstrated improvement in muscle mass or strength in elderly men or women.

Anatomical and physiological studies have shown that the number of motor units (i.e., the number of spinal motor neurons) supplying limb muscles remains fairly constant up to age 60. Beyond that, healthy individuals typically lose about half of their motor units between ages 60 and 80.5 Sprouting of terminal axons from remaining motor neurons initially compensates for those that are lost, however as this process continues, muscle fibers are inevitably left to atrophy without nerve supply. This neurogenic atrophy is likely the major cause of sarcopenia.1, 2

Changes in Muscle Dynamics

Two major types of motor units can be distinguished by their morphologic and physiologic characteristics. In Type 1 motor units, small motor neurons innervate muscle fibers with slow contraction times. Type 2 motor units contain larger motor neurons and muscle fibers that contract more quickly. Aging muscles may show a shift toward the slower contractions of Type 1 units for a few reasons. First, aging leads to selective Type 2 fiber atrophy. Whether this simply reflects decreased physical activity or some other more specific feature of aging muscles is not clear. Secondly, muscle fibers may actually transform from Type 2 to Type 1 as a result of the denervation and reinervation that follows loss of motor neurons.6

The predominance of Type 1 fiber contraction in aging muscles inhibits the ability to make quick, forceful movements. This poses particular problems for rapid postural reflexes important in maintaining balance. In addition to overall muscle weakening and proprioceptive deficits (described below), slowing of postural adjustments presents a major risk for falls in the elderly.

Therapeutic Considerations for the Aging Neuromuscular System

The literature regarding testosterone replacement for sarcopenia presents a mixed picture. Meta-analyses have suggested that injected testosterone can produce a moderate increase in muscle mass and strength in older men.7 Concerns over adverse effects temper any current enthusiasm. In particular, no large, prospective studies have looked at rates of prostate cancer in older men receiving testosterone supplementation.8

Growth hormone supplementation has not demonstrated improvement in muscle mass or strength in elderly men or women. Furthermore, the addition of growth hormone to a resistance exercise program does not appear to confer additional benefit. Adverse effects including carpal tunnel syndrome, hyperglycemia, edema and orthostatic hypotension led to high drop-out rates in treatment groups of some studies.9

Relatively few clinical trials have evaluated the muscular effects IGF-1 administration. A study assessing a two
month course of IGF-1 complexed to a binding protein, found that grip strength improved by 11%. The effect of estrogen replacement on sarcopenia has also received little study to date. Reported effects of estrogen on lean body mass have been mixed and changes in strength or contraction speed have yet to be investigated.10

Exercise, in the form of resistance training, appears to be the most effective treatment to counteract muscular decline in the elderly. Resistance training programs can achieve the same percentage gain in muscle mass and strength at age 80 as they do in young adults. Although the mechanism is not understood, resistance training also increases whole muscle contraction speed with an associated improvement in balance. This likely reflects adaptive coordination among different motor units since the contraction speed of individual muscle fibers may actually decrease with resistance training.

AGING IN PERIPHERAL SENSORY NERVES

Signs of peripheral sensory loss become increasingly prevalent with advancing age. Loss of ankle reflexes and decreasing distal vibration sense are particularly common. One study revealed that at least one of these deficits occurred in 26% of individuals aged 74-84 and in 54% of those older than 85.11 Correspondingly, anatomic studies have documented lower numbers of sural nerve fibers and physiologic studies have shown lower amplitudes of sural nerve response in “normal” older individuals.

Since these findings are so common, they are often considered part of “normal aging.” This notion overlooks the impact of peripheral sensory deficits on balance and gait in the elderly. A number of studies have documented that peripheral sensory loss is an important risk factor for falls. In some studies, the existence of lower extremity neuropathy in elderly individuals is not frequently reversible, simple preventive measures including use of a cane, nightlights and shower chairs should not be neglected.

NEUROPATHIC PAIN

The age-related changes discussed above concern the largest sensory fibers. Evaluation of small caliber sensory fibers is more challenging but crucial to understanding neuropathic pain. This is an important issue for aging populations given the striking predominance of certain neuropathic pain conditions in the elderly.12 In contrast to the clear age-related loss of large sensory fibers, anatomic studies have demonstrated relative preservation of small-caliber, pain sensing fibers in the elderly. This raises an interesting possibility regarding the development of post-herpetic neuralgia, a condition which is rare below the age of 50 but complicates 20-40% of zoster cases past the age of 60. Studies testing sensory function in patients with post herpetic neuralgia have indicated that vibratory sensory loss (presumably due to large-fiber failure) is more prominent than small-fiber (pain and temperature) deficit. This suggests that preferential large fiber loss with aging may be an important risk factor for the development of neuralgias and neuropathic pain. If small sensory fibers are relatively preserved, they may present an important target for treatments. The use of local or topical agents aimed at small fibers could supplement or replace systemic medications that are limited by adverse reactions in elderly patients.

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Disclosure of Financial Interests

The author has no financial interests to disclose.

Discussion of off-label usage of any products or services

*use of supplemental testosterone, growth hormones and IGF-1 to reduce sarcopenia is investigational

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