



Orentreich  
Foundation for the  
Advancement of  
Science, Inc.

# VitalLongevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

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## Frailty

Most of us have been surprised when a seemingly healthy, elderly person became severely disabled or perhaps died after a minor trauma, such as a fall, infection, or surgery, whereas another individual of the same age and apparent health profile sailed through with no problems. Why such different outcomes?

Lack of resiliency and poor outcome after stress very likely reflect the constellation of frailty characteristics (phenotype) (Table 1), any three of which increase risk of falls, disability, hospitalization, and even death. This issue discusses the relatively new concept of frailty as a distinct clinical state with measurable components and that predicts adverse health outcomes. The ability to recognize frail individuals, that is, with diminished reserve capacity, could influence lifestyle choices and guide therapy decisions, for example, whether to operate. Frailty can occur prematurely; its early recognition allows intervention at a stage when it will be most beneficial. Pre-frailty, the presence of any two components, carries a high risk of becoming frail and an intermediate risk of the same adverse events. Very early detection of pre-frailty awaits the development of more sensitive stress tests.

### Frailty Characteristics (Phenotype)

#### Any three or more:

- Unintended weight loss (more than 10 pounds in a year)
- Sarcopenia (low muscle mass and weakness)
- Fatigue (exhaustion)
- Slow walking speed
- Low physical activity

Table 1.

irreversible nutritional deficits. The biggest culprit: nothing by mouth (NPO) orders that fail to provide nutrients intravenously or any other way. Undernourished persons experience more infections and much higher death rates in-hospital and within 90 days whether they remain in the hospital or not.

**Advice** If hospitalized, request that high-protein supplements be provided earlier rather than later and that persistent nausea be treated. Inquire as to what will be done to compensate for NPO orders. Ask for levels of serum albumin and hemoglobin (routine tests) (Table 2) at admission and in follow-ups; decreasing levels could indicate PEM, which reduces the production of these proteins. Ask to be maintained in positive energy balance (weight-gaining) if at all possible, which can make all the difference between recovery or decline.

## Sarcopenia

Sarcopenia, the reduction of muscle mass and strength with age, can result from PEM, inactivity, or

declines in growth hormone (GH) (somatopause) and DHEA (adrenopause) (VitalLongevity, December 2005). Notably, insulin resistance in muscle can also be a major factor. Insulin stimulates muscle protein synthesis; older muscles do not respond optimally to its signal, creating an imbalance between protein synthesis and breakdown. Sarcopenia significantly increases risk of falls and all-cause mortality. In US adults over age 70 sarcopenia is a stronger predictor of mortality than is obesity.

A reduction in grip strength, in the absence of osteo- or rheumatoid arthritis of the hand, is a fairly good indicator of sarcopenia's onset. A simple device for monitoring grip strength, a dynamometer, can be purchased for under \$300 ([www.dynamometer-muscletesting.net](http://www.dynamometer-muscletesting.net); 1-800-572-2531) or your physician can assess grip strength during yearly physicals. Between the ages of 50 and 85, an annual grip-strength loss of 1.3 pounds in men and 0.7 pounds in women is average. A decline of as little as 4 pounds can be meaningful.

**Advice** High-intensity progressive resistance training, which increases both muscle size and strength and stimulates GH production, can reverse sarcopenia. Unfortunately, those who stand to gain the most (inactive

## Weight Loss

A cardinal sign of impending frailty—unintended weight loss of more than 10 pounds in one year not due to cancer or other disease—generally reflects protein-energy malnutrition (PEM). Lack of appetite due to diminished taste or smell, tooth/gum problems, reduced access to supermarkets or cooking capability, and poor food selection (high carb/low protein) can all contribute to PEM. Although 'frail' conjures an image of extreme thinness, many frail individuals, particularly women (who are twice as likely as men to be frail), have a high percentage of body fat or body mass index (BMI). When these women lose weight, they lose muscle rather than fat. Protein-rich high-energy supplements such as Boost®, in addition to, not in lieu of, regular meals, can help prevent PEM. Reversal of nutritional deficits, however, is notoriously difficult. Also, if you have PEM and happen to be hospitalized, you're likely to develop greater and potentially

seniors with poor muscle quality) are the least likely to consider exercise. Included with this issue is a Harvard Health Letter on Exercise and Age: A Prescription for Mature Adults.

Nutritional supplementation can help. What does not work is substitution of regular food with equivalent calories of a supplement. Good evidence suggests that current protein intake guidelines for elderly adults are too low and that much higher levels of essential amino acids would be beneficial. The essential amino acid leucine, in particular, stimulates muscle protein synthesis after exercise or an overnight fast. One strategy for preserving muscle mass over age 70 is to increase overall protein intake while consuming 80% of the day's protein allotment during one meal (protein-pulse feeding), along with 2.5 grams of leucine. This tactic maximizes the increase of blood amino acids to the higher levels required by older muscles while reducing the inefficient carbohydrate energy source. If you have chronic kidney or liver disease, consult your physician first.

Low vitamin D (<10 ng/mL) is strongly associated with frailty, contributing to sarcopenia through impaired neuromuscular function. Supplementation of at least 800 IU/day is generally warranted (VitaLongevity, September 2005) and can halve fall risk. As a biomarker of PEM, serum albumin in the low-normal range predicts future strength decline in older men and women. Depressed mood also carries risk of steep strength decline, particularly in older men with low body weight; antidepressant therapy can be very effective.

## Slow Walking Speed/Inactivity

A brisk walk 30 minutes a day can add three years to life, yet the frail generally can't walk 1000 yards without difficulty. Low muscle power (endurance) is associated with mortality regardless of strength. Speed and coordination decline due to age-associated impairments in motor control systems.

Two simple tests can be performed: "gait-time", the time to

walk a measured course, and "get up and go time", the time to rise from an armchair, walk ten feet, turn, walk back, and sit down. A simpler observation: the subject stops walking when talking (because walking requires too much attention) can indicate frailty and predict falls in the elderly. Even self-reported level of function in walking one-half mile and climbing 10 steps can provide reliable information and help uncover a preclinical stage of physical disability.

**Advice** Exercise is by far the best prescription. The oldest can still benefit from balance training and aerobic exercises, showing significant gains in functional capacity.

Test	Normal Range
Albumin	3.2 - 4.6 g/dL
Hemoglobin	12.0 - 16.0 g/dL
DHEA-S	
men > 60 years of age	20 - 213 µg/dL
women > 60 years of age	10 - 115 µg/dL
IGF-1 (adults)	50 - 300 ng/mL
Vitamin D, 25-dihydroxy	10 - 55 ng/mL

Table 2.

Anemia, frequently associated with the frail phenotype and often of unknown cause, contributes to poor physical performance; subclinical anemia can signal the transition to frailty. Unfortunately, physicians tend to overlook subclinical to moderate anemia and many cases go untreated. Anemia alone, not necessarily due to poor diet or iron deficiency, carries a three-fold

risk of falling. Other causes of anemia include blood loss, chronic inflammation, and kidney disease. Hemoglobin, the protein that carries oxygen in red blood cells, should be greater than 13g/dL in men and 12g/dL in women. Hemoglobin levels should be monitored regularly, particularly after a fall. Low levels of insulin-like growth factor-1 (IGF-1) are also associated with slow walking speed, but raising IGF-1 levels by giving GH remains controversial.

Older men given GH for one month showed improvements in measures of balance and physical performance, such as a more stable one-legged stance and a faster stair climb. In the short-term, however, GH treatment increases insulin resistance and its long-term effects on cancer risk are unknown.

**Prevention is key** Many practical reasons exist for assessing a variety of physiological functions, particularly in the elderly, with the goal of preserving health into very old age. Although certain aspects of frailty can be reversed, being alert to early warning signs and taking prompt action reap far greater rewards.

### Information for Donors

The Orentreich Foundation for the Advancement of Science, Inc., was founded in 1961. OFAS is a non-profit institution dedicated to biomedical research to prevent, halt, or reverse those disorders that decrease the quality or length of life. It is duly registered with the US Internal Revenue Service as an Operating Private Foundation under Section 4942(j)(3).

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