Definitions / Biology of Frailty

Harvey Jay Cohen, MD

SIOG

November 05, 2011
FRAILTY - DEFINITIONS

Fried
A state of age-related physiologic vulnerability resulting from impaired homeostatic reserve and a reduced capacity of the organism to withstand stress.

Rockwood
A precarious balance easily perturbed.

Clipp
A breeze could tip him over.
CLINICAL SYNDROME of FRAILTY

Symptoms
- Weight loss
- Weakness
- Fatigue
- Anorexia; decreased food intake
- Inactivity

Signs
- Sarcopenia
- Osteopenia
- Balance and gait abnormalities
- Deconditioning
- Undernutrition
- Slow gait speed

Risk
- Decreased resiliency/ability to respond to stressors
Unconventional Views of Frailty

Special Article

Frailty Thy Name Is . . . Phrailty?

Heather E. Whitson,¹,² Jama L. Purser,¹ and Harvey J. Cohen¹,²
Whitson, JGMS 62:728, 2007
Whitson, JGMS, 62:728, 2007
PATHWAYS TO MORTALITY

ENVIRONMENT

GENETICS

INDEPENDENCE → VULNERABILITY → FRAILTY → FUNCTIONAL DECLINE → DEATH

DISEASE/DISORDER

PHYSIOLOGIC DYSREGULATION
FRAILTY DEFINITIONS

OBJECTIVE

1. Phenotypic*
a. Weight Loss
b. Exhaustion
c. Weakness
d. Slow Walking Speed
e. Low Physical Activity

2. Deficit Accumulation Index**
a. Total # potential deficits
b. Actual # of deficits
c. $b \div a = \text{index}$

*Fried, J Gerontol A 56: M146, 2001
Physiologic systems: Hematologic, immune, endocrine, adiposity, neuromuscular, micronutrients

Fried LP et al. *J of Geron* 64A: 1049, 2009
CONTRIBUTORS TO FRAILTY

- Aging
- Osteopenia
- Sarcopenia
- Immune Dysregulation
- Neuroendocrine Dysregulation
- Disease
- Medication
- Nutrition
- Catabolism
- Chronic conditions
- Deconditioning
- Falls/Injuries

FRAILTY
HOMEOSTATIC RESERVE

Fries, 1981
FUNCTION AND MORTALITY

From Fries, 1981
**AGE-RELATED PHYSIOLOGIC SYSTEM DECLINES CENTRAL TO THE SYNDROME OF FRAILTY**

<table>
<thead>
<tr>
<th>Sarcopenia</th>
<th>Immune Dysregulation</th>
<th>Neuroendocrine Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>† Skel muscle mass</td>
<td>↑ Memory cells</td>
<td>† Growth hormone</td>
</tr>
<tr>
<td>† Vo2max</td>
<td>† Naive cells</td>
<td>† Estrogen</td>
</tr>
<tr>
<td>† Strength exer. tol</td>
<td>† IL-2</td>
<td>† Testosterone</td>
</tr>
<tr>
<td>† Thermoreg</td>
<td>↑ IgG, IgA</td>
<td>Cortisol dysteg</td>
</tr>
<tr>
<td>† Energy expend</td>
<td>↑ IL-6, IL-1β</td>
<td></td>
</tr>
<tr>
<td>↑ Insulin resist</td>
<td>† Mitogen resp.</td>
<td>↑ Sympath tone</td>
</tr>
</tbody>
</table>
Inflammation - Coagulation Interface and Frailty

- Aging
- Inflammation → IL6 cytokines → Acute Phase Reactions (CRP) → Organ Dysfunction
- Organ Dysfunction ≈ Frailty
- Chronic Multiple Organ Dysfunction Syndrome
  - Endothelial Damage/Microthrombi

Injury/Disease

Coagulation → Cascade → D-dimer
DYNAMICS OF FRAILTY

Sarcopenia

↓ GH, sex steroid Cortisol dysregulation

↑ Catabolic cytokines

Neuroendocrine dysregulation

↑ Catabolic cytokines

immune dysfunction

Cortisol dysregulation
Cellular Factors in Loss of Homeostasis

• Apoptosis
• Senescence
• Repair
  - Autophagy
The sign in the West Virginia lunch counter read:
Don’t criticize the coffee.
You may be old and weak yourself someday.