Homeostasis & Allostasis

Vitruvian Man
Leonardo Da Vinci
Stress:
In biology, any change (stressor) in the environment that may tend to alter an existing equilibrium and trigger counteracting responses at molecular, cellular, and systemic levels to preserve/reestablish such an equilibrium and insure adaptation.

Claude Bernard, (1813-1878, Prof. of Physiology at the Collège de France, Paris), suggests that the equilibrium or steady state of the “milieu intérieur” is to remain constant to allow for optimal function and survival.
Types of Stress

- Examples of Physical/Chemical Stress
  - High/low extreme temperatures
  - Physical injury
  - Hemorrhage
  - Hypoglycemia, etc.

- Examples of Psychological/Emotional Stress
  - Fear
  - Cognition of danger
  - Memories
  - Sorrow or joy
  - Hate or love, etc.

Homeostasis
From Walter B. Cannon (1871-1945)
Wisdom of the Body, 1932

From Greek: *homeo* “the same” *stasis* “state”

Indicates that for optimal function of the organism, a steady state (or equilibrium) must be achieved

This “constancy” of the internal environment allows survival despite continuing changes in the external environment (stress)
From left to right: F. Skelton, R. Guillemin (Nobel Prize 1977), Prof. C. LeBlond, P.S. Timiras

The Nobel Prize was awarded for the identification of the hypothalamic hypophysiotropic hormones.
**Homeodynamics**

A *constant* environment obtained through a series of dynamic adjustments

This continual need for adjustment is implicated in the term **“allostasis”**

(From Greek *allo* “different” *stasis* “state”)

Emphasizes the dynamism of adaptive responses to stress

This adaptation to stress is often achieved with a price -- a declining ability to adapt and/or an increased pathology and disease

*Prof. T. Seeman, Geriatrics, UCLA (UCB alumna)*
Figure 10.11
Progressive stages of homeostasis from adjustment (health) to failure (death)
### Table 10.7

<table>
<thead>
<tr>
<th>Functions Stimulated by Stress:</th>
<th>Functions Inhibited by Stress:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>All functions not immediately necessary for defense and survival are decreased:</td>
</tr>
<tr>
<td>• Increased cardiac rate</td>
<td>• Decreased growth</td>
</tr>
<tr>
<td>• Elevated blood pressure</td>
<td>• Decreased appetite (anorexia)</td>
</tr>
<tr>
<td>• Increased blood coagulation</td>
<td>• Decreased reproductive function and sex drive</td>
</tr>
<tr>
<td>• Redistribution of blood from peripheral (skin) and internal systems (gastro-intestinal) to heart, skeletal muscles, brain</td>
<td>• Decreased circulation in tissues not involved in stress response</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>• Decreased response to pain</td>
</tr>
<tr>
<td>• Increased respiratory ventilation</td>
<td>• Decreased immune function</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td>• Decreased thymus size</td>
</tr>
<tr>
<td>• Increased glycogen mobilization</td>
<td>• Decreased thymic hormones and cytokines</td>
</tr>
<tr>
<td>• Increased glycemia</td>
<td>• Increased lipolysis</td>
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<tr>
<td>• Increased lipolysis</td>
<td><strong>Hormonal</strong></td>
</tr>
<tr>
<td><strong>Hormonal</strong></td>
<td>• Increased CRH, ACTH, glucocorticoids</td>
</tr>
<tr>
<td>• Increased vasopressin, NGF</td>
<td>• Increased catecholamines (E &amp; NE)</td>
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<tr>
<td>Pathophysiologic Responses During Stress</td>
<td></td>
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<tr>
<td>------------------------------------------</td>
<td></td>
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<tr>
<td><strong>During Stress</strong></td>
<td></td>
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<tr>
<td>Energy storage ceases because:</td>
<td></td>
</tr>
<tr>
<td>† sympathetic activity</td>
<td></td>
</tr>
<tr>
<td>(i.e. increased vigilance/ arousal)</td>
<td></td>
</tr>
<tr>
<td>‡ parasympathetic activity</td>
<td></td>
</tr>
<tr>
<td>‡ insulin secretion</td>
<td></td>
</tr>
<tr>
<td>Access to energy storage is facilitated</td>
<td></td>
</tr>
<tr>
<td>and energy storage steps are reversed because of:</td>
<td></td>
</tr>
<tr>
<td>† glucocorticoid secretion</td>
<td></td>
</tr>
<tr>
<td>† epinephrine/ norepinephrine secretion</td>
<td></td>
</tr>
<tr>
<td>† glucagon secretion</td>
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</tbody>
</table>
Pathophysiologic Responses After Stress

If physiologic responses are insufficient and adaptation is incomplete, symptoms of poor health are registered (e.g. loss of energy when freeing energy from storage and returning to storage)

Examples of consequences:
- Muscle wasting
- Diabetes (Type 2)
- Ulcers, colitis, diarrhea
- Inhibition of growth (in childhood)
- Osteoporosis (in old age)
- ↓ LHRH, ↓ testosterone
Figure 10.10
Some physiologic and pathologic responses to stress in selected organs
Table 10.9
Risk Factors (Allostatic Load)
Endangering Health and Shortening Life Span

Elevated Physiologic Indices (at risk)
- Systolic blood pressure: ≥ 148 mm Hg
- Diastolic blood pressure: ≥ 83 mm Hg
- Waist-hip ratio: ≥ 0.94
- Total cholesterol-High Density Lipoprotein ratio: ≥ 5.9
- Total glycated hemoglobin level: ≥ 7.1%
- Urinary cortisol level: ≥ 25.7 mg/g creatinine
- Urinary epinephrine level: ≥ 5 mg/g creatinine
- Urinary norepinephrine level: ≥ 48 mg/g creatinine

Lowered Physiologic Indices (at risk)
- HDL cholesterol level: ≤ 1.45 mmol/L
- DHEA (Dehydroepiandrosterone) level: ≤ 2.5 µmol/L
Janus is the Roman God of gates and doors, of beginnings and endings and, hence, is represented by a double faced head; generally placed on the gates of the city, the menacing face looking towards the outside of the city ready to defend it against any attackers, the benevolent face turned towards the city is a protector and promoter of prosperity and good health.
Moderate stress of short duration
Allostatic Load weak or absent

Severe and prolonged stress
Allostatic Load progressive & severe

**Incidence of Cardiovascular Diseases**

**Cognitive Alterations**

- Moderate stress of short duration
  - Allostatic Load weak or absent
  - stimulate:
    - vigilance
    - attention
    - memory storage

- Excessive stress of long duration
  - Allostatic Load progressive & severe
  - reduce:
    - number of neurons
    - neurotransmitter balance
    - memory storage

Figure IV: Protection contre Pathologie: fonction cérébrale et mémoire
Moderate & Regular Physical Exercise

Allostatic Load weak or absent

Cardiovascular function
Energy mobilization
Immune efficacy
Cognition & vigilance
Mass & strength of muscle & bone

Physical Exercise

Excessive & prolonged physical exercise or lack of regular exercise

Allostatic Load Progressive & increasing

Atherosclerosis
Obesity
Incidence of cardiovascular diseases
Immunosuppression
Depression, anxiety, memory loss
Bone fragility
Muscle atrophy & weakness
Hormesis

• A new term, from the Greek “I excite.”
  – Excitation induced by physical or psychological stress

• Stimulation of any system by a stimulus of relatively moderate intensity & short duration
  – In contrast to a strong stimulus of long duration that will induce destabilization

• Recently, several lines of research indicate that hormesis may promote longevity