Why are there so many more mechanisms to raise blood pressure than to lower BP?

- Physiological adjustments counter biological problems
  ∴ Most important/common problem must be *low* BP
- Problems from hypertension generally occur after reproductive years, so less subject to natural selection
- Extreme hypotension = "shock"

Circulatory Shock

Excessively low BP

Symptoms include:

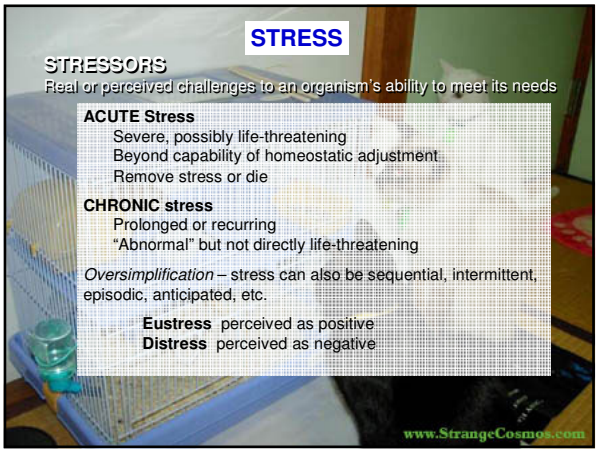
- Hypotension (<90 systolic; <50 MAP)
- Cool, clammy skin (sympathetic activation)
- Disorientation or unconsciousness (low blood to brain)
- Fast heart rate, weak pulse
- Urine formation much reduced or stops
- Drop in blood pH (↑ lactic acid)

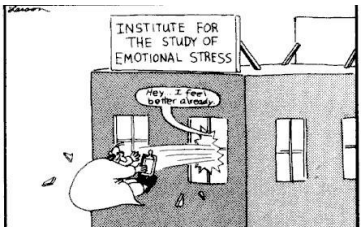
Causes of Shock

- **hypovolemic shock**
  caused by inadequate blood volume
  "Hemorrhagic shock" = due to bleeding (~20% of blood volume)
- **cardiogenic shock**
- **distributive shock** (due to widespread vasodilation)
  - **anaphylactic shock**
    caused by allergic reaction; histamines
  - **septic shock**
    "blood poisoning"
    serious infections & high fever cause widespread vasodilation
  - **neurogenic shock**
- **obstructive shock** (blockage of blood flow)

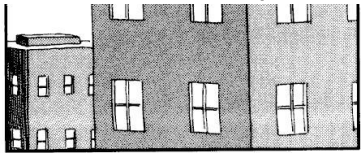
Why is there so much hypertension today?

- Evolutionary history
- Multi-factorial (no single reason)
- Risk factors vs. causation
- Genetics (2x risk if family history)
- Diet
  - High fat + cholesterol = arteriosclerosis
  - High salt, retain more water in blood
  - Deficiency of minerals?
- Low exercise
- Obesity
- Race/Ethnicity (African Americans > European Ams)
- Stress (sympathetic activation, cortisol)





Hormones and Sympathetic Nervous System mediate the stress response



Mechanisms of Communication Between Cells

mechanism	transmission	chemicals	affects
Direct	gap junctions	ions, solutes	neighbor cells
Synaptic	neuron synapse	neurotransmitters	specific target cells
Paracrine	ECF	paracrine factors	local cells
Endocrine	bloodstream	hormones	systemic
Pheromonal	volatile (air)	pheromones	other individuals

HORMONES

Hormones: chemical messenger molecules produced by endocrine organs, released into the bloodstream for transport to other cells.

Hormones can affect virtually any cell in the body (that has a receptor) and produce "long-term" physiological effects.

Mechanisms of action:

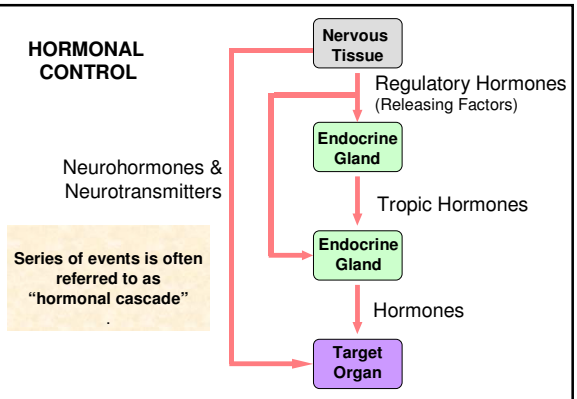
- Activate genes to stimulate synthesis of enzyme or protein
- Alter rate of protein synthesis
- Activate/deactivate an existing enzyme
- Change membrane potential / permeability

Steroid hormones

(lipid derived) can cross the cell membrane and directly affect structures in cytoplasm or nucleus.

Non-steroidal hormones

Require membrane receptors (G-protein, 1-TMS, ion channel) and usually act through 2nd messengers (cAMP, cGMP, Ca^{++})



Patterns of Hormonal Interaction

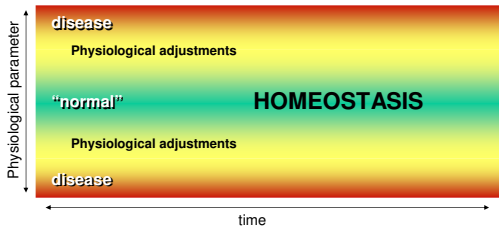
- **Antagonistic** – opposite effects
- **Synergistic** – additive effects
- **Permissive** – 1st needed for 2nd to function
- **Integrative** – produce different, but complementary functions

Homeostasis:

State of functional equilibrium of body; maintaining "constant" internal state

negative feedback loops make adjustments to keep the body functioning within specific parameters

"Disease" generally reflects body drifting away from homeostasis

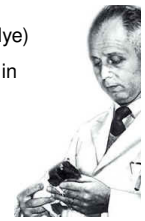


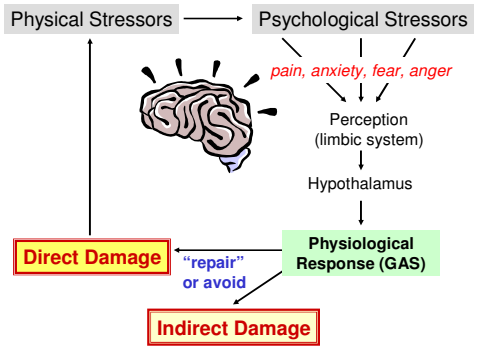
HORMONES and STRESS

General Adaptation Syndrome (H. Selye)

physiological response to stress occurs in three phases:

- Alarm
- Resistance
- Exhaustion

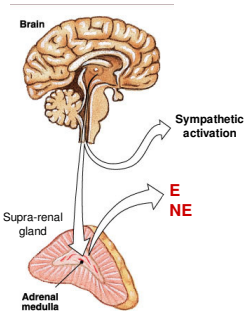




1. ALARM PHASE

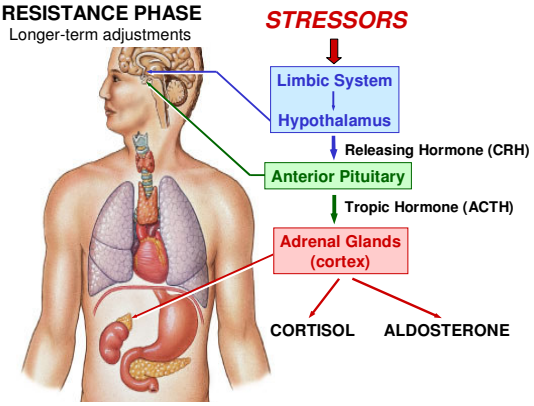
Immediate/Short-Term Response to Stress

- Detection and Awareness
- CNS Arousal
- Response
  sympathetic activation
  NE, E as hormones



2. RESISTANCE PHASE

Longer-term adjustments



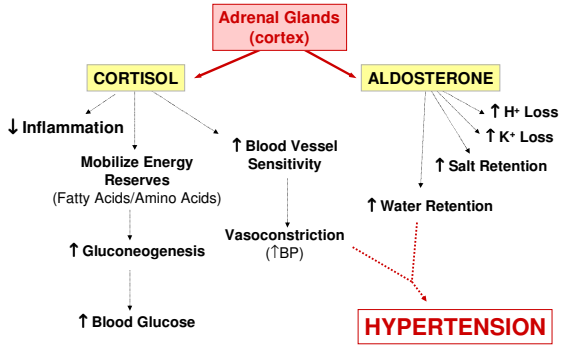
HPA Axis (Hypothalamus → pituitary → adrenal)

Glucocorticoids (CORTISOL)

- Gluconeogenesis from fatty acids and amino acids in liver
- Sensitizes blood vessels (increased constriction)
- Reduces *inflammation* (anti-inflammatory)
  Inflammation = nonspecific defense; swelling, redness, pain

Mineralocorticoids (Aldosterone)

- Sustain blood volume and BP
- Increased H^+ secretion by kidneys
- Increased salt retention = increased water retention
- Increased K^+ loss



Why stress → hypertension?

Much of resistance phase prepares body for excessive body fluid losses (bleeding)

1. ↑ blood clotting
2. ↑ RBC count (spleen contraction + produce new RBCs)
3. ↓ kidney filtration (save water)
4. ↑ aldosterone (salt & water retention)
5. ↑ ADH (anti-diuretic hormone = water retention)

3. EXHAUSTION PHASE

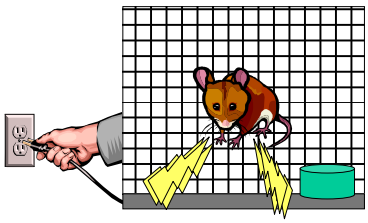
***"Diseases of Adaptation"* appear when homeostasis not achieved, stress is not removed.**

- exhaustion / depletion of energy reserves
- electrolyte imbalance
- enlarged adrenals
- lymphoid tissue atrophy
- hypertension

Probably contributes to other diseases, esp. through ↓ immune function

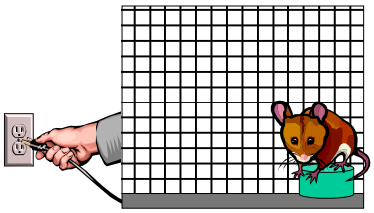
arteriosclerosis, menstrual problems, headaches, insomnia, allergies, depression, ulcers

Endocrine response to stress



Measure levels of:
- Dopamine
- Epinephrine
- Cortisol (glucocorticoids)

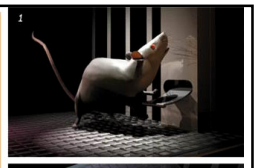
Endocrine response to stress



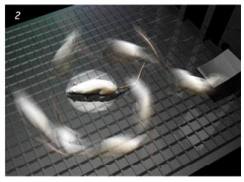
Measure levels of:
- Dopamine
- Epinephrine
- Cortisol (glucocorticoids)

Can push lever to avoid painful stimulus

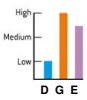
D = dopamine
G = glucocorticoids
E = epinephrine

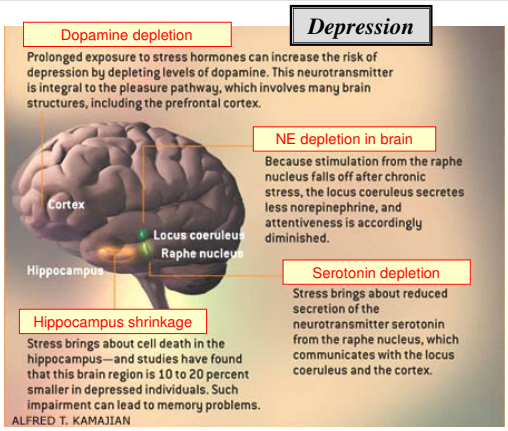


Lever no longer works (anxiety)



Chronic Stress (depression)





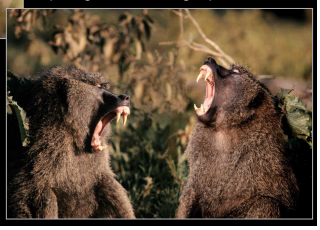
The endocrine response to stress affects numerous behaviors in different vertebrates, from fish & amphibians to humans.

- Arousal and attention
- Locomotor activity
- Sensory thresholds (pain perception)
- Dispersal
- Exploratory behavior
- Thermoregulation
- Memory and learning
- Feeding behavior
- Aggression
- Social dominance
- Reproduction

STRESS in the WILD
(Robert Sapolsky)

Savanna Baboons (*Papio cynocephalus*)

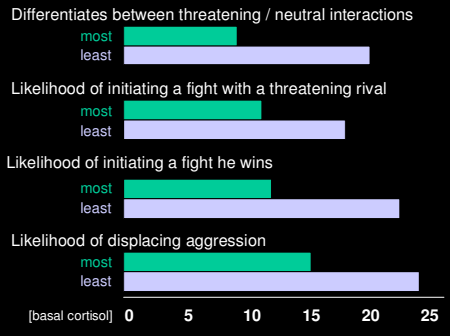
- Rigid dominance hierarchies through fighting, display
- Observe group interactions, individual personalities
- Measure cortisol & testosterone levels in animals of different rank
- Examine response to stressor (being shot w/dart gun)



Low ranking males
- Higher circulating cortisol levels
- Endorphin and cortisol increase in response to stress (dart in butt)
- Testosterone drops in response to stress

Dominant males
- Lower circulating cortisol levels
- Endorphin and cortisol increase in response to stress
- Testosterone spikes in response to stress

Dominance Style



Sapolski's interpretation:

- ***Know which threats are real***
- ***Take control where you can***
- ***Have an outlet for stress***

Stress (real or anticipated) produces physiological changes, primarily due to the hormones that are released.

Things that alter perception of stress can have real physiological effects

→ this is a major contributor to the scientific basis to placebo effect.

"Personality" affects the physiological response to stress.

...AND YOU THINK YOU HAVE STRESS..