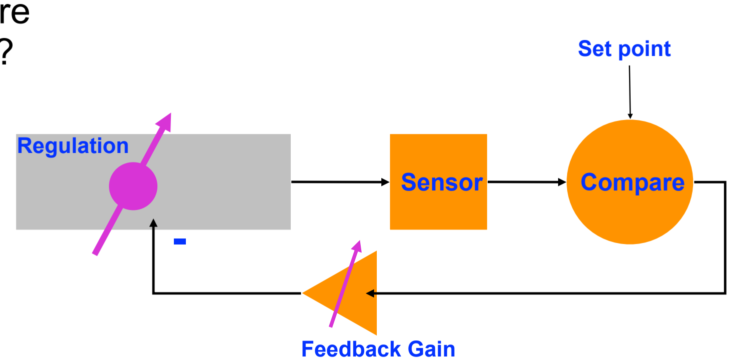
Control of Circulation

Bioengineering/Physiology 6000

Physiologic Control Systems

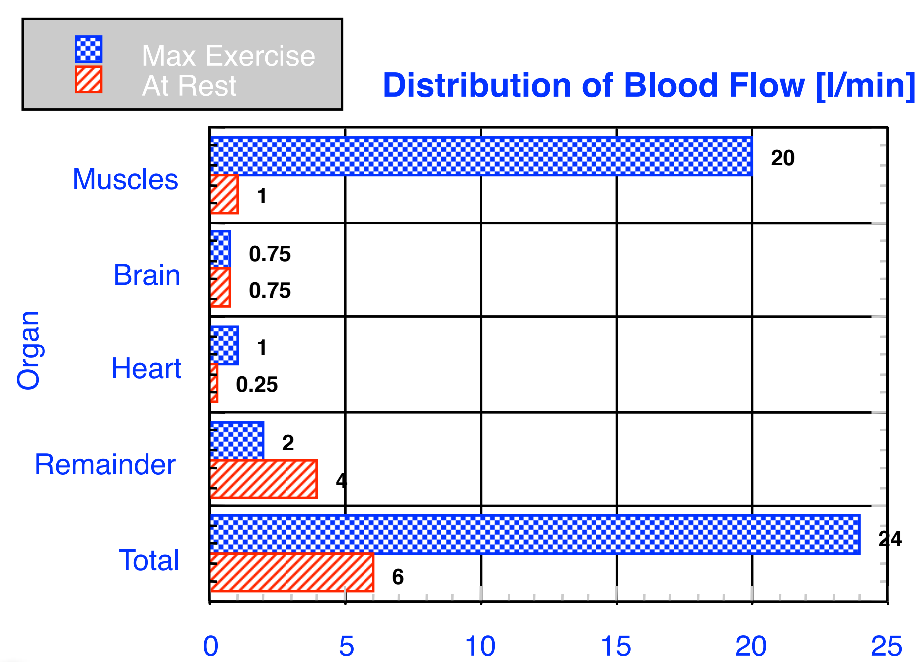
- Goal: overall effect of the system
- Process steps: pathways, basic mechanisms
- Points of regulation: where can we alter the process?
  - uni/bi-directional?
  - time to action?
- Sensors
  - local or remote?
  - direct or indirect?
- Feedback mechanisms: control
  - pathways, gain, time to action
  - set point determination



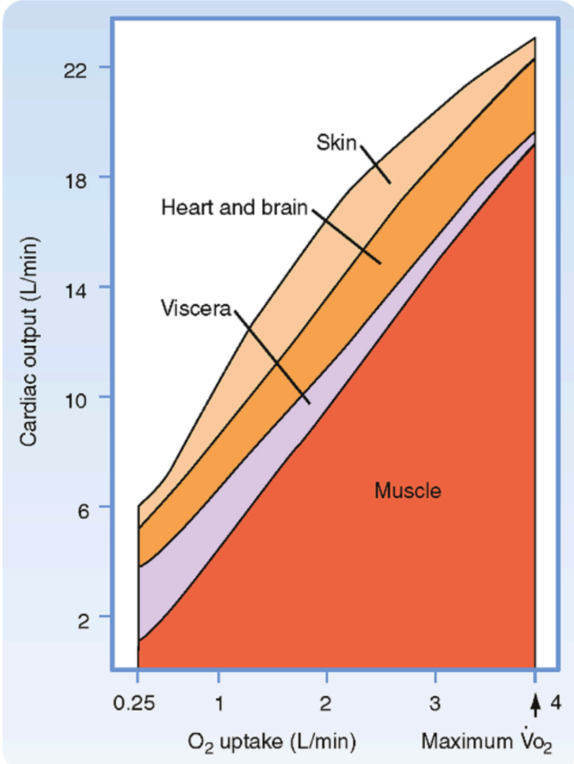
Control of the Circulation Overview

- Goal: adjust circulation so that adequate blood flow is provided to all tissues; secondary goal is to provide proper pressure in capillaries for fluid balance.
- Process steps and regulation points:
  - Cardiac output (rate and stroke volume)
  - Peripheral circulation
    - arteriole diameter, resistance changes
    - hormonal influence on vessels (pharmacomechanical coupling)
    - ANS modulation: mostly sympathetic
  - Blood pressure
    - depends on cardiac output and peripheral resistance
    - fluid balance, adjust blood volume
- Sensors: Local and remote; pressure, chemo
- Feedback: Local and remote, fast and slow

Response to Exercise



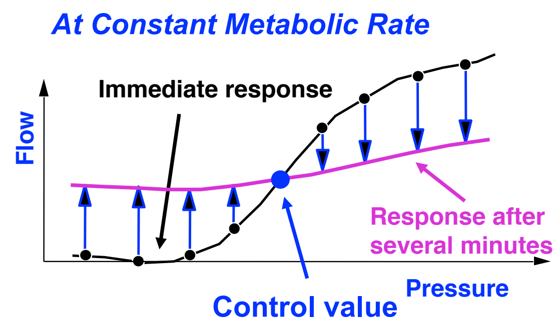
Another View of Exercise

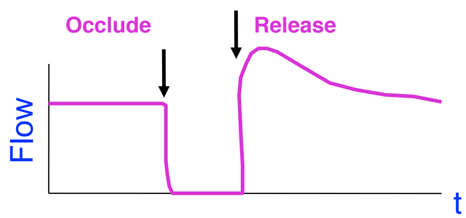


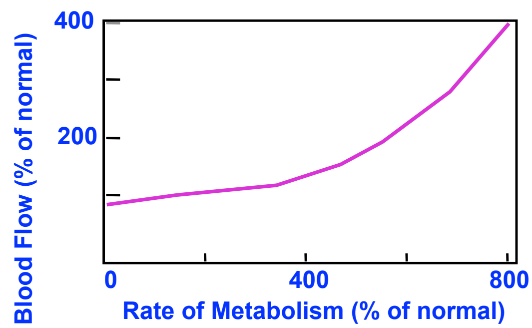
Local Control

Local Regulation: the Data

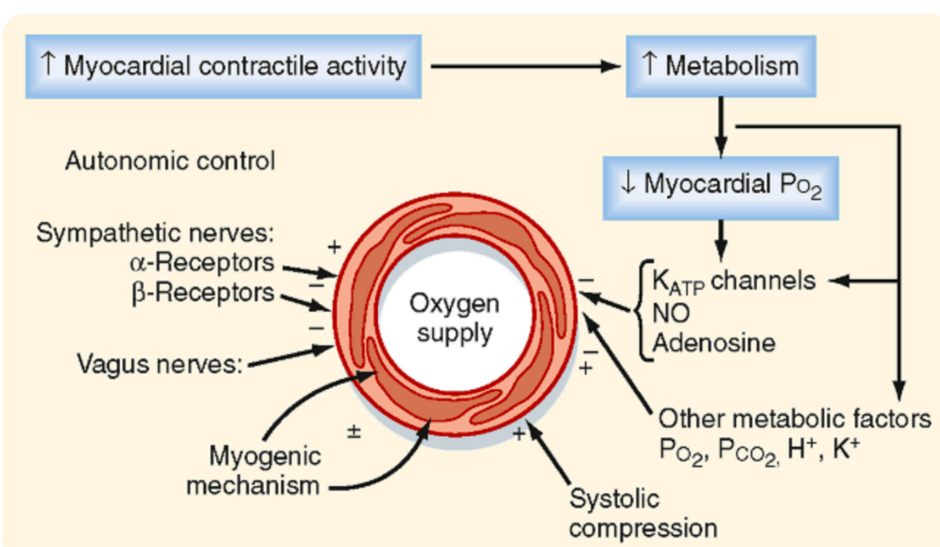
- Regulation Mechanisms
  - Change in resistance of the vessels
    - myogenic or metabolic reflexes
  - Vascularization: angiogenesis, collaterals
    - long term response (and more powerful)
- Sensors
  - stretch, metabolites, ions



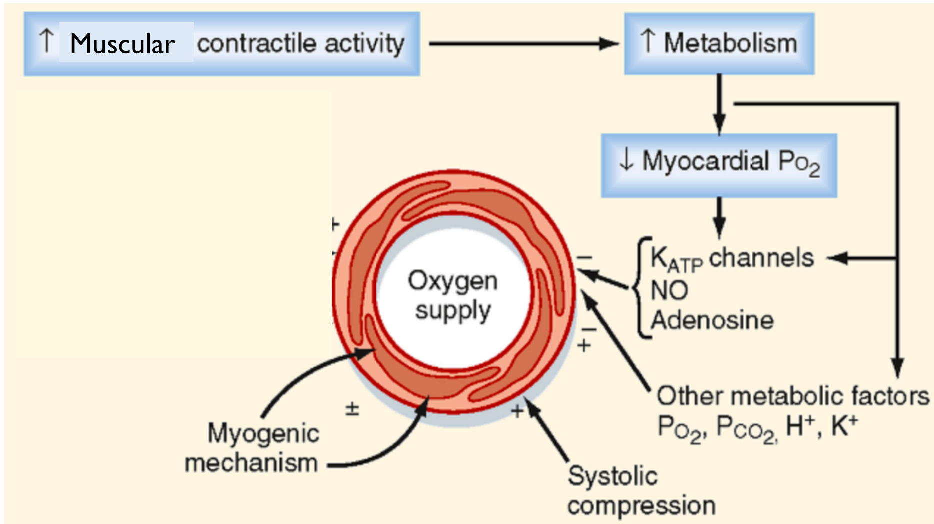




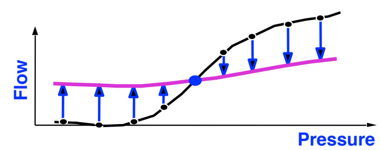
Control of Vascular Flow



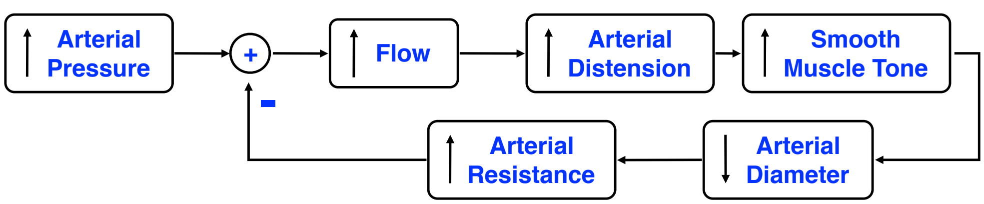
Local Control



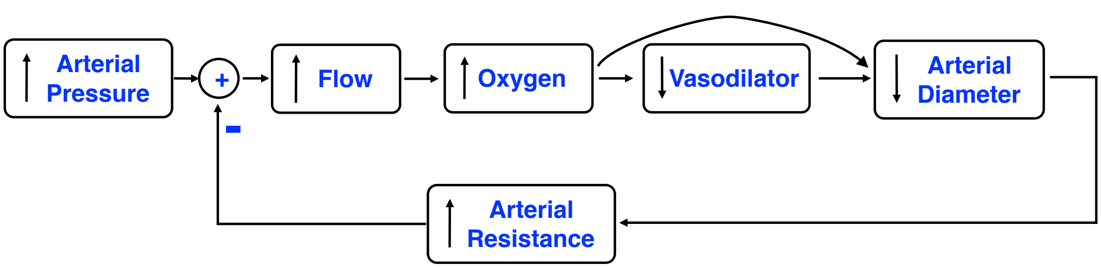
Autoregulation: Feedback Mechanisms



Myogenic Mechanism

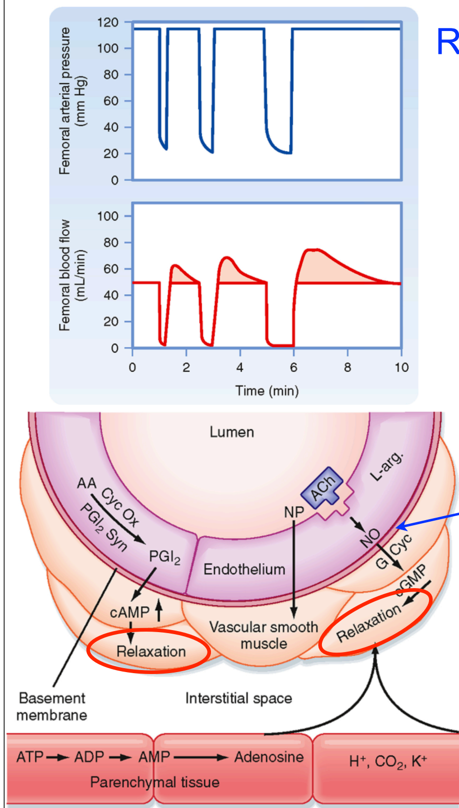


Metabolic Mechanism

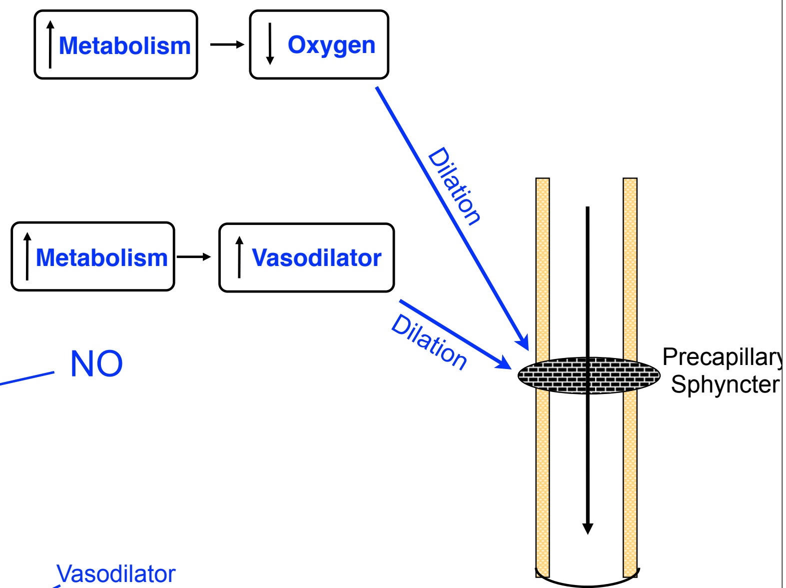


- Details of mechanisms not clear

Metabolic Feedback Mechanism



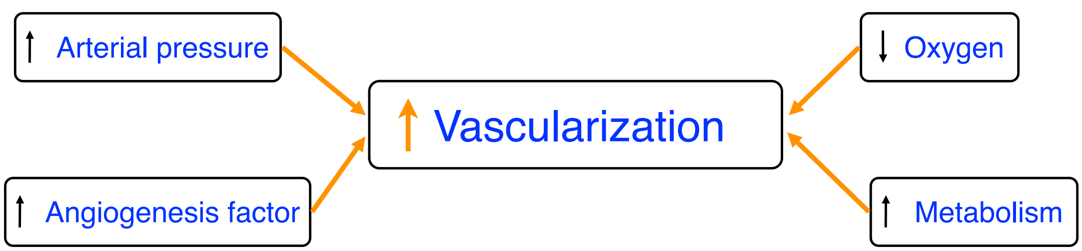
Reactive Hyperemia



NO

Vasodilator substances (linked to exercise)

Long Term Local Regulation

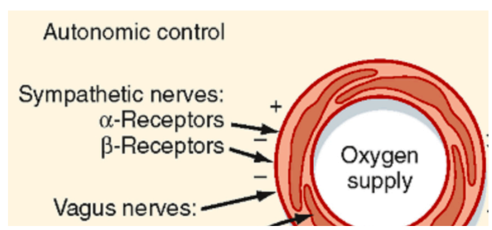


- Factors
  - Time: hours to days in infants; weeks to never in aged
  - Angiogenisis factor: attracts buds that break from vessels walls
  - Collateral circulation: metabolically driven, leads to bypass
- Examples
  - Coarction of the aorta(congenital: large differences in pressure even though flow is normal)
  - Retrolental fibroplasia: sudden drop in oxygen concentration in premature babies leads to vessel growth

Note: long term regulation more powerful than short!!

Central Control

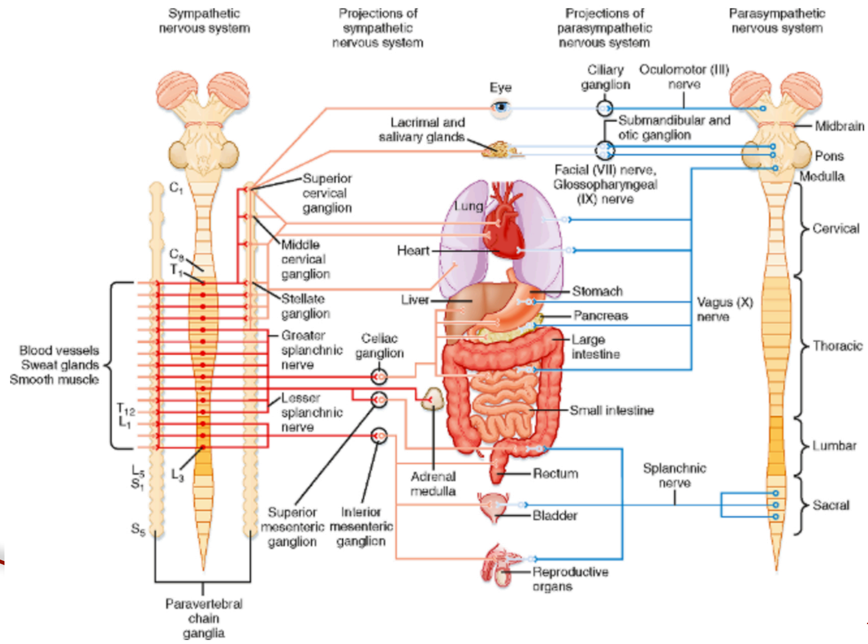
Central Regulation of Blood Flow/Pressure



- Process Steps
  - Hormonal
    - Most important mechanism, especially long term
    - Many substances involved but norepinephrine is major player
    - Main effect is vasodilation via β receptors in vascular smooth muscle
  - Central (ANS)
    - Sympathetics influence venous more than arterial vessels
    - Parasympathetic only minor role
    - Main effect is vasoconstriction via α receptors in vascular smooth muscle
- Sensors
  - Pressure, stretch, chemo, psychological

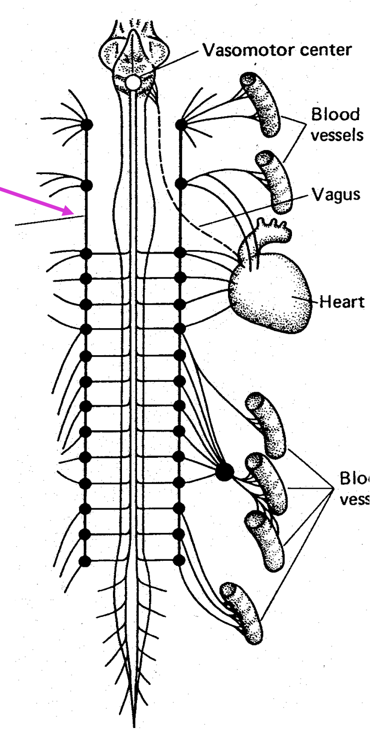
Autonomic Nervous System

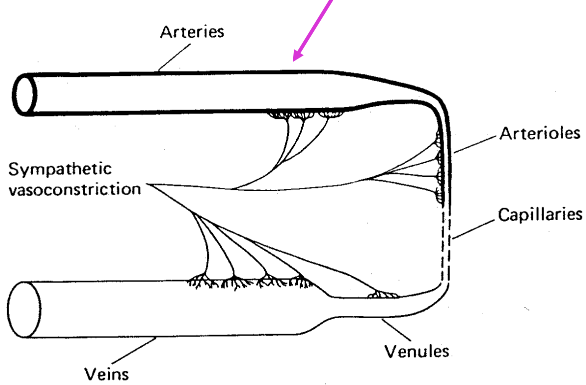
See Eckert Figure 8-18, page 296



Autonomic Innervation of the Circulation

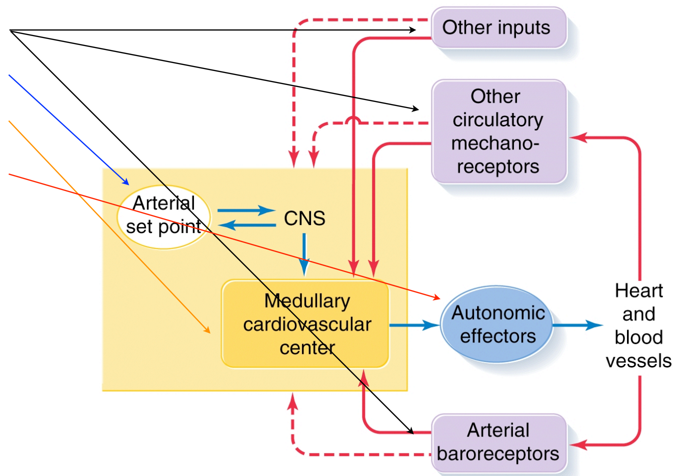
- Sympathetics release norepinephrine to both constricting (α) and relaxing (β) receptors in the vascular smooth muscle.
- Parasympathetics have little direct influence





Central Control Overview

- Distributed sensors
- Pressure set point
- Integrator (CNS)
- Actuation via ANS



Vasoconstrictive Substances

Substance	Source	Action
Norepinephrine	adrenal medulla	vasoconstrictive in almost all cases (α-receptors).
Epinephrine	adrenal medulla	vasoconstrictive except in skeletal and cardiac muscle where vasodilative (β-receptors)
Angiotensin	kidneys/plasma	powerful constrictor in response to drop in P_a
Vasopressin (Antidiuretic Hormone)	Hypothalamus/ pituitary	even more powerful vasoconstrictor; important in case of major hemmorhage and regulating water retension in the kidney

Vasodilator Substances

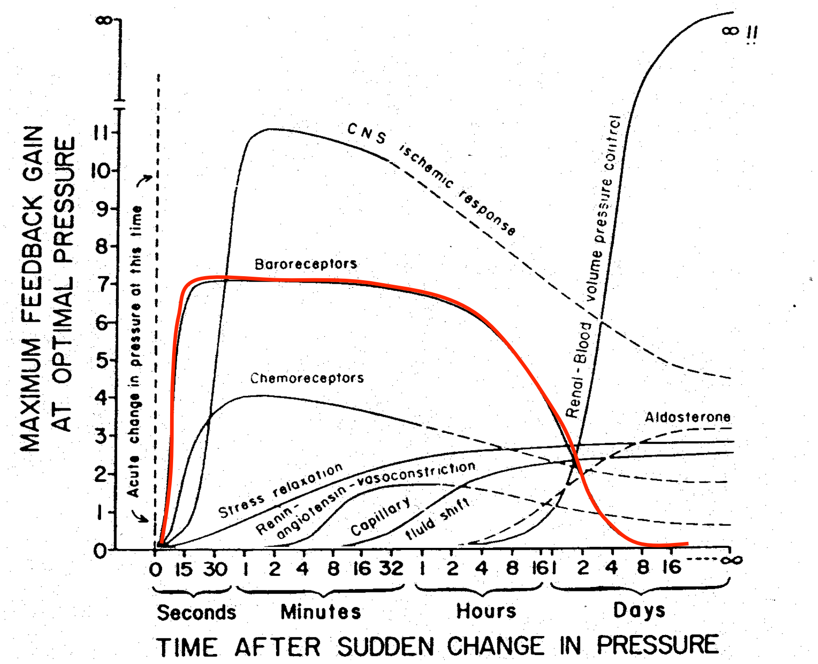
Substance	Source	Action
Bradykinin	plasma and tissue fluids	dilation, increases permeability; role unclear but may be activated by tissue injury
Seratonin	chromaffin tissue, intestines	can be both dilator and vasoconstrictor, depending on tissue; role even less clear
Histamine	all tissues	not important in normal circulation but does cause dilation and increased capillary permeability in damaged areas, leading to edema.
Prostoglandins	all tissues	usually dilator, but can cause constriction; effect usually local but role unclear; subject of extensive research.

Effects of Ions

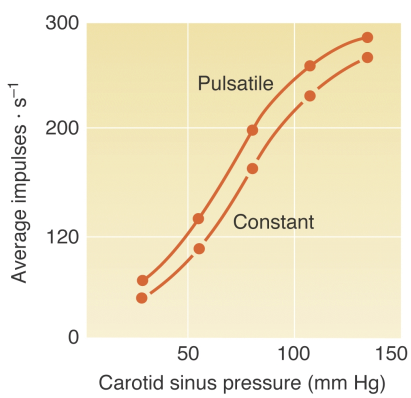
Substance	Action
Ca^{+2}	vasoconstriction via direct influence on smooth muscle cells
K^{+}_{e}	dilation via inhibition of smooth muscle (raise resting potential)
Mg^{+2}	dilation through inhibition of smooth muscle (blocks Ca channels by ion replacement mechanism?)
H^{+}	drop in pH causes dilation in most tissues; rise in pH causes first constriction, then dilation
CO_2	mild vasodilation in most tissues, marked in brain, but its main action is via other central control mechanisms

Regulation of Arterial Pressure

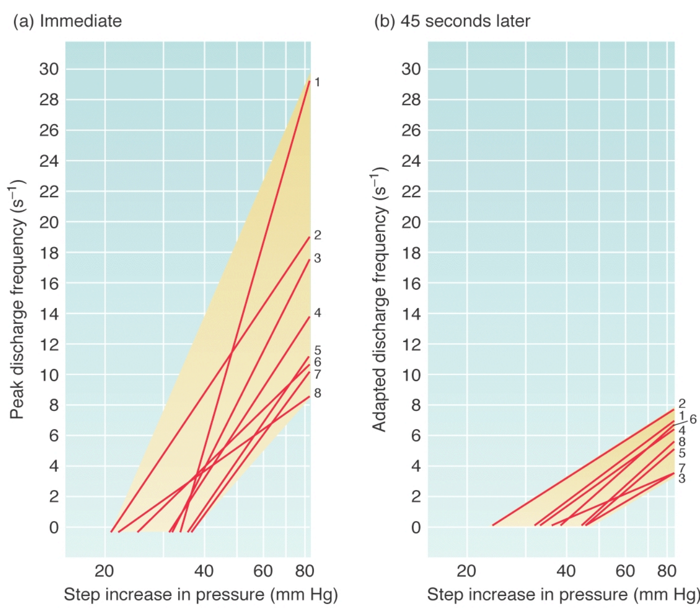
- Critical for homeostasis
- Both fast and slow components
- Fast do not last, slow are most powerful



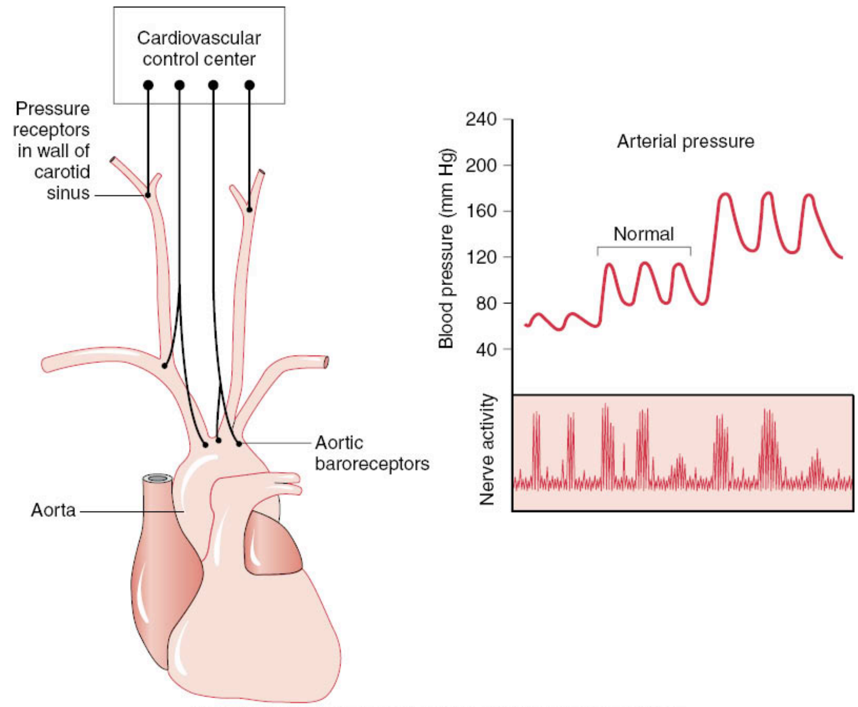
Baroreceptors



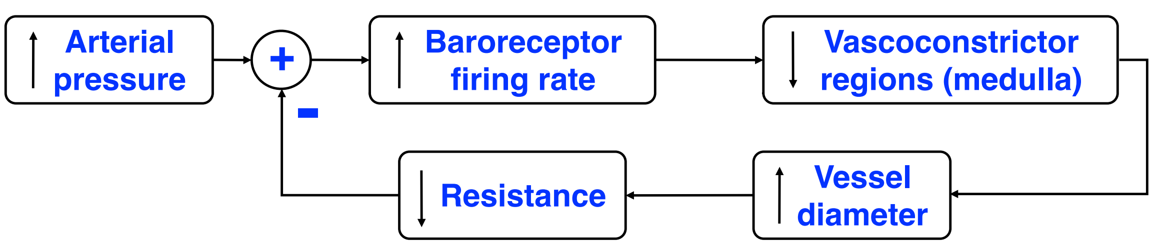
- Found in carotid sinus, aortic arch and subclavian, common carotid, pulmonary arteries
- Respond differently to pulsatile vs. constant response



Baroreceptor System



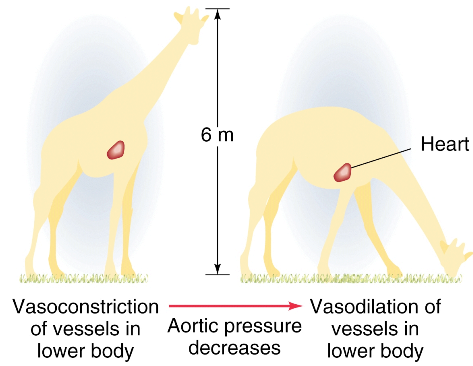
Arterial Baroreceptor Reflex

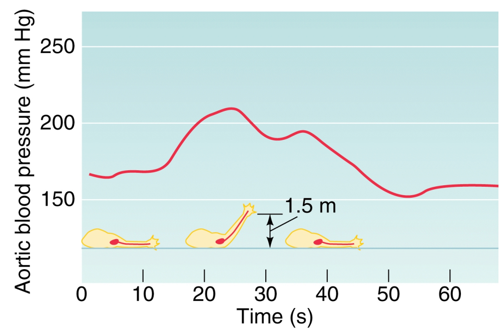


- Most important in the short term
- Response varies across vessels
- Gain is variable (time, hypertension, NE)

Venous Response to Posture

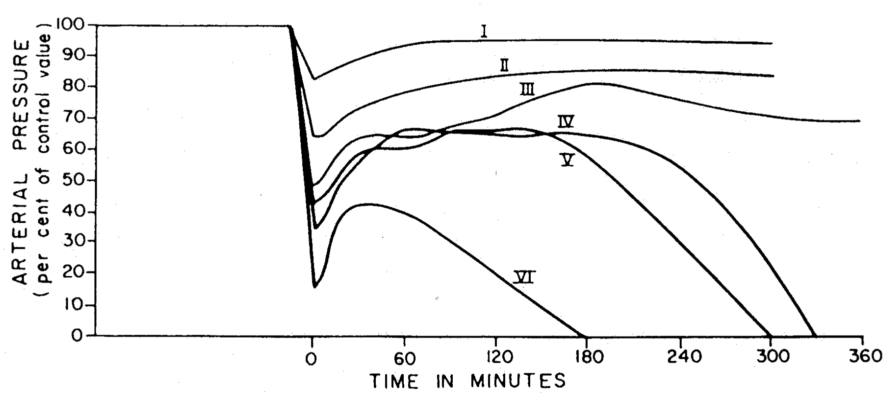
- Vasoconstriction to maintain venous return
  - Inadequate over time
  - Blood pooling, fainting
- Long necked animals require more active regulation
  - Aortic pressures: 160--200 mm Hg
  - Rapid regulation of vasodilation
  - Kidney especially critical
- Blood pooling in fish tails
  - Large, central return veins
  - Accessory caudal heart





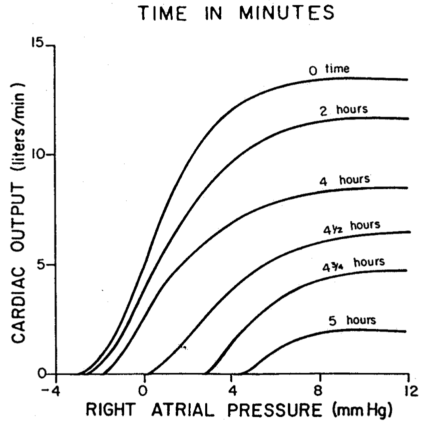
Hemorrhage and Shock: Examples

I-VI: increasing duration of hemorrhage



Function curves for different times after hemorrhage

- animal bled until P_A = 30 mm Hg and maintained at this pressure for indicated time
- measured cardiac function curves at indicated time points



In progressive shock, heart eventually suffers!

Hemorrhage and Shock: Basics

- Blood loss leads to drop in venous return and blood pressure
- Resulting shock can be progressive or nonprogressive
- Response represents balance of compensatory and decompensatory mechanisms
- End result?
  - a dynamic battle between negative and positive feedback
  - can reach a point of no return (damage is too extensive for recovery)
  - rapid treatment (replacement) is imperative!

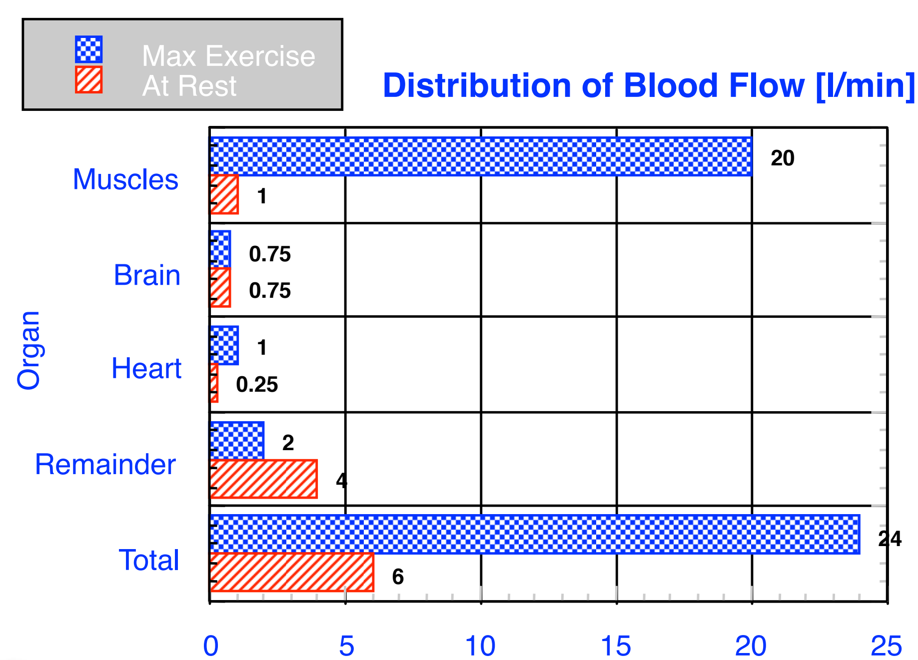
Hemorrhage and Shock: Compensatory Mechanisms

- Baroreceptor reflex: increased HR, vasoconstriction, recruitment of blood reservoirs (cold skin)
- Cerebral ischemia: massive central response!!
- Chemoreceptor responses: adds to vasoconstriction and increase respiration (good for increasing venous return)
- Reabsorption of fluid from the tissues, due to atrial hypotension upsetting normal fluid balance
- Humoral (catecholamine) response: up to 50x normal levels in the blood
- Vasopressin/Renin/Angiotensin: all potent vasoconstrictors and increase kidney water retention

Hemorrhage and Shock: Decompensatory Mechanisms

- Cardiac failure: coronary hypotension leads to failure and reduction in CO (see lower panel of Figure two slides before)
- Acidosis: reduced flow leads to drop in pH, which further compromises contraction and response to vasoconstrictors
- CNS Depression: hypoxia compromises central control
- Blood clotting: increases at first, which can block vessels and affect both heart and brain; decreases later and promotes internal bleeding

Response to Exercise



Response to Exercise I

- Heart rate
  - Release of parasympathetic tone
  - Increase in sympathetic stimulation
  - 4-5 fold increase possible, function of exercise level
- Stroke volume
  - Increases, can even double
  - Frank-Starling plays small role at moderate exercise, larger role at high intensity exercise
- Venous return
  - Increases due to venous constriction and respiration

What happens to TPR?

Key Messages

- Vascular control is essential, multifaceted, and complex (we have only touched the surface)
- Local mechanisms
  - Myogenic
  - Metabolic
- Central mechanisms
  - Baroreceptor system
  - Venous response
- Exercise as example