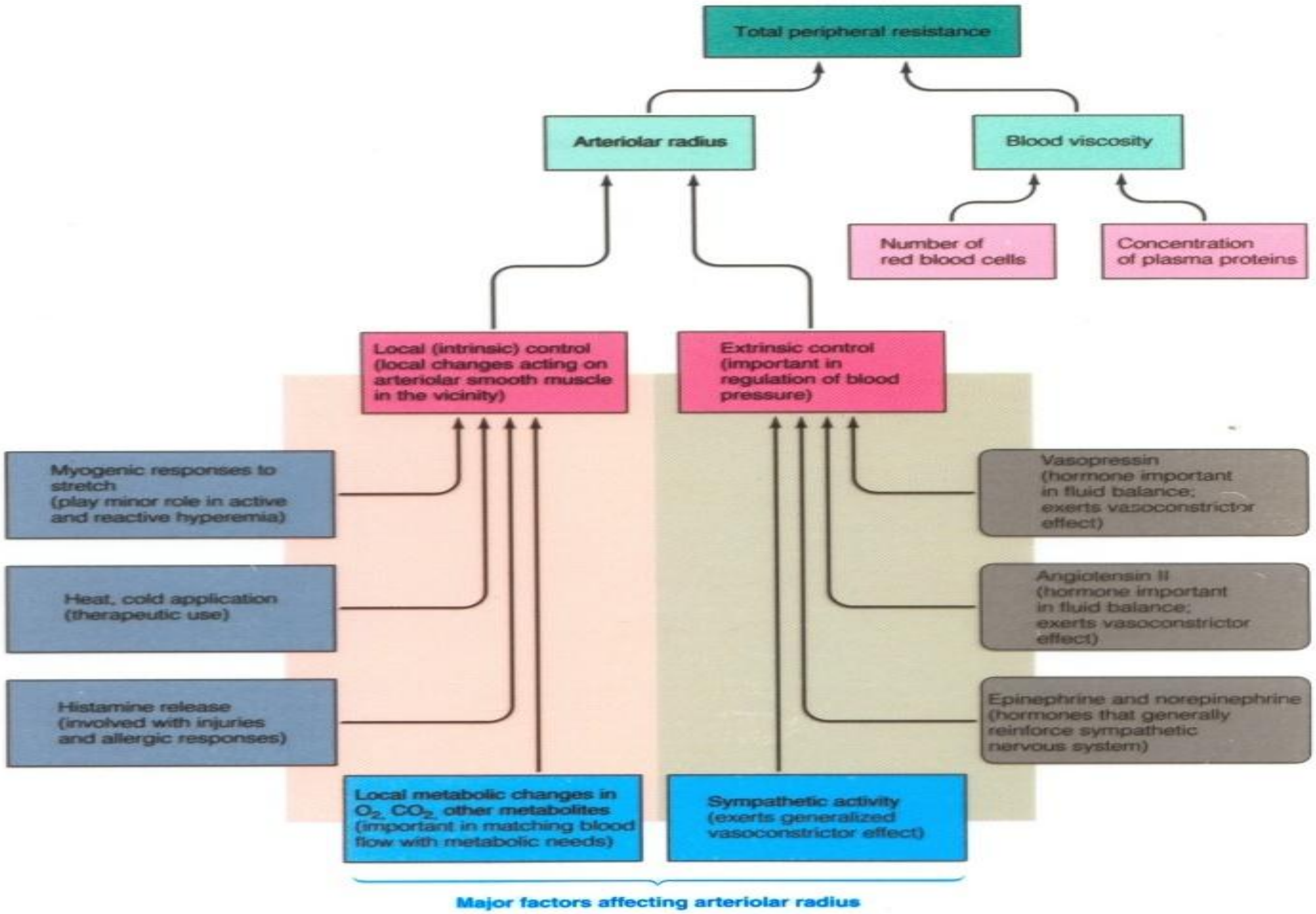
Blood Pressure Regulation 2

Faisal I. Mohammed, MD,PhD

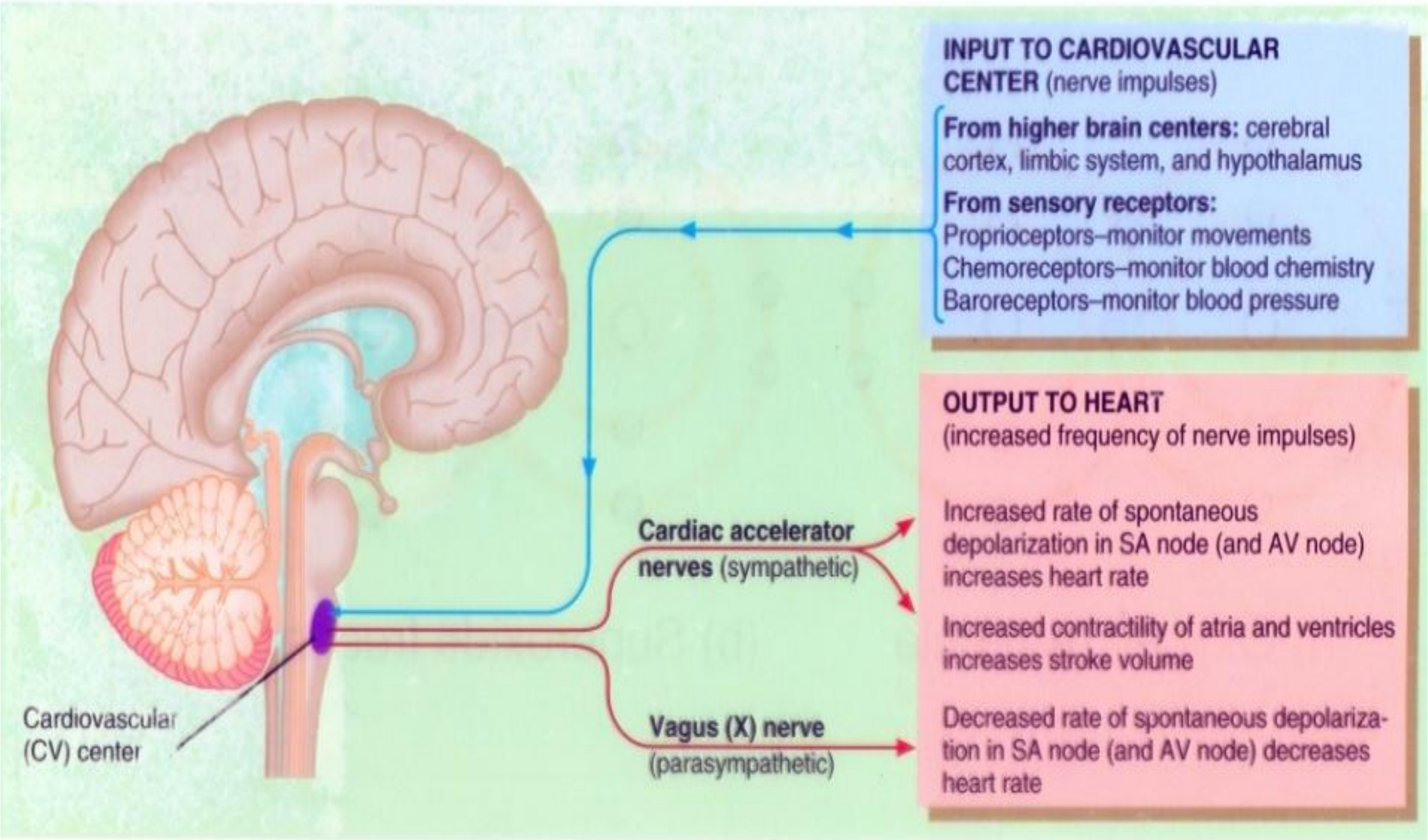
Objectives

- Outline the intermediate term and long term regulators of ABP.
- Describe the role of Epinephrine, Antidiuretic hormone (ADH), Renin-Angiotensin-Aldosterone and Atrial Natriuretic Peptide (ANP) in BP regulation
- Point out the role of Kidney-body fluid system in long term regulation of BP
- Follow up the responses of the circulatory shock

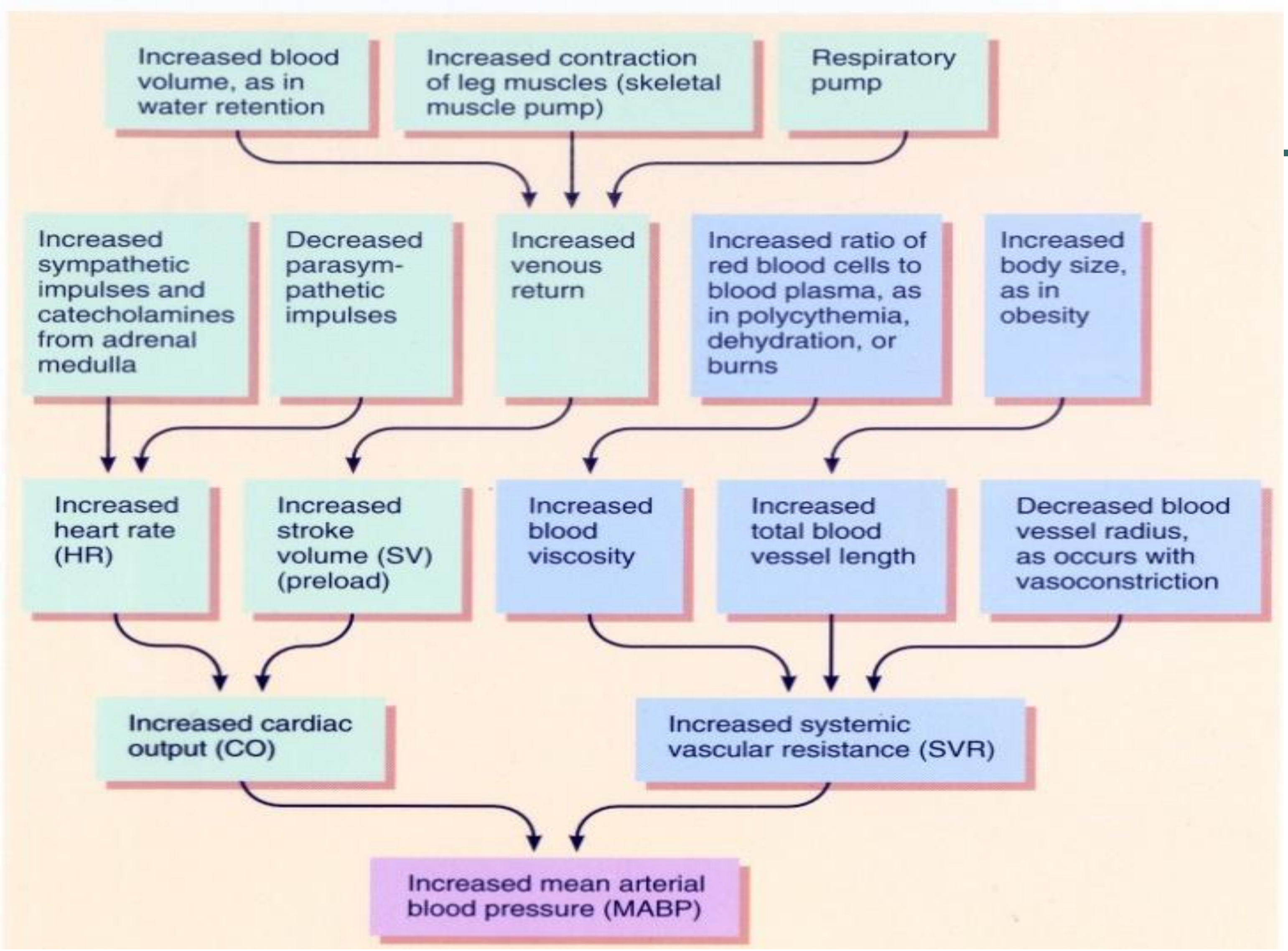
Factors affecting Total Peripheral Resistance



Nervous Control of the Heart



Factors that affect the Mean Arterial Pressure



Intermediate / Long term Regulation of BP

1. Epinephrine – Adrenal medulla system
   works as intermediate term needs ~ 10 min. to work causes vasoconstriction

2. ADH (vasopressin) system needs ~ 30 min to work causes vasocnstriction

Long term Regulation of BP…cont

3. Renin-Angiotensin-Aldosterone system ~ 1 hour to be effective

Angiotensinogen (14 a.a peptide) converted into Angiotensin I (10 a.a peptide) by Renin that come from afferent arteriolar cell, the angiotensin I is converted into angiotensin II (8 a.a peptide) by Angiotensin converting enzyme mainly in the lungs.

Angiotensin II (A II) is very potent vasoconstrictor. AII also stimulates aldosterone synthesis and secretion from the adrenal coretx (Zona glomerulosa), aldosterone increases Na^+ reabsorption from the renal nephrone and so water.

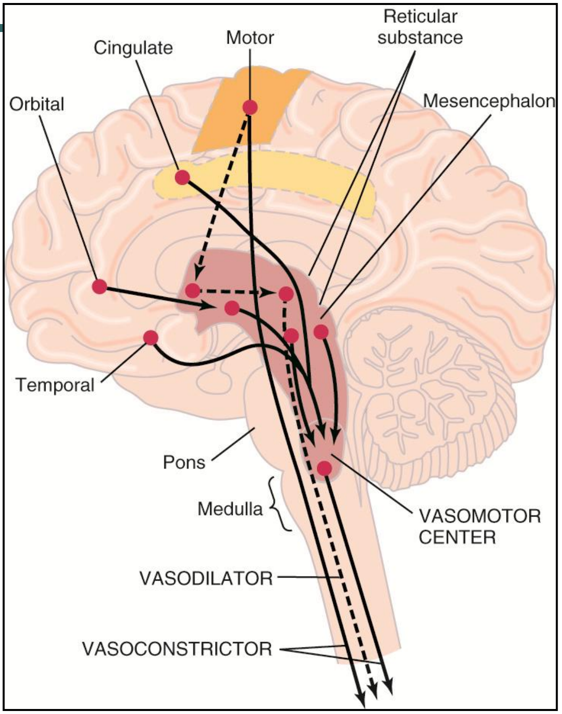
AII is also a positive inotropic agent

Long term Regulation of BP …cont

4. Atrail Natriuretic peptide (ANP): An 28 a.a peptide released mainly from the Rt. Atrium in response to stretch. It causes increase in GFR so increase Na^+ and water. Its concentration decreases when BP is low and its concentration increases if BP is high, mainly due volume overload

CNS Ischemic Response

- CNS Ischemic response is activated in response to cerebral ischemia.
- Reduced cerebral blood flow causes CO2 buildup which stimulates vasomotor center thereby increasing arterial pressure.
- CNS Ischemic response is one of the most powerful activators of the sympathetic vasoconstrictor system.



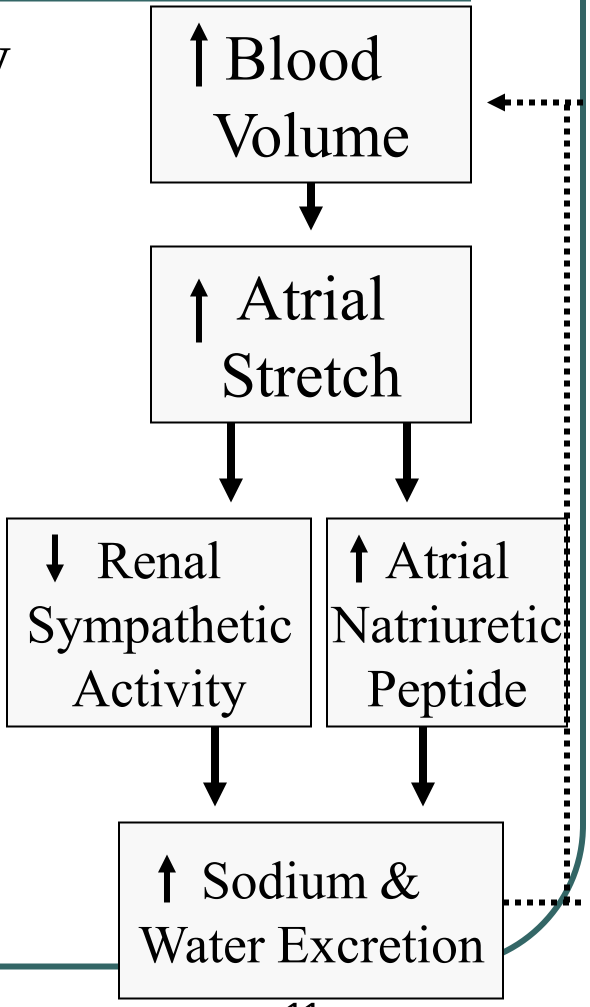
Cerebral Ischemia → ↑CO_2 → **Vasomotor Center** → **↑Sympathetic Activity** → **↑Arterial Pressure**

CNS Ischemic Response

- CNS Ischemic response is not activated until pressure falls below 60mmHg; greatest activation occurs at pressures of 15-20mmHg.
- Cushing reaction is a special type of CNS ischemic response.
- Prolonged CNS ischemia has a depressant effect on the vasomotor center.

Atrial and Pulmonary Artery Reflexes

- Low pressure receptors in atria and pulmonary arteries minimize arterial pressure changes in response to changes in blood volume.
- Increases in blood volume activates low pressure receptors which in turn lower arterial pressure.
- Activation of low pressure receptors enhances Na^+ and water by:
  - Decreasing rate of antidiuretic hormone
  - Increasing glomerular filtration rate
  - Decreasing Na^+ reabsorption



Bainbridge Reflex

- Prevents damming of blood in veins atria and pulmonary circulation.
- Increase in atrial pressure increases heart rate.
- Stretch of atria sends signals to VMC via vagal afferents to increase heart rate and contractility.

Atrial Stretch → **Vagal afferents** → **↑ Vasomotor Center (vasoconstrictor)** →  **↑ Heart rate Contractility**

Blood Pressure Regulation

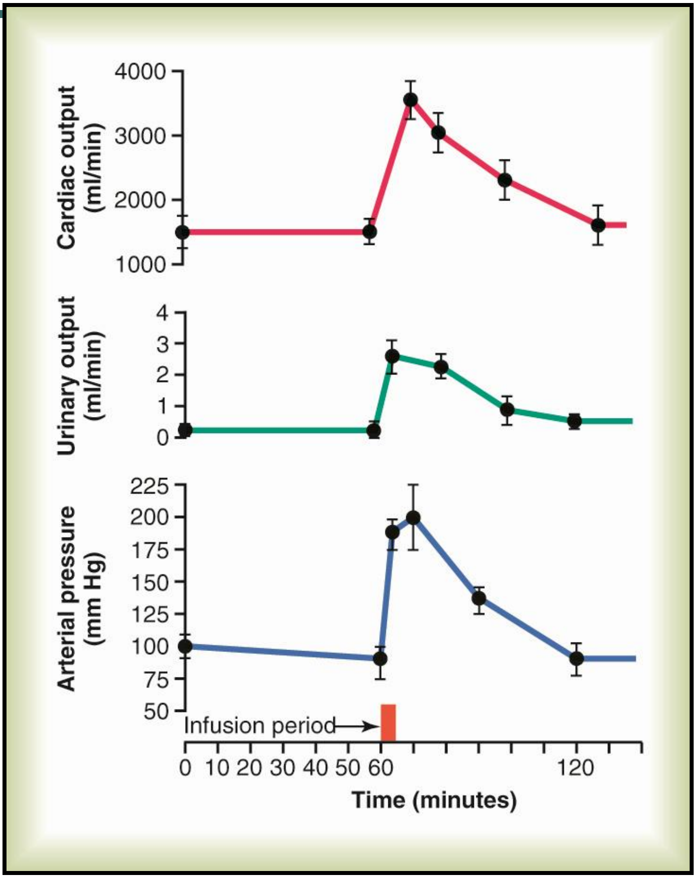
- Mean Arterial Pressure (MAP) = 1/3 systolic pressure + 2/3 diastolic pressure

$$CO = \frac{MAP}{TPR}$$

$$MAP = CO * TPR$$

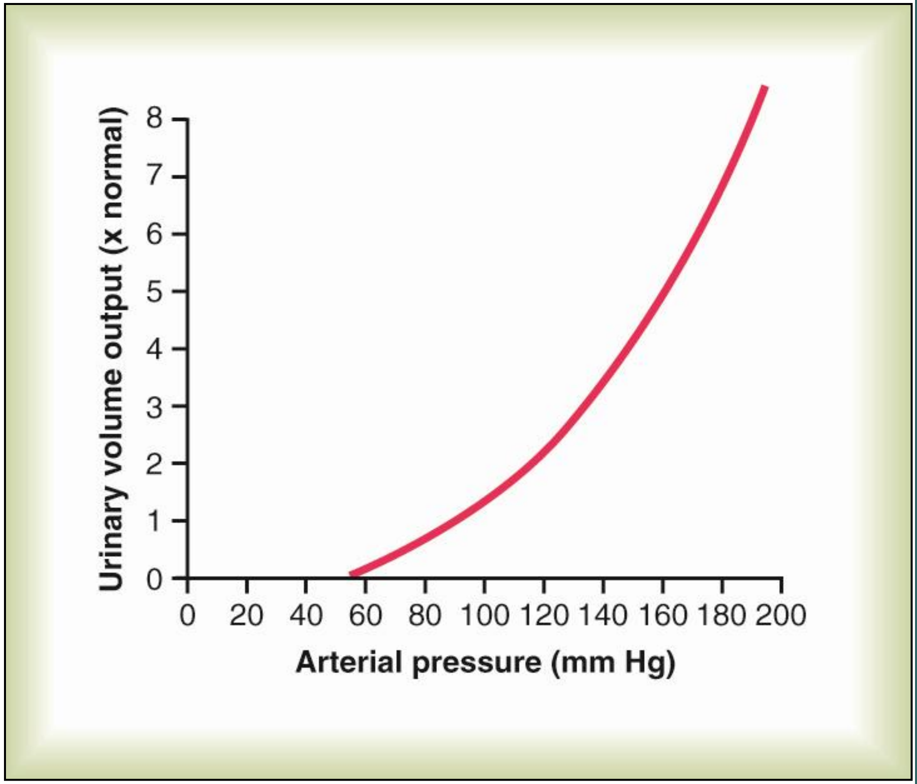
Renal Body Fluid System for Long Term Arterial Pressure Control

- Plays a dominant role in long term pressure control.
- As extracellular fluid volume increases arterial pressure increases.
- The increase in arterial pressure causes the kidneys to lose Na and water which returns extracellular fluid volume to normal.



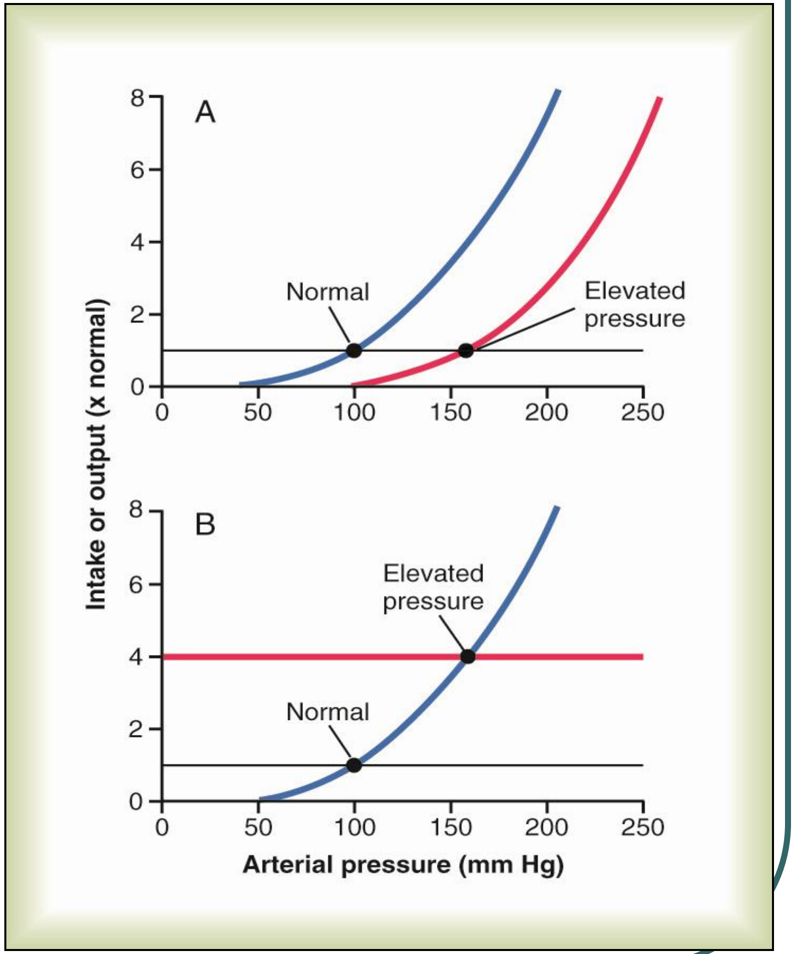
Pressure Natriuresis and Diuresis

- The effect of pressure to increase water excretion is called pressure diuresis.
- The effect of pressure to increase Na excretion is called pressure natriuresis.



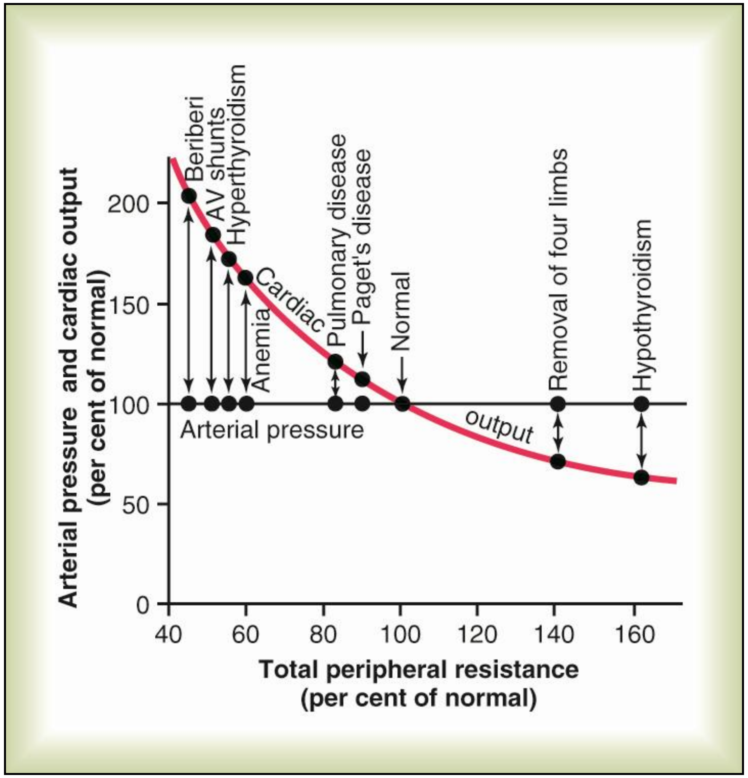
Graphical Analysis of Renal Body Fluid Mechanism

- The major determinants of long-term arterial pressure control.
  - Based on renal function curve
  - Salt and water intake line
- Equilibrium point is where intake and output curves intersect.
- Renal body fluid feedback system has an infinite gain.



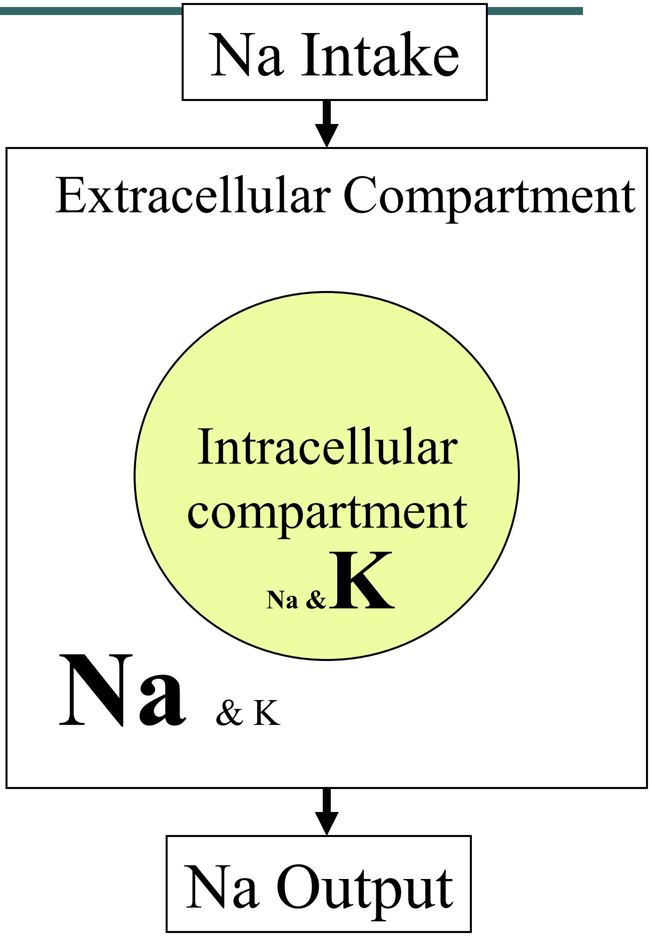
Failure of Total Peripheral Resistance to Elevate Long-term Arterial Pressure

- Changes in TPR does not affect long-term arterial pressure level.
- One must alter the renal function curve in order to have long-term changes in arterial pressure.
- Changing renal vascular resistance does lead to long-term changes in arterial pressure .

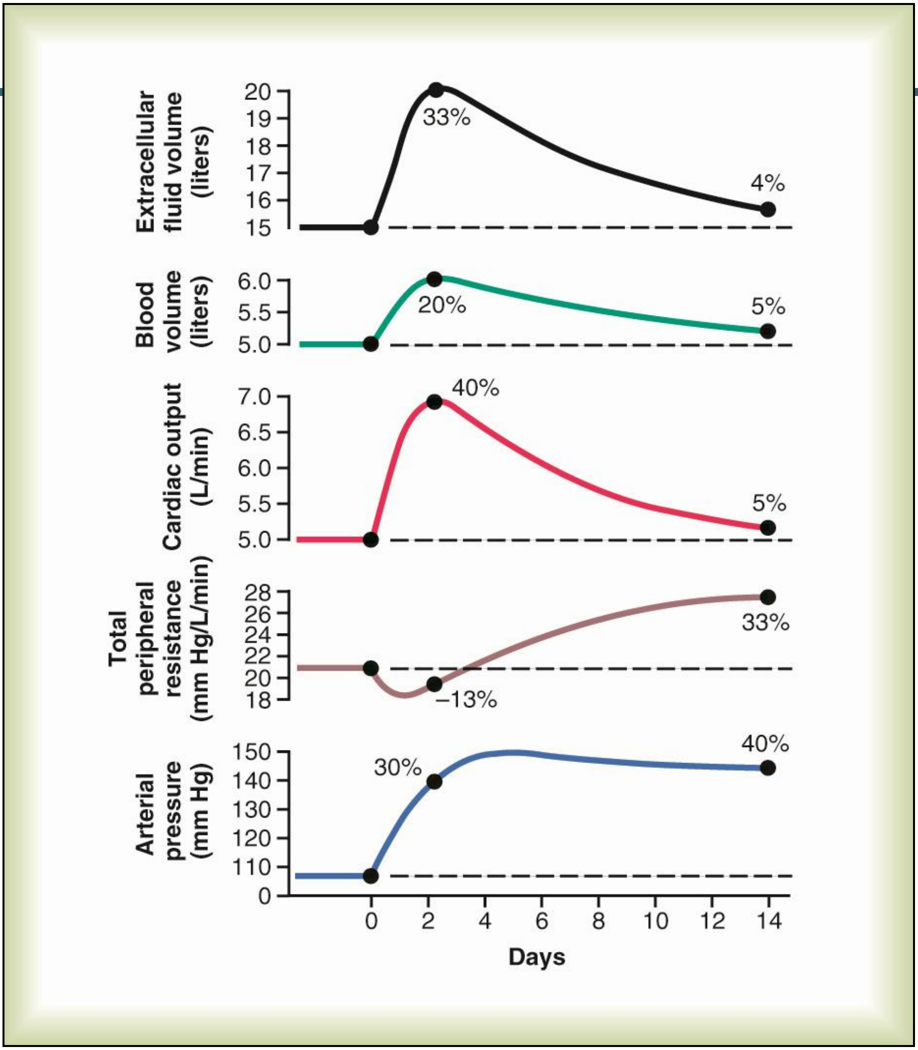


Sodium is a Major Determinant of ECFV

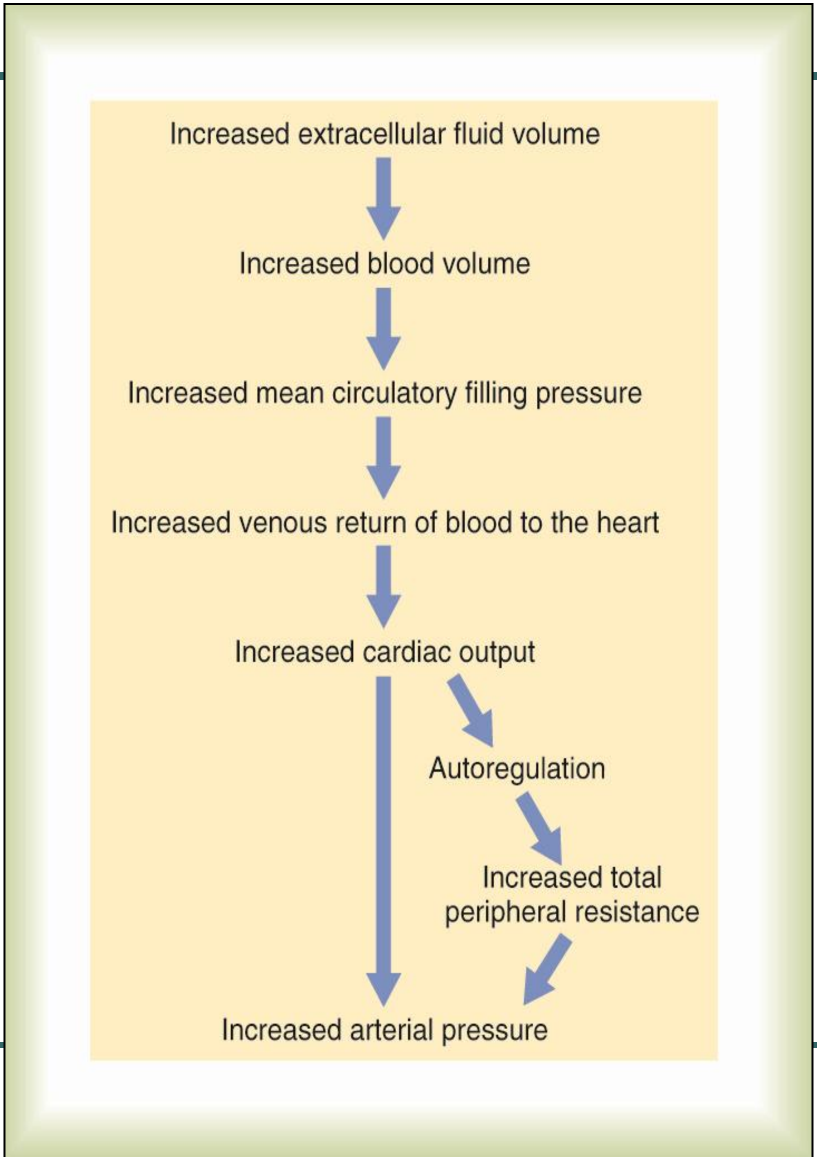
- As Na^+ intake is increased; Na^+ stimulates drinking, increased Na^+ concentration stimulates thirst and ADH secretion.
- Changes in Na^+ intake leads to changes in extracellular fluid volume (ECFV).
- ECFV is determined by the balance of Na^+ intake and output.



Volume Loading Hypertension

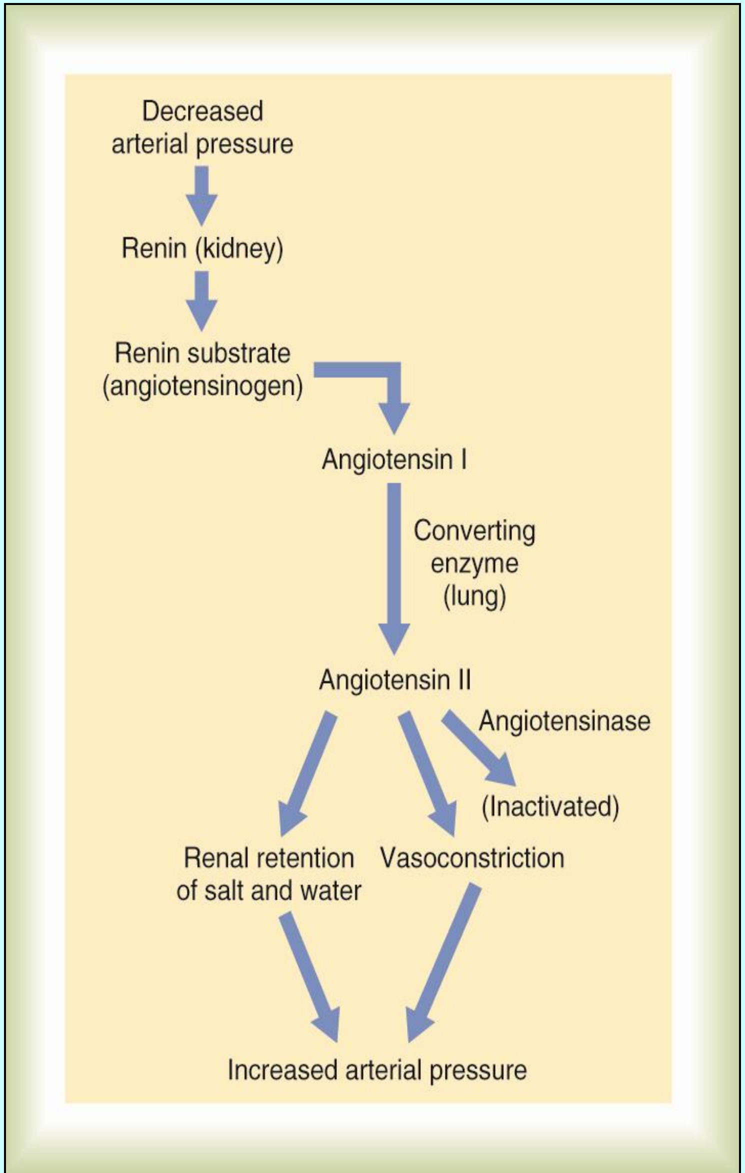


Effect of ECFV on Arterial Pressure



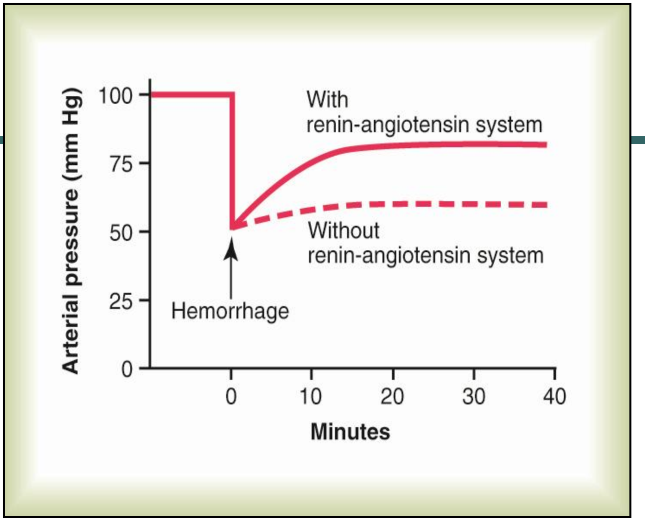
Renin-Angiotensin System

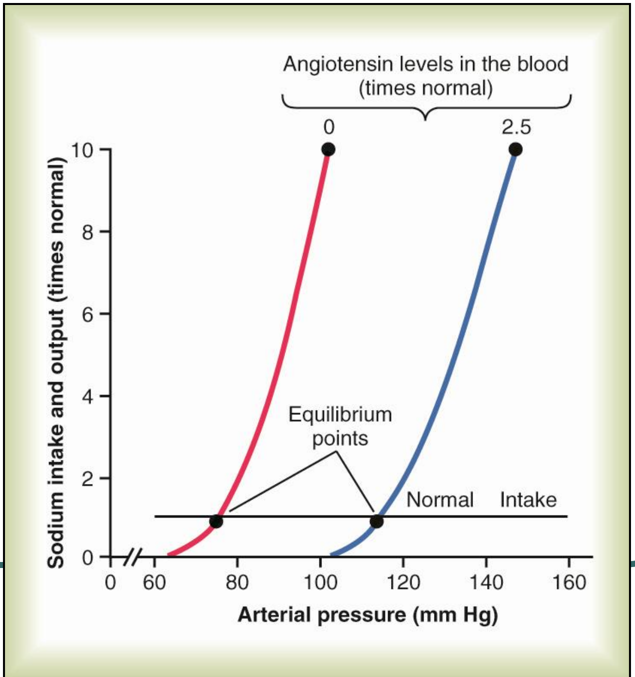
- Renin is synthesized and stored in modified smooth muscle cells in afferent arterioles of the kidney.
- Renin is released in response to a fall in pressure.
- Renin acts on a substance called angiotensinogen to form a peptide called angiotensin I.
- AI is converted to AII by a converting enzyme located in the endothelial cells in the pulmonary circulation.



Actions of the Renin Angiotensin System

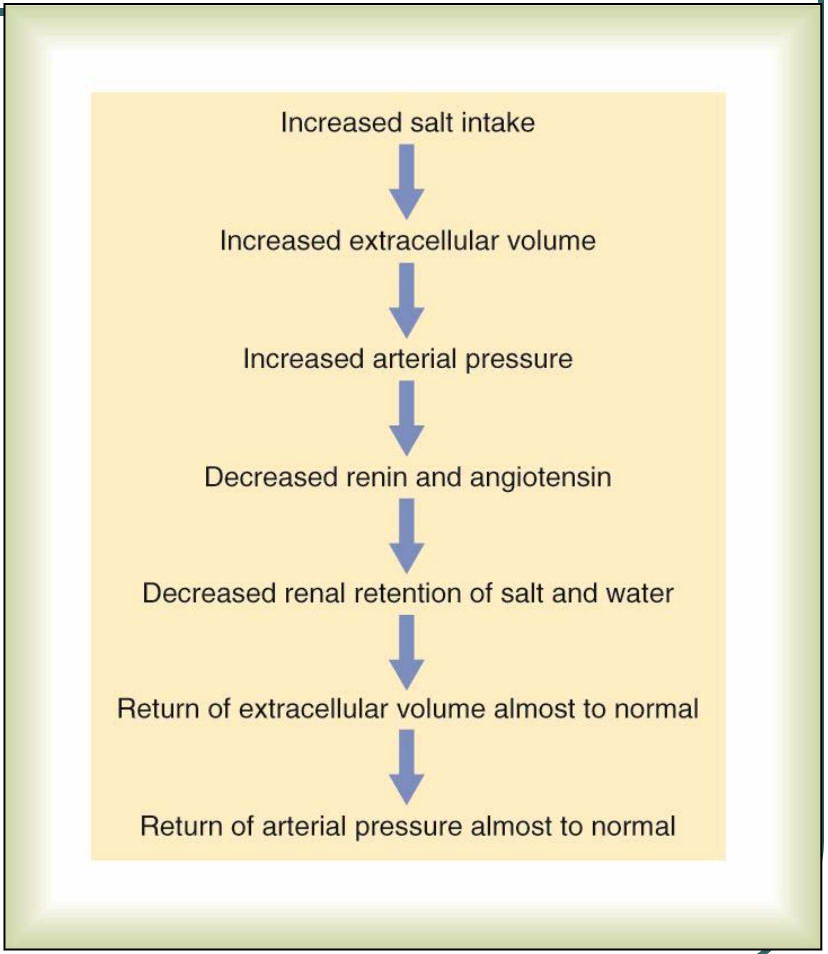
- Causes vasoconstriction
- Causes Na^+ retention by direct and indirect acts on the kidney
- Causes shift in renal function curve to right



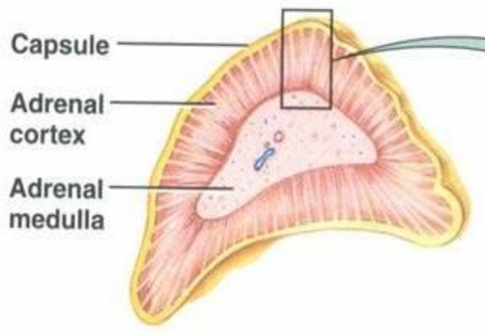


Renin Angiotensin System: Effect of Na^+ Intake

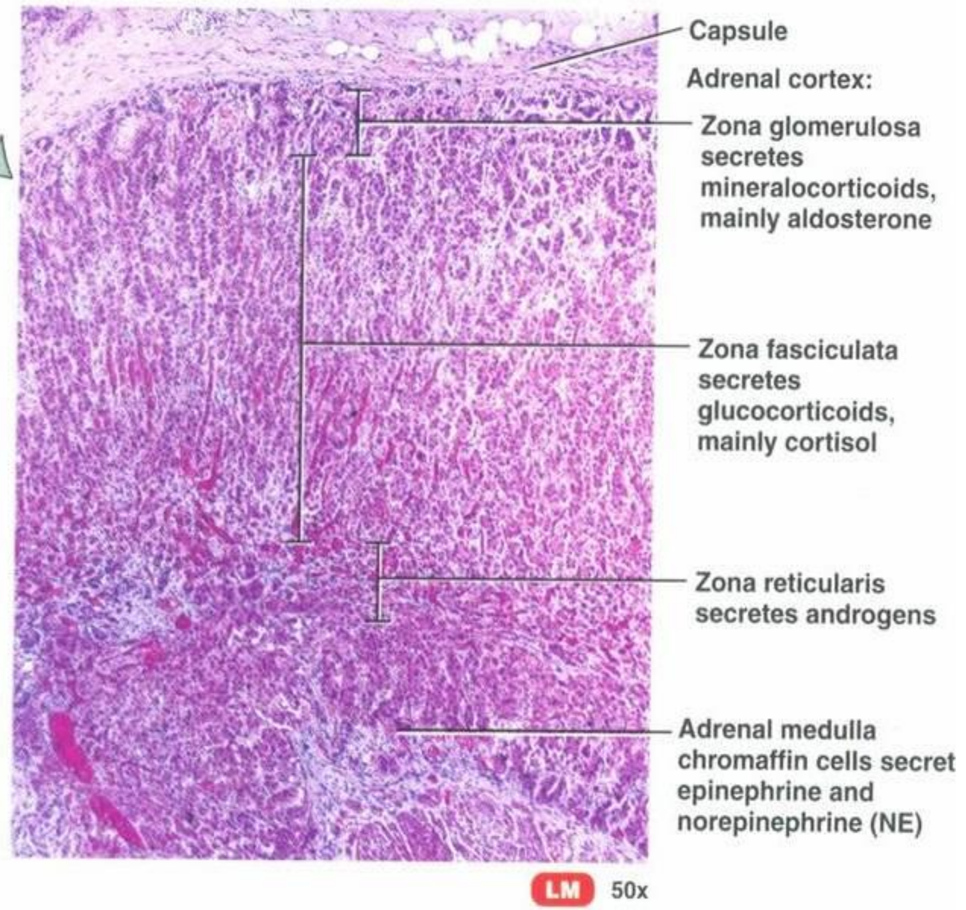
- RAS is important in maintaining a normal AP during changes in Na^+ intake.
- As Na^+ intake is increased renin levels fall to near 0.
- As Na^+ intake is decreased renin levels increase significantly.
- RAS causes the Na^+ loading renal function curve to be steep.



Adrenal Gland as the source of Aldosterone (cortex) and Epinephrine (medulla)

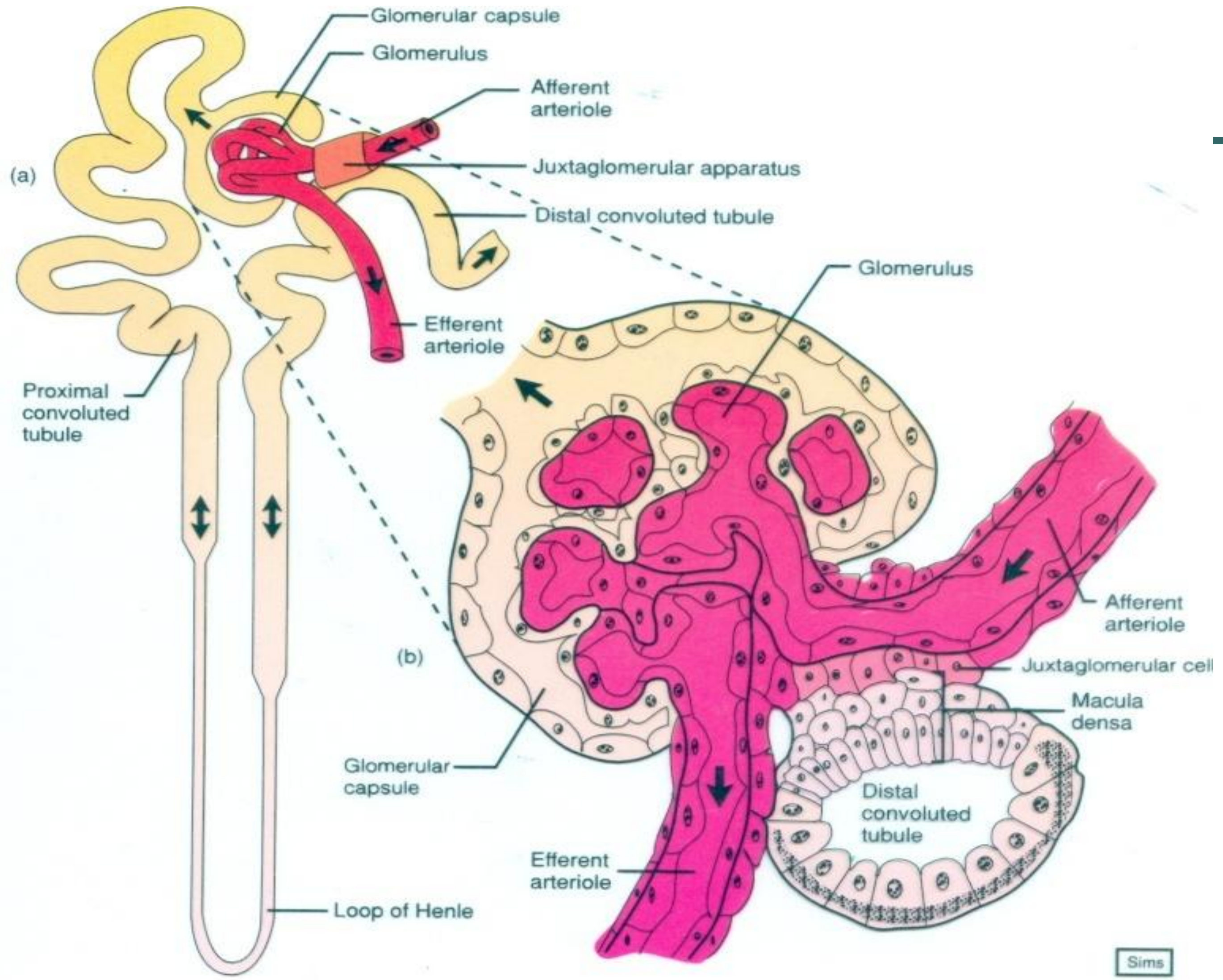


Section through left adrenal gland



(c) Subdivisions of the adrenal gland

Juxtaglomerular Apparatus



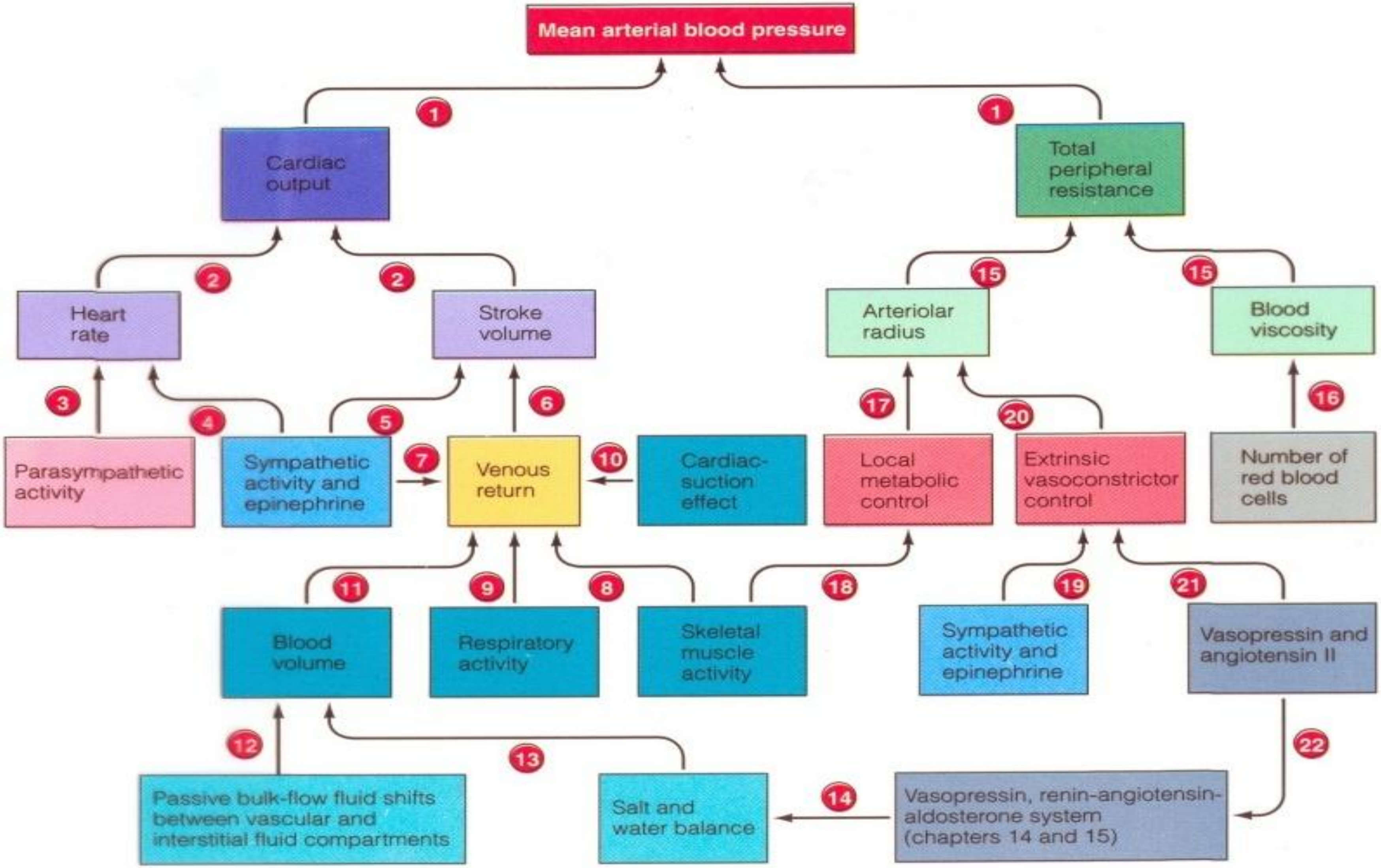
Factors Which Decrease Renal Excretory Function and Increase Blood Pressure

- Angiotensin II
- Aldosterone
- Sympathetic nervous activity
- Endothelin

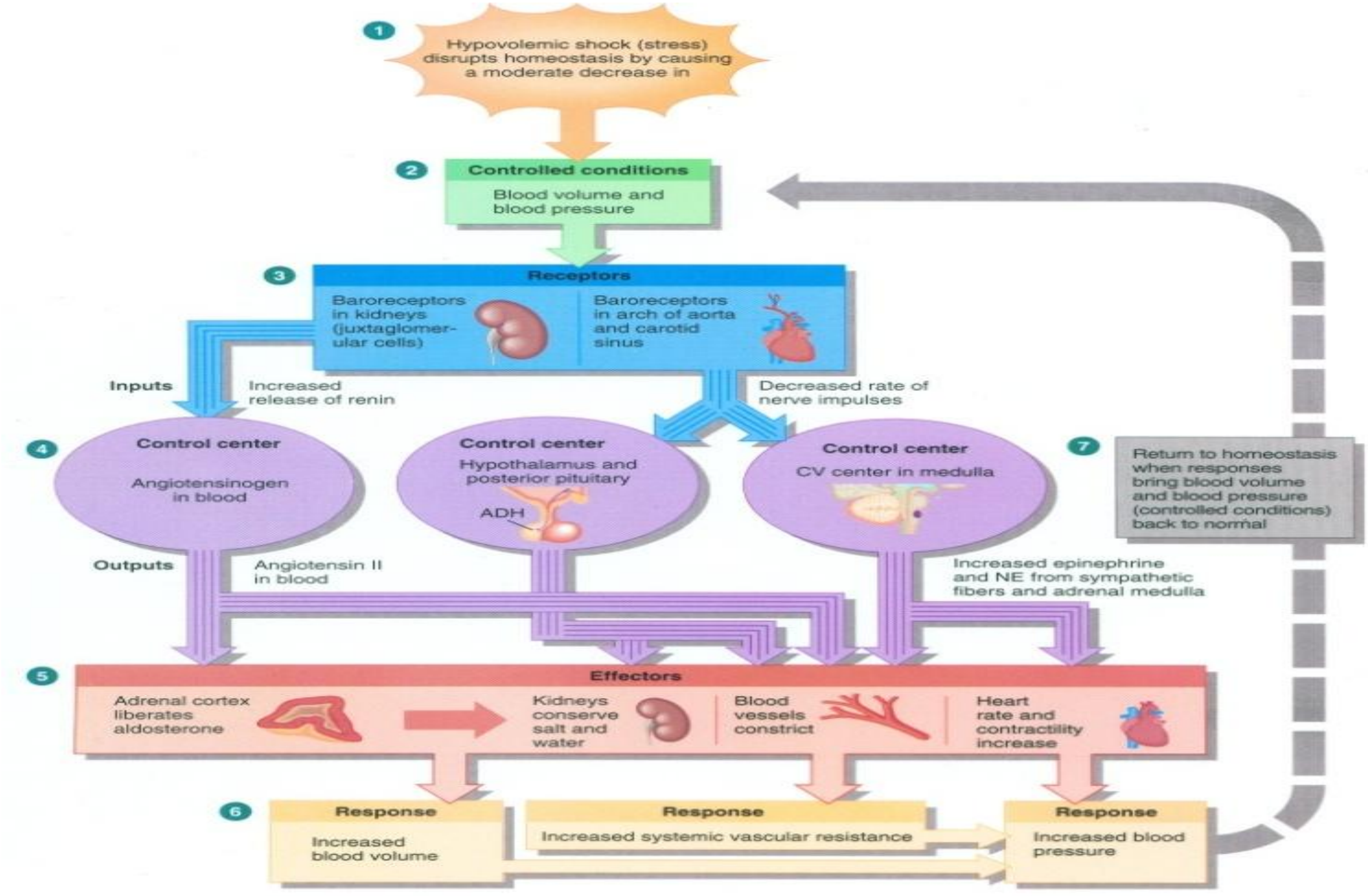
Factors Which Increase Renal Excretory Function and Reduce Blood Pressure

- Atrial natriuretic peptide
- Nitric oxide
- Dopamine

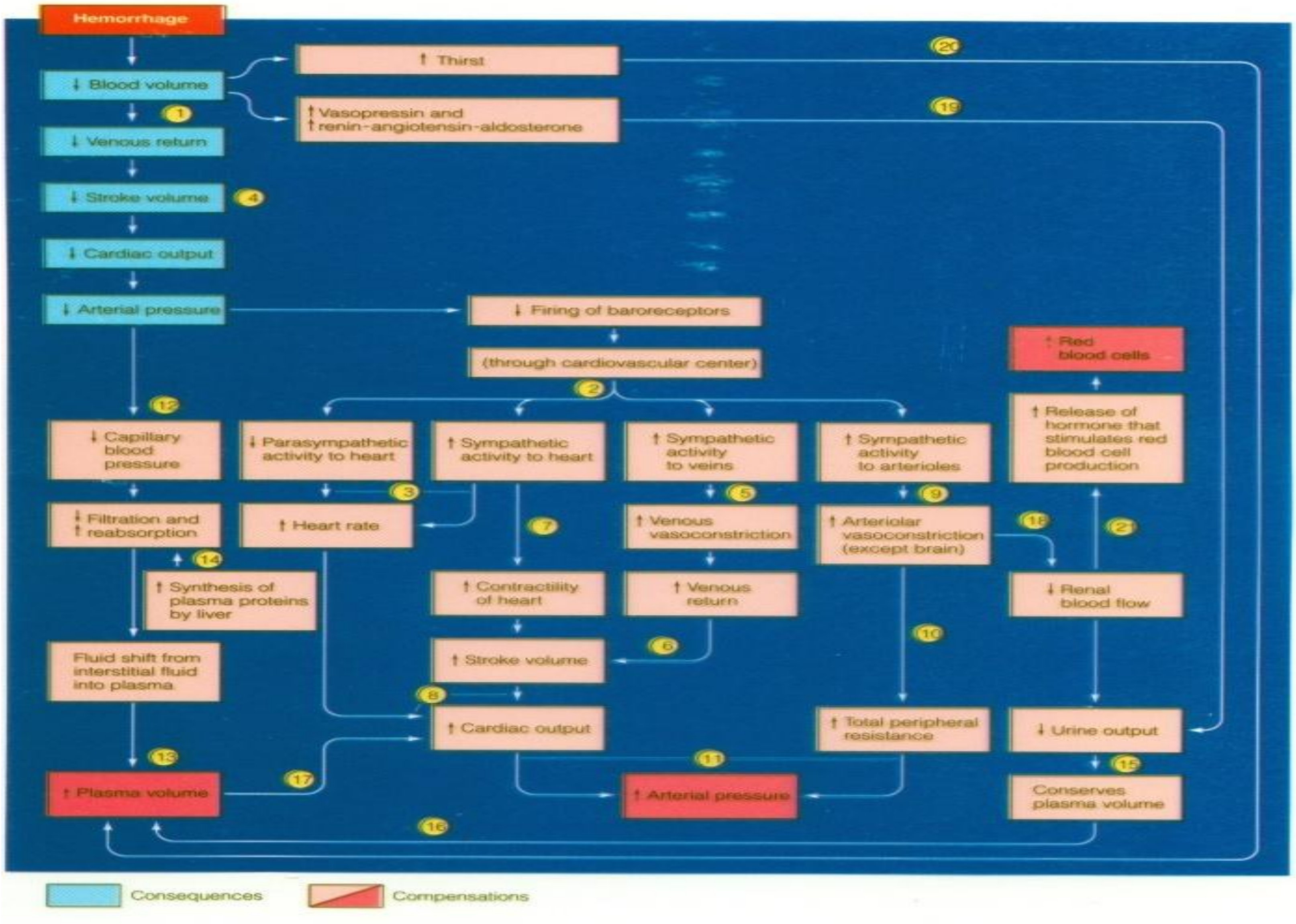
Determinants of Mean Arterial BP



Negative Feedback Cycle of Elevated BP



Consequences and Compensations of Hemorrhage



Thank You

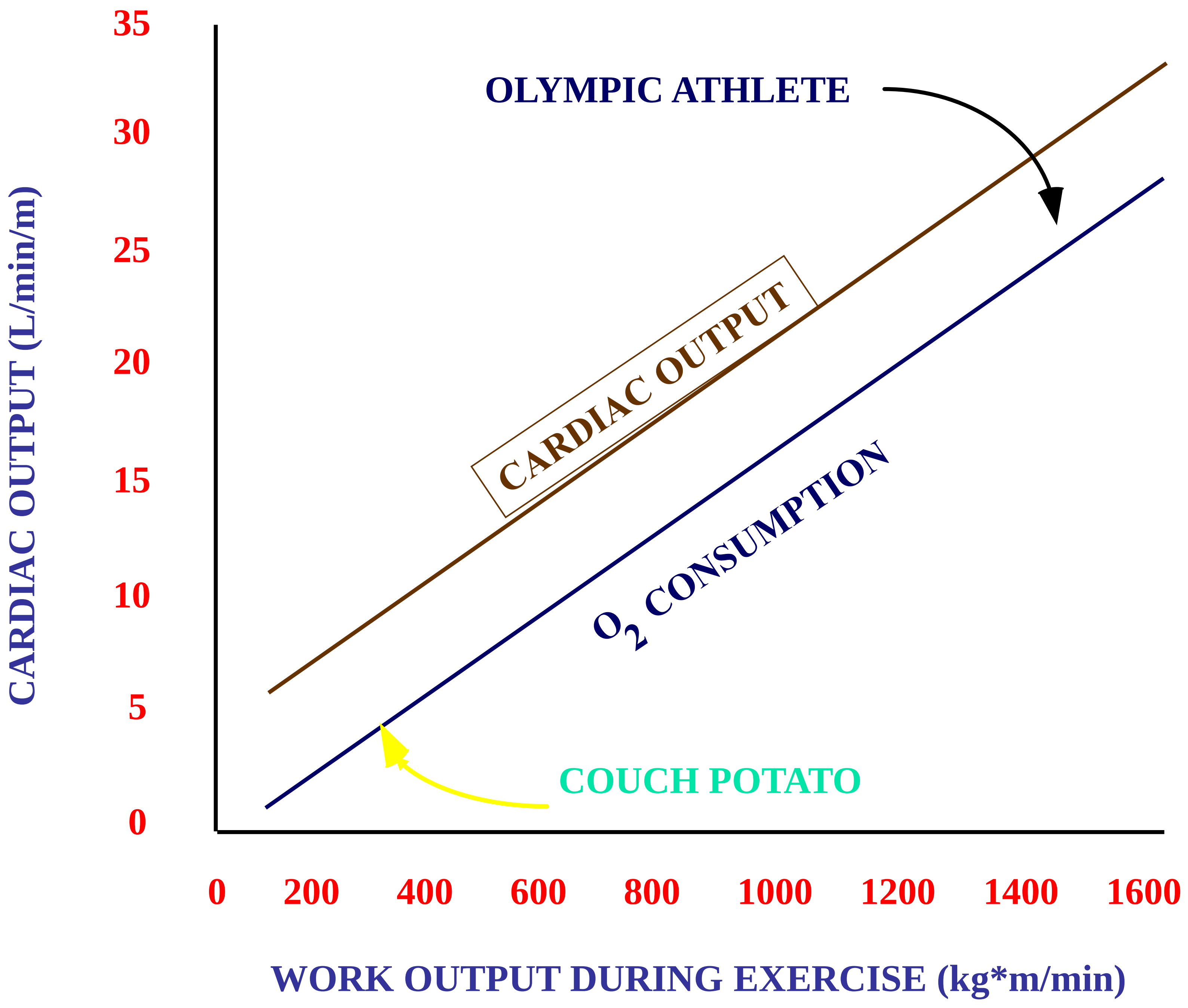
Control of blood tissue blood flow

Objectives

- List factors that affect tissue blood flow.
- Describe the vasodilator and oxygen demand theories.
- Point out the mechanisms of autoregulation.
- Describe how angiogenesis occurs.
- Inter-relat how various humoral factors affect blood flow.

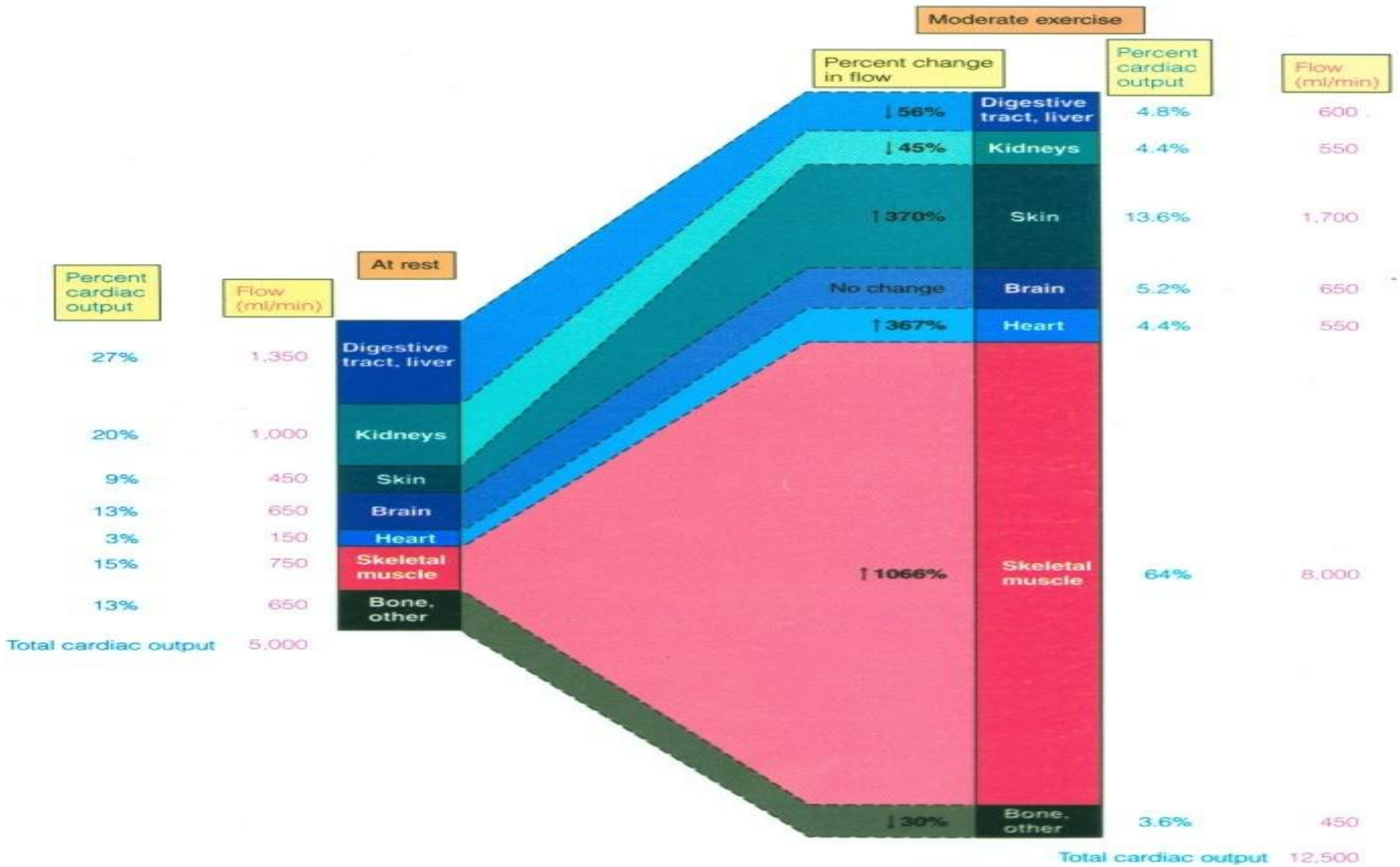
Local Control of Blood Flow

- Each tissue controls its own blood flow in *proportion to its needs.*
- Tissue needs include:
  1) delivery of *oxygen* to tissues
  2) delivery of *nutrients* such as glucose, amino acids, etc.
  3) removal of carbon dioxide hydrogen and other *metabolites* from the tissues
  4) transport various *hormones* and other substances to different tissues
- Flow is closely related to *metabolic rate of tissues.*



35
30
25
20
15
10
5
0
CARDIAC OUTPUT (L/min/m)
OLYMPIC ATHLETE
CARDIAC OUTPUT
O_2 CONSUMPTION
COUCH POTATO
0
200
400
600
800
1000
1200
1400
1600
WORK OUTPUT DURING EXERCISE (kg*m/min)

Magnitude & Distribution of CO at Rest & During Moderate Exercise



Variations in Tissue Blood Flow

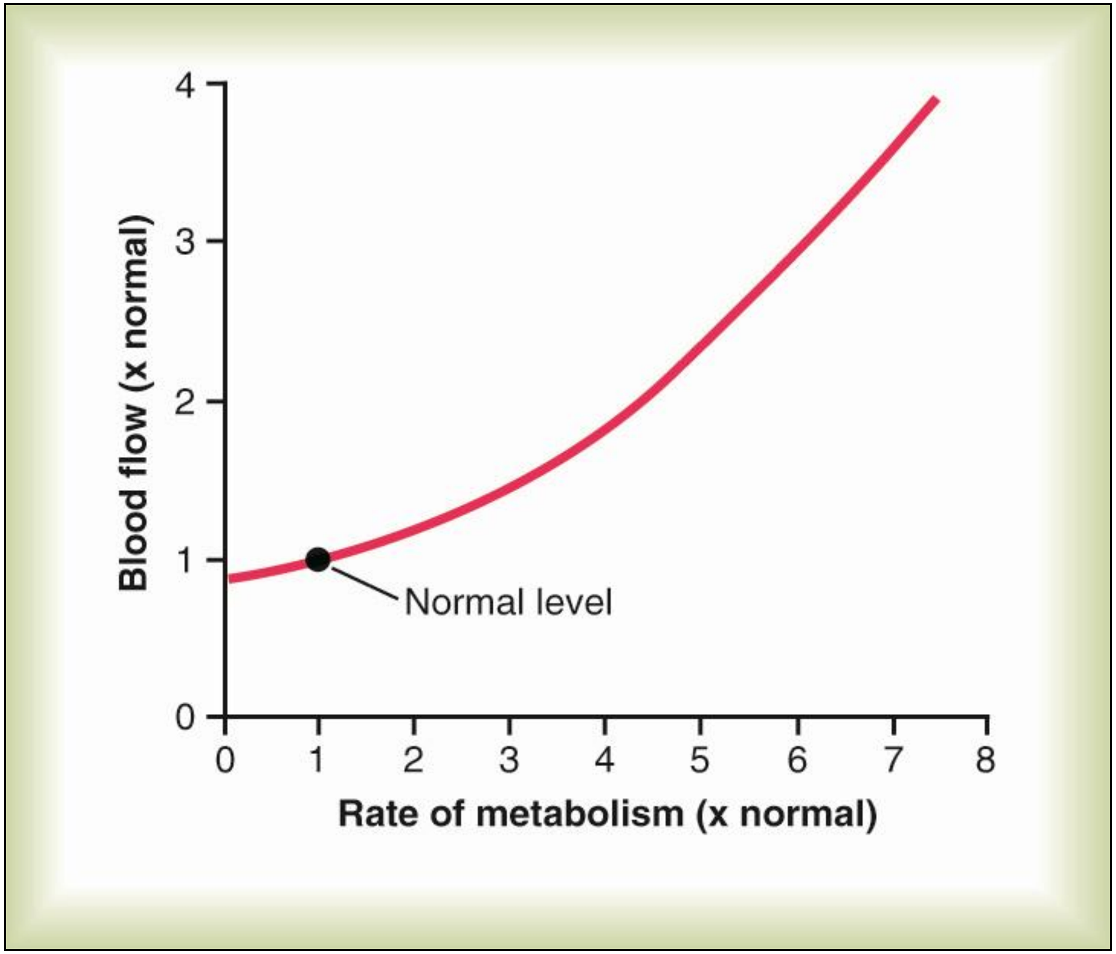
	Per cent	ml/min	ml/min/ 100 gm
Brain	14	700	50
Heart	4	200	70
Bronchi	2	100	25
Kidneys	22	1100	360
Liver	27	1350	95
Portal	(21)	(1050)	
Arterial	(6)	(300)	
Muscle (inactive state)	15	750	4
Bone	5	250	3
Skin (cool weather)	6	300	3
Thyroid gland	1	50	160
Adrenal glands	0.5	25	300
Other tissues	3.5	175	1.3
Total	100.0	5000	---

Acute Control of Local Blood Flow

- Increases in *tissue metabolism* lead to increases in blood flow.
- Decreases in *oxygen availability* to tissues increases tissue blood flow.
- Two major theories for local blood flow are:
  1) *The vasodilator theory*
  2) *Oxygen demand theory*

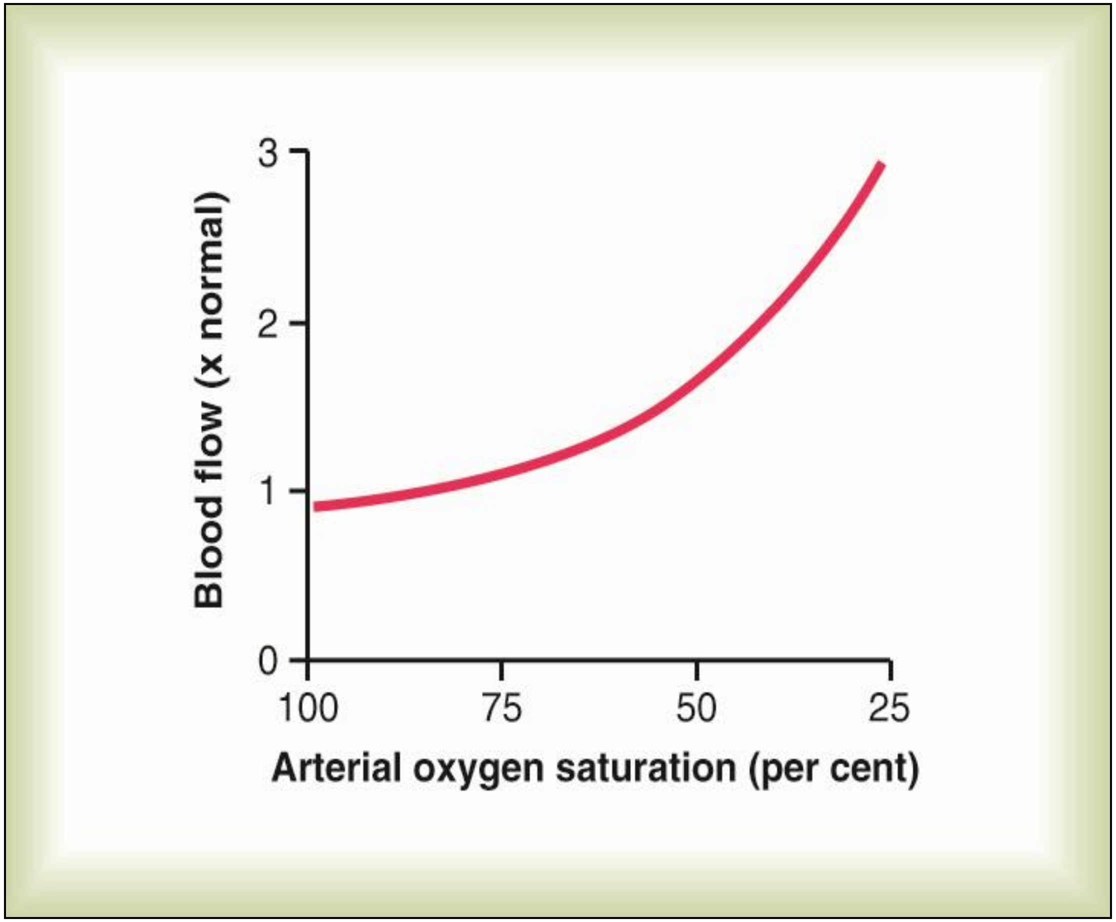
Effect of Tissue Metabolic Rate on Tissue Blood Flow

↑ Tissue Metabolism ⟶ ↑Blood Flow



Effect of Tissue Oxygen concentration on Blood Flow

↓ **Tissue Oxygen Concentration** ← ↑ **Blood Flow**



Relationship between Pressure, Flow, and Resistance

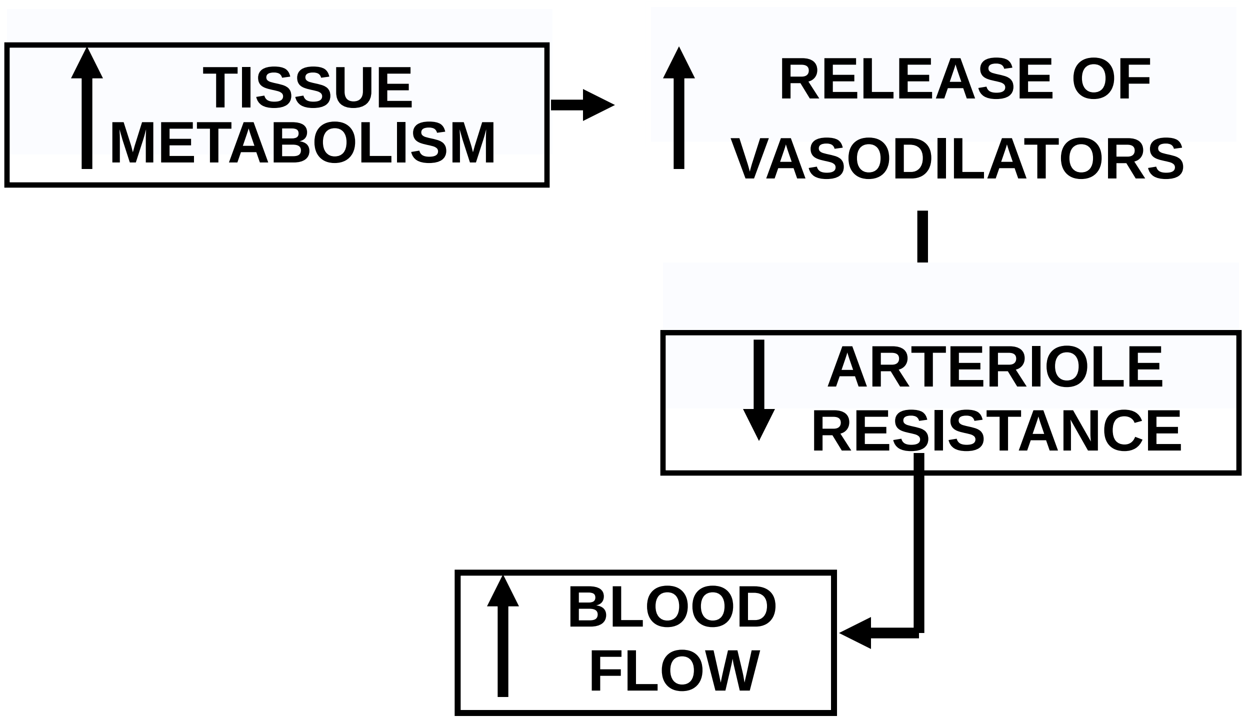
- $F = \Delta P/R$
- *Flow* (F) through a blood vessel is determined by:

  1) The *pressure difference* (Δ P) between the two ends of the vessel

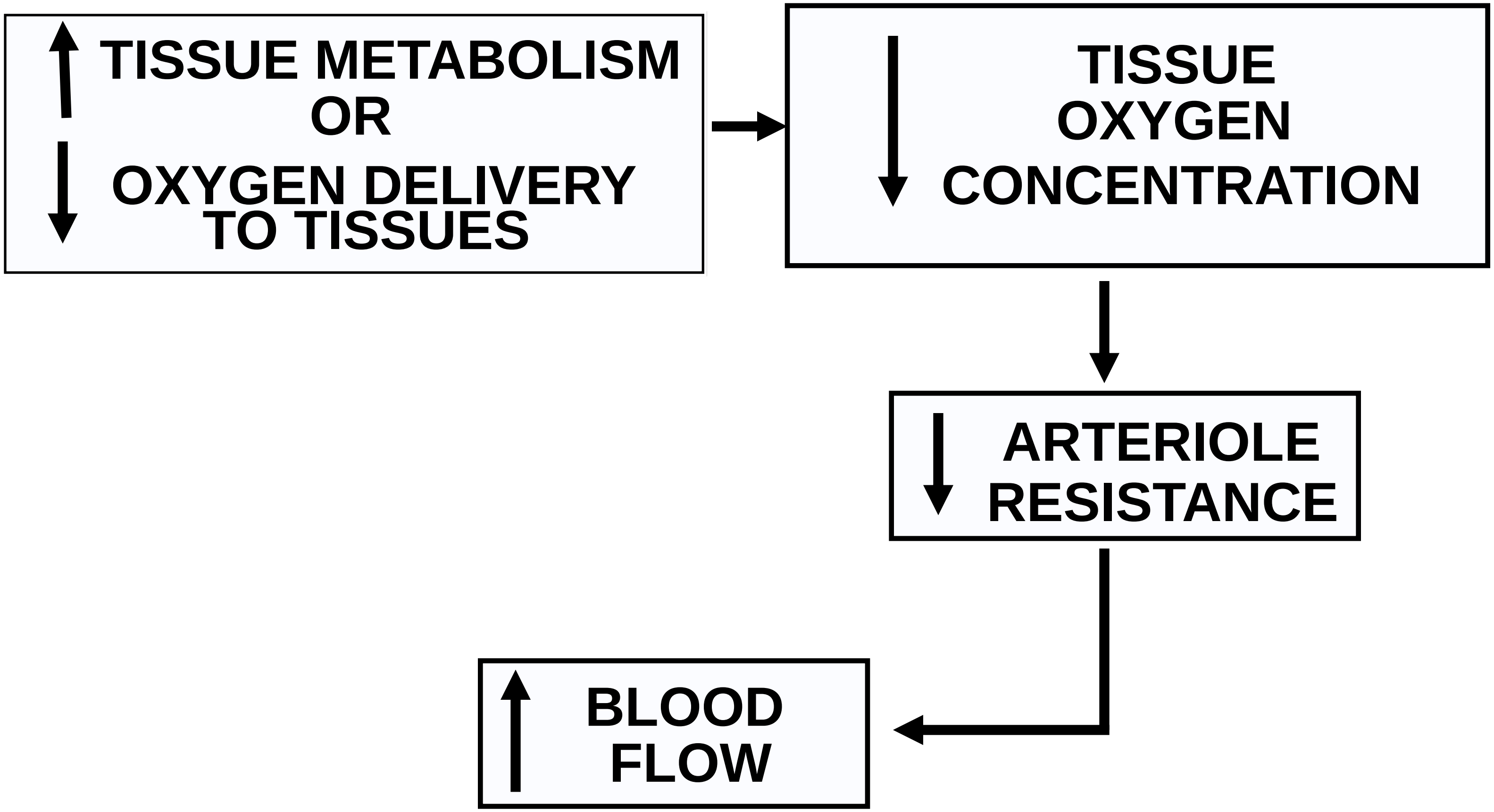
  2) *Resistance* (R) of the vessel

Vasodilator Theory for Blood Flow Control

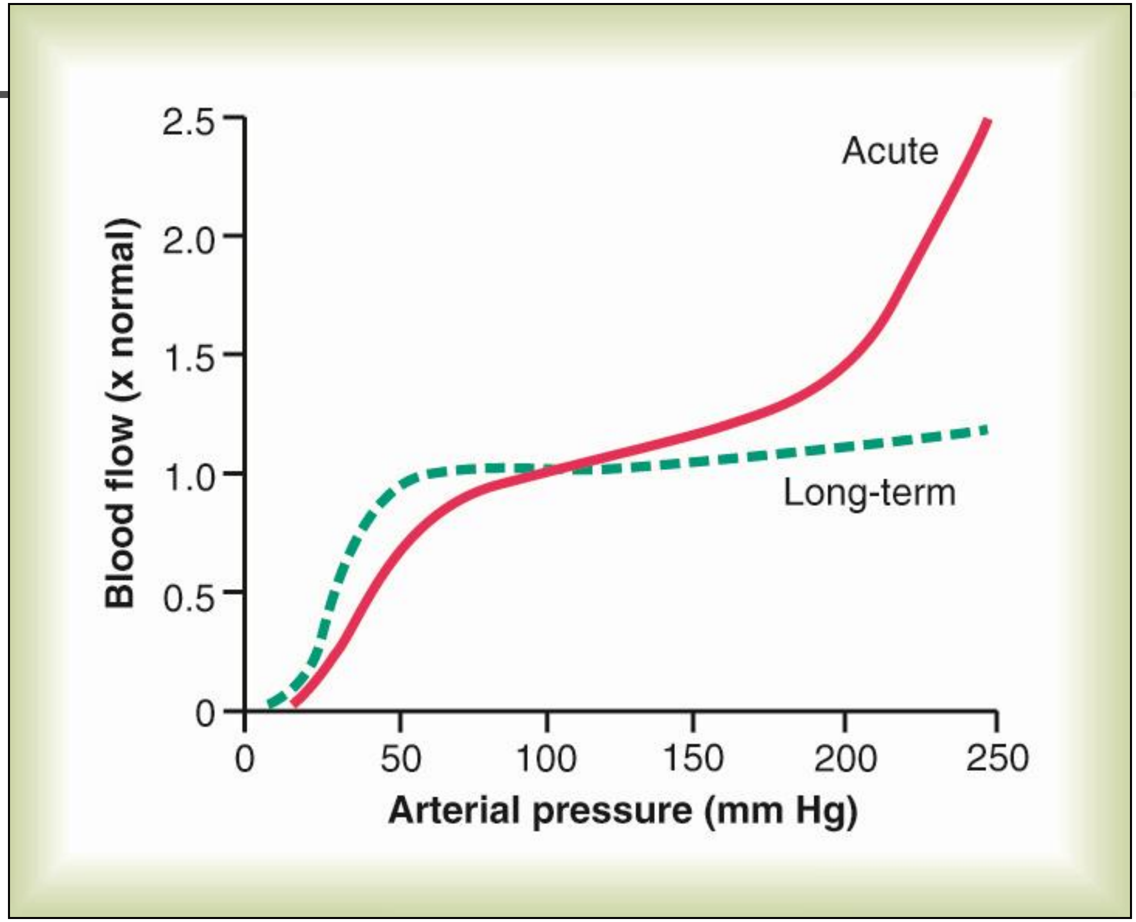
- Local Vasodilators: **Adenosine**, **CO2**, **Lactic acid**, **ADP compounds**, **Histamine**, **K^+ ions**, **H^+ ions**, **Prostacyclin**, **Bradykinin**, **and Nitrous oxid (NO)**



Oxygen Demand Theory for Blood Flow Control



Autoregulation of Blood Flow



Autoregulation - ability of a tissue to maintain blood flow relatively constant over a wide range of arterial pressures.

Blood Flow Autoregulation Theories

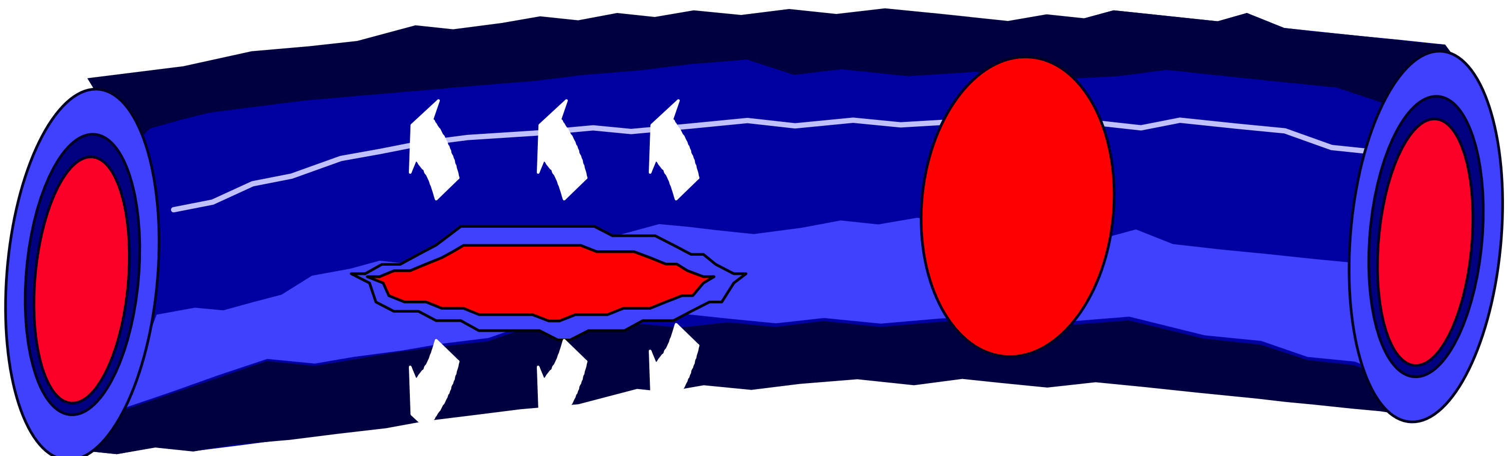
- *Metabolic theory* suggests that as arterial pressure is decreased, oxygen or nutrient delivery is decreased resulting in release of a vasodilator.

- *Myogenic theory* proposes that as arterial pressure falls the arterioles have an intrinsic property to dilate in response to decreases in wall tension.

- Certain tissues have *other mechanisms* for blood flow control the kidneys have a feedback system between the tubules and arterioles and the brain blood flow is controlled by carbon dioxide and hydrogen ion conc.

Laplace's Law: Myogenic mechanism

TENSION = PRESSURE X RADIUS
(dynes/cm) (dynes/cm^2) (cm)



↑ PRESSURE ⟶ ↑ TENSION ⟶ ↓ RADIUS

(to maintain tension constant)

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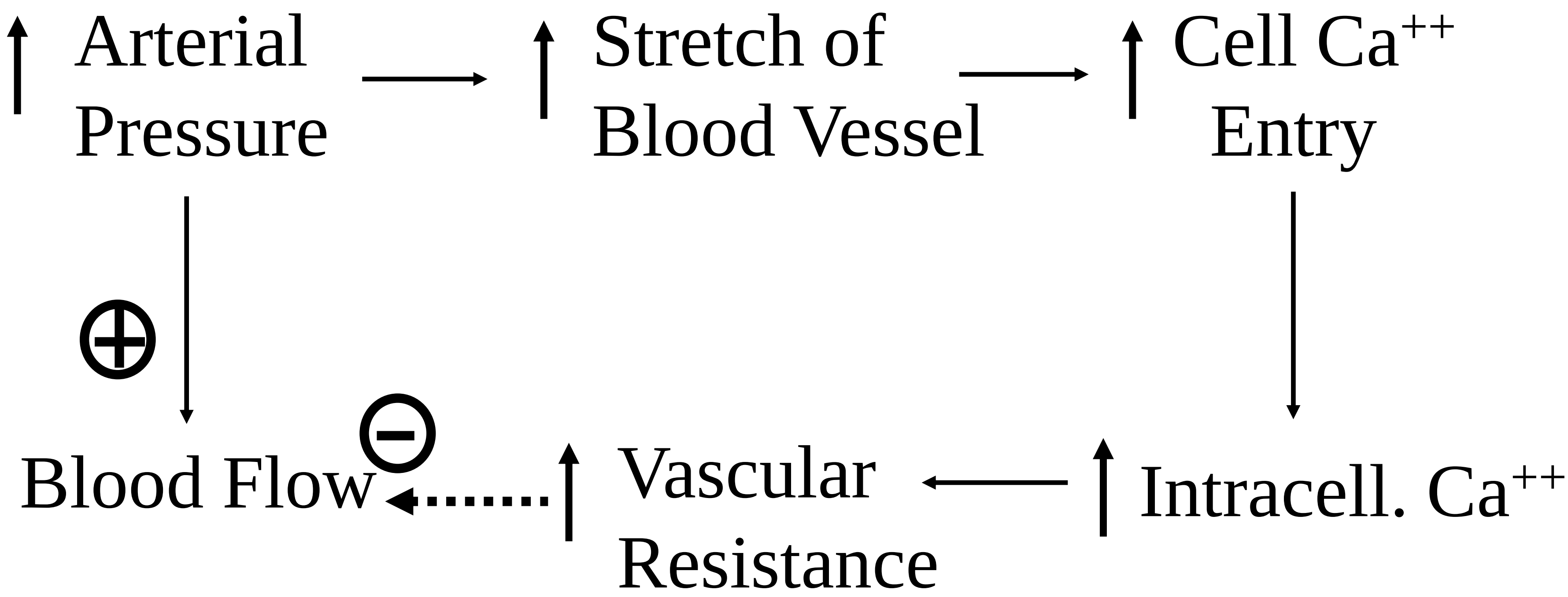
(to maintain tension constant)

Myogenic Mechanism



Myogenic Mechanism

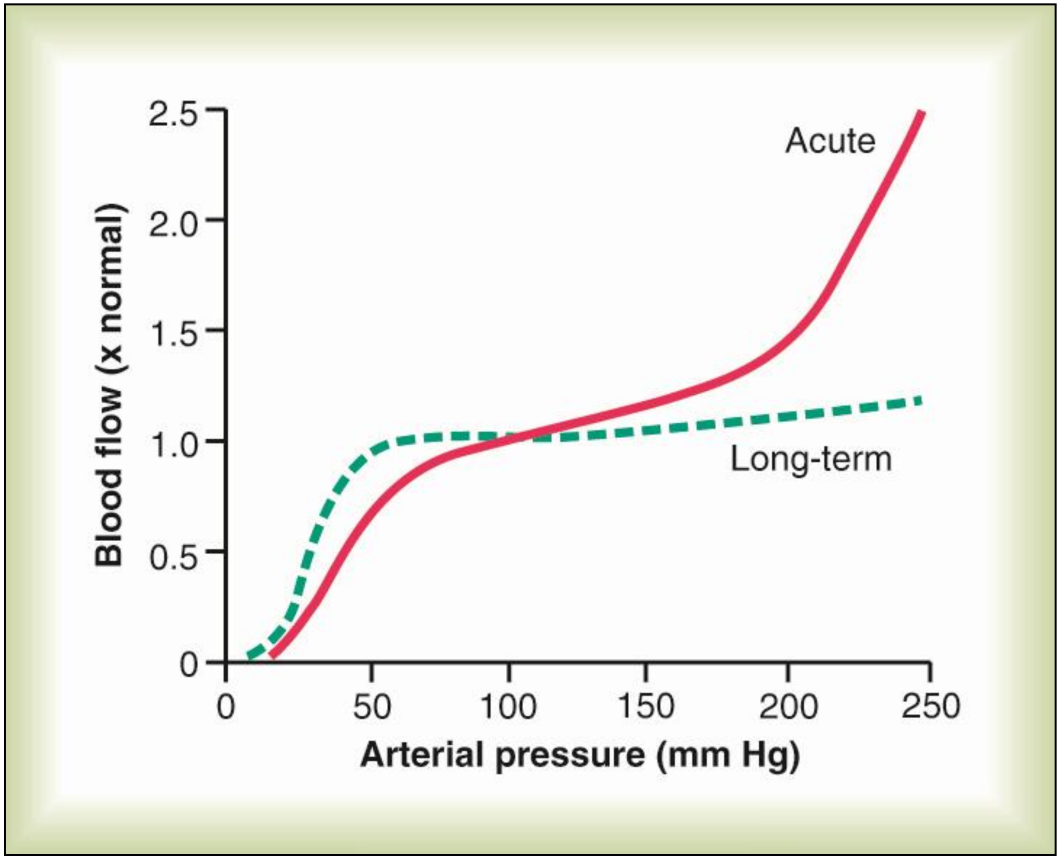
↓ Arterial Pressure → ↓ Stretch of Blood Vessel → ↓ Cell Ca^{++} Entry

Blood Flow ← ↓ Vascular Resistance ← ↓ Intracell. Ca^{++}

Long-term Regulation of Blood Flow

- Long-term regulatory mechanisms which control blood flow are more effective than acute mechanism.
- Long-term local blood flow regulation occurs by changing the degree of vascularity of tissues (***size and number of vessels***).
- *Oxygen* is an important stimulus for regulating tissue vascularity.

Long-term Regulation of Blood Flow



Angiogenesis

- *Angiogenesis* is the growth of new blood vessels.
- Angiogenesis occurs in response to angiogenic factors released from:
  1) ischemic tissue
  2) rapidly growing tissue
  3) tissue with high metabolic rates
- Most angiogenic factors are ***small peptides*** such as vascular endothelial cell growth factors (VEGF), fibroblast growth factor (FGF), and angiogen.
- Example of angiogenesis is ***Retrolental Hyperplasis***

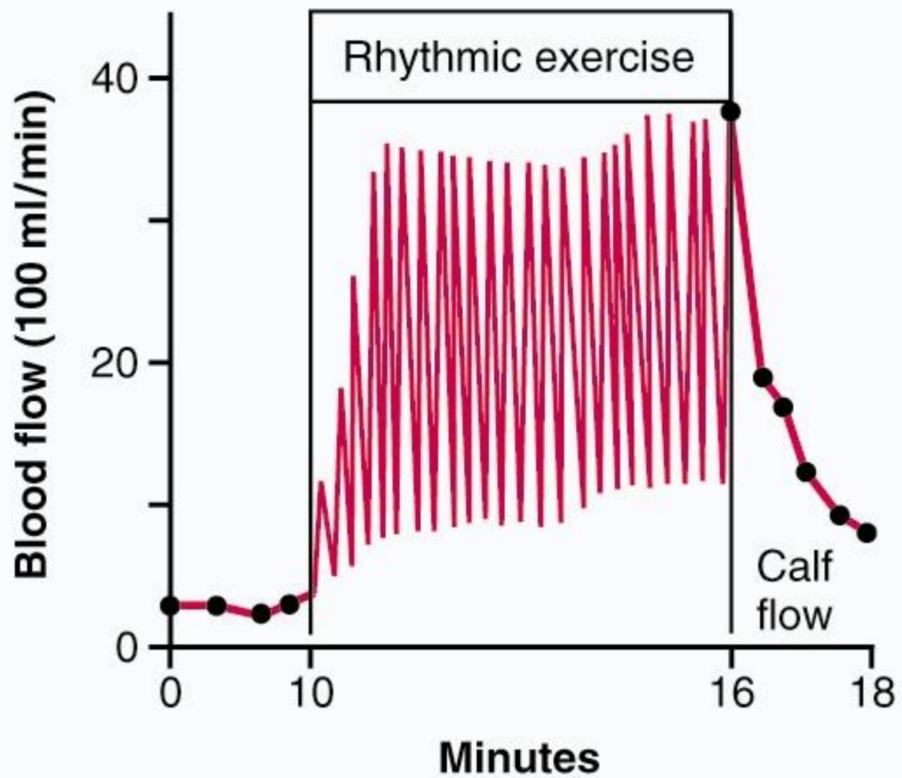
Humoral Regulation of Blood Flow

- Vasoconstrictors
  - Norepinephrine and epinephrine
  - Angiotensin
  - Vasopressin
  - Endothelin
- Vasodilator agents
  - Bradykinin
  - Serotonin
  - Histamine
  - Prostaglandins
  - Nitric oxide

Blood Flow: Skeletal Muscle Regulation

- Muscle blood flow can increase tenfold or more during physical activity as vasodilation occurs
  - Low levels of epinephrine bind to β receptors
  - Cholinergic receptors are occupied
- Intense exercise or sympathetic nervous system activation result in high levels of epinephrine
  - High levels of epinephrine bind to α receptors and cause vasoconstriction
    - This is a protective response to prevent muscle oxygen demands from exceeding cardiac pumping ability

Exercise and Muscle Blood Flow



Muscle Blood Flow During Exercise

- Can - 20 fold during exercise.
- Muscle makes up a large portion of body mass Þ great effect on Cardiac output.
- Resting blood flow = 3 to 4 ml/min/100 gm muscle.
- Oxygen delivery can be increased by increasing the extraction ratio from 25% up t0 75%
- Capillary density -’s markedly.
- Most blood flow occurs between contractions.

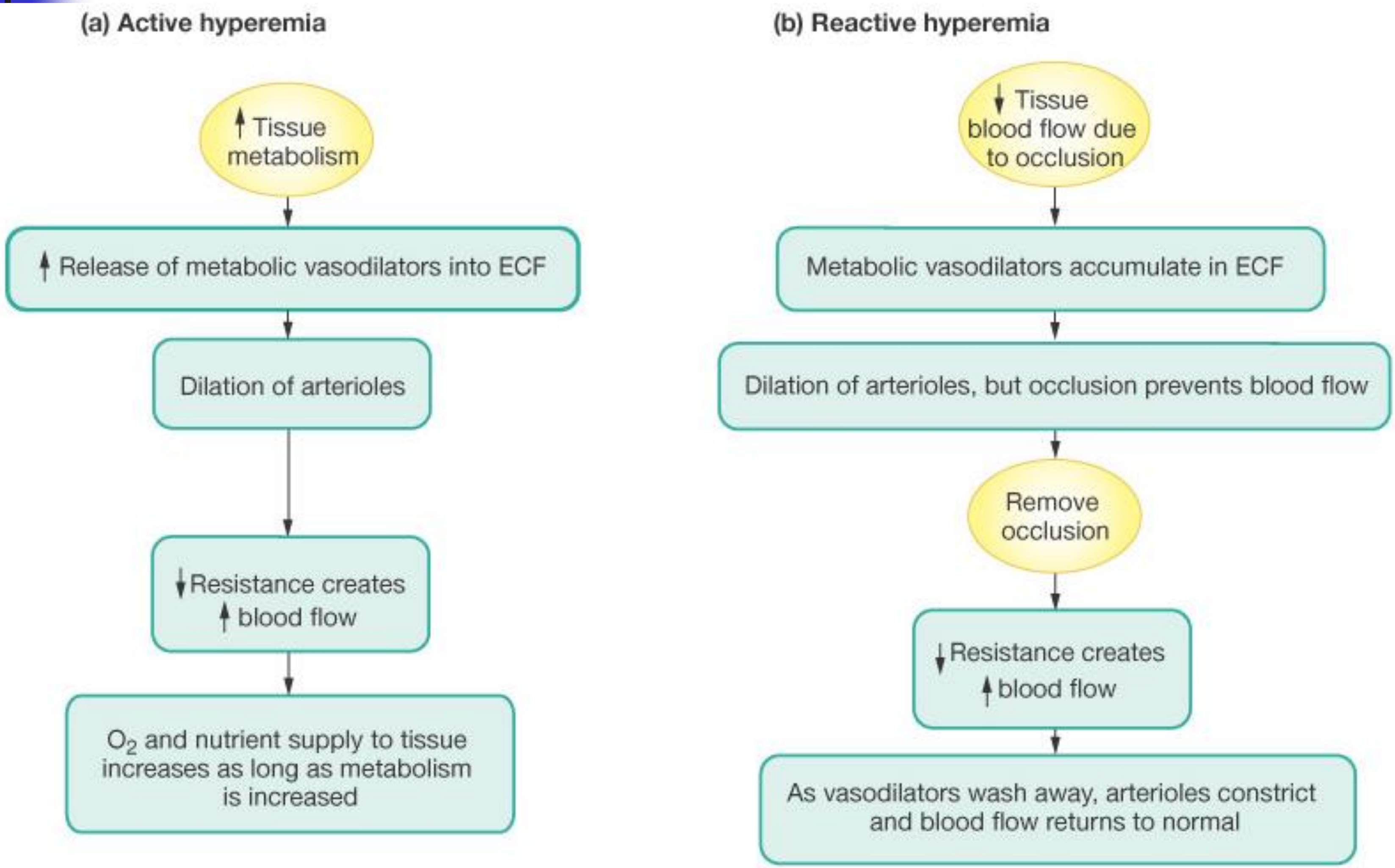
Local Regulation of Muscle Blood Flow during Exercise

- $\downarrow O_2$ during exercise affects vascular smooth muscle directly $\Rightarrow$ vasodilation.
- Vasodilators (which ones?)
  1. K^+
  2. Adenosine
  3. Osmolality
  4. EDRF (nitric oxide)

Nervous Regulation

- Sympathetic release of norepinephrine (mainly α).
- Adrenals release epinephrine (β and α) norepinephrine (α + a little β).
  - β receptors $\Rightarrow$ vasodilation mainly in muscle and the liver.
  - α receptors $\Rightarrow$ vasoconstriction in kidney and gut.

Arteriole Resistance: Control of Local Blood Flow



Thank You

Special circulations, Coronary, Pulmonary…

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Objectives

- Describe the control of blood flow to different circulations (Skeletal muscles, pulmonary and coronary)
- Point out special hemodynamic characteristic pertinent to each circulation discussed

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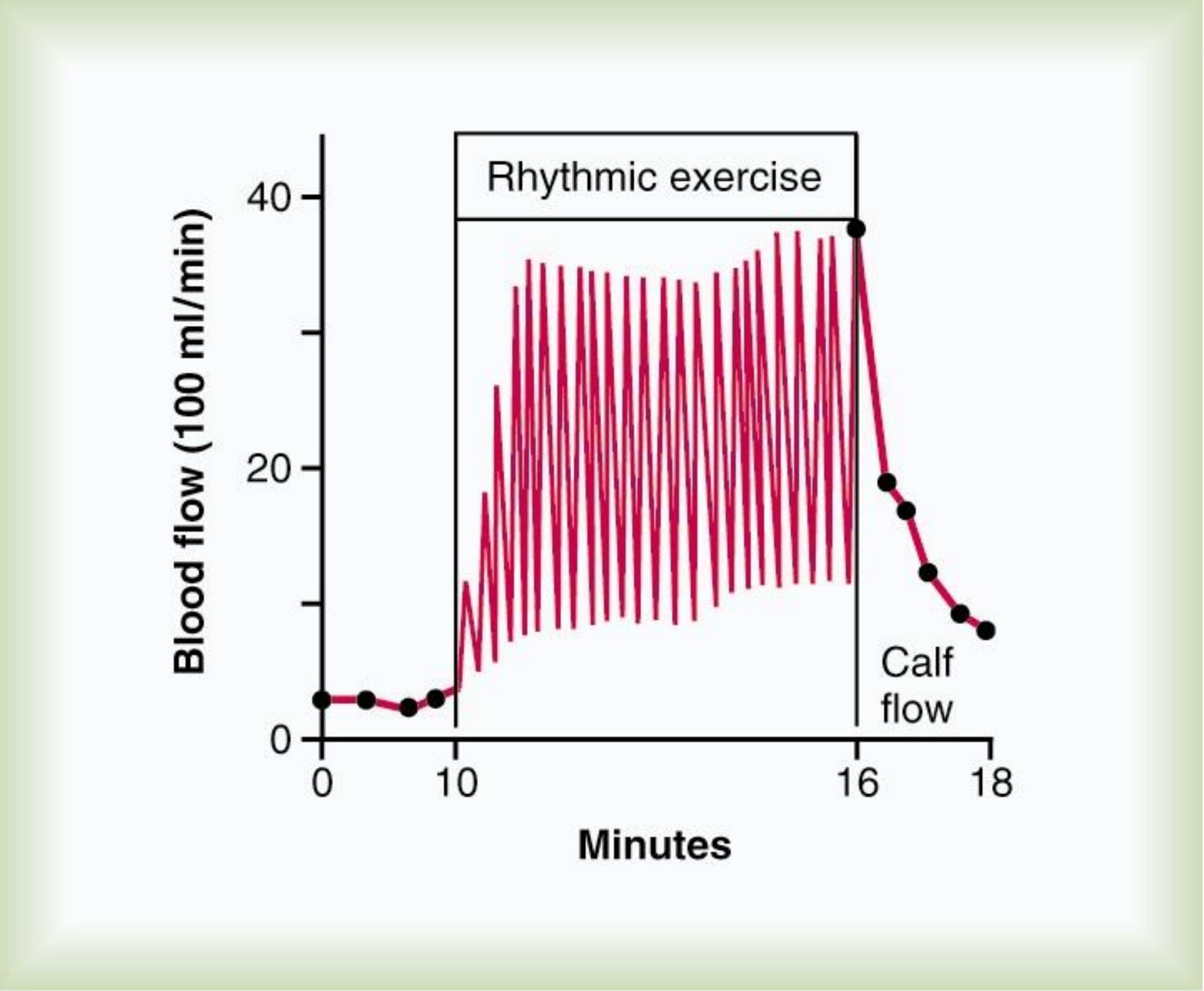

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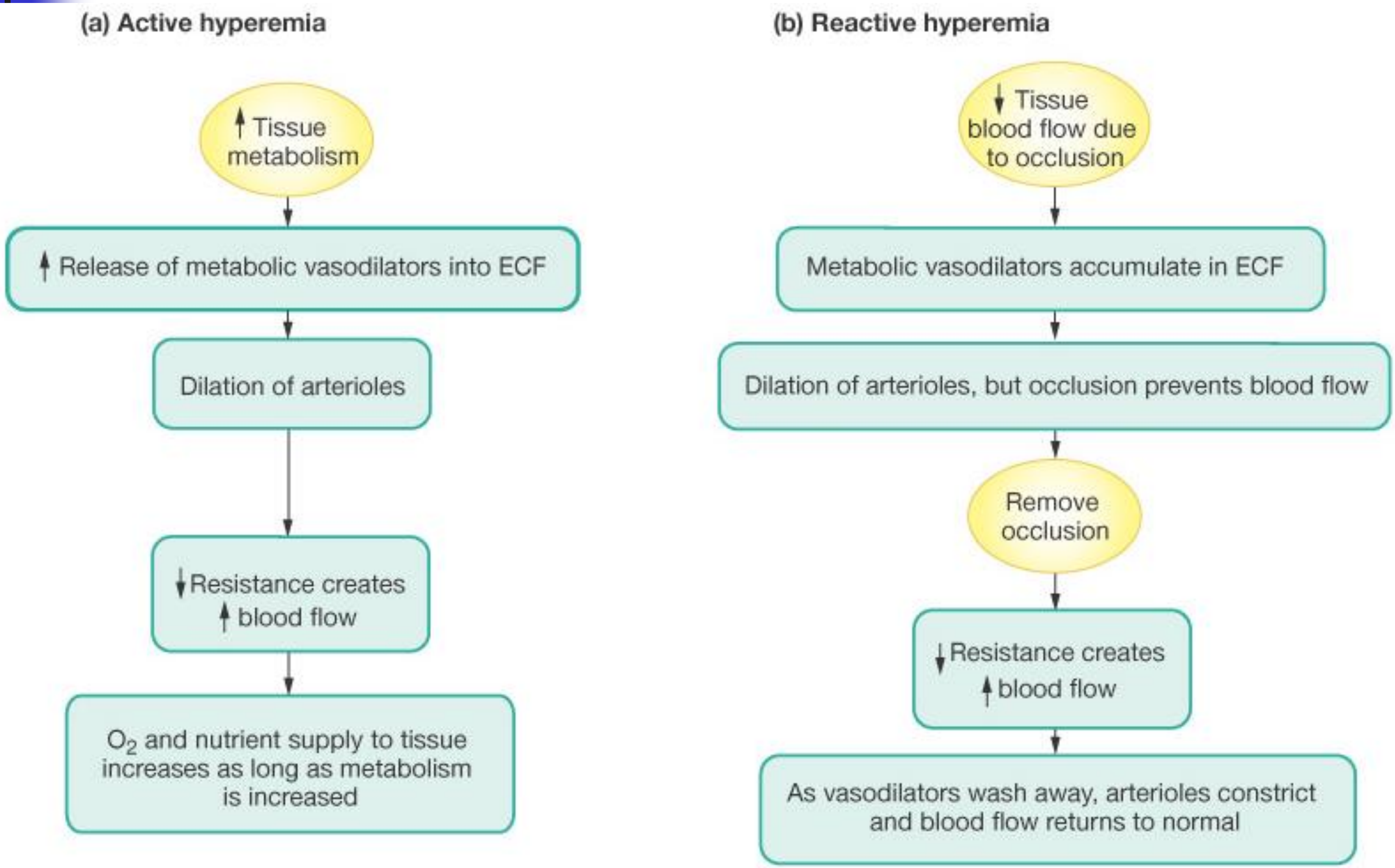
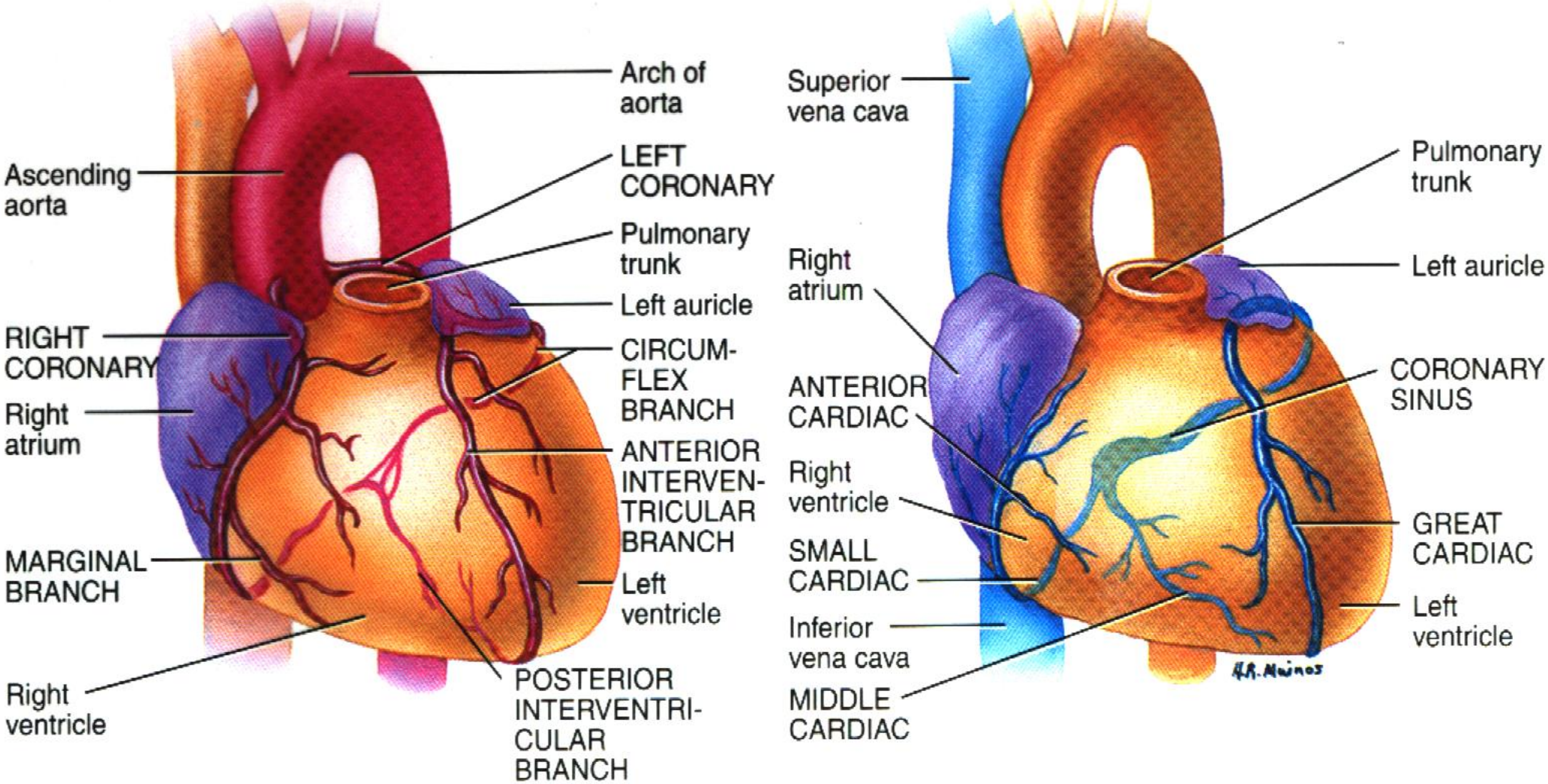


Blood Flow: Heart

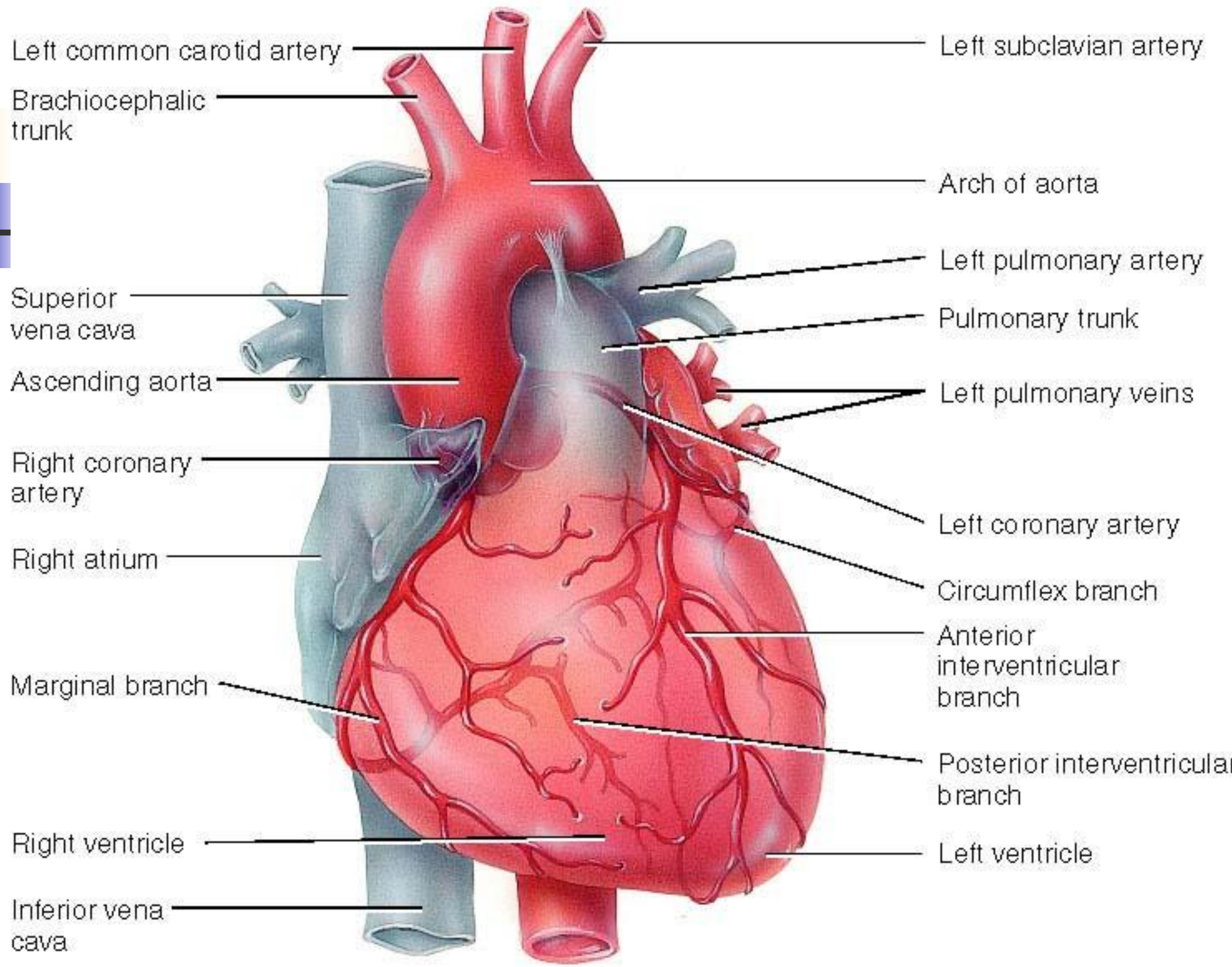
- Small vessel coronary circulation is influenced by:
  - Aortic pressure
  - The pumping activity of the ventricles
- During ventricular systole:
  - Coronary vessels compress
  - Myocardial blood flow ceases
  - Stored myoglobin supplies sufficient oxygen
- During ventricular diastole, oxygen and nutrients are carried to the heart
- Extraction ratio is maximum (75%) during rest so an increase demand for oxygen means an increase blood flow



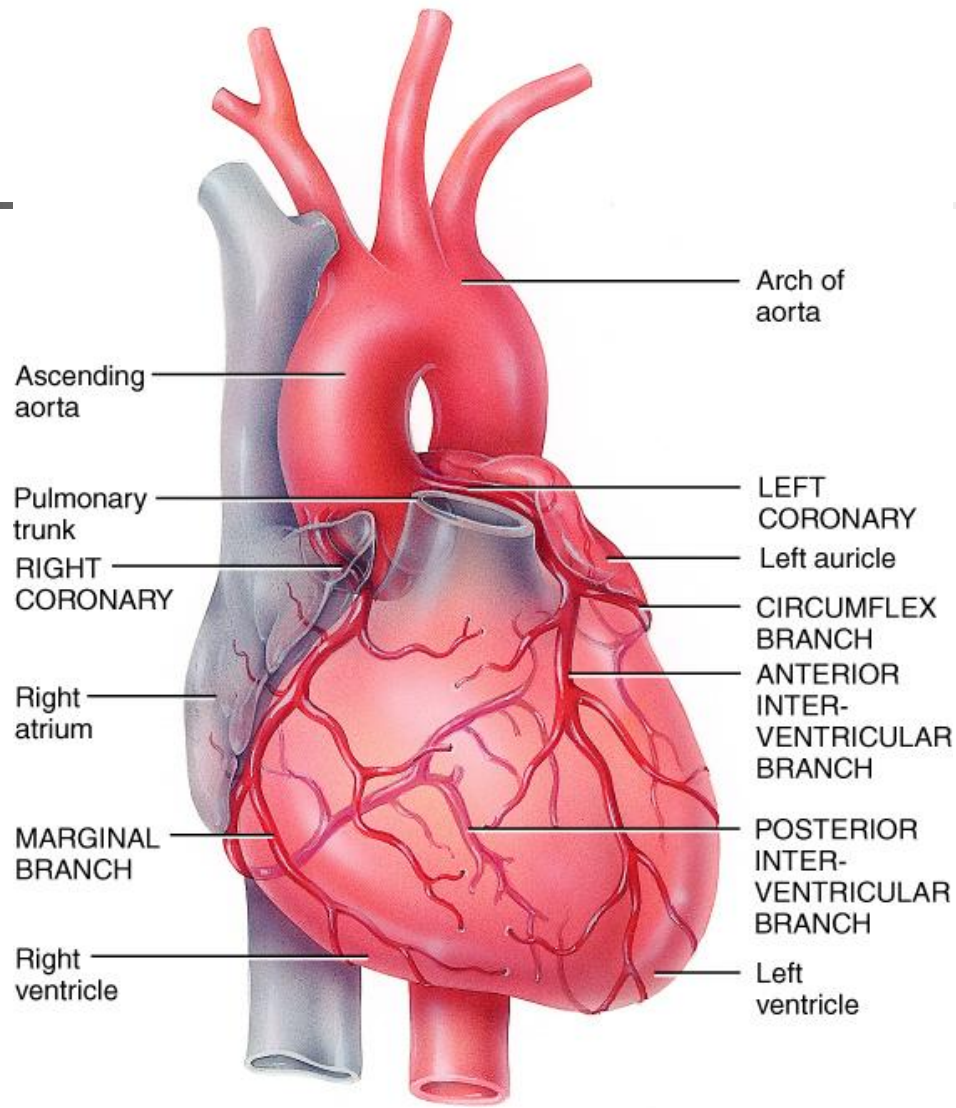
(a) Anterior view of coronary arteries

(b) Anterior view of coronary veins

CORONARY CIRCULATION

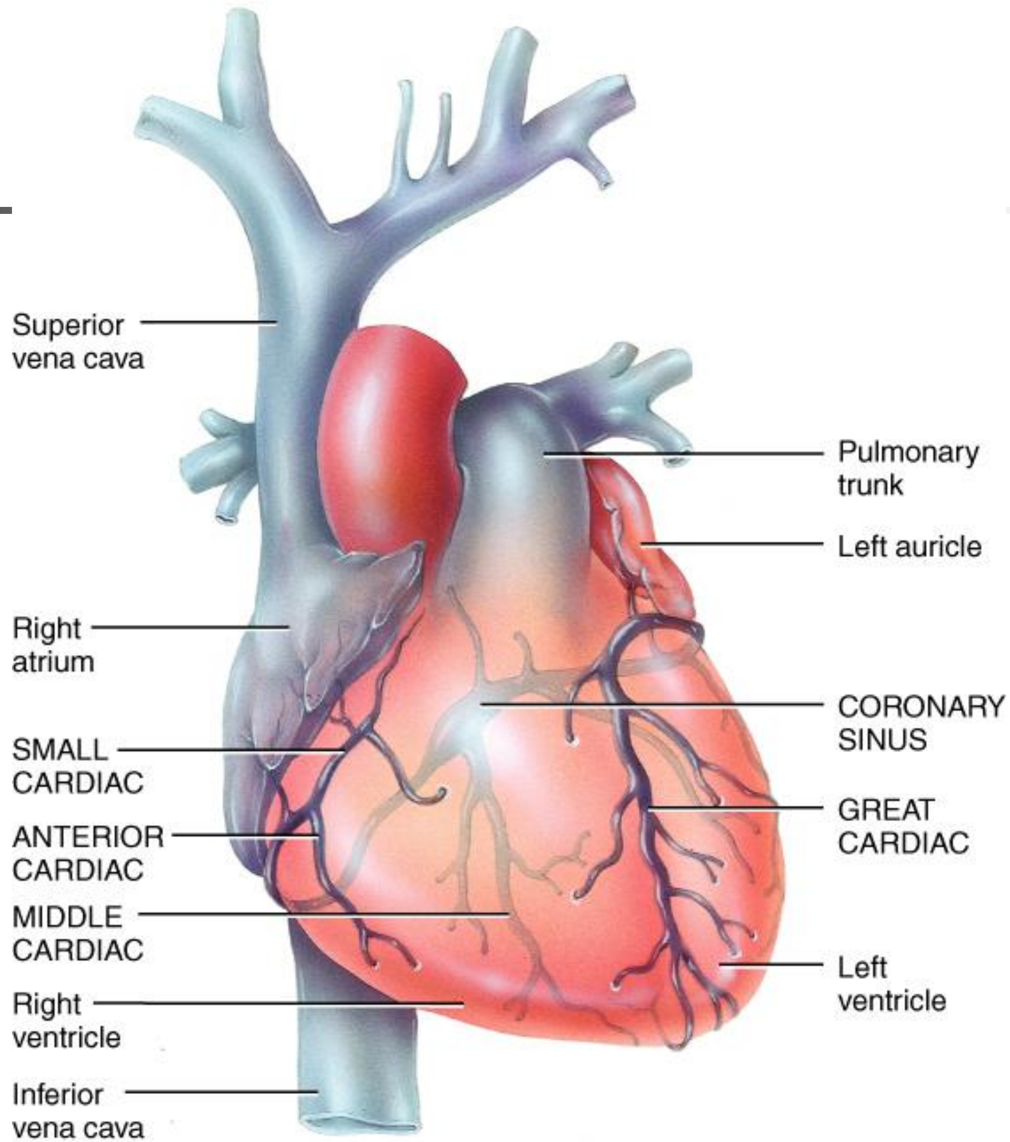

Left common carotid artery
Brachiocephalic trunk
Superior vena cava
Ascending aorta
Right coronary artery
Right atrium
Marginal branch
Right ventricle
Inferior vena cava
Left subclavian artery
Arch of aorta
Left pulmonary artery
Pulmonary trunk
Left pulmonary veins
Left coronary artery
Circumflex branch
Anterior interventricular branch
Posterior interventricular branch
Left ventricle

21.19



(a) Anterior view of coronary arteries

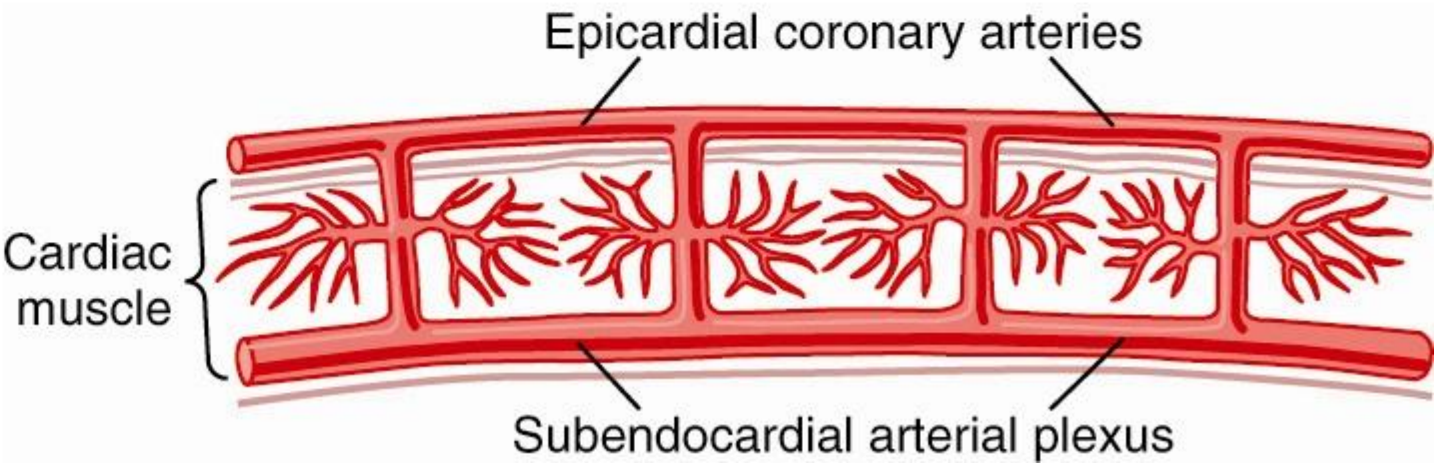
20.08a



(b) Anterior view of coronary veins

20.08b

Epicardial and Subendocardial Vasculature



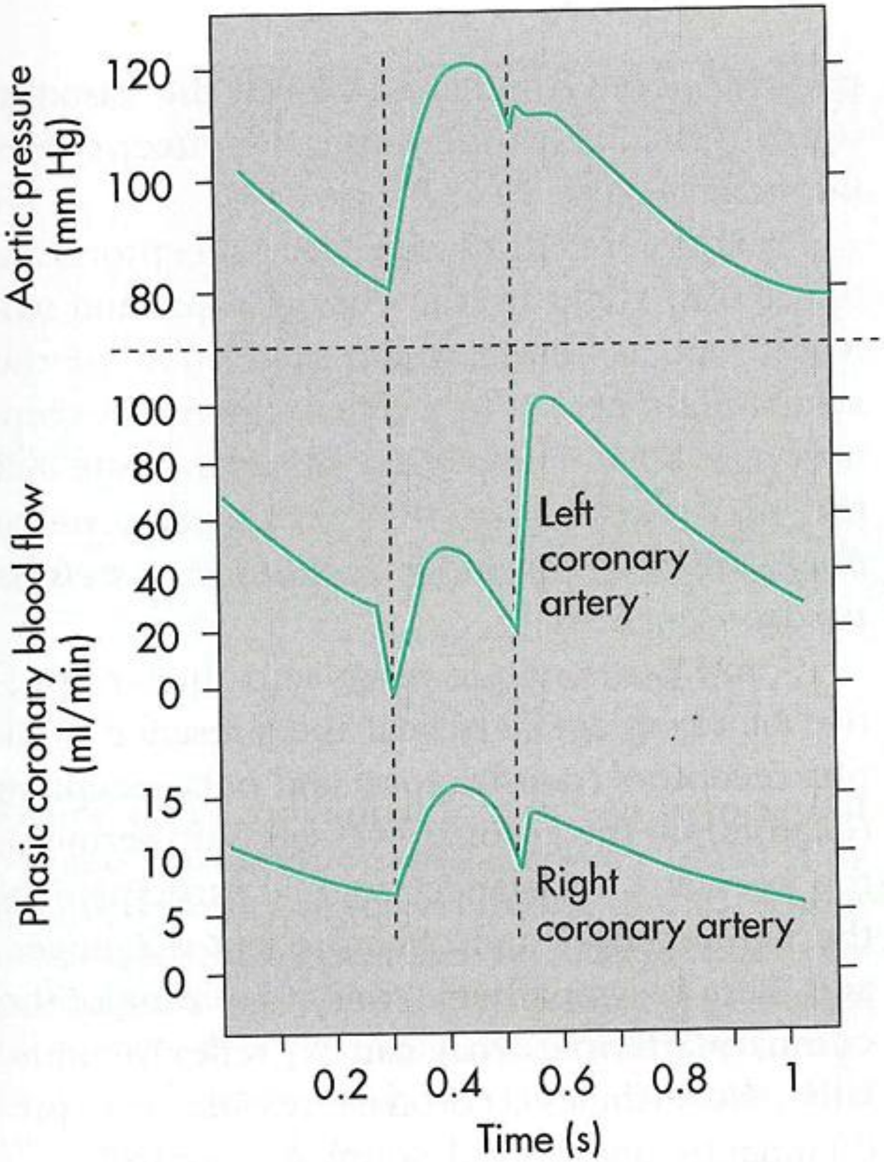
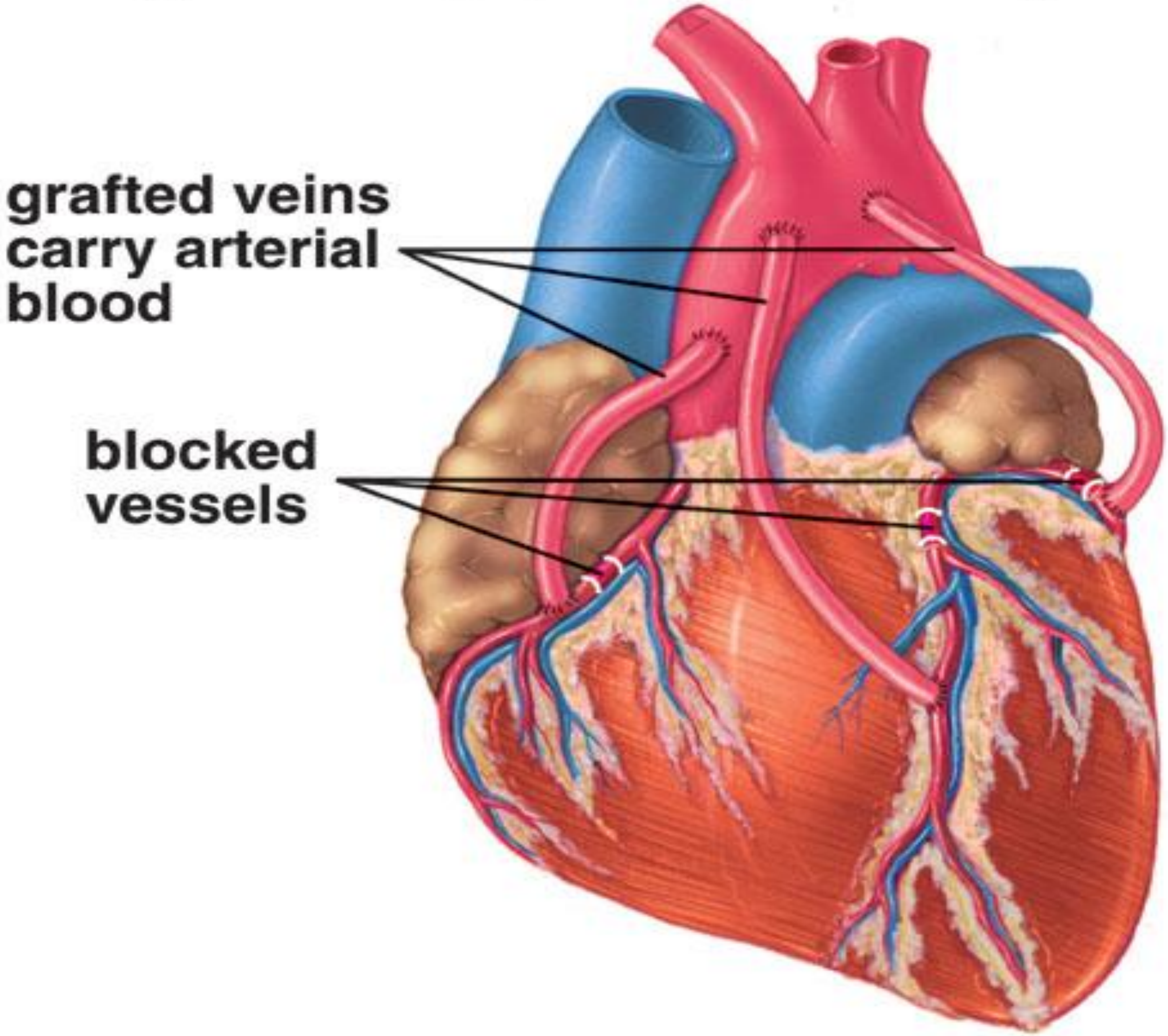
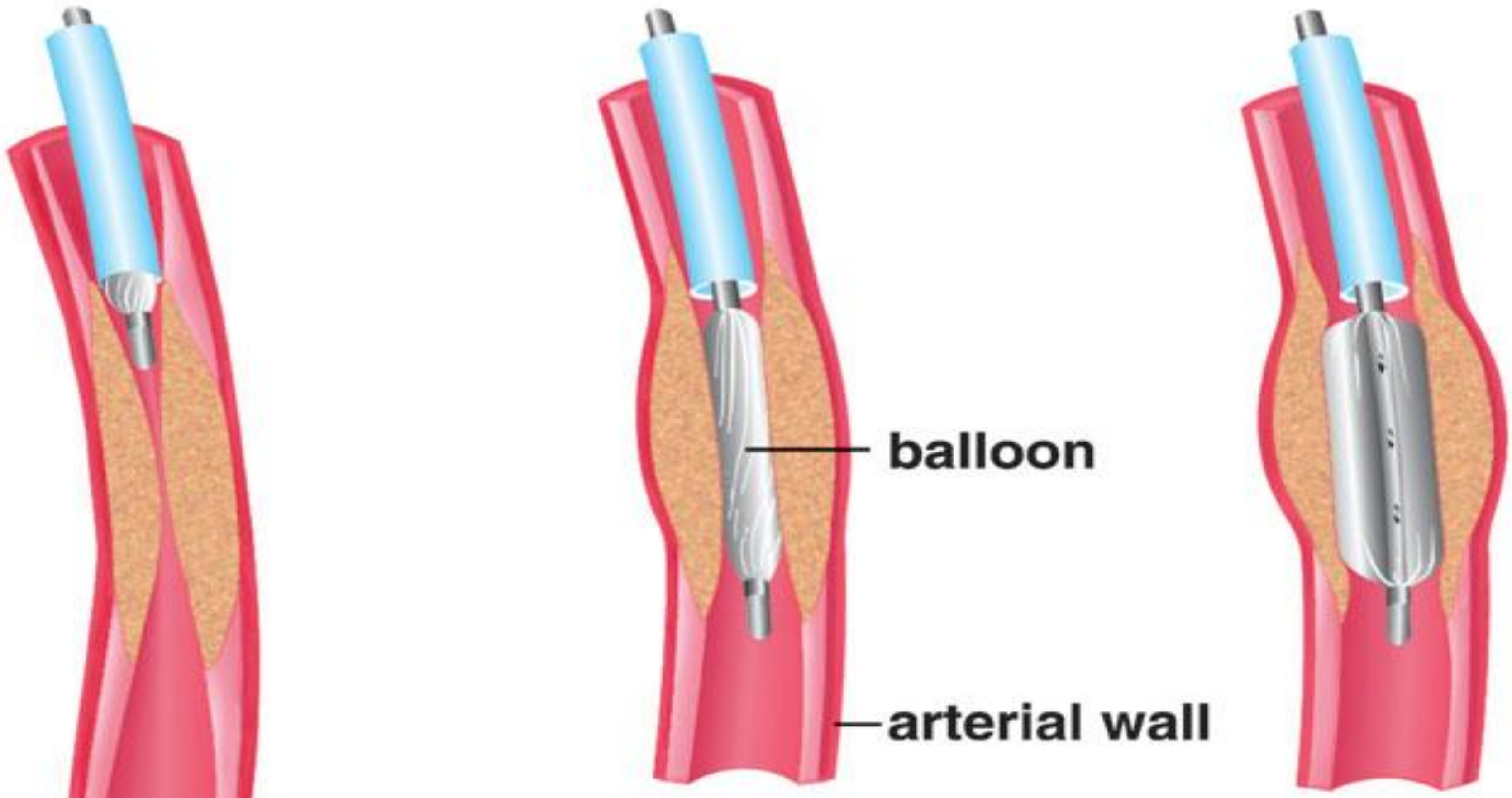


Figure 10-3 ■ **Comparison of phasic coronary blood flow in the left and right coronary arteries.**

Coronary bypass operation



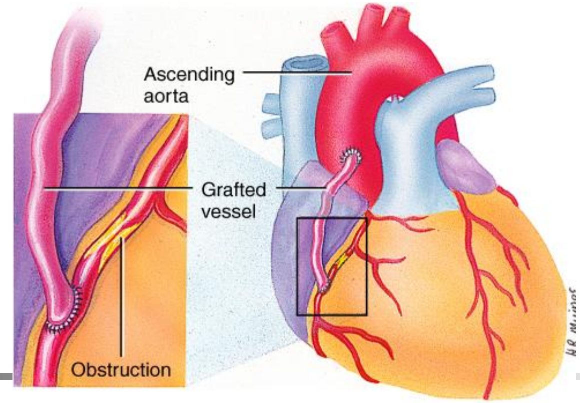
Angioplasty



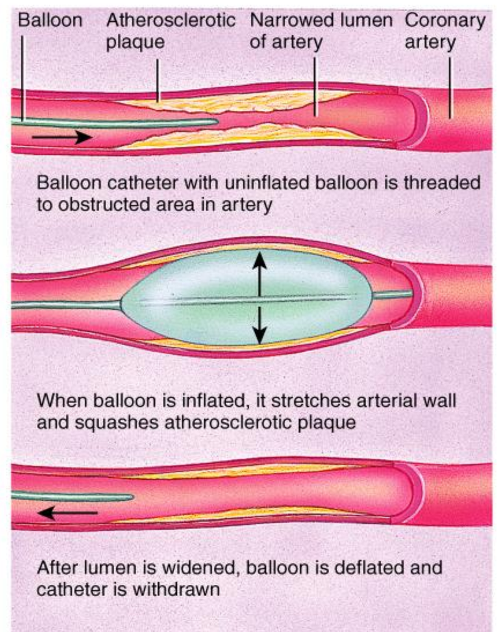
a. Artery is closed.

b. Balloon is released.

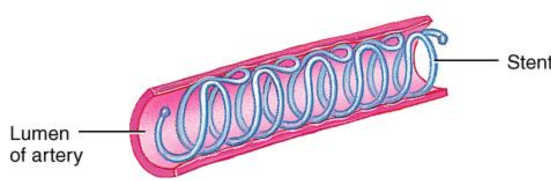
c. Balloon is inflated.



(a) Coronary artery bypass grafting (CABG)



(b) Percutaneous transluminal coronary angioplasty (PTCA)



(c) Stent in an artery

20.20

Blood Flow: Brain

- Blood flow to the brain is constant, as neurons are intolerant of ischemia
- Metabolic controls – brain tissue is extremely sensitive to declines in pH, and increased carbon dioxide causes marked vasodilation
- Myogenic controls protect the brain from damaging changes in blood pressure
  - Decreases in MAP cause cerebral vessels to dilate to insure adequate perfusion
  - Increases in MAP cause cerebral vessels to constrict

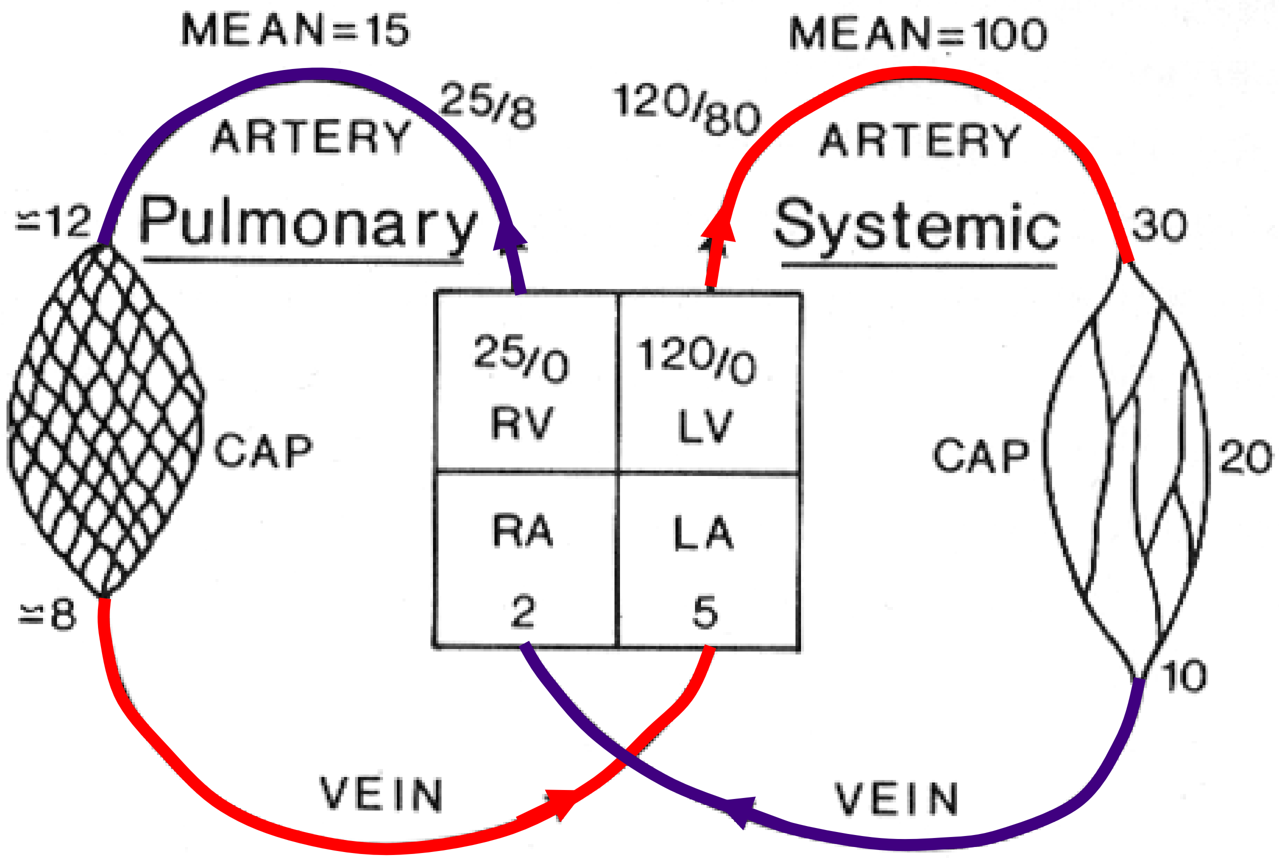
Blood Flow: Brain

- The brain can regulate is own blood flow in certain circumstances, such as ischemia caused by a tumor
- The brain is vulnerable under extreme systemic pressure changes
  - MAP below 60mm Hg can cause syncope (fainting)
  - MAP above 160 can result in cerebral edema

Blood Flow: Skin

- Blood flow through the skin:
  - Supplies nutrients to cells in response to oxygen need
  - Aids in body temperature regulation and provides a blood reservoir
- Blood flow to venous plexuses below the skin surface:
  - Varies from 50 ml/min to 2500 ml/min, depending upon body temperature
  - Is controlled by sympathetic nervous system reflexes initiated by temperature receptors and the central nervous system

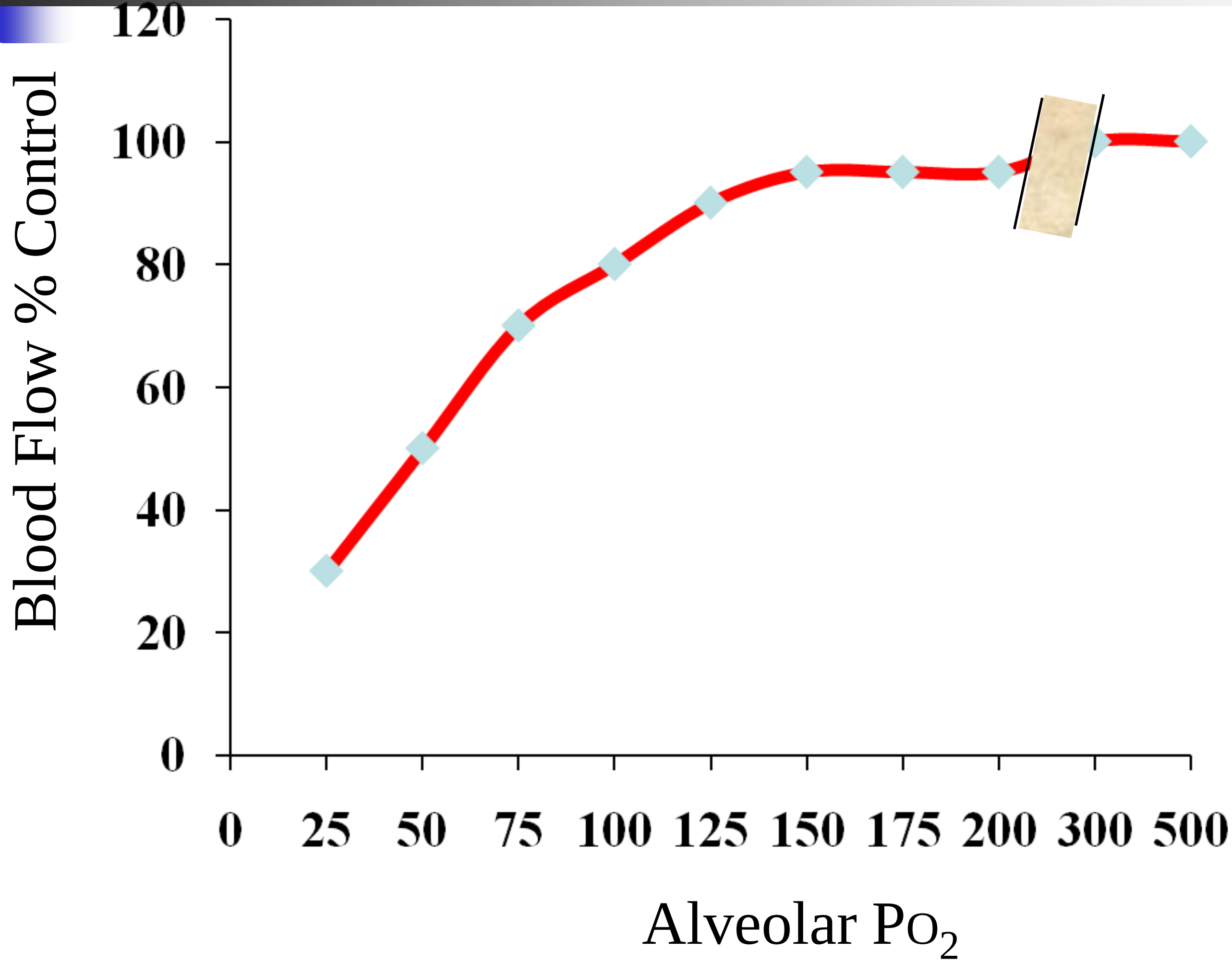
Characteristics of the Pulmonary Circulation



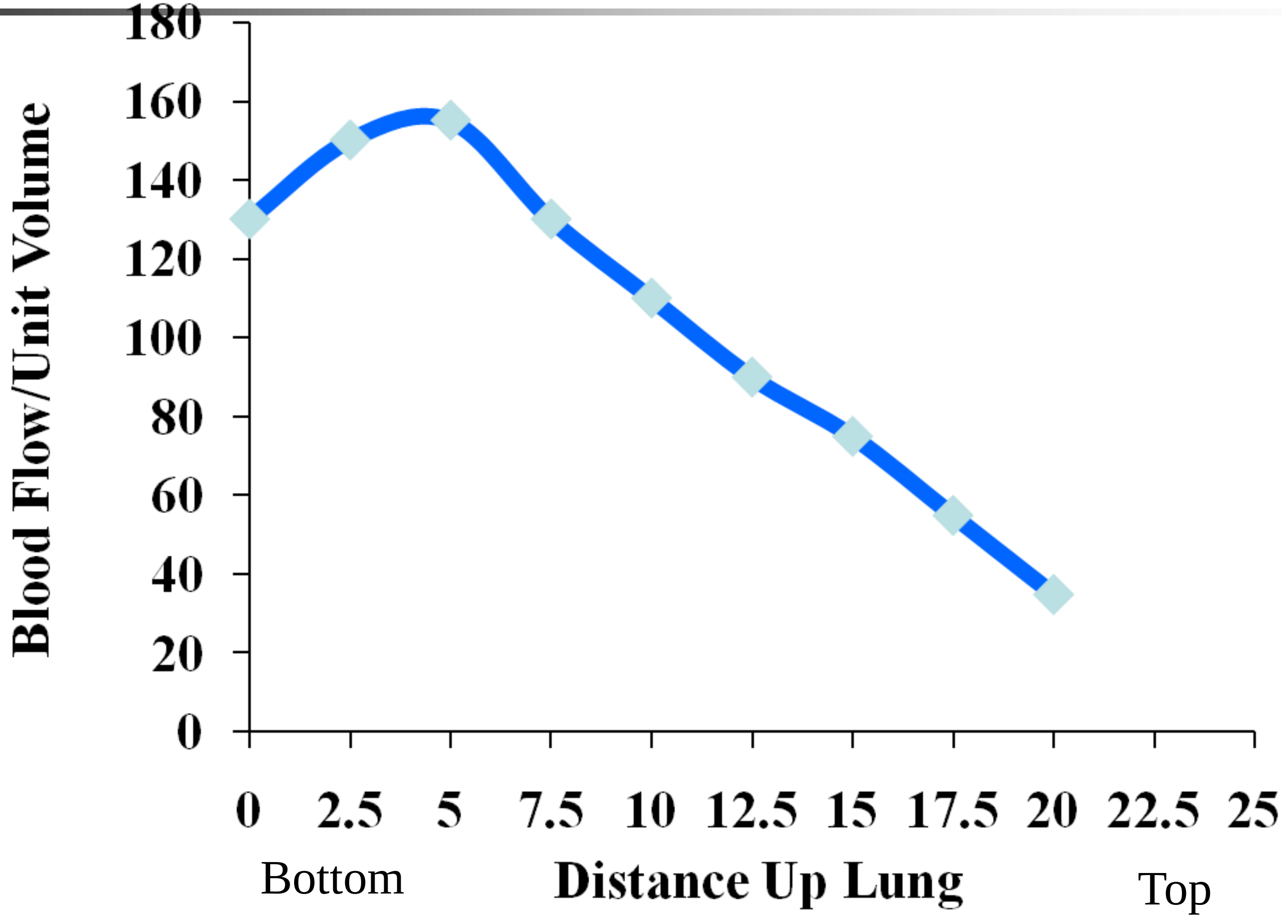
Blood Flow: Lungs

- Blood flow in the pulmonary circulation is unusual in that:
  - The pathway is short
  - Arteries/arterioles are more like veins/venules (thin-walled, with large lumens)
    - They have a much lower arterial pressure (24/8 mm Hg versus 120/80 mm Hg)
  - The autoregulatory mechanism is exactly opposite of that in most tissues
    - Low oxygen levels cause vasoconstriction; high levels promote vasodilation
    - This allows for proper oxygen loading in the lungs

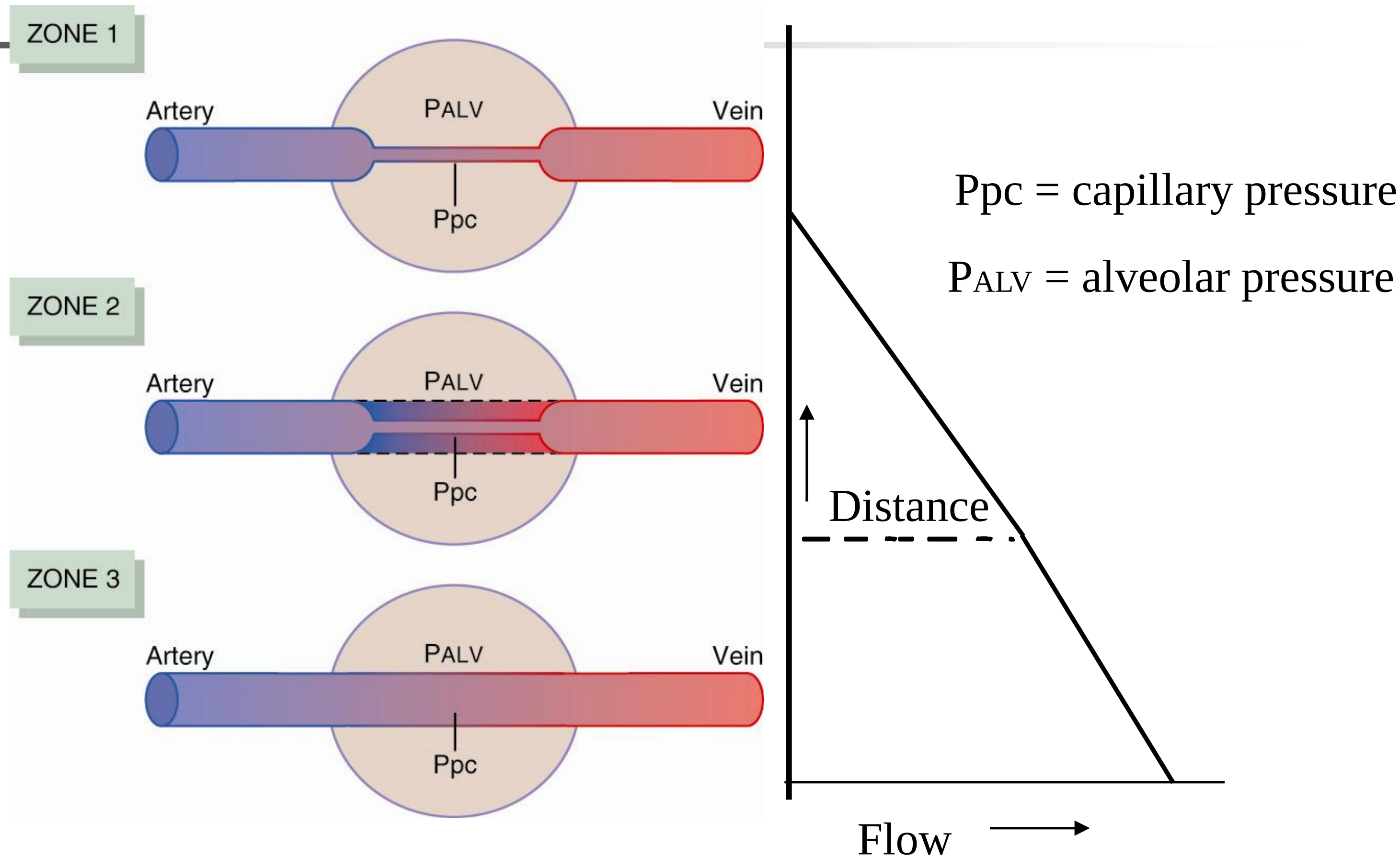
Effect of Po_2 on Blood Flow



Distribution of Blood Flow



Hydrostatic Effects on Blood Flow



Thank You