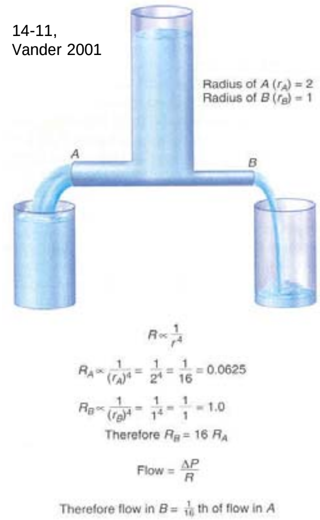
Lecture 26
24 March 2008

Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2008

Kevin Bonine & Kevin Oh

1. Circulation (Ch 23)

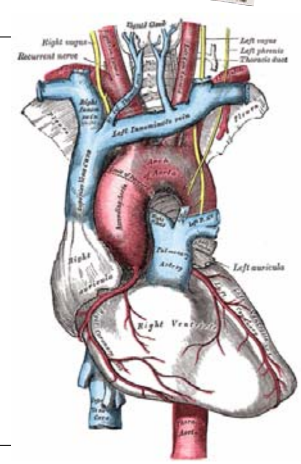
14-11,
Vander 2001



http://eebweb.arizona.edu/eeb_course_websites.htm

Housekeeping, 24 March 2008

<u>Upcoming Readings</u>
Mon 24 Mar: Ch 23
Wed 26 Mar: Ch 23
LAB Wed 26 Mar: no reading
Fri 28 Mar: Ch 23
Mon 31 Mar: Ch 24



Lab discussion leaders: 09 April
1pm – none
3pm – Nina

Lab discussion leaders: 02 April
1pm – Vangie & Christina
3pm – Prasun & Ajay

Vertebrate
Circulation

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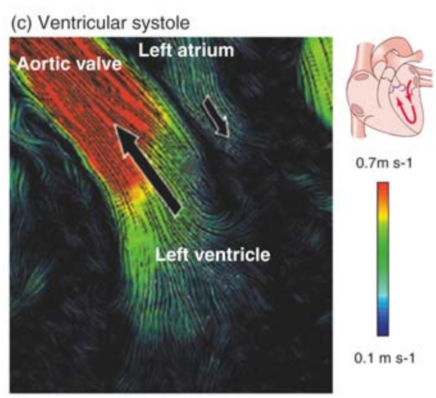
1. Circulation
2. Heart Muscle
3. Heart Function
4. Diving Response



12-10 Randall et al.

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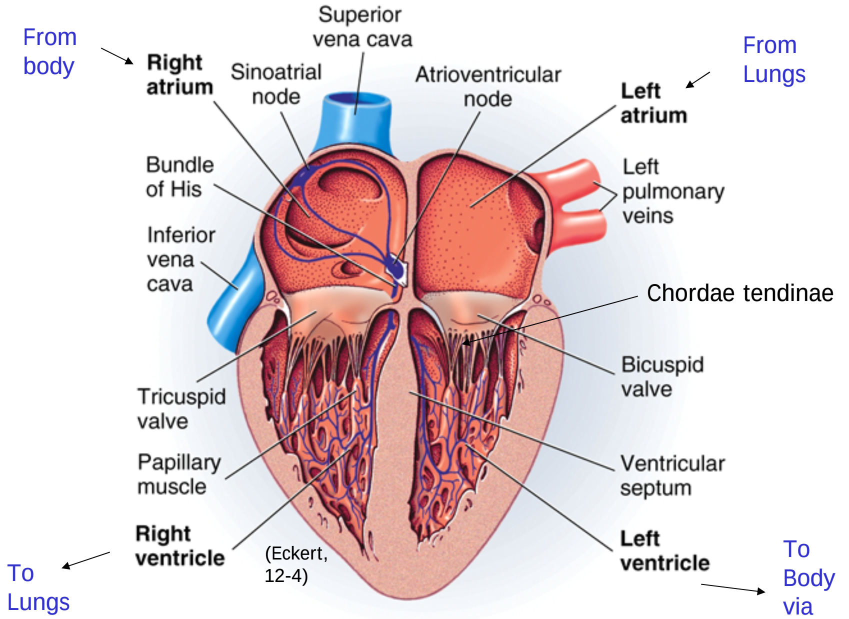

Mammalian Heart

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Vertebrate Circulation (too big for diffusion!)

Heart is main propulsive organ

Arterial system
- -distributes blood
- -regulates pressure

Capillaries
- -transfer between blood and tissues

Venous system
- -return blood to heart
- -storage reservoir

Divided into Central and Peripheral

Focus on Mammalian Circulation with some exceptions

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Gravity and BP

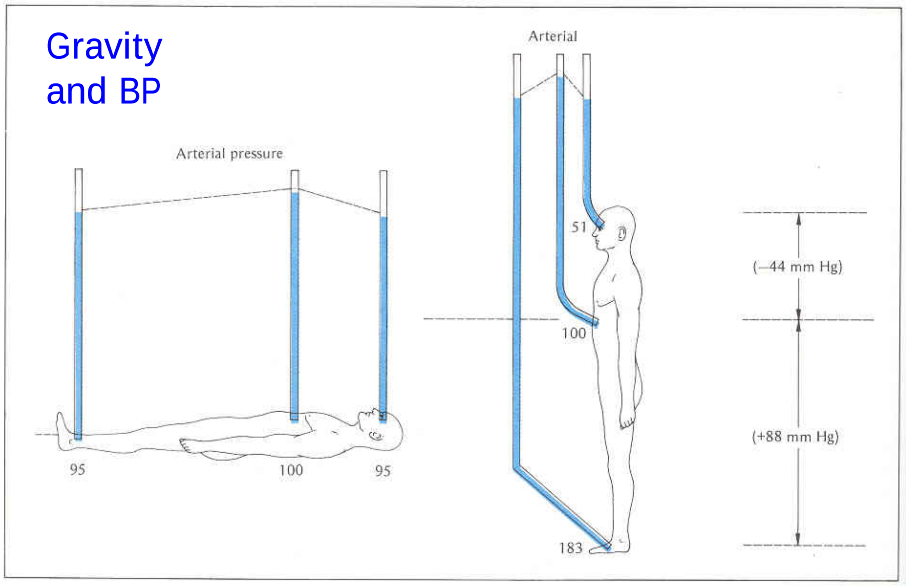
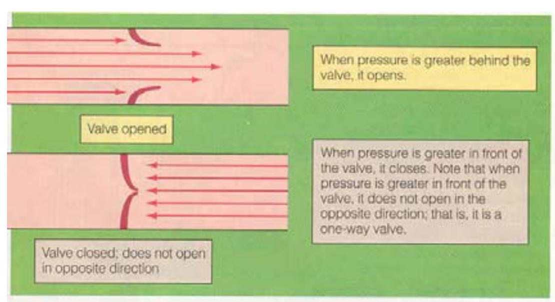


FIGURE 3.15 Arterial and venous pressures in a man as he assumes different postures. The figures indicate the pressures at various points in relation to the pressure in the right atrium of the heart. (1 mm Hg = 0.13 kPa). [Modified from Burton 1972]

Knut Schmidt_Nielsen 1997

Circulatory Roles and Components

Valves control direction of blood flow



Sherwood 1997

Figure 9-4 Mechanism of Valve Action

Smooth muscle controls diameter of peripheral vessels, thereby altering resistance and flow to different tissues

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Circulatory Roles and Components

-Gases (CO_2, O_2)
-Nutrients
-Waste
-Hormones
-Antibodies
-Salts
-etc.

-Temperature
Regulation

-Blood volume 5-10%
of body volume

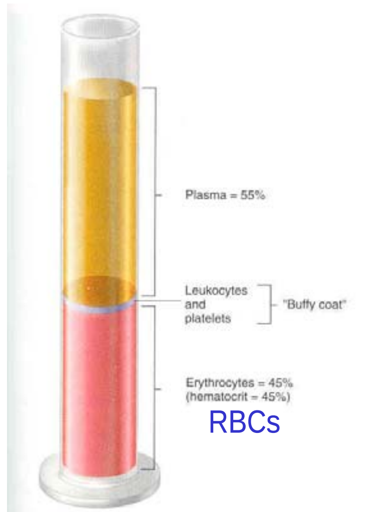


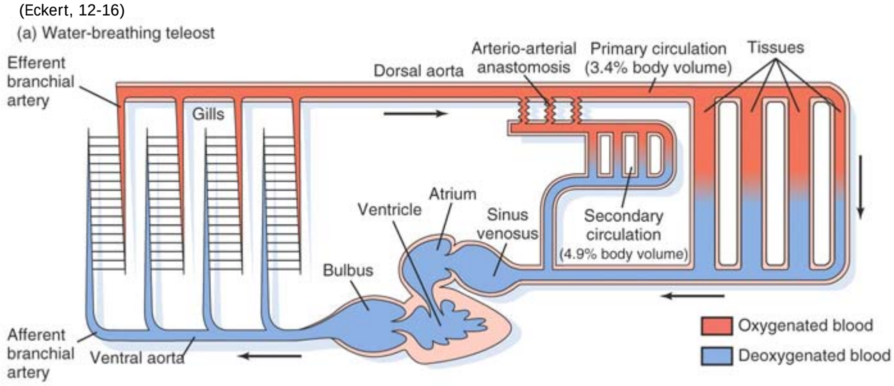
FIGURE 14–1 Vander 2001
Measurement of the hematocrit—the percentage of blood volume that is erythrocytes—by centrifugation. The presence of a thin layer of leukocytes and platelets between the plasma and red cells explains why, in this example, the value for plasma determined by centrifugation should actually be slightly less than 55 percent.

Development of Terrestrial Circulatory System:

gills simple (and linear):
1. Blood goes to gills
2. O2-rich blood goes to tissues
3. O2-poor blood goes to heart
4. Blood gets pumped back to gills

lungs more complex because get 2 circuits in parallel:
1. Pulmonary circuit (lower pressure)
2. Systemic circuit (higher pressure)

(Eckert, 12-16)



Fish Circulation through gills

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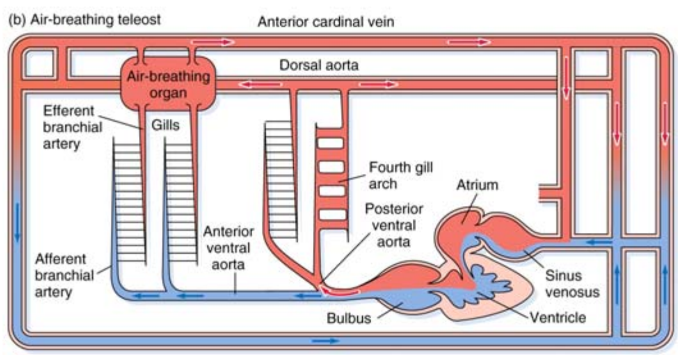
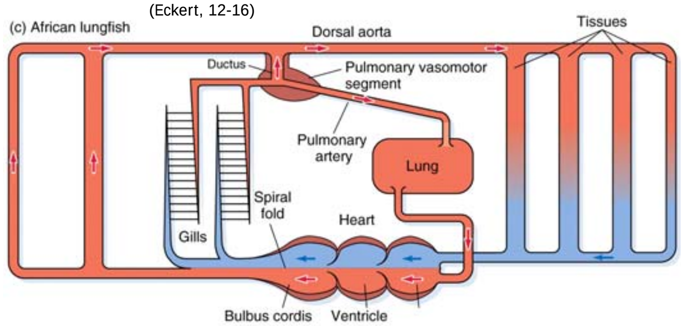
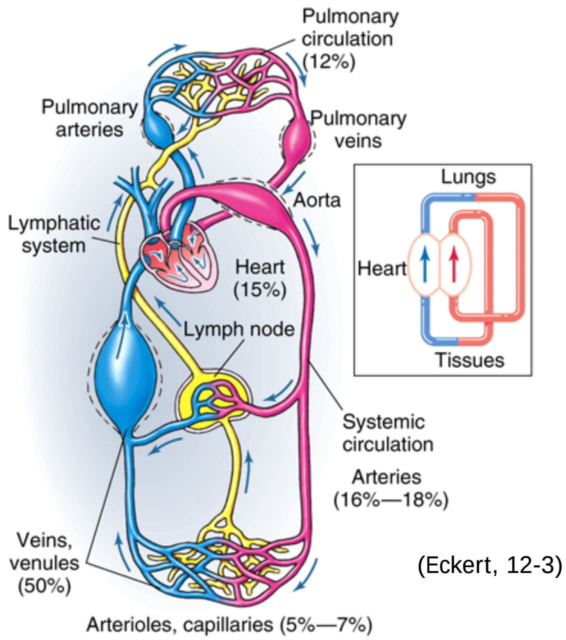
Addition of lungs more complicated

Water vs. air



(Eckert, 12-16)





(Eckert, 12-3)

Mammalian Circulation

Two parallel closed circuits:

1. Pulmonary (lower press.)
2. Systemic

Note venous reservoir

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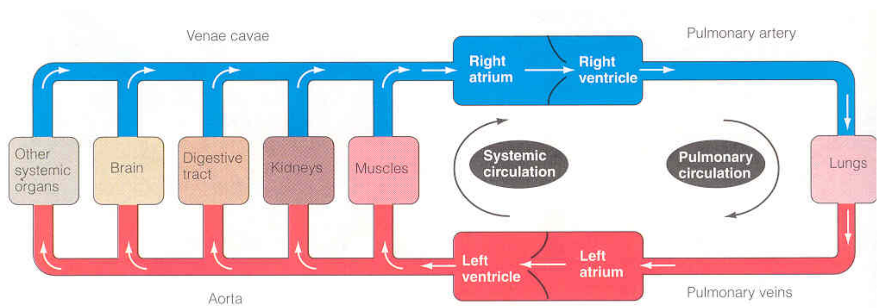
Tissue Beds in Parallel, not Series



9-3, Sherwood 1997

All cells within 2-3 cells of a capillary

Can control amount of flow to each tissue independently

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In addition to Heart,

Blood also moved via

1. Elastic recoil of arteries
2. Squeezing of vessels during body movement
3. Peristaltic contractions of smooth muscle in vessels

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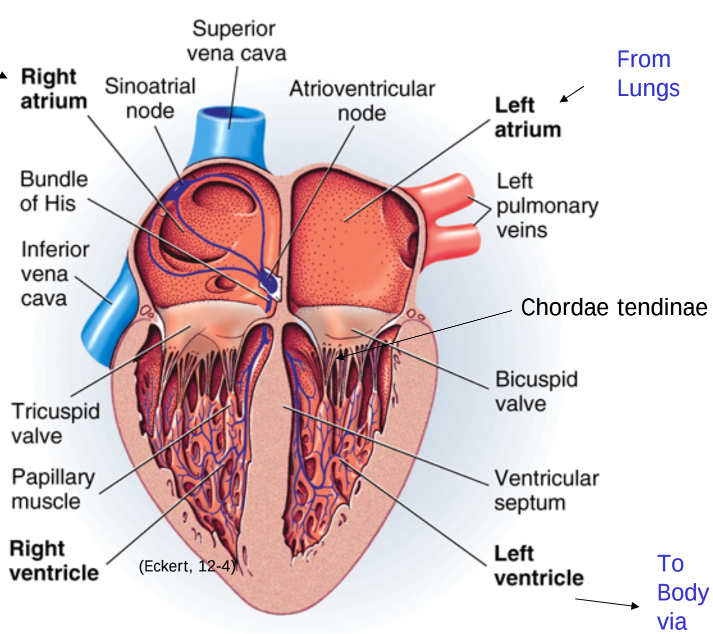
From body

From Lungs



To Lungs

To Body via AORTA

Mammalian Heart

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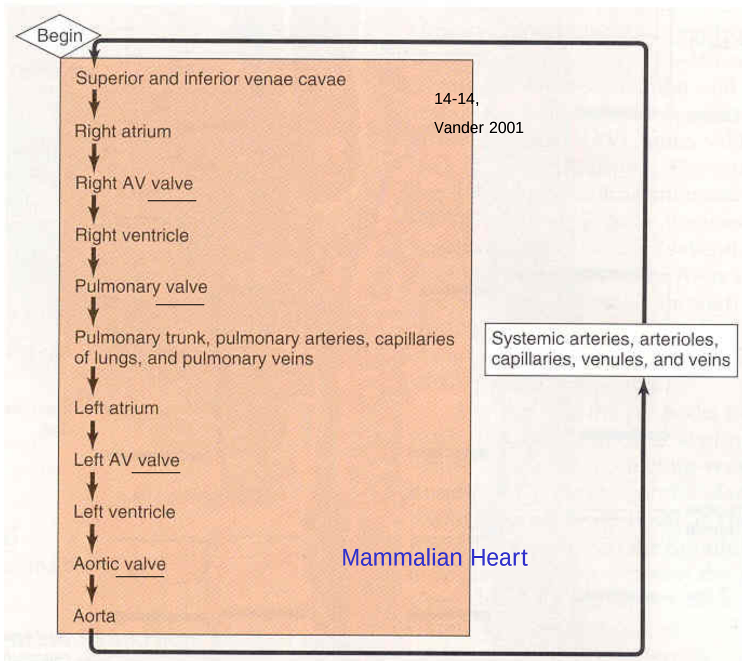
No valves
as Enter
Atria



Non-Mammalian Heart Examples:

Amphibians and Reptiles (except crocodilians) with
3 chambers (= one ventricle, two atria)

- incomplete ventricular septum
- BUT separate rich and poor blood
- AND alter pressure in systemic and pulmonary
- able to alter flow to systemic or pulmonary circuit

Cardiovascular System

Amphibians:

only vertebrates where O_2 poor blood to skin
(as well as to lungs)

adults with paired pulmocutaneous arteries
divide into two branches
1. Pulmonary
2. Cutaneous (to flanks and dorsum)

skin provides 20-90% O_2 uptake
30-100% CO_2 release

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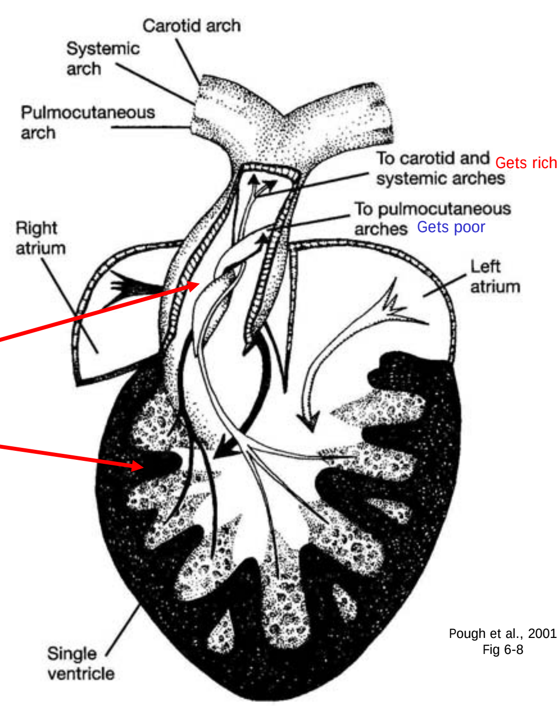
Cardiovascular System

FROG Heart

conus arteriosus
w/ spiral valve

trabeculae
(create channels)

role of Tb and HR



Pough et al., 2001
Fig 6-8

Cardiovascular System

Reptilian Heart (not crocs)

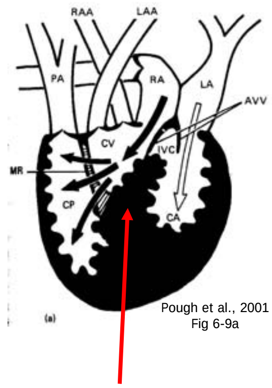
(no conus arteriosus, no spiral valve)

2 systemic arches and
one pulmonary artery
from single ventricle

BUT, single ventricle functions as THREE

3-chambered heart anatomically
5-chambered heart functionally

RAA = right aortic arch
LAA = left aortic arch
PA = pulmonary artery



Pough et al., 2001
Fig 6-9a

Muscular Ridge

RA = right atrium
LA = left atrium

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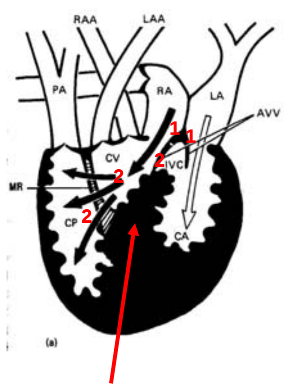
Reptilian Heart (not crocs)
not "primitive"

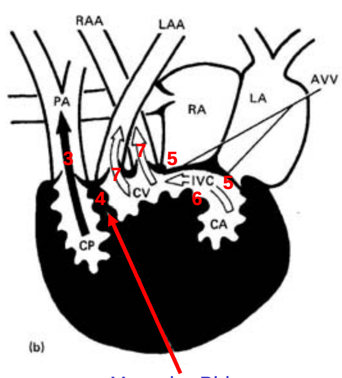
3-chambered heart anatomically
5-chambered heart functionally

RAA = right aortic arch
LAA = left aortic arch
PA = pulmonary artery



Muscular Ridge

IVC = intraventricular canal
AVV = atrioventricular valve



Muscular Ridge

Pough et al., 2001
Fig 6-9

CP = cavum pulmonale
CV = cavum venosum
CA = cavum arteriosum

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Reptilian and Amphibian Circulation

Cardiac Shunts (in 3-chambered heart)

1. temperature regulation
2. breath holding (diving, turtle in shell, inflated lizards)
3. stabilize O_2 content of blood when breathe intermittently

R to L

O_2 poor to systemic via aortic arches
(short delay between valves opening)

L to R

O_2 rich to pulmonary artery
(longer delay between valves opening)

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Mammalian fetus:

Ductus arteriosus (R -> L shunt, lung bypass)
- -pulmonary artery to systemic arch
- -when lung inflate resistance down (pulm)
- -when lose placental circ. resistance up (syst)
- -closes at birth

Foramen ovale (interatrial shunt R -> L)
- -hole in wall between atria
- -closes at birth

Bird chick:

Chorioallantois
= network of vessels under shell surface

Interatrial septum
-R -> L shunt, lung bypass
-closes after hatching

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Electrical Activity in the Mammalian Heart

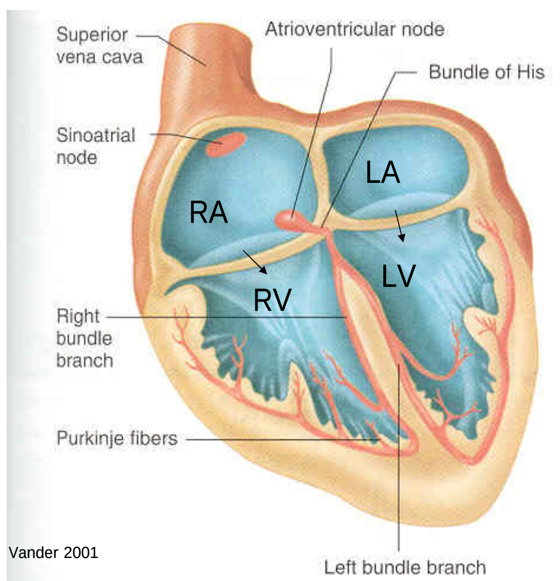
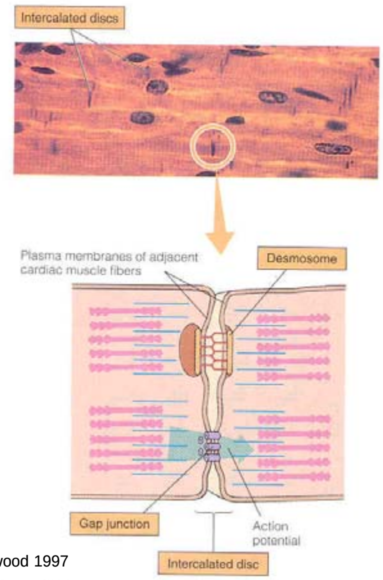


FIGURE 14–16
Conducting system of the heart.

Influenced by autonomic NS



Sherwood 1997

Figure 9-8 **Organization of Cardiac Muscle Fibers** Adjacent cardiac muscle cells are joined end to end by intercalated discs, which contain two types of specialized junctions: desmosomes, which act as spot rivets mechanically holding the cells together, and gap junctions, which permit action potentials to spread from one cell to adjacent cells.

Cardiac Cells electronically linked by Gap Junctions

(except from atrial to ventricular cells...)

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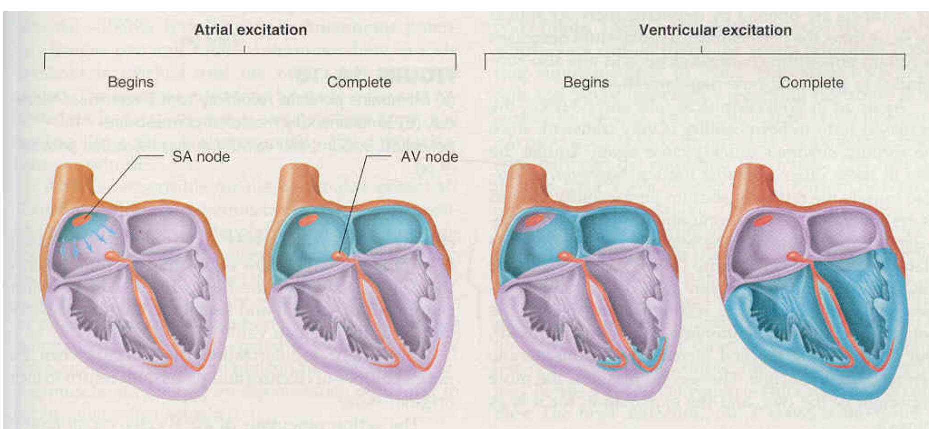
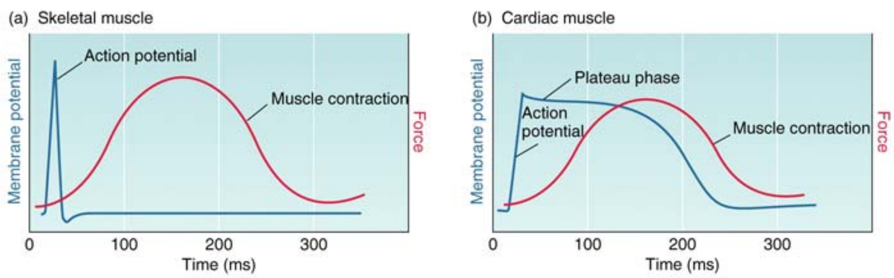
Electrical Activity in the Mammalian Heart



Vander 2001

FIGURE 14–17
Sequence of cardiac excitation. The blue color denotes areas that are depolarized. Impulse spread from right atrium to left atrium is via the atrial muscle cells where the atria contact each other in their shared wall.
Adapted from Rushmer.

Recall AP and refractory period differences…



(Eckert, 12-7)

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Types of Cardiac Cells:

A. Contractile

B. Conducting

~ autorhythmic

SA node
AV node

~ fast-conducting

Internodal
Interatrial
Bundle of His
Purkinje
Etc.

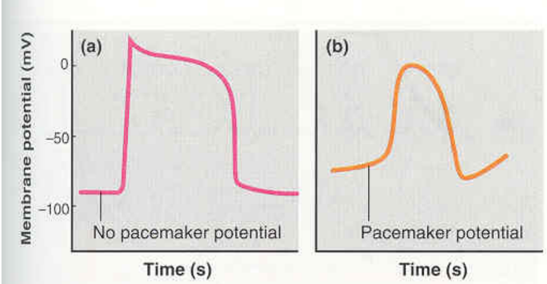

FIGURE 14–19 Vander 2001
Comparison of action potentials in (a) a ventricular muscle cell (from Figure 14–18) and (b) a sinoatrial (SA)-nodal cell. The most important difference is the presence of the pacemaker potential in the SA node.

Types of Cardiac Cells:

A. Contractile

B. Conducting

- 1° autorhythmic

  SA node
  AV node

- 1° fast-conducting

  Internodal
  Interatrial
  Bundle of His
  Purkinje
  Etc.

Pacemakers:

-Normally HR driven by SA node

-Others are Latent pacemakers

-Called Ectopic pacemaker when node other than SA driving HR

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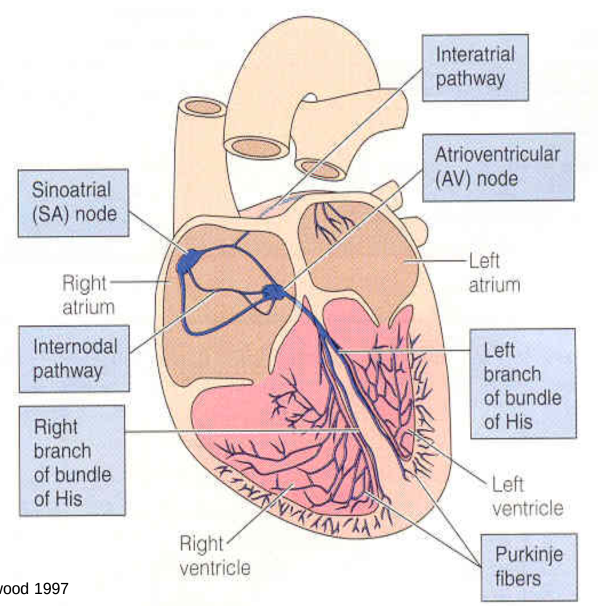

Sherwood 1997

Figure 9-11 Specialized Conduction System of the Heart

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Sherwood 1997

Figure 9-12 **Different Autorhythmic Rates** (a) Recording from autorhythmic cell A. (b) Recording from autorhythmic cell B. Because Cell A has a faster rate of depolarization, it reaches threshold more quickly than Cell B and therefore generates action potentials more rapidly.

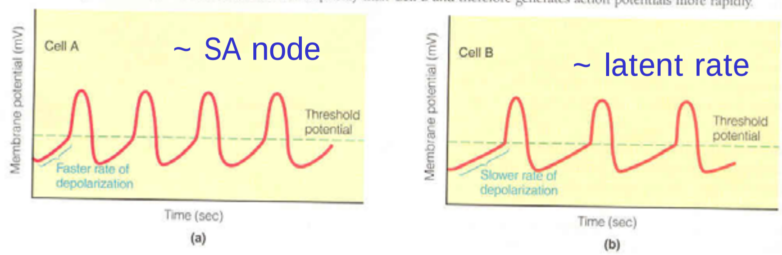

Table 9-1

Normal Rate of Action Potential Discharge in Autorhythmic Tissues of the Heart

Tissue	*Action Potentials Per Minute**
SA node (normal pacemaker)	70–80
AV node	40–60
Bundle of His and Purkinje fibers	20–40

*In the presence of parasympathetic tone; see p. 206.

Sherwood 1997

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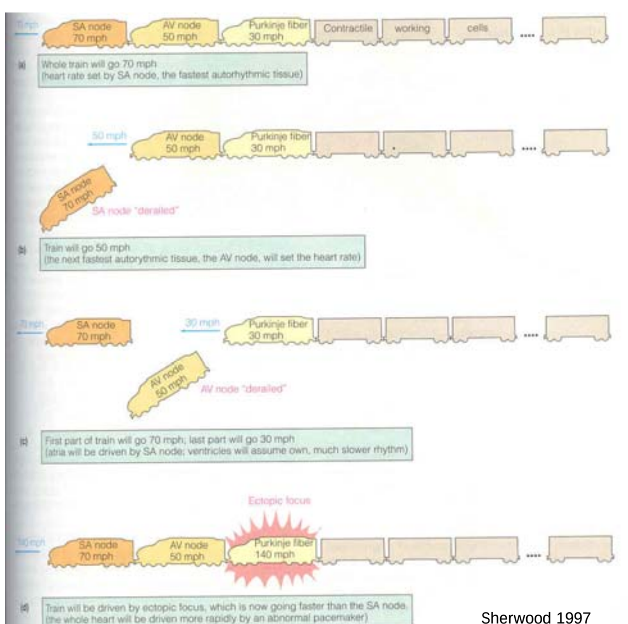
The Heart Rate Train



SA

AV

other

oops

Sherwood 1997

Figure 9-13 **Analogy of Pacemaker Activity** (a) Normal pacemaker activity by the SA node. (b) Takeover of pacemaker activity by the AV node when the SA node is nonfunctional. (c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in a condition of heart block even though the SA node is still functioning. (d) Takeover of pacemaker activity by an ectopic focus.

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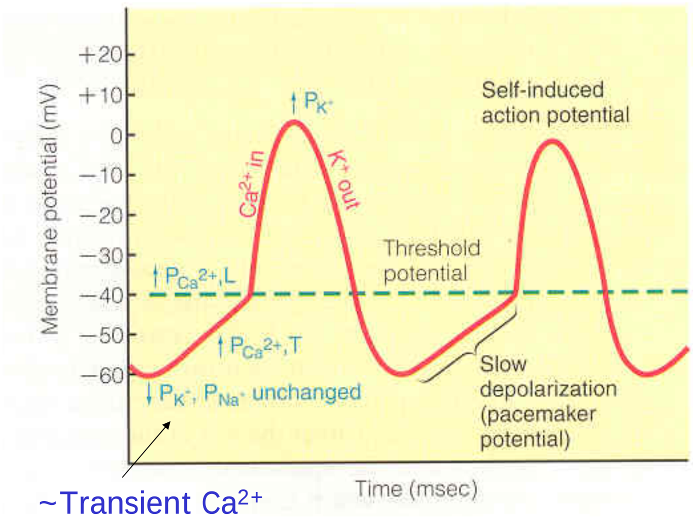
9-11, Sherwood 1997



Which way would you alter channel permeabilities to speed or slow HR??

~Transient Ca^{2+} channels

K^+, Na^+

Autorhythmic Cardiac Muscle (e.g. SA node)

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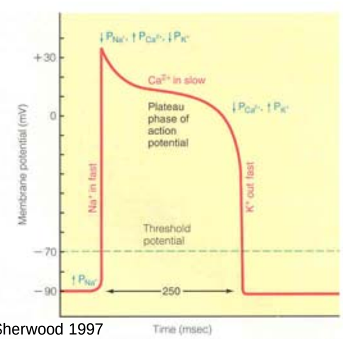
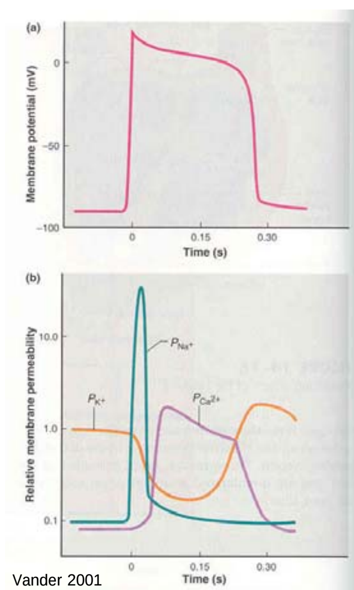


Sherwood 1997

Figure 9-15 Action Potential in Contractile Cardiac Muscle Cells The action potential in cardiac contractile cells differs considerably from the action potential in cardiac autorhythmic cells (compare with Fig. 9-10). The membrane potential of cardiac contractile cells remains at a resting potential of −90 mV until excited. Similar to most excitable cells, the rising phase of the action potential is caused by a fast Na^+ influx and the falling phase by a fast K^+ efflux. Unique to cardiac contractile cells, the membrane potential is maintained near the peak of the action potential for several hundred milliseconds. This plateau phase of the action potential results from a slow influx of Ca^{2+} coupled with a marked decrease in K^+ permeability.

Contractile Cardiac Muscle

Ca^{2+} current maintains plateau



Vander 2001

FIGURE 14–18
(a) Membrane potential recording from a ventricular muscle cell. (b) Simultaneously measured permeabilities P to potassium, sodium, and calcium during the action potential of (a).

Cardiac Muscle (the other striated muscle)

-Small muscle fiber cells with only one nucleus

-Individual fibers are connected to neighbors electronically via gap junctions

-Two types of fibers:

1. Contractile (similar to skeletal muscle)
2. Conducting (including pacemaker cells)
   Do not contract, but transmit electrical signal

-Cardiac contraction myogenic (arises within heart)

Can be influenced by autonomic nervous system (alpha, beta adrenoreceptors increase [Ca2+])

-Long-lasting AP with long plateau phase, and long refractory period - why?

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Cardiac Muscle (the other striated muscle)

-Intracellular calcium from SR and across plasma membrane (unlike in skeletal)

-Dihydropyridine receptors in T-tubules are voltage-activated calcium channels

-Ryanodine receptors then release more calcium from SR into the cytoplasm (calcium-induced calcium release)

-During relaxation, Calcium pumped actively back into SR and out across plasma membrane

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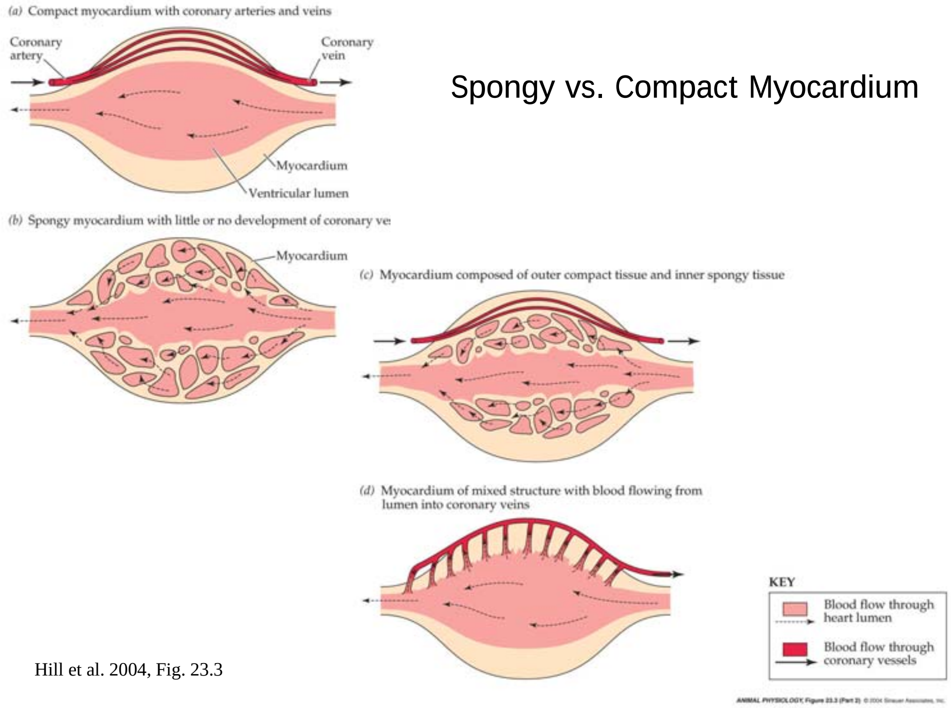
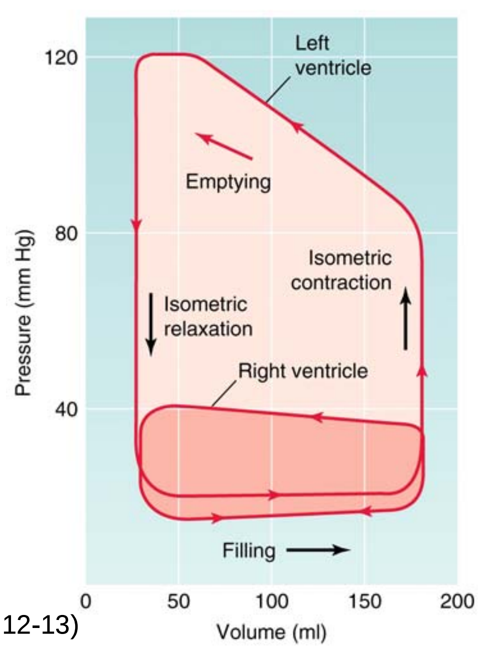
Spongy vs. Compact Myocardium



Hill et al. 2004, Fig. 23.3

Heart Work Loops



(Eckert, 12-13)

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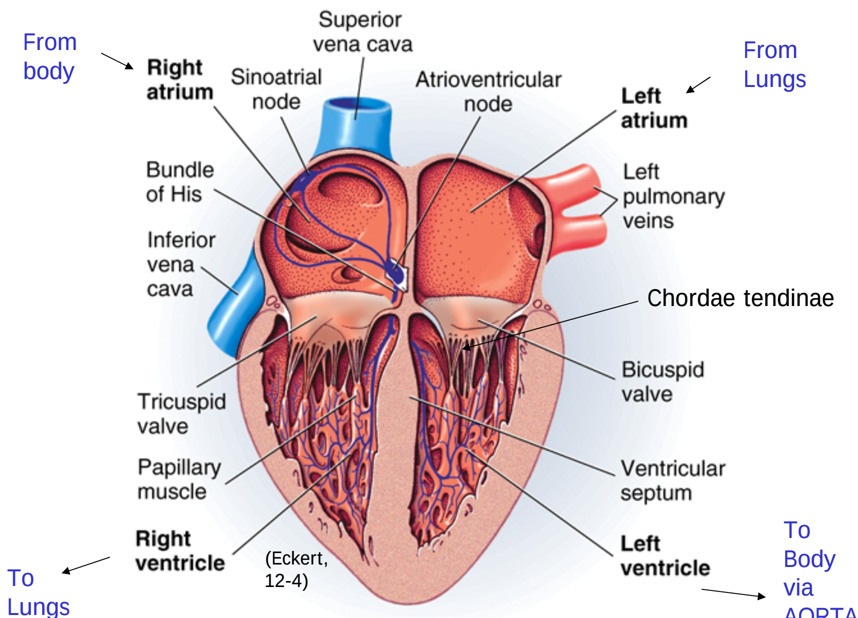

Mammalian Heart

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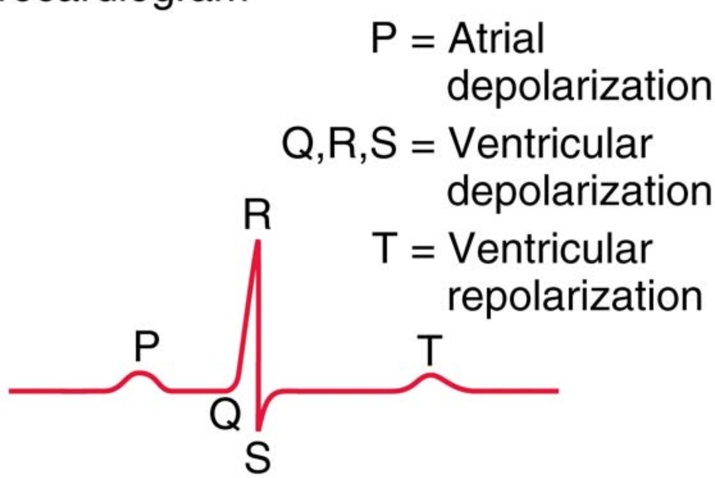
(a) Electrocardiogram

(Eckert, 12-8)



(Q,R,S masks atrial repolarization)

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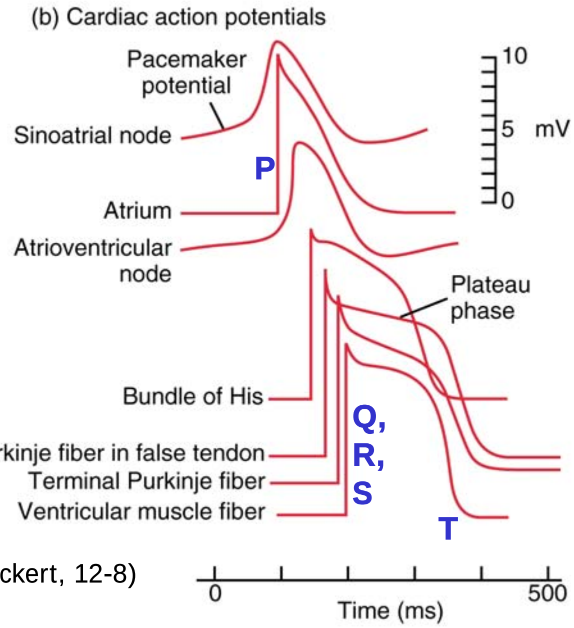

(Eckert, 12-8)

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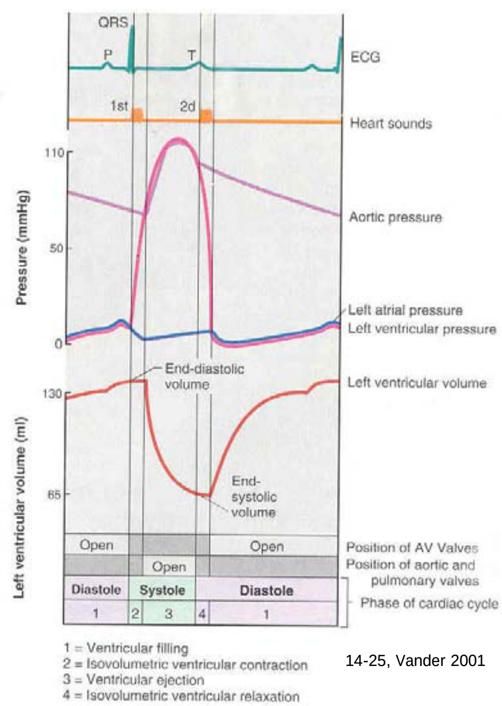
Wiggers Diagram

Valves open/close where pressure curves cross



14-25, Vander 2001

760 mmHg
= 1 atm
= 9.8 m blood

1:2

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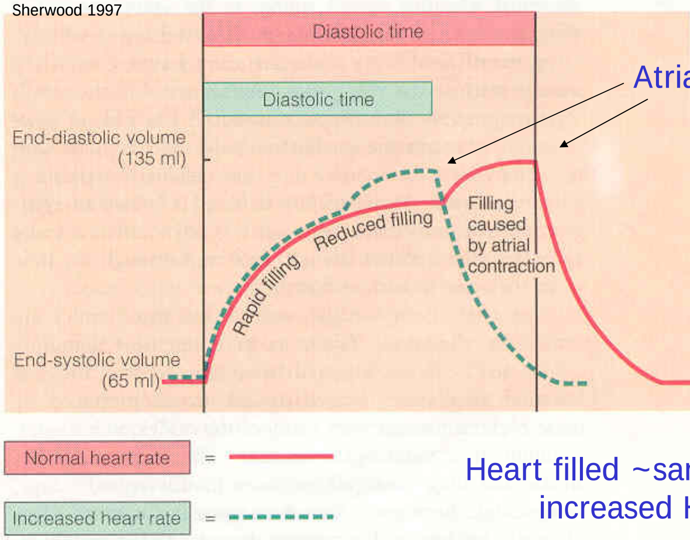
Figure 9-22 **Ventricular Filling Profiles during Normal and Rapid Heart Rates** Because much of ventricular filling occurs early in diastole during the rapid-filling phase, filling is not seriously impaired when diastolic time is reduced as a result of an increase in heart rate.

Sherwood 1997



Atrial Kick

Heart filled ~same with increased HR

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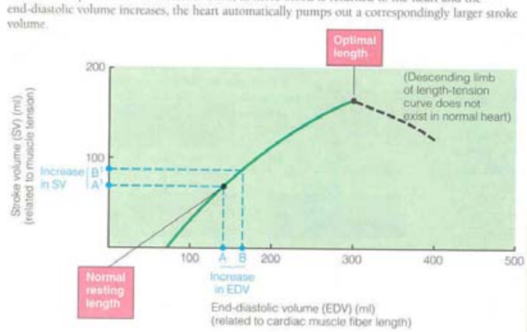
Sherwood 1997

Figure 9-26 **Intrinsic Control of Stroke Volume (Frank-Starling Curve)** The cardiac muscle fiber's length, which is determined by the extent of venous filling, is normally less than the optimal length for developing maximal tension. Therefore, an increase in end-diastolic volume (that is, an increase in venous return), by moving the cardiac muscle fiber length closer to optimal length, increases the contractile tension of the fibers on the next systole. A stronger contraction squeezes out more blood. Thus, as more blood is returned to the heart and the end-diastolic volume increases, the heart automatically pumps out a correspondingly larger stroke volume.



Frank-Starling Curve

Systole = Ventricular Emptying

Diastole = Ventricular Filling (rest)

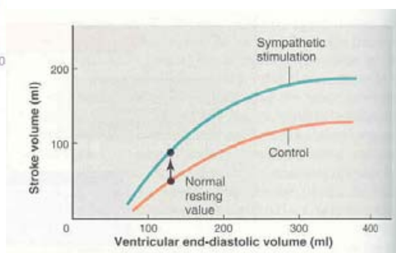


FIGURE 14–30 Vander 2001

Effects on stroke volume of stimulating the sympathetic nerves to the heart. Stroke volume is increased at any given end-diastolic volume; that is, the sympathetic stimulation has increased ventricular contractility.

Cardiac Output:

CO = cardiac output (ml/min from 1 ventricle)

SV = stroke volume (ml/beat from 1 ventricle)

= EDV – ESV (end-diastolic – end-systolic volume)

HR = heart rate (beats/min)

CO = HR x SV

MABP = CO x TPR

MABP = DP + 1/3(SP-DP)

- Heart can utilize different types of energy sources (unlike brain)

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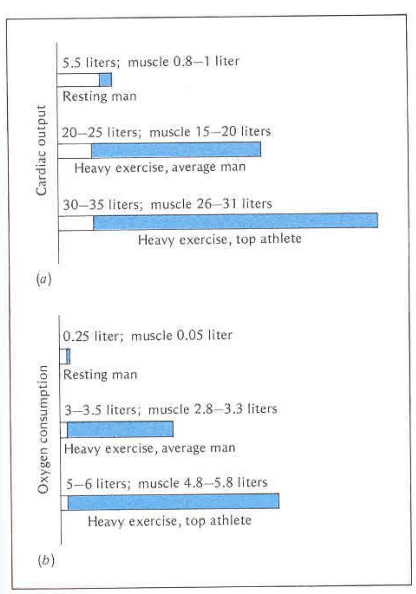

Figure 3.19 Distribution of total blood flow (cardiac minute volume) (a) and of oxygen consumption (b) between the muscles (shaded bars) and all other parts of the body (unshaded bars). Data for resting man, heavy exercise in a normal man, and heavy exercise in a top athlete. All values are in liters per minute. [Folkow and Neil 1971]

Cardiac Output 6x

Exercise

Oxygen Consumption X 20

Knut Schmidt-Nielsen 1997

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Cardiac Output Control

Sympathetic speeds heart rate
and increases contractility

1. Norepinephrine binds to $beta_1$ adrenergic receptors
2. Increases cAMP levels and phosphorylation
3. Activates cation channels (Na^+) and increases HR

4. Epi and Norepi activate alpha and $beta_1$ adrenoreceptors which increase contractility and rate of signal conduction across heart

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How increase contractility?

More Ca^{2+}

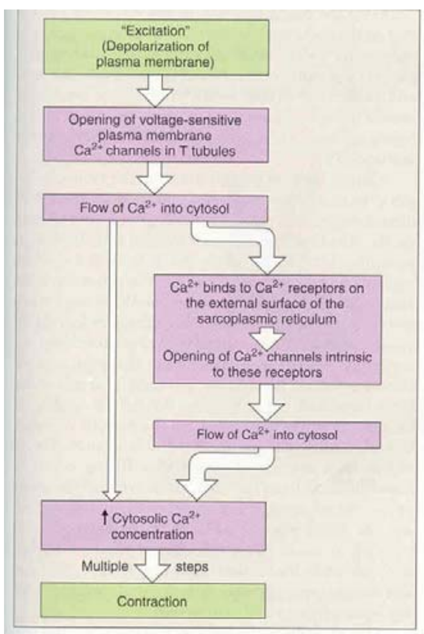
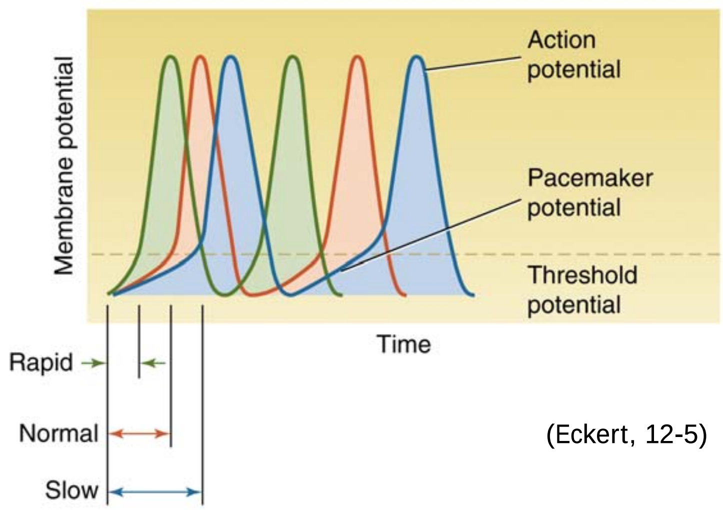


FIGURE 14–22 Vander 2001
Excitation-contraction coupling in cardiac muscle.

50

HR control

Parasympathetic vs. Sympathetic



(Eckert, 12-5)

HR control

Parasympathetic slows heart rate

-Innervate Atria (Vagus nerve = Xth cranial nerve)

-Cholinergic (ACh)

-Alter SA node pacemaker potential by ⇑ K^+ permeability

⇓ Ca^{2+} permeability

Parasympathetic innervation of AV node slows passage of signal between atria and ventricles

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Peripheral Circulation

- Endothelium lining vessels
- Middle layer with smooth muscle (esp. arteries)
- Outer fibrous layer

Capillaries with ~ only Endothelium

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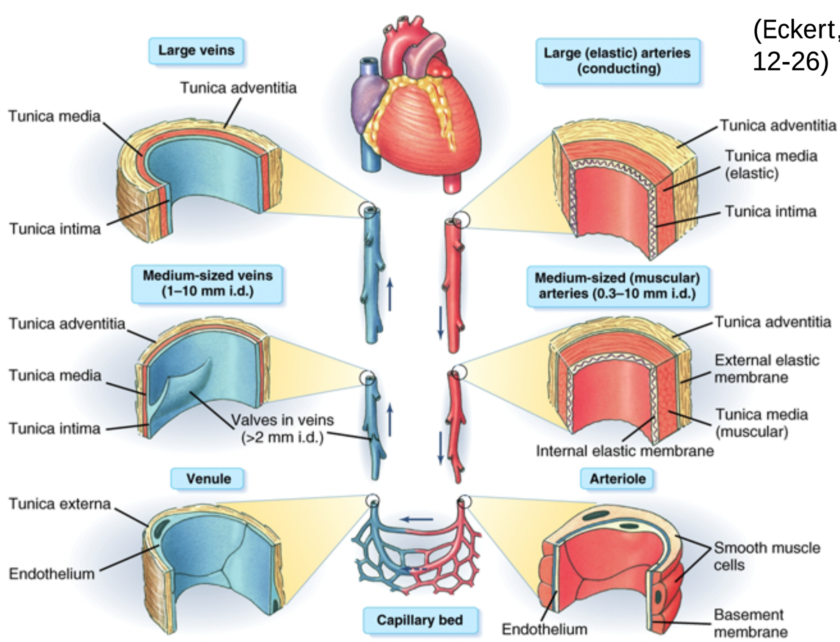
(Eckert, 12-26)



Peripheral Circulation

Compliance vs. Elasticity

~ Veins vs. Arteries

Volume Reservoir vs. Pressure Reservoir

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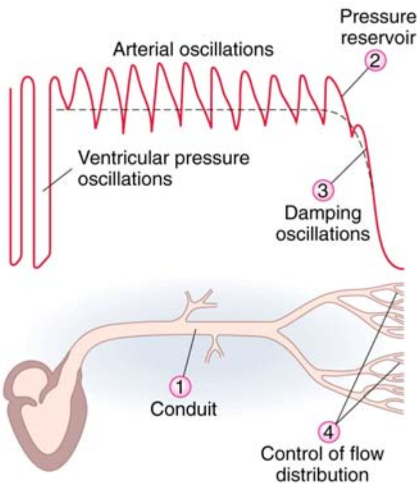
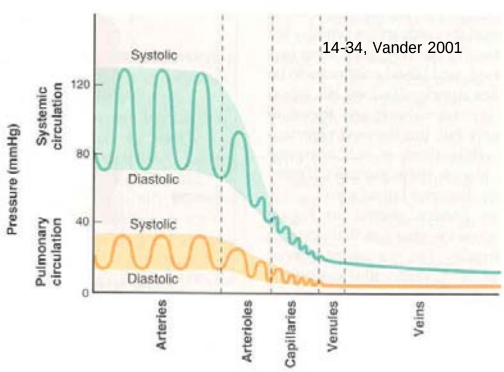
Volume Reservoir vs. Pressure Reservoir



(Eckert, 12-27)



~Constant P and Q at Capillaries!

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Venous System

- low pressure (11 mm Hg or less)
- thin walled veins with less muscle
- more compliant and less elastic
- valves
- blood moved by skeletal muscle (and smooth)
- breathing creates vacuum (low pressure) in chest to aid blood flow to heart

Microcirculation

- endothelium in capillaries is permeable

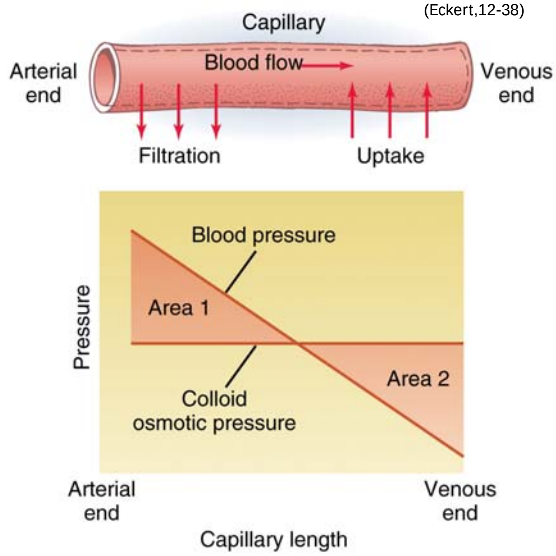
1. continuous
2. Fenestrated (kidney, gut)
3. Sinusoidal (liver, bone)

Less permeable ↓ More permeable

- Movement across walls, between walls, in vesicles

- Bulk Flow...

Bulk Flow…



Fluid Pressure
vs.
Osmotic Pressure

Faster than diffusion

Filtration > Uptake

Lymph System to return excess fluid

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Bulk Flow…

- Edema
- Starvation
- Lungs
- Kidneys

Lymph System

- No RBCs; therefore not red
- Drains interstitial spaces
- has valves and smooth musculature
- empties into thoracic duct at vena cavae
- transport system for large hormones and fats into blood stream
- filariasis, elephantiasis
- Reptiles and Amphibians with lymph hearts

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Circulatory System Regulation

1. Feed Brain and Heart First
2. Next Feed Tissues in Need
3. Maintain volume, prevent edema, etc.

Baroreceptors
Chemoreceptors
Mechanoreceptors
Thermoreceptors

Info. integrated at Medullary Cardiovascular Center
medulla oblongata and pons

Depressor Center → Parasympathetic Effectors

Pressor Center → Sympathetic Effectors

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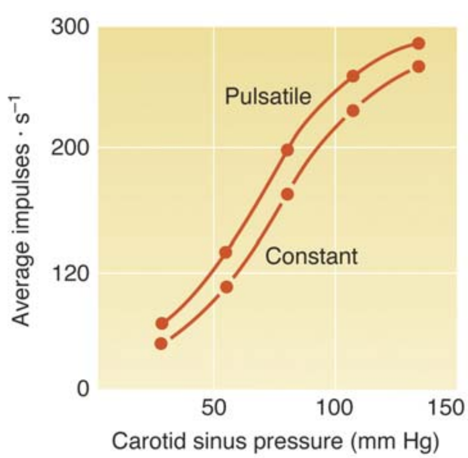
Circulatory System Regulation

Baroreceptors increase AP firing rate when BP increases

Sensed at carotid sinus, aortic arch, subclavian, common carotid, pulmonary

Usually leads to Sympathetic suppression to decrease BP

(Eckert, 12-43)



Circulatory System Regulation

Arterial Chemoreceptors in carotid and aortic bodies

(More details when discuss ventilation)

e.g., low O_2, high CO_2, low pH
leads to bradycardia and peripheral vasoconstriction
(diving and not inflating lungs)

What about when not diving?

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Circulatory System Regulation

Cardiac Mechanoreceptors and Chemoreceptors

Alter heart rate AND blood volume

e.g.,
ANP (Atrial Natruiretic Peptide) released in response to stretch

- leads to increased Na^+ excretion
and therefore greater urine output

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Circulatory System Regulation

Extrinsic vs. Local Control

↓

Neuronal or
Hormonal

Most arterioles with sympathetic innervation

Also respond to circulating catecholamines:

-At high levels, alpha adrenoreceptors are stimulated → vasoconstriction (to increase BP)

-At low levels, $beta_2$ adrenoreceptors are stimulated → vasodilation (to increase flow to tissue)

-Response depends on tissue type, receptor type(s), level of catecholamines (epi, norepi), etc.

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Circulatory System Regulation

Extrinsic vs. Local Control

stretch

temp.
O_2
CO_2
pH
adenosine
K^+

Decreased O_2 levels with opposite effect in lungs

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Circulatory System Regulation

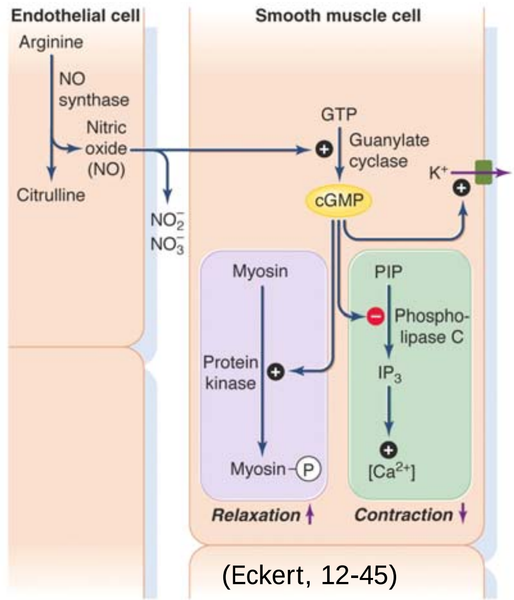
Extrinsic vs. Local Control

NO (nitric oxide)

Released from
vascular endothelium:

-Vasodilation
-Relaxation

-Viagra acts by blocking
breakdown of cGMP



(Eckert, 12-45)

Circulatory System Regulation

Extrinsic vs. Local Control

Histamine

Released in response
to injury of connective
tissue and leukocytes:

-Vasodilation

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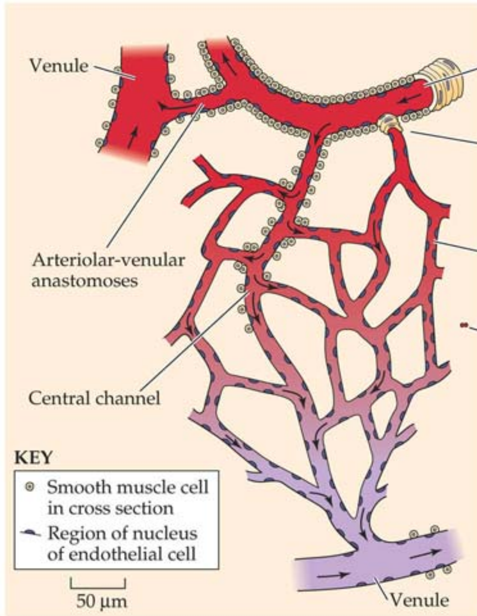
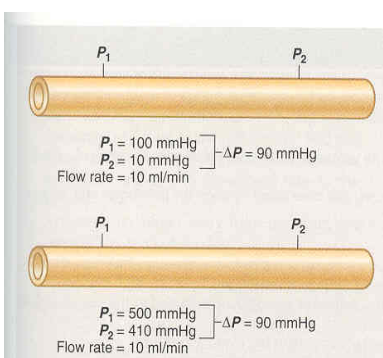


(Hill et al., 2004
Fig 23.11)

Hemodynamics in Vessels

Flow depends primarily on pressure gradient and resistance

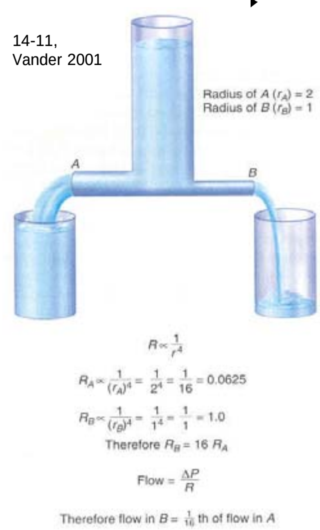


Vander 2001

FIGURE 14–10

Flow between two points within a tube is proportional to the pressure difference between the points. The flows in these two identical tubes are the same (10 ml/min was selected arbitrarily), because the pressure differences are the same.

14-11,
Vander 2001



Hemodynamics

Use to approximate flow

- Poiseuille's Law:

Pressure Gradient

Flow rate

radius^4

$$Q = \frac{(P_1 - P_2)\pi r^4}{8L\eta}$$

length

viscosity

Small change in radius → large change in flow rate

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Hemodynamics

- From Poiseuille's Law:

Pressure Gradient

Resistance

length

viscosity

$$R = \frac{(P_1 - P_2)}{Q} = \frac{8L\eta}{\pi r^4}$$

Flow rate

radius^4

Small change in radius → large change resistance

Modifiable if vessel distensible under pressure

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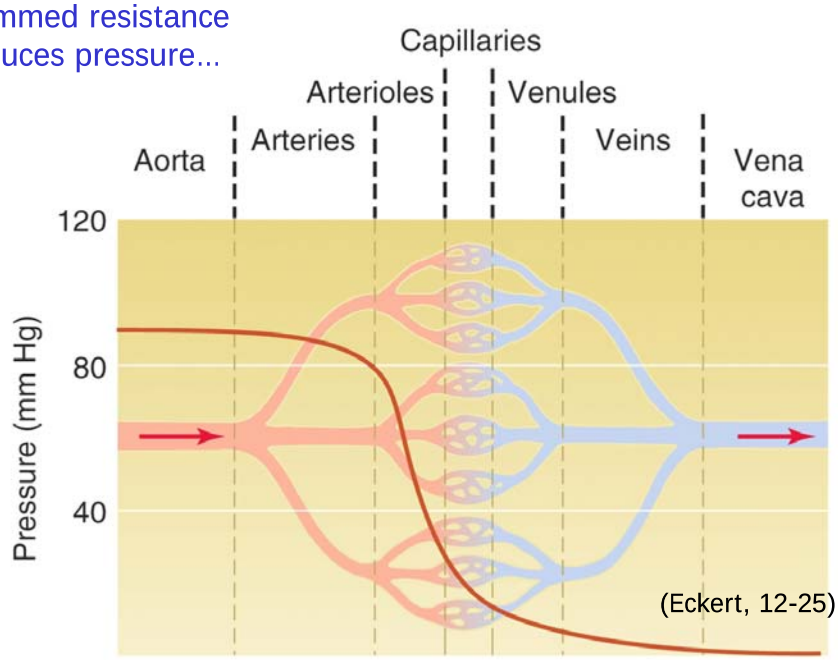
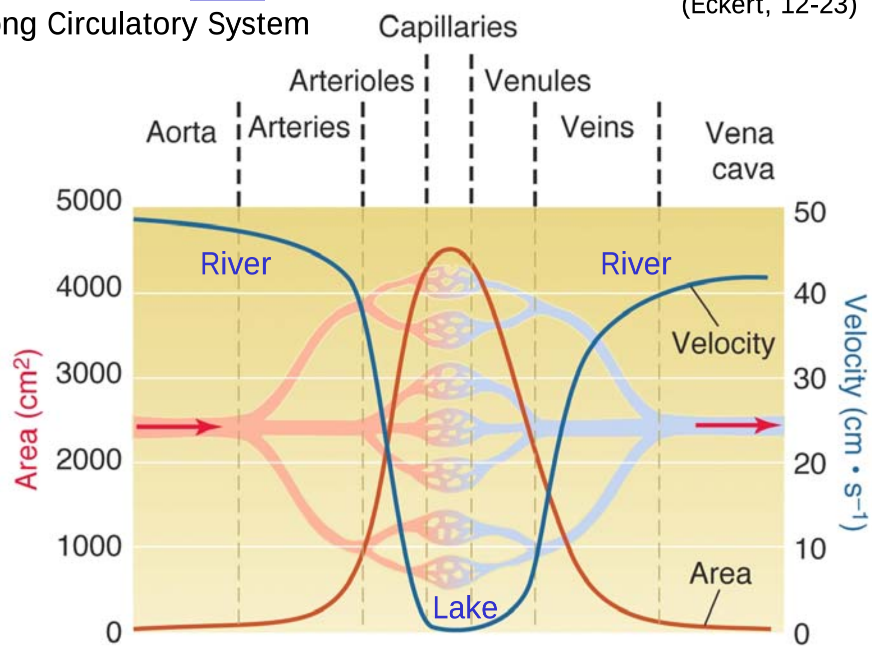
Summed resistance reduces pressure...



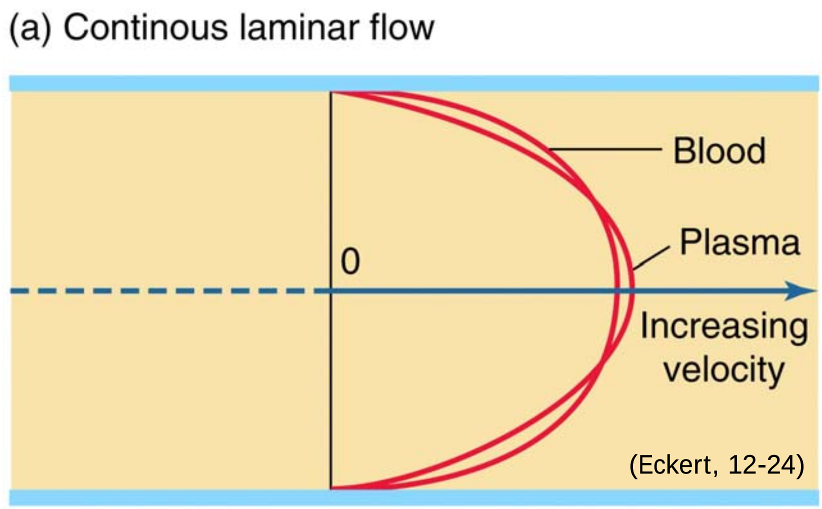
(Eckert, 12-25)

Total Flow Rate <u>same</u> all along Circulatory System

(Eckert, 12-23)



Shapes of curves slightly different because of RBCs (viscosity)



Why does blood in the lower extremities of aquatic organisms not pool as it may do in legs of humans, giraffes, etc.?

FISH:

Blood tends to pool in tail b/c inertia and compression waves when swimming

-Veins in middle of body
-Accessory caudal (tail) heart in some species

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