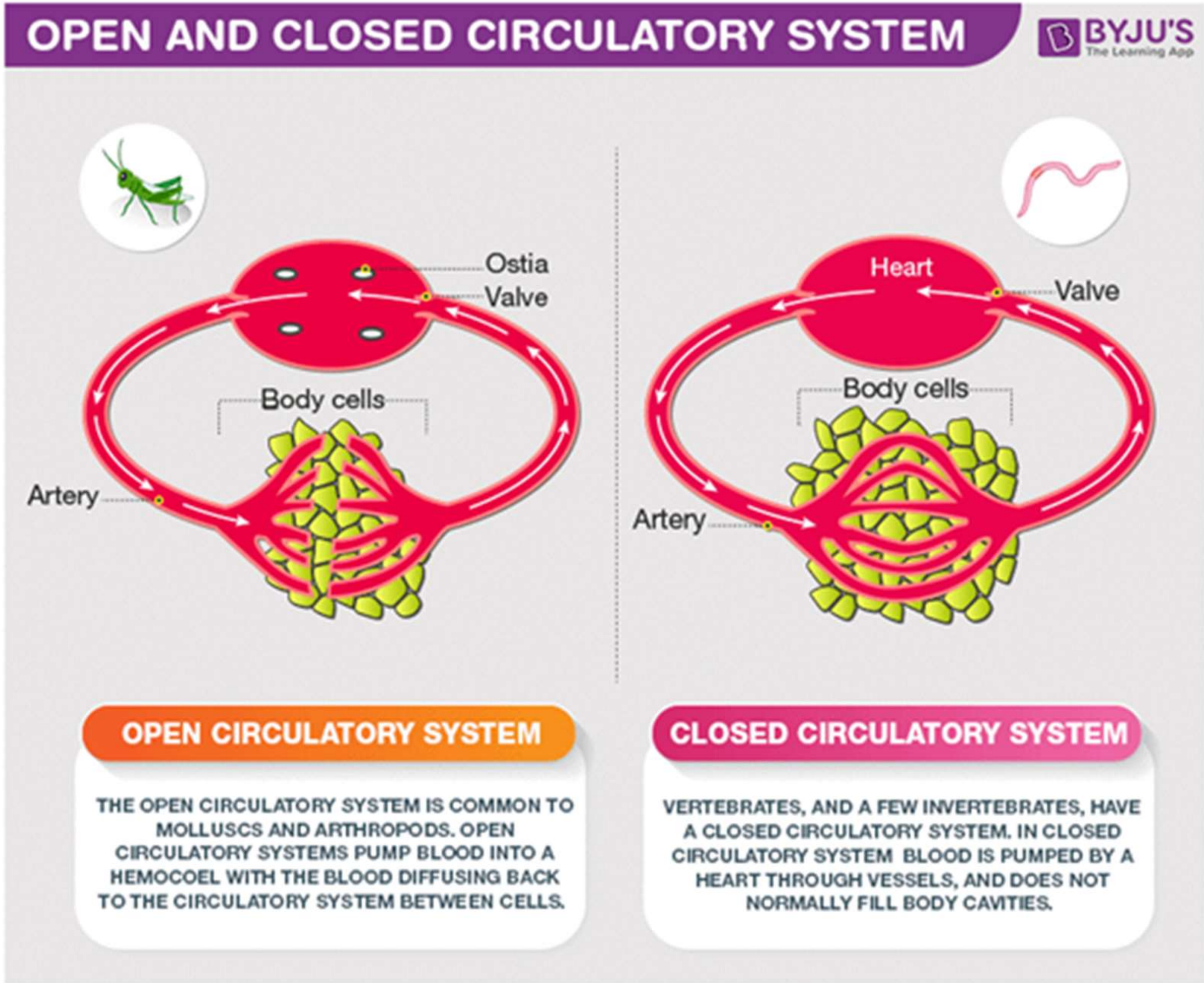
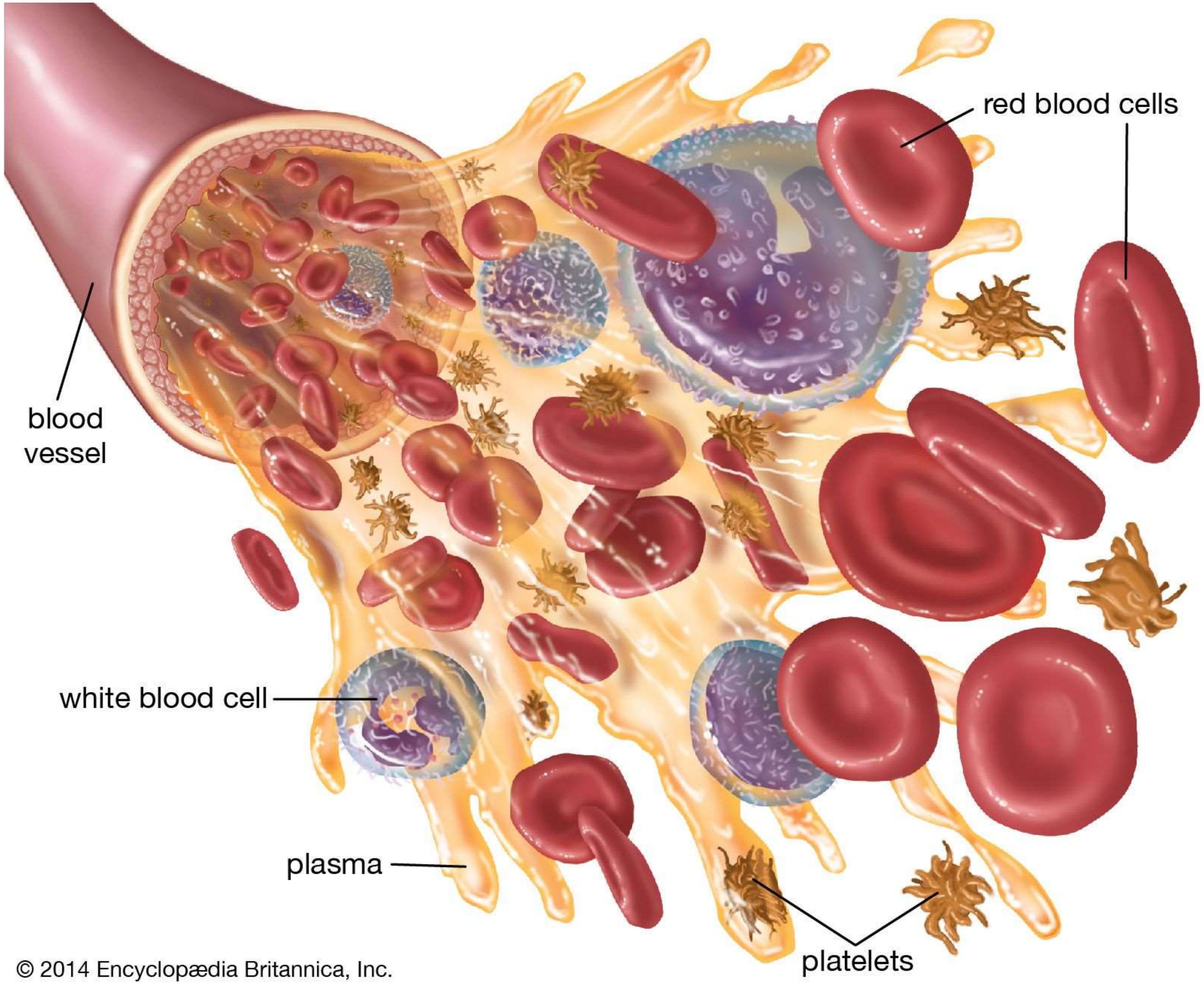
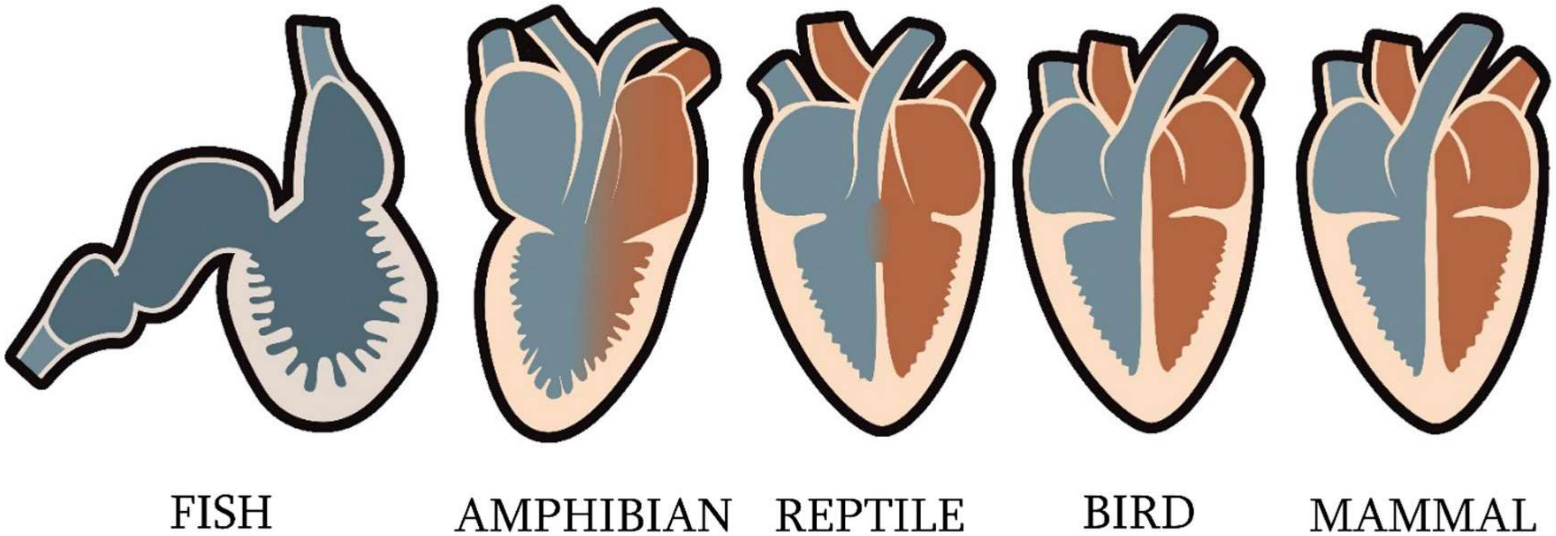

TIME FOR
RECAP

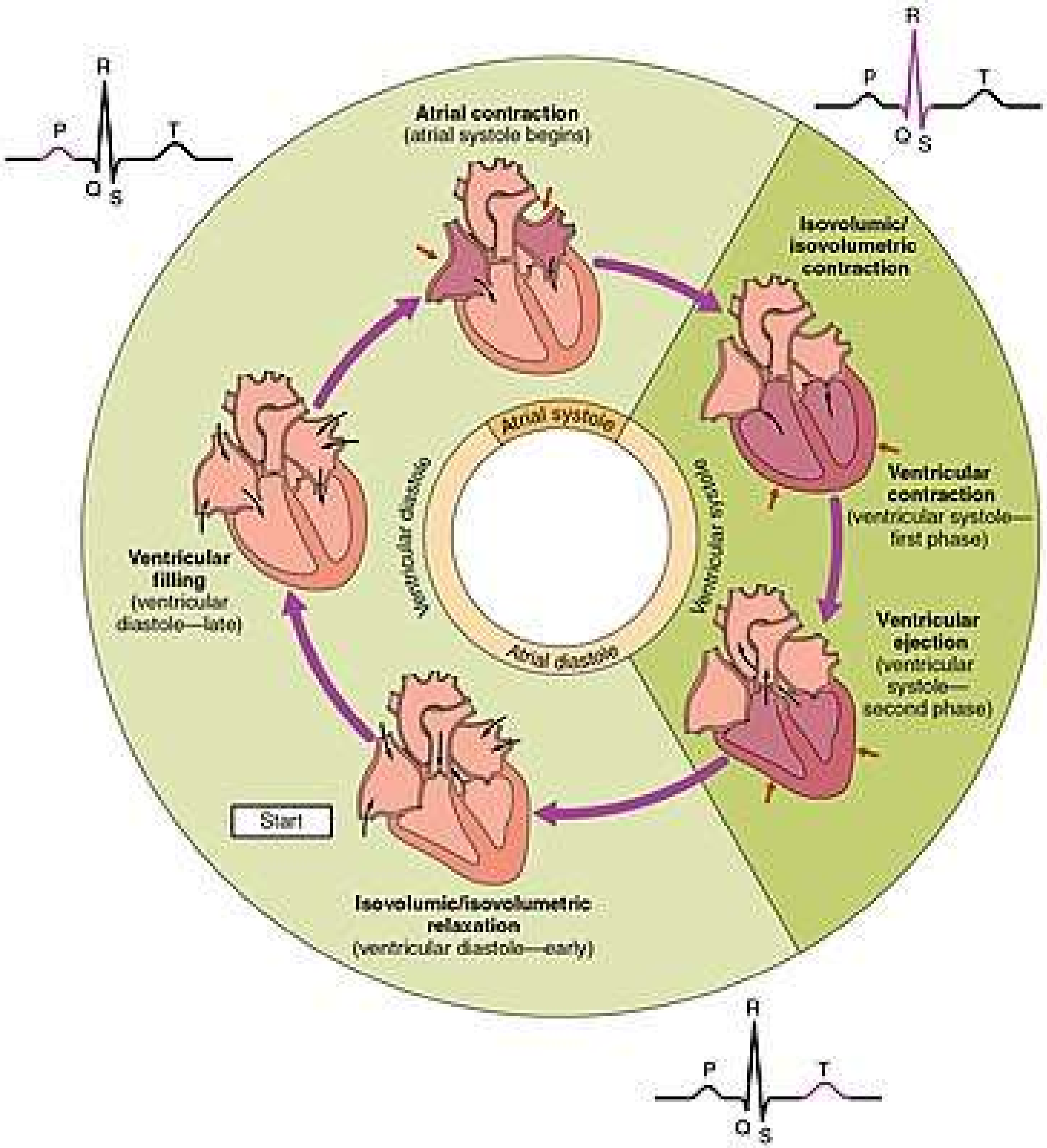


Circulatory systems evolved to overcome diffusion, which is extremely slow over all but very small distances, by creating bulk transport. Circulatory systems have up to three distinct components: fluid, pump, and vessels.


red blood cells
blood
vessel
white blood cell
plasma
platelets

Pumping mechanisms include flagella, extrinsic skeletal muscles, peristaltic muscular pumps, and hearts (chamber muscle pumps). Many animals have primary hearts aided by auxiliary pumps, such as two extra hearts in cephalopods to aid gill flow. Arthropod hearts are dorsally located and have many valved openings.




R
P
T
Q
S
Atrial contraction
(atrial systole begins)
Isovolumic/
isovolumetric
contraction
Ventricular
contraction
(ventricular systole—
first phase)
Ventricular
ejection
(ventricular
systole—
second phase)
Isovolumic/isovolumetric
relaxation
(ventricular diastole—early)
Ventricular
filling
(ventricular
diastole—late)
Start
Atrial systole
Ventricular systole
Atrial diastole
Ventricular diastole

Cardiac output and its control

The most important physiological parameter of a heart is undoubtedly the cardiac output: the volume of blood per minute pumped by a heart to the body.

C.O. = heart rate × stroke volume

(volume per minute) (beats per minute) (volume pumped per beat or stroke)

Animal	Cardiac Output	=	Heart Rate	×	Stroke Volume
Blue Whale:	2,100,000 mL/min	=	6 beats/min*	×	350,000 mL/beat
Horse:	13,500 mL/min	=	30 beats/min	×	450 mL/beat
Human:	4,900 mL/min	=	70 beats/min	×	70 mL/beat
Shrew:	1 mL/min	=	1,000 beats/min	×	0.001 mL/beat
Pigeon:	195.5 mL/min	=	115 beats/min	×	1.7 mL/beat
Trout (10°C):	17.4 mL/min	=	37.8 beats/min	×	0.46 mL/beat

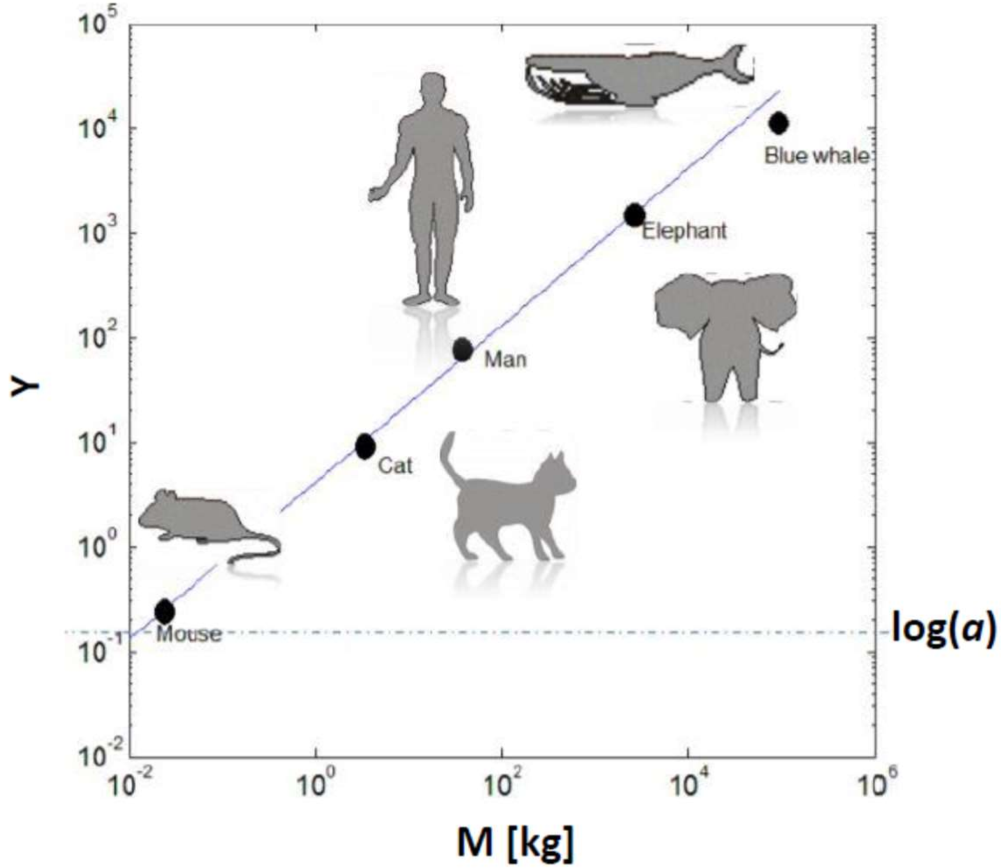
The “universal law of allometric scaling” for a parameter **Y** is expressed by the allometric equation: $\mathbf{Y = aM^b}$ oppure $\mathbf{\log Y = \log a + b \log M}$

where:

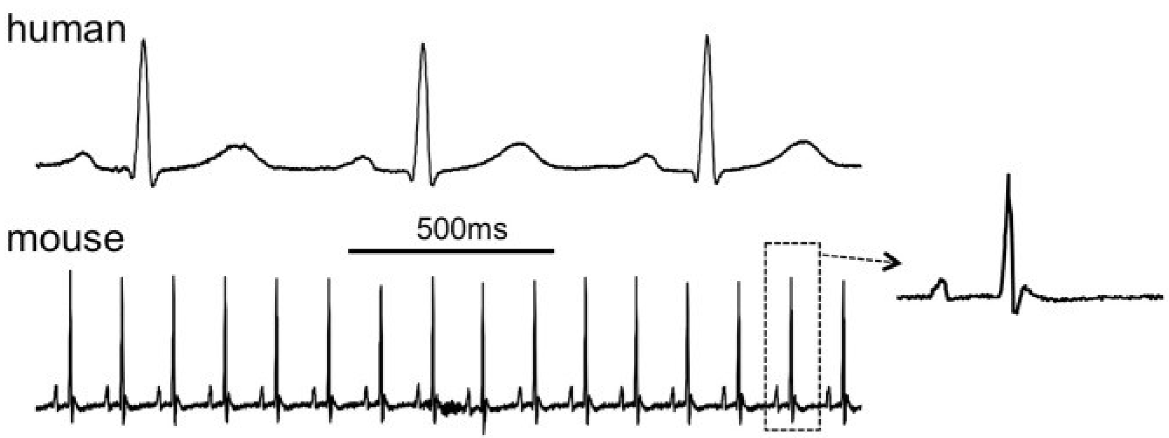
M is a measure of body zine

a is a normalization constant

b represents the scaling exponent.



PARAMETER	EXPONENT VALUE	MEANING
Cells size [m] Blood velocity [m/s] Pressure gradients [Pa]	b = 0	Parameter and body mass are indipendent
Volumes (bone, blood…) [m^3]	b = 1	Parameter and body mass are directly proportional (isometric scaling)
Metabolic rates [J/s] Flow rates (haematic, respiratory…) [m^3/s]	b = 3/4	Parameter increases slower than body mass
Radii of aorta and trachea [m]	b = 3/8	Parameter increases slower than body mass
Frequencies (cardiac, respiratory…) [Hz]	b = - 1/4	Parameter decreases when body mass increases
Bone mass [kg]	b = 4/3	Parameter increases faster than body mass

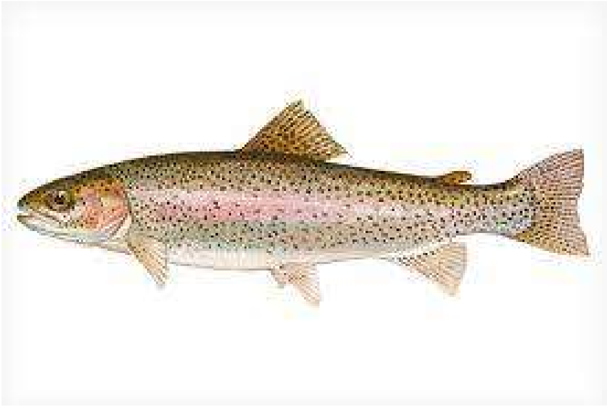


Effect of temperature

Yellowfin Tuna	Cardiac Output	=	Heart Rate	×	Stroke Volume
25°C:	43.5 mL/min	=	106 beats/min	×	0.41 mL/beat
10°C:	19.8 mL/min	=	19.6 beats/min	×	1.01 mL/beat

Yellowfin tuna, a partly endothermic fish with high metabolic rate.

Even if they are able to warm various tissues including some skeletal muscles, their hearts remain near ambient temperature because the *coronary* circulation.



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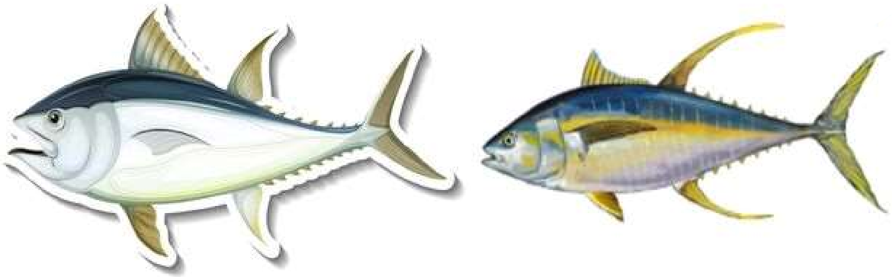
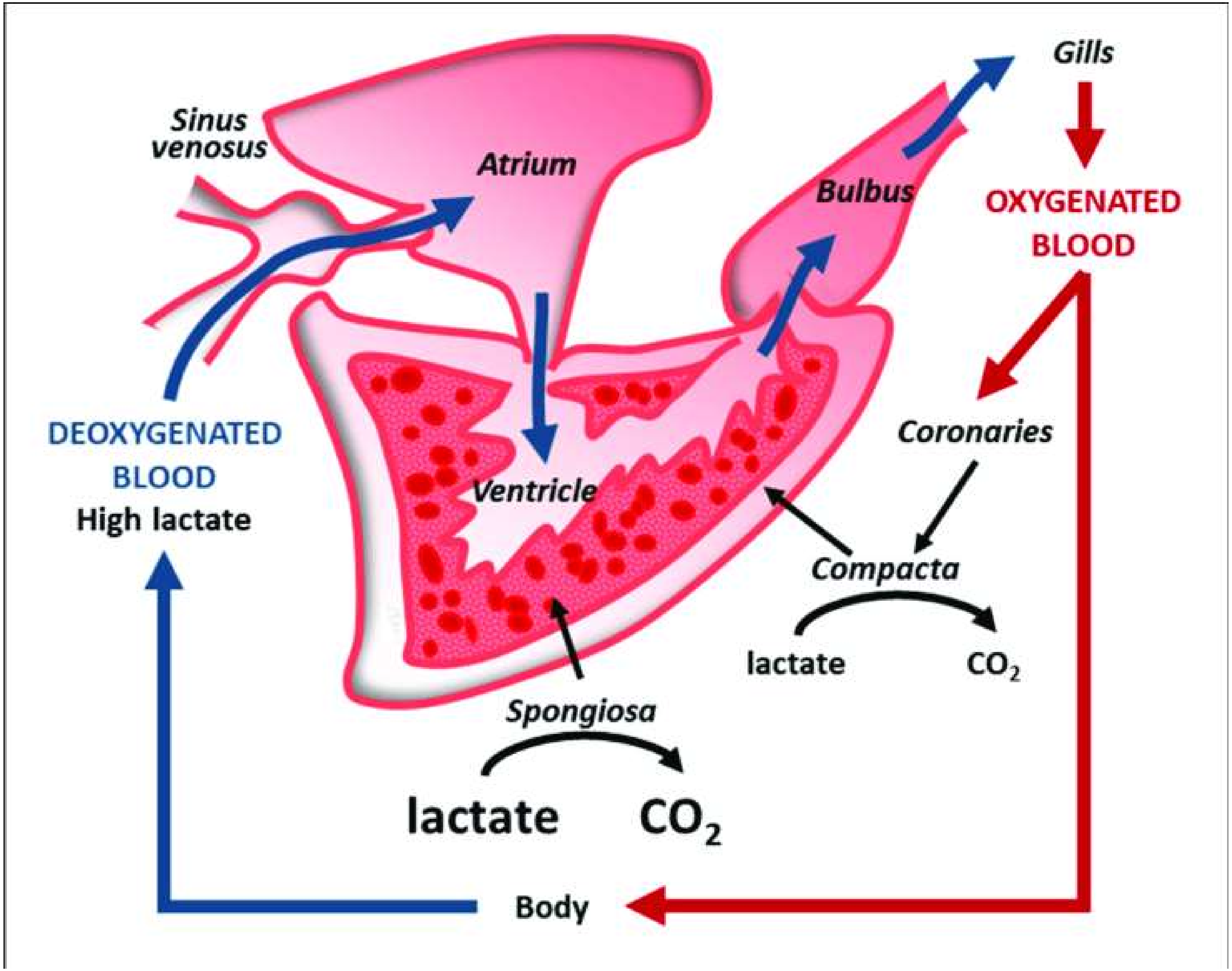
10°C:	19.8 mL/min	=	19.6 beats/min	×	1.01 mL/beat

The tuna does not do well at this temperature, presumably because of its higher metabolic demands it receives blood directly from the gills, which are at ambient temperature



Bluefin Tuna
vs
Yellowfin Tuna

Blank et al. J Exp Biol, 2004

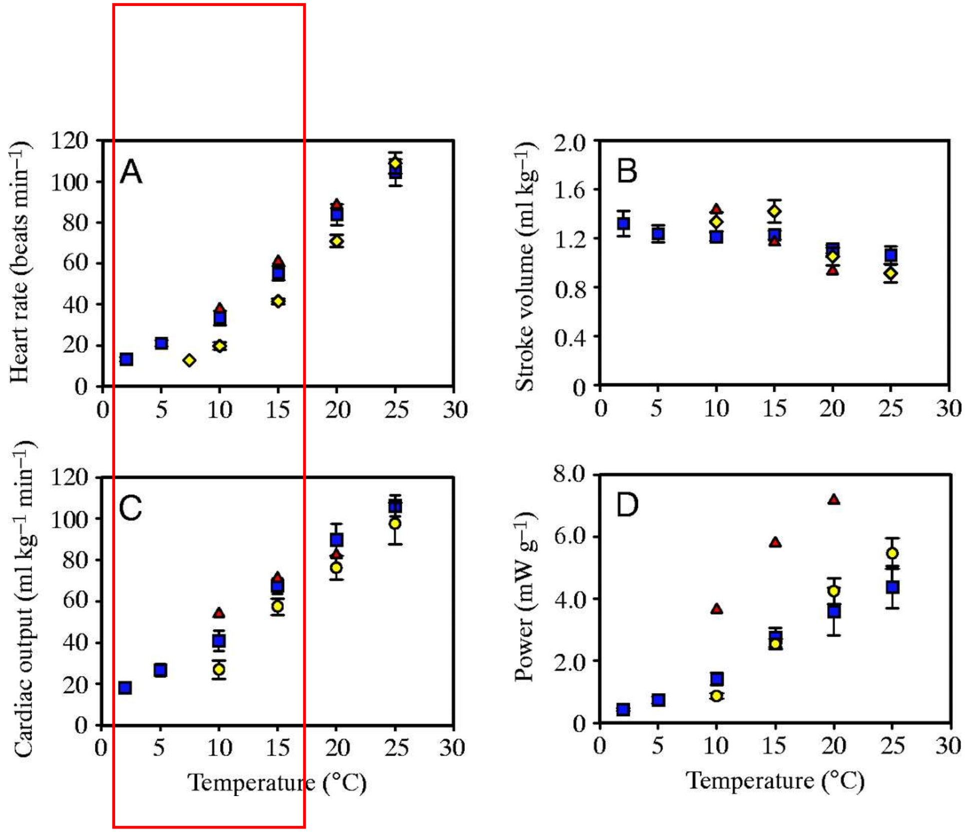


Gills
Sinus venosus
Atrium
Bulbus
OXYGENATED BLOOD
DEOXYGENATED BLOOD
High lactate
Coronaries
Ventricle
Compacta
lactate
CO_2
Spongiosa
lactate
CO_2
Body

Journal of Experimental Biology

Jason M. Blank,Jeffery M. Morrissette,Ana M. Landeira-Fernandez,Susanna B. Blackwell,Thomas D. Williams,Barbara A. Block, In situ cardiac performance of Pacific bluefin tuna hearts in response to acute temperature change, J Exp Biol, 2004, Fig. 3.

Fig. 3.



In situ cardiac performance of Pacific bluefin tuna hearts in response to acute temperature change

Effect of development

Broiler Chicks	Cardiac Output	=	Heart Rate	×	Stroke Volume
4 weeks old:	253 mL/min	=	362 beats/min	×	0.70 mL/beat
6 weeks old:	434 mL/min	=	328 beats/min	×	1.33 mL/beat

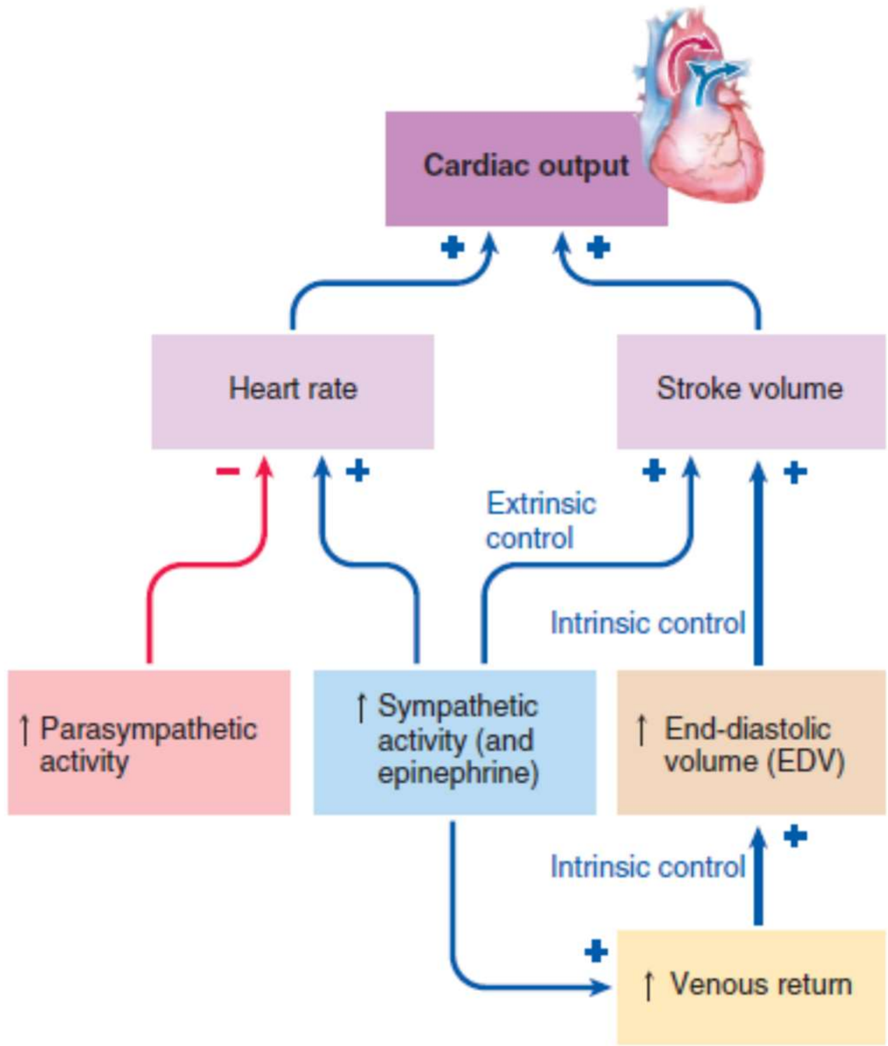


FIGURE 9-29 Control of cardiac output. Cardiac output equals heart rate times stroke volume. Heart rate in turn is increased by sympathetic activity and decreased by parasympathetic activity, while stroke volume is increased by sympathetic activity and higher venous return.

Legge di Frank-Starling

la forza di contrazione aumenta all'aumentare del volume ventricolare prima della contrazione (volume telediastolico). L'aumento del volume telediastolico si ha sia per un maggior ritorno venoso (PRECARICO), sia per una maggior resistenza arteriosa (POSTCARICO).

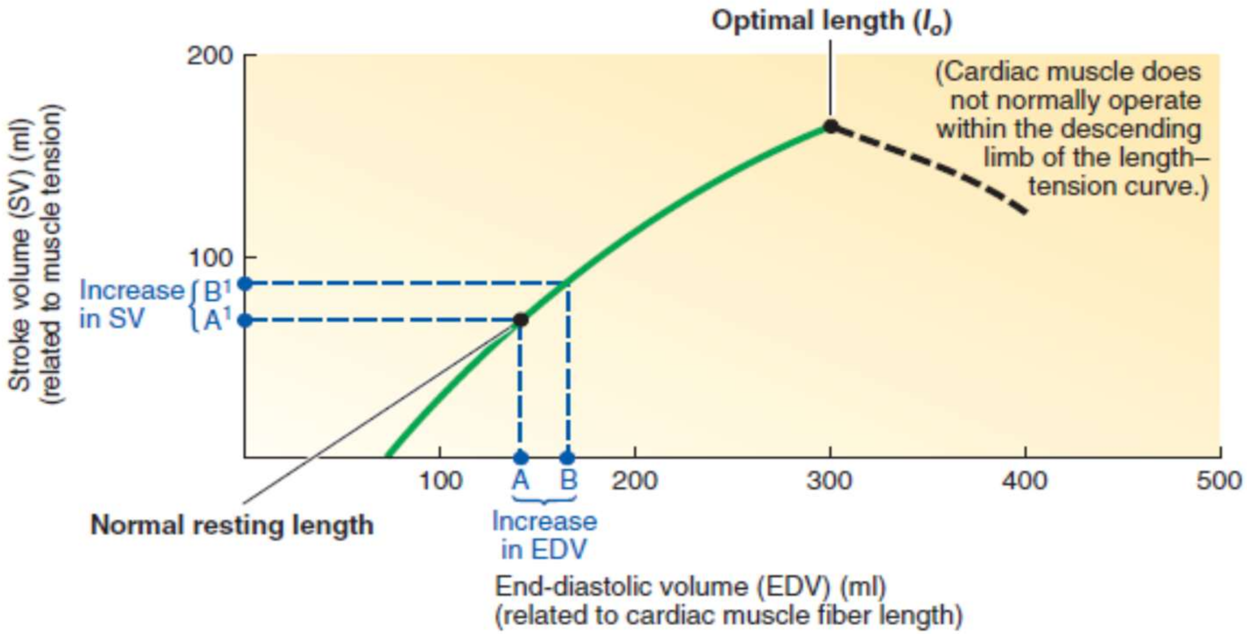


FIGURE 9-30 Intrinsic control of stroke volume (Frank-Starling curve). The cardiac muscle fiber's length, which is determined by the extent of venous filling, is normally less than the optimal length for developing maximal tension. Therefore, an increase in end-diastolic volume (that is, an increase 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.

Physics of fluid flow

Hemodynamic flow law:

$$Q = \Delta P/R$$

where:

Q = flow rate of fluid through a vessel (quantity per unit time)
ΔP = pressure gradient, or $P1 - P2$, where
P1 = pressure at the inflow end of a vessel
P2 = pressure at the outflow end of a vessel
R = resistance of blood vessels

Pressure gradient

The pressure gradient—the difference in pressure between the beginning and end of a vessel—is the main driving force for flow through the vessel; that is, blood flows from an area of higher pressure (P1) to an area of lower pressure (P2) down a pressure gradient (ΔP).

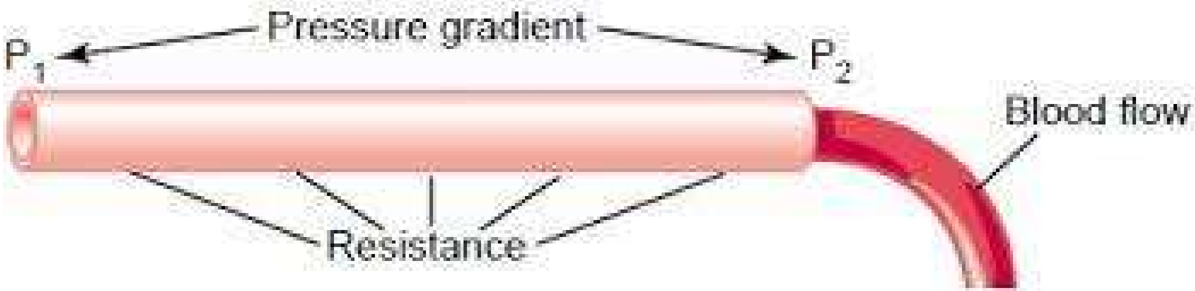
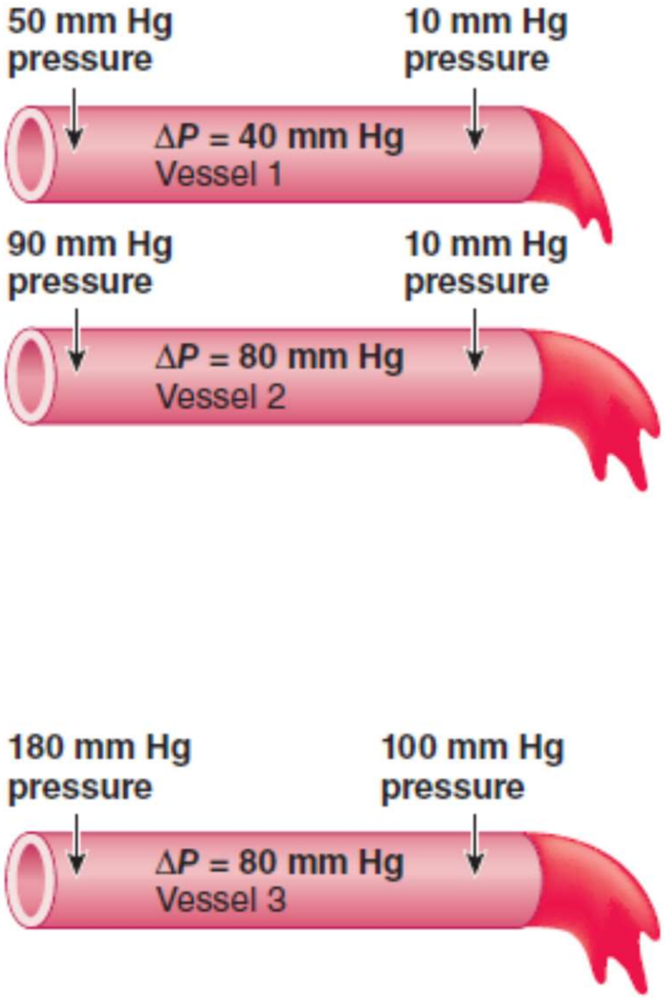
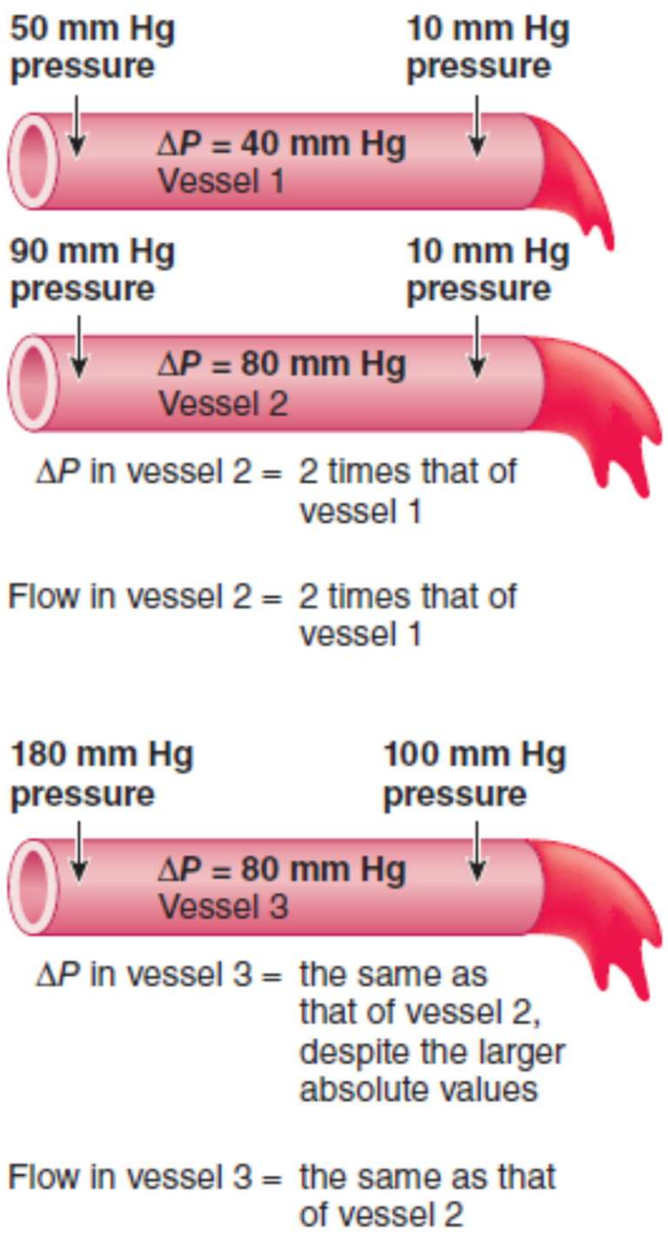
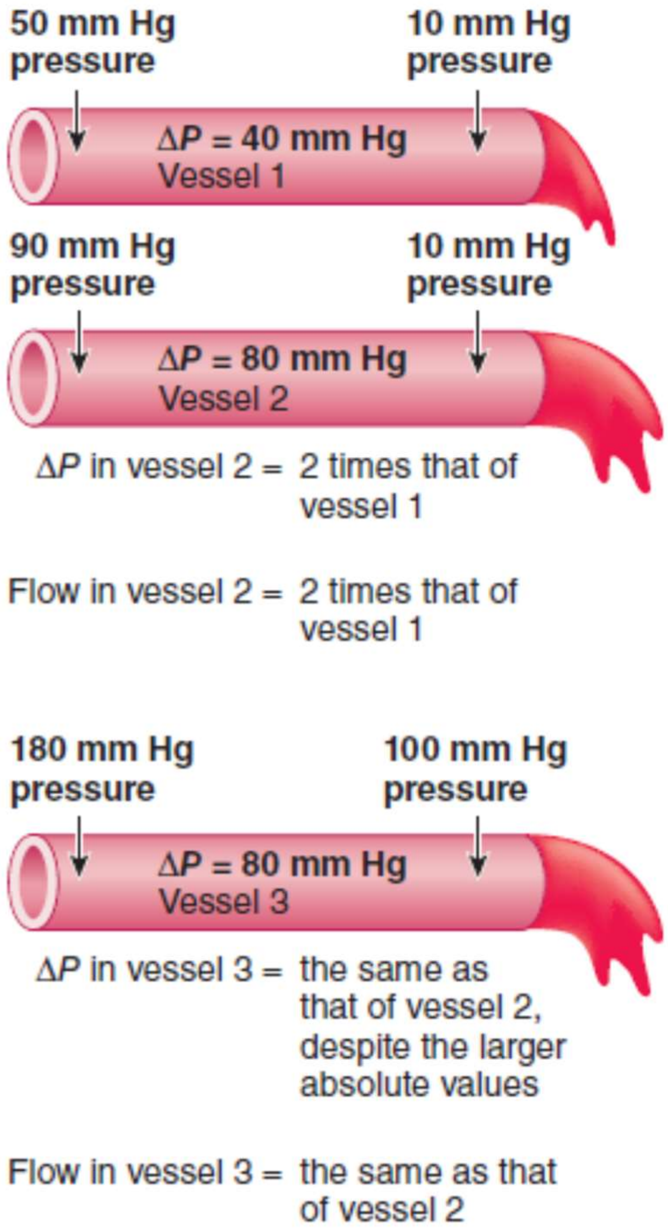


Figure 14–3

Interrelationships among pressure, resistance, and blood flow.

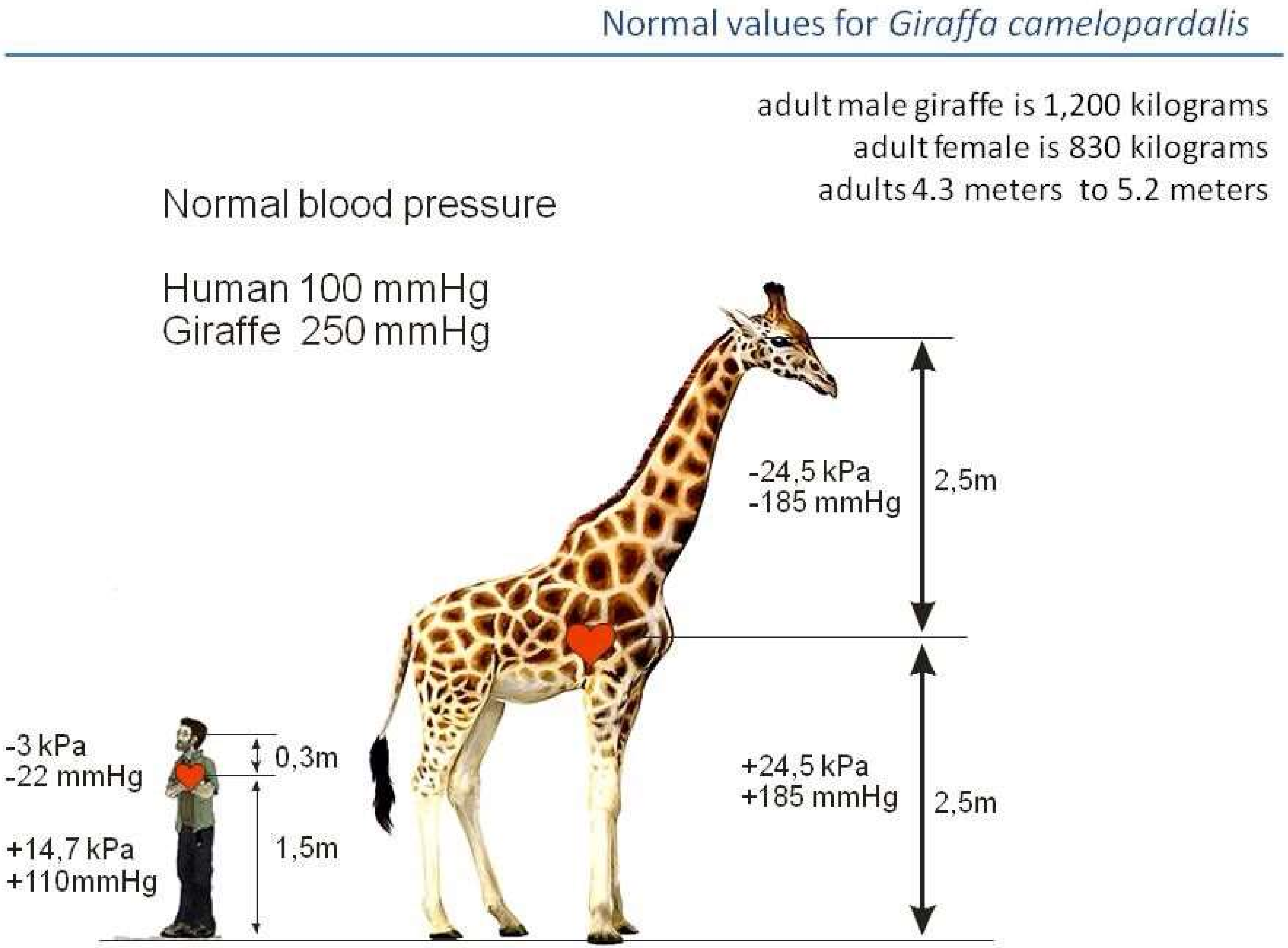

50 mm Hg
pressure
10 mm Hg
pressure
ΔP = 40 mm Hg
Vessel 1
90 mm Hg
pressure
10 mm Hg
pressure
ΔP = 80 mm Hg
Vessel 2
180 mm Hg
pressure
100 mm Hg
pressure
ΔP = 80 mm Hg
Vessel 3

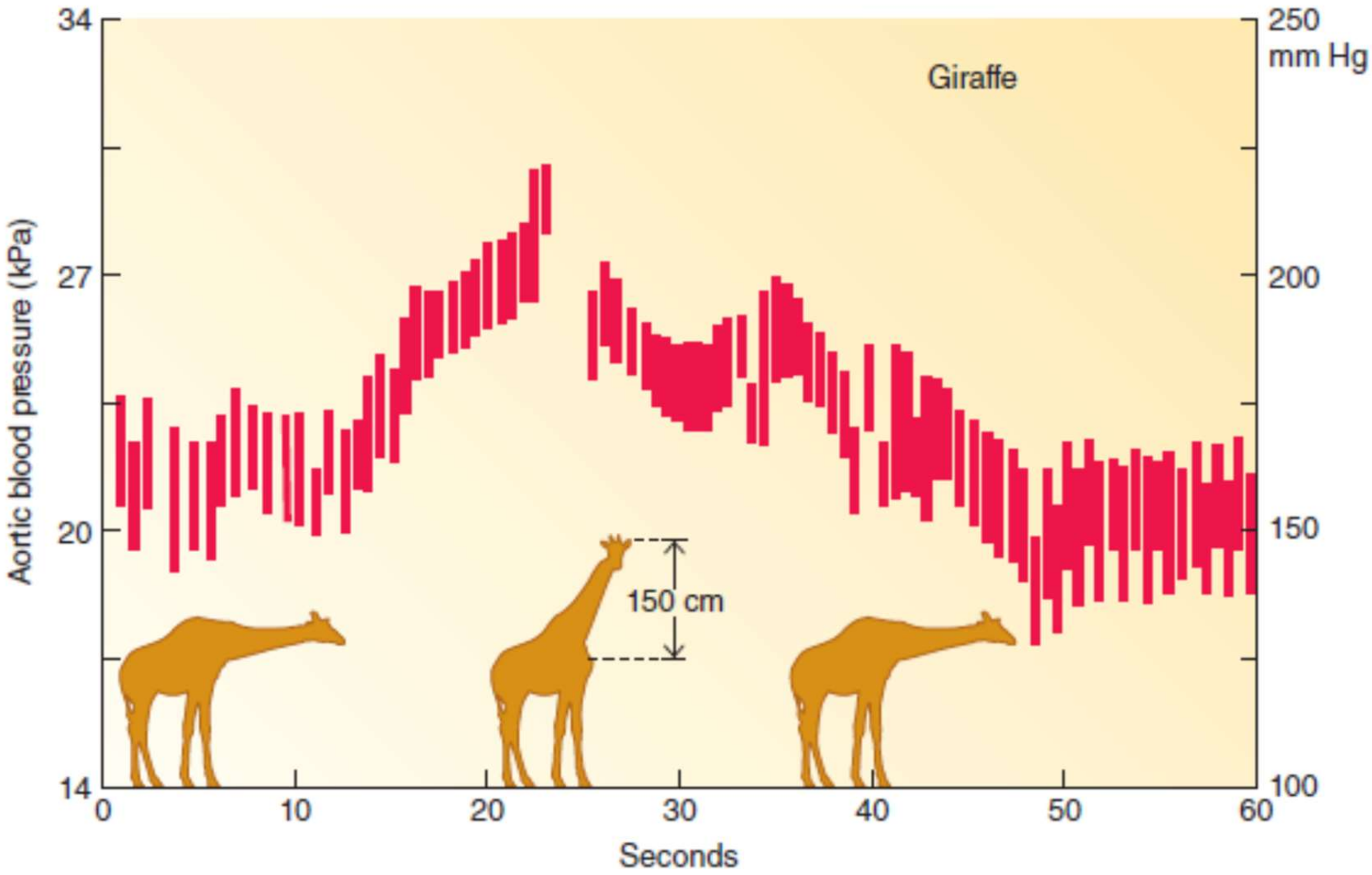

50 mm Hg pressure
10 mm Hg pressure
ΔP = 40 mm Hg
Vessel 1
90 mm Hg pressure
10 mm Hg pressure
ΔP = 80 mm Hg
Vessel 2
ΔP in vessel 2 = 2 times that of vessel 1
Flow in vessel 2 = 2 times that of vessel 1
180 mm Hg pressure
100 mm Hg pressure
ΔP = 80 mm Hg
Vessel 3
ΔP in vessel 3 = the same as that of vessel 2, despite the larger absolute values
Flow in vessel 3 = the same as that of vessel 2



- ✓ The greater the pressure gradient forcing blood through a vessel, the greater the rate of flow through that vessel

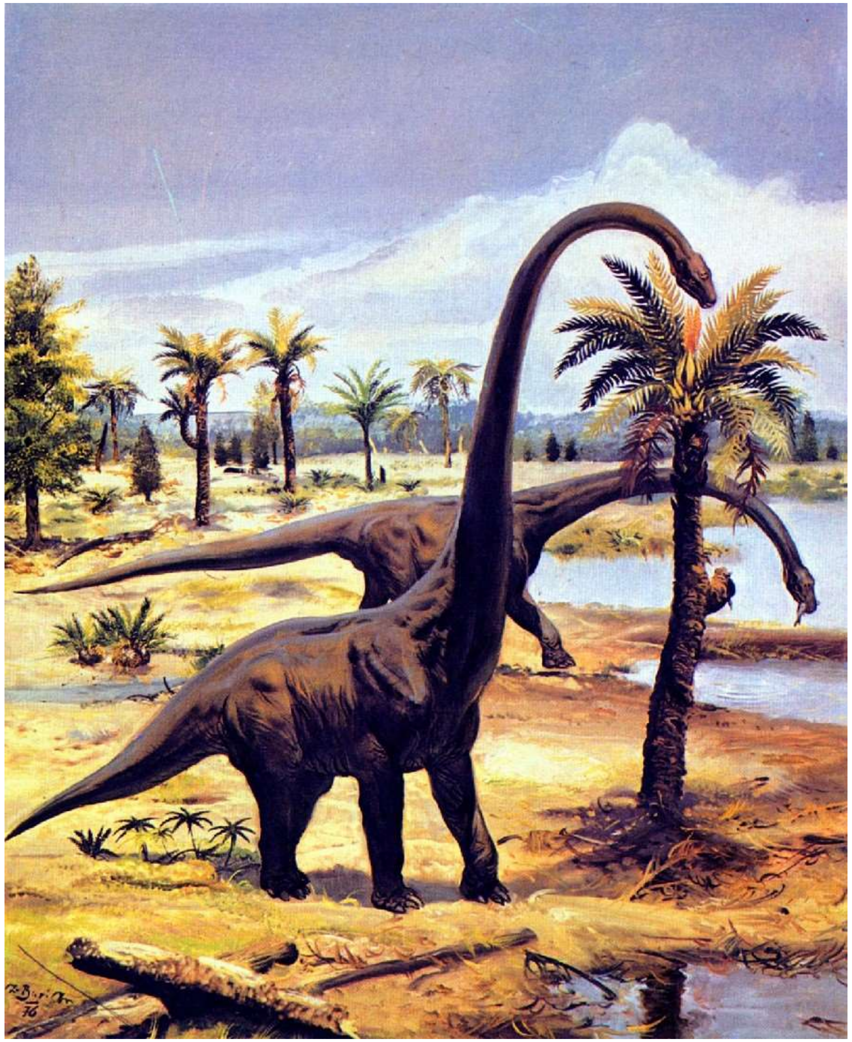
Gravity


Normal values for *Giraffa camelopardalis*
adult male giraffe is 1,200 kilograms
adult female is 830 kilograms
adults 4.3 meters to 5.2 meters
Normal blood pressure
Human 100 mmHg
Giraffe 250 mmHg
-24,5 kPa
-185 mmHg
2,5m
+24,5 kPa
+185 mmHg
2,5m
-3 kPa
-22 mmHg
0,3m
+14,7 kPa
+110mmHg
1,5m



To to ensure oxygen supply to its brain, the average driving pressure needs to be about 200 mm Hg!

How could a brachiosaur pump blood to its brain?

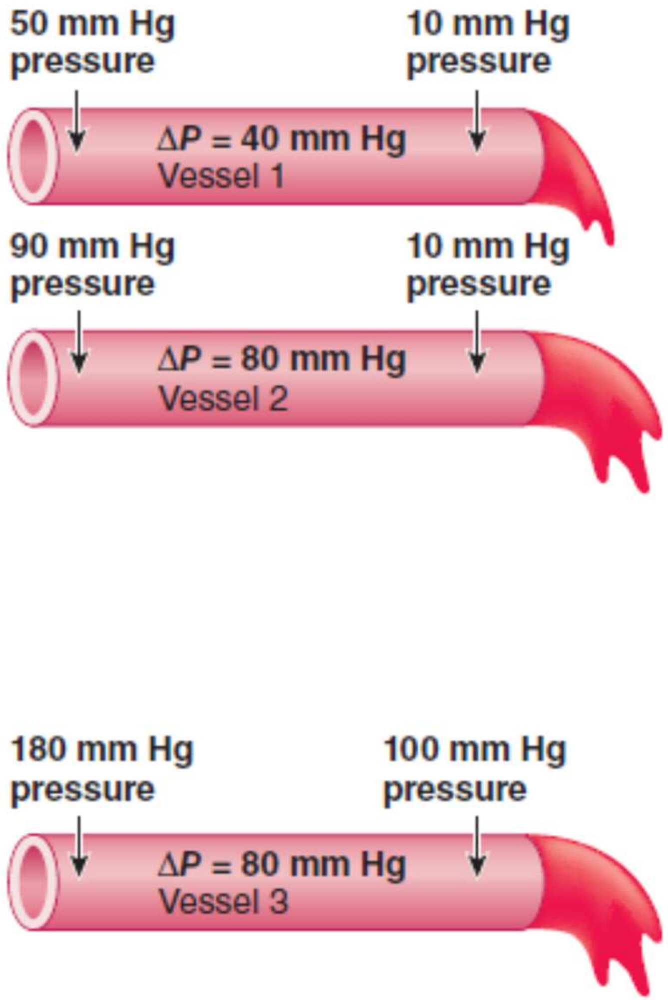


Choy and Altman, 1992, Lancet https://doi.org/10.1016/0140-6736(92)91722-K

Resistance

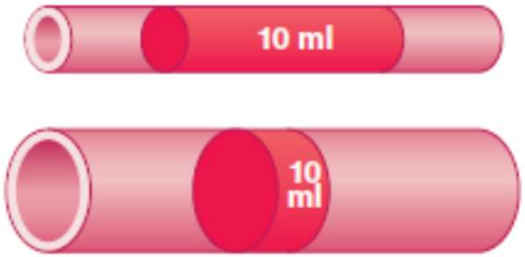
$$Q = \Delta P / R$$

The other factor influencing flow rate through a vessel is the resistance (R), which is a measure of the hindrance to blood flow through a vessel caused by friction between the moving fluid and the stationary vascular walls.



- ✓ Contraction of the heart imparts pressure to the blood, but because of frictional losses (resistance), the pressure decreases as blood flows through a vessel

- ✓ When resistance increases, the pressure gradient ΔP must increase correspondingly to maintain the same flow rate. Accordingly, when the vessels offer more resistance to flow, the heart must work harder to maintain adequate circulation.

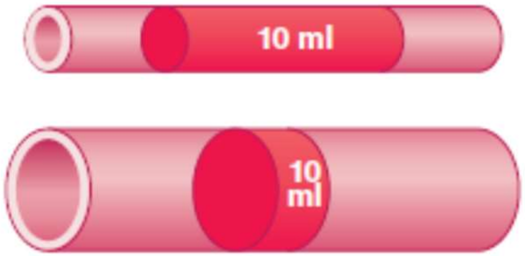


(a) Comparison of contact of a given volume of blood with the surface area of a small-radius vessel and a large-radius vessel

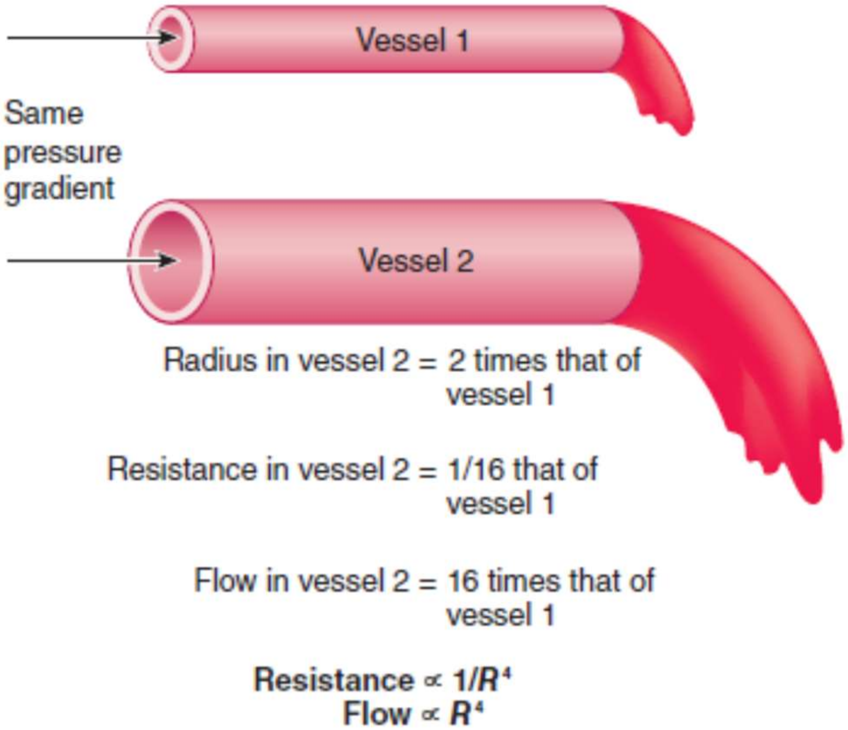
The exact relationship, for idealized laminar, non-pulsatile flow in a rigid tube, is:

$$R = 8\eta L/\pi r^4$$

viscosity of the fluid, η
Vessel *length, L*
vessel *radius, r*



(a) Comparison of contact of a given volume of blood with the surface area of a small-radius vessel and a large-radius vessel



(b) Influence of vessel radius on resistance and flow

The exact relationship, for idealized laminar, non-pulsatile flow in a rigid tube, is:

$$R = 8\eta L/\pi r^4$$

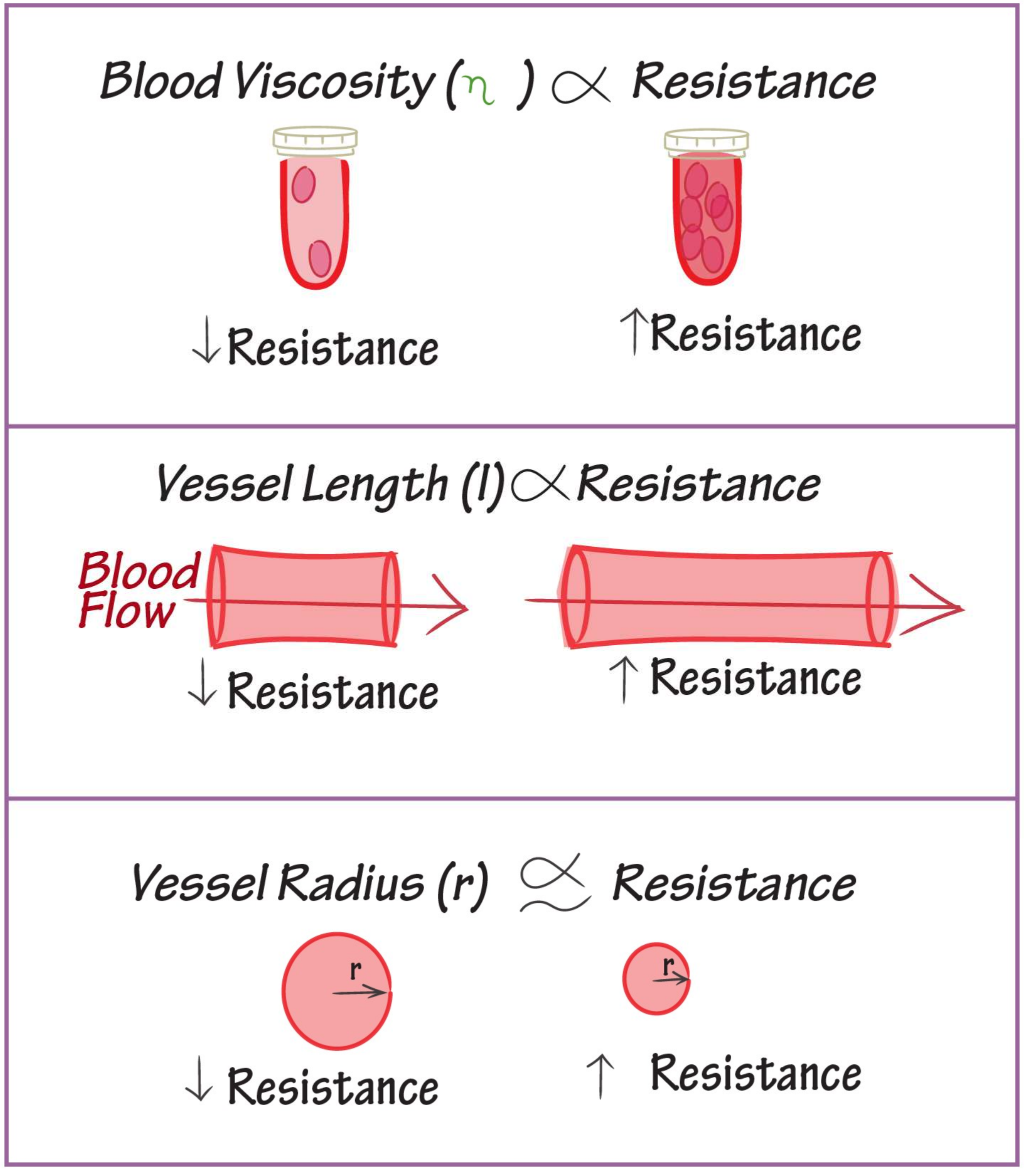
viscosity of the fluid, η

Vessel *length, L*

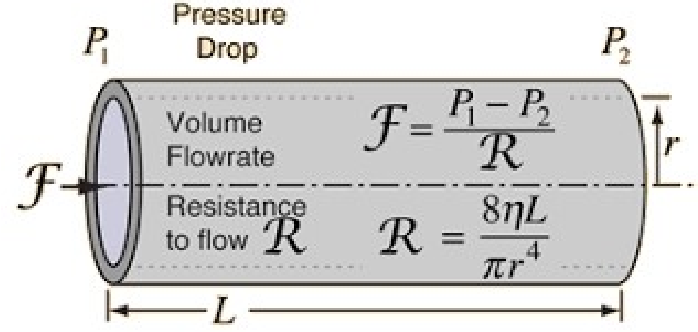
vessel *radius, r*

$$R = 8\eta L/\pi r^4$$

Determinants of Resistance:



Poiseuille's Law

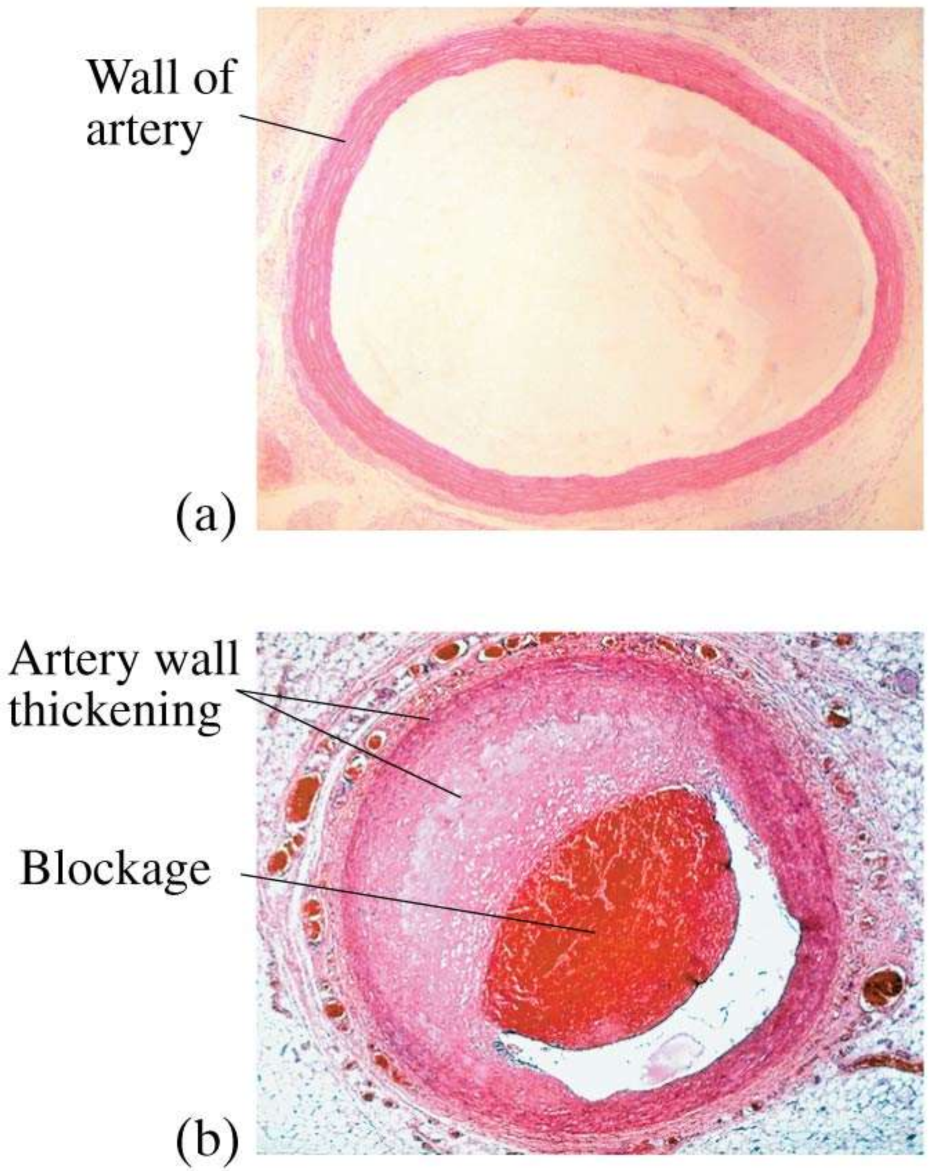


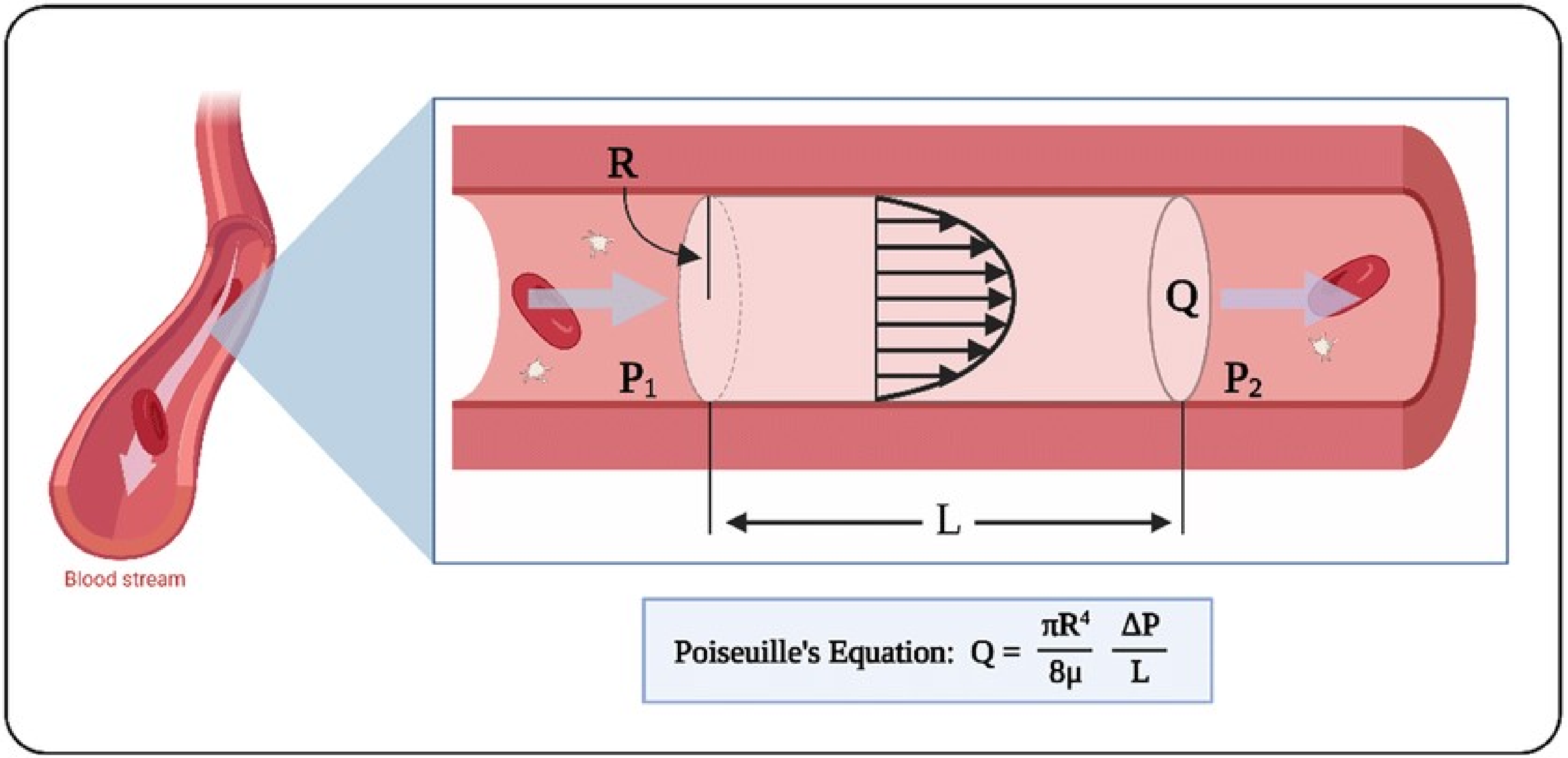
The rate of flow in a fluid in a round tube depends on the viscosity of the fluid, the pressure difference, and the dimensions of the tube.

$$Q = \frac{\Delta P \pi r^4}{8 \eta l}$$

Q = volume flux
ΔP = change in pressure
r = pipe or vessel radius
η = viscosity
l = pipe or vessel length

The volume flow rate is proportional to the pressure difference, inversely proportional to the length of the tube and to the pressure difference, and proportional to the fourth power of the radius of the tube.

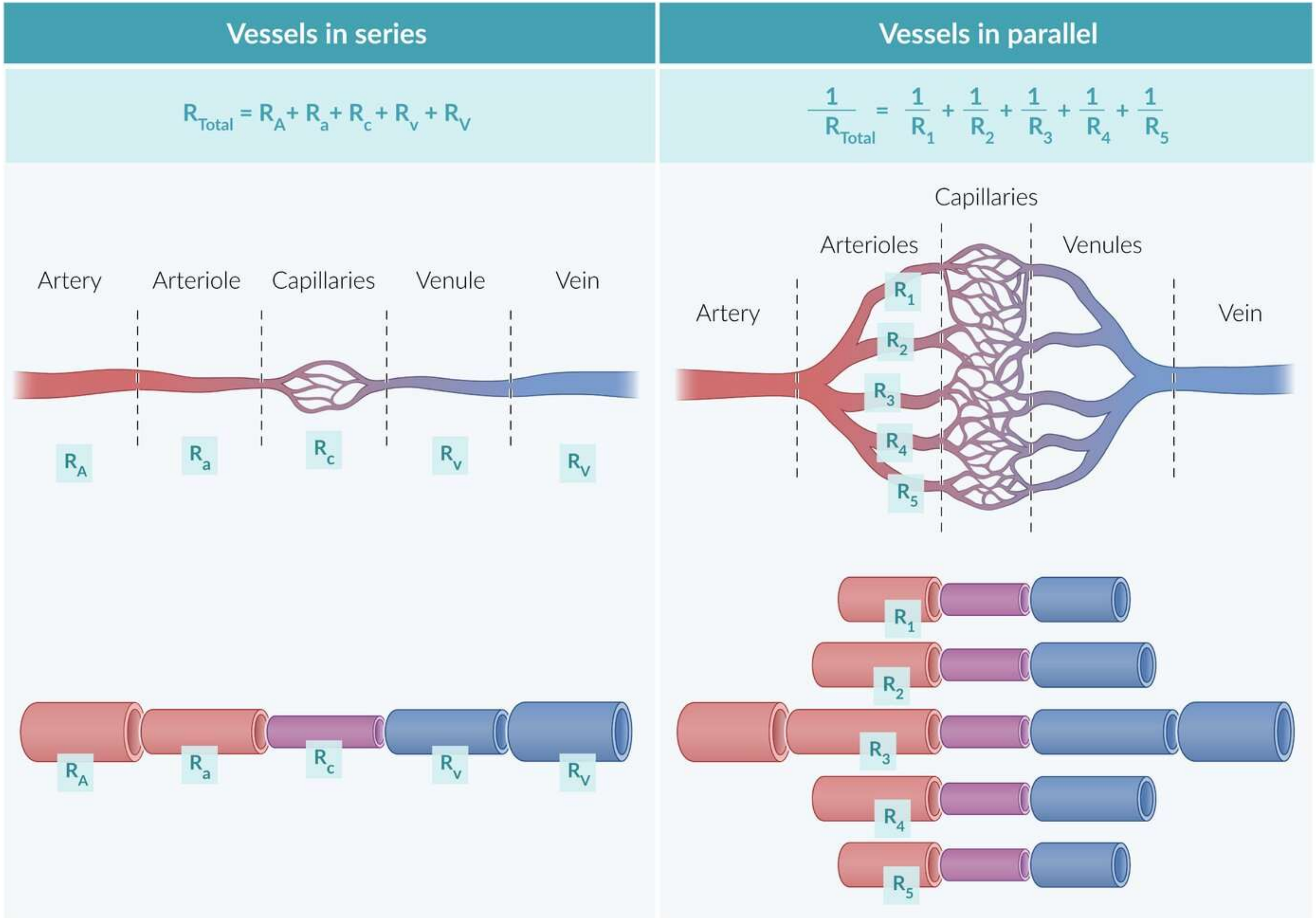

Wall of artery
(a)
Artery wall thickening
Blockage
(b)



This has consequences for blood flow—if the radius of the artery is half what it should be, the pressure has to increase by a factor of 16 to keep the same flow.

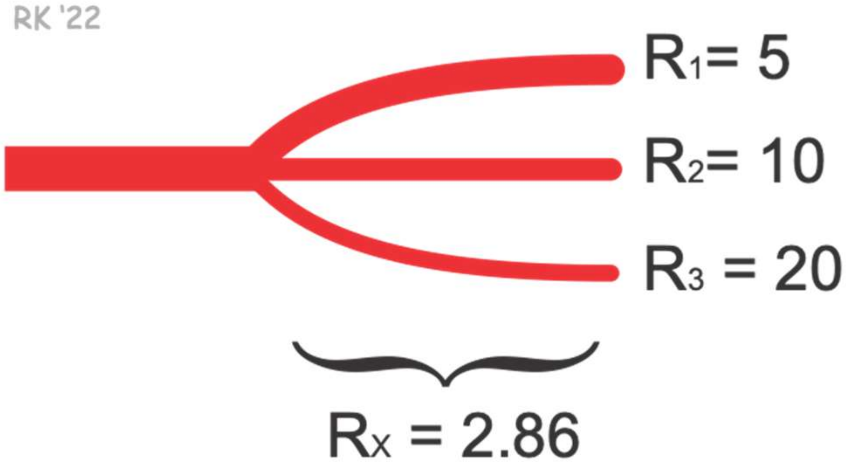
Usually, the heart cannot work that hard, but blood pressure goes up as it tries.

how is flow directed and regulated?



Assume, $R_A = 20$, $R_a = 50$, $R_c = 20$, $R_v = 6$, $R_V = 4$

Therefore, $R_T = 20 + 50 + 20 + 6 + 4 = 100$ *mm Hg / ml / s*

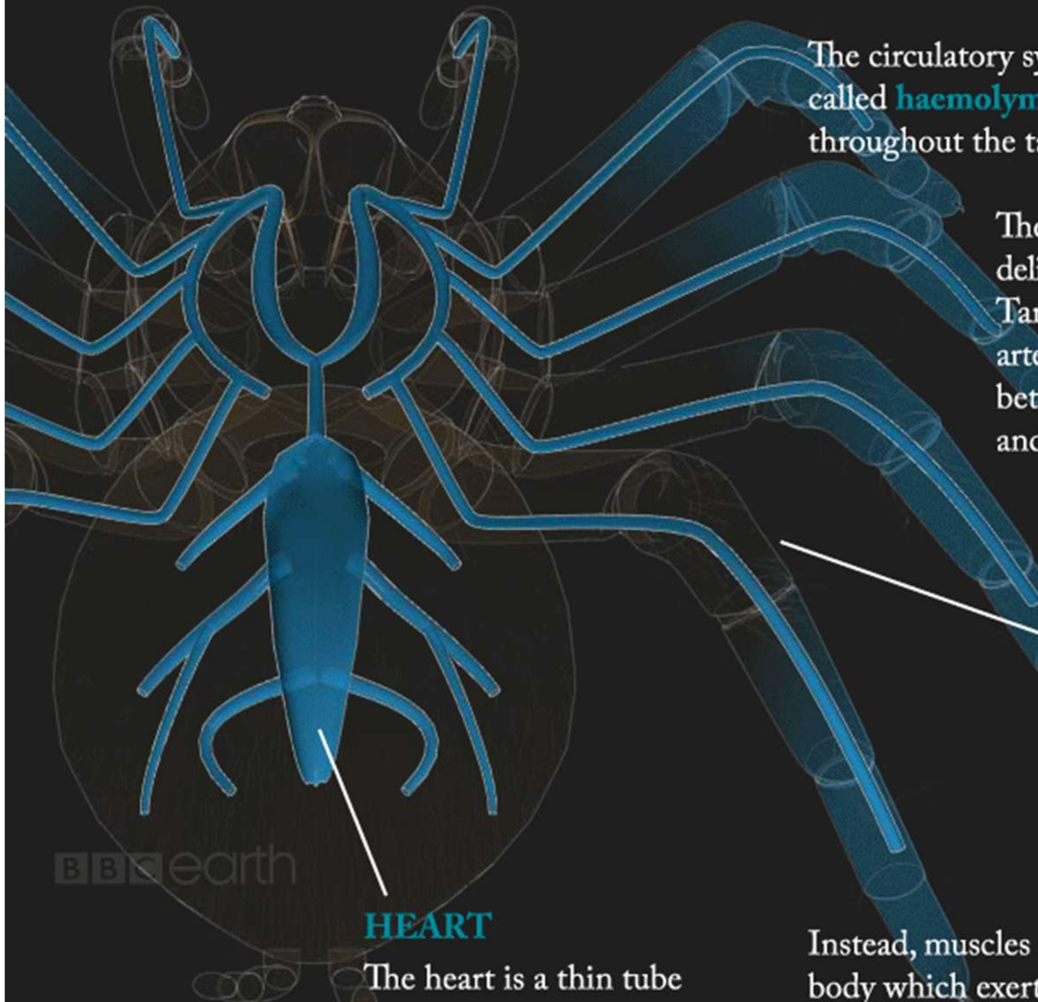


$$R_X = \frac{1}{1/R_1 + 1/R_2 + 1/R_3}$$

1.The total resistance of a network of parallel vessels is less than the resistance of the vessel having the lowest resistance. Therefore, a parallel arrangement of vessels reduces resistance to blood flow. That is why capillaries, which have the highest resistance of individual vessels because of their small diameter, comprise only a small portion of the total vascular resistance of an organ or microvascular network.

2.When there are many parallel vessels, changing the resistance of a few of these vessels will have a relatively small effect on total resistance for the segment.

CIRCULATION & MOVEMENT



The circulatory system is filled with a clear fluid called **haemolymph** which pumps from the heart throughout the tarantula's body.

There's no network of capillaries to deliver blood to tissues as in humans. Tarantula blood flows through arteries into pockets (called **lacunae**) between tissues, bathing the tissue, and eventually back to the heart.

HEART

The heart is a thin tube on the inside-top surface of the abdomen.

MOVEMENT

Tarantulas have flexor muscles that contract to curl legs inward, however, some leg joints lack extensor muscles to extend them outward again.

Instead, muscles are tightened within the spider's body which exerts pressure on blood in the legs, causing them to extend; something like squeezing one side of a water balloon.

When tarantulas and other spiders die, their legs curl permanently inward.

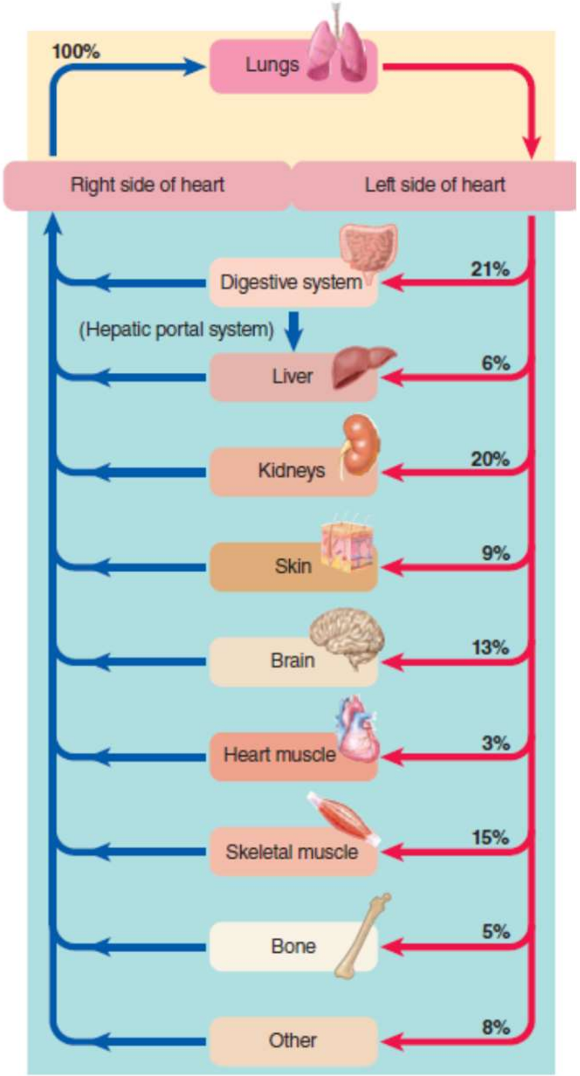
Circulatory Pathways and Vessels: Closed Circulation

Parallel and series flow are both important for reconditioning the blood.

The organs that recondition the fluid may receive substantially more blood than necessary to meet their basic metabolic needs so they can perform homeostatic adjustments.

- ✓ To maximize gas exchange with the environment, gills of most fishes and lungs of birds and mammals receive all of the blood flow, that is, in series.
- ✓ Similarly, all blood flows from the heart of a cephalopod to its two gills, then to its two auxiliary (branchial) hearts.

Distribution of cardiac output at rest

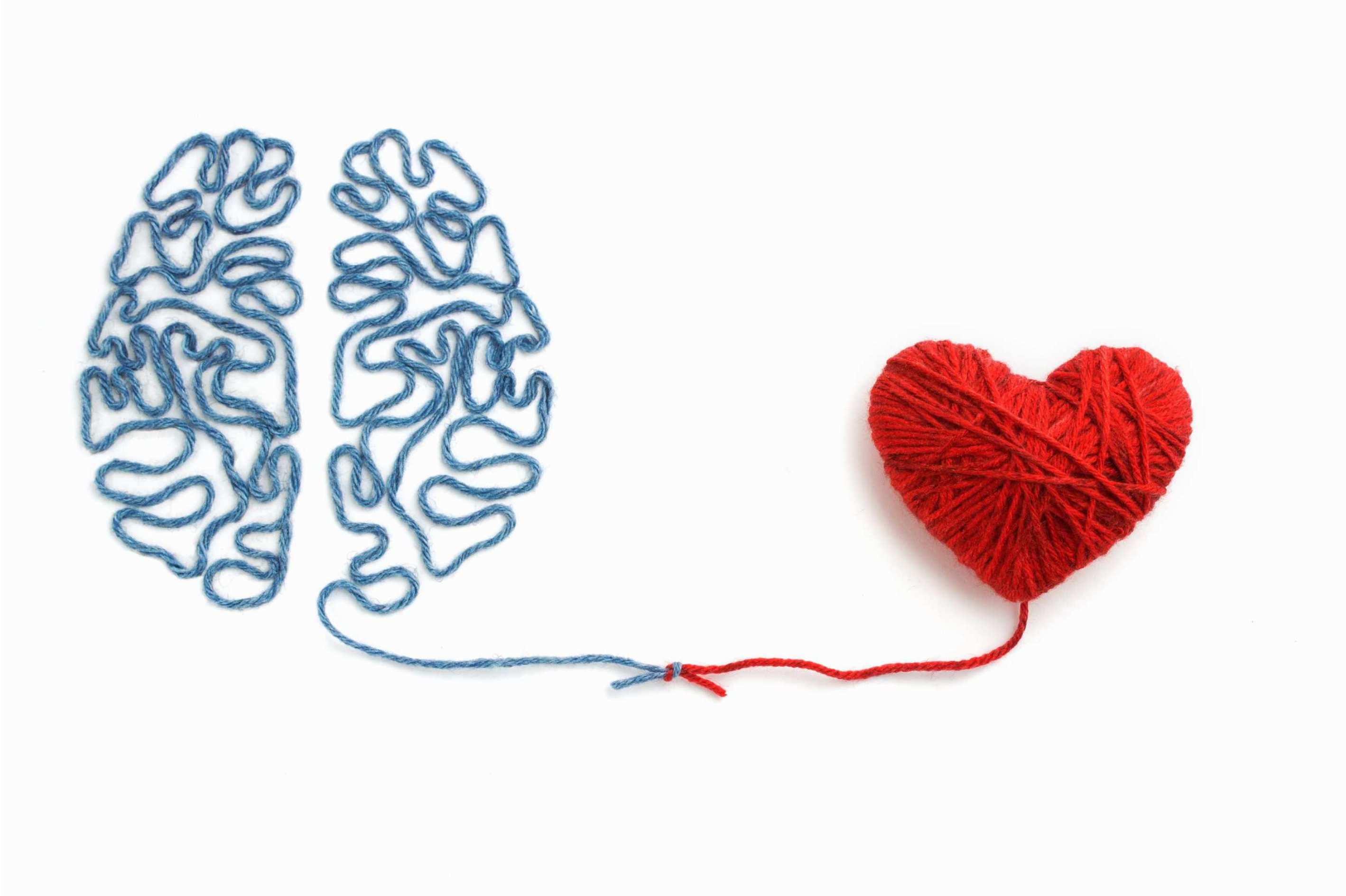


Values are for a typical human.

The lungs receive all the blood pumped out by the right side of the heart, whereas the systemic organs each receive a portion of the blood pumped out by the left side of the heart.

This distribution of cardiac output can be adjusted as needed.

Because reconditioning organs receive blood flow in excess of their own needs, they can withstand temporary reductions in blood flow much better than can organs that do not have this extra margin of blood supply.



WHAT IS A ZEBRAFISH?

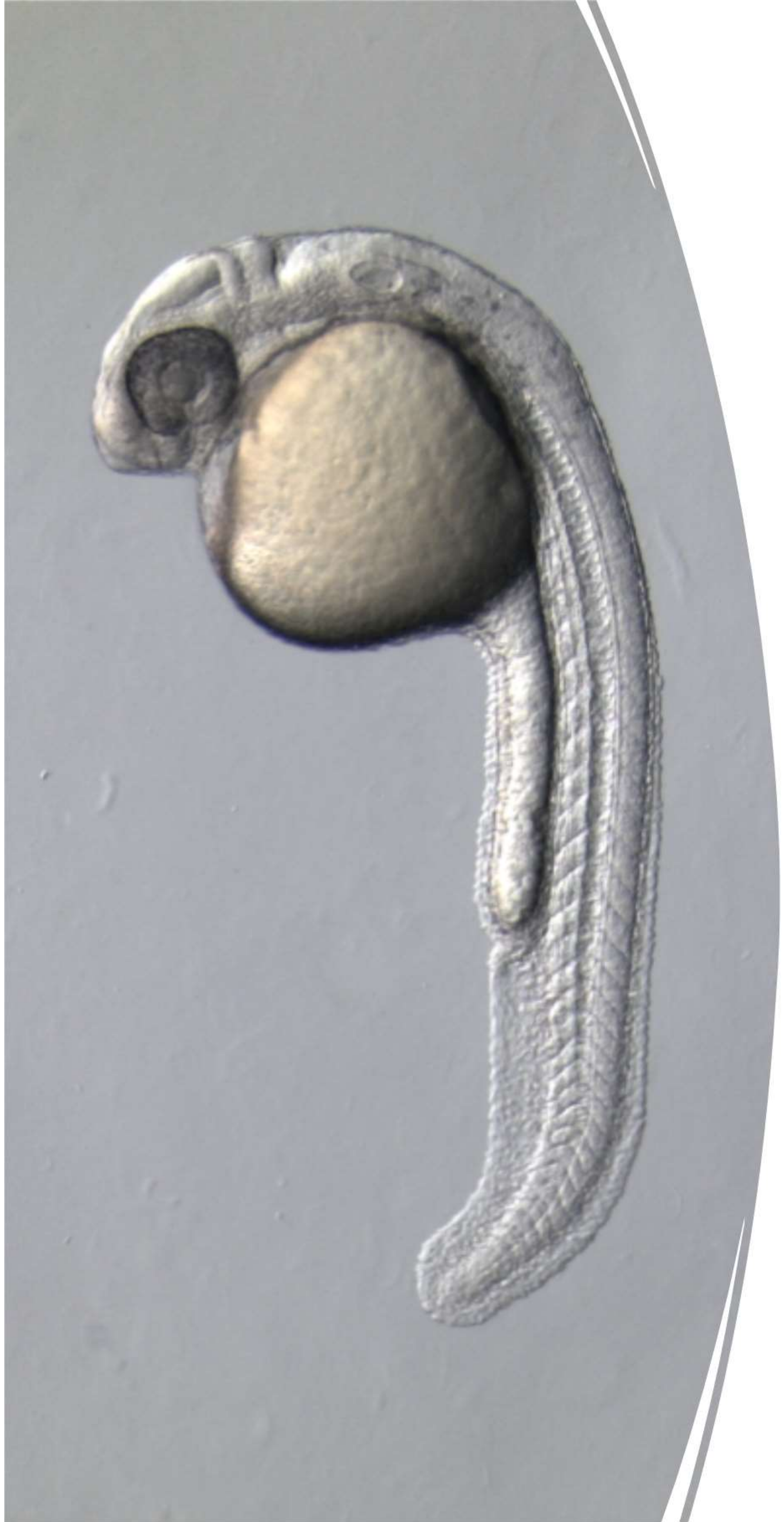
- *Danio rerio*
- Small freshwater fish from South Asia.
- 4 cm long when fully grown.
- Common aquarium fish.
- Very easy to look after.

WHAT IS A MODEL ORGANISM?

- Non-human species widely studied to understand human disease.

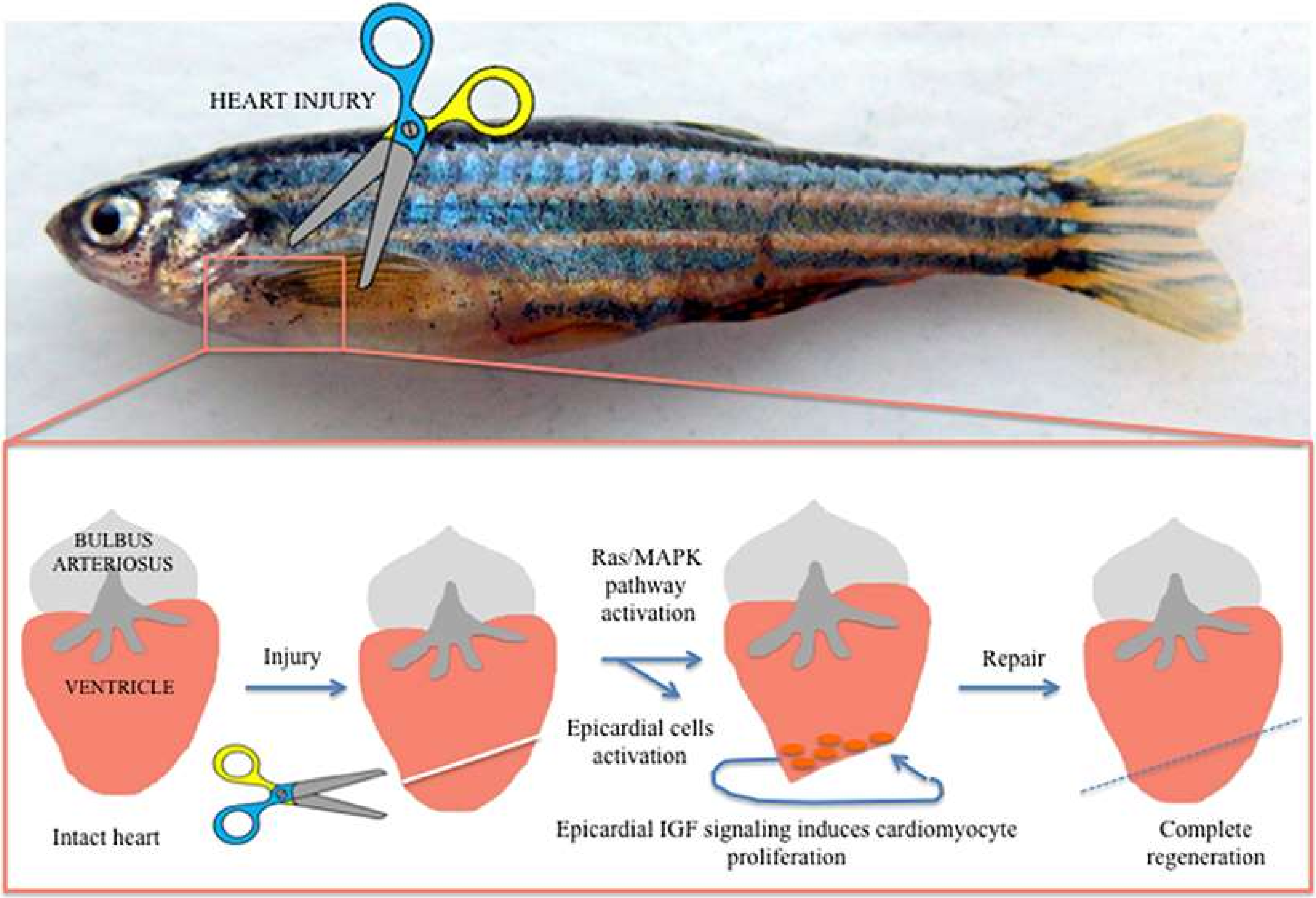
- Model organisms are used when experimentation using humans is unfeasible or unethical.

Zebrafish are good genomic models



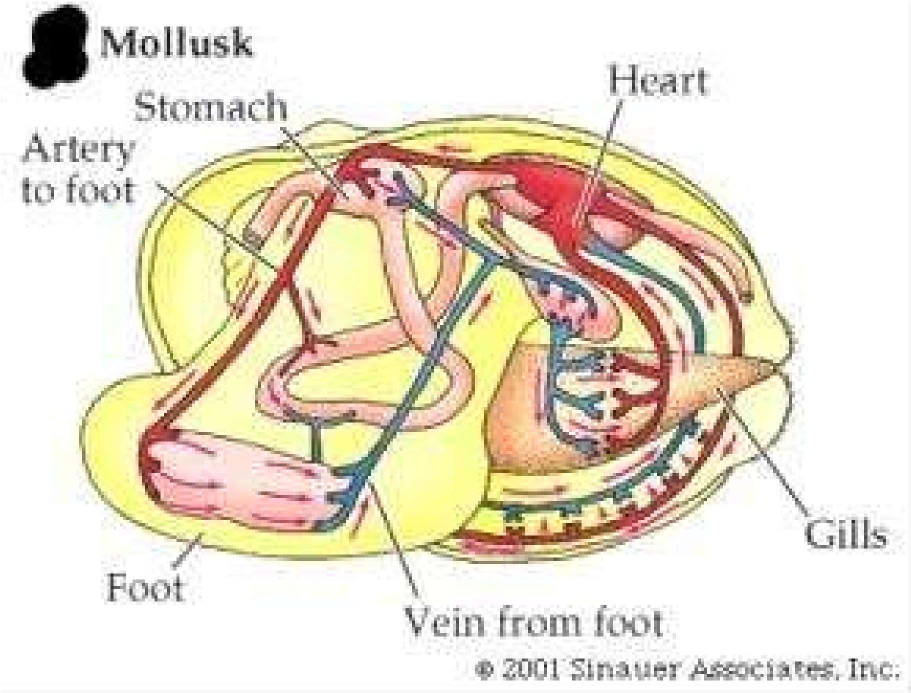
WHY USE ZEBRAFISH?

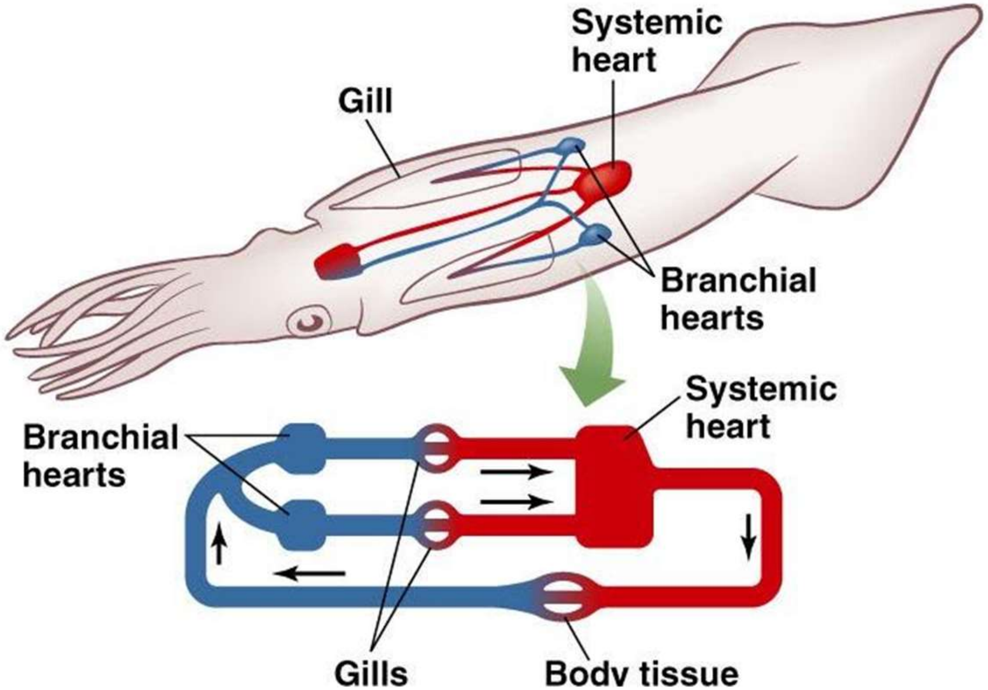
- Small size.
- It develops quickly. All major organs present within 5 days post fertilisation.
- Short generation time (3-4 months).
- Produces 300-400 eggs every 2 weeks.
- Translucent embryos.
- Lots of genome resources available.



Beffagna 2019, Front. Cardiovasc. Med https://doi.org/10.3389/fcvm.2019.00107

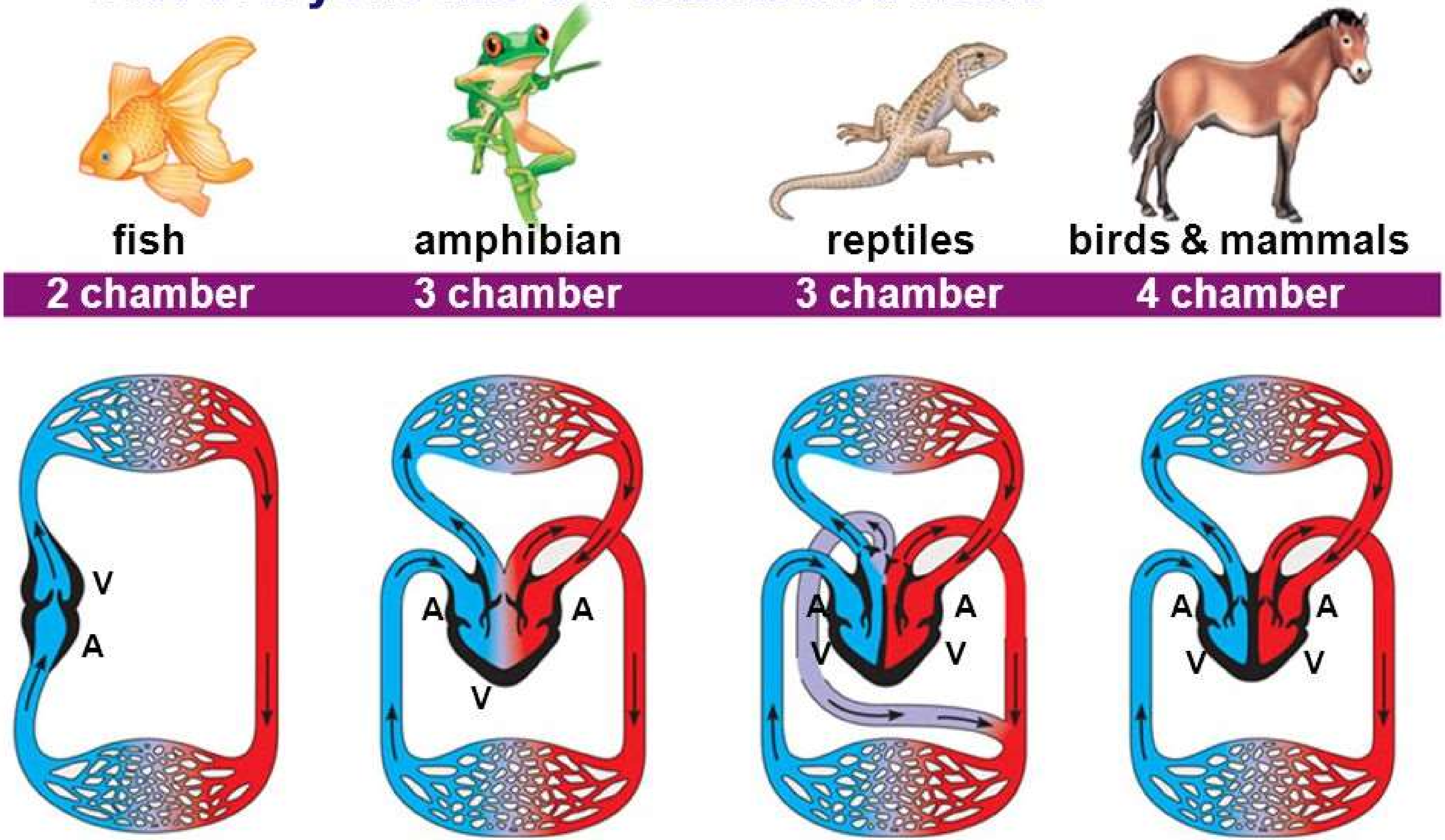
Closed systems are often said to have evolved in the most metabolically active animals because they allow more rapid and more precise control of oxygen delivery to the tissues that need it the most.





Evolution of circulatory system

Not everyone has a 4-chambered heart

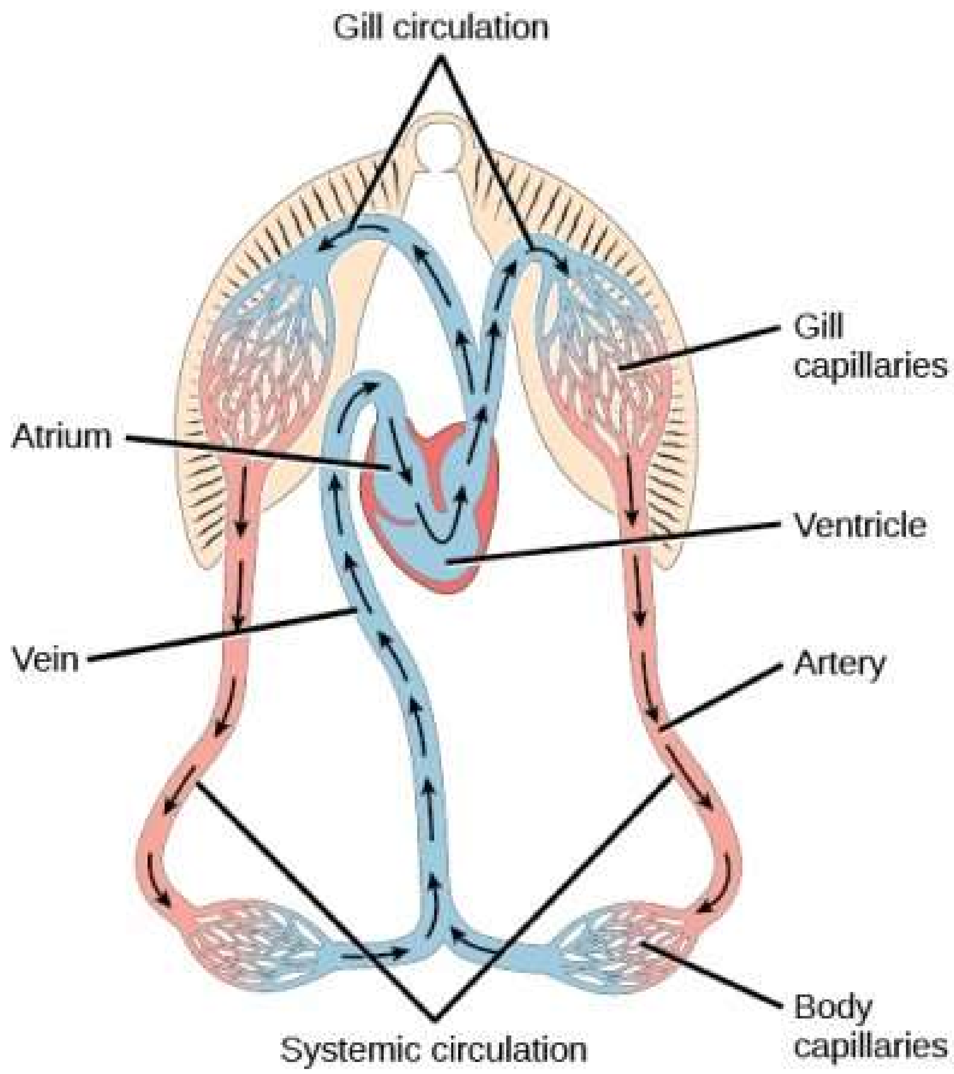


Fish have the simplest circulatory systems of the vertebrates: blood flows unidirectionally from the two-chambered heart through the gills and then the rest of the body.

1. **Gill circulation**

2. **Systemic circulation**

Systemic heart → gills → body organs and sinuses → (auxiliary hearts) → systemic heart



(a) Fish

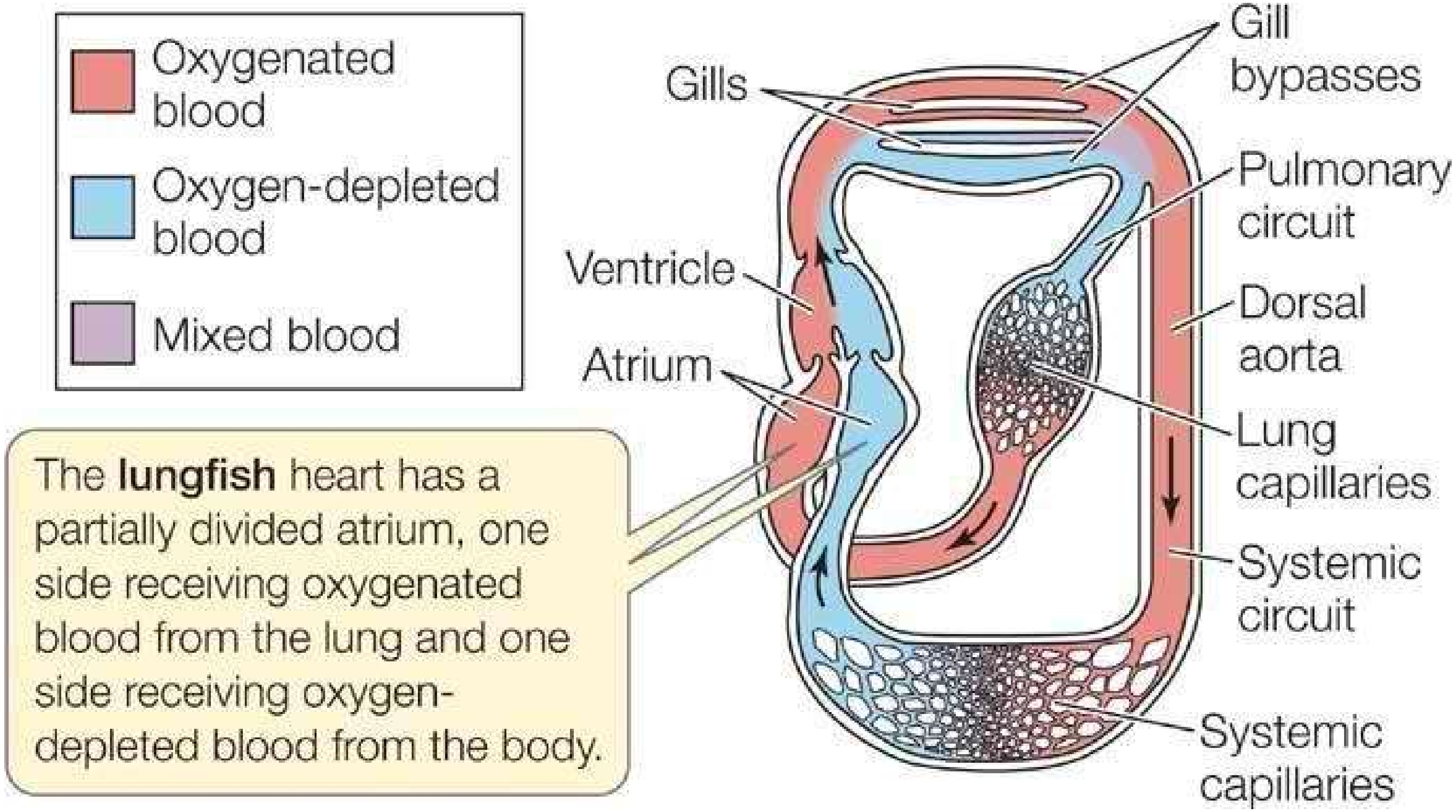
The result is a limit in the amount of oxygen that can reach some of the organs and tissues of the body, reducing the overall metabolic capacity of fish.

In amphibians, reptiles, birds, and mammals, blood flow is directed in two circuits: one through the lungs and back to the heart, which is called pulmonary circulation, and the other throughout the rest of the body and its organs including the brain (systemic circulation).

Air-breathing fishes such as lungfish evolved new respiratory organ, the lung, in addition to gills.

This required a separate circuit, because the lung is not always used by these fishes.

In lungfish, the flow to the lungs occurs after the gills, where the blood can either go to the body (during water breathing), or be diverted to the lungs (during air breathing)



Right side of heart → gills → body organs →
right side of heart (water breathing)
Right side of heart → gills → lungs → left side of heart →
body organs → right side of heart (air breathing)

The vertebrate vascular system evolved from one circuit to two separate circuits

In the vertebrates, the closed system presumably began as a simple loop:

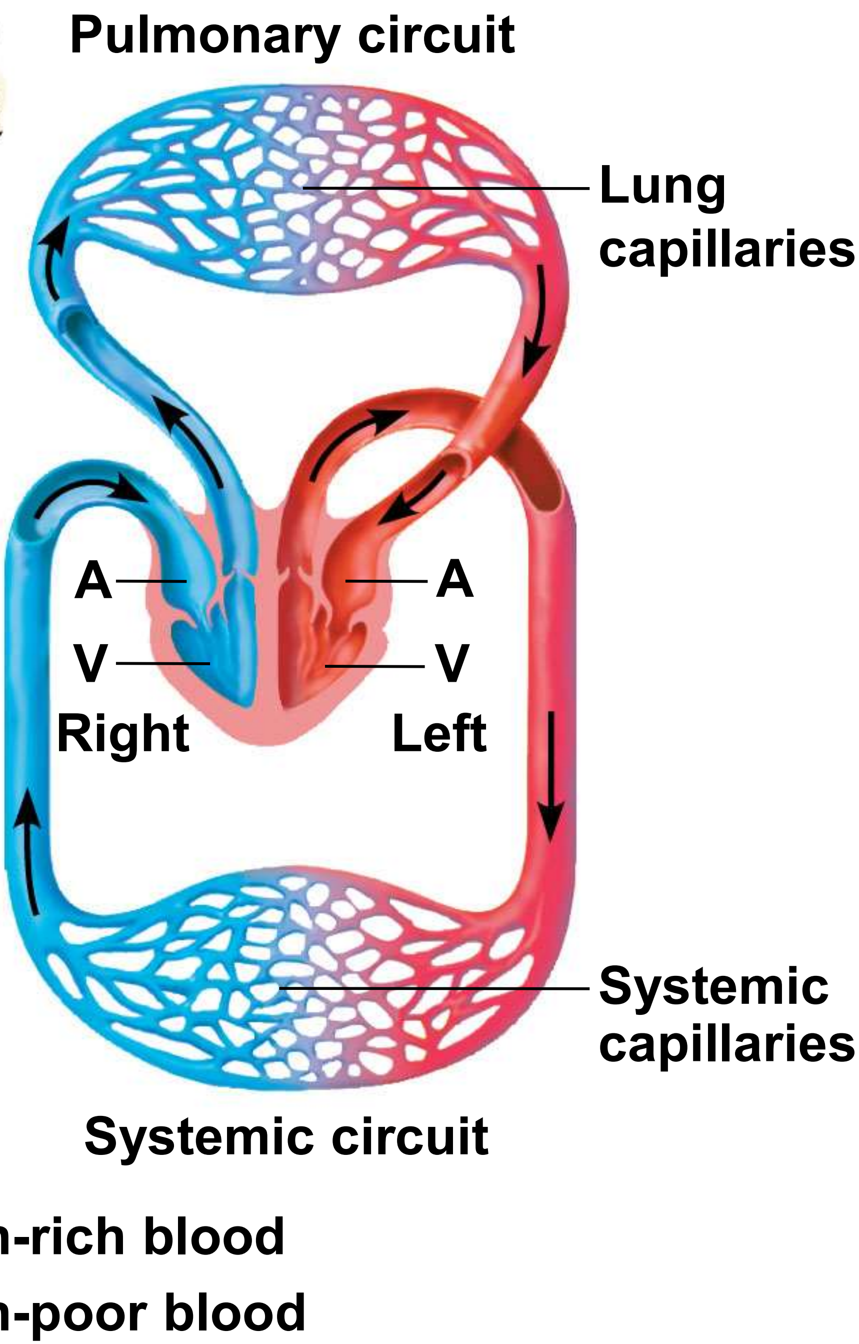
Heart → artery → gills → aorta and branching parallel arteries → arterioles → capillaries in body organs → veins → heart

As we noted earlier, the flow to the gills is in series with the rest of the circulation, with the rest of the flow in a parallel.

While useful for maximal gas exchange, series flow creates a problem because the tiny diameters of the capillaries in the gills create an enormous resistance to flow.

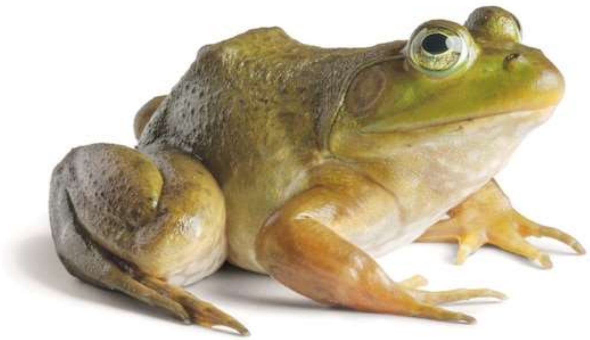
Double circulation

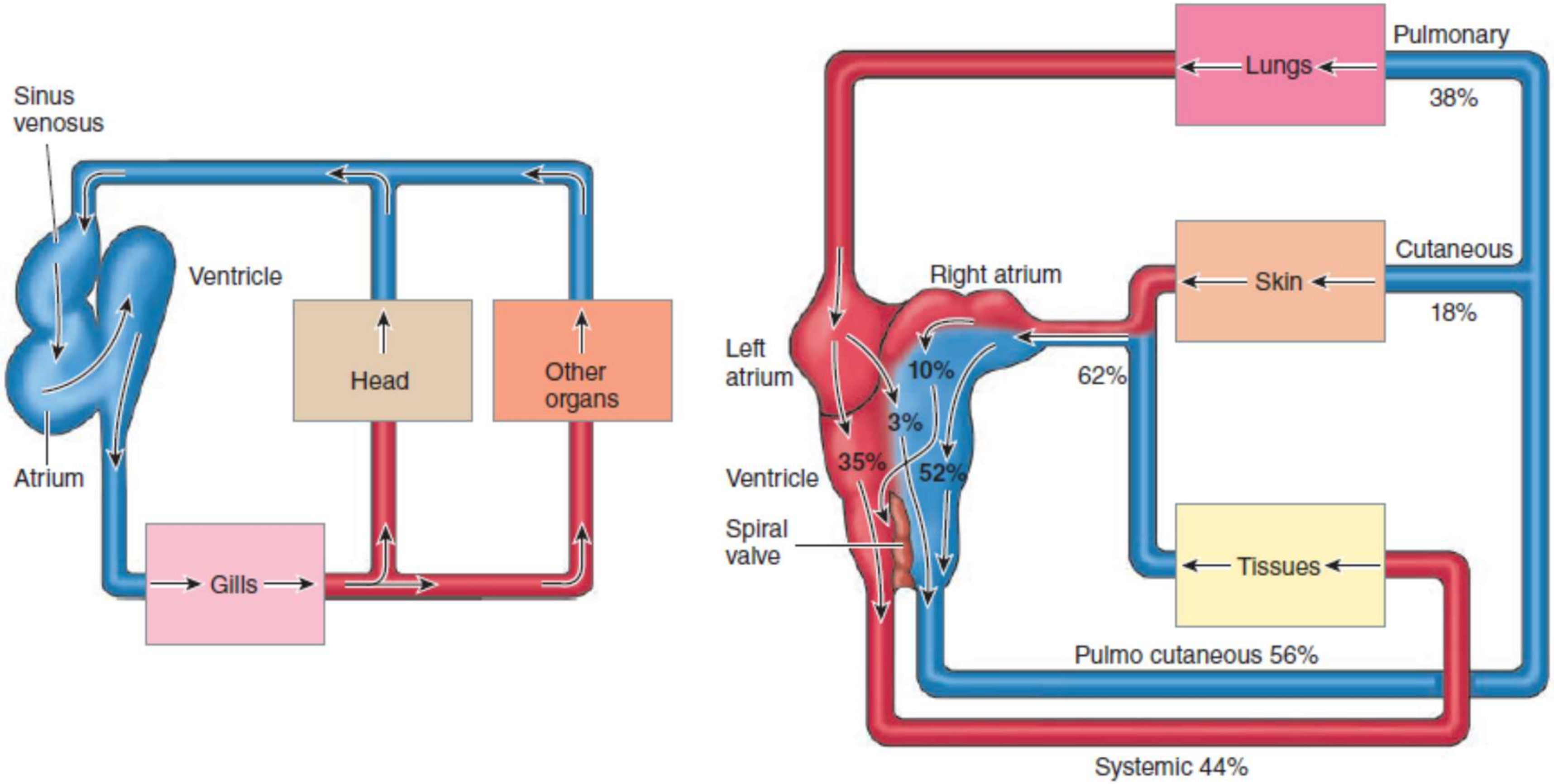
- Amphibian, reptiles, and mammals have **double circulation**
- Oxygen-poor and oxygen-rich blood are pumped separately from the right and left sides of the heart



- In reptiles and mammals, oxygen-poor blood flows through the **pulmonary circuit** to pick up oxygen through the lungs
- In amphibians, oxygen-poor blood flows through a **pulmocutaneous circuit** to pick up oxygen through the lungs and skin
- Oxygen-rich blood delivers oxygen through the **systemic circuit**
- Double circulation maintains higher blood pressure in the organs than does single circulation

Adaptations of Double Circulatory Systems

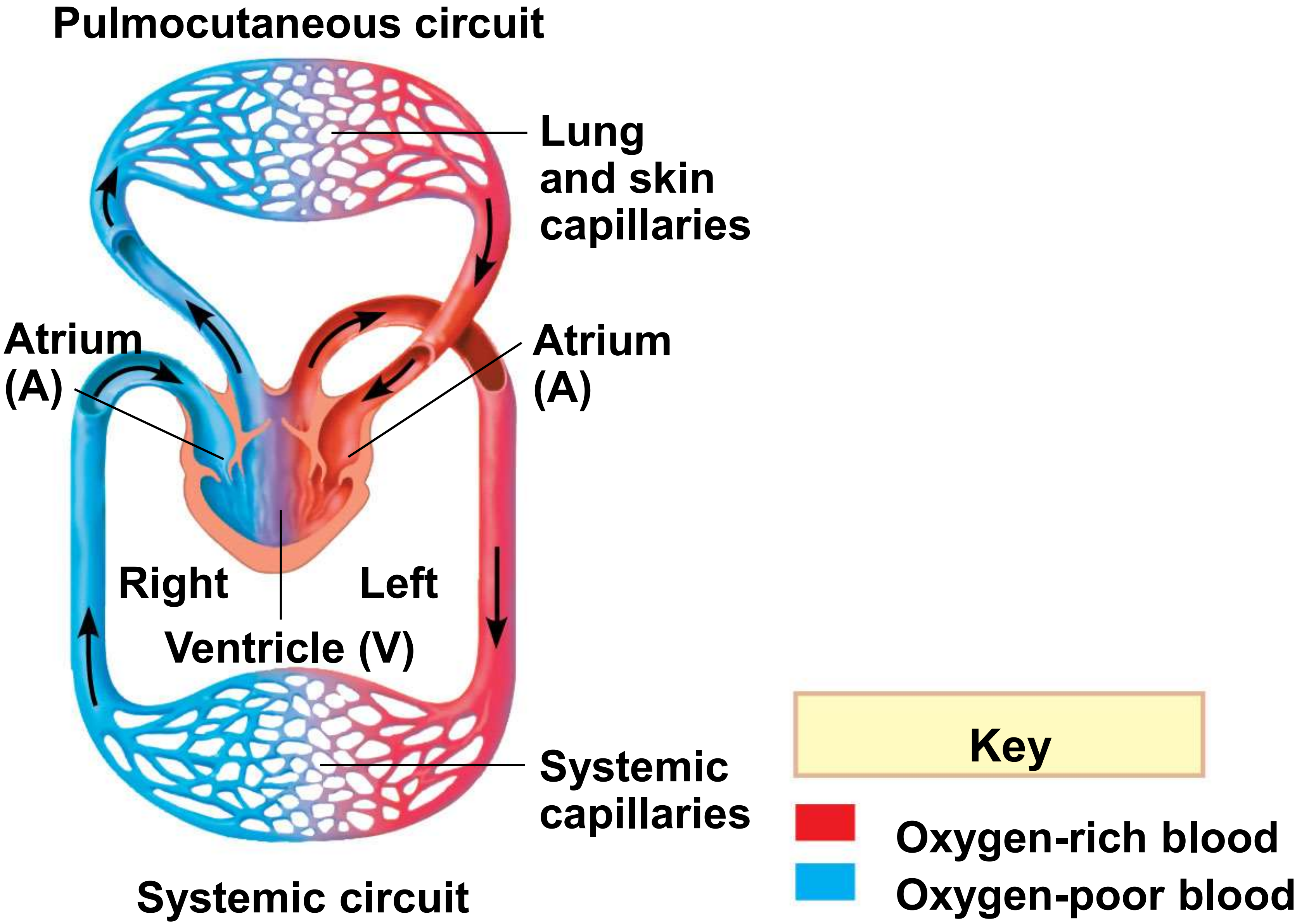




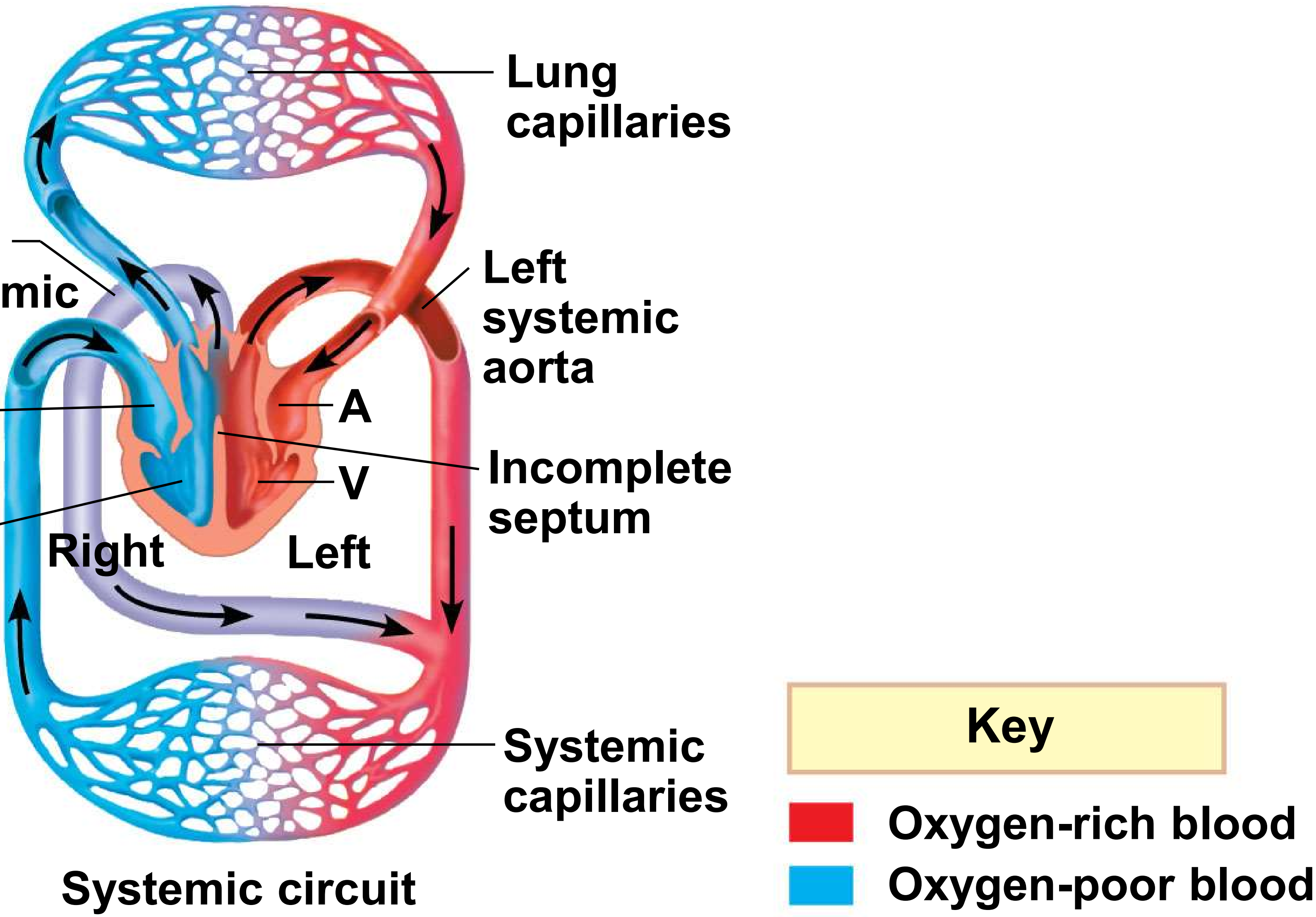
(a) Flow in a bony fish

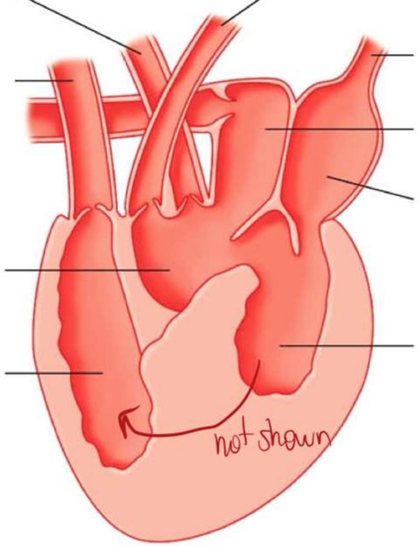
(b) Flow in a bullfrog

Amphibians


Pulmocutaneous circuit
Lung
and skin
capillaries
Atrium
(A)
Atrium
(A)
Right
Left
Ventricle (V)
Systemic
capillaries
Systemic circuit
Key
Oxygen-rich blood
Oxygen-poor blood

Reptiles

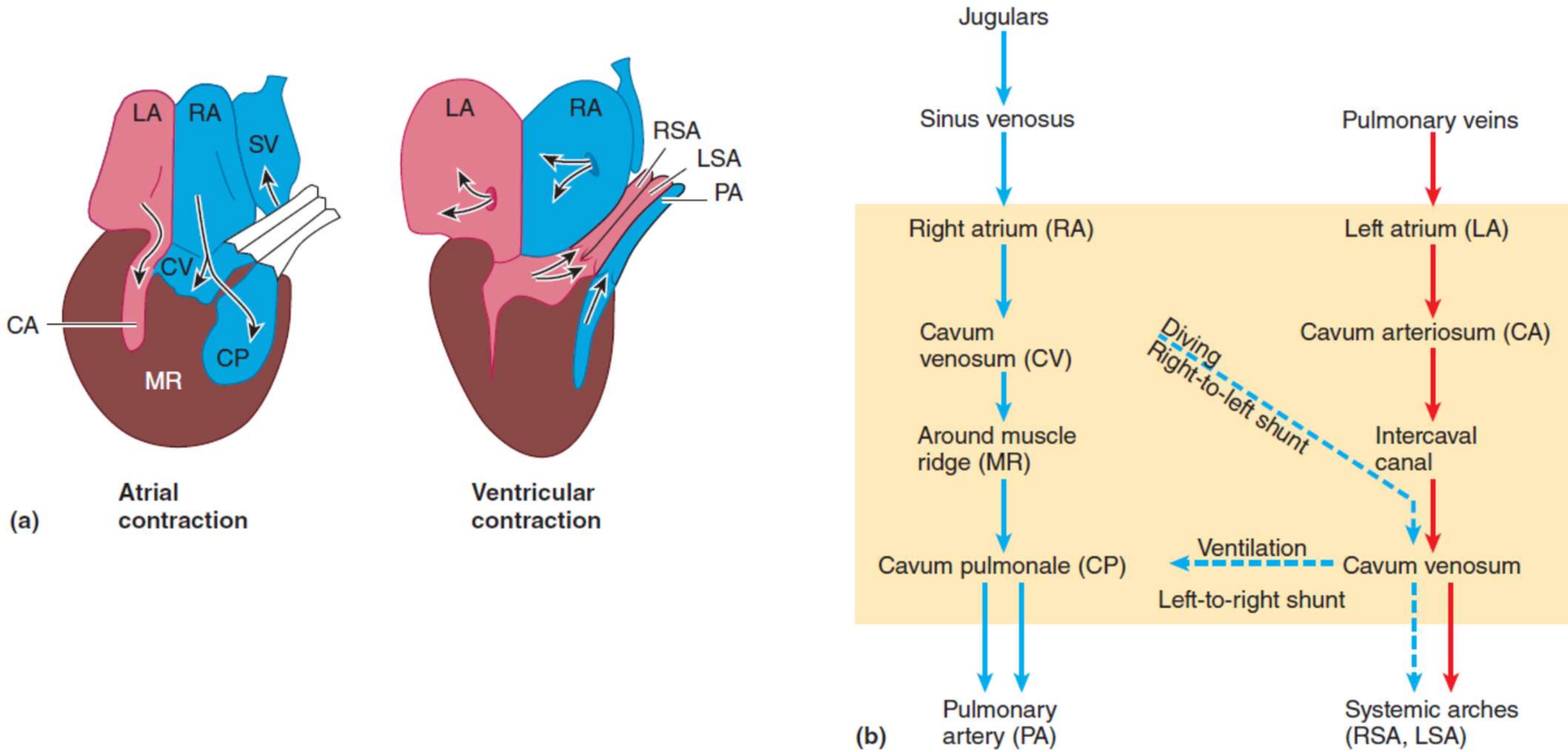

Pulmonary circuit
Lung capillaries
Right systemic aorta
Left systemic aorta
Atrium (A)
A
Incomplete septum
V
Ventricle (V)
Right
Left
Systemic capillaries
Systemic circuit
Key
Oxygen-rich blood
Oxygen-poor blood



(a) Cardiac anatomy of non-crocodilian reptiles

the ventricle is different. In most reptiles, it is one large chamber but has two large subchambers partially divided by thick muscle rather than a true septum: the *cavum arteriosum* and *cavum pulmonale*.

At the top of both (and connected to both) is a small third subchamber, the *cavum venosum*.



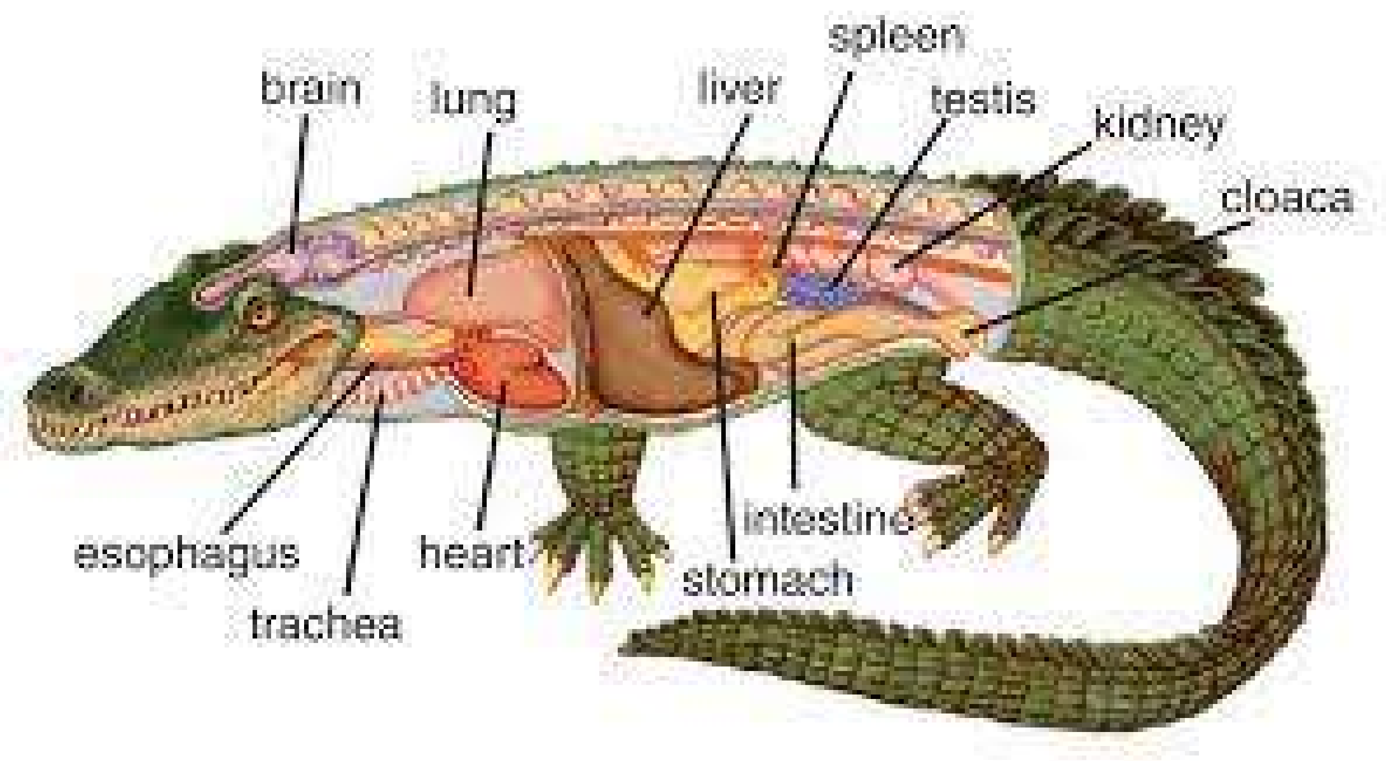
Breathing air

Right atrium → c. venosum → c. pulmonale → lungs →left atrium → c. arteriosum → c. venosum → body organs → right atrium

Diving

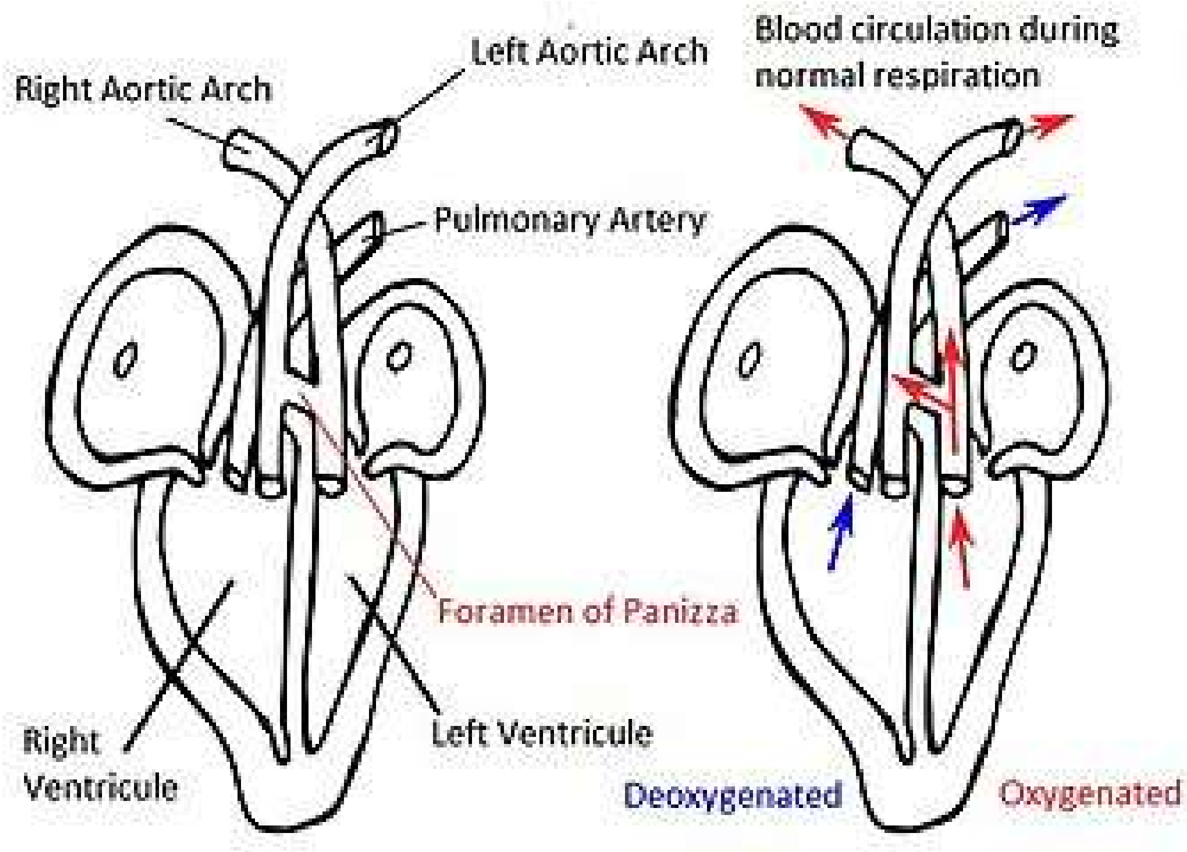
Right atrium → c. venosum → body organs → right atrium

Alligators and crocodiles are the most primitive animals to exhibit a four-chambered heart.

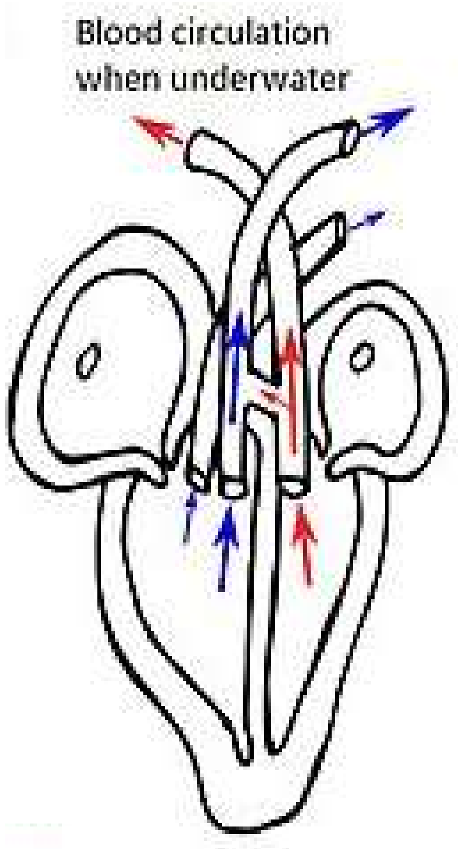


Crocodilians have a completely separated ventricle with deoxygenated blood from the body, or systemic circulation, in the right ventricle and oxygenated blood from the lungs, or pulmonary circulation, in the left ventricle, as in birds and mammals.

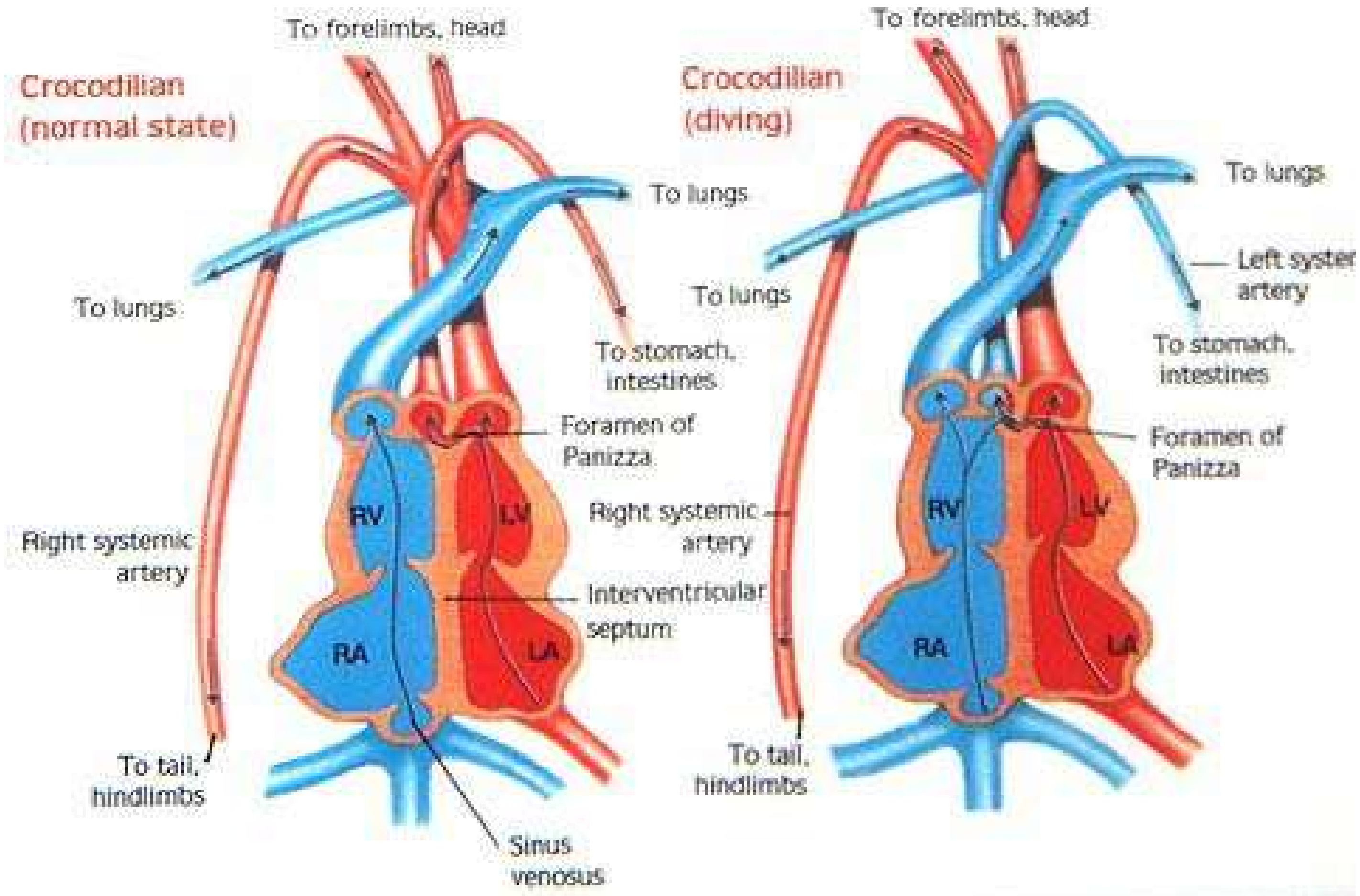
Two vessels, the left aorta and the pulmonary artery, exit the right ventricle. Blood from the right ventricle goes to the lungs through the pulmonary artery, as in mammals and birds.



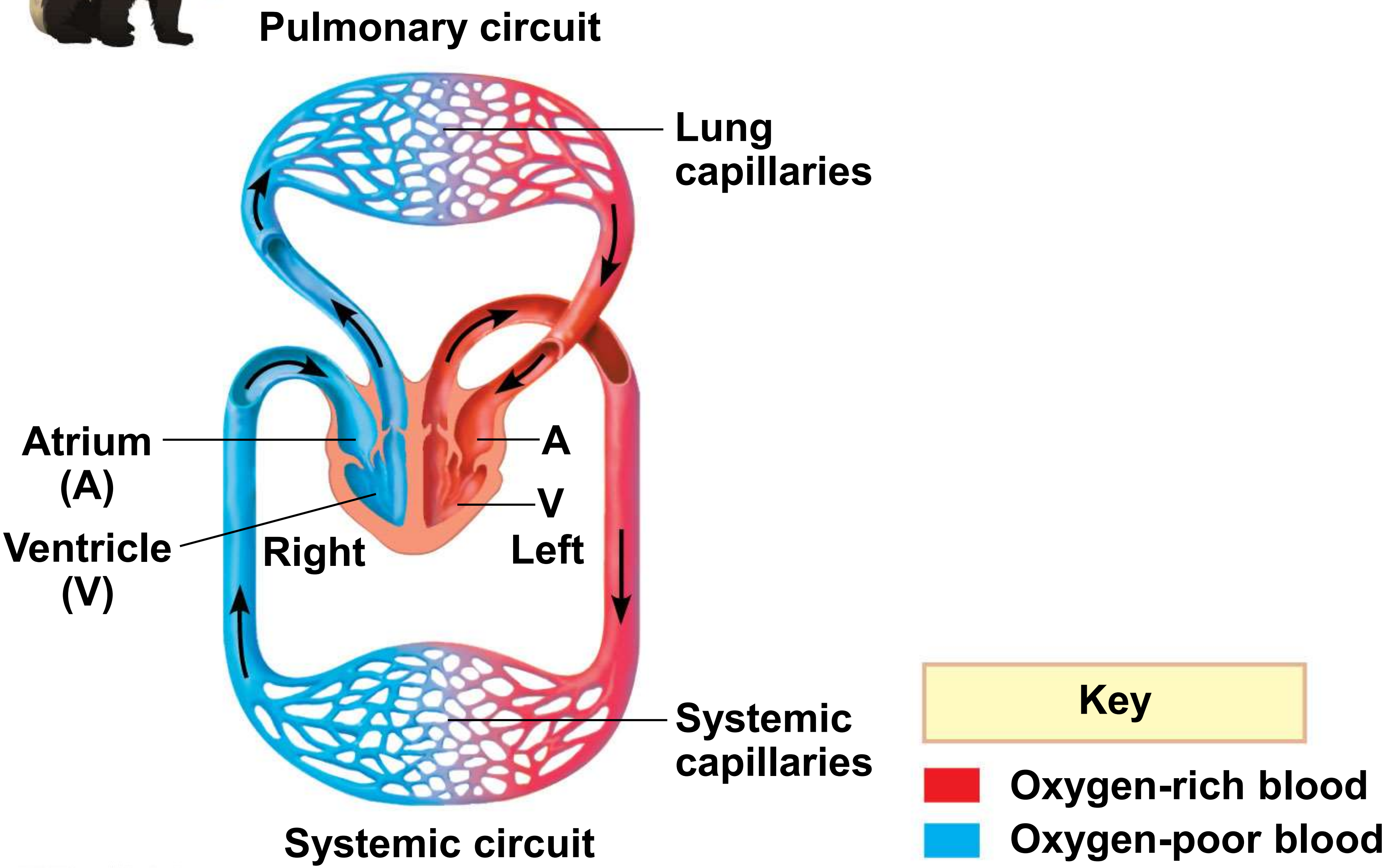
Right atrium → right ventricle → lungs → left atrium →
left ventricle → body organs → right atrium



However, during long periods of submergence (i.e., while the animal waits for prey or stays underwater waiting for prey to rot) a unique valve leading to the pulmonary artery contracts, pressure in the right ventricle can increase, and blood can leave the right ventricle, enter the left aortic arch, and therefore bypass the pulmonary circulation.


Crocodilian
(normal state)
To forelimbs, head
To lungs
To lungs
To stomach,
intestines
Foramen of
Panizza
RV
LV
Right systemic
artery
Interventricular
septum
RA
LA
To tail,
hindlimbs
Sinus
venosus
Crocodilian
(diving)
To forelimbs, head
To lungs
To lungs
Left syster
artery
To stomach,
intestines
Foramen of
Panizza
RV
LV
Right systemic
artery
RA
LA
To tail,
hindlimbs

Mammals and Birds



Mammals and Birds

- Mammals and birds have a four-chambered heart with two atria and two ventricles
- The left side of the heart pumps and receives only oxygen-rich blood, while the right side receives and pumps only oxygen-poor blood
- Mammals and birds are endotherms and require more O_2 than ectotherms

Right atrium → right ventricle → lungs → left atrium →
left ventricle → body organs → right atrium

Researchers think this complete separation evolved independently in birds and mammals and was necessary for the high endothermic metabolisms of these vertebrates.

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LETTERS

Reptilian heart development and the molecular basis of cardiac chamber evolution

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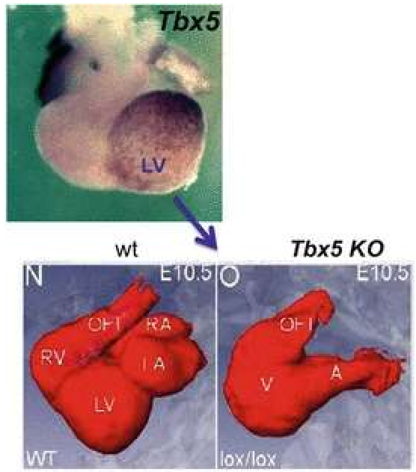

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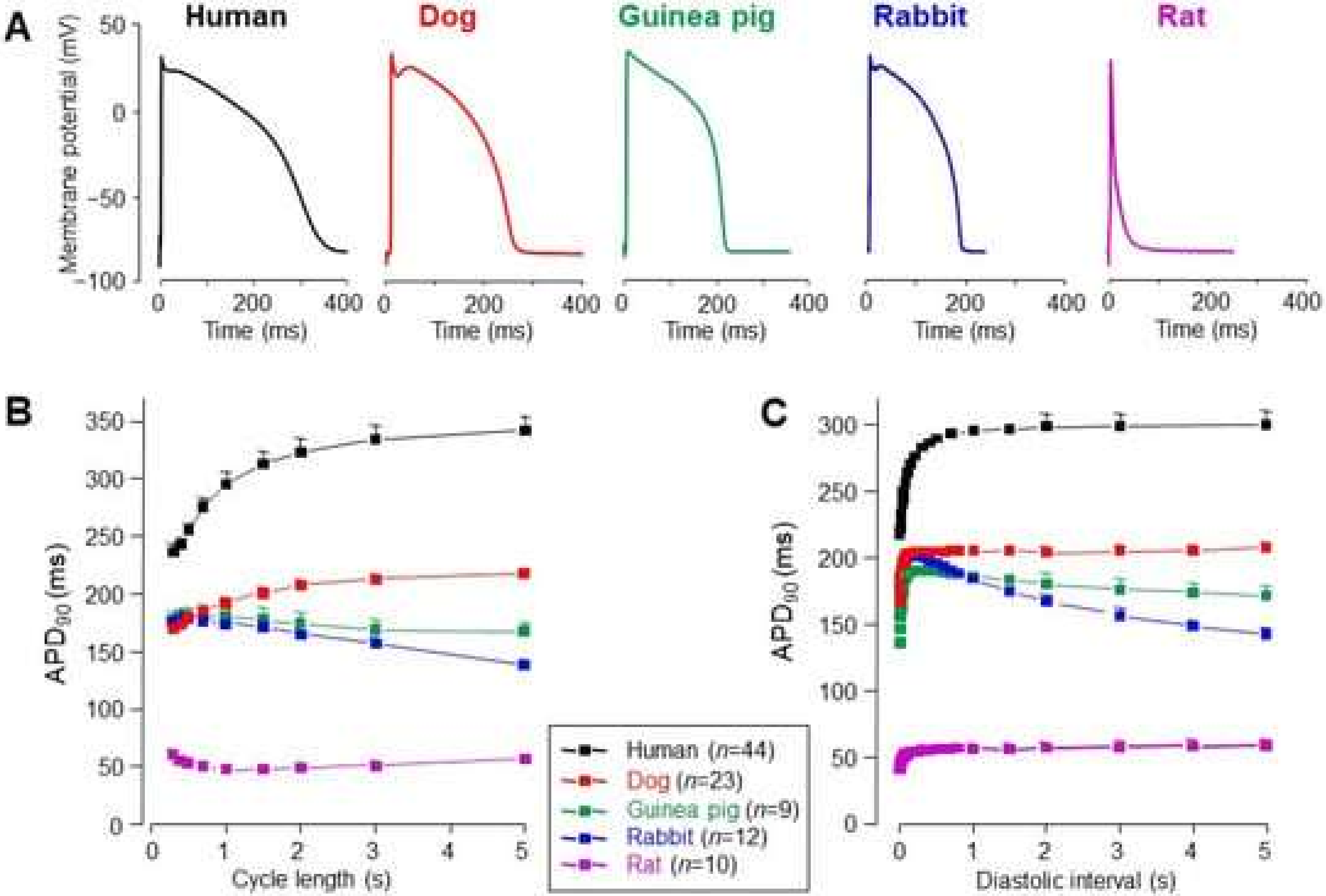
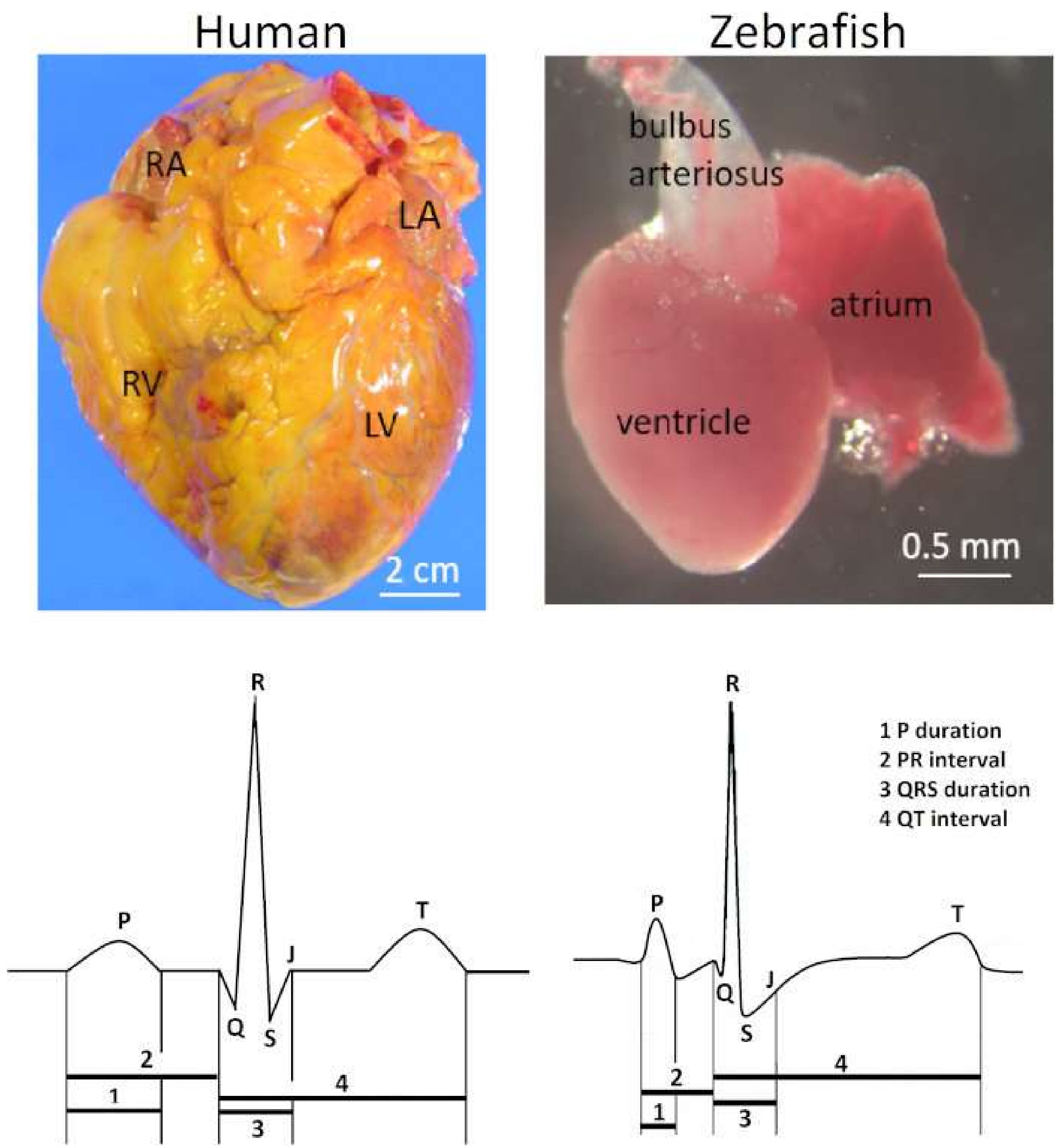
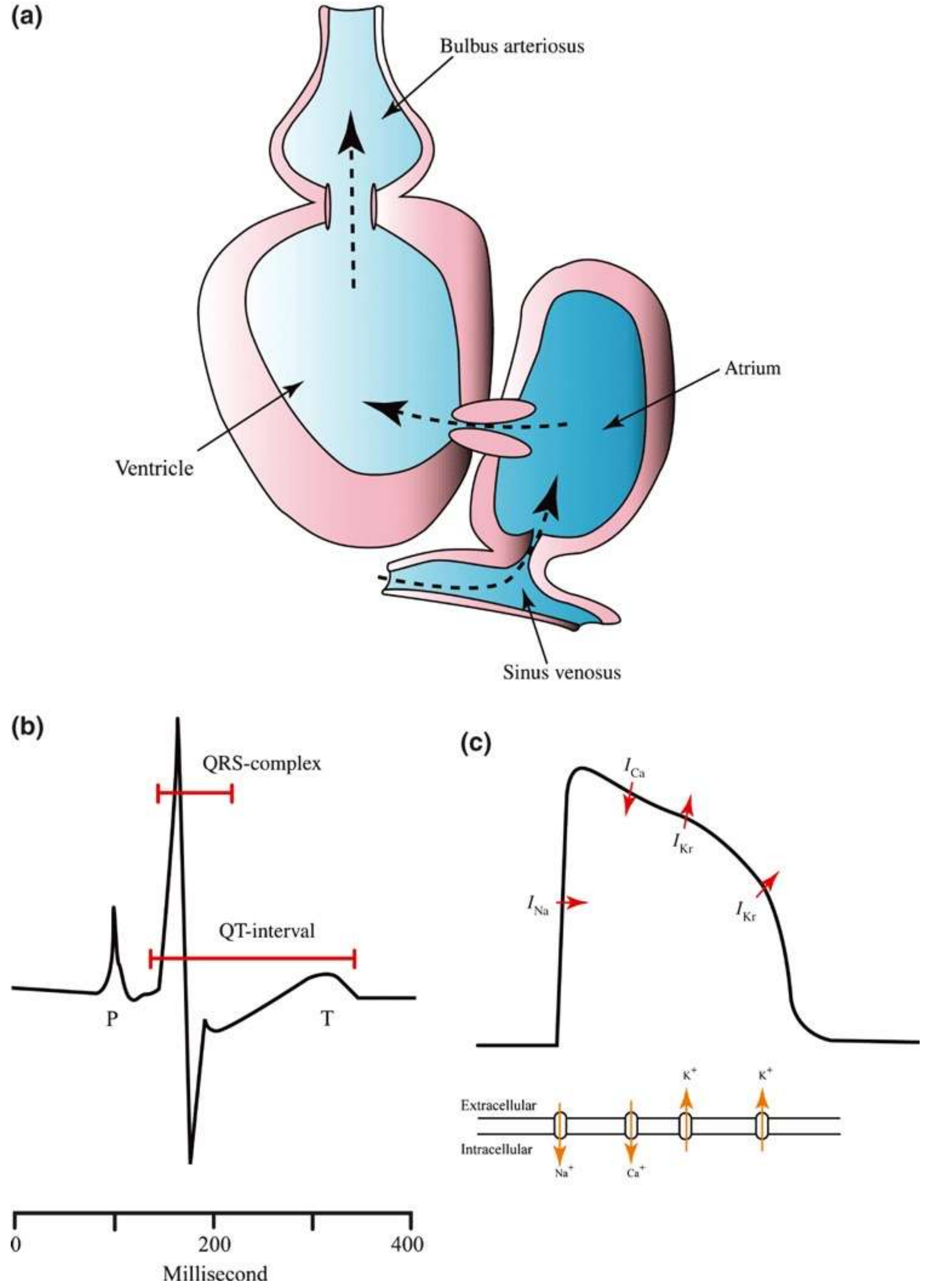
The zebrafish issue



A
Human
Dog
Guinea pig
Rabbit
Rat
Membrane potential (mV)
Time (ms)
B
APD90 (ms)
Cycle length (s)
C
Diastolic interval (s)
Human (n=44)
Dog (n=23)
Guinea pig (n=9)
Rabbit (n=12)
Rat (n=10)


Human
Zebrafish
RA
LA
RV
LV
2 cm
bulbus
arteriosus
atrium
ventricle
0.5 mm
R
P
T
J
Q
S
1
2
3
4
1 P duration
2 PR interval
3 QRS duration
4 QT interval



(a)
Bulbus arteriosus
Atrium
Ventricle
Sinus venosus
(b)
QRS-complex
QT-interval
P
T
0
200
400
Millisecond
(c)
I_{Ca}
I_{Kr}
I_{Na}
I_{Kr}
K^+
K^+
Extracellular
Intracellular
Na^+
Ca^+