Overview of Lecture:
Circulation, gas exchange
see the schedule for reading and watching assignments

Bullet Points:
• Plasma membrane transport
• Circulatory Systems:
  None – just diffusion
  Closed single loop: low press.
  Closed double loop: high-low
• Hearts & Chambers
• Prenatal shunting & Adult Diving
• Fantastic voyage - loop-de-loop!
• Human ECG
• Blood pressure & flow
• Capillaries – time-sharing blood
• Central control
  negative feedback:
   sympathetic & parasympathetic
• Local control: just say NO
• Sex and blushing
Learning Goals:

1. Be able to compare and contrast the circulatory systems of a fish and a mammal, highlighting differences that are functionally important for the hot, high-energy “lifestyle” of mammals. A good answer will consider the pressure driving flow through systemic and respiratory capillary beds and the pressure drops across these beds.

2. Be able to describe the points of passage in the “fantastic voyage, loop-de-loop” that a blood cell would take to make a complete circuit through the human circulatory system, beginning in the right ventricle and ending in the right atrium.

3. Be able to explain why blood in a human has to be carefully “time shared” across capillary beds. Where is blood-flow control across capillary beds primarily exerted? Explain the central push-pull control exerted by the parasympathetic and sympathetic nervous systems. Explain the local control mediated by NO.

4. How does viagra work? What is blushing and why is it such a strange form of social communication?
Be sure to watch (the 3rd one is a little long)
Every living cell is an open system, importing resources & exporting wastes across the lipid plasma membrane.

Channel & Transport proteins built into the membrane play key roles in regulating transport.

- **Diffusion**: Hydrophyllic channels facilitate diffusion: water & simple solutes
- **Facilitated diffusion**: Carrier proteins selectively admit glucose & big stuff
- **ATP-dependent enzymes pump ions up gradient**: 
  - Na\(^+\)-K\(^+\) exchange pump

ATP - adenine triphosphate
In **unicellular protists**, each cell is in direct contact with the external environment & diffusion to and from the membrane is adequate.

**Diffusion is inefficient over distances of more than a few millimeters;** diffusion time is proportional to the square of the distance [from Fick’s law]: if it takes ~1 sec for a given quantity of glucose to diffuse 100 μm, it will take ~100 seconds for it to diffuse 1 mm and almost 3 hours to diffuse 1 cm.

The **branching gastrovascular cavities** of colentrate & flatworms → body wall only two cells thick; each cell in direct contact with medium; ensuring that ... diffusion distances are short & a circulatory system is unnecessary.

{**plasma** → interstitial fluid} & the surfaces that exchange gases, nutrients & wastes with the external environment. Diffusion [see Fick’s law] only has to bridge the 1st or last few mm.
The heart of simple chordates like lancelets is little more than a muscular tube in the main artery that contracts in peristaltic waves.

A fish heart is basically just a tube with 4 chambers in series. The Sinus Venosus & Atrium collect venous blood, the Ventricle & Conus Arteriosus pump it in a peristaltic wave to capillary beds. The Sinus Venosus serves as 'pacemaker' of peristaltic waves; in mammals, the homologous pacemaker is the sinoatrial (SA) node.
The evolution of lungs in **amphibians** {lost in thin ‘lungless’ salamanders} is associated with two separate circuits: the **pulmocutaneous circuit** to the lungs & skin, the **systemic circuit** to the other tissues {double loop w/ single capillary bed per loop}

Amphibians have a **three-chambered heart**: the Right Atrium (& sinus venosus) collect O\(_2\) depleted systemic blood, the Left Atrium collects O\(_2\) rich pulmonary blood. The pulmonary and systemic blood mixes {a little} in the **single Ventricle** {mixing keeps both circuits low pressure}

**Turtles, snakes & lizards also have double circulation** with pulmonary (lung) and systemic circuits, but one ventricle w/ some mixing.

Ridges (septa) & valves allow shunting of blood from one circuit to the other, [useful for long periods underwater.

**note:** this shunting from pulmonary to systemic happens in fetuses of placental mammals, but isn’t supposed to happen in adult mammals – later
Birds and mammals evolved from different reptilian ancestors; their four-chambered hearts evolved independently, an example of convergent evolution.

In fetal mammals, the lungs are nonfunctional & the pulmonary circuit is bypassed. Systemic venous blood entering the right atrium is shunted directly into the left atrium through an opening called the foramen ovale, which is supposed to close at birth, when the pulmonary circuit opens.

Two separate circuits allow
↓ pressure pulmonary
↑ pressure systemic
2 < 6

Note hepatic portal system:
2 capillary beds in series.
Also a hypothalamus-pituitary portal
Each day the average heart pumps about 2,000 gallons of blood.

In a 70-year lifetime, an average human heart beats more than 2.5 billion times.

Watch: https://www.youtube.com/watch?v=v3b-YhZmQu8

note: how bundle branches [of His] & purkinji fibers reverse direction of contraction: atria top down ventricles bottom up

The normal ECG has the following features:

Rewiring the Heart: Stem Cell Therapy to Restore Normal Cardiac Excitability and Conduction
DOI: 10.2174/157488809787169066

The best way to correct some types of bradycardia (slower than normal heartbeat) is with a heart pacemaker. Pacemakers have helped thousands of people of all ages and all walks of life overcome problems associated with serious arrhythmias.
Blood pressure & flow (flow ~ pressure/resistance ~ pressure X area)

‘Law of Continuity’ - liquid is incompressible and same volume must pass each cross-section per unit time, ∴ \( \uparrow \) cross-section \( \rightarrow \downarrow \) velocity

[Bernoulli's Equation; ‘still waters run deep’]

Note: no pressure in veins to push blood up to heart! Contracting skeletal muscles squeeze the veins. Flaps within the veins act as one-way valves that keep blood moving only toward the heart. If we sit or stand too long, the lack of muscular activity causes our feet to swell with stranded blood.
Humans are circulating ~5 liters (~10.6 pints) of blood through ~60,000 miles of capillaries with a total surface of ~1000 m². 5l of blood cannot fill the heart, arteries, veins and all the capillaries at once.

Capillaries in the brain, heart, kidneys, and liver get priority and are usually open. Other tissue capillary beds take turns “time sharing” blood; prioritizing by need.

In anaphylactic shock, a hyper-allergic reaction results in massive release of histamines which dilate too many capillaries, dropping blood pressure. Epinephrine {aka adrenalin: normally from sympathetic NS and also adrenal medulla - ‘fight or flight’} should be given to raise the blood pressure by constricting blood vessels in guts.
The autonomic nervous system innervates cardiac & smooth muscle, and glands – not under conscious control.

**Parasympathetic division**
- Constricts pupil of eye
- Stimulates salivary glands
- Slows heart
- Constricts bronchi in lungs
- Stimulates activity of stomach and intestines
- Stimulates activity of pancreas
- Stimulates gallbladder
- Promotes voiding from bladder
- Promotes erection of genitals

**Sympathetic division**
- Dilates pupil of eye
- Inhibits salivary gland secretion
- Relaxes bronchi in lungs
- Accelerates heart
- Inhibits activity of stomach and intestines
- Inhibits activity of pancreas
- Stimulates glucose release from liver; inhibits gallbladder
- Stimulates adrenal medulla
- Inhibits voiding from bladder
- Promotes ejaculation and vaginal contractions

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**Ach**
- Relax: slow heart
- constrict pupils
- Rest & Digest

**Nepi**
- Excite: speed heart
- dilate pupils
- Fight or Flight

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**http://www.mhhe.com/biosci/ap/vander/student/olc/index.htm**

**https://en.wikipedia.org/wiki/Norepinephrine**  [Nepi is both a neurotransmitter & hormone]

The general function of norepinephrine is to mobilize the brain and body for action. … in the so-called **fight-or-flight** response. … increases arousal and alertness, … **increases heart rate and blood pressure**, triggers the release of glucose from energy stores, **increases blood flow to skeletal muscle, reduces blood flow to the gut**, [by dilating or constricting arteriole and pre-capillary sphincter smooth muscle]
Arterial blood pressure is normally regulated within a narrow range, typically ranging from 85 to 100 mmHg in adults. This is accomplished by negative feedback systems incorporating pressure sensors (i.e., baroreceptors) that sense the arterial pressure. The most important arterial baroreceptors are in the carotid sinus and in the aortic arch. These receptors respond to stretching of the arterial wall so that if arterial pressure suddenly rises, the walls of these vessels passively expand, which increases the firing frequency of action potentials generated by the receptors. If arterial blood pressure suddenly falls, decreased stretch of the arterial walls leads to a decrease in receptor firing.
Flow follows need.

The role of nitric oxide on endothelial function.
The vascular endothelium is a monolayer of cells
between the vessel lumen and the vascular smooth muscle cells.
Nitric oxide (NO) is a soluble gas continuously synthesized from the amino acid
L-arginine in endothelial cells by the enzyme nitric oxide synthase (NOS).
This substance has a wide range of biological properties
that maintain vascular homeostasis,
including modulation of vascular muscle tone,
regulation of local cell growth, and protection of the vessel …,

Individual tissues have the ability to signal their own needs for increased blood.
{paracrine signals are local cell-to-cell chemical messengers}
The messenger molecule nitric oxide (NO)
is synthesized by endothelial tissues in need of oxygen
and diffuses across cell membranes.
It causes the smooth muscle of the arteriole walls
and precapillary sphincters to relax
and the vessels to dilate.
[local, autonomous negative feedback regulation of
blood flow and distribution to meet local O₂ demand;
Humans are circulating ~5 liters (~10.6 pints) of blood through ~60,000 miles of capillaries with a total surface of ~1000 m². 5l of blood cannot fill the heart, arteries, veins and all the capillaries at once. At any given time, only about 5-10% of the body’s capillaries have blood flowing through them.

Capillaries in the brain, heart, kidneys, and liver get priority and are usually open. Other tissue capillary beds take turns “time sharing” blood; prioritizing by need.

Good Circulation Is Essential For Good Health...

...This is especially true for organs that require the most circulation including:

- the heart,
- kidneys,
- liver,
- and healthy functioning sex organs.
Vascular smooth muscle (VSM) cells surround arteries and arterioles, contracting and relaxing the arteries to regulate blood pressure. ...

Relaxation ... is triggered by nitric oxide (NO) ... activates an enzyme [GC] that manufactures cyclic guanosine monophosphate (cGMP). cGMP, directs the smooth muscle cells to relax, leading to the dilation of ... arterioles [and increased local blood flow].

Immediately following release of NO and production of cGMP; another enzyme, phosphodiesterase type 5 (PDE-5), is activated. [PDE-5 has localized distribution in body]

**PDE-5 destroys cGMP**
The result is contraction of vascular smooth muscle and decreased blood flow [where PDE-5 is]
The reddening of the face from a blush is due to the relaxation of the muscular coats of the small arteries, by which the capillaries become filled with blood; arteriole & sphincter smooth muscle relaxed via sympathetic (‘involuntary’) nerves.

We have now to consider,

**why should the thought that others are thinking about us affect our capillary circulation?**

consider the idea of an ‘involuntary’ signal from your subconscious brain to your social partners via your autonomic nervous system and facial capillary beds!

Recent findings … reveal that if you ever find yourself in a pickle after, say, committing a social offence or being caught in an embarrassing mishap, the presence or absence of blushing can help determine if you’ll be forgiven by others.