Carnegie
Fall 2019

TOPIC: The Heart

- A transport system pump, hollow blood vessels are delivery routes
- Enclosed in mediastinum of thorax
- Extends obliquely from the second rib to fifth intercostal space (12-14cm)
- 2/3 of mass lies on the left side, the right side on the diaphragm
- Broad, flat base towards right shoulder, it's apex points towards left hip
- 3 layers: pericardium, myocardium, and endocardium

1. **Pericardium**
- Outer covering of heart
- Double walled, fibro-serous sac

a. **Fibrous pericardium**
- Protects, anchors heart to surrounding
- Prevents overfilling of heart

b. **Serious pericardium**
- Two layers, parietal and visceral (epicardium)
- In between the layers is the fluid filled pericardial cavity

2. **Myocardium**
- Mostly cardiac muscle, it's the bulk of the heart
- Cardiac muscle cells are tethered to one another by connective tissue fibres arranged in circular bundles:
- Link heart parts together
- Reinforce myocardium internally
- Anchor cardiac muscle fibers
- Vessel/valve support
- Direct spread of action potential across pathways

3. **Endocardium**
- Layer of endothelium and connective tissue layer on the inner myocardial surface
- Continuous with endothelium linings of vessels leaving/entering heart

The heart has 2 atria and 2 ventricles
Interatrial septa-> separate the atria
Interventricular septa-> separate ventricles
The heart has 2 exterior grooves:

- Coronary sulcus and anterior-posterior interventricular sulcus

1. **Atria:** Receiving Chambers

- Small, thin walled
- Need only convey blood to ventricles
- Deoxygenated, blood enters via the right atrium via three veins:

1. The superior vena cava returns blood from body regions superior to the diaphragm
2. The inferior vena cava returns blood from body areas below the diaphragm
3. The coronary sinus collects blood draining from the myocardium

- The left atrium has four pulmonary veins, oxygenated blood goes in here

Pectinate Muscles:

- Parallel ridges in the walls of the right atria of the heart
- Has muscle fibers arranged in a comb like fashion, can stretch and improve volume of atrium

Fossa Ovalis

- Depression in the right atrium of heart, the remnant of a thin fibrous sheet that covered the foramen ovule during fetal development

Foramen Ovale

- A small hole located in the septum, which is the wall between the two upper atriums
- Allows oxygenated blood coming from the umbilical vein to bypass the pulmonary circulation in the fetus

Ventricles: Discharging Chambers

- Pumps of the heart, walls much thicker, especially the left ventricle
- Right ventricle pumps blood to pulmonary trunk
- Left ventricle pumps blood to aorta
- Internal walls have muscle bundles: trabeculae carnae (irregular ridges of muscle) , papillary muscles(valve function)

Heart valves

- Blood flow is unidirectional, enforced by 4 heart valves

1. **atrioventricular valves:**

- There are two, one located at each atrial-ventricular junction
- They prevent backflow into the atria when the ventricles contract
- The right AV valve, the tricuspid valve= has three flexible cusps(flaps of endocardium reinforced by CT)
- The left AV valve, the mitral valve: has two cusps, resembles a tall pointed hat, also known as bicuspid valve

Each valve have tiny white collagen cords called chordae tendinea, these anchor the cusps to papillary muscles. When the heart is relaxed, the AV flaps hang limply and blood flow occurs. When the ventricles contract, the blood is compressed and the flap edges meet, closing the valve.
They act as tethers that anchor the flaps in their closed position, if they were not anchored, they would be blown upward into the atria like an umbrella blown inside out.
Papillary muscles contract and chordae tendineae tighten to prevent valve flaps from entering the atria

2. **Semilunar valves:**

- Paired, the aortic and pulmonary valves, from ventricles to either pulmonary or systemic circuits
- Prevent backflow into ventricles

pulmonary valve= right ventricle to pulmonary artery

- Aortic valve= left ventricle to aorta
- Valves open and close in response to pressure
- As ventricles contract and pressure rises, blood is pushed up against SL valves, forcing them open
- As ventricles relax, pressure decreases, blood flows back and the cusps are filled and valves close.

Valvular insufficiency : forces the heart to repump the same blood over and over because the valve does not close properly and blood backflows
Valvular stenosis: the valve flaps become stiff and constrict the opening . The constricted opening forces heart to contract more forcibly than normal
Both types of valve problems may weaken heart over time as heart workload increases.

Pathway of a RBC in the heart:

1. Oxygen poor blood returns from body tissues back to heart
2. Goes to superior/inferior vena cava/ coronary sinus
3. Goes to right atrium
4. Goes to right ventricle
5. Goes to pulmonary trunk
6. Goes to two pulmonary arteries to the lungs (pulmonary circuit) to be oxygenated
7. Oxygen rich blood returns to the heart via the four pulmonary veins
8. Goes to left atrium then left ventricle ten aorta
9. Oxygen rich blood is delivered to the body tissues (systemic circuit)

Equal volumes pumped into pulmonary and systemic circuits, but 2 ventricles have unequal workload

1. **Pulmonary circuit** (right ventricle): short, low-pressure circulation , left side of heart
2. **Systemic circuit**(left ventricle): long pathway with 5x resistance, right side of heart

Walls of left ventricle are 3x thicker than those of the right

Coronary Circulation

- Shortest, but one of the most important
- Right and left coronary arteries from base of aorta, encircle heart in coronary sulcus (atrioventricular groove)
- Left coronary artery runs toward the left side of the heart and then divides into two major branches
- The right coronary artery courses to the right side of the heart and also divides into two branches
- Provide a blood flow to the myocardium
- The functional blood supply of heart

Anastomoses provide alternate routes for nourishment if a given artery begins to be obstructed
Total occlusion means: actively deliver blood when heart is relaxed, largely ineffective when ventricles contracting
Heart is 1/200 of the body's weight but requires 1/20 of the body's blood.

Diseases of Coronary Vessels
Angina pectoris: thoracic pain caused by deficiency in blood delivery to the myocardium. It may result from stress-induced spasms of coronary arteries or increased physical demands on the heart. The myocardial cells are weakened by temporary lack of oxygen but do not die.
Myocardial Infarction: commonly called a heart attack. Cells do die, dead tissue replaced by noncontractile scar tissue

Coronary Venous supply begins with capillaries

Compare the physiological properties of cardiac muscle fibers with skeletal muscle fibers

	;keletal	**;ardiac**
;tructure	Striated, long, cylindrical, nultinucleate	Striated, short, branched, one or two nuclei per cell
Gap junctions between cells	no	yes
Contracts as a unit	No, motor units are stimulated ndividually	Yes, gap junctions allow this
T tubules	abundant	Fewer, wider
Sarcoplasmic reticulum	Elaborate, has terminal cisterns	Less elaborate, no terminal cisterns

;ource of ca for :ontraction	;R	;R and extracellular fluid
;upply of ATP	\erobic and anaerobic (fewer nitochondria)	\erobic only (more mitochondria)

1. Desmosomes for strong cell-cell adhesion during contraction
2. Gap junctions for electric coupling-> functional syncytium(a single coordinated unit)

Heart contraction is stimulated by action potentials
Action potential: signal
Muscle twitch: response
Contractile cardiac muscle cells: conduct impulses that are responsible for pumping blood to the body
Autorhythmic cardiac muscle cells:
action impulses originate in here, these cells are self-excitable so they can generate an AP without external stimulation
-they have an unstable resting potential that continuously depolarizes spontaneously

<u>**Special Characteristics Of Cardiac Muscle cells:**</u>

1. Stimulation: auto-rhythmicity of cardiac cells, can self-stimulate
2. The heart contracts as a unit (all or none)
3. Influx of calcium from ECF triggers calcium release from sarcoplasmic reticulum
4. Absolute refractory period: 250 msec vs 1-2msdc for action potential stimulating skeletal muscle. This period is almost as long as the contraction itself which prevents tetanic contractions, also allows the heart to fill again
5. Heart relies almost exclusively on aerobic respiration

Activation of contraction basically as in skeletal muscle

Pacemaker: The SA node is a pacemaker
Pacemaker potentials -> action potentials

<u>**In autorhythmic cells, action potential is due to:**</u>

1. <u>**Pacemaker potential**</u>
- This slow depolarization is due to opening of Na channels and closing of K channels. Membrane potential is never a flat line
2. <u>**Depolarization**</u>
- The action potential begins when the pacemaker potential reaches threshold. Depolarization is due to calcium influx thorough channels
3. <u>**Repolarization**</u>
- is due to calcium channels inactivating and K channels still open which allows K efflux and brings the membrane potential back to its most negative voltage.

Sequence of excitation

1. **SA node:** generates impulses and sets the pace for the heart as a whole, for this reason it is the pacemaker
2. **Atrioventricular node (AV):** depolarization spreads via gap junctions to the AV node. The impulse is delayed here for about 0.1 second, allowing the atria to respond and complete contraction before ventricles contract. Slowest part, once through , impulse travels very fast through the rest.
3. **AV bundle:** the only electrical connection between the atria and ventricles, as there's no gap junctions.
4. **Right and left bundle branches:** AV bundle splits into two pathways, the right and left bundle branches which go towards the hearts apex.
5. **Purkinje fibers**: long strands of barrel shaped cells with few myofibrils. Penetrates into the heart apex, and then turns into the ventricular walls. They excite the cells of interventricular septum

Bottleneck is from atria to ventricles because_______
0.22 sec from initiation at SA node to depolarization of last of ventricular cells

Rate of SA node depolarization regulated by ANS(autonomic nervous system):
1**) parasympathetic ns:** decreases diastolic depolarization rate
"the brakes", slows down the heart
2) **sympathetic ns:** increases depolarization and repolarizing rates,
"the accelerator", speeds up the heart

Under resting conditions, tonic parasympathetic output to have a dampening effect on heart rate

Bradycardia: heart rate that's too slow
Tachycardia: heart rate that's faster, more than 100 times per minute.
Sinus rhythm: a normal heart beat, with respect to heart rate and rhythm Between 60 to 100 beats per minute.

Electrocardiogram: records electrical changes during heart activity, relies on conductible activity of body fluids. A typical ECG has three waves or deflections. Records only voltage and time, shows only electrical events, but from these we can deduce contractile events.

1. **P wave**: lasts about 0.08s and results from movement of depolarization wave from the SA node through atria. Atria will contract after 0.01 second and depolarize.
2. **QRS complex**: ventricular depolarization and precedes contraction.
3. **T-wave:** ventricular repolarization, repolarization is slower.

Abnormal activation of the heart

- Correct sequence of activation needed for the heart to function as a pump

Ventricular fibrillation: heart beats with rapid, erratic, impulses
2nd degree heart block: AV node becomes completely refractory to conduction
Non-functional SA node (junctional rhythm): heartbeat originates from the AV node

Systole: contraction of heart, pumping out
Diastole: relaxation of heart, filing with blood
Cardiac cycle: atrial systole+ diastole -> ventricular systole +diastole.

- Includes all events associated with the blood flow through the heart in one complete heart beat,

Dichroitic notch: a small downward deflection, It represents closure of the aortic or pulmonic valve

Phases of the Cardiac Cycle:

1. **Ventricular filling:** mid to late diastole

- Pressure in heart is low, returning blood is flowing through atria and to the ventricles. Aorta and pulmonary valves are closed.
- Following depolarization(P wave), the atria contracts, and blood is compressed, atrial pressure rises and residual blood propels into the ventricles.
- Ventricles are now in the last part of their diastole as they have maximum volume (end diastolic volume)
- The atria then relaxes and the ventricles depolarize (QRS complex)
- Atrial diastole for the rest of the cycle

2. **Isovolumetric contraction**

- As the atria relax, ventricles begin to contract
- Pressure increase and AV valves close, the isovolumetric contraction pause is when the ventricles are completely closed and the blood volume in the chambers remains constant as they contract.
- As pressure keeps rising, it finally exceeds the pressure in the arteries. This stage ends with the SL valves are forced open.

3. **Ventricular ejection:**

- Blood rushes from ventricles into the aorta pulmonary trunk
- Pressure in aorta reaches 120 mm Hg.

4. **Isovolumetric relaxation: early diastole**

- Following the peak of the T wave, the ventricles relax. Ventricular pressure drops and blood in the aorta and pulmonary trunk flow back to the heart , closing the SL valves. The beginning of isovolumetric relaxation phase

5. **Back to step 1:**

- Atria continued in diastole and have been filling, when pressure of atria> Ventricular pressure, AV valves open and we are back at step 1.

75 beats/minute: each cardiac cycle= 0.8 seconds
Atrial systole: 01 seconds

Ventricular systole: 0.3 seconds
Quiescent period: 04 seconds

2 features driving cardiac cycle:

a. Blood flow through heart controlled entirely by pressure changes
b. Blood flows from higher to lower pressure through any available opening

2 distinguishable sounds can be heard through a stethoscope

- Heart sounds due to vibrations of heart/chest due to valve closure

a. **First heart sound**: closure of AV valves= beginning of systole
b. **Second heart sound**: closure of semilunar valves= end of systole

Heart murmurs:

- Due to **valvular obstruction** -> high velocity jet of blood through narrow opening-> higher pitch of sounds
- Due to **valvular insufficiency** -> leakage of blood back causes sounds when there should be silence

Abnormal blood flow

Pulmonary valve stenosis: the narrowed pulmonary valve causes the blood to be turbulent and noisy which is heard as a heart murmur.

Cardiac output (CO): amount of blood pumped from left ventricle into aorta/minute

- Average CO for resting, healthy male -> 5L/minute
- CO= HR X SV
- HR= heart rate.   SV= stroke volume
- CO increases 4-5 times in a fit person
- CO increases 7 times in a well-trained marathon runner
- Notion of cardiac reserve: the difference between resting and maximal CO

Regulation of Stroke Volume

- SV Is the difference between end diastolic volume and end systolic volume
- Preload, contractibility, and afterload

1. **Preload:**

- The degree to which cardiac muscle cells are stretched before they contract
- The higher the preload, the higher the stroke volume, Frank Starling law of the heart, the heart will pump whatever volume of blood it receives
- Most important factor is venous return -> amount of blood returning to heart and distend its ventricles. Increasing this will increase EDV and thus impact the SV.
- Cardiac muscle has optimal length for contraction= length-tension relationship. Resting=shorter than optimal length
- FS mechanism ensures that each ventricle pumps same volume over a period of time

2. **Contractibility:**

- Contractile strength achieved at a given muscle length.
- Independent of muscle stretch and EDV
- Contractibility rises when more ca enters. Enhanced contractibility means more blood is ejected from the heart so ESV is lower
- Increased sympathetic stimulation also increases contractibility .
- Norephedrine initiates a cyclic AMP second messenger system that increases ca entry.
- Digoxin increases heart contractibility
- Parasympathetic ns antagonizes the sympathetic stimulation

3. **Afterload**

- Back pressure exerted by arterial blood
- Afterload is the pressure that the ventricles must overcome to eject blood.
- In healthy individuals, afterload is not a major determinant of stroke volume but in people with hypertension, afterload is important as it reduces ability of ventricles to eject blood.

Regulation of Heart Rate:

Factors increasing heart rate: positive chronotropic factors
Factors decreasing heart rate: negative chronotropic factors

1. **ANS regulation of heart rate**

- Emotional or physical stressors activate the sympathetic nervous system and norepinephrine is released, causing threshold to be reached more quickly, SA nodes fire more and heart beats faster
- Parasympathetic division reduces heart rate when stressful situation is passed.
- Resting conditions: both visions continuously send impulses to the SA node, but the dominant influence is inhibitory(parasympathetic ns is dominant), therefore heart is said to show vagal tone
- Tachycardia: fast resting heart rate, leads to reduced CO as it promotes fibrillation.

2. **Chemical regulation**

- Hormones-> epinephrine enhances heart rate and contractibility. Thyroxine also enhances effects of epinephrine and norepinephrine.
- Ions-> normal heart function depends on having normal levels of ions. Plasma electrolyte imbalances pose real dangers.

3. **Body temperature**

- Heat increases heart rate, cold decreases it, useful for surgery

What are the effects of chronically elevated blood pressure on cardiac muscle cells?

- Myocardium must exert more force to open the aortic valve and pump the same amount of blood. Eventually, stress takes a toll and myocardium is much weaker