Chapter 20

The Heart

heart anatomy
located in the mediastinum, the medial cavity, of the thorax
lungs flank the heart and partially obscure

lies slightly to the left of the midline

apex points down towards the left

base is the broader upper aspect where the great vessels emerge

layers of the heart wall
1. epicardium or visceral pericardium
   outer thin layer of mesothelium
   is simple squamous epithelium
   some areolar tissue
   has adipocytes

2. myocardium
   1. mainly cardiac muscle
   2. thickest layer
   3. contains tissue to conduct electrical current
   4. contains a connective tissue fiber skeleton: the fibrous skeleton of the heart
      1. anchors cardiac muscle
      2. reinforces cardiac muscle
      3. provides support for great vessels
      4. limits spread of action potentials to specific pathways

3. endocardium
   1. single layer of endothelium attached to a thin layer of connective tissue
   2. lines the heart chambers
   3. is continuous with the endothelial linings of the blood vessels
   provides a none clotting surface
chamber and great vessels of the heart
heart has four chambers
right and left atria
right and left ventricles

atria
are the receiving chambers and receive blood returning to the heart
only need to contract enough to push blood into the ventricles
thus are thin walled
don’t contribute to the pumping of blood throughout the body

ventricles
1. right and left are separated by interventricular septum
2. make up most of the heart mass
3. are the discharging chambers thus are more massive
   right ventricle pumps out the pulmonary trunk to the lungs (low oxygen blood) so generate little pressure
   left pumps out the rest of the body (the systemic circulation) and must generate greater pressure so is larger than right

Blood flow through the chambers of the heart (pp. 723)
1. blood enters right atria via three vessels
   1. inferior vena cava
   2. superior vena cava
   3. coronary sinus

2. blood passes by right AV valve (tricuspid valve)
3. blood enters right ventricle
4. blood is forces out the right ventricle passed the pulmonary semilunar valve
5. blood enters pulmonary trunk with splits into right and left pulmonary arteries
6. blood is sent to lungs

7. blood returns form lungs via one of four pulmonary veins (two rights and two lefts)
8. blood enters left atria
9. blood passes left AV valve (bicuspid valve)
10 blood enters **left ventricle**
11. blood is forced passed **aortic semilunar valve**
12. blood enters **aorta** and is sent to body minus the lungs via
   - brachiocephalic a,
   - left carotid a,
   - left subclavian a
   - descending aorta

1. out the aorta return to right atria = **systemic circulation**
2. out the pulmonary trunk return to left atria = **pulmonary circulation**

   equal volume of blood passes through both circuits but
   work load is different

**pulmonary circuit** is short and low pressure circuit so
right ventricle has to pump less

**systemic circuit** is long and requires high pressure
   thus the left ventricle is much larger (3X)

The heartbeat

**Cardiac Physiology**

The primary function of the heart is to propel blood though out the pulmonary and
systemic circulatory loops.

This is accomplished by the contraction of the cardiocytes that make up the heart

contraction of the heart’s contractile cells is triggered by **action potentials** that originate at the heart

There are types of cardiocytes
1. Specialized **conduction cells**
   - that make up the conduction system and are designed to
     rapidly conduct electrical current

2. **Contractile cells**
   - These are the cells that shorten which pushes the blood from the heart
     Are 99% of all cardiocytes

   Contractile cells are more common
All cardiocytes have the ability to depolarize spontaneously producing action potentials

For example:
- isolated atrial cells depolarize thus contract (beat) 60 times per min
- isolated ventricular cells depolarize thus contract 20-40 times per min

The cells that depolarize fastest will set the rate or **pace** of heart contractions

Under normally conditions the cells that pace the heart are located at the top of the right atrium.
- This piece of tissue is called the **Sinoatrial node (SA node)** or the **pacemaker**

From these pacemaker cells the action potentials spread across the heart along a **conduction pathway**

**Conduction system for the spread of electrical activity across the heart**

**Sinoatrial node**
- located in rear wall of **right atrium** near opening of superior vena cava
- has fastest rhythm (80-100 a.p./min) & normally overrides all others
  - this is were the **pacemaker cells are found** and is also called the **cardiac pacemaker**

Action potential travels through walls of atria causing wave of atrial depolarization followed by a wave of **atrial contraction**
- its rate of depolarization sets the heart rate (**sinus rhythm**)  

**Internodal pathways**
- Connects SA node to atrioventricular (AV) node,
  - Consists of three major bands of conduction cells that branch through out the atria
    - Takes about 50 msec for the action potential to travel the internodal pathway
    - Along the way the contractile cells of the atria are stimulated to depolarize and produce action potentials
Action potentials spread form cell-to-cell via gap junctions (electrical synapses).
Following depolarization the contractile cells of the atria contract and push blood into the ventricles.

The electrical events occurring in the atria do not pass to the ventricles due to a band of tissue called the fibrous skeleton that breaks the gap junction connections between atrial cells and ventricular cells. Due to a slow conduction speed down the internodal pathway, the atria will completely depolarize before the action potential reaches the next part of the conduction pathway, the AV node.

**Atrioventricular node**
Large node located at the junction between the atria and the ventricles in right posterior portion of interatrial septum.

AV nodal cells are smaller in diameter and have few gap junctions thus has a much slower rate of action potential propagation.
Takes about 100 msec for action potential to through AV node.

Slower conduction speed in nodal fibers, allows complete atrial depolarization before action potential spreads to ventricles.
Thus allow the atria to contract and finish filling the ventricles with blood before the ventricles contract.

Under normal conditions the AV node can generate action potentials at a max rate of 230/min. This sets the maximum ventricular contraction rate (heart rate) at 230 beats/min.
If the SA node and thus atria contract faster it can not result in a faster rate of ventricular contraction (the AV is the bottle neck).

After the AV node depolarizes the action potential next spreads to the AV bundle of His.

**AV Bundle of His**
Only electrical connection between atria & ventricles.
Fiber skeleton insulates the rest of the atria from ventricles.
Divides into right & left bundle branches as it passes through the ventricular septum
  
  Left is larges and supplies the larger left ventricle

Both branches travel down towards the apex of the heart where they fan out into smaller Purkinje fibers

**Purkinje fibers**
  
  Pass through ventricular myocardium
  
  Fast rate of action potential generation and serve to synchronize ventricular contraction
  
  the contraction of the ventricles starts at the apex so that all blood is forced up and out

  action potentials spreads from cell to cell via gap junctions all alone the conduction pathway and from cardiocyte to cardiocyte

  By the time the action potential has reached the ventricular muscle at the apex the atria have completed their contraction maximizing the blood in the ventricles and the ventricles can now start to contract to expel the blood from the heart

**Generation of the electrical activity of the heart**
  
  The heart generates its own electrical activity and this electrical activity triggers the heart (cardiocytes) to contract which pumps the blood

  What is responsible for this electrical activity (action potentials)?

  **Generation of the action potential at the pacemaker cells**
  
  The SA node (pacemaker cells) spontaneously depolarizes (fires) 70-80 times per minute
  
  This occurs because the SA nodal cells have an unstable resting membrane potential

  1. negative charges accumulate inside the cells as it repolarizes from the last action potential
  2. the negative charges repel negative charges that are part of a special type of sodium channel
  3. this repulsion opens the sodium channel and now a lot of sodium enters the cell (sodium permeability goes up)

    This sodium channel is called the slow spontaneously opening sodium channel
4. now the membrane potential drops from -60mv until it reaches a **threshold** value (around -40mv)
   this opens **fast voltage-sensitive calcium channels**
5. now calcium rapidly enter to further depolarize the cell (not sodium like in nerve and skeletal muscle)
6. the entry of calcium neutralizes negative charges further, opening adjacent voltage sensitive calcium channels
   thus the action potential is propagated by calcium channels
5. the fast calcium channels and the slow spontaneously opening sodium channel close while voltage-sensitive potassium channels open this causes repolarization

As the cell repolarizes negative charges are accumulating inside the pacemaker cell
   This will now start to repel the negative charges on the spontaneously opening sodium channel starting the cycle over
   Thus the pacemaker cells have an unstable resting membrane potential

**Spread of electrical activity**

Once a pacemaker cell has depolarized (generated an action potential) this electrical charge spreads by the passing of positive charges from one cell to the next via gap junctions
   Thus the first cell to generate an action potential will force the adjacent cells to depolarize due to the attachment through gap junctions

   Therefore the action potential will spread quickly across and down the conduction pathway until it reaches the atria and ventricles where the contractile cells are

**electrical events at the contractile cells**

1. through gap junctions positive charges enters the cells and depolarizes a small area of membrane opening **fast voltage-sensitive sodium channels**
2. this allows more sodium to enter thus opening adjacent fast voltage-sensitive sodium channels
   thus the action potential is propagated by sodium channels
3. as the fast voltage-sensitive sodium channels start to close a second type of channel opens called the **slow voltage-sensitive calcium channel**

4. this channel lets positively charged calcium enter the cell and holds the cell depolarized for about 150 msec  
   (this results in a **plateau** on the action potential)

5. repolarization begins when the voltage sensitive calcium channel will slowly close and voltage-sensitive potassium channels will slowly open to repolarize the cell

**Reason for a plateau:**
- results in a long depolarization (200 msec) thus have strong muscle contraction  
  (not a twitch)
- a long absolute refractory period so no tetanus  
  absolute refractory period lasts until relaxation phase of contraction begins

**Role of the action potential**
- Results in opening calcium channels that let in 20% of the total calcium  
  Makes the heart very sensitive to changes in blood calcium levels  
  Makes these channels important targets for drug therapies

  Stimulates the smaller sarcoplasmic reticulum to release the other 80% of calcium

**Role of calcium**

**excitation-contraction-coupling**
- 1. the action potential will be propagated down the T tubules  
  causing the sarcoplasmic reticulum to release calcium

- 2. the calcium from the ER and the calcium that entered from ion channels will bind to troponin  
  This moves tropomyosin exposing a myosin binding site on actin

Now have cross bridge formation and power stroke resulting in filaments sliding = contraction  
contraction = pumping

**Innervation of the heart**
the heart produces its own heart (sinus) rhyme but the autonomic nervous system alters the heart rate according to changes in the body's needs. Integration site for all this information is located in the medulla oblongata:

**Cardiovascular center**

**cardioinhibitory**
parasympathetic

**cardioacceleratory**

sympathetic

1) cardioinhibitory region gives rise to axons that travel as part of the **vagus nerve** (X) traveling down neck and form part of the **cardiac plexus**

parasympathetic fibers release ACh which open K channels and 1) slightly **hyperpolarize** the heart tissue and also 2) slows the **rate of depolarization** when the spontaneous sodium channel opens, this slows the rate of action potential formation and therefore heart rate.

at rest slows heart rate to 75 beats/min

2) Cardioacceleratory region gives rise to axons that travel down the spinal cord and exit at the lower cervical, upper thoracic region forming the **cardiac nerve** which joins with fibers from the vagus to form the **cardiac plexus**

sympathetic activity accelerates the heart rate by releasing norepinephrine which binds to beta-1 receptors which results in opening calcium channels speeding up the pacemakers' rate of depolarization so have a faster and stronger heart rate.

under max exercise may increase heart rate to 220 beats/min

above this rate there won't be enough time to fill the ventricles

**Input** to the ANS inform about changes in body needs

**Five major sources**

1. Proprioceptors – rate of changes in position of limbs & muscles during physical activity
2. Chemoreceptors - monitor chemical changes in blood
   i.e. rising CO2 and acid levels

3. Baroreceptors - monitor blood pressure in major arteries & veins
   Inform about drops in overall blood pressure as active tissues
   vasodilate when active

4. Higher brain centers
   Inform the autonomic centers about upcoming activities, i.e.
   just before a race

5. Atrial stretch receptors
   When wall of atria are stretched by increase in venous return
   increases sympathetic activity to heart

The cardiac cycle

The cardiac cycle is the period between the start of one heartbeat and the beginning of
the next
the cycle includes alternating periods of contraction and relaxation

 contraction (systole) peak pressure produced during heart contraction.
120 mm Hg (left vent)

 relaxation (diastole) lowest pressure produced during heart relaxation.
80 mm Hg (left vent)

 don’t forget there is a systole and a diastole for both the atria and the ventricles

Note: most of the time the discussion of cardiac cycle concentrates on the left atria and
ventricle due to its high pressures. Be aware the same events are occurring on the right side but
at lower pressures.

Both the right and the left sides of the heart pump the same volumes of blood. If not you have
some form of congestive heart failure.

periods of the cardiac cycle

1. period of ventricular filling
   Ventricles are in diastole
AV valves are open
Semilunar valves are closed

**a. passive ventricular filling phase**

- pressure in heart is low
- atria are in diastole
- ventricles are in late diastole
- blood returning into the heart is passively flowing through the atria into the ventricles
- blood pressures in the sup. and inf. vena cava is greater than in the atria

At the end of the passive filling will see the P wave on the ECG.

**b. active ventricular filling phase**

- the atria contract (systole) which propels blood out of the atria into the ventricles
- this will “top off” the ventricles
- atria will now start to relax (diastole) this allows blood to flow backward into the atria causing the AV valves to close
- this makes the first heart sound
  - this marks the end of period of ventricular filling

- ventricles now have max amount of blood which is called the end-diastolic volume

- at the very end of this period you will see the start of the QRS wave on the ECG

**2. period of ventricular systole**

- ventricles start the contract while atria continues to relax

  **isovolumetric contraction phase**

- at the start both the AV and the semilunar valves are closed
- have a fixed volume

- so the first half of the period of ventricular systole is called isovolumetric contraction phase

- pressure quickly rises, overcoming the pressure in the aorta and pulmonary trunk
this forces open the semilunar valves

**ventricular ejection phase**

now blood is forces out of the heart so second part of the period is called **ventricular ejection phase**

amount of blood left in the ventricle after ventricular ejection phase is over is called **end-systolic volume**

at the very end of this period you will see the T wave on the ECG

as blood is ejected the pressure in the ventricle starts to rapidly drop

3. **period of isovolumetric relaxation**

ventricles enter **early diastole** and relax so pressure in ventricles drops quickly (also drops due to blood ejection)

this allows blood to flow back into the heart from the aorta and pulmonary trunk which shuts the semilunar valves (**second heart sound**)

closure of the left semilunar valves is followed by a brief rise in pressure called the **dicrotic notch**

due to elastic recoil of the aortic walls

all heart valves are now closed so have a fixed volume of blood or **isovolumetric relaxation phase**

this fixed volume of blood is the smallest volume in the ventricles and is called the **end systolic volume**

While ventricles were in systole the atria have been in diastole and filling

once pressure in the atria is higher than in the ventricles the, AV valves will open and start the cycle over (period #1)

**heart sounds**

S1 (lubb) the closing of the AV vales

End of period of ventricular filling

S2 (dupp) the closing of the semilunar valves

Start of period of isovolumetric relaxation

S3 opening of AV vale
Is sound of blood rushing into the atria
Occurs at the start of ventricular filling (passive phase)
S4 contraction of the atria
Due to blood rushing into the ventricles when the atria contracts
Occurs during the active phase of ventricular filling

**EKG**

- P wave occurs during period ventricular filling
- QRS wave starts during period of ventricular filling
- T wave occurs during period of isovolumetric relaxation

**Cardiodynamics**

The movements and forces generated during cardiac contractions

Body activities and therefore the needs of the body change from minute to minute. How is the blood supply adjusted to meet the changing needs of peripheral tissues?

**Cardiac output**

- amount of blood pumped from each ventricle in one minute (5 -6 L/min)

\[ \text{CO} = \text{SV} \times \text{HR} \]

both heart rate & stroke volume can vary

Stroke volume - amount of blood pumped from a ventricle per beat (70-80 ml)

\[ \text{SV} = \text{EDV} - \text{ESV} \]

- EDV = end diastolic volume
  - volume of blood in ventricle at the end of ventricular diastole
- ESV = end systolic volume
  - volume of blood remaining in ventricle at the end of ventricular systole

ejection fraction is the percentage of the EDV represented by the SV

for example:

  EDV of 110ml and SV of 80ml

\[ \text{Ejection fraction} = \frac{80}{110} = 72\% \]
Resting cardiac output

\[ \text{CO (ml/min)} = \text{HR (75beats/min)} \times \text{SV (70 ml/beat)} \]

\[ \text{CO} = 5250\text{ml/min or } 5.25\text{ L/min} \]

Cardiac reserve

difference between resting and maximal cardiac output

is about 5 to 6 times the resting CO

5.25 L/min up to 30 L/min

Trained athletes max is 40L/min

Control of cardiac output

precise adjustments of CO are necessary to insure tissues receive adequate blood flow under varying conditions

what changes cardiac output

\[ \text{(CO} = \text{SV} \times \text{HR}) \]

changes in heart rate
changes in stroke volume

Factors affecting stroke volume:

Remember SV is the difference between the end-diastolic volume and the end-systolic volume

Thus any thing that changes EDV or ESV will change SV

1. Factors changing EDV

Is the amount of blood a ventricle contains at the end of diastole just before a contraction begins

Affected by two factors

**Filling time** - the duration of ventricular diastole

The faster the heart rate the shorter the filling time

Reduces filling time = reduced EDV = reduced stroke volume = reduced cardiac output

**Venous return** - the blood flow rate back to the heart

Affected by changes in

cardiac output,

blood volume,

patterns of peripheral circulation,
skeletal muscle activity, rate and depth of breathing

An increase in venous return = increase in EDV = increase in cardiac output

2. Factors changing ESV
The amount of blood that remains in the ventricle at the end of contraction (systole)

Affected by three factors
- Preload
- Contractility
- Afterload

Preload
the degree of stretch experienced by ventricular muscle cells during ventricular diastole
is directly proportional to the EDV
the greater EDV the greater preload

if the sarcomere resting length is longer (in optimal range), the contraction is stronger & the fibers shorten more production a more forceful contraction (length tension relationship).
Results in more blood pumped from the heart or decrease in the ESV = increase in stroke volume = increase in cardiac output
An increase in preload increases the ejection fraction. It is not just more in = more out. It is more in = a better pumping action by the ventricle

Frank-Starling Law - any factor that increases preload produces a stronger contraction

At rest have low preload so high ESV and low stroke volume

During exercise preload increases so have lower ESV and higher stroke volume

Contractility
Is the amount of force produced during a contraction at a given preload
(is independent of muscle stretch (preload))

results from changing the levels of free calcium inside the myocytes
the increase in calcium results in more actin and myosin fibers interacting
thus a stronger contraction thus more complete ejection of blood

**lowers ESV thus increase SV**

**inotropic effects**
(anything that changes contractility)

**ANS:**

- sympathetic output of norepinephrine binding to beta 1 receptors increases contractile force
  positive inotropic agent

- parasympathetic output of ACh hyperpolarizing the tissue
  negative inotropic

**Hormones:**

- epinephrine & norepinephrine from adrenal medulla increases force
  bind to alpha and beta receptors to increase force of contraction
  positive inotropic agent

- glucagon & thyroid hormone
  positive inotropic agent

**Drugs:**

- digitalis
  positive inotropic agent

- beta blockers
propranolol, timolol, metoprolol
negative inotropic agents

calcium channel blockers
nifedipine and verapamil
negative inotropic agents

Afterload
force produced by contracting ventricle necessary to exceed
aortic pressure & open aortic valve,
higher aortic pressure or pulmonary trunk pressure = higher
afterload which extends the time the ventricle spends in
isovolumetric contraction & reduces time the heart spends in
isometric contraction (ejection phase),
thus high afterload = increase in ESV and decrease in
SV

afterload is increased by
constriction of peripheral blood vessels
circulatory blockage
valve stenosis

Role of heart rate in controlling cardiac output
CO = SV x HR

Heart rate
Can be altered by positive and negative chronotropic effects
1. ANS

Negative chronotropic effects
Pacemaker cells of S-A node establish base rate at 80-100/min
Parasympathetic (Vagus) output decreases rate
to 70-80/min
Parasympathetic stimulation can reduce the CO
by 10 to 20%
An increase in blood pressure will stretch
baroreceptors in the carotid arteries and aorta
This stimulates the cardioinhibitory
center while inhibiting the
cardioacceleratroy center and activates the vagus to release ACh

**Positive chronotropic effects**
- parasympathetic withdraw
- increase to **80-100bpm**
- sympathetic activity
- increase over **200bpm**

sympathetic stimulation can increase CO by 50 to 100%

low blood pressure as perceived by the baroreceptors will shut down the cardioinhibitory center and let the cardioacceleratroy center turn on thus the cardiac nerve will be activated releasing norepinephrine and epinephrine

chemoreceptors in same location will active the cardioacceleratroy center when blood CO2 and acid levels increase and O2 levels decrease

2. **Hormones**
   - epi and norepinephrine from adrenal medulla
   - thyroid hormones
   - both have positive chronotropic effects

3. **Cardiac reflexes**
   - Bainbridge reflex
     - Increase in **venous return** will stretch the atria (nodal cells)
     - Stimulates the cardioacceleratroy center (sympathetic stimulation) with increases heart rate

4. **Changes in ion concentration**
   - low extracellular potassium (hypokalemia) hyperpolarizes the pacemaker, moving it from threshold for APs and lowers heart rate. In extreme cases the heart will be unable to depolarize and will stop in diastole
high extracellular potassium (hyperkalemia) depolarizes the pacemaker and raises the heart rate. Extreme hyperkalemia the cells will depolarize and be unable to repolarize. The heart will stop in systole

5. Temperature
   positive chronotropic effect
      elevated temperature increases heart rate
      speeds the opening of channels
   
   negative chronotropic effect
      lower temperature slows rate
      slows the opening of channel

closing words about increase in heart rate and the affects on cardiac output as heart rate increases the ventricular filling time decreases so this would tend to lower cardiac output

up to 160-180 bpm's the combination of increased venous return and increased contractility compensates for reduced filling time so that stroke volume increases.

over this amount the stroke volume falls but cardiac output continues to rise do to the increase in heart rate

over 220-240 cardiac output starts to fall do to a major decline in stroke volume do to drop in ventricular filling time