1. Heart
   a. Generates the pressure that propels blood thru blood vessels.
   b. Separates oxygenated and deoxygenated blood separate.
   c. Helps regulates the body's blood supply.
2. Heart position
   a. W/i the mediastinum, the medial cavity of the thorax.
   b. Apex rests on the superior diaphragmatic surface and points toward the left hip.
   c. Base points towards the right shoulder.
   d. Medial to the lungs, anterior to the esophagus and vertebrae, and posterior to the sternum.
3. Pericardium
   a. Encloses the heart.
   b. Outermost layer is the fibrous pericardium – a collagenous structure that protects and anchors the heart and prevents it from distending.
   c. Deeper is the serous pericardium, a 2 layered serous membrane.
   d. Parietal serous pericardium is the outer of the 2 and abuts the fibrous pericardium.
   e. Visceral serous pericardium is the inner of the 2 and is the external covering of the heart and is a.k.a. the epicardium.
   f. Parietal and visceral layers are continuous with one another where the great vessels leave the heart.
   g. Pericardial cavity is the space btwn the parietal and visceral layers and contains serous fluid, which reduces friction.
4. Heart wall
   a. Divided into 3 layers.
   b. Epicardium
      i. Most superficial and is a.k.a. visceral serous pericardium.
      ii. Composed of simple squamous epithelium overlaying thin loose CT.
   c. Myocardium
      i. Middle layer.
      ii. Primarily cardiac muscle, but also contains blood vessels, nerves, and CT.
      iii. Myocardial CT forms a dense network known as the fibrous skeleton, which supports the heart valves, acts as origin/insertion for the cardiac muscle cells, and helps direct the spread of electrical activity within the heart along defined pathways.
   d. Endocardium.
      i. Inner layer
      ii. Consists of endothelium (simple squamous epithelium) resting on a layer of thin CT.
      iii. Lines the heart chambers and its folds create the heart valves.
5. Heart Chambers
   a. 2 superior atria and 2 inferior ventricles.
   b. Thin interatrial septum divides the 2 atria
   c. Tthick interventricular septum divides the 2 ventricles.
6. Heart consists of 2 pumps connected in series.
   a. Each pump sends blood to a different circuit.
   b. Pulmonary circuit runs btwn the heart and the lungs.
   c. Systemic circuit runs btwn the heart and the rest of the body tissues.
   d. Right side of the heart receives deO_2 blood from the systemic circuit and pumps it thru the pulmonary circuit.
   e. Left side of the heart receives O_2 blood from the pulmonary circuit and pumps it thru the systemic circuit.
7. Atria
   a. Heart's receiving chambers.
   b. Small and thinly muscled. Large muscle mass is unnecessary, since atrial contraction propels only a small amount of blood to the ventricles.
8. Right atrium
   a. Receives deO_2 blood from the systemic circuit via 3 vessels:

            i. Superior vena cava carries blood from arms, head, and upper tors
            ii. Inferior vena cava carries blood from the legs, abdomen, and pelvis
            iii. Coronary sinus carries blood from the coronary circulation – which nourishes the heart wall.
    b. Sends blood to right ventricle thru tricuspid orifice, via the tricuspid valve.
9. Left atrium
    a. Receives O_2 blood from the pulmonary circuit via the 4 pulmonary veins.
    b. Sends blood to left ventricle thru mitral (bicuspid) orifice, via the mitral (bicuspid) valve.
10. Fossa ovalis
    a. Remnant of the foramen ovale, a hole in the fetal atrial septum.
        i. Fetal blood flowed through the hole from RA to LA thus bypassing the pulmonary circuit (since the fetal lungs are neither developed nor oxygenated).
11. Left and right auricles
    a. Muscular pouches connected to the left and right atria.
    b. Function as reservoirs for blood.
12. Ventricles
    a. Large, muscular chambers.
    b. Thick musculature is necessary because they are the actual pumps.
    c. Contain muscular ridges known as trabeculae carneae as well as muscular bulges known as papillary muscles.
13. Right ventricle
    a. Discharges blood into the pulmonary trunk, the first vessel of the pulmonary circuit.
    b. Separated from the pulmonary trunk by the pulmonary semilunar valve
14. Left ventricle
    a. Discharges blood into the aorta, the first vessel of the systemic circuit.
    b. Separated from the aorta by the aortic semilunar valve.
    c. More muscular than the RV.
        i. Necessary because the LV pumps blood a farther distance and against greater pressure (note – RV and LV pump the same volume of blood per beat).
15. Systemic and pulmonary circuits

Systemic circuit:

L ventricle → Aorta → Systemic arteries → Syst. capillaries → Syst. veins → Venae cavae → R atrium

Pulmonary circuit:

R ventricle → Pulmonary trunk → Pulm. arteries → Pulm. capillaries → Pulm. veins → L atrium

    a. If we combine the 2 circuits, note that we have 2 pumps in series:

L atrium → L ventricle → Systemic Blood Vessels → R atrium → Right ventricle → Pulmonary blood vessels → L atrium

16. Ways in which the systemic circuit differs from the pulmonary circuit
    a. Longer
    b. Much larger blood volume.
    c. Its blood is under far greater pressure.
    d. Resistance to blood movement is also far greater.
    e. Systemic arteries are O_2 rich & CO_2 poor. Pulmonary arteries are O_2 poor & CO_2 rich. Systemic veins are O_2 poor and CO_2 rich. Pulmonary veins are O_2 rich and CO_2 poor.
17. Coronary circuit
    a. Network of blood vessels supplying/draining the 3 heart layers.
    b. Needed b/c the heart requires a prodigious amount of O_2 and nutrients, and little O_2 or nutrients can diffuse thru the thick myocardium.

c. Basic pathway of blood in the coronary circuit is:

L ventricle → Aorta → Coronary arteries → Cor. capillaries → Cor. veins → Cor. sinus → R atrium

18. 4 Heart valves
    a. Ensure 1-way flow within the heart.
    b. 2 atrioventricular valves separating the atria from the ventricles
    c. 2 semilunar valves separating the ventricles from their great vessels.
19. AV valves
    a. Consist of a flap of endothelium with a core of connective tissue.
    b. Tricuspid valve has 3 flaps and prevents backflow of blood from the RV to the RA.
    c. Mitral (bicuspid) valve prevents backflow from the LV to the LA
    d. AV valve flaps are attached to strings of collagen called chordae tendineae.
    e. Chordae tendineae attach to papillary muscles in the ventricle wall.
    f. Blood goes thru an AV valve from atria to the ventricle when atrial BP > ventricular BP.
        i. At this time the chordae tendineae are slack, and papillary muscles are relaxed.
    g. When the ventricle contracts:
        i. Ventricular BP > atrial BP.
        ii. Blood will attempt to flow down its pressure gradient back into the atria. This pushes the valve flaps towards the atria (closing them).
        iii. Chordae tendineae tighten as papillary muscles contract thus preventing the valve flaps from flipping up (prolapsing) into the atrium.
    h. Note that the chordae tendinae and papillary muscles do NOT close the AV valves themselves. Blood's attempt to backflow is what pushes the valves shut.
20. Semilunar valves
    a. Aortic semilunar valve prevents backflow from the aorta into the LV.
        i. ASV is pushed open when LV BP exceeds aortic BP. It's forced shut when aortic BP exceeds LV BP.
    b. Pulmonary semilunar valve prevents backflow from the pulmonary trunk into the RV.
        i. PSV is pushed open when RV BP exceeds pulmonary trunk BP. It's forced shut when pulmonary trunk BP exceeds RV BP.
    c. Note that b/c the semilunar valves are "pocket valves" they have no need for associated chordae tendineae or papillary muscles.
21. Cardiac muscle
    a. Comprises the bulk of the heart wall.
    b. Involuntary
    c. 2 types of cardiac muscle cells – contractile cells and autorhythmic cells.
    d. Contractile cells
        i. 99%
        ii. Generate the force involved in pumping.
        iii. Striated, short, and branched.
    e. Autorhythmic cells
        i. 1%
        ii. Spontaneously depolarize to set the rate of contraction.
22. Intercalated discs
    a. Link cardiac muscle cells together mechanically and electrically.
    b. Contain 2 separate structures: gap junctions and desmosomes.
    c. Gap junctions
        i. Protein channels that allow ions to flow btwn adjacent cells.
        ii. Create an electrical connection btwn cardiac muscle cells.
        iii. Allow the depolarization wave initiated by autorhythmic cells to spread through the cardiac musculature.
            1. Electrical excitation of cardiac muscle cells causes an increase in intracellular Ca^{2+} levels. Calcium binds w/ troponin to produce contraction via the familiar sliding filament mechanism.

iv. Allows the heart to function as a single coordinated unit (functional syncytium), which helps maximize its efficiency.

d. Desmosomes

i. Protein filaments that physically connect adjacent cardiac muscle cells and prevent them from separating during contraction.

23. Fibrous skeleton of the heart

a. Dense irregular CT w/i the heart.

b. Provides origins and insertion points for cardiac contractile cells.

c. Supports heart valves

d. Separates the atria from the ventricles both physically and electrically

24. Intrinsic control of heart rate

a. Performed by the autorhythmic

b. 5 main groups of autorhythmic cells:

i. Sinoatrial node – group of autorhythmic cells near opening of the SVC.

ii. Atrioventricular node – group of ACs in inferior IA septum near tricuspid orifice.

iii. Atrioventricular bundle – group of ACs in the superior IV septum.

iv. Right and left bundle branches – group of ACs in middle & inferior IV septum.

v. Purkinje fibers – separate autorhythmic cells that wind through the ventricles.

c. The above list also gives the path of the electrical conduction system within the heart.

d. All autorhythmic cells have the ability to rhythmically and spontaneously depolarize.

e. SA node cells have the fastest rate of depolarization

i. They set the pace for other autorhythmic cells as well as the rest of the heart. \

ii. SA node is known as the pacemaker of the heart.

f. Spread of depolarization:

SA node cells depolarize.

→ Depolarization wave travels to atrial contractile cells.

↓ Atrial contractile cells contract. Note that the right atrium begins to contract before the left.

↓ Depolarization wave travels to AV node. Depolarization wave is briefly delayed, allowing atria to complete contracting before the ventricles begin.

↓ Depolarization wave travels down AV bundle & bundle branches. *(Fibrous skeleton prevents it from traveling directly from atria to ventricles)*

↓ Depolarization wave travels thru the ventricles via Purkinje fibers.

↓ Ventricular contractile cells depolarize and then contract.

g. W/o any input (neural or hormonal), the inherent rate of SA node depolarization determines heart rate.

i. Normal uninfluenced rate is roughly 100 depolarizations per minute.

h. Fibrous skeleton of the heart electrically isolates the atria and the ventricles. The AV bundle is the only electrical connection btwn them.

i. Ventricular depolarization and contraction begin at the apex of the heart and proceed upward. This allows blood to be propelled up out of the ventricles into the great vessels.

25. Extrinsic control of heart rate

a. Refers to factors originating outside of cardiac tissue that affect heart rate.

b. Most extrinsic control is nervous or endocrine in nature.

26. Medulla oblongata contains 2 cardiac centers that can alter the heart's activity.

a. Cardioacceleratory center

        i. Projects via the cardiac sympathetic nerves to the SA node, AV node, and the ventricular myocardium.
        ii. These neurons release NE, which increases contraction rate and force.
    b. Cardioinhibitory center
        i. Contains parasympathetic neurons that project (via the vagus nerve, CN X) to the SA node and AV nodes. T
        ii. These neurons release ACh, which causes a decrease in heart rate but no change in the heart's contractile strength.
    c. At rest, both parasympathetic and sympathetic neurons are releasing neurotransmitters onto the heart, but the parasympathetic branch is dominant.
    d. During stress, exercise, and excessive heat the sympathetic influence is dominant.

27. Heart sounds
    a. 2 associated with each heart beat.
    b. 1^{st} heart sound
        i. LUB
        ii. Caused by the shutting of the atrioventricular valves
        iii. Occurs at the onset of ventricular contraction.
    c. 2^{nd} heart sound
        i. DUP
        ii. Caused by the shutting of the semilunar valves
        iii. Occurs at the end of ventricular contraction.
28. Cardiac cycle
    a. Refers to all events associated with blood flow thru the heart during one heartbeat.
    b. Includes the contraction (systole) and relaxation (diastole) of all 4 chambers.
    c. Divided into 4 parts: ventricular filling, isovolumetric contraction, ventricular ejection, and isovolumetric relaxation.
    d. We'll discuss the cardiac cycle in terms of the left side of the heart, but analogous events are occurring on the right side.
29. Ventricular filling
    a. LA BP is lower than the BP of the pulmonary vasculature, so blood enters the left atrium.
    b. LA BP is greater than LV BP, so blood enters the LV.
    c. B/c LA BP is greater than LV BP, the mitral valve is pushed open.
    d. LV BP is less than aortic BP. As a result, blood tries to back flow from the aorta into the LV and this forces the aortic semilunar valve closed.
    e. Neither atrial nor ventricular muscle is contracting. Both are in diastole.
    f. About 80% of the ultimate ventricular volume will enter in this passive manner.
    g. At the end of ventricular filling, while the LV is still relaxing, the LA depolarizes and contracts.
        i. This pushes roughly the final 20% of blood into the LV.
        ii. LV now has the maximum volume it will contain during this particular cycle.
            1. This is the end diastolic volume (EDV). (Typically = 130mL).
    h. For the rest of the cycle, the LA will be in diastole.
30. Isovolumetric contraction
    a. LV depolarizes, contracts, and LV BP rises quickly almost immediately exceeds LA BP.
    b. Blood is pushed upward shutting the mitral valve– creating the 1^{st} heart sound (LUB).
    c. However, the opening of the aortic semilunar valve requires much more pressure than was necessary to close the mitral valve.
    d. So after the mitral valve is shut, the LV continues to contract and its BP rises, but until LV BP exceeds aortic BP, the aortic semilunar valve remains shut.
    e. Thus, during this period, the AV and semilunar valves are shut and the volume within the LV is not changing. Hence this phase is known as "iso" "volumetric" contraction.
31. Ventricular ejection
    a. LV BP now exceeds aortic BP (80mmHg), the semilunar valve is forced open, and blood is ejected from the LV into the ascending aorta.
    b. Not all of the blood in the LV is ejected. The amount remaining after ventricular contraction is known as the end systolic volume (ESV). A typical value is 70mL.

        i. This gives a reserve amount of blood that could also be ejected if necessary (e.g., during exercise).
    c. Amount of blood ejected during this phase is known as the stroke volume.
        i. Stroke volume is the difference btwn end diastolic and end systolic volumes: SV=EDV-ESV.
        ii. A more vigorous contraction will result in a decreased ESV and an increased SV.

32. Isovolumetric relaxation
    a. Once the LV has completed contracting, its BP falls and quickly becomes less than aortic BP and blood tries to back flow, which shuts the semilunar valve– creating the 2nd heart sound (DUP).
    b. However, it takes a bit longer for the LV BP to drop below the LA BP – and cause the mitral valve to open.
    c. During this time, as LV BP is falling, the AV and semilunar valves are shut and LV volume is not changing.
    d. Once LV BP falls below LA BP (which is rising as blood returns to the heart), the mitral valve will open and the cycle will begin anew with another round of ventricular filling.
33. LV vs. RV
    a. Note that the events on the left side of the heart during a normal cardiac cycle are mirrored by the events on the right side of the heart.
    b. Both the right and the left side of the heart contract at the same rate.
    c. They have identical stroke volumes on average.
    d. The only difference is the pressure involved. The LV must contract harder to open its semilunar valve. This is because the systemic circuit is under a much higher pressure than the pulmonary circuit. The left and right ventricle must have identical stroke volumes. If LV SV > RV SV, then blood would back up in the systemic circuit. If LV SV < RV SV, then blood would back up in the pulmonary circuit.
34. Cardiac output
    a. Amount of blood pumped by each ventricle in one minute.
    b. Product of heart rate and stroke volume: CO(mL/min) = HR(beats/min) x SV(mL/beat).
    c. Changes in either stroke volume or heart rate can alter cardiac output.
    d. During exercise, cardiac output can increase dramatically.
35. Nervous system regulation of heart rate.
    a. Increases in heart rate are achieved by:
        i. Increase in cardioacceleratory center activity. This increases sympathetic nerve activity and increases NE release on the heart.
        ii. Decrease in cardioinhibitory center activity. This decreases parasympathetic nerve activity and decreases ACh release on the heart.
    b. Decreases in heart rate are achieved by:
        i. Decrease in cardioacceleratory center activity. This decreases sympathetic nerve activity and decreases NE release on the heart.
        ii. Increase in cardioinhibitory center activity. This increases parasympathetic nerve activity and increases vagus nerve activity (a.k.a. vagal tone), and increases ACH release on the heart.
36. Relationship btwn heart rate and stroke volume
    a. Note that if heart rate changes without a change in contractility (the strength of the contraction), stroke volume will change also. This is because changing the heart rate alters the filling time (i.e., the time btwn beats during which the heart fills up with blood).
37. Hormonal influences on heart rate.
    a. Epinephrine, released by the adrenal medulla (an endocrine organ found atop the kidney), increases HR.
    b. Thyroxine, released by the thyroid gland (located in the anterior neck), increases HR.
38. Other factors that raise heart rate
    a. Increased body temperature and chemicals such as caffeine, nicotine, and ephedrine.
39. Other factors that decrease heart rate
    a. Decreased body temperature and drugs such as beta blockers.

40. Regulation of stroke volume
    a. Depends on 3 main variables: preload, contractility, and afterload.
41. Preload
    a. Refers to the degree of ventricular stretch during filling.
    b. An increase in heart muscle is stretched (up to a point), causes increased contractile force
    c. Increased in stretch causes more optimum cross-bridge formation btwn actin and myosin and a stronger contraction, thus ejecting a larger volume.
    d. Frank-Starling law states: *"What returns to the heart will get pumped out of the heart."*
    e. As venous return (the volume of blood returning to the heart per minute) increases, EDV increases, and stroke volume increases.
    f. A decrease in HR will increase the filling time and thus increase EDV (and preload).
    g. An increase in venous pressure will also increase EDV (and preload).
    h. The stroke volume is greatly influenced by changes in preload.
42. Contractility
    a. Strength of the heart's contraction independent of its degree of stretch.
    b. Increase in contractility will result in an increase in stroke volume and a decrease in end systolic volume.
    c. Factors that increase contractility include: increased cardioacceleratory activity; and hormones such as epinephrine and thyroxine.
43. Afterload
    a. Pressure that must be overcome to open the semilunar valve and eject blood.
    b. Equivalent to arterial blood pressure.
    c. Increase in arterial BP will increase afterload. This makes the heart expend more time/energy on opening the semilunar valve and less on ejecting blood.
    d. Thus, an increase in afterload will cause stroke volume to decrease and end systolic volume to increase.
    e. However, it takes a significant increase in afterload before the pumping output of the heart is hampered.