Cardiovascular medicine

I-Med

Outline

- Overview anat and physiology
- Introduction to cardiovascular disorders
- Diagnosis of cardiovascular diseases
- Disorders of rhythm
- Disorders of the heart
- Vascular diseases

Anatomy overview

- **1. Function**
- **Cardiovascular** = Heart, Arteries, Veins, Blood

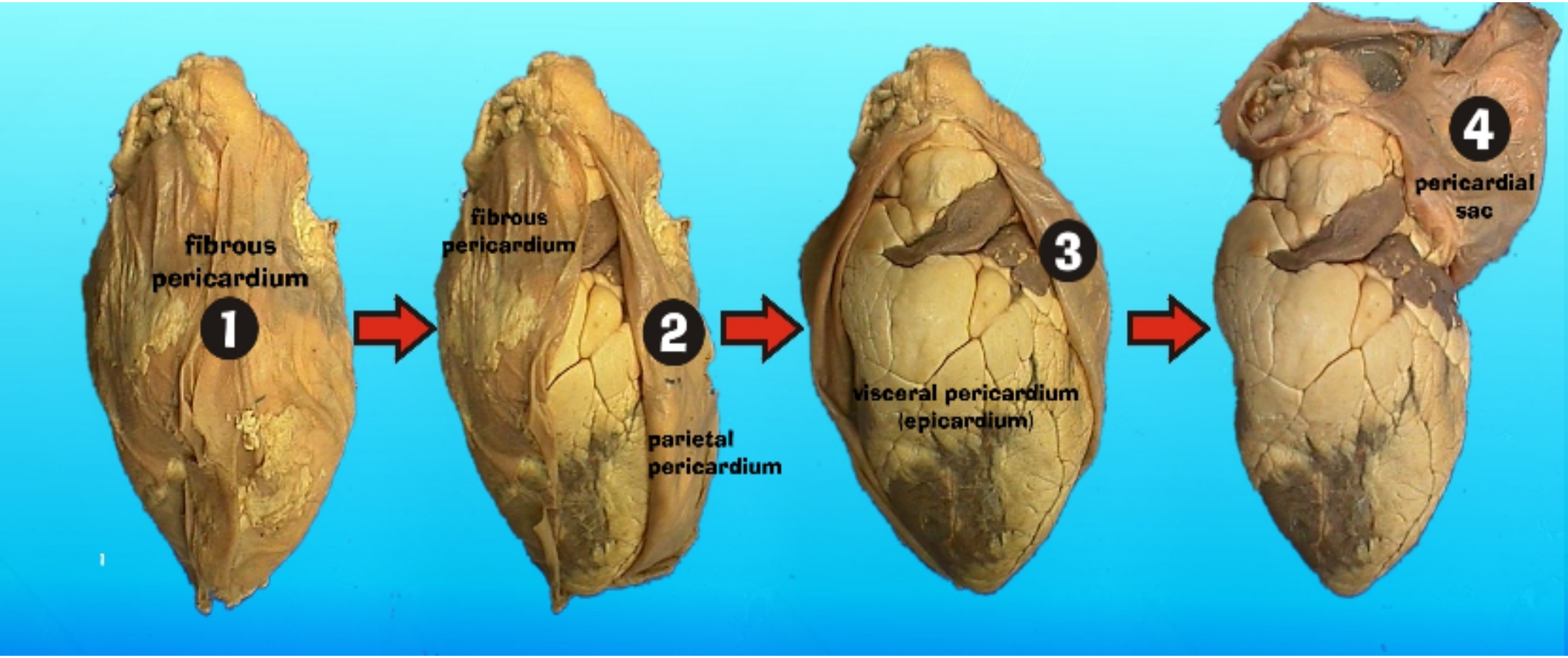
- ***Function:***
  - Transportation
  - Blood = transport vehicle
  - Carries oxygen, nutrients, wastes, and hormones
  - Movement provided by pumping of heart

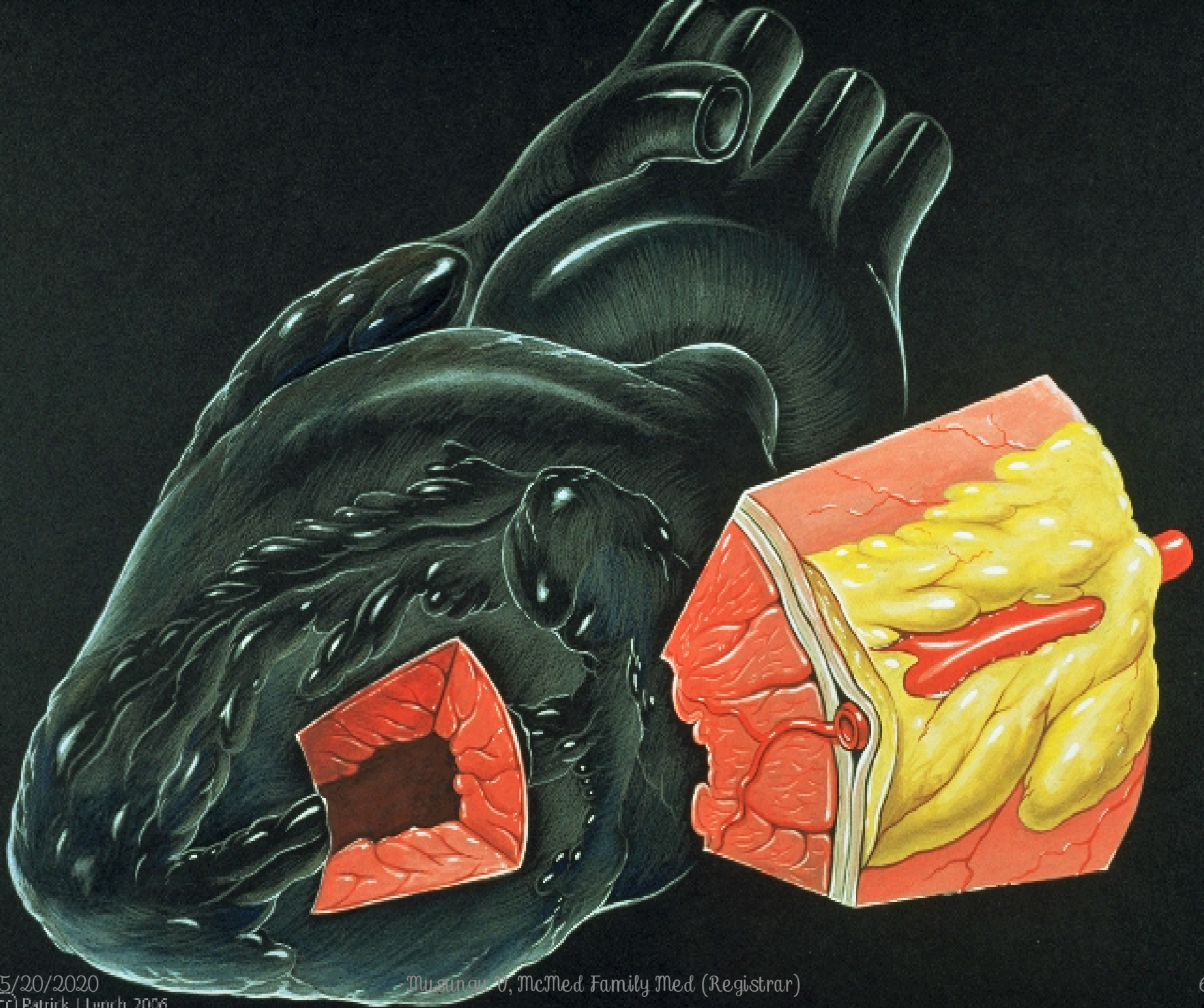
(2) Cardiac Tissues

- **Outermost = Pericardium & Epicardium**
  - Pericardium is a membrane anchoring heart to diaphragm and sternum
  - Pericardium secretes lubricant (serous fluid)
  - Epicardium is outermost muscle tissue

- **Middle = Myocardium**
  - Contains contractile muscle fibers

- **Innermost = Endocardium**
  - Lines Cardiac Chambers

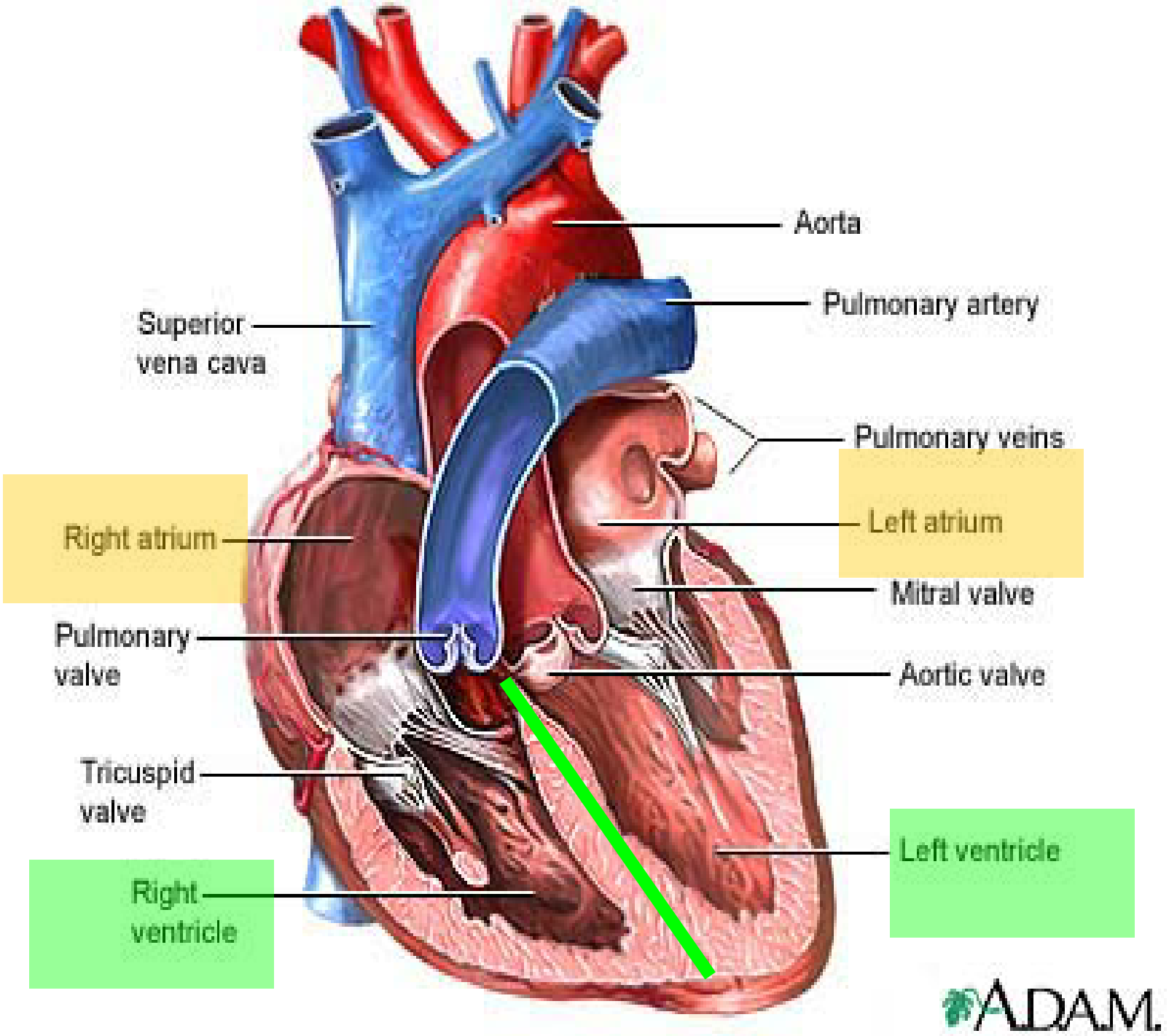

fibrous pericardium
1
fibrous pericardium
2
parietal pericardium
3
visceral pericardium (epicardium)
4
pericardial sac



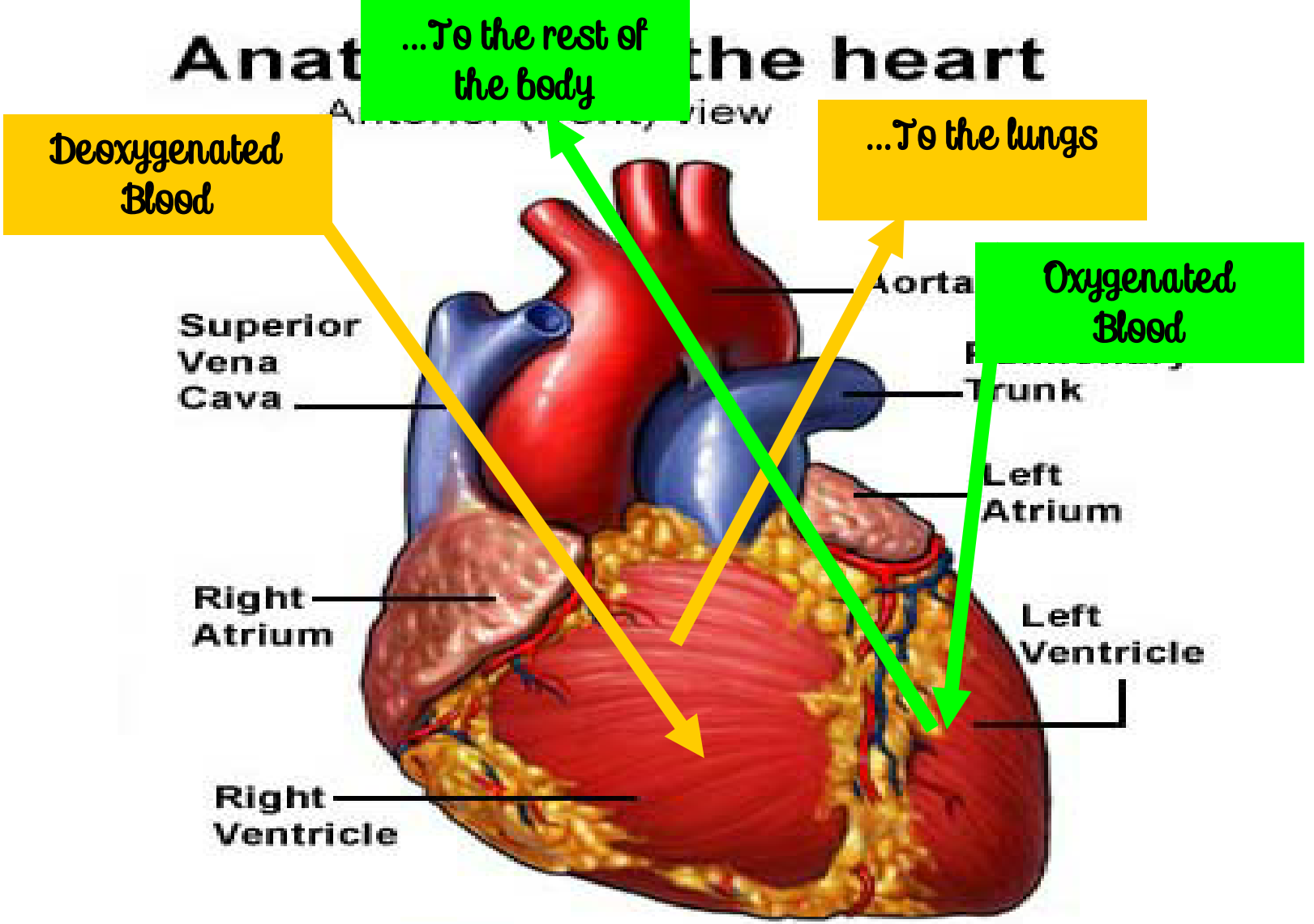
(3) Cardiac Chambers

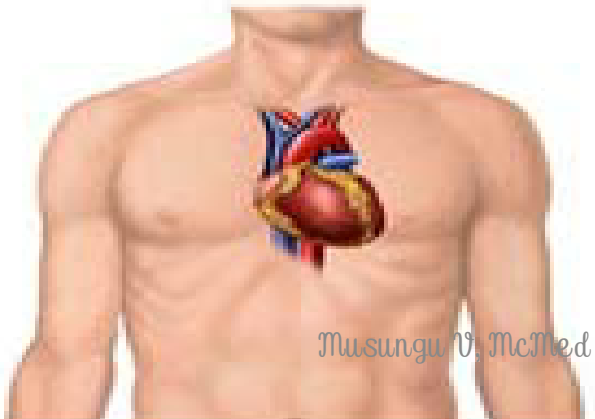
- ***Human heart has 4 chambers***
  - **2 Atria**
    - Superior = primary receiving chambers, do not actually pump
    - Blood flows into atria
  - **2 Ventricles**
    - Pump blood
    - Contraction = blood sent out of heart + circulated

- ***Chambers are separated by septum…***
  - Due to separate chambers, heart functions as double pump


Aorta
Pulmonary artery
Superior vena cava
Pulmonary veins
Left atrium
Right atrium
Mitral valve
Pulmonary valve
Aortic valve
Tricuspid valve
Left ventricle
Right ventricle
A.D.A.M.

Anat the heart



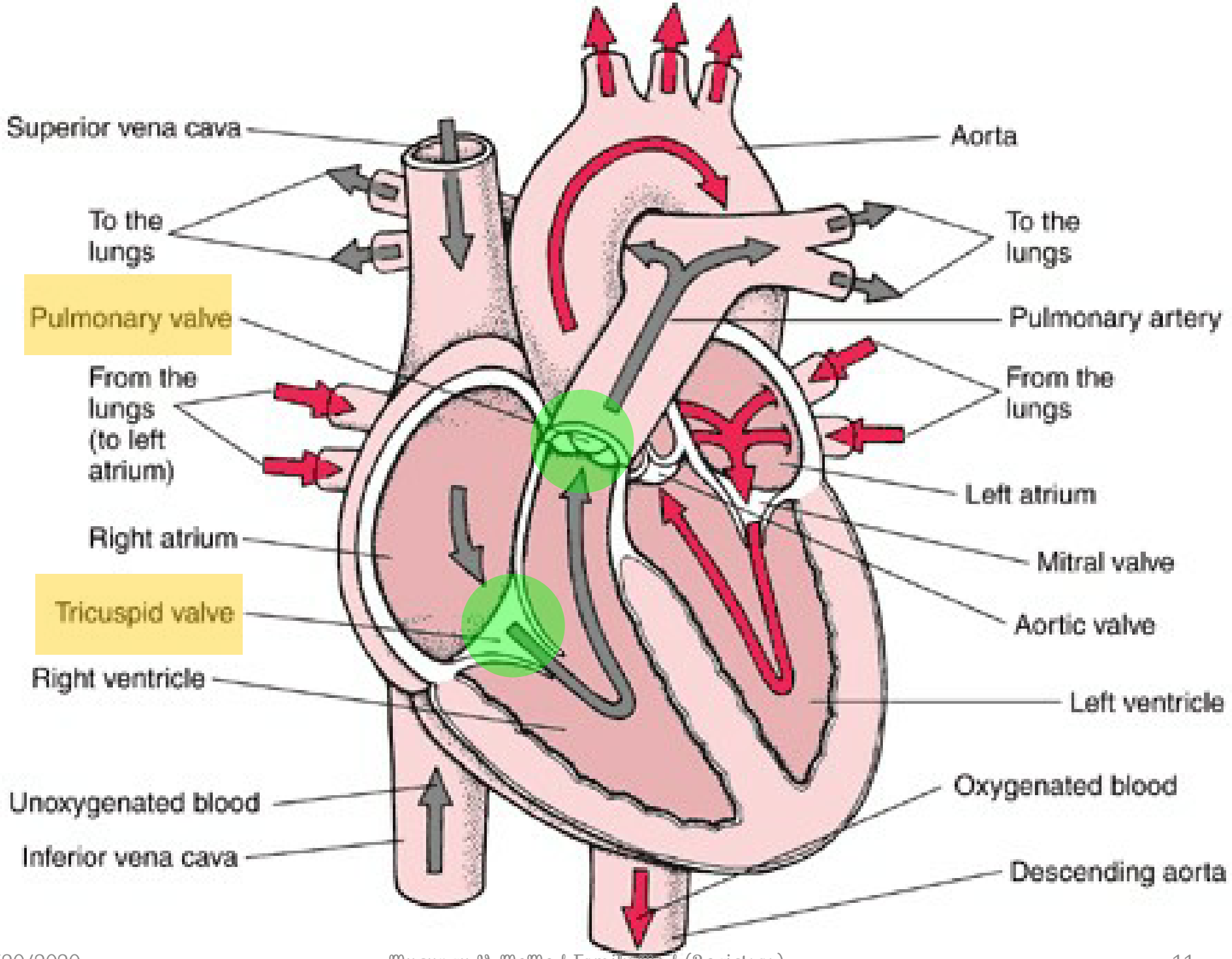


Location of heart within the body

(4) Pulmonary Circulation

- **Pulmonary** = Deoxygenated Blood
- Involves Right Side of Heart

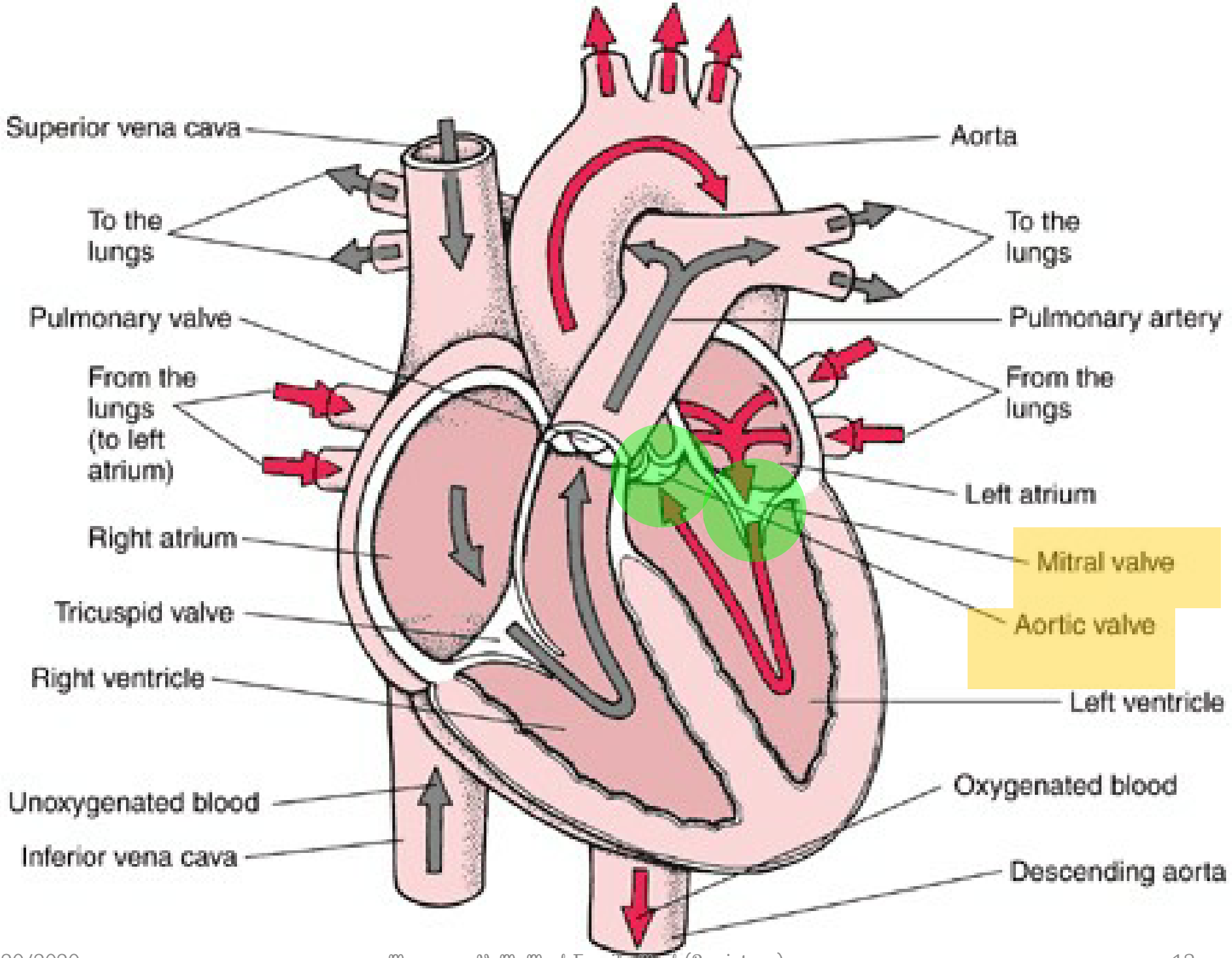
- ***Pathway:***
  1. Superior / Inferior Vena Cava
  2. Right Atrium → Tricuspid Valve
  3. Right Ventricle → Pulmonary Semilunar Valve
  4. Left Pulmonary Artery
  5. Lungs


Superior vena cava
Aorta
To the lungs
To the lungs
Pulmonary valve
Pulmonary artery
From the lungs (to left atrium)
From the lungs
Left atrium
Right atrium
Mitral valve
Tricuspid valve
Aortic valve
Right ventricle
Left ventricle
Unoxygenated blood
Oxygenated blood
Inferior vena cava
Descending aorta

(5) Systemic Circulation

- **Systemic** = Oxygenated Blood
- Involves Left Side of Heart

- ***Pathway:***
  1. Left Pulmonary Vein
  2. Left Atrium → Bicuspid Valve
  3. Left Ventricle → Aortic Semilunar Valve
  4. Aorta
  5. All Other Tissues


Superior vena cava
Aorta
To the lungs
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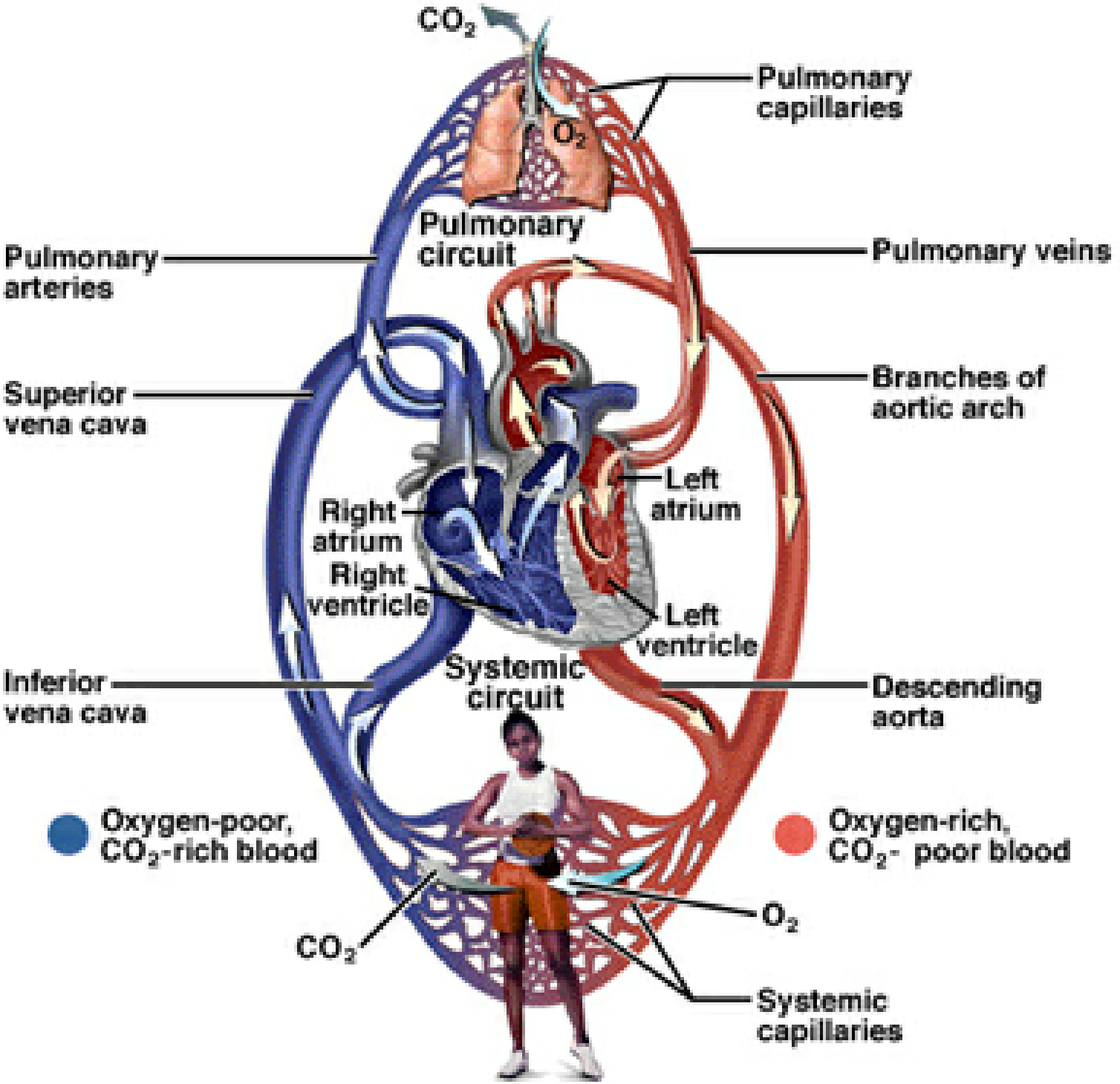
Unoxygenated blood
Oxygenated blood
Inferior vena cava
Descending aorta


CO_2
Pulmonary capillaries
O_2
Pulmonary circuit
Pulmonary arteries
Pulmonary veins
Superior vena cava
Branches of aortic arch
Left atrium
Right atrium
Right ventricle
Left ventricle
Systemic circuit
Inferior vena cava
Descending aorta
Oxygen-poor, CO_2-rich blood
Oxygen-rich, CO_2- poor blood
O_2
CO_2
Systemic capillaries

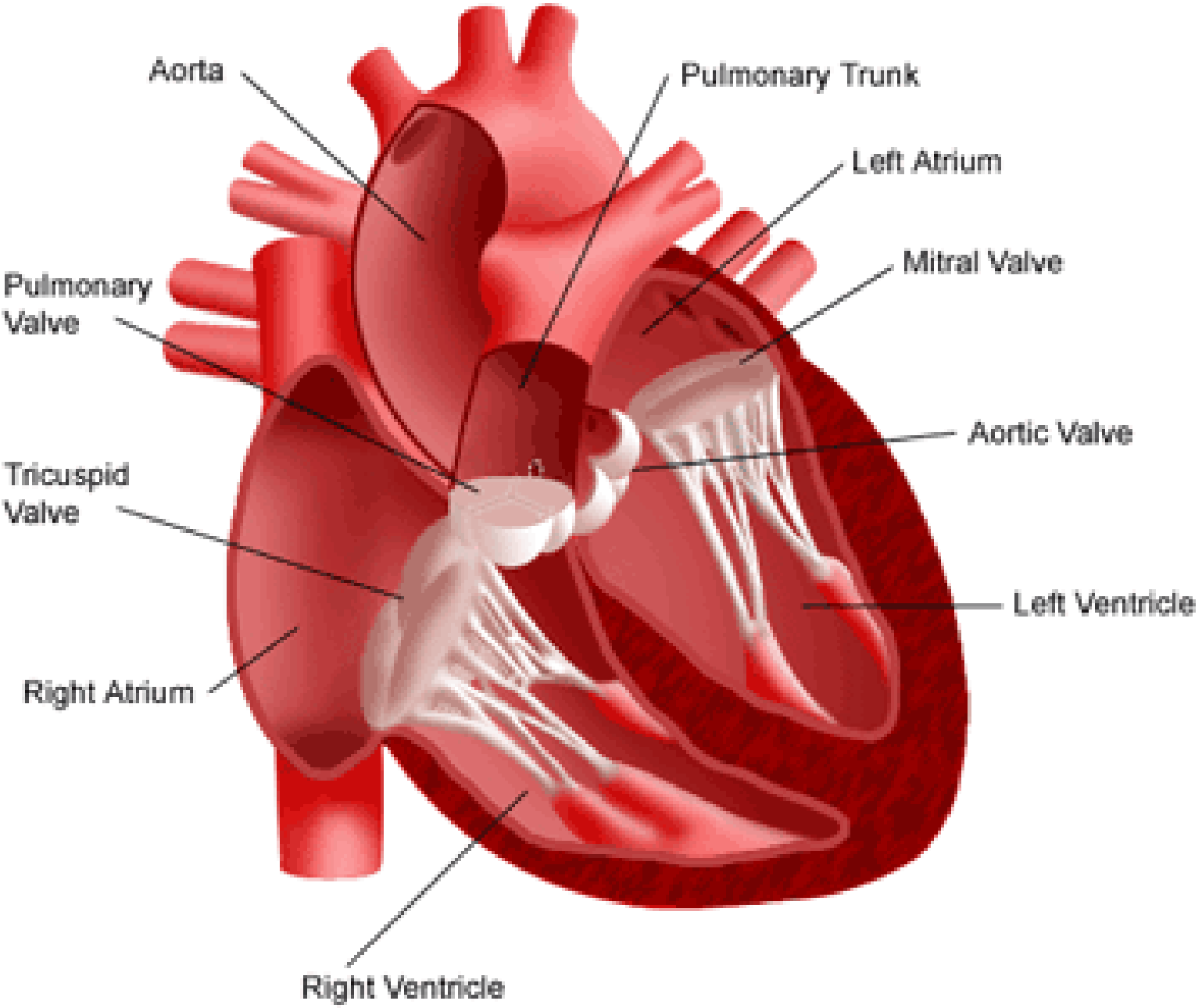
(6) Cardiac Valves

[4 main valves]

- ***When the heart is relaxed…***
  - Blood passively fills atrium
  - Flows right past tricuspid / bicuspid valves
  - Semilunar Valves remain shut

- ***When the heart contracts (pumps)…***
  - Tricuspid / Bicuspid valves swing up and shut
  - Blood ejected out of ventricle
  - Semilunar Valves open up

Valves of the Heart



Cardiovascular Physiology

Cardiovascular System Function

- Functional components of the cardiovascular system:
  - Heart
  - Blood Vessels
  - Blood
- General functions these provide
  - Transportation
    - Everything transported by the blood
  - Regulation
    - Of the cardiovascular system
      - Intrinsic & extrinsic
  - Protection
    - Against blood loss
  - Production/Synthesis

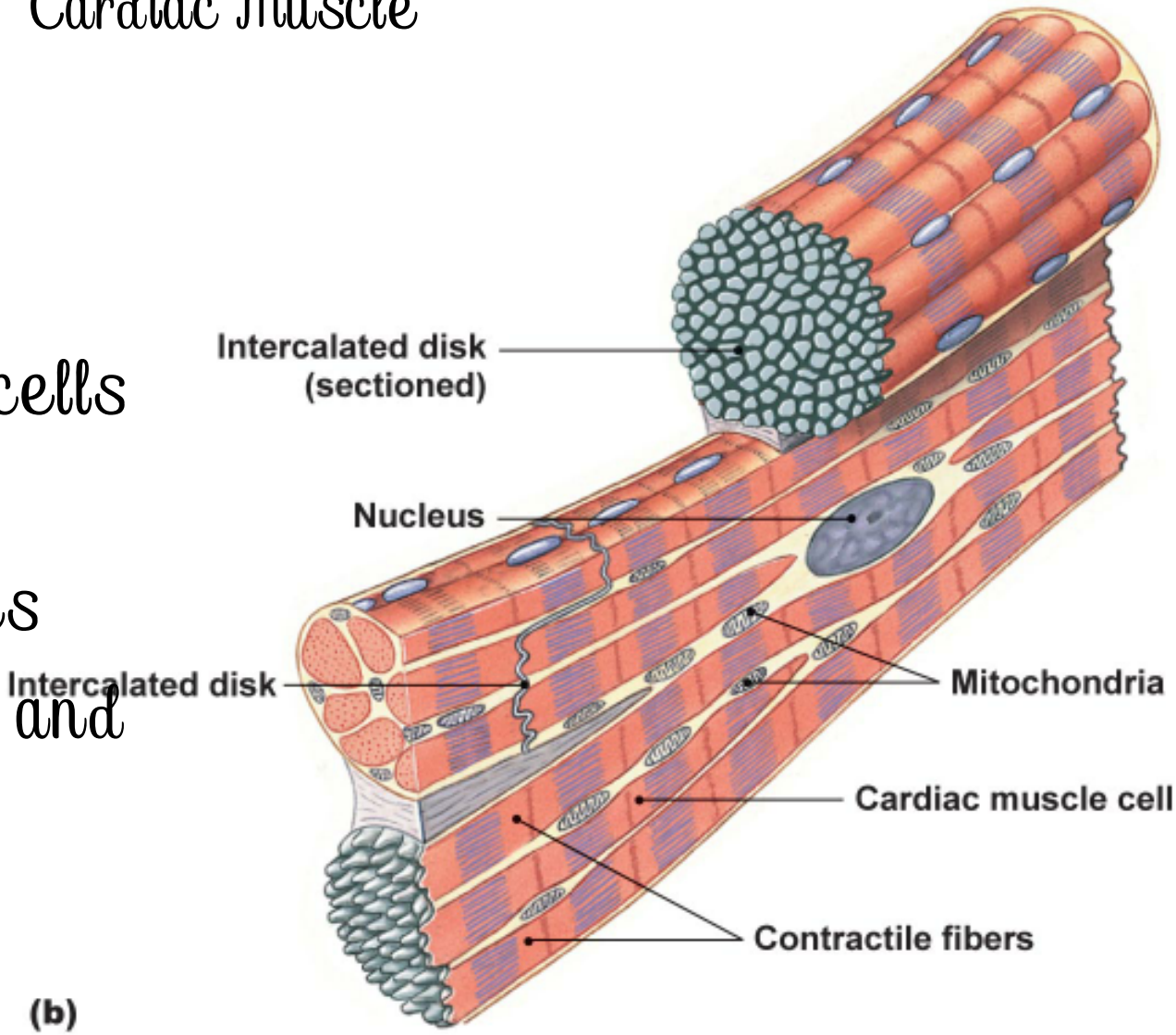
Cardiovascular System Function

- To create the "pump" we have to examine the Functional Anatomy
  - Cardiac muscle
  - Chambers
  - Valves
  - Intrinsic Conduction System

Functional Anatomy of the Heart

Cardiac Muscle

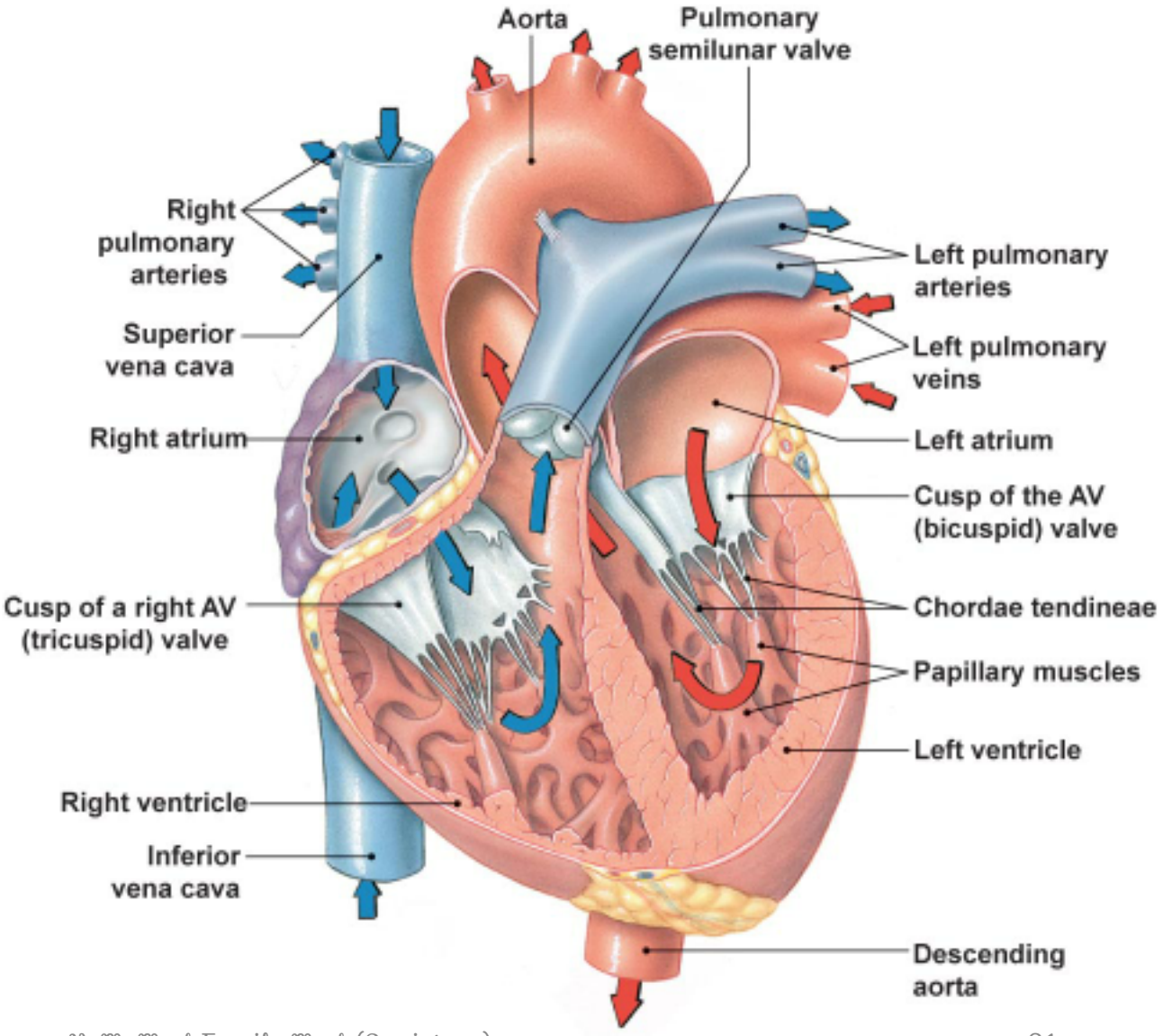
- Characteristics
  - Striated
  - Short branched cells
  - Uninucleate
  - Intercalated discs
  - T-tubules larger and over z-discs



Functional Anatomy of the Heart

Chambers

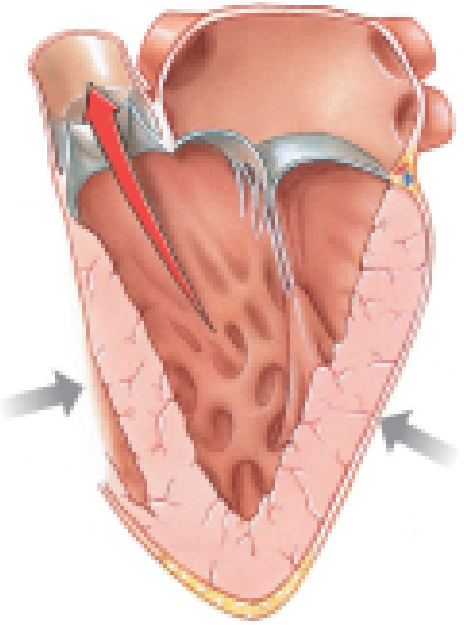
- 4 chambers
  - 2 Atria
  - 2 Ventricles
- 2 systems
  - Pulmonary
  - Systemic

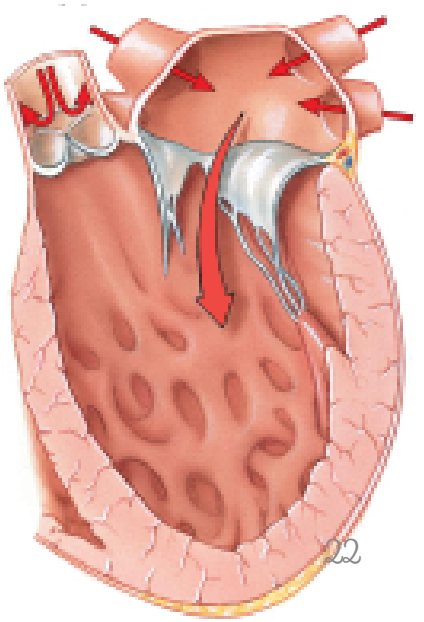


Functional Anatomy of the Heart

Valves

- Function is to prevent backflow
  - Atrioventricular Valves
    - Prevent backflow to the atria
    - Prolapse is prevented by the chordae tendinae
      - Tensioned by the papillary muscles
  - Semilunar Valves
    - Prevent backflow into ventricles

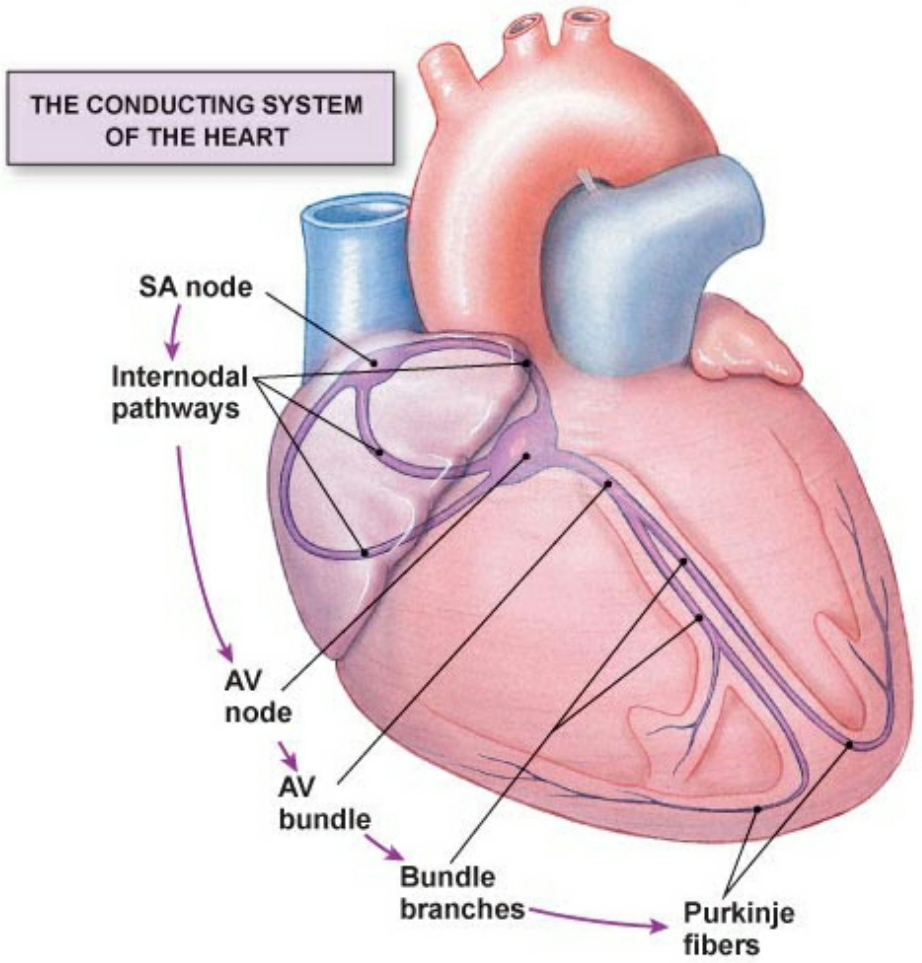




Functional Anatomy of the Heart

Intrinsic Conduction System

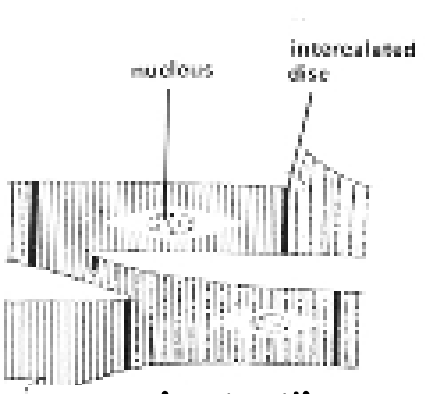
- Consists of "pacemaker" cells and conduction pathways
  - Coordinate the contraction of the atria and ventricles



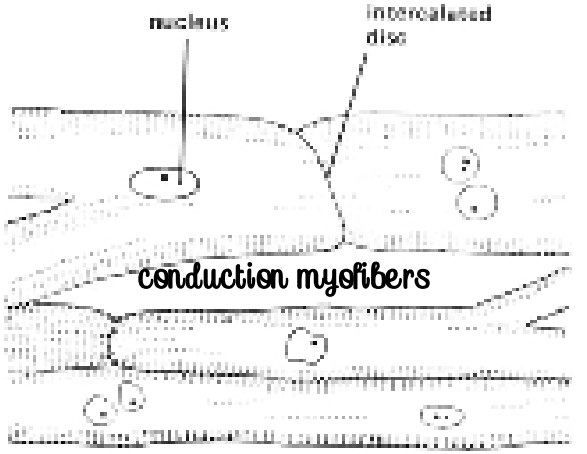
Myocardial Physiology

Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells
  - Smaller than contractile cells
  - Don't contain many myofibrils
  - No organized sarcomere structure
    - do not contribute to the contractile force of the heart

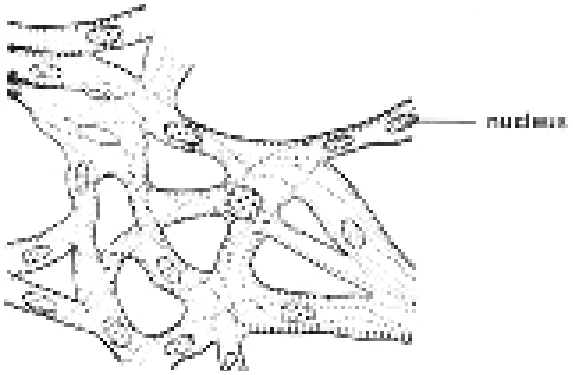


normal contractile myocardial cell



B

SA node cell



AV node cells

Myocardial Physiology

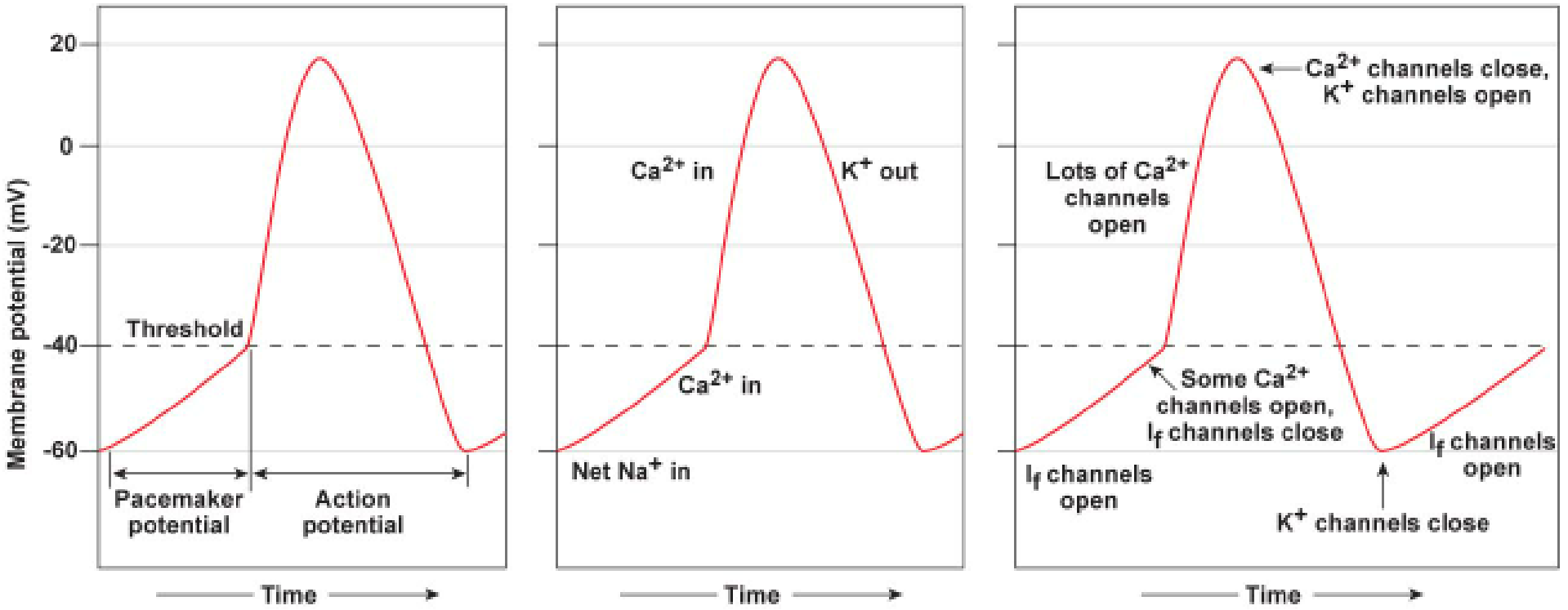
Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells
  - Unstable membrane potential
    - "bottoms out" at -60mV
    - "drifts upward" to -40mV, forming a pacemaker potential
  - Myogenic
    - The upward "drift" allows the membrane to reach threshold potential (-40mV) by itself
    - This is due to
      1. Slow leakage of K^+ out & faster leakage Na^+ in
         - » Causes slow depolarization
         - » Occurs through I_f channels (f=funny) that open at negative membrane potentials and start closing as membrane approaches threshold potential
      2. Ca^{2+} channels opening as membrane approaches threshold
         - » At threshold additional Ca^{2+} ion channels open causing more rapid depolarization
         - » These deactivate shortly after and
      3. Slow K^+ channels open as membrane depolarizes causing an efflux of K^+ and a repolarization of membrane

Myocardial Physiology

Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells



Myocardial Physiology

Autorhythmic Cells (Pacemaker Cells)

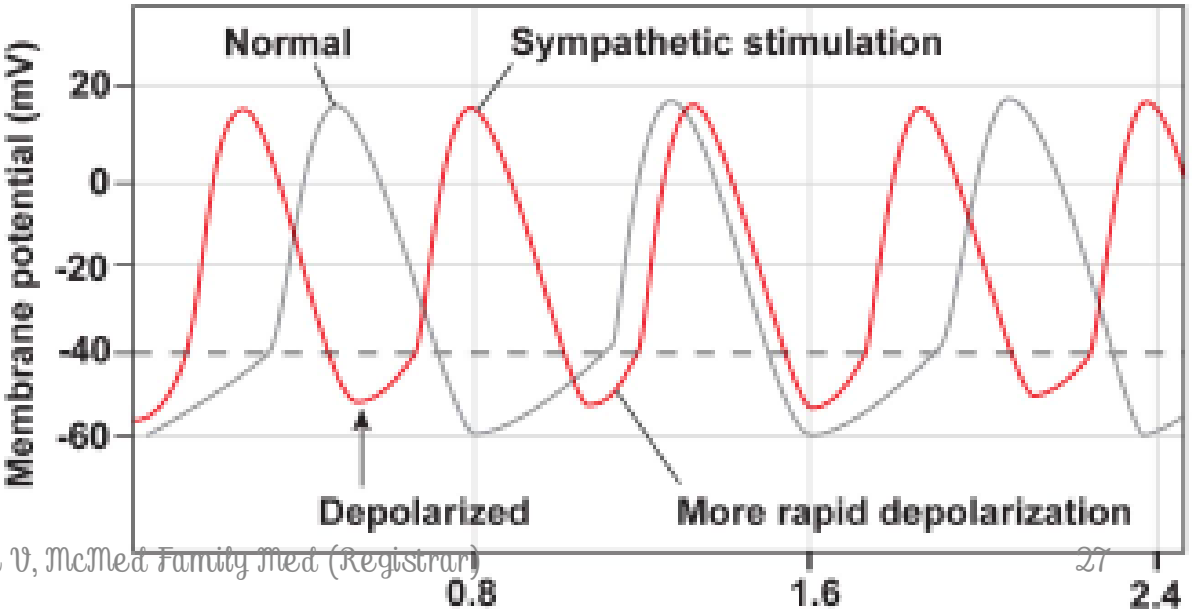
- Altering Activity of Pacemaker Cells
  - Sympathetic activity
    - NE and E increase I_f channel activity
      - Binds to β_1 adrenergic receptors which activate cAMP and increase I_f channel open time
      - Causes more rapid pacemaker potential and faster rate of action potentials

Sympathetic Activity Summary:

increased chronotropic effects
↑heart rate

increased dromotropic effects
↑conduction of APs

increased inotropic effects
↑contractility



Myocardial Physiology

Autorhythmic Cells (Pacemaker Cells)

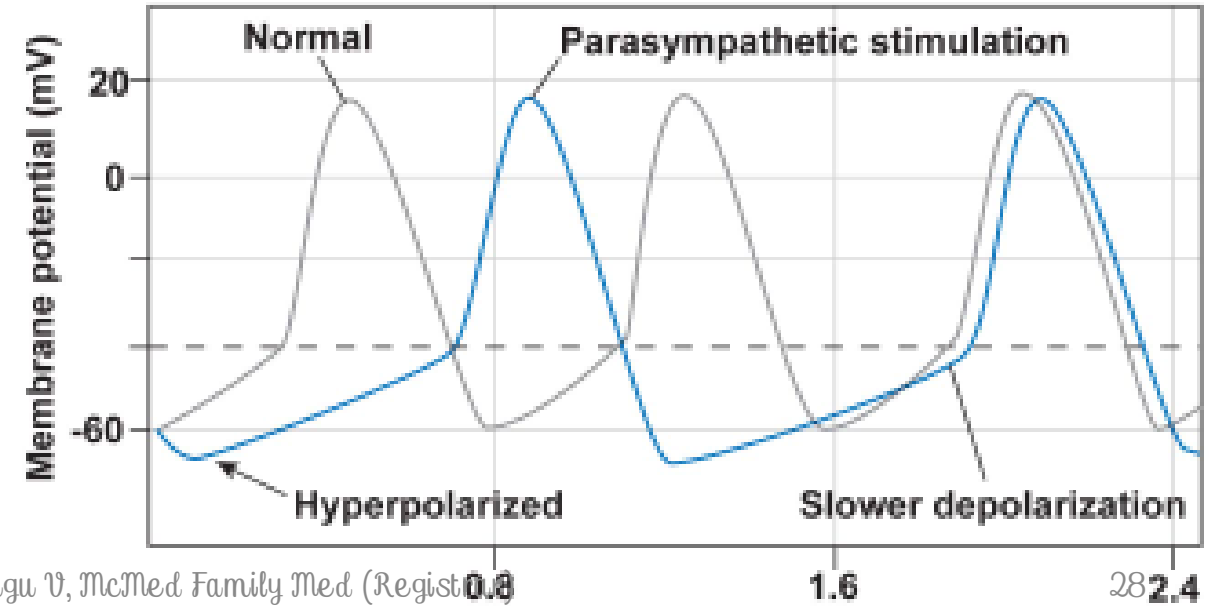
- Altering Activity of Pacemaker Cells
  - Parasympathetic activity
    - ACh binds to muscarinic receptors
      - Increases K^+ permeability and decreases Ca^{2+} permeability = hyperpolarizing the membrane
        - » Longer time to threshold = slower rate of action potentials

Parasympathetic Activity Summary:

decreased chronotropic effects
↓heart rate

decreased dromotropic effects
↓ conduction of APs

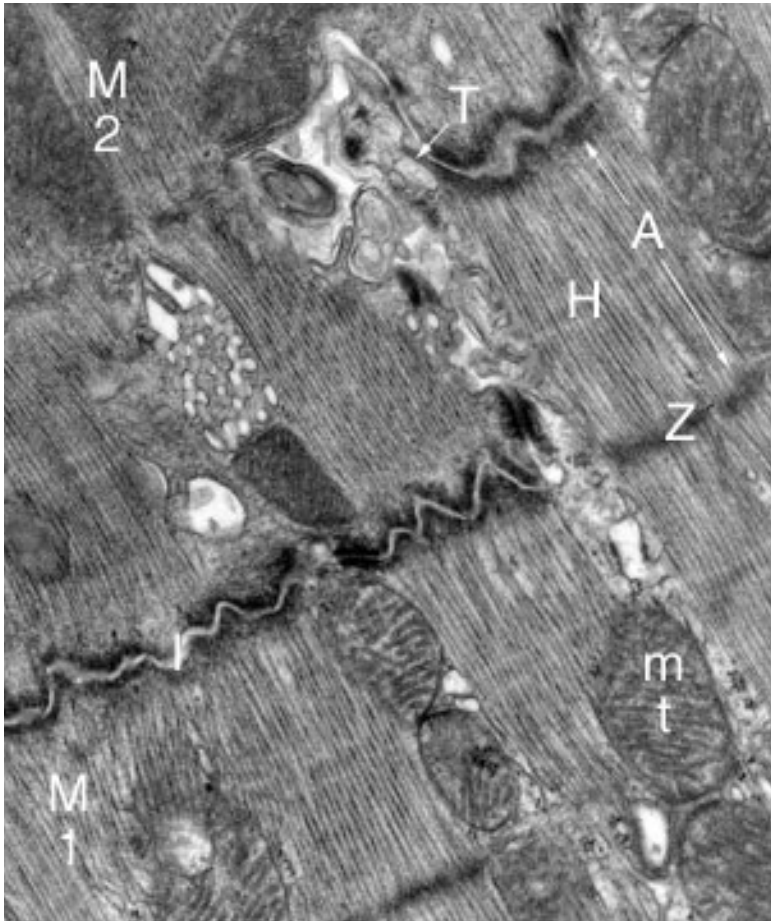
decreased inotropic effects
↓ contractility



Myocardial Physiology

Contractile Cells

- Special aspects
  - Intercalated discs
    - Highly convoluted and interdigitated junctions
      - Joint adjacent cells with
        - » Desmosomes & fascia adherens
      - Allow for synticial activity
        - » With gap junctions
  - More mitochondria than skeletal muscle
  - Less sarcoplasmic reticulum
    - Ca^{2+} also influxes from ECF reducing storage need
  - Larger t-tubules
    - Internally branching
  - Myocardial contractions are graded!



Myocardial Physiology

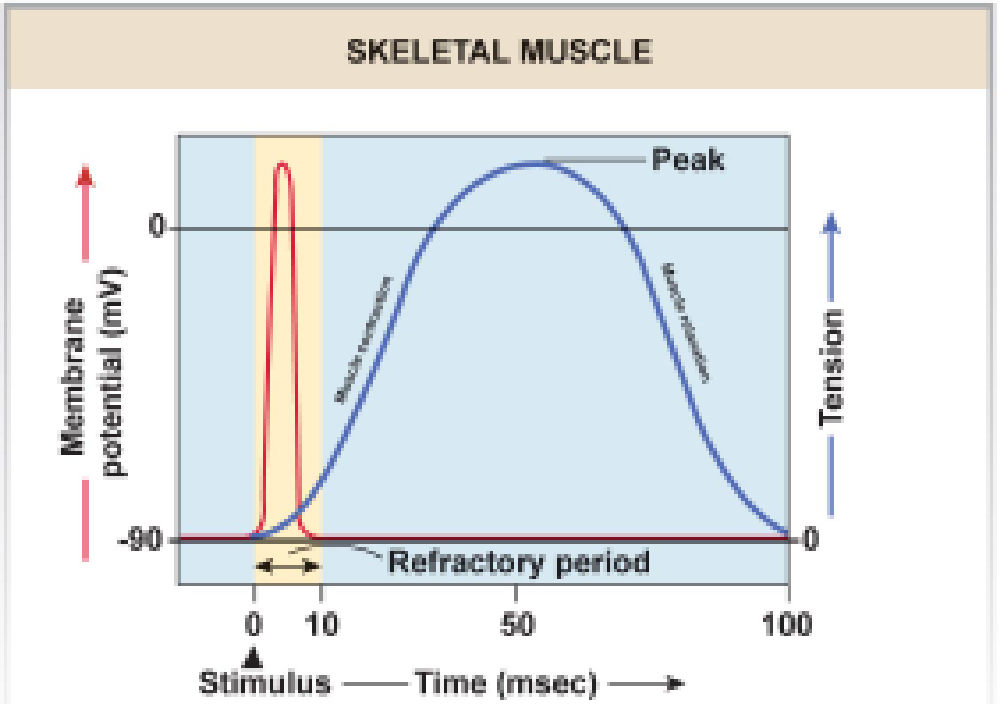
Contractile Cells

- Special aspects
  - The action potential of a contractile cell
    - Ca^{2+} plays a major role again
    - Action potential is longer in duration than a "normal" action potential due to Ca^{2+} entry
    - Phases
      - 4 – resting membrane potential @ -90mV
      - 0 – depolarization
        - » Due to gap junctions or conduction fiber action
        - » Voltage gated Na^{+} channels open… close at 20mV
      - 1 – temporary repolarization
        - » Open K^{+} channels allow some K^{+} to leave the cell
      - 2 – plateau phase
        - » Voltage gated Ca^{2+} channels are fully open (started during initial depolarization)
      - 3 – repolarization
        - » Ca2+ channels close and K+ permeability increases as slower activated K+ channels open, causing a quick repolarization
  - What is the significance of the plateau phase?

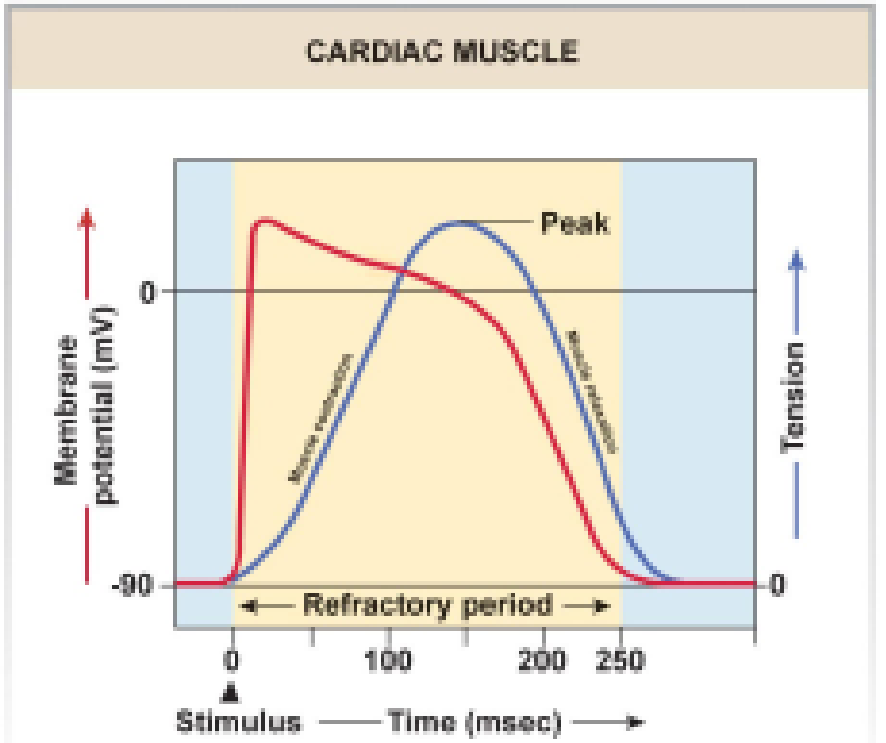
Myocardial Physiology

Contractile Cells

- Skeletal Action Potential vs Contractile Myocardial Action Potential



(a) **Skeletal muscle fast-twitch fiber:** The refractory period (yellow) is very short compared with the amount of time required for the development of tension.

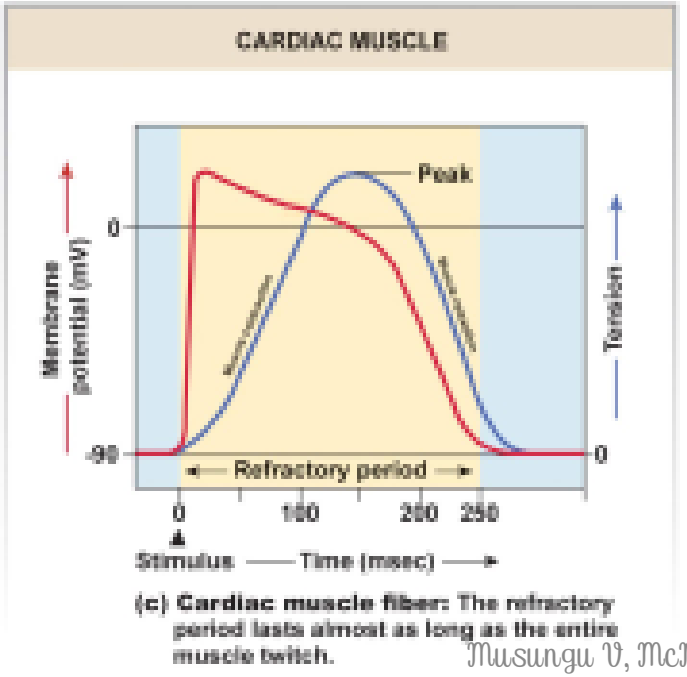


(c) **Cardiac muscle fiber:** The refractory period lasts almost as long as the entire muscle twitch.

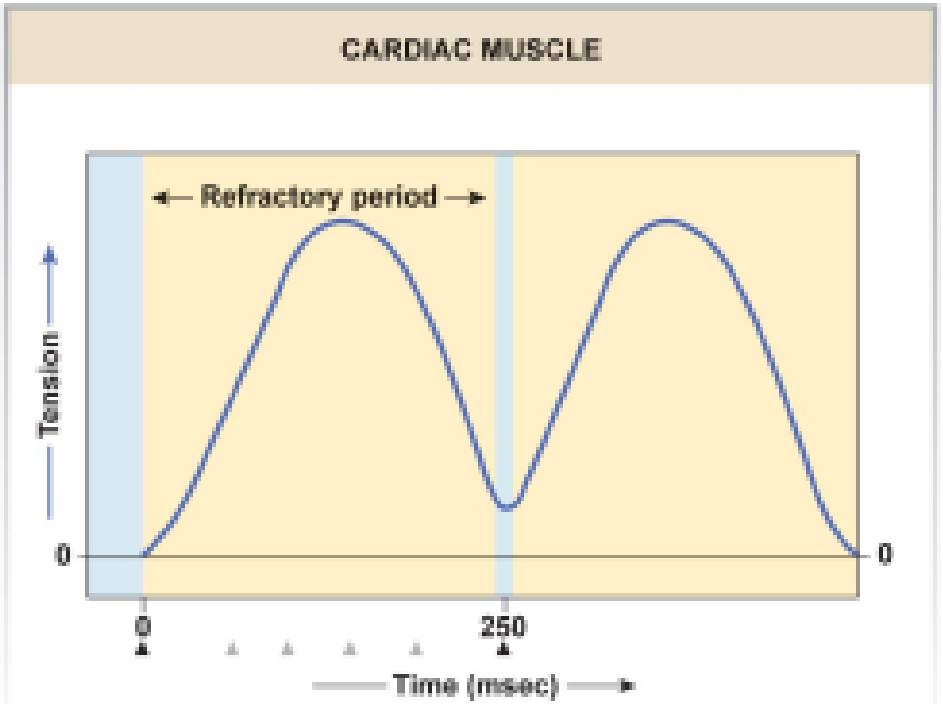
Myocardial Physiology

Contractile Cells

- Plateau phase prevents summation due to the elongated refractory period
- No summation capacity = no tetanus
  - Which would be fatal



(c) Cardiac muscle fiber: The refractory period lasts almost as long as the entire muscle twitch.



(d) Long refractory period in a cardiac muscle prevents tetanus.

Summary of Action Potentials

Skeletal Muscle vs Cardiac Muscle

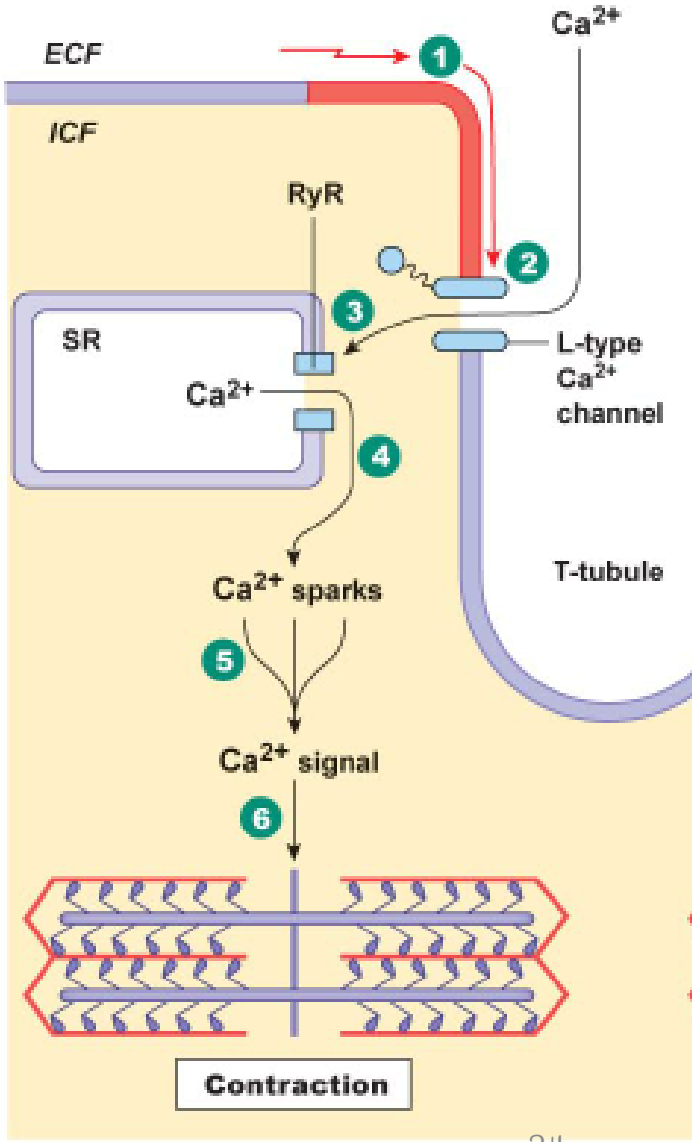
TABLE 14-3 Comparison of Action Potentials in Cardiac and Skeletal Muscle

	SKELETAL MUSCLE	CONTRACTILE MYOCARDIUM	AUTORHYTHMIC MYOCARDIUM
Membrane potential	Stable at −70 mV	Stable at −90 mV	Unstable pacemaker potential; usually starts at −60 mV
Events leading to threshold potential	Net Na^+ entry through ACh-operated channels	Depolarization enters via gap junctions	Net Na^+ entry through I_f channels; reinforced by Ca^{2+} entry
Rising phase of action potential	Na^+ entry	Na^+ entry	Ca^{2+} entry
Repolarization phase	Rapid; caused by K^+ efflux	Extended plateau caused by Ca^{2+} entry; rapid phase caused by K^+ efflux	Rapid; caused by K^+ efflux
Hyperpolarization	Due to excessive K^+ efflux at high K^+ permeability when K^+ channels close; leak of K^+ and Na^+ restores potential to resting state	None; resting potential is −90 mV, the equilibrium potential for K^+	Normally none; when repolarization hits −60 mV, the I_f channels open again. ACh can hyperpolarize the cell.
Duration of action potential	Short: 1–2 msec	Extended: 200+ msec	Variable; generally 150+ msec
Refractory period	Generally brief	Long because resetting of Na^+ channel gates delayed until end of action potential	None

Myocardial Physiology

Contractile Cells

- Initiation
  - Action potential via pacemaker cells to conduction fibers
- Excitation-Contraction Coupling
  1. Starts with CICR (Ca^{2+} induced Ca^{2+} release)
     - AP spreads along sarcolemma
     - T-tubules contain voltage gated L-type Ca^{2+} channels which open upon depolarization
     - Ca^{2+} entrance into myocardial cell and opens RyR (ryanodine receptors) Ca^{2+} release channels
     - Release of Ca^{2+} from SR causes a Ca^{2+} "spark"
     - Multiple sparks form a Ca^{2+} signal

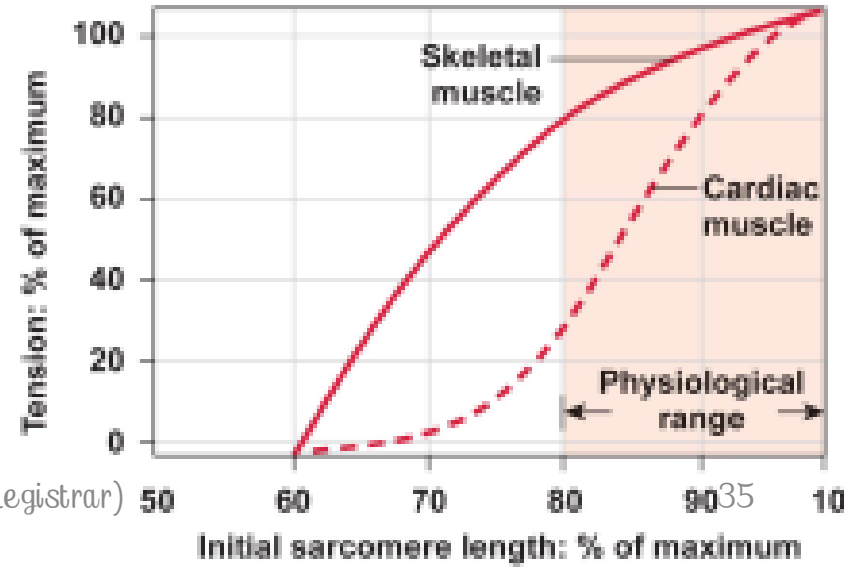


Spark Gif

Myocardial Physiology

Contractile Cells

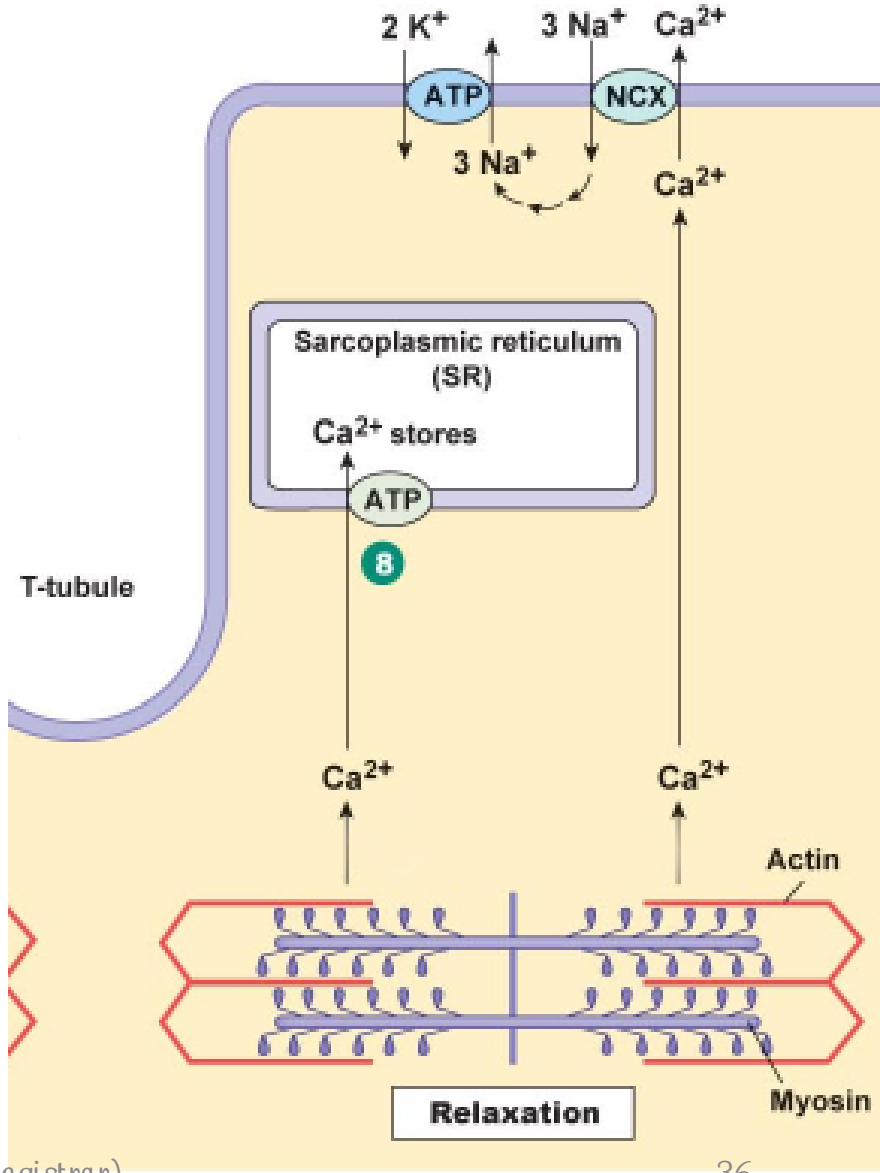
- Excitation-Contraction Coupling cont…
  2. Ca^{2+} signal (Ca^{2+} from SR and ECF) binds to troponin to initiate myosin head attachment to actin
- Contraction
  - Same as skeletal muscle, but…
  - Strength of contraction varies
    - Sarcomeres are not "all or none" as it is in skeletal muscle
      - The response is graded!
        - » Low levels of cytosolic Ca^{2+} will not activate as many myosin/actin interactions and the opposite is true
    - Length tension relationships exist
      - Strongest contraction generated when stretched between 80 & 100% of maximum (physiological range)
      - What causes stretching?
        - » The filling of chambers with blood



Myocardial Physiology

Contractile Cells

- Relaxation
  - Ca^{2+} is transported back into the SR and
  - Ca^{2+} is transported out of the cell by a facilitated Na^{+}/Ca^{2+} exchanger (NCX)
  - As ICF Ca^{2+} levels drop, interactions between myosin/ actin are stopped
  - Sarcomere lengthens



Cardiac Cycle

Coordinating the activity

- Cardiac cycle is the sequence of events as blood enters the atria, leaves the ventricles and then starts over
- Synchronizing this is the Intrinsic Electrical Conduction System
- Influencing the rate (chronotropy & dromotropy) is done by the sympathetic and parasympathetic divisions of the ANS

Cardiac Cycle

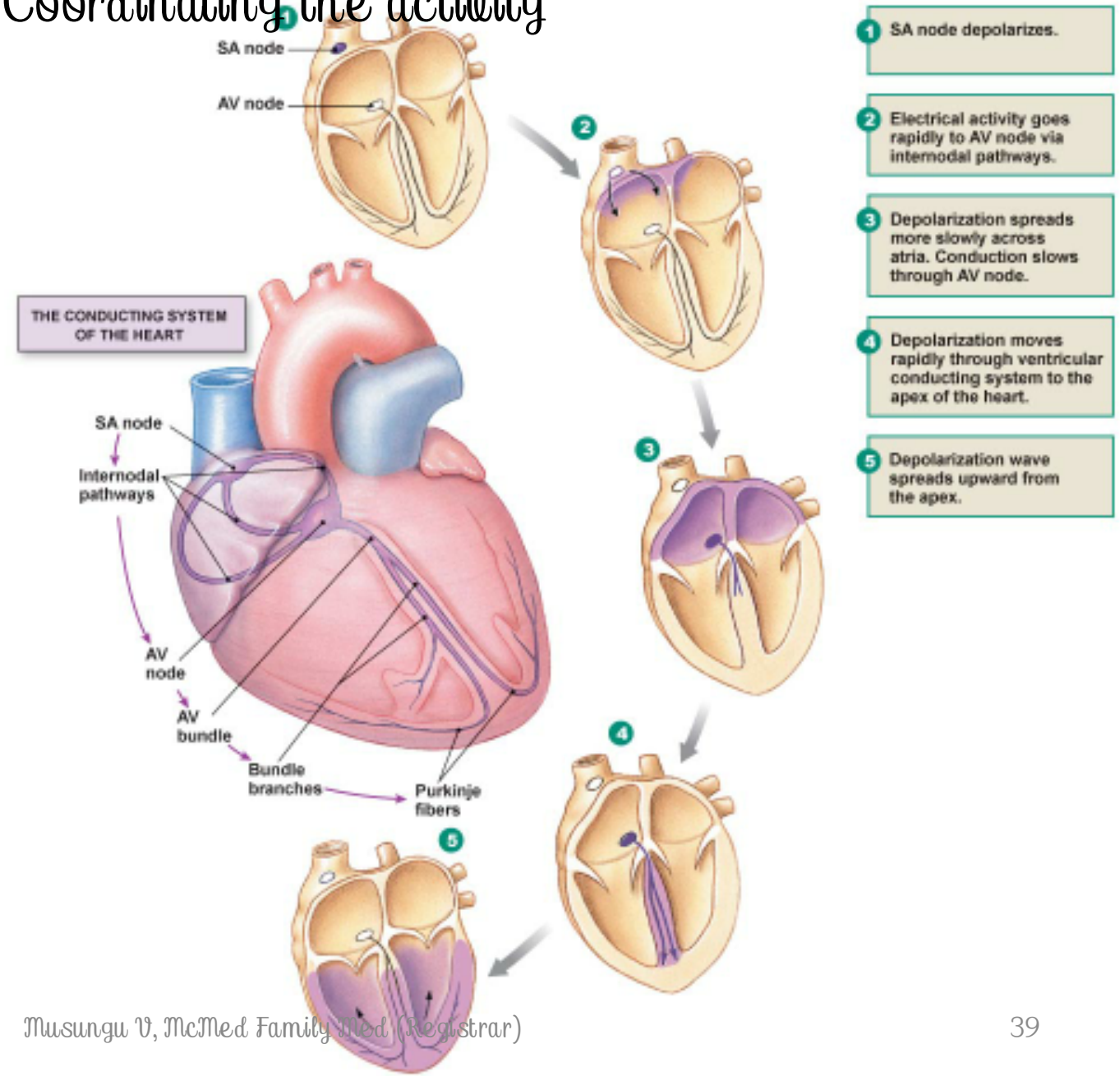
Coordinating the activity

- Electrical Conduction Pathway
  - Initiated by the Sino-Atrial node (SA node) which is myogenic at 70-80 action potentials/minute
  - Depolarization is spread through the atria via gap junctions and internodal pathways to the Atrio-Ventricular node (AV node)
    - The fibrous connective tissue matrix of the heart prevents further spread of APs to the ventricles
    - A slight delay at the AV node occurs
      - Due to slower formation of action potentials
      - Allows further emptying of the atria
  - Action potentials travel down the Atrioventricular bundle (Bundle of His) which splits into left and right atrioventricular bundles (bundle branches) and then into the conduction myofibers (Purkinje cells)
    - Purkinje cells are larger in diameter & conduct impulse very rapidly
      - Causes the cells at the apex to contract nearly simultaneously
        - » Good for ventricular ejection

Cardiac Cycle

Coordinating the activity

- Electrical Conduction Pathway

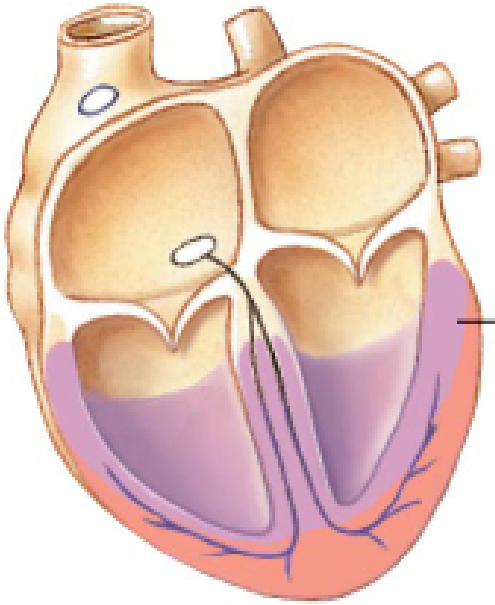


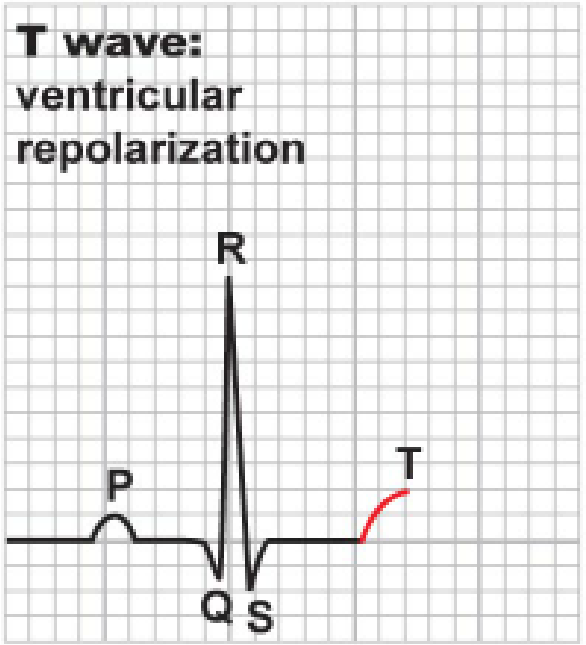
Cardiac Cycle

Coordinating the activity

- The electrical system gives rise to electrical changes (depolarization/repolarization) that is transmitted through isotonic body fluids and is recordable
  - The ECG!
    - A recording of electrical activity
    - Can be mapped to the cardiac cycle

ELECTRICAL EVENTS OF THE CARDIAC CYCLE





Cardiac Cycle

Phases

- Systole = period of contraction
- Diastole = period of relaxation
- Cardiac Cycle is alternating periods of systole and diastole
- Phases of the cardiac cycle
  1. Rest
     - Both atria and ventricles in diastole
     - Blood is filling both atria and ventricles due to low pressure conditions
  2. Atrial Systole
     - Completes ventricular filling
  3. Isovolumetric Ventricular Contraction
     - Increased pressure in the ventricles causes the AV valves to close... why?
       - Creates the first heart sound (lub)
     - Atria go back to diastole
     - No blood flow as semilunar valves are closed as well

Cardiac Cycle

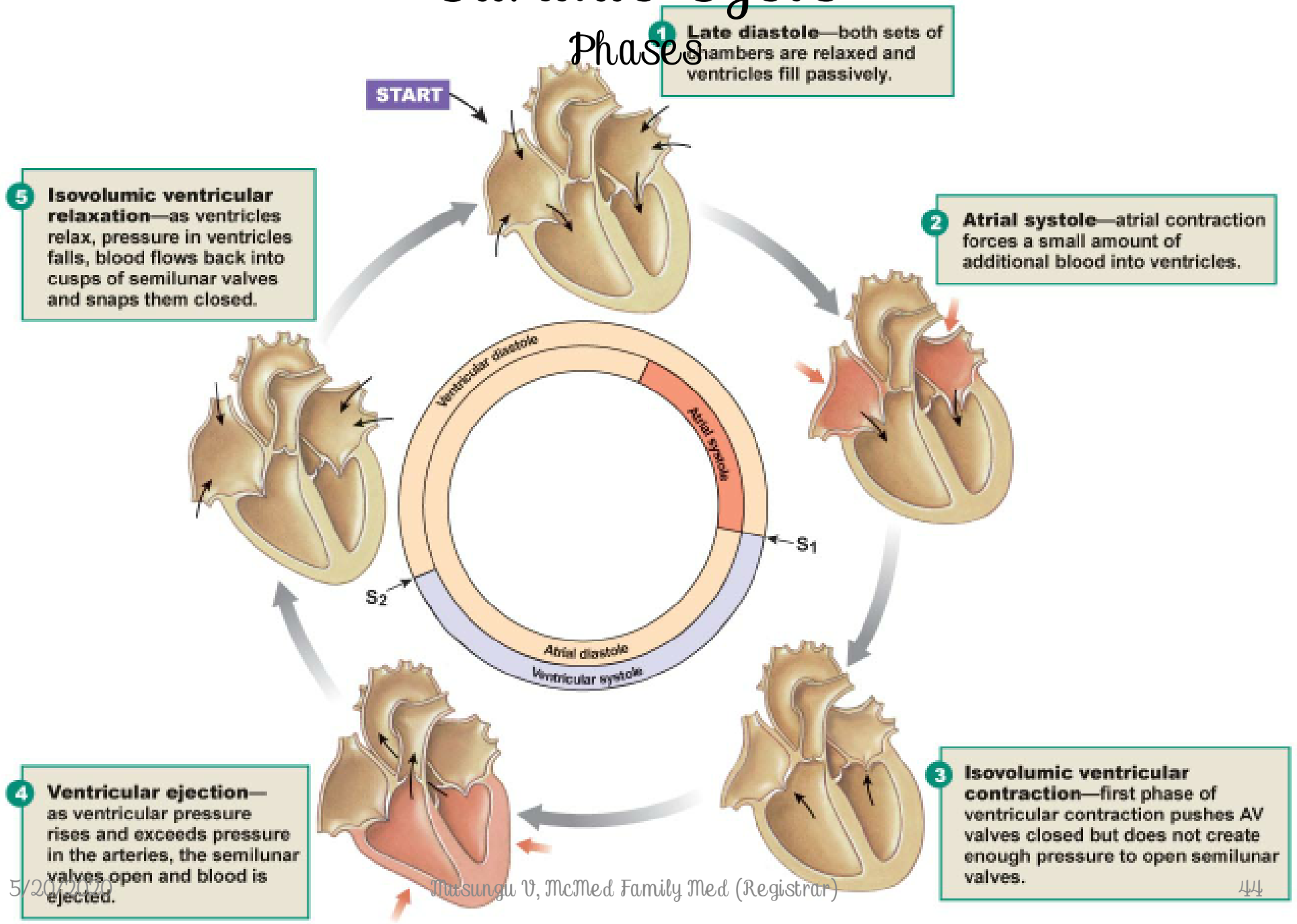
Phases

- Phases of the cardiac cycle
  4. Ventricular Ejection
     - Intraventricular pressure overcomes aortic pressure
       - Semilunar valves open
       - Blood is ejected
  5. Isovolumetric Ventricular Relaxation
     - Intraventricular pressure drops below aortic pressure
       - Semilunar valves close = second heart sound (dup)
     - Pressure still hasn't dropped enough to open AV valves so volume remains same (isovolumetric)

  Back to Atrial & Ventricular Diastole

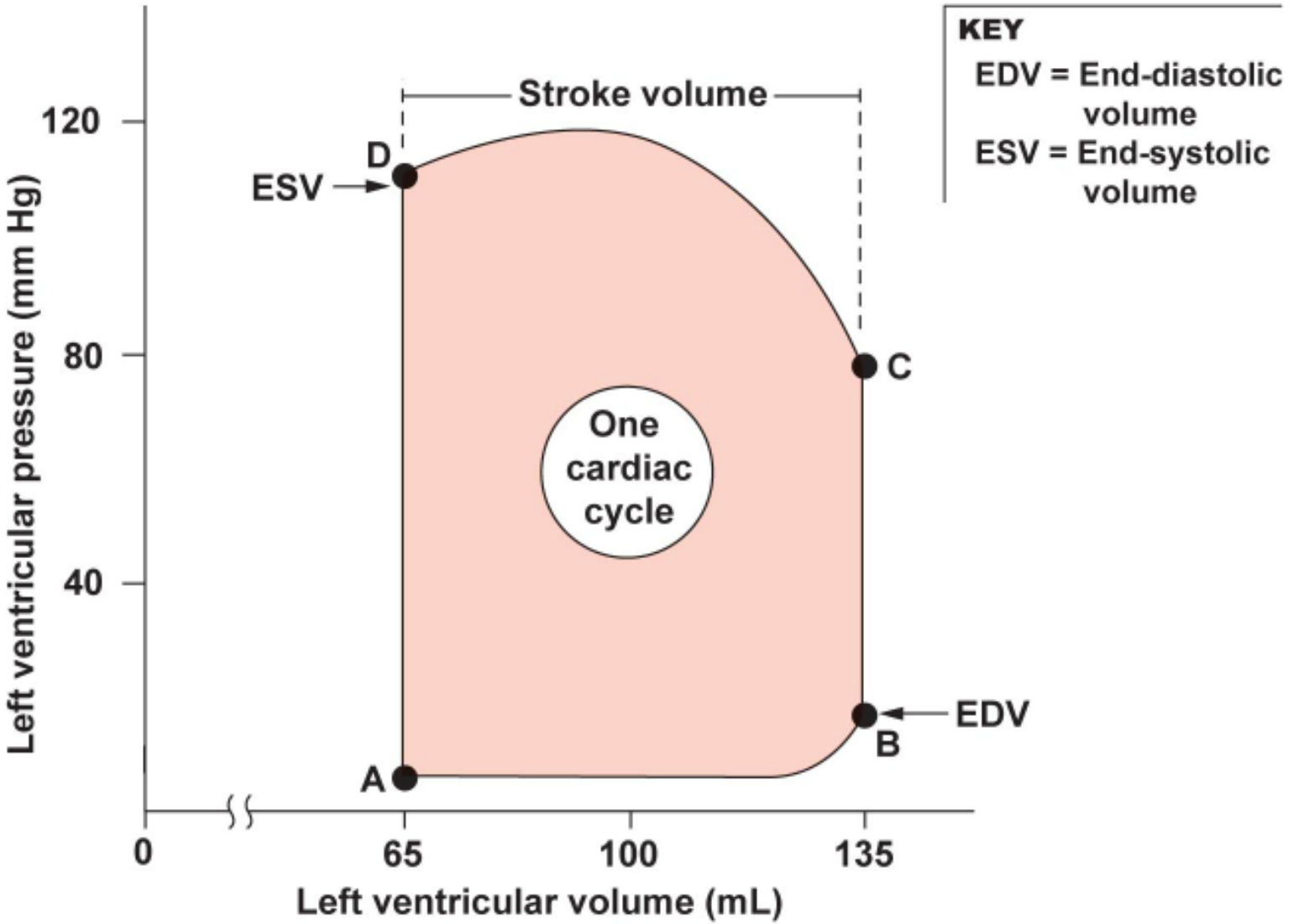
Cardiac Cycle

Phases



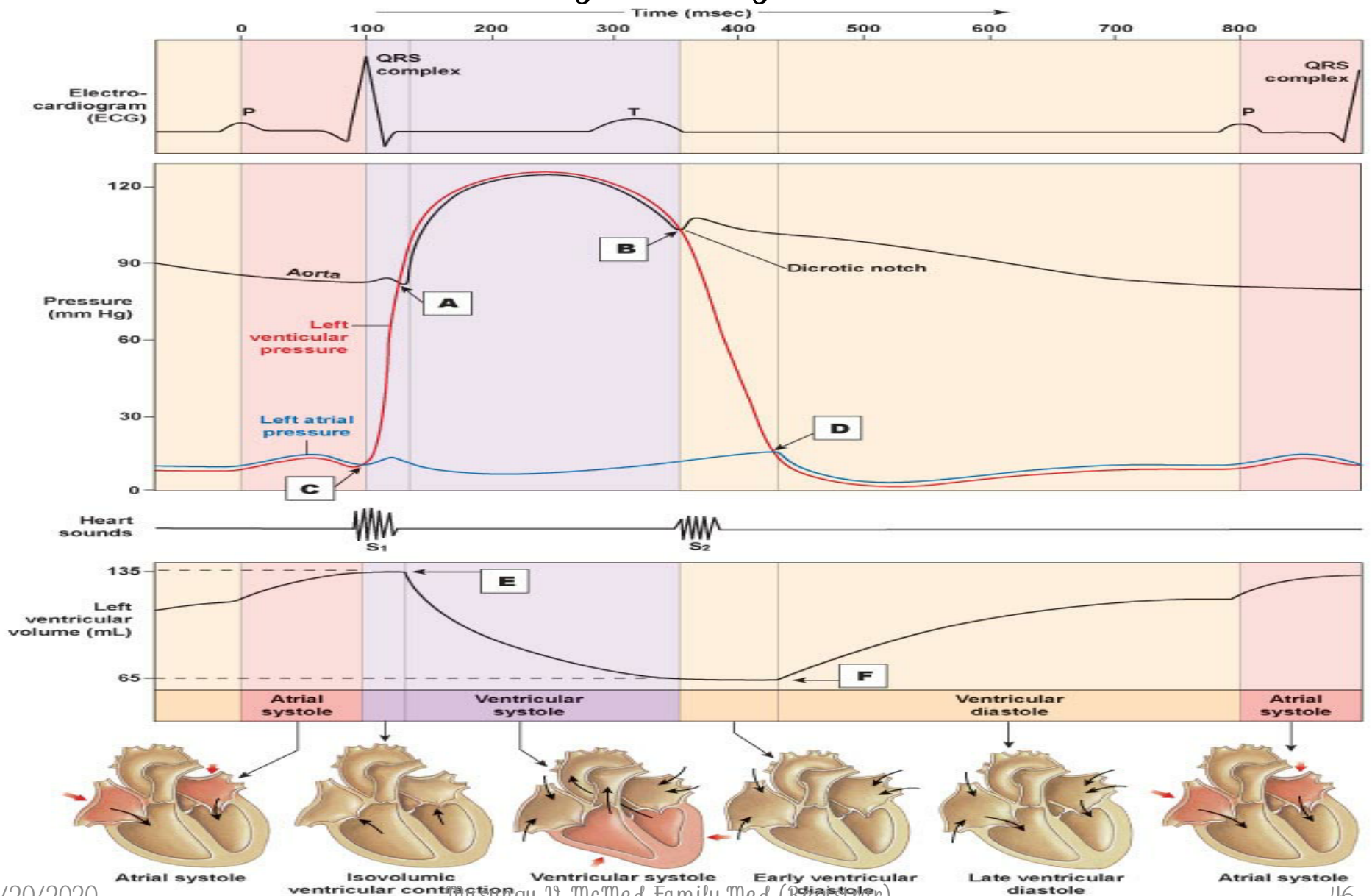
Cardiac Cycle

Blood Volumes & Pressure

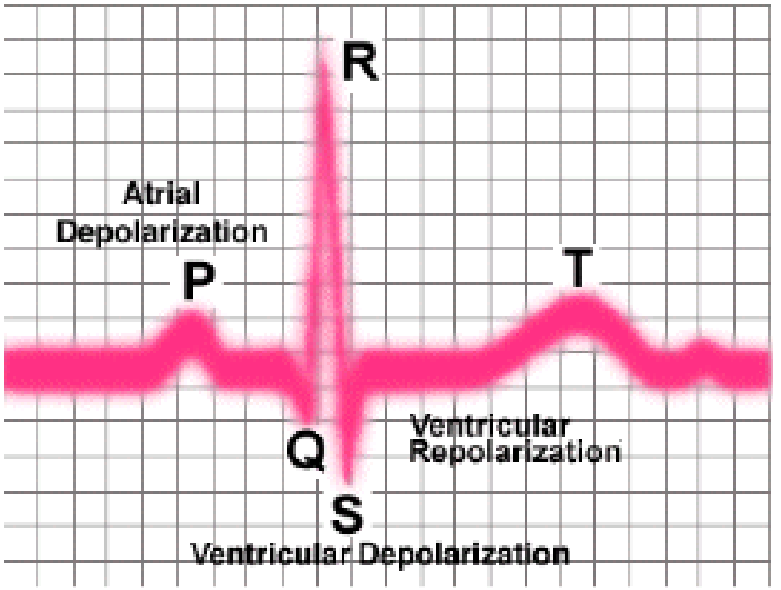


Cardiac Cycle

Putting it all together!



Wave Interpretation



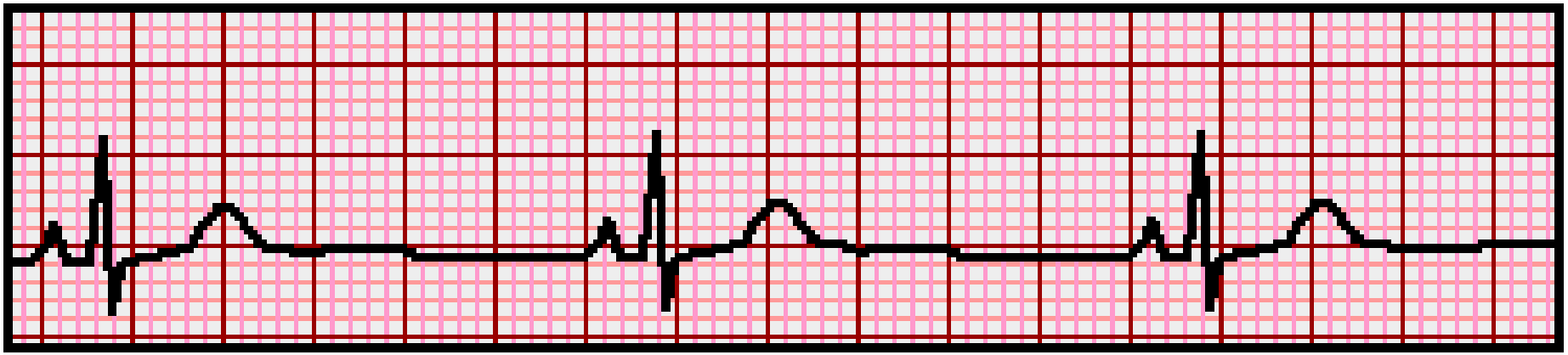
- P Wave = contraction of atria
- PQ Wave = signal arrives at AV node slowing down a bit to allow ventricles to fill with blood
- Q Wave = signal moves to Bundle of His and divides into the bundles and Purkinje fibers
- R Wave = contraction of left ventricle
- S Wave = contraction of right ventricle
- T Wave = ventricles relaxing

Rule of 300

- Take the number of "big boxes" between neighboring QRS complexes, and divide this into 300. The result will be approximately equal to the heart rate

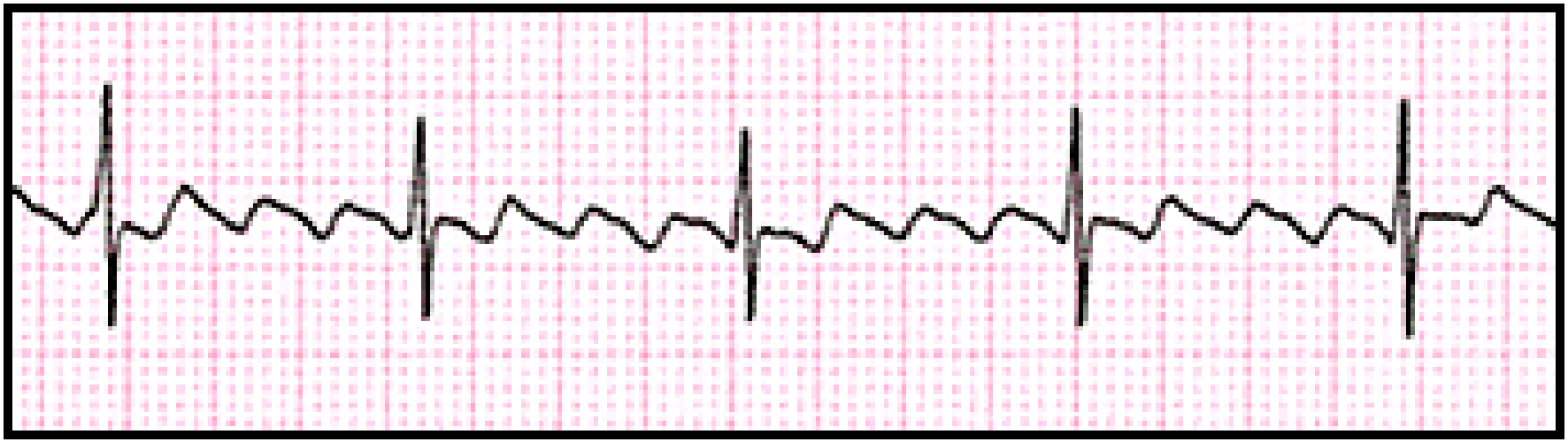
- Although fast, this method only works for regular rhythms.

What is the heart rate?



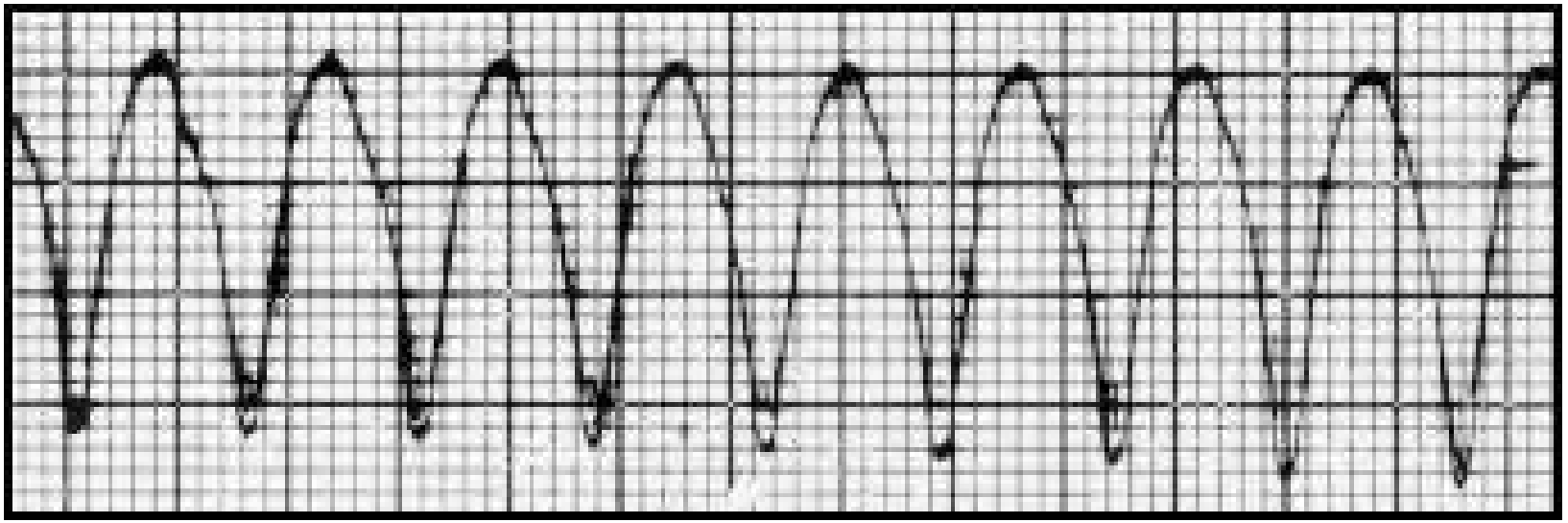
(300 / 6) = 50 bpm

What is the heart rate?



(300 / ~ 4) = ~ 75 bpm

What is the heart rate?



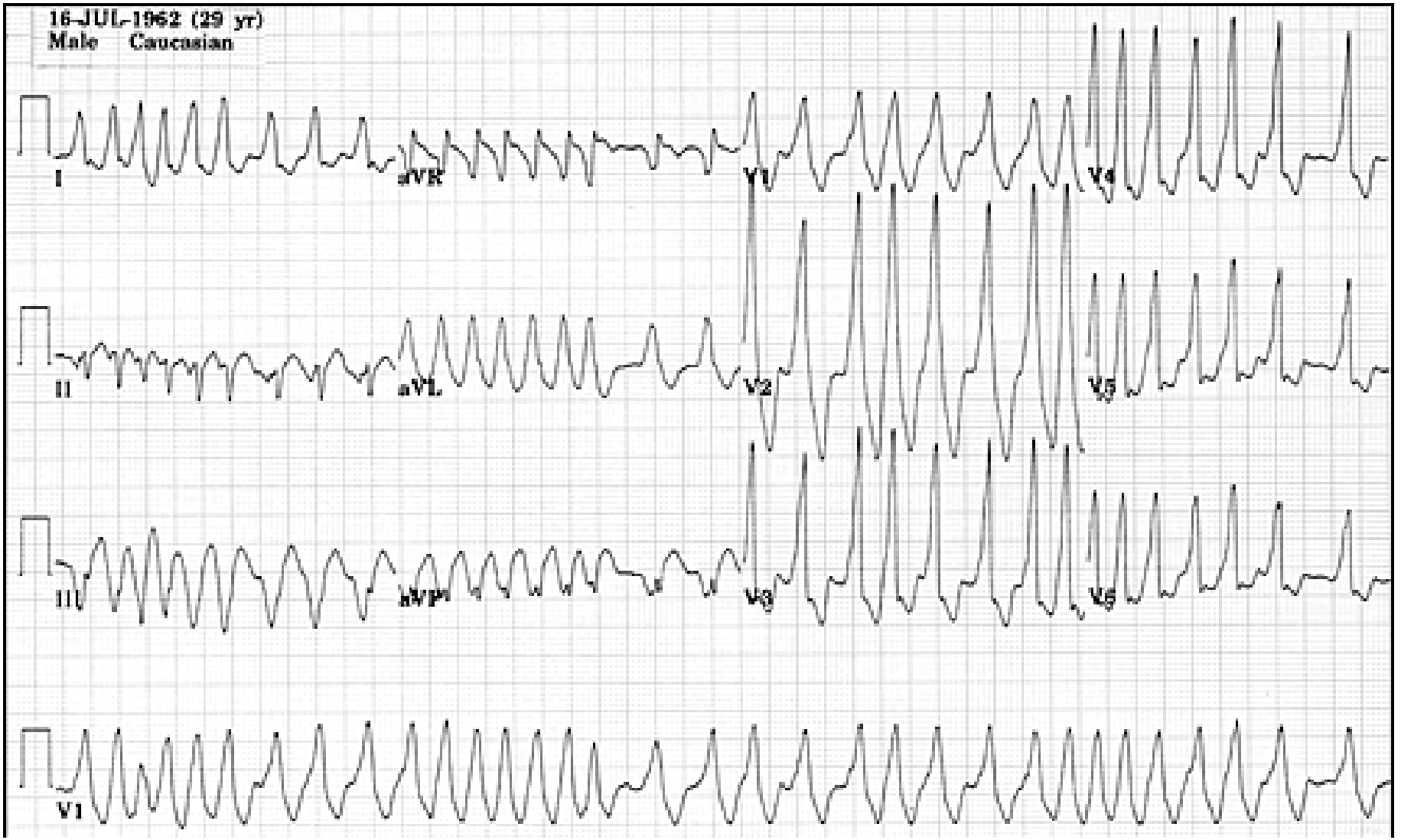
(300 / 1.5) = 200 bpm

10 Second Rule

- As most EKGs record 10 seconds of rhythm per page, one can simply count the number of beats present on the EKG and multiply by 6 to get the number of beats per 60 seconds.

- This method works well for irregular rhythms.

What is the heart rate?



33 x 6 = 198 bpm

Diagnosis of cardiovascular disease

- History taking (very important) complete and thorough
- Physical examination
  - Skin
    - Central cyanosis occurs with significant right-to-left shunting at the level of the heart or lungs, allowing deoxygenated blood to reach the systemic circulation.
    - Peripheral cyanosis or acrocyanosis, usually related to reduced extremity blood flow due to small vessel constriction, as seen in patients with severe heart failure, shock, or peripheral vascular disease; it can be aggravated by the use of -adrenergic blockers

- Jaundice
  - Could mean advanced heart failre with cardiac cirrhosis
- Head and neck
  - Dentition and oral hygiene should be assessed in every patient both as a source of potential infection and as an index of general health
  - A high-arched palate is a feature of Marfan syndrome and other connective tissue disease syndromes

- Check for distended neck veins(sign of right atrium congestion)

– Chest

- scars at the site of pacemaker/defibrillator generator implantation may provide the first clue regarding an underlying cardiovascular disorder in patients unable to provide a relevant history
- A prominent venous collateral pattern may suggest subclavian or vena caval obstruction
- Thoracic cage abnormalities; pectus carinatum ("pigeon chest") and pectus excavatum ("funnel chest").

- Straight back syndrome refers to the loss of the normal kyphosis of the thoracic spine seen in patients with mitral valve prolapse (MVP)
- Obstructive lung disease is suggested by a barrel chest deformity, especially with tachypnea, pursed-lip breathing, and use of accessory muscles
- severe kyphosis and compensatory lumbar, pelvic, and knee flexion of ankylosing spondylitis should prompt careful auscultation for a murmur of aortic regurgitation

- Abdomen
  - liver is frequently enlarged and tender in patients with chronic heart failure
  - Splenomegaly may be a feature of infective endocarditis, particularly when symptoms have persisted for weeks or months
  - Ascites is a nonspecific finding but may be present with advanced chronic right heart failure.
  - presence of an arterial bruit over the abdomen suggests high-grade atherosclerotic disease

- Extremities
  - Clubbing implies the presence of central right-to-left shunting, although it has also been described in patients with endocarditis
  - Lower extremity or presacral edema + elevated JVP defines volume overload ;- a feature of chronic heart failure or constrictive pericarditis
  - Lower extremity edema in the absence of jugular venous hypertension may be due to lymphatic or venous obstruction
  - A Homan's sign (posterior calf pain on active dorsiflexion of the foot against resistance) is neither specific nor sensitive for deep venous thrombosis.
  - Muscular atrophy or the absence of hair along an extremity is consistent with severe arterial insufficiency or a primary neuromuscular disorder.

Assessment of blood pressure

- Blood pressure is best measured in the seated position with the arm at the level of the heart, using an appropriately sized cuff, after 5–10 min of relaxation.
- The cuff should be inflated to 30 mmHg above the expected systolic pressure and the pressure released at a rate of 2–3 mmHg/s
- Systolic and diastolic pressures are defined by the first and fifth Korotkoff sounds, respectively.
- Very low (even 0 mmHg) diastolic blood pressures may be recorded in patients with chronic, severe AR or a large arteriovenous fistula because of enhanced diastolic "run-off."

- Blood pressure should be measured in both arms, and the difference should be less than 10 mmHg.
- blood pressure differential that exceeds this threshold may be associated with
  - atherosclerosis
  - inflammatory subclavian artery disease,
  - supravalvular aortic stenosis,
  - aortic coarctation,
  - aortic dissection.

- Orthostatic hypotension is defined by a fall in systolic pressure >20 mmHg or in diastolic pressure >10 mmHg in response to assumption of the upright posture from a supine position within 3 minutes

- Arterial Pulse
  - *Pulsus paradoxus* refers to a fall in systolic pressure >10 mmHg with inspiration that is seen in patients with
    - pericardial tamponade,
    - massive pulmonary embolism,
    - hemorrhagic shock,
    - severe obstructive lung disease,
    - tension pneumothorax

- Read
  - Heart sounds
  - Murmurs

Investigations in cardiovasclar diseases

- Electrocardiogram
- Echo cardiogram
- Diagnostic cardiac catheterization
- Cardiac enzymes (troponin I and T)
- CK-MB

Cardiac catheterization

- Diagnostic cardiac catheterization and coronary angiography are considered the gold standard in the assessment of the anatomy and physiology of the heart and its associated vasculature (rare in kenyan set up)
- Indications include
  - Chest pain syndrome
  - Unstable angina
  - Severe plmonary edema
  - Read more, harrisons principles of i-Med, 18th edition

HEART FAILURE

- Definition
  - Heart failure (HF) is a clinical syndrome that occurs in patients who, because of an inherited or acquired abnormality of cardiac structure and/or function, develop a constellation of clinical symptoms (dyspnea and fatigue) and signs (edema and rales) that lead to frequent hospitalizations, a poor quality of life, and a shortened life expectancy.

– Epidemiology

- worldwide, with more than 20 million people affected
- overall prevalence of HF in the adult population in developed countries is 2%
- Prevalence increase with age, and affects 6–10% of people over age 65
- women constitute at least one-half the cases of HF because of their longer life expectancy
- HF patients are now broadly categorized into two groups:
  - HF with a depressed EF (commonly referred to as *systolic failure*)
  - HF with a preserved EF (commonly referred to as *diastolic failure*).

- Etiology of heart failure
  - Myocardial infarction
  - Myocardial ischemiaa
  - Chronic pressure overload
  - Toxic/drug-induced damage
  - Hypertension
  - Obstructive valvular disease
  - Pulmonary heart diseases e.g pulmonary embolism
  - High output states e.g thyrotoxicosis

Global picture of HF

- Rheumatic heart disease remains a major cause of HF in Africa and Asia in the young.
- Hypertension is an important cause of HF in the African and African-American populations.
- Chagas' disease is still a major cause of HF in South America.
- anemia is a frequent concomitant factor in HF in many developing nations.
- diabetes accelerates atherosclerosis and often is associated with hypertension.

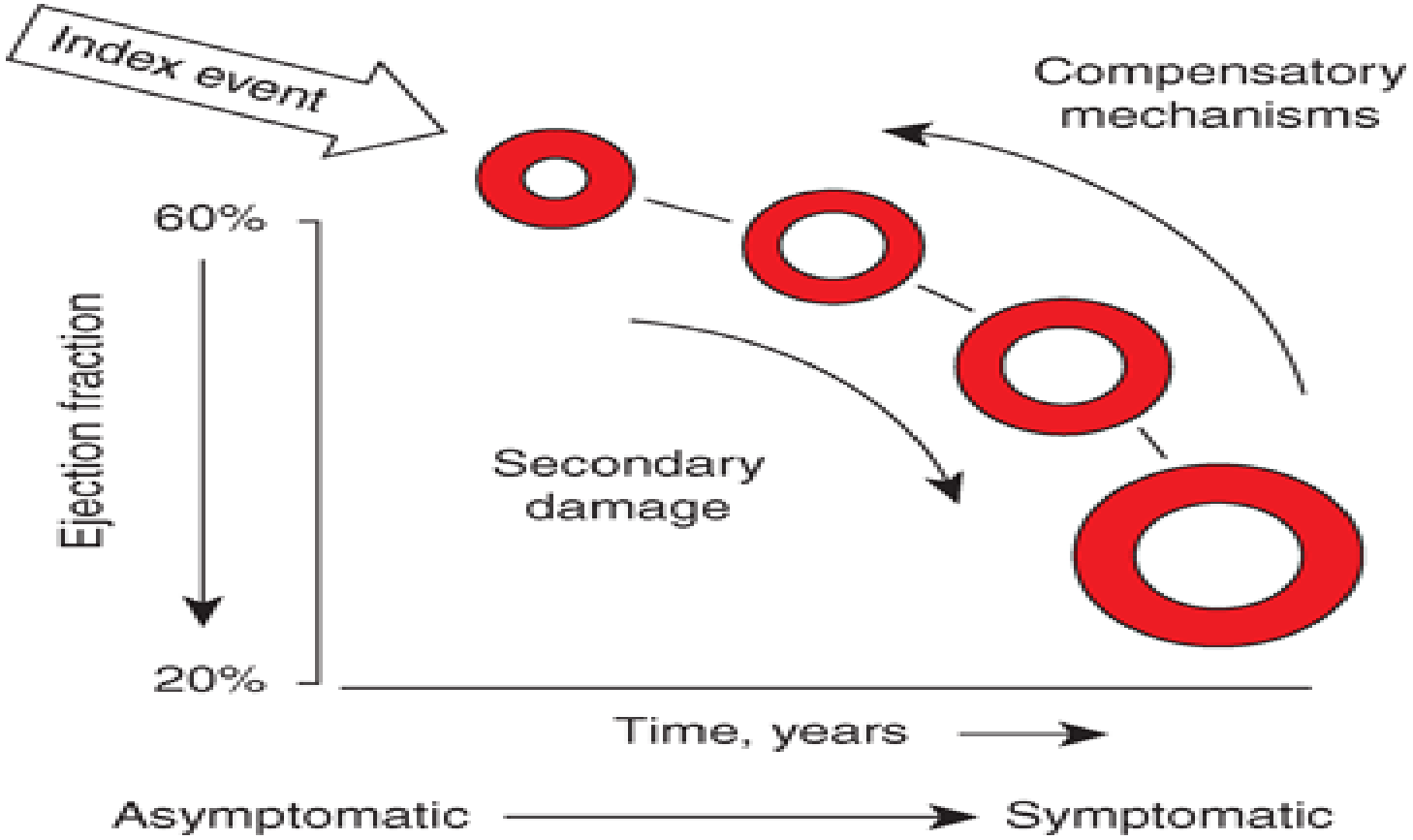
Prognosis of HF

- 30–40% of patients die within 1 year of diagnosis and 60–70% die within 5 years, mainly from worsening HF or as a sudden event (probably because of a ventricular arrhythmia).
- patients with symptoms at rest [New York Heart Association (NYHA) class IV] have a 30–70% annual mortality rate
- patients with symptoms with moderate activity (NYHA class II) have an annual mortality rate of 5–10%

New York Heart Association Classification (NYHA)

- **Class I:** Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.
- **Class II** Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
- **Class III** Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
- **Class IV** Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Pathogenesis of HF



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

Pathogenesis of heart failure with a depressed ejection fraction

- Heart failure begins after an index event produces an initial decline in the heart's pumping capacity.
- After this initial decline,compensatory mechanisms are activated, *(adrenergic nervous system, the renin-angiotensin-aldosterone system, and the cytokine system)*
- In the short term, these systems are able to restore cardiovascular function to a normal thus pt remains asymptomatic.
- with time the sustained activation of these systems can lead to secondary end-organ damage with worsening left ventricular remodeling and subsequent cardiac decompensation.

Activation of neurohormonal systems in heart failure.

- The decreased cardiac output in HF patients results in an "unloading" of high-pressure baroceptors in the left ventricle, carotid sinus, and aortic arch.
- This leads to a loss of inhibitory parasympathetic tone to the central nervous system (CNS), leading to increased efferent sympathetic tone, and non-osmotic release of arginine vasopressin (AVP) from the pituitary.
- AVP aka ADH is a powerful vasoconstrictor that increases the permeability of the renal collecting ducts, leading to the reabsorption of free water.
- These also activate efferent sympathetic nervous system pathways that innervate the heart, kidney, peripheral vasculature, and skeletal muscles.

continued

- Sympathetic stimulation of the kidney leads to the release of renin, *(raise angiotensin II and aldosterone).* These promotes salt and water retention and leads to vasoconstriction of the peripheral vasculature, myocyte hypertrophy, myocyte cell death, and myocardial fibrosis.
- these neurohormonal mechanisms facilitate short-term adaptation by maintaining blood pressure, and hence perfusion to vital organs **BUT!!**
- the same neurohormonal mechanisms contribute to end-organ changes in the heart and the circulation and to the excessive salt and water retention in advanced HF.

Basic Mechanisms of Heart Failure

- Systolic failure
  - myocyte hypertrophy
  - alterations in the contractile properties of the myocyte
  - progressive loss of myocytes (necrosis, apoptosis, and autophagic cell death).
  - adrenergic desensitization,
  - abnormal myocardial energetics and metabolism
  - reorganization of the extracellular matrix with dissolution of structural collagen weave *(does not provide structural support to the myocytes*).

Basic Mechanisms of Heart Failure

- The biologic stimuli for these profound changes(previous slide) include
  - mechanical stretch of the myocyte
  - circulating neurohormones (norepinephrine, angiotensin II)
  - inflammatory cytokines [TNF],
  - other peptides and growth factors (endothelin),
  - reactive oxygen species (superoxide).
- The sustained overexpression of above contribute to the progression of HF.
- this is the clinical rationale for using pharmacologic agents that antagonize these systems ***[e.g., angiotensin-converting enzyme (ACE) inhibitors and beta blockers] in treating patients with HF.***

Basic Mechanisms of Heart Failure

- Diastolic dysfunction
  - Myocardial relaxation is (ATP)-dependent process regulated by uptake of cytoplasmic calcium into the SR and extrusion of calcium by sarcolemmal pumps.
  - reductions in ATP concentration, (ischemia), interfere with these processes thus slowed myocardial relaxation.
  - If LV filling is delayed (e.g., from hypertrophy or fibrosis), LV filling pressures remain elevated at end diastole.
  - An increase in heart rate disproportionately shortens the time for diastolic filling thus elevated LV filling pressures
  - Elevated LV end-diastolic filling pressures leads to increased pulmonary capillary pressures (contribute to the dyspnea experienced by patients with diastolic dysfunction).
  - **impaired myocardial relaxation, increased myocardial stiffness secondary to cardiac hypertrophy and increased myocardial collagen content all contribute to diastolic failure.**
  - diastolic dysfunction can occur alone or in combination with systolic dysfunction in patients with HF.

Left Ventricular remodeling

- refers to the changes in LV mass, volume, and shape and the composition of the heart that occur after cardiac injury or abnormal hemodynamic loading conditions.
- It may contribute to the progression of HF by mechanical burdens that are produced by the changes in the geometry of the remodeled LV.
- LV wall thinning occurs as the left ventricle begins to dilate. Together with the increase in afterload created by LV dilation, leads to *afterload mismatch* **(contribute further to a decrease in stroke volume).**
- high end-diastolic wall stress to lead to:
  - hypoperfusion of the subendocardium (worsen LV function,)
  - increased oxidative stress, **(activates TNF and interleukin 1),**
  - sustained expression of stretch-activated genes (**angiotensin II, endothelin, and TNF**) and/or stretch activation of hypertrophic signaling pathways.
- Increasing LV dilation also results in tethering of the papillary muscles with resulting incompetence of the mitral valve apparatus and functional mitral regurgitation, **(worsens hemodynamic overloading of the ventricle).**
- Thus LV remodeling contribute to the progression of HF.

Symptoms

- Dyspnea
  - Due to pulmonary congestion with accumulation of interstitial or intra-alveolar fluid, which activates juxtacapillary J receptors, which in turn stimulate the rapid, shallow breathing characteristic of cardiac dyspnea.
- Orthopnea
  - defined as dyspnea occurring in the recumbent position, is usually a later manifestation of HF than is exertional dyspnea
  - results from redistribution of fluid from the splanchnic circulation and lower extremities into the central circulation during recumbency, with a resultant increase in pulmonary capillary pressure

Symptoms

- Paroxysmal nocturnal dysnea
  - refers to acute episodes of severe shortness of breath and coughing that occur at night and awaken the patient from sleep, usually 1–3 hours after the patient retires.
  - Results from increased pressure in the bronchial arteries leading to airway compression, along with interstitial pulmonary edema that leads to increased airway resistance
  - In orthopnea pt relieved by sitting upright at the side of the bed with the legs in a dependent position, but with PND cough and wheezing persist even after they have assumed the upright position

Symptoms

- Cheyne stoke respirations
  - periodic respiration or cyclic respiration
  - present in 40% of patients with advanced HF and usually is associated with low cardiac output.
  - caused by a diminished sensitivity of the respiratory center to arterial P_{co2}

Other symptoms

- Patients with HF also may present with gastrointestinal symptoms.
- Anorexia, nausea, and early satiety associated with abdominal pain and fullness are common **(related to edema of the bowel wall and/or a congested liver).**
- Congestion of the liver and stretching of its capsule may lead to right-upper-quadrant pain.
- Cerebral symptoms such as confusion, disorientation, and sleep and mood disturbances occur in patients with severe HF, particularly elderly patients with cerebral arteriosclerosis and reduced cerebral perfusion.
- Nocturia is common in HF and may contribute to insomnia.

Physical Examination

- The purpose of the examination is to help determine the cause of HF as well as to assess the sewerity of the syndrome.

General appearance and VO

- In mild or moderately severe HF, the patient appears to be in no distress at rest except for feeling uncomfortable when lying flat for more than a few minutes.
- In severe HF, the patient must sit upright, may have labored breathing, and may not be able to finish a sentence because of shortness of breath.
- Systolic blood pressure may be normal or high in early HF, **(reduced in advanced HF due to severe LV dysfunction).**
- pulse pressure may be diminished ***signifies reduction in stroke volume***.
- Sinus tachycardia is a nonspecific sign caused by increased adrenergic activity.
- cool peripheral extremities and cyanosis of the lips and nail beds (caused by excessive adrenergic activity) **peripheral vasoconstriction**

Jugular venous pressure

- Examination of the jugular veins provides an estimation of right atrial pressure.
- The jugular venous pressure is best appreciated with the patient lying recumbent, with the head tilted at 45°.

Pulmonary Examination

- Pulmonary crackles result from the transudation of fluid from the intravascular space into the alveoli.
- In patients with pulmonary edema, rales may be heard widely over both lung fields and may be accompanied by expiratory wheezing (cardiac asthma).
- Crackles present in patients without concomitant lung disease are specific for HF.
- rales are absent in patients with chronic HF.
- Pleural effusions result from the elevation of pleural capillary pressure and the resulting transudation of fluid into the pleural cavities.
- Since the pleural veins drain into both the systemic and the pulmonary veins, pleural effusions occur most commonly with biventricular failure.
- pleural effusions are often bilateral in HF, when they are unilateral, they occur frequently in the right pleural space.

Abdomen and extremities

- Hepatomegaly is an important sign in patients with HF. When present, the enlarged liver is tender and may pulsate during systole if tricuspid regurgitation is present.
- Ascites, (late sign), occurs due to increased pressure in the hepatic veins.

- **READ CARDIAC EXAMINATION (HEART SOUNDS)**

Cardiac Cachexia

- With severe chronic HF, there may be marked weight loss and cachexia.
- mechanism of cachexia is not entirely understood,
- Possible explanation includes
  - elevation of the resting metabolic rate;
  - anorexia, nausea, and vomiting due to congestive hepatomegaly and abdominal fullness;
  - elevation of circulating cytokines such as TNF;
  - impairment of intestinal absorption due to congestion of the intestinal veins.
- When present, cachexia signifies poor overall prognosis

Diagnosis

- straightforward when the patient presents with classic signs and symptoms of HF
- the signs and symptoms of HF are neither specific nor sensitive
- key to making the diagnosis is to have a high index of suspicion (high risk patients)
- additional laboratory testing should be performed

Routine laboratory testing

- Complete blood count
- UECs
- LFTS
- Urinalysis
  - Selected patients should have assessment for diabetes mellitus (fasting serum glucose or oral glucose tolerance test), dyslipidemia (fasting lipid panel), and thyroid abnormalities (thyroid-stimulating hormone level).

Radiologic investigations

- Echo cardiogram
  - assess cardiac rhythm and determine the presence of LV hypertrophy or a prior MI (presence or absence of Q waves) as well as to determine QRS width to ascertain whether the patient may benefit from resynchronization therapy
- Electro cardiogram (electrical activity)
- Chest Xray
  - provides useful information about cardiac size and shape, state of the pulmonary vasculature, and may identify noncardiac causes of the patient's symptoms

Biomarkers

- useful adjunctive tools in the diagnosis of patients with HF.
- Both B-type natriuretic peptide (BNP) and N-terminal pro-BNP, (released from the failing heart), are sensitive markers for the presence of HF with depressed EF;
- Note that natriuretic peptide levels
  - increase with age and renal impairment,
  - more elevated in women,
  - elevated in right HF from any cause.
  - Levels can be falsely low in obese patients .
- serial measurements of BNP not recommended as a guide to HF therapy.
- Other biomarkers, such as *troponin T and I, C-reactive protein, TNF receptors, and uric acid*, may be elevated in HF and provide important prognostic information.

Differential diagnosis of HF

- Renal failure
- Acute respiratory distress syndrome
- Pulmonary edema
  - Among others

TREATMENT OF HF

- HF should be viewed as a continuum that is composed of four interrelated stages
  - *Stage A* includes patients who are at high risk for developing HF but do not have structural heart disease or symptoms of HF (e.g., patients with diabetes mellitus or hypertension).
  - *Stage B* includes patients who have structural heart disease but do not have symptoms of HF (e.g., patients with a previous MI and asymptomatic LV dysfunction)
  - *Stage C* includes patients who have structural heart disease and have developed symptoms of HF (e.g., patients with a previous MI with dyspnea and fatigue
  - Stage D includes patients with refractory HF requiring special interventions (e.g., patients with refractory HF who are awaiting cardiac transplantation).

Treatment continued

- In this continuum, every effort should be made to prevent HF by treating the preventable causes of HF (e.g., hypertension) and also treating the patient in stages B and C with drugs that prevent disease progression (e.g., ACE inhibitors and beta blockers) and by symptomatic management of patients in stage D.