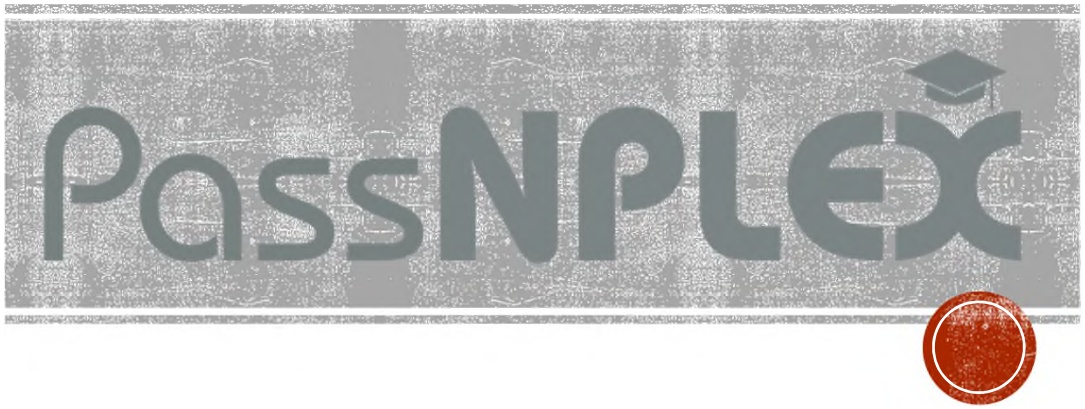


CARDIOVASCULAR SYSTEM

CARDIOVASCULAR SYSTEM

- Embryology & Anatomy
- Physiology
- Biochemistry
- Pathology

SAMPLE CASE 1

Post-mortem microscopic examination of the proximal end of the left anterior descending coronary artery from a 41-year-old female reveals a thrombotic occlusion arising from an atherosclerotic plaque.

1. Hypercholesterolemia was implicated in the pathogenesis of her atherosclerosis. In the synthesis of cholesterol, what is the key regulating enzyme?
   A. Phosphodiesterase
   B. HMG-CoA reductase
   C. Cholesterol desmolase
   D. Cholesterol synthetase

4

- **Answer:** B - HMG-CoA reductase

- Phosphodiesterases break phosphodiester bonds (ex. cyclic nucleotide phosphodiesterase)
- Cholesterol desmolase cleaves a six carbon group from cholesterol. It is the committing and rate-limiting step in steroid biosynthesis.
- Cholesterol synthetase does not exist.

5

SAMPLE CASE 2

A 4-week old male has a ventricular septal defect. Physical examination reveals asystolic murmur, but there is no evidence of cyanosis. Echocardiography shows a left-to-right shunt through a defect in the membranous part of the interventricular septum.

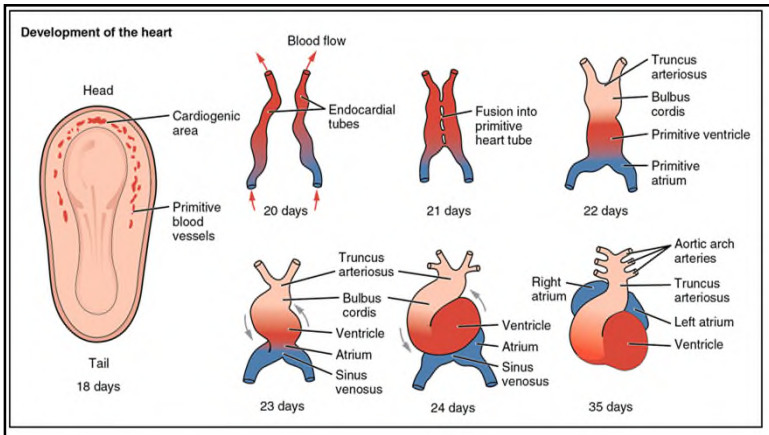
1. The membranous interventricular septum is normally formed by the _____.
   A. Sinus venosus
   B. Septum primum
   C. Septum secundum
   D. Endocardial cushions

6

- **Answer:** D – Endocardial cushions play a role in the proper formation of the heart septa.

- The sinus venosus is a large cavity which precedes the atrium on the venous side of the heart. It exists in the embryonic heart between the two venae cavae.
- The cavity of the primitive atrium that becomes subdivided into right and left chambers by the **septum primum**.
- **The septum secundum** grows downward from the upper wall of the atrium to the right of the primarly septum and ostium secundum. Shortly after birth it fuses with the septum primum and results in the closure of the foramen ovale,

EMBRYOLOGY & ANATOMY



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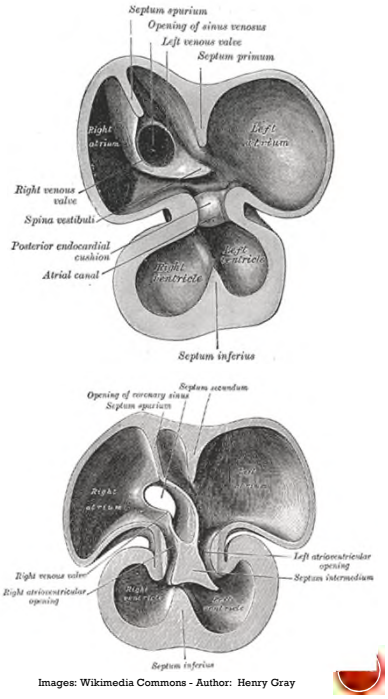

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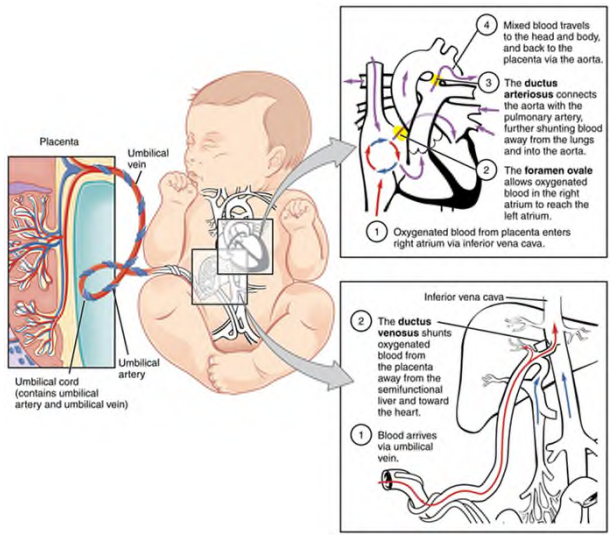
FETAL CIRCULATION



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Major external and internal structures are established from **weeks 4-8** however, they function minimally at this time.

Name Changes After Birth

Foramen ovale → Fossa ovalis

Ductus venosus → Ligamentum venosum

Ductus arteriosus → Ligamentum arteriosum

Umbilical vein → Ligamentum teres

Umbilical arteries → Medial umbilical ligaments

CARDIAC MUSCLE

- **Striated muscle**
  - Light (I bands-no thick filaments) and dark (A bands- single thick filament) cross-bands
  - Myofibrils = contractile units
    - Composed of myosin (thick) and actin (thin) filaments
- Muscle cells are branched and arranged in units called sarcomeres.
  - Intercalated disks and gap junctions allow rapid flow of depolarization signal
- Cardiac muscle cells have a rhythm and contract spontaneously

VESSEL WALL LAYERS

Tunica intima
- Endothelium – **simple squamous epithelium**
- Subendothelium – loose connective tissue
- Basement membrane
- Arteries contain an internal elastic lamina.

Capillaries do NOT contain these three layers!

Tunica media
- Contains **smooth muscle**
- Large arteries contain an external elastic lamina

Tunica adventitia
- Contains **collagen and elastic fibers**
- Protects the vessel, prevent over expansion, and anchors it to surrounding tissue

VESSEL TYPES

Capillaries

- Connect the arterial and venous systems
- Walls contain ONLY tunica intima
- Involved in the exchange of nutrients, oxygen and waste products.

- Continuous – no pores or fenestrae
- Fenestrated – pores with a pore diaphragm
- Sinusoidal – irregular channels or blood pools

Arteries

- Carry oxygenated blood (some exceptions)

Elastic = conducting arteries
Muscular = distributing arteries
Arterioles = smallest type that have a narrow lumen and thick muscular wall

Veins

- Carry deoxygenated blood (some exceptions)

Small, medium, large

- Medium sized veins have one-way valves to resist gravity.
- Large veins have longitudinal smooth muscle and a tunica adventitia

Venules are the smallest type of vein.

CARDIAC MUSCLE LAYERS

Endocardium
- Internal layer
- Covers the valves

Myocardium
- Composed of cardiac muscle

Epicardium
- Outermost layer which is also considered the visceral layer of the serous pericardium
- Fibrous skeleton forms the valve rings and helps anchor muscle fibers.

RIGHT ATRIUM

Receives venous blood from the **SVC, IVC, and coronary sinus**

Sulcus terminalis = vertical groove that separates the rough and smooth parts of the arterial wall, externally

Crista terminalis = same as above but internally

Sinus venarum = smooth space between the openings of the SVC and IVC.

Pectinate muscles = muscular ridges in the atria

Fossa ovalis = depression on the interatrial septum

Atrioventricular orifice is found on the top of the tricuspid valve

Sinoarterial node (aka pacemaker) is found in the superior end of the sulcus terminalis near the opening of the SVC.

Artrioventricular node is found on the ventricular side of interartrial septum near the coronary sinus

Coronary sinus = opening between right AV and IVC orifices

LEFT ATRIUM

- Forms the base of the heart
- Shares the fossa ovalis with the right atrium
- Interatrial septum
- A.V. orifice (top of the mitral valve)
- Left auricle

- Contains the entrance of the right and left pairs of pulmonary veins

RIGHT VENTRICLE

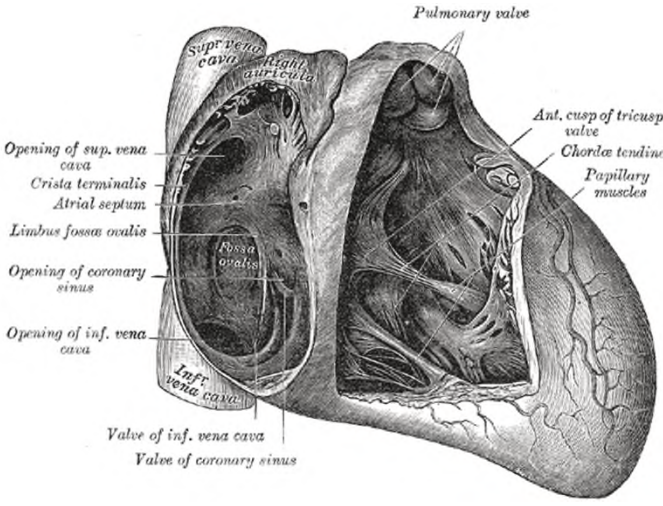
- Trabeculae carnae = muscular elevations in the heart wall
- Chorae tendinae attach the septal cusps of the AV valves to the ventricle walls
- Papillary muscles attach the tendinous cords to the ventricular walls
  - Anterior, posterior, and septal
- Conus arteriosis is a conical prolongation of the right ventricle where the pulmonary arteries emerge.
- Septomarginal trabecula carries the right bundle branch of the AV bundle
- Interventricular septum = muscular wall that separates the left and right ventricles
- Pulmonary trunk exits the right ventricle

LEFT VENTRICLE

Main pump of the heart

- Walls are thick due to the high pressure
- Papillary muscles
- Chordae tendinae
- Mitral valve
- Interventricular septum
- Trabeculae carnae
- Left bundle branch

- AV bundle – conducts impulses from the AV node



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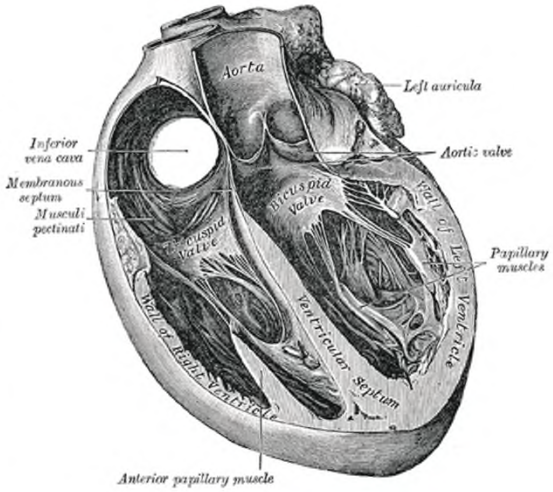

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PERICARDIUM

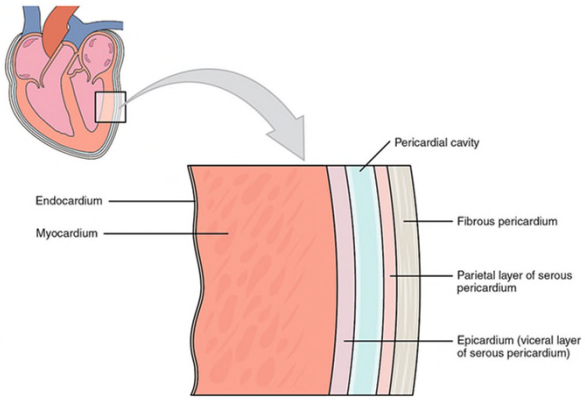
- Double-walled fibroserous sac

Layers

- Fibrous pericardium (external)
- Parietal layer of serous pericardium (internal)
- Visceral layer of serous pericardium
  - Reflected onto the heart

Pericardial cavity

- Space between the parietal and visceral layers of serous pericardium



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CARDIAC SURFACES

Apex of the heart is directed anteriorly and to the left

Base = posterior aspect

Diaphragmatic = interior surface

Anterior = sternocostal surface

Pulmonary = left surface which is located in the cardiac impression of the left lung

Pulmonary Arteries

- Right and left
- Moves venous blood from the right ventricle to the lungs

Pulmonary Veins

- Right and left
- Two from each lung
- Carry oxygenated blood to the left atrium

Aorta

- Ascending
  - From the aortic valve
  - Aortic sinuses hold blood to prevent valve leaflets from adhering to the aortic wall

CARDIAC VALVES

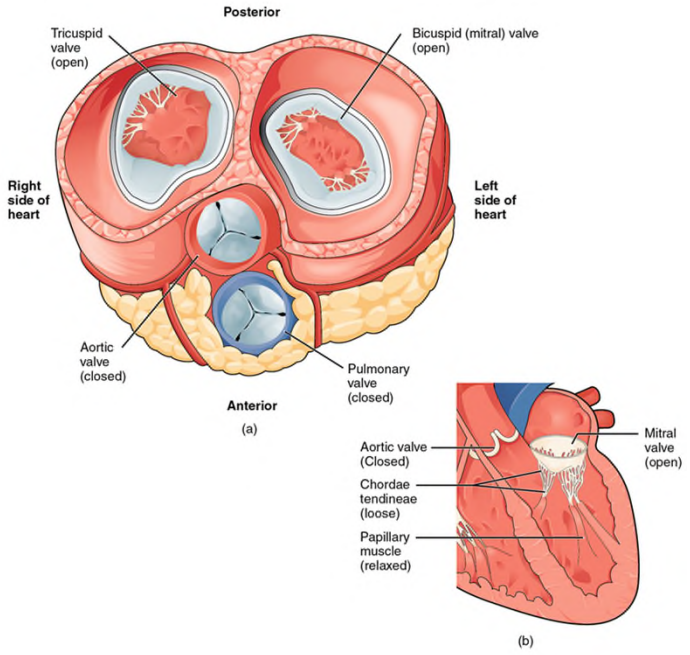
S1 sound

- Closure of the mitral and tricuspid (AV) valves (isometric contraction)
- Beginning of systole

S2 sound

- Closure of the aortic and pulmonic valves (isometric relaxation)
- Beginning of diastole

- **AV valves** prevent the backflow into atria during systole.
- **Semilumar valves** prevent the backflow into ventricles from the arteries at the end of the ventricular systole.
- Valves can be **impacted by regurgitation and stenosis**.



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VASCULAR DYSFUNCTION

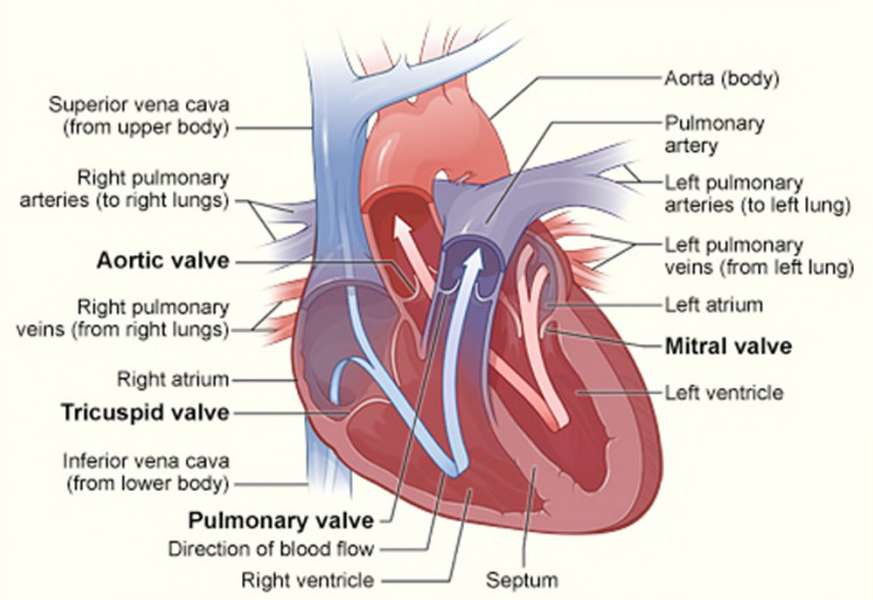
During Diastole

- A – Aortic
- R – Regurgitation
- M - Mitral
- S – Stenosis

- P – Pulmonic
- R – Regurgitation
- T – Tricuspid
- S – Stenosis

Regurgitation occurs **early diastole**

Stenosis occurs **late diastole.**



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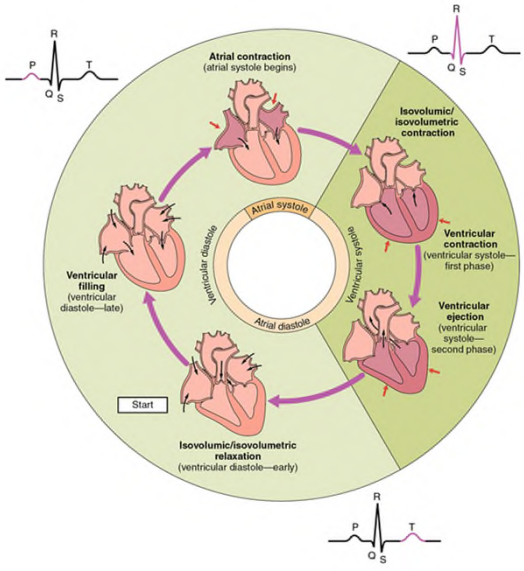
PHYSIOLOGY

CARDIAC CYCLE



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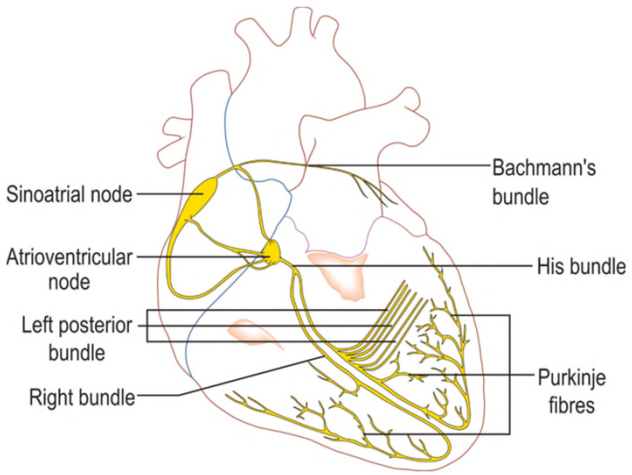
ELECTRICAL CONDUCTION



- **SA node** firing rate is 60-100 depolarizations/minute **without neural or hormonal input**.
- The depolarization wave is **delayed momentarily** (about 0.1 seconds) at the **AV node.**
- Then travels to the **bundle of His** to the **purkinje system** before reaching the ventricles.

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MID-LATE DIASTOLE

- Ventricle fill passively
- AV valves are open
- Aortic and pulmonary valves are closed
- Pressure increases in both atria
- The SA node fires at the end of diastole causing the atria to depolarize and contract.

SYSTOLE

Early

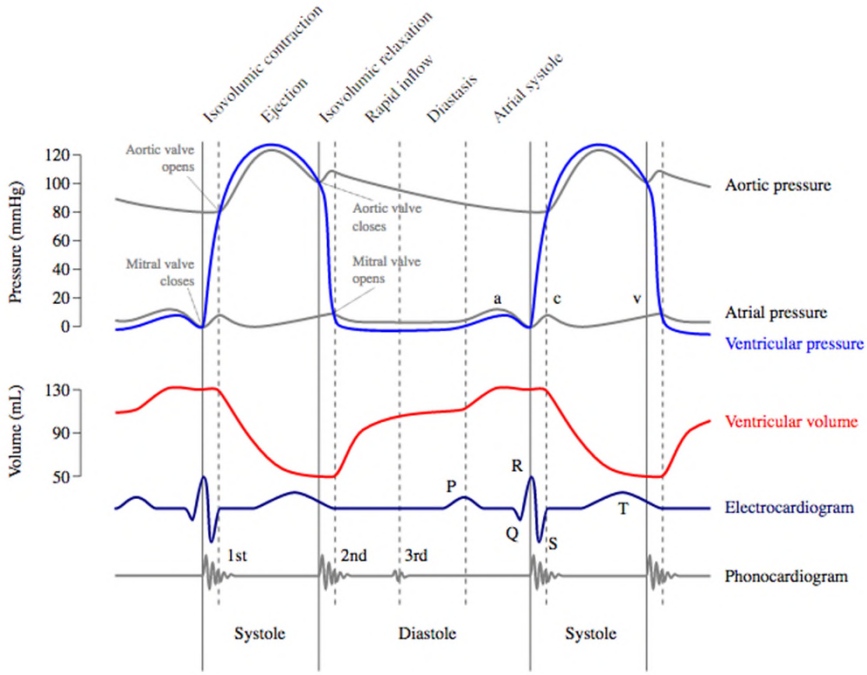
- Pressure within the ventricles increases early in this phase causing the AV valves to close.
- Aortic and pulmonary valves remain closed and ventricular pressure continues to rise.

Late

- Aortic and pulmonary valves are forced open causing blood to enter the aorta and pulmonary trunk.
- End-systolic volume is the remaining ventricular blood.

EARLY DIASTOLE

- Brief repolarization phase
- Ventricles relax and pressure drops rapidly
- Aortic and pulmonary valves close and the AV valves remain closed
- Atrial pressure quickly exceeds ventricular pressure causing the AV valves to open.



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HEART BLOCK

Primary
- Elongation of PR interval

Secondary
- Mobitz 1: Elongation of the PR interval until TWO atrial depolarizations occur.
- Mobitz II: Non-conducting P waves with no elongation of the PR interval and likely to progress to complete heart block

Complete
- No QRS wave (Bundle branch block)

DEFINITIONS

Frank-Starling Law
- Stroke volume increase proportionally to an increase in the volume of blood filling the heart.

Stroke volume (SV)
- The volume of blood pumped from one ventricle during each contraction

Cardiac Output (CO)
- CO = SV x heart rate (HR)
- Increased stretch and ANS stimulation affect CO

Force of contraction changes in the presence of:
- Increased end diastolic volume or increased cardiac stretch
- Sympathetic stimulation

HEART RATE

Parasympathetic nervous system

- Right vagus nerve decreases the intrinsic rate of the SA node at rest
- Left vagus nerve slows conduction at the AV node and decreases the force of contraction by the aria (not the ventricles).

Sympathetic nervous system

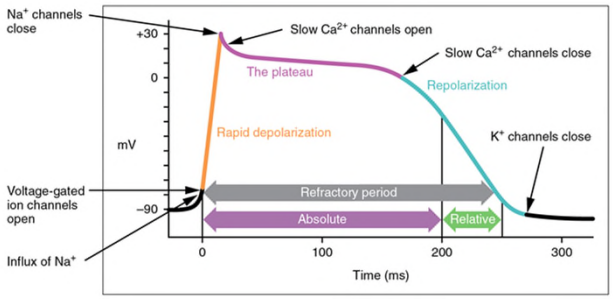
- Increases the rate in times of stress (increased frequency, conduction, force of contraction of the atria and ventricles)

Thyroid hormones

- Cause a slower and more sustained increased in heart rate
- Enhance the effects of epinephrine and norepinephrine of the heart

CARDIAC MUSCLE

- Cardiac cells connect via **intercalated discs**
  - Contain **desmosomes** that anchor them together during contraction
  - **Gap junctions** allow ions to pass between cells
- **Striated, short, fat, branched, and interconnected**
- Na+ permeability toward its resting value is not accompanied by membrane polarization
- Membrane remains depolarized at a plateau of about 0 mV because K+ channels remain closed.
  - Ca2+ channels open causing Ca2+ from the sarcoplasmic reticulum.
- Cardiac **action potentials are 100 times longer than skeletal muscle APs**
- **Absolute refractory period is longer** in order to prevent tetanic contractions in myocytes.



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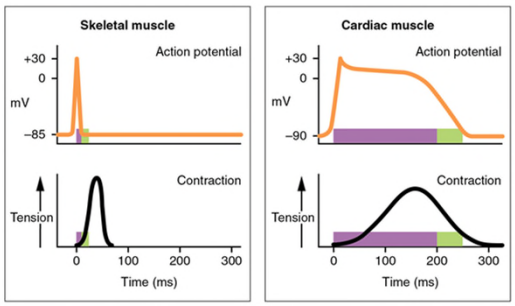

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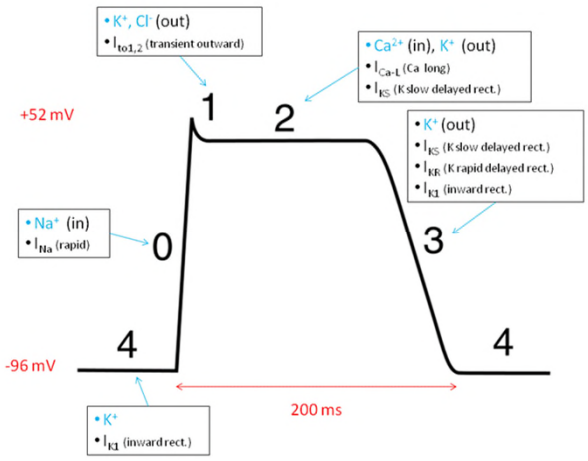

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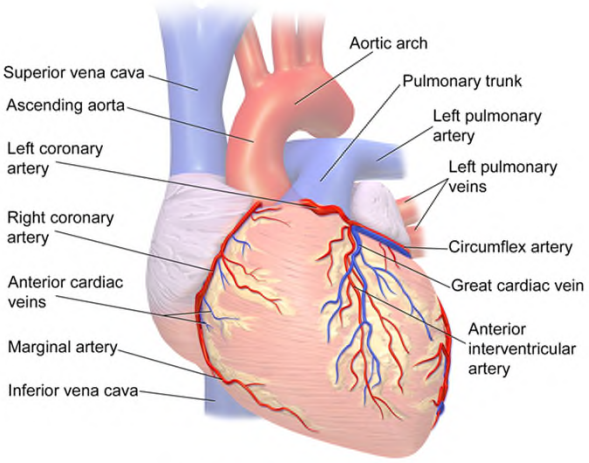
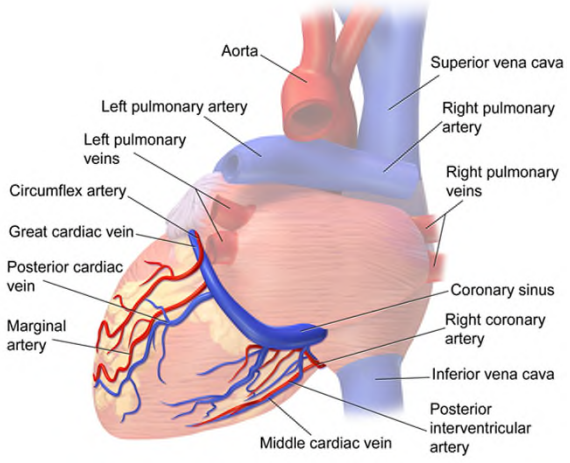
CORONARY CIRCULATION



Coronary Circulation (Anterior)



Coronary Circulation (Posterior)

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CORONARY ARTERIES

- Supply the epicardium and myocardium
- LCA and RCA are the first branches off the aorta

Coronary Artery	Right Coronary Artery (RCA)	Left Coronary Artery (LCA)
Origin/location	From right aortic sinus and runs along the AV groove	From the left aortic sinus and run along the coronary groove
Branches	SA nodal artery, right marginal branch, AV nodal branch, posterior interventricular branch	SA nodal artery, anterior interventricular branch, circumflex branch, left marginal branch
Anastomoses	Anterior interventricular branches of the LCA and the circumflex artery.	Posterior interventricular branch of the RCA
Supplies	AV and SA nodes, right atrium, most of the right ventricle, part of the left ventricle, part of the AV septum.	SA node, left atrium, most of the left ventricle, part of the right ventricle, IV septum

CORONARY VEINS

- Empty into the coronary sinus
- Coronary sinus receives blood from:
  - Anterior interventricular (great cardiac) – ascends in the anterior interventricular groove
  - Posterior interventricular (middle cardiac) – ascends the posterior interventricular groove
  - Left posterior ventricular
  - Left marginal
  - Small cardiac – runs along the coronary groove with the marginal artery
- Great cardiac vein drains the areas that are supplied by the LCA
- The middle and small cardiac veins drain the areas supplied by the RCA.

CORONARY CIRCULATION REGULATION

Adenosine and nitric oxide

- Autocrine transmitters that change coronary artery resistance in response to oxygen demand.

Sympathetic nerve input

- Initial vasoconstriction via the activation of alpha-1 adrenergic receptors found on coronary blood vessels.
- Vasodilation follows and is mediated by local production of nitric oxide and the activation of beta-1 adrenergic receptors found on myocardial cells.

Parasympathetic nerve input

- Direct coronary vasodilation

SYSTEMIC CIRCULATION

- Arterial System
- Venous System
- Lymphatic System

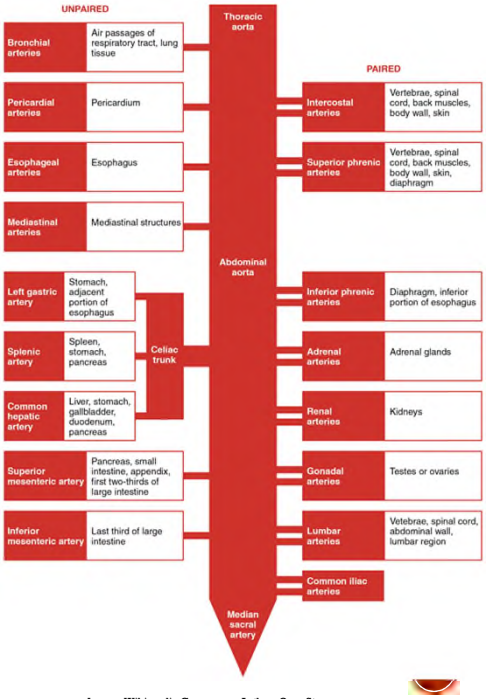
ARTERIAL SYSTEM

Thoracic aorta

- T4 in the posterior mediastinum and runs left of T5-T12
- Branches:
  - Left bronchial arteries
  - Two esophageal arteries
  - Pericardial arteries
  - Mediastinal arteries
  - 9 pairs of intercostal arteries
  - Subcostal arteries
  - Superior phrenic arteries

Abdominal aorta

- After the thoracic aorta passes through the aortic hiatus in the diaphragm (T12 level)
- Branches
  - Celiac trunk (T12 level)
  - Superior mesenteric artery (L1 level)
  - Inferior mesenteric artery (L3 level)



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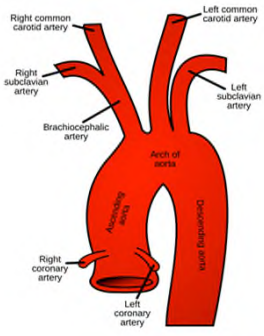
Head & Neck

Aortic arch

- Branches:
  - Left common carotid, left subclavian artery (left side), brachiocephalic trunk (right side)
    - Brachiocephalic trunk divides into:
      - Right common carotid and right subclavian artery



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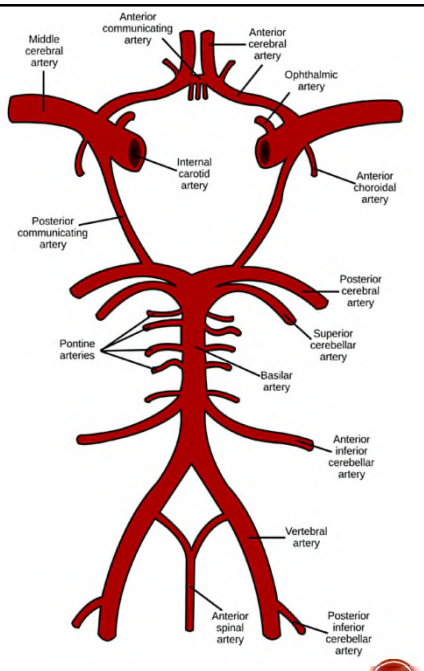
Common carotids → internal & external carotid arteries

- Internal carotid
  - No branches in the neck
  - Main artery supplying the brain and orbits
- External carotid
  - Supplies structures external to the skull
  - 8 branches:
    - Superior thyroid, lingual, facial, ascending pharyngeal, occipital, posterior auricular, and terminates as the maxillary and superficial temporal arteries

Brain

- Supplied by the internal carotid and vertebral arteries
- Anterior brain supplied by:
  - Internal carotid arteries enter the cranial cavity through the carotid canals (temporal bone) and travel to the cavernous sinus.
- Posterior brain supplied by:
  - Basilar artery branches (formed by the vertebral arteries)
- **Circle of Willis**
- Anterior communicating artery
- Anterior cerebral arteries
- Internal carotid arteries
- Posterior communicating arteries
- Posterior cerebral arteries



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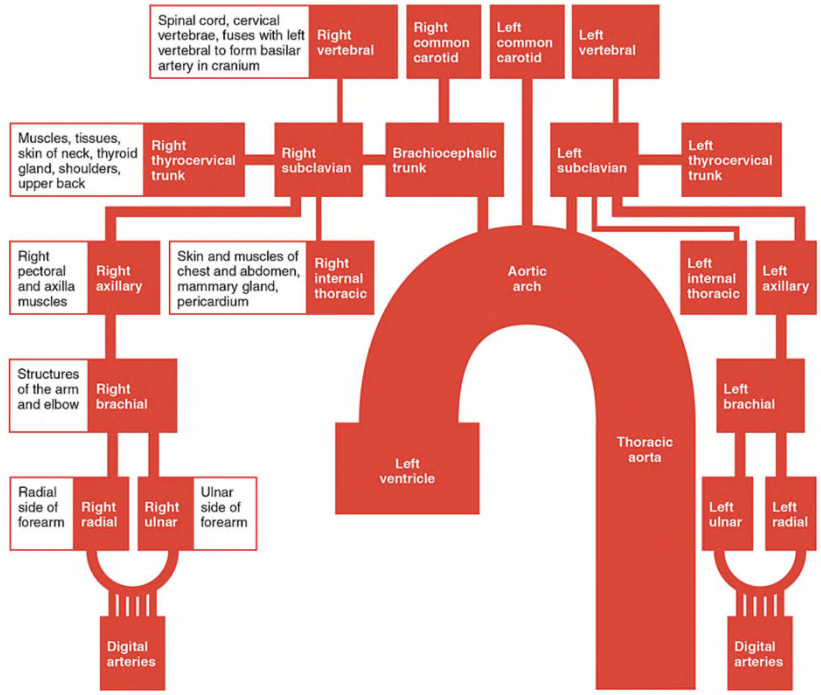
Spine

- 3 longitudinal arteries form channels in the pia matter
  - Anterior spinal artery
  - Two posterior spinal arteries

Thorax

- Left and right internal thoracic arteries from the left and right subclavian arteries
- Anterior intercostal artery branches off the internal thoracic artery.
- Highest intercostal artery branches from the costocervical trunk
- 1st two posterior intercostal arteries branch from the highest intercostal artery
- The remaining posterior intercostal arties come from the thoracic aorta
- Internal thoracic arteries terminate into:
  - Musculophrenic and superior epigastric arteries



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Abdomen

- Abdominal aorta branches into the celiac trunk, superior and inferior mesenteric arteries.
- Celiac trunk → left gastric, splenic, common hepatic arteries

Artery & Additional Branches	Organ Supplied
Left gastric artery	Distal portion of the esophagus, lesser curvature of the stomach
Splenic artery	Spleen, greater curvature of the stomach, body of the pancreas
Hepatic artery - Left and right hepatic	Liver, gallbladder, duodenum, pancreas
Superior mesenteric artery - Ileocolic, middle and right colic	Liver, gallbladder, duodenum, pancreas
Inferior mesenteric artery - Left colic, sigmoid, superior rectal	Descending and sigmoid colon, proximal part of the rectum
Left and right renal arteries - Inferior suprarenal arteries	Suprarenal glands (also supplied by the superior suprarenal artery and the middle suprarenal artery)

Abdomen (continued)

- Common iliac arteries
  - Branch from the abdominal aorta (level of L4)
  - Further divides into an internal and external iliac branch
- Internal iliac supplies the pelvic organs and muscles
- External iliac supplies the superficial abdomen and pelvic areas
  - Becomes the femoral artery after passing through the inguinal ligament

Pelvis

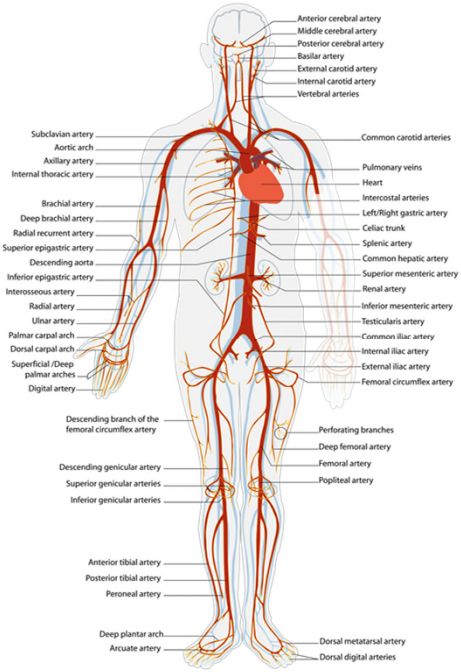
- Internal iliac → posterior and anterior divisions
- Anterior division primarily supplies the pelvis
  - Branches: obturator, internal pudendal, inferior vesical, middle rectal, uterine, vaginal, and internal pudendal arteries.
  - Inferior rectal artery is a branch off of the internal pudendal artery

Upper Limb

- The subclavian artery → axillary artery after passing under the 1st rib
- Axillary artery has 3 parts each of which have arteries that branch off it.
  - Superior thoracic artery (1st)
  - Thoracoacromial and lateral thoracic arteries (2nd)
  - Subscapular and anterior and posterior circumflex humeral arteries (3rd)
- The axillary artery → brachial artery → divides into the ulnar and radial arteries at the cubital fossa.
- Radial artery → deep palmar artery
- Ulnar artery → superficial palmar artery

Lower Limb

- Femoral artery → popliteal artery
  - Branches:
    - Profunda (deep) femoral artery
    - Medial circumflex artery
    - Lateral circumflex artery
- Popliteal artery
  - Branches:
    - Anterior tibial artery → dorsalis pedis artery
    - Posterior tibial artery → lateral and medial plantar arteries



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VENOUS SYSTEM

Superior Vena Cava

- Located right of the midline
- Empties into the right atrium.
- Formed by the joining of the right and left brachiocephalic veins
  - Subclavian vein drains the upper extremities
  - External jugular vein drains most of the scalp and side of the face.
    - Terminates as the subclavian vein
  - Internal jugular vein drains blood from the anterior face, brain, cervical viscera, and deep neck muscles
    - It starts at the jugular foramen and merges with the subclavian vein to form the brachiocephalic vein

Inferior Vena Cava

- Right of the midline
- Empties into the right atrium
- Formed by the junction of the right and left common iliac veins
  - The following veins drain into the IVC
    - Lumbar, gonadal, renal, suprarenal, hepatic, and inferior phrenic
      - The left gonadal and suprarenal veins → left renal vein

Head & Neck

Cranium

- Diploic veins drain the anterior, frontal, poterior temporal, and occipital lobes
- Emissary veins connect the dural venous sinuses and the veins outside the cranium.
- Meningeal veins drain into the plexi.

Dura matter sinuses

- Found between the periosteal and meningeal layers of the dura
- Blood is drained through these sinuses to the internal jugular veins
- Inferior and superior sagittal, straight transverse, occipital, sigmoid, cavernous, intercavernous, inferior and superior petrosals, basilar, and sphenoparietal sinuses
- Confluence of sinuses = where the straight, occipital, superior sagittal, and transverse sinuses meet.

Spine

- External and internal venous plexi are formed the spinal veins
- Basivertebral veins drain into both venous plexi
- Intervertebral veins

Thorax

- Azygos
  - Right side of the vertebral column
  - Accessory hemiazygos vein is on the left side
  - Drain the thoracoabdominal walls and the back into the SVC
- Brachiocephalic is formed by the subclavian veins and the internal jugular vein
- Internal thoracic vein drains into the brachiocephalic vein

Abdomen

- Portal vein collects blood from the abdominal organs and transports it to the liver.
- Hepatic vein drains the liver and empties into the IVC.
  - Contains blood from the portal vein and hepatic arteries
- Splenic vein empties into the portal vein
  - Joins the inferior mesenteric and superior mesenteric veins
- Mesenteric veins
  - The superior mesenteric vein drains the small intestine, ascending colon, proximal ½ of the transverse colon, and part of the stomach/
    - Empties into the portal vein
  - Distal ½ of the transverse colon, descending colon, pancreas, spleen, part of the stomach is drained by the inferior mesenteric vein.
    - Empties into the splenic vein

Pelvis

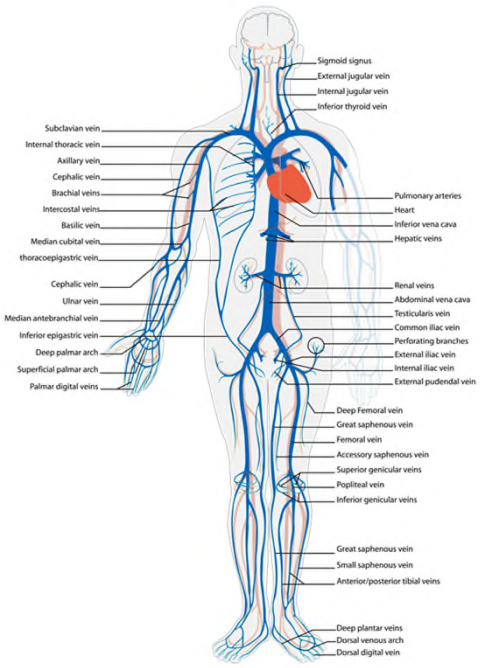
- External iliac vein
  - Previously the femoral vein before passing by the inguinal ligament
  - Forms the common iliac vein after combining with the internal iliac vein
- Internal iliac vein
  - Runs from the lesser pelvis from the upper border of the greater sciatic notch to the edge of the pelvis

Upper Limb

- Cephalic vein
  - From the dorsal venous network of the lateral aspect of the hand
  - Empties into the axillary vein
- Basilic vein
  - From the dorsal venous network of the medial aspect of the hand
  - Merges with the axillary vein
- Median antebrachial vein
  - From the dorsum of the thumb and runs along the anterior aspect of the forearm between the basilic and cephalic veins.
- Brachial vein → axillary vein
- Axillary vein becomes the subclavian vein at the lateral border of the 1st rib
- Venae comitantes is a pair of veins that run close to an artery so the pulsations help venous return.
- Subclavian vein joins the internal jugular vein to form the brachiocephalic.

Lower limb

- Common iliac vein is formed by the external and internal iliac veins.
- Saphenous veins
  - Dorsal vein of the great toe and dorsal venous arch of the foot form the great saphenous vein
    - Empties into the femoral vein
  - Dorsal vein of the little toe and dorsal venous arch of the foot form the small saphenous vein
    - Empties into the popliteal vein found in the popliteal fossa
- Tibial veins
  - Anterior and poterior tibial veins form the popliteal vein
- Popliteal vein
- Femoral vein
  - The popliteal vein becomes the femoral vein at the adductor hiatus
  - Becomes the external iliac proximal to the inguinal ligament



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BLOOD FLOW

- Flow = pressure difference/resistance

Poiseuille's Law

- Velocity of the blood flow through the capillaries is directly proportional to the radius of the capillary (to the 4^{th} power) and the pressure on the blood
- Inversely proportional to the blood viscosity and the length of the capillary

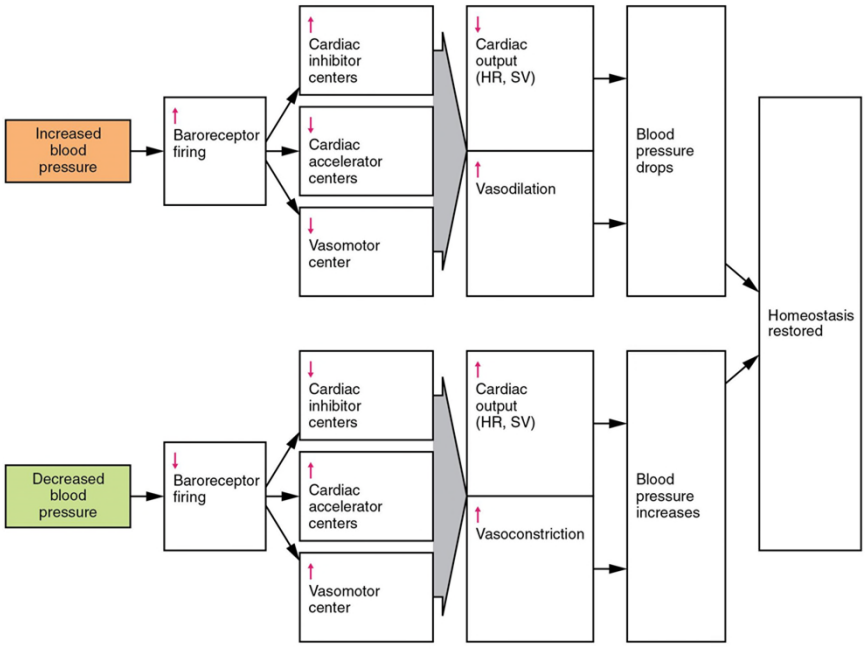
BLOOD PRESSURE

- Mean arterial pressure (MAP) = Cardiac output (CO) x total peripheral resistance (TPR)

Short-term Nervous Regulation

- Baroreceptors – found in the common carotids and aortic arch
  - Regulator of arterial blood pressure
  - An increased in arterial pressure causes increased firing of the arterial baroreceptors → compensatory decrease in CO and TPR
- Chemoreceptors – found in the aortic arch and carotid arteries

  PO2 decreases/PCO2 increases (pH drops) → chemoreceptors transmit impulses to the medulla → increased sympathetic stimulation & decreased parasympathetic stimulation → increased HR, increased vasoconstriction and contractility → increased MAP



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Short-term hormonal regulation

- Adrenal medulla hormones
  - Adrenal glands → NE (vasoconstriction) and Epi (increases CO → generalized vasoconstriction)
- Atrial natriuretic factor causes a decreases in blood volume and vasodilation
- Antidiuretic hormone (ADH) causes the kidneys to conserve water
- Angiotensin II
  - Released in response to renin by the kidney when there is inadequate renal perfusion
  - Causes vasoconstriction
- Endothelium derived factors
- Inflammatory chemicals
  - Histamine, kinins, etc. = potent vasodilators and increased capillary permeability

Local Controls

- Autoregulation
  - Blood flow is adjusted automatically in proportion to its requirement
  - The diameter of local arterioles that feed the capillary beds of each organ is modified
- Metabolic control
  - Vasodilation results when declining levels of nutrients or increasing levels of metabolic byproducts
- Long-term autoregulation
  - Increase in the number of vessels or existing vessels enlarge to compensate for prolonged change in nutrient requirements

Nervous System Controls

- Sympathetic nervous system
  - NE, Epi → vasoconstriction
- Parasympathetic nervous system
  - Ach → vasodilation

VENOUS PRESSURE CONTROL

- Total blood volume determines venous pressure
- The smooth muscle cells of the veins are innervated by sympathetic neurons and stimulated by NE

Muscle pump

- Skeletal muscle contractions causes the compression of veins.

Respiratory pump

- The descending of the diaphragm during inspiration increases the intra-abdominal pressure → squeezes the local veins
- The pressure within the thorax decreases at the same time allowing the thoracic veins to expand.

CAPILLARY EXCHANGE

Hydrostatic pressure = force exerted by a fluid on a wall

- Capillary hydrostatic pressure/filtration pressure pushes fluid through the capillary wall into the interstitium.
- Interstitial hydrostatic pressure = fluid pressure outside the capillaries

Osmotic/oncotic pressures = pressure created by the presence of large, non-diffusible molecules

- These molecules draw water into the capillary
- Capillary oncotic pressure
- Interstitial oncotic pressure is lower because it contains fewer proteins than blood

EDEMA

- Increased arterial BP increases capillary hydrostatic pressure and pushes fluid out
- Increased capillary permeability allows proteins and fluids to leave the capillaries
- Decreased fluid returns to capillaries is generally due to an imbalance in oncotic pressure between the sides of the capillary membrane.
- Blockage of lympathic drains → build up in the interstitum and increases interstitial hydrostatic pressure.

EFFECTS OF EXERCISE

Acute

- CO increases due to the ↑HR and small ↑ in SV.
  - ↑HR due to ↓parasympathetic stimulation and ↑ sympathetic stimulation of the SA node.
- Increased SV due to:
  - ↑ ventricular contractility from neural stimulation
  - ↑ venous return (muscle pumps)
  - ↑ inspiration
  - Easier flow through dilated skeletal muscle arterioles
- CO shifts to increase the flow to the muscles, skin, and heart.
- MAP increases due to the increased CO and increased TPR

Adaptive Effects

- Increased CO mainly due to increased SV
  - Thicker myocardium and increased contractility
- Increased oxidative capacity due to an increase in mitochondria
- HR decreases at rest because the heart is more efficient
- Increased insulin sensitivity as a result of increased skeletal muscle glucose utilization.

BIOCHEMISTRY

BIOCHEMISTRY

- Fatty acids
- Fatty acid oxidation
- Triglycerides
- Ketones
- Regulation of adipose tissue metabolism
- Phospholipids
- Cholesterol
- Lipoproteins

FATTY ACIDS

- Long chain organic acids (4-24 carbon atoms)
  - Composed of single carboxyl group and a long, nonpolar hydrocarbon "tail"
- Either free form or esterified to glycerol
- Number of double bonds between carbon atoms determines the degree of saturation.
  - Unsaturated fatty acids naturally occur in the cis form

- Saturated lipids = butter, animal fat, coconut oil
- Monounsaturated lipids = olive oil, avocados, canola oil
- Polyunsaturated lipids = flax seed oil, walnuts, EPO, cold water fish

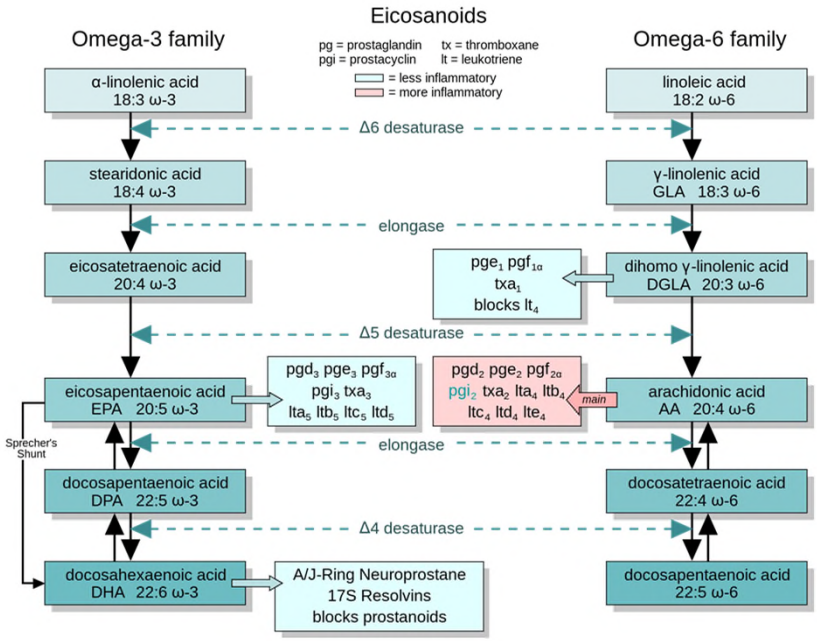
Fatty acid	# of carbons	Saturation
Palmitic	16	Saturated
Stearic	18	Saturated
Oleic (omega-9)	18	Monounsaturated (Δ9)
Linoleic (omega-6)	18	Di-unsaturated (Δ9,12)
Linolenic (omega-3)	18	Tri-unsaturated (Δ9,12,15)
Arachidonic	20	Tetra-unsaturated (Δ5,8,11,14)

ESSENTIAL FATTY ACIDS

- Linoleic and alpha-linolenic acid (polyunsaturated fatty acids)
- Required to make eicosanoic molecules
  - thromboxanes, leukotrienes, lipoxins, prostraglandins

EFA metabolism

- Linoleic acid (omega-6)
  - Gamma-linolenic acid (GLA), dihomogamma-linolenic acid (DGLA), and AA
- Arachidonic acid (considered semi-essential)
  - Produced from gamma-linolenic acid
- Alpha-linolenic acid (omega-3)
  - Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)



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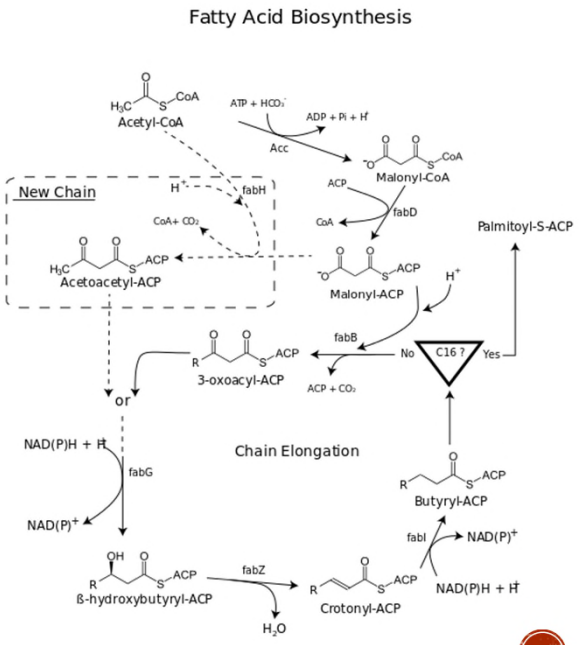
SHORT-CHAIN FATTY ACIDS

- Butyrate is an example
- 2-6 carbon atoms
- Preferred energy source for colon epithelial cells
- play an important role in the absorption of salt and water

FATTY ACID SYNTHESIS

- Glucose and protein → fat
- Occur when NADH, ATP, and citrate levels are high.
- Acyl intermediates of fatty acid synthesis are covalently bonded to acyl carrier protein (ACP)
- De novo lipogenesis occurs in the cytosol (up to 16 carbons in length - palmitate)
- Chains longer than 16 carbons are formed by elongation
  - Occurs in liver cells' smooth endoplasmic reticulum
  - Involves the addition of two carbon units to the carboxyl end via elongase



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- Lipogenesis occurs primarily in liver.
  - Enzymes can be found in the cytoplasm of adipose cells, mammary gland cell, and some kidney cells.

Acetyl-CoA → malonyl CoA via acetyl-CoA carboxylase (**rate limiting enzyme**)

- Requires **biotin**
- Enzyme is inhibited by:
  - Glucagon, epinephrine-induced phosphorylation, malonyl-CoA, or palmitoyl-CoA
- Enzyme is activated by a high concentration of citrate and insulin.

- **Pantothenic acid** is required to hold enzyme complexes together that are used for the remaining reactions.
- **NADPH** is needed in two reactions.

FATTY ACID OXIDATION

- Primary pathways for the catabolism of saturated fatty acids
- Occurs in the mitochondria
- Two-carbon fragments are removed from the carboxyl end of long-chain FAs producing acetyl-CoA
- Prior to oxidation the long-chain fatty acid is activated by ATP and coenzyme A
  - Forms fatty acyl-CoA which is transported across the mitochondrial membrane via carnitine acyltransferase I

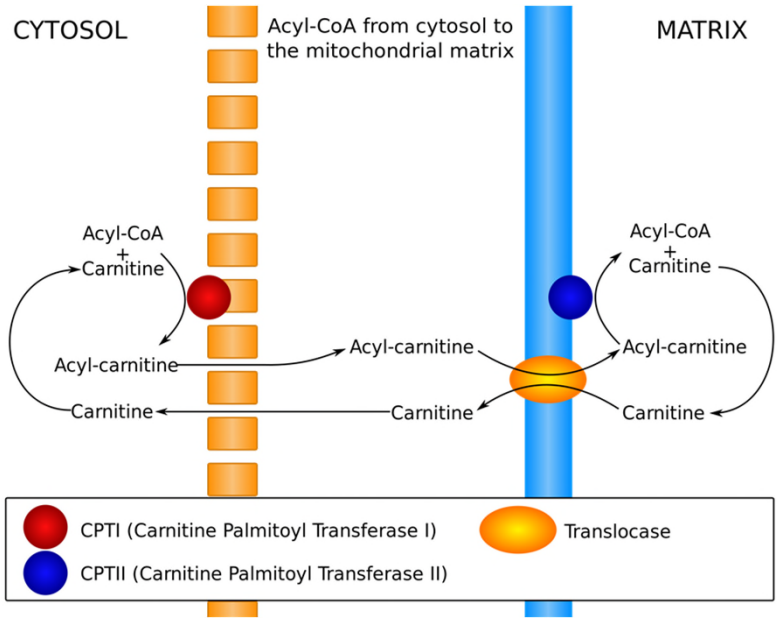
4 reactions that work on the beta-carbon of fatty acyl-CoA:

1. Acyl CoA → enoyl-CoA (forms a double bond)
   - via acyl CoA dehydrogenase, uses FAD
2. Enoyl CoA → beta-hydroxyacyl CoA
   - Via enoyl CoA hydratase (water is then added across the double bond)
3. Beta-hydroxylacyl-CoA → beta-ketoacyl-CoA
   - Via beta-hydroxylacyl CoA dehydrogenase, uses NAD
4. Beta-ketoacyl CoA → Acyl CoA (minus 2 carbons) + 2 Acetyl CoA
   - Via thiolase (cleavage occur between the alpha- and beta-carbons)

- Acetyl-CoA enters the Krebs cycle while the fatty acyl-CoA cycles back to the first step until it is completely degraded into acetyl-CoA.

- 1 $FADH_2$ and 1 NADH are produced which are used in the ETC to produce ATP

- Occurs in skeletal and cardiac muscle
- In the liver, acetyl-CoA is ultimately converted into ketone bodies to be used as energy in other tissues.
- Fatty acid oxidation is controlled by the demand for ATP.
  - Adequate carbohydrate/glucose, ATP, malonyl-CoA inhibits the carnitine acyltransferase 1 transporter
  - When ATP levels are low, epinephrine, norepinephrine, and glucagon stimulate lipolysis in order to provide fatty acids for oxidation.
- Short and medium chain fatty acids cross the mitochondrial membrane easily.
- Carnitine is requires to transport long chain fatty acids.



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TRIGLYCERIDES

- Glycerol base that has been esterified with 3 fatty acid chains
- Major functions:
  - Component of cell membranes
  - Storage form of fatty acids
  - Metabolites act as intracellular messengers and hormones
- Synthesis occurs primarily in the liver but occurs in the adipose tissue as well.
  - Triacylglycerol acts as energy storage
- Most triglycerides are exported with cholesterol, cholesterol esters, phospholipid, and protein to form VLDLs

TRIGLYCERIDE SYNTHESIS

First step is glycerol phosphate synthesis via one of two pathways

- Addition of two fatty acids from fatty acyl CoA (pathothenic acid)
- Removal of phosphate
- Addition of a third fatty acid

Pathway 1 (Glycolysis to form DHAP)

- Hydrogenation via glycerol-P dehydrogenase using NADH (niacin)

Pathway 2

- Phosphorylation of glycerol by glycerol kinase using ATP

- Insulin promotes the conversion of carbohydrates to triglycerides.
- Glucagon and epinephrine causes mobilization of triglycerides via triacylglycerol lipase.

KETONE BODIES

Acetate, acetoacetate, beta-hydrobutyrate

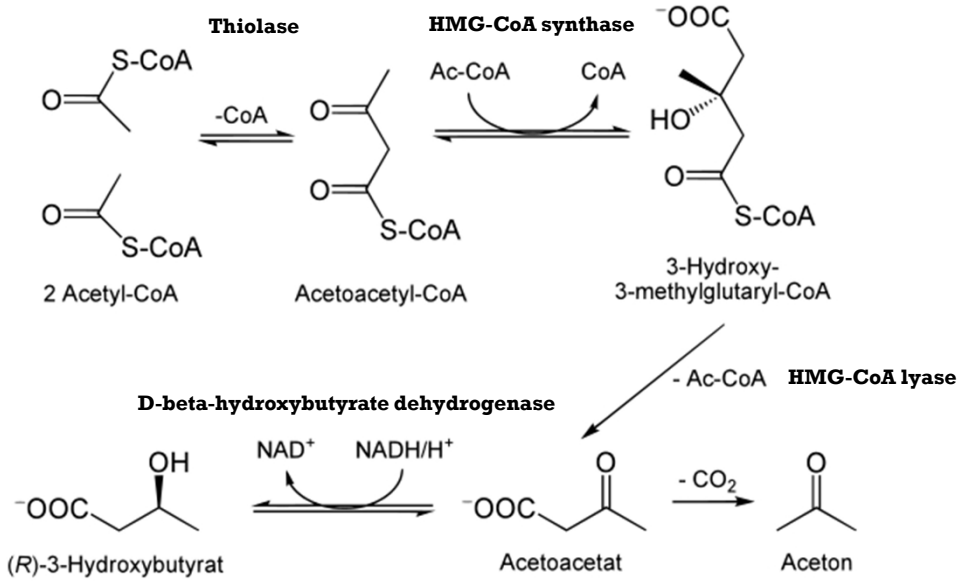
- Can be taken up by the muscles, kidneys, heart and brain and oxidized into energy

Synthesis

- Glucose cannot be synthesized from FAs
- Acetyl-CoA from beta-oxidation of fats can be shunted into forming ketones in liver mitochondria.

Regulation

- Liver can only generate ketones from free FAs floating in the blood
- Carnitine acyltransferase I transporter
- Level of oxaloacetate to draw acetyl-CoA into the Krebs cycle.



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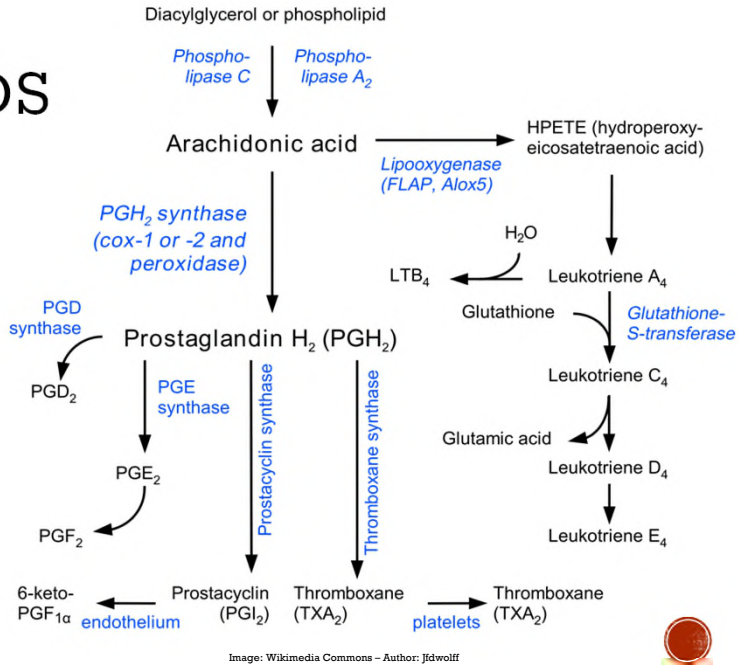
EICOSANOIDS

- Prostaglandins, thromboxanes, prostacyclin, leukotrienes
- Prostaglandin synthesis is regulated by cycloxygenase



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PHOSPHOLIPIDS

Alcohol attached by a phosphodiester bridge to either a diacylglycerol or sphingosine

- Usually composed of a glycerol backbone, two fatty acid chains, and a phosphorylated alcohol
  - Fatty acid chains are esterified at C1 & C2 of the glycerol-3-phosphate
  - Alcohol head group is esterified to the phosphate group on C3
- Non-membrane bound phospholipids
  - Bile, lung surfactant, plasma lipoprotein particles
- Major component of cell membranes is phosphatidylcholine (lecithin)

Cephalins

- Phospholipids derived from glycerol where the primary and secondary hydroxyl groups are esterified with a long-chain fatty acid or monoserine ester of phosphoric acid.
- Contain **amino alcohols ethanolamines or serines**

Sphingomyelin

- Derived from **sphingosine** NOT glyercol
- Have a **phosphorylated choline** group attached

Cardiolipin

- Two molecules of phosphatidic acid esterified through their phosphate groups to an additional molecule of glycerol
- **Antigenic**

PHOSPHOLIPID SYNTHESIS

- Synthesized in the smooth endoplasmic reticulum
  - CDP-activated polar head group is used
  - CDP-activated 1,2-diacylglyerol and an inactivated polar head group
- Basic group is added to phosphatidic acid or 1,2-diacylglycerol
- Most phospholipids have:
  - A saturated fatty acid on carbon one (C-1)
  - An unsaturated fatty acid on carbon two (C-2)

Phosphatidylcholine (PC) (Lecithins)

- C-1: palmitic or stearic acid
- C-2: oleic, linoleic, or linolenic acid
- Dipalmitoyl lecithin is a component of pulmonary surfactant and the major phospholipid found in the extracellular lipid layer lining the pulmonary alveoli.
- Phosphatidylserine and phosphatidylethanolamine can be converted to PC
- PS→ PE → PC

Phosphatidylethanolamine (PE)

- C-1: palmitic or stearic acid
- C-2: a long chain unsaturated fatty acid

Phosphatidylserine (PS)

- Composed of similar fatty acid to PE
- Can serve as a source of PE through a decarboxylation reaction

Phosphatidylinositol (PI)

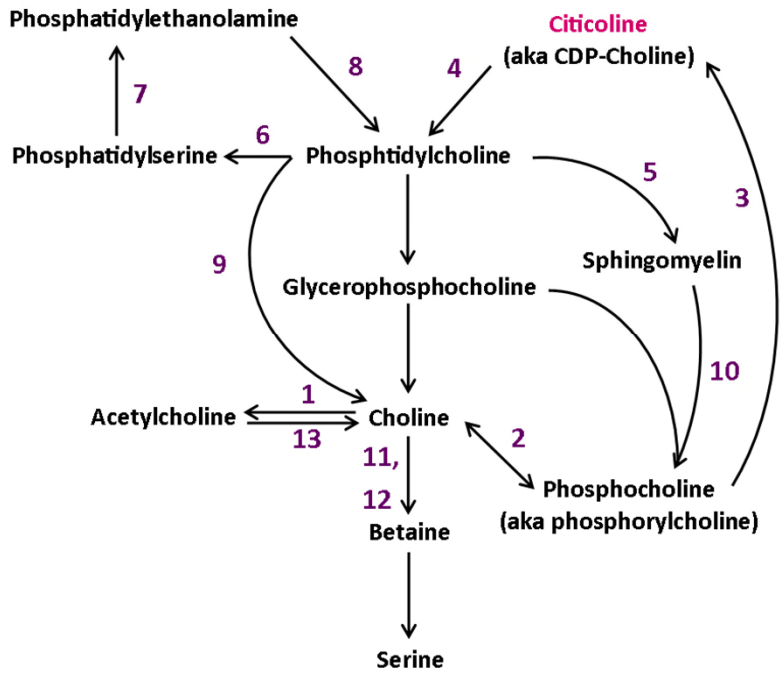
- C-1: almost exclusively stearic acid
- C-2: arachidonic acid
- Important for intracellular transducer of signals coming from the plasma membrane

Phosphatidylglycerol (PG)

- High concentrations in the membrane of the mitochondria and in pulmonary surfactant.

Diphosphatidylglycerol (DPG) (AKA cardiolipin)

- Found in the inner mitochondrial membrane and pulmonary surfactant



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PHOSPHOLIPID DEGRADATION

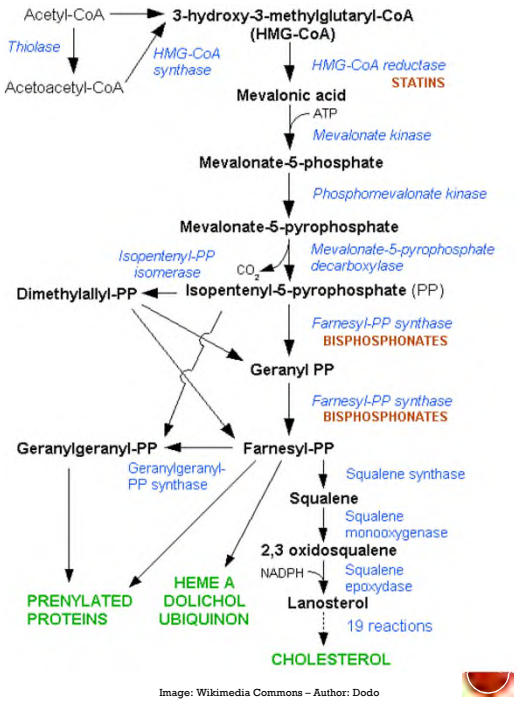
- Phospholipases, A1 and A2 remodel the acyl groups in phospholipids
- Products of these reactions are called lysophospholipids
  - Can be substrates for acyl transferases
  - Can accept acyl groups from other phospholipids (via lysolectithin acyltransferase (LLAT))
- Phospholipase A2 can release arachidonic acid from the C-2 position
  - Arachidonate is used as a substrate for the synthesis of prostaglandins and leukotrienes

CHOLESTEROL

- Primarily synthesized in the liver and intestines
- Derived
- Precursor to:
  - Steroid hormones
  - Bile acids
  - Adrenocortical hormones
  - Vitamin D
- Regulates cell membrane fluidity

CHOLESTEROL SYNTHESIS

- Cytosol of most nucleated cells
- **HMG-CoA reductase is the rate-limiting enzyme**
  - Inhibited by cholesterol or bile salts in the liver
  - Stimulated by insulin
- Cholesterol also feeds back to inhibit the transcription of HMG-CoA reductase and synthase enzymes.
- Cholesterol binds LDL receptors and shuts down cholesterol synthesis.



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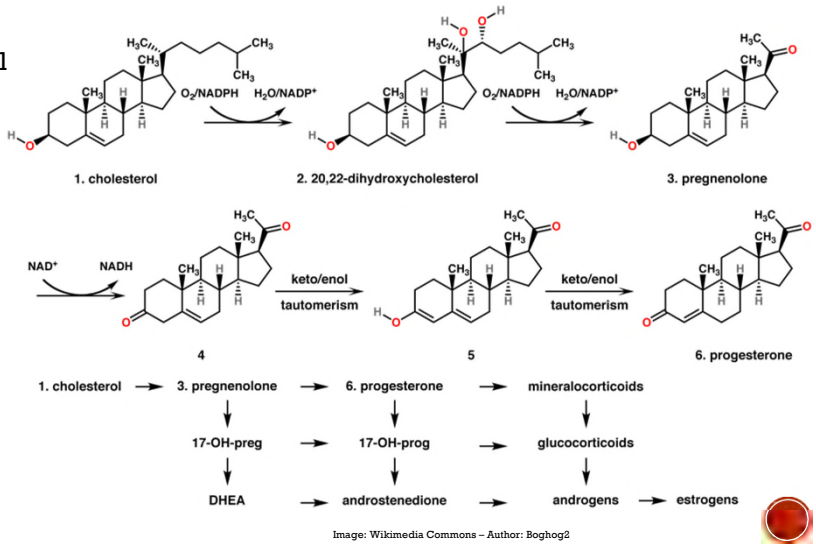
STEROID SYNTHESIS

- A 6-carbon group is cleaved from cholesterol by **desmolase**
  - **committing and rate-limiting step in steroid biosynthesis**
- **Pregnenolone** is the product which moves to the cytosol.



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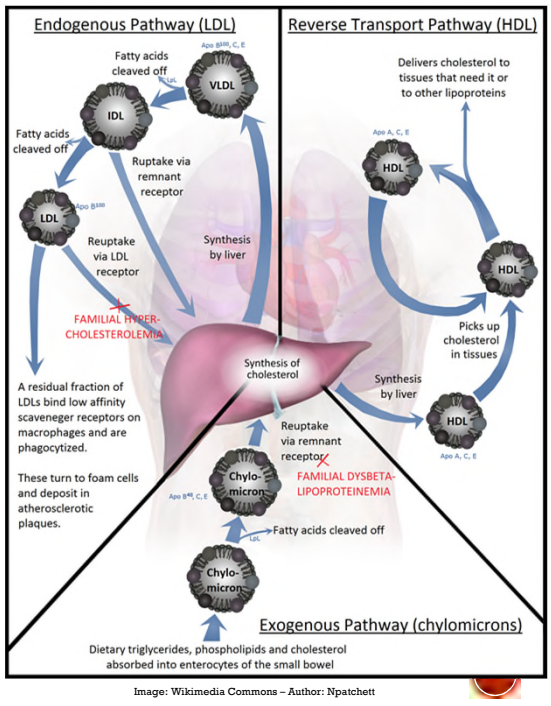
LIPOPROTEINS

- Lipids are bound to water-soluble proteins for transport in the blood
- Apoproteins, phospholipids, and free cholesterol form a membrane around a core of cholesterol esters and triglycerides.

LIPOPROTEIN METABOLISM

- Dietary lipids are turned into chylomicrons in the intestines and absorbed via lacteals.
- Lipoprotein lipase (LPL) removed fatty acids from triglycerides and apoA and C are transferred to HDL.
- Chylomicron remnant are taken up by the apoE receptor into hepatocytes.
- VLDL is formed by the lipids from the chylomicron remnant being packaged with apoB-100 primarily and C and E.
- LPL removes fatty acids from VLDL to form IDL and ultimately LDL (apoC & E are shed)
- LDL is taken up by the hepatocytes via the LDL receptor.
- HDL is formed in the intestines and liver with small amount of lipid.
  - Gradually accumulates fatty acids and cholesterol from LDL via phospholipid transfer protein (PLTP)
  - Scavenges cholesterol from the periphery via lecithin:cholesterol acyltransferae (LCAT)
- Cholesterol can be transferred to LDL via the cholesterol ester transfer protein and to the liver via SR-B! receptor.



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Lipoprotein	Apo	Origin	Degraded location	Role
Chylomicron	B-48	Intestines	Periphery	Fatty acid transport
Chylomicron remnant	B-48	Periphery	Liver	Fatty acid transport
VLDL	B-100	Liver	Liver, periphery	LDL precursor
IDL	B-100	Periphery	Liver, periphery	LDL precursor
LDL	B-100	Periphery	Liver, periphery	Transports cholesterol to the periphery
HDL	A	Liver, intestines	Liver	Transports cholesterol to the liver
Lp(a)	(a)	Liver	Liver	Unknown

CHYLOMICRONS

- Largest lipoprotein
- Primarily composed of exogenous triglycerides
- Produced in the intestines after a fatty meal
- Degraded by LPL to release triglycerides
  - Leaving a smaller chylomicron remnant which is taken up by the liver

VERY LOW-DENSITY LIPOPROTEINS (VLDL)

- Delivers fatty acids for fuel or storage
- Primarily made of endogenous triglycerides
- Mainly produced in the liver
- LPL releases free fatty acids from VLDL
  - Becomes smaller and more dense → creates LDL

INTERMEDIATE-DENSITY LIPOPROTEINS (IDL)

- Between VLDL and LDL in size
- Higher levels of IDL are linked to increased risk of atherosclerosis

LOW-DENSITY LIPOPROTEINS (LDL)

- Primarily composed of cholesterol esters
- Transported to the periphery from the liver
- All cells have LDL receptors and take LDL up via endocytosis

HIGH-DENSITY LIPOPROTEINS (HDL)

- Removes unesterified cholesterol from the periphery and transports it to the liver
- Mainly made in the liver and to a lesser extent the small intestine
- HDL apo A1 induces LCAT to catalyze the transfer of fatty acids from phosphatidyl choline to cholesterol
  - Forms cholesterol esters in the core of HDL.
- Aids chylomicrons and VLDL in unloading their fatty acids from triglycerides by activating LPL.

LIPOPROTEIN (A)

- Composed of LDL combined with apo(a)
- Formed in the liver
- Function is unknown

PATHOLOGY

PATHOLOGY

- Hypertensive heart diseases
- Congestive heart failure
- Ischemic heart disease
- Valvular heart disease
- Primary myocardial diseases
- Pericardial disease
- Congenital heart disease
- Hemodynamic conditions
- Vascular conditions
- Vascular neoplasms
- Infectious vascular diseases

HYPERTENSIVE HEART DISEASES

- Pulmonary hypertension
- Systemic hypertension

PULMONARY HYPERTENSION

- >25 mm Hg average pressure in the pulmonary veins, arteries, or capillaries
- Due to increased pulmonary vascular resistance (>30-50% of pulmonary arterial tree is occluded)
- Right ventricle cannot maintain CO, severe hypotension develops leading to cardiogenic shock
- Dyspnea, fainting, dizziness, dry cough, angina (all worse with exertion), peripheral edema
  - Pulmonary venous HTN causes orthopnea

Group 1 (Pulmonary arterial hypertension, PAH)
- Idiopathic, familial, associated with a systemic disease (scleroderma, congenital shunts, HIV infection, toxins, drugs, etc.)

Group II (associated with left heart disease)
- Atrial or ventricular disease
- Valvular disease (most commonly mitral stenosis)

Group III (associated with lung diseases/hypoxemia)
- COPD, interstitial lung disease, chronic high-altitude exposure, sleep apnea, developmental lung abnormalities

Group IV (thromboembolic)

Group V (misc.)

SYSTEMIC HYPERTENSION

- Elevated systolic and/or diastolic blood pressure
  - Measured on 3 separate occasions
- Excess salt with low potassium intake, chronic inflammation, low magnesium, chronic stress or anxiety, insulin resistance, renal hormone imbalance, obesity, arteriosclerosis
- Complications include chronic renal failure, retinopathy, aneurysm ruptures, congestive heart failure
- High pressure causes chronic damage and can affect any organ sensitive to minor vascular damage.
- Most are asymptomatic for a long period of time.
  - Very high pressure can cause dizziness, blurry vision, and headaches.

Stage	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	➢160	≥ 100

CONGESTIVE HEART FAILURE

- Left-sided
- Right-sided

CONGESTIVE HEART FAILURE

- CO is maintained by various compensatory mechanism to create higher than normal filling pressure and large increases in atrial pressure → myocardial hypertrophy results
- The brain and kidneys suffer forward deficit (low blood supply)
  - Renal failure, dementia, confusion (cough if right-sided CHF)
- Blood builds up in the liver and spleen resulting in backward deficits
  - Caput medusae, esophageal varices, hepatosplenomegaly, ascites, hemorrhoids
- Fatigue, rales, cough, dyspnea, orthopnea, palpitations, tachypnea, cyanosis, edema, jugulovenous, lateral displacement of point of maximal impulse

TYPES OF CHF

Systolic
- Inadequate systolic emptying, reduced ejection fraction, more common

Diastolic
- Inadequate diastolic filling, normal ejection fraction, less common

Right-sided CHF "Blue bloater"
- Renal hypoxia (fluid retention, pitting edema), pleural effusion and ascites, enlarged and congested liver and spleen, neck venous distension
- Lung disease leads to right ventricular failure initially followed by left-sided failure
- Due to left-sided CHF, left-sided lesions (mitral stenosis), pulmonary hypertension, cardiomyopathy and diffuse myocarditis, tricuspid or pulmonary valvular disease

Left-sided CHF "Pink puffer"
- Dyspnea and orthopnea due to pulmonary congestion and edema, pleural effusion with hydrothorax, reduced renal perfusion and therefore water and salt retention, cerebral anoxia
- Caused by ischemic heart disease (i.e. MI), hypertension, aortic and mitral valvular disease, cardiomyopathy, myocarditis

ISCHEMIC HEART DISEASE

- General overview
- Angina pectoris
- Chronic ischemic heart disease
- Myocardial infarction

ISCHEMIC HEART DISEASE

- Damage to the heart occurs due to a reduction in blood flow to tissues
- Reduced coronary blood flow – partial or complete occlusion
- Increased myocardial demand
  - Pregnancy, exercise, hyperthyroidism, infections
- Decreased oxygen in the blood
  - Anemia, carbon monoxide poisoning, congenital right-to-left shunts
- Complications include angina pectoris, myocardial infarction, chronic ischemic heart disease, ischemic stroke, intermittent claudication, sudden cardiac death, thromboembolic disease

ANGINA PECTORIS

- Episodic chest pain due to insufficient oxygen supply to the myocardium
- Pain or discomfort in jaw, back, epigastrium, shoulders, or neck
  - Dyspnea, nausea, or diaphoresis may occur during an attack

Stable
- Severe narrowing of the coronary arteries
- Occurs during exertion and relieved by rest or nitroglycerin

Unstable
- Unpredictable → can occur at rest or sleep
- Nitroglycerin DOES NOT bring relief

Prinzmetal's
- Caused by vasospasm
- Can occur at rest
- Nitroglycerin brings relief

CHRONIC ISCHEMIC HEART DISEASE

- No acute event unless an asymptomatic myocardial infarction occurred earlier
- Slowly proceeds to congestive heart failure
- Small areas of scar tissue are found in the heart as a result of numerous small, subclinical MIs.

MYOCARDIAL INFARCTION (MI)

- Coagulation necrosis of the myocardium due to ischemia

Transmural

- Myocardial necrosis that spans the endocardium to pericardium usually results from an occlusion in the proximal portion of a coronary artery

Subendocardial

- Myocardial necrosis is limited to the inner 1/3 of the heart wall generally a result of a partial coronary occlusion or an occlusion within the heart's vascular tree.

- Sudden crushing chest pain (radiating into neck, jaw, left arm, back, or shoulders), nausea, vomiting, dyspnea, feeling of impending doom, palpitations, cyanosis

Complications:

- Arrthythmias
- Myocardial rupture – within 4-10 days after an MI; can cause blood to enter the pericardial sac, cardiac tamponade, and death.
- Mural thrombosis – a thrombus may form over the infarct and can lead to an embolism
- Ventricular aneurysm (dilation of the ventricle)
- Ruptured papillary muscle

VALVULAR HEART DISEASES

- Aortic stenosis/insufficiency
- Mitral stenosis/insufficiency
- Endocarditis
- Mitral valve prolapse
- Rheumatic heart disease
- Carcinoid heart disease

AORTIC STENOSIS

- Generally congenital but can be a result of rheumatic disease
- Aortic valve becomes calcified that causes outflow to be obstructed leading to left ventricular hypertrophy.
- Most commonly due to calcification of a congenitally bicuspid aortic valve
- Chest pain, syncope, dyspnea on exertion, palpable chest thrill/heave
- Diamond shaped crescendo-decrescendo systolic murmur, which lasts throughout systole
- Best heard in the right upper sternal border

MITRAL STENOSIS

- Narrowing of the mitral valve
- Main cause is Rheumatic fever
- Shortness of breath, fatigue, feet or leg swelling, heart palpitations, dizziness/fainting, chest discomfort
- Complications include pulmonary hypertension and edema, heart failure, cardiac hypertrophy, and atrial fibrillation.

ENDOCARDITIS

- Inflammation of the endocardium
- Most of the damage is done to the valves (vegetations)
- Infective endocarditis due to bacterial and sometimes fungal infection of the endocardium.

Acute

- *Staphylococcus aureus*
- Often secondary to an infection elsewhere
- More virulent organisms

Subacute

- *Streptococcus viridans*
- More common in patients with congenital heart disease or pre-existing valvular heart damage (i.e. rheumatic valvular disease)
- Less virulent organisms

MITRAL VALVE PROLAPSE

- Mitral valve leaflets are enlarged (protrude into the left atrium) and the chordae tendinae are elongated.
- Mid-systolic click and sometimes a late systolic murmur (mitral regurgitation)
- Generally benign and asymptomatic but can result in mitral regurgitation
  - Hyper-sympathetic syndrome, palpitations, orthostatic hypotension, fatigue, chest pain
- More susceptible to **endocarditis**

RHEUMATIC HEART DISEASE

- Sequelae of a Group A beta hemolytic *Streptococcus pyrogens* infection
- Strep Ab cross-react with the heart tissue (type II hypersensitivity reaction)
- Inflammation occurs in all 3 layers:
  - Endocarditis
  - Myocarditis
  - Pericarditis
- Other symptoms include:
  - Aschoff bodies (granulomatous inflammatory lesions), erythema marginatum (trunk/extremities), migratory polyarthritis, fever, subcutaneous nodules, chorea, malaise, elevated ESR

CARCINOID HEART DISEASE

- Carcinoid syndrome occurs when a rare cancerous tumor called a carcinoid tumor secretes certain chemicals, primarily **serotonin**, into the bloodstream.
- **Carcinoid tumors occur most commonly in the gastrointestinal tract or lungs**.
- Fibrotic endocardial plaques can occur which are associated heart valve dysfunction that classically involves the tricuspid valve.
- Initial symptoms include fatigue and dyspnea.
- Skin flushing, excessive diarrhea, right-sided heart disease, and bronchoconstriction.

PRIMARY HEART DISEASE

- Cardiomyopathies
- Myocarditis

CARDIOMYOPATHIES

Dilated/Congestive
- Leads to ventricular dilation and right- & left-sided heart failure
- Most commonly due to chronic death of myocardial cells and lesser due to acute myocardial inflammation
- Fibrosis occurs in the left and right ventricles causing dyspnea on exertion and easy fatiguing.
  - Cough, edema (legs, ankles, feet), or even liver problems can occur which can cause ascites.
- Causes include viral infection, hypothyroidism, toxin exposure, post-partum, thiamine deficiency

Restrictive
- Rigid ventricular walls (primarily the left) which causes decreased output
- Due to diffuse infiltration of hardening substances (ex. iron) or chronic inflammation
- Hypertrophy → fibrosis
- Dyspnea on exertion, edema, orthopnea, arrhythmias

Hypertrophic
- Significant ventricular hypertrophy not due to outflow obstruction such as aortic valve diseases or hypertension
- Anterior leaflet of mitral valve is misplaced
- Congenital, acquired, idiopathic forms
- Syncope and sudden death

MYOCARDITIS

- Inflammation of the myocardium which can lead to chronic health issues and sudden death
- Bacterial infection can follow sepsis which causes neutrophil invasion
- Symptoms include: chest pain, palpitations, fever, CHF, fatigue, systolic murmur, dysnea

- Bacterial (strep, staph, gonococcus, diphtheria)
- Viral (Coxsackie, influenza, echo viruses, parvovirus B19)
- Parasitic (trichinosis, toxoplasmosis)
- Rickettsial (Lyme, Chagas disease, Rocky Mountain spotted fever, typhus)
- Autoimmune (SLE, PSS, sarcoidosis, vasculitis, rheumatic fever)
- Toxic (carbon monoxide, snake venom, iron, copper, arsenic)
- Certain drugs

PERICARDIAL DISEASE

- Metastatic disease
- Pericardial effusions
- Pericarditis

METASTATIC DISEASE

- Neoplastic tumors can spread to the pericardium via retrograde lymphatic extension, direct contiguous extension, hematogenous spread, transvenous extension
  - Lung or breast cancer, lymphoma, melanoma
- Dyspnea, anterior thoracic pain, pleurisy, peripheral edema, cough
- Complications include pericardial effusion and pressure on the heart can lead to CHF or other cardiac functional impairment

PERICARDIAL EFFUSIONS

- Excess fluid within the pericardial space (>30-50 ml)
- Hydropericardium – increased serous transudate in the pericardial space due to system edema
  - CHF, nephrotic syndrome, chronic liver disease
- Hemopericardium – accumulation of blood in the pericardial space (cardiac tamponade)
  - Perforation or myocardial rupture post-MI
  - Cardiac tamponade restricts the filling of the heart and results in arrhythmia and can lead to sudden cardiac death.
- Dyspnea, chest pain, palpitations - symptoms are worse on exertion
- Viral pericardial effusions generally spontaneously resolve without treatment

PERICARDITIS

Inflammation of the pericardial sac which can lead to pericardial fibrosis

- Primary disease is idiopathic
- Secondary disease due to rheumatic fever, infections, or drugs.

Symptoms include: dyspnea, palpitations, chest pain – symptoms are worse on exertion

- More serious cases or infections can cause fever, myalgia, fatigue, athralgia

Risk factors include medications, autoimmune disease, cancer, systemic viral infections, chronic heart and lung disease

Complications:

- Fibrinous pericarditis can progress to constrictive pericarditis
- CHF
- Cardiac tamponade

Fibrinous

- Iatrogenic or autoimmune
- Adhesions restrict heart activity causing a loud friction rub

Serous

- Non-infectious and heart function is not impaired by fluid levels

Suppurative

- Infectious and can spread. Adhesions with cardiac hypertrophy and signs of heart failure

Hemorrhagic

- Trauma, tuberculosis, cancer
- Results in acute death or constrictive pericarditis

Constrictive

- Involves scarring and calcification and results from the above forms and other trauma.
- Heart cannot not expand and constriction of the vena cavas can heart right heart failure symptoms

CONGENITAL HEART DISEASE

- Bicuspid aortic valve
- Patent ductus arteriosus
- Septal defects
- Tetralogy of Fallot

BICUSPID AORTIC VALVE

- Most common malformation of the aortic valve
- Generally asymptomatic
- Can cause aortic stenosis resulting in a systolic murmur
- Can lead to heart failure due to this outflow obstruction

PATENT DUCTUS ARTERIOSUS

- Ductus arteriosus fails to close after birth.
- Results in a portion of oxygenated blood to flow back to the lungs
- Early presentation includes laboured breathing and poor weight gain
- Tachycardia, dyspnea, "machine-like" heart murmur, cardiomegaly, widened pulse pressure, cyanosis of the lower extremities
- If left untreated it can lead to congestive heart failure

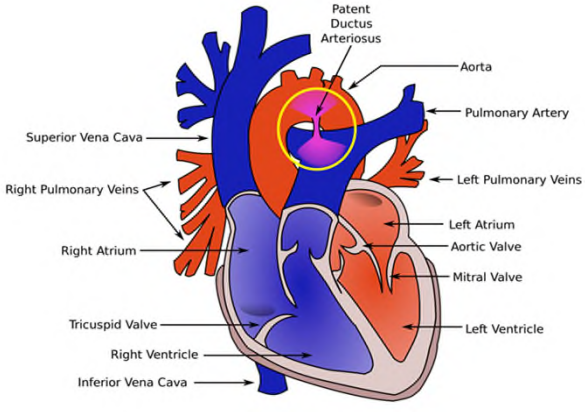

Image: Wikimedia Commons – Author: BrownCow

SEPTAL DEFECTS

- Most often in the membranous region of the ventricular septum
- Ventricular Septal Defect
  - Opening in the wall between the right and left ventricles due to incomplete closure of the membranous septum
  - Can lead to pulmonary hypertension and eventual right-sided heart failure, cyanosis
- Atrial Septal Defect
  - Patent foramen ovale

TETRALOGY OF FALLOT

Four congenital defects found together:

- Ventricular septal defect
- Pulmonary stenosis
- Overriding aorta
- Hypertrophy of the right ventricle

- Cyanosis at birth, tendency to squat to reduce right to left shunting

HEMODYNAMIC CONDITIONS

- Embolism
- Hemorrhage
- Infarction
- Edema
- Shock
- Thrombosis

EMBOLISM

- Embolism = undissolved substance in the blood that doesn't belong there
- Obstructs the flow of blood causing ichemia, infarction, and necrosis.
- Piece of thrombus has broken off and entered the blood stream and becomes trapped somewhere else (thromboembolism)
- Symptoms include acute pain, sudden collapse, MI, stroke, pulmonary embolism but some can be asymptomatic.
- Sudden death can occur

HEMORRHAGE

- Blood leaves the vessels and enters tissue space or out of the body

Acute
- Sudden, massive escape of blood

Chronic
- Low-grade, mild leaking

- Causes include platelet deficiencies or inhibition, vitamin C deficiency, blood thinners, trauma, etc.
- Complications include hemorrhagic shock (>15% blood loss) eventually causes death and chronic blood loss can cause iron deficiency

INFARCTION

- Obstruction of blood supply (ischemia) resulting in localized necrosis
- Anemic
  - Areas with no collateral blood supply
  - Kidney, heart, spleen
- Hemorrhagic
  - Collateral blood supply to be insufficient
  - Gastrointestinal, lung

EDEMA

- Accumulation of an excessive amount of fluid in the cells or tissue space.
- Caused by increased hydrostatic pressure, increased capillary permeability, increased sodium retention, decreased oncotic pressure, lymph obstruction

Exudate

- Fluid with high protein content, often contains inflammatory cell
  - Serous – no inflammatory cells
  - Fibrinous – large amount of fibrin
  - Purulent – large amount of cellular debris
  - Suppurative – purulent exudate accompanied by significant liquefaction necrosis

Transudate

- Low protein contain, imbalance in Starling's forces, generally not associated with inflammation
  - Ascites – fluid accumulation in the abdominal cavity
  - Pleural effusion – fluid accumulation in the pleural cavity
  - Edema – lymphatic obstruction

SHOCK

- Insufficient blood flow to vital organs
- Hemorrhagic, distributive, obstruction, cardiogenic
- Causes include decreased cardiac output due to hemorrhage or severe liver failure, widespread peripheral vasodilation due to sepsis or severe trauma

Types

- Hypovolumic – burns, trauma, diarrhea, vomiting
- Cardiogenic – most commonly due to MI, liver failure
- Septic – most commonly due to Gram –ve infections → endotoxemia → peripheral vasodilation and injury to vessels
- Neurogenic due to severe trauma resulting in peripheral vasodilation

Stages

Compensated/early/non-progressive shock

- Increased heart rate, respiratory rate, and peripheral resistance

Decompensated/progressive shock

- Vessel musculature fails, vasodilation occurs, and less blood gets to the heart causing hypotension
- Cells are injured and die due to lack of oxygen

Irreversible

- 1st acute tubular necrosis occurs in the kidney then full renal failure occurs.
- Severe metabolic acidosis, coma, heart failure

THROMBOSIS

Virchow triad

- Endothelial injury
- Abnormal blood flow
- Hypercoagulability

- Thrombi (clotted blood) are initiated by damage to endothelial cells
- Venous or arterial thrombi can become loose and cause embolisms
- Arterial thrombi can narrow the lumen of vessels causing ischemia
- Venous stasis or partially obstructed vessels are risk factors
  - Cardiac failure, prolonged bed rest, pregnancy, varicose veins
- Thrombophlebitis – acute inflammation of the vein
- Phlebothrombosis – no inflammation

VASCULAR CONDITIONS

- Aneurysms
- Aortic dissection
- Arteriosclerosis, atherosclerosis
- Familial hypercholesterolemia
- Giant cell arteritis (temporal arteritis)
- Peripheral vascular disease
- Pulmonary embolism
- Raynaud's syndrome
- Thromboangiitis obliterans (Buerger's disease)
- Deep vein thrombosis
- Varicose veins
- Vasculitis

ANEURYSMS

- Occur in arteries that have weakness or thinness their wall which causes an expansion
- Can rupture and cause hemorrhage and damage.
- Saccular – asymmetrical, spherical bulge in the side of a vessel
- Fusiform – symmetrical expansion
- Generally asymptomatic but symptoms can include: dizziness, hypotension, severe headache, back pain, pulsatile mass, abdominal pain
- Copper deficiency is a risk factor
- Secondary atherosclerosis, vasculitis, smoking, can be congenital

AORTIC DISSECTION

- Arch of the aorta or descending thoracic aorta
- Tearing of the intima (longitudinal intraluminal tear)
- Acute < 2 weeks
- Chronic > 2 weeks
- Tearing pain in the chest or interscapular region, neck, and/or jaw pain, syncope, abdominal pain, hypotension, paresthesia
- Associated with connective tissue disease, atherosclerosis, and hypertension

ARTERIOSCLEROSIS, ATHEROSCLEROSIS

Arteriosclerosis = thickening and loss of elasticity of arterial walls.

Atherosclerosis

- Involves the large elastic arteries
  - Thrombi, emboli, ischemia, infarction, hemorrhaga, aneurysm
- Most commonly the aorta, coronary, common iliac, femoral, popliteal, internal carotid and cerebral arteries

Most widely accepted etiology:

- Damage to the vascular endothelium disturbs blood flow causing fibrous plaques/atheromas.
- Simple plaques coalesce into larger plaques.
- Ridges are formed and they begin to crack and fissure resulting in a complicated plaque.
- Thrombi form over the cracks and fissures which can break off and form emboli.

FAMILIAL HYPERCHOLESTEROLEMIA

- **Autosomal dominant** genetic disorder (LDLR gene on chromosome 19)
- **Partial or complete absence of LDL receptors**
  - Leads to reduced or absent hepatic clearance, hypercholesterolemia, premature atherosclerosis
- Generally asymptomatic but signs can include xanthelasma palpebrarum, tendinous xanthomatosis, and arcus senilis corneae
- Coronary and peripheral artery disease are complications.

GIANT CELL ARTERITIS

- AKA **temporal arteritis**
- Granulomas are formed in the small to medium-sized arteries of the head
  - Branches of the carotid especially the temporal artery
- Tenderness and nodules over the artery, temporary vision loss, headache, polymyalgia rheumatica, facial pain, increased ESR

PERIPHERAL VASCULAR DISEASE (PAD)

Arterial

- Intermittent claudication (pain with walking), peripheral pulses may be obscured
- Complications include thromboembolism and death

Venous

- Chronic dull aching in legs, dusky colouration, stasis ulcers, loss of hair, dependent leg edema, lichenification, pulses are intact
- Complications include thrombophlebitis and ulceration

PULMONARY EMBOLISM

- Acute – occlusion of the vessel
- Chronic - > 50% diameter reduction
- Hypoxemia, hyperventilation, and tissue damage result.

RAYNAUD'S SYNDROME

- **Vasospasms** in the **arterioles** of the extremities
  - Triggered by cold and emotional stress
  - Fingers and toes turn white, blue, then pink (**Tricolour change**)

Raynaud's disease
- No underlying disease, recurrent vasospasm of small arteries and arterioles

Raynaud's phenomenon
- Secondary to a disorder - often autoimmune diseases
  - SLE, scleroderma, atherosclerosis, Buerger's disease

- Ulceration and gangrene can occur.

THROMBOANGIITIS OBLITERANS

- Inflammatory disease of the small- to medium-sized arteries and veins of the extremities
- Causes ischemia and pain
- Nodular phlebitis, gangrene, distal claudication, and necrosis can occur.
- **Smoking is a major risk factor**

DEEP VEIN THROMBOSIS (DVT)

- Thrombophlebitis – acute inflamamtion
- Phlebothrombosis – no inflammation

- Most commonly found in the **deep veins of the leg**
- Causes swelling, redness, pain, warmth in the affected extremity
- Emboli can result that travel to the lungs and cause a pulmonary infarction

- Risk factors include smoking, prolonged bed rest, recent pregnancy, fractures, estrogen containing birth control pill, obesity, polycythemia

VARICOSE VEINS

- Tortuous, dilated veins
- Most commonly affects the superficial veins of the lower extremity
- Caused by increased venous pressure and/or valve failure
  - Pregnancy, obesity, thrombophlebitis, prolonged standing

VASCULITIS

- **Autoimmune attack and inflammation of blood vessels**
- Fever, fatigue, weight loss, lethargy, weakness, multi-organ dysfunction

Large vessel disease – symmetric hypertension, absent pulses, claudication, bruits, shoulder/hip arthralgia, visual disturbances
- Giant cell arteritis
- Takayasu's arteritis

Medium vessel disease – skin nodules and ulcers, digital gangrene, hypertension, oligoarthritis, myalgia, athralgia, microaneurysms, livedo reticularis
- Polyarteritis nodosa
- Kawasaki's disease

Small vessel disease – splinter hemorrhages, uveitis, urticaria, purpura, neuropathy, glomerulonephritis, vestibular lesions, ischemic bowel
- Wegener's granulomatosis
- Henoch-Schonlein purpura
- Churg-Strauss syndrome

VASCULAR NEOPLASMS

- Hemangiomas
- Kaposi's sarcoma

HEMANGIOMAS

- Benign tumors made of hyperplastic blood vessels
- Lesions can be flat or raised and are red or purple in colour
- Do not become enlarged
- Can cause issues if inside organs because they can rupture, compress structures, disrupting normal blood flow

Capillary hemangioma – tangle of loosely packed capillary-like channels
- Skin, subcutaneous tissue, spleen, liver, or kidneys

Cavernous hemangioma – large cavernous vascular spaces in skin, mucosal surfaces, spleen, liver, kidney, or brain.
- Associated with Hippel-Landau disease which results in large hemangiomas of the brain/eye and internal organs.

KAPOSI'S SARCOMA

- **Malignant** tumor of lympathic epithelium
- Causes vascular channels within the lymphatics that cause them to fill with blood
- Reddish-purple to dark-blue cutaneous macules, nodules, or plaques
- Result of a **herpes virus-8 infection**
- **Immunocompromised** are at risk of developing these tumors
- High mortality rate in transplant and AIDS patients

INFECTIOUS VASCULAR DISEASES

- Bacterial endocarditis
- Chagas disease
- Lyme disease
- Rocky Mountain Spotted Fever
- Viral hemorrhagic fever
- Viral myocarditis

BACTERIAL ENDOCARDITIS

- See endocarditis slide

CHAGAS DISEASE

- ***Trypanomasoma cruzi*** infection via triatomine bugs
  - Infected bugs deposit feces containing trypomastigotes on the skin while biting
  - Invade macrophages and turn into amastigotes and multiply.
  - Trypomastigotes are released into the tissue and blood and infect myocardial, muscle, reticuloendothelial, and nervous system cells.
- Generally asymptomatic initially
- Fever, lymphadenopathy, hepatomegaly, acute myocarditis, meningoencephalitis, malaise occur 1-2 weeks later (acute phase)
- Complications include cardiomyopathy, heart failure, apical aneurysms, thromboembolism, megacolon, megaesophagus

LYME DISEASE

- Infection with ***Borrelia burgdorferi*** via ticks
  - **Spirochete** that can be visualized with dark field microscopy or Giemsa stain
- Serological testing of IgM or IgG Ab to the spirochete

Stages

- 1st (3-32 days after tick bite)
  - Spreading circular red rash with a white center (erythema migrans)
  - Flu-like symptoms and lympadenopathy
- 2nd (months after primary lesion)
  - Cardiovascular and neurological symptoms
  - Bell's palsy, peripheral neuropathy, heart block
- Final
  - Large joint arthritis (knee), other systemic symptoms

ROCKY MOUNTAIN SPOTTED FEVER

- ***Rickettsia rickettsii*** infection via *Dermacentor* ticks
- Widespread vasculitis that affects the coronary vessels
- Flu-like illness, petechiae, GI pain, myalgias, arthralgias, purpural rash (starts on limbs and moves to the trunk)
- Severe cases can result in edema, DIC, circulatory collapse
- Lethal without antibiotics

VIRAL HEMORRHAGIC FEVER

- Viruses trigger widespread **vascular damage** leading to multi-organ damage or failure.
- **Enveloped RNA viruses**

Dengue fever

- Transmitted by *A. aegypti* mosquito
- Influenza-like symptoms initially then severe pain in joints and muscles, maculopapular rash, leukopenia, and lymphadenopathy
- Dengue hemorrhagic fever results in shock and hemorrhaging that can be fatal.

Hantavirus pulmonary syndrome

- Spread via rodents
- Fever, dyspnea, cough, diarrhea, respiratory distress and failure, lympocytosis, fatigue, thrombocytopenia
- Renal failure and/or pulmonary hemorrhage and other areas of hemorrhage

VIRAL MYOCARDITIS

- See myocarditis slide

KEY POINTS

- Embryonic changes to the heart
- Major branches of the coronary arteries/veins
- Major branches off the aorta
- Where vessels change their names (i.e. femoral → popliteal)
- Steps of the cardiac cycle including heart sounds
- Cardiac muscle contraction process
- Difference between cardiac and skeletal muscle contraction
- Valvular dysfunctions – diastolic vs systolic
- Rate-limiting enzymes and their cofactors
- Lipoproteins

PRACTICE QUESTIONS

1. What is the source of the left anterior descending coronary artery?
   A. Aortic sinus
   B. Circumflex artery
   C. Left coronary artery
   D. Right coronary artery

2. 4-week-old male with a ventricular septal defect develops infective endocarditis and experiences fever, septic emboli within his lungs. Which pathogenic bacteria is most likely the cause of his sepsis?
   A. Streptococcus viridans
   B. Staphylococcus aureus
   C. Haemophilus influenzae
   D. Staphylococcus epidermis

ANSWERS

- 1. C – Left coronary artery divides into the left anterior descending artery and the circumflex branch.
  - The aortic sinus is a dilation of the ascending aorta located above the aortic valve.
  - The right coronary artery branches into the posterior descending artery and the right marginal artery.

- 2. A – Streptococcus viridans is more common in patients with congential heart disease such as ventricular septal defect.
  - Endocarditis due to *Staphylococcus aureus* infection is often secondary to an infection elsewhere.
  - Haemophilus influenzae and Staphylococus epidermis are not implicated in endocarditis.

IN THE NEXT SECTION…

- **Section 3: Endocrine System**