

SECTION III

High-Yield Organ Systems

“Symptoms, then, are in reality nothing but the cry from suffering organs.”
—Jean-Martin Charcot

“Man is an intelligence in servitude to his organs.”
—Aldous Huxley

“When every part of the machine is correctly adjusted and in perfect harmony, health will hold dominion over the human organism by laws as natural and immutable as the laws of gravity.”

—Andrew T. Still

► Approaching the Organ Systems	280
► Cardiovascular	283
► Endocrine	329
► Gastrointestinal	363
► Hematology and Oncology	409
► Musculoskeletal, Skin, and Connective Tissue	449
► Neurology and Special Senses	499
► Psychiatry	571
► Renal	597
► Reproductive	631
► Respiratory	679

► APPROACHING THE ORGAN SYSTEMS

In this section, we have divided the High-Yield Facts into the major **Organ Systems**. Within each Organ System are several subsections, including **Embryology**, **Anatomy**, **Physiology**, **Pathology**, and **Pharmacology**. As you progress through each Organ System, refer back to information in the previous subsections to organize these basic science subsections into a “vertically integrated” framework for learning. Below is some general advice for studying the organ systems by these subsections.

Embryology

Relevant embryology is included in each organ system subsection. Embryology tends to correspond well with the relevant anatomy, especially with regard to congenital malformations.

Anatomy

Several topics fall under this heading, including gross anatomy, histology, and neuroanatomy. Do not memorize all the small details; however, do not ignore anatomy altogether. Review what you have already learned and what you wish you had learned. Many questions require two or more steps. The first step is to identify a structure on anatomic cross section, electron micrograph, or photomicrograph. The second step may require an understanding of the clinical significance of the structure.

While studying, emphasize clinically relevant material. For example, be familiar with gross anatomy and radiologic anatomy related to specific diseases (eg, Pancoast tumor, Horner syndrome), traumatic injuries (eg, fractures, sensory and motor nerve deficits), procedures (eg, lumbar puncture), and common surgeries (eg, cholecystectomy). There are also many questions on the exam involving x-rays, CT scans, and neuro MRI scans. Many students suggest browsing through a general radiology atlas, pathology atlas, and histology atlas. Focus on learning basic anatomy at key levels in the body (eg, sagittal brain MRI; axial CT of the midthorax, abdomen, and pelvis). Basic neuroanatomy (especially pathways, blood supply, and functional anatomy), associated neuropathology, and neurophysiology have good yield. Please note that many of the photographic images in this book are for illustrative purposes and are not necessarily reflective of Step 1 emphasis.

Physiology

The portion of the examination dealing with physiology is broad and concept oriented and thus does not lend itself as well to fact-based review. Diagrams are often the best study aids, especially given the increasing number of questions requiring the interpretation of diagrams. Learn to apply basic physiologic relationships in a variety of ways (eg, the Fick equation, clearance equations). You are seldom asked to perform complex calculations. Hormones

are the focus of many questions; learn where and how they are synthesized, their regulatory mechanisms and sites of action.

A large portion of the physiology tested on the USMLE Step 1 is clinically relevant and involves understanding physiologic changes associated with pathologic processes (eg, changes in pulmonary function with COPD). Thus, it is worthwhile to review the physiologic changes that are found with common pathologies of the major organ systems (eg, heart, lungs, kidneys, GI tract) and endocrine glands.

Pathology

Questions dealing with this discipline are difficult to prepare for because of the sheer volume of material involved. Review the basic principles and hallmark characteristics of the key diseases. Given the clinical orientation of Step 1, it is no longer sufficient to know only the “buzzword” associations of certain diseases (eg, café-au-lait macules and neurofibromatosis); you must also recognize the clinical descriptions of these high-yield physical exam findings.

Given the clinical slant of the USMLE Step 1, it is also important to review the classic presenting signs and symptoms of diseases as well as their associated laboratory findings. Delve into the signs, symptoms, and pathophysiology of major diseases that have a high prevalence in the United States (eg, alcohol use disorder, diabetes, hypertension, heart failure, ischemic heart disease, infectious disease). Be prepared to think one step beyond the simple diagnosis to treatment or complications.

The examination includes a number of color photomicrographs and photographs of gross specimens that are presented in the setting of a brief clinical history. However, read the question and the choices carefully before looking at the illustration, because the history will help you identify the pathologic process. Flip through an illustrated pathology textbook, color atlases, and appropriate Web sites in order to look at the pictures in the days before the exam. Pay attention to potential clues such as age, sex, ethnicity, occupation, recent activities and exposures, and specialized lab tests.

Pharmacology

Preparation for questions on pharmacology is straightforward. Learning all the key drugs and their characteristics (eg, mechanisms, clinical use, and important adverse effects) is high yield. Focus on understanding the prototype drugs in each class. Avoid memorizing obscure derivatives. Learn the “classic” and distinguishing toxicities of the major drugs. Do not bother with drug dosages or brand names. Reviewing associated biochemistry, physiology, and microbiology can be useful while studying pharmacology. There is a strong emphasis on ANS, CNS, antimicrobial, and cardiovascular agents as well as NSAIDs. Much of the material is clinically relevant. Newer drugs on the market are also fair game.

Cardiovascular

“As for me, except for an occasional heart attack, I feel as young as I ever did.”

—Robert Benchley

“Hearts will never be practical until they are made unbreakable.”

—*The Wizard of Oz*

“As the arteries grow hard, the heart grows soft.”

—H. L. Mencken

“Nobody has ever measured, not even poets, how much the heart can hold.”

—Zelda Fitzgerald

“The art of medicine has its roots in the heart.”

—Paracelsus

“It is not the size of the man but the size of his heart that matters.”

—Evander Holyfield

The cardiovascular system is one of the highest yield areas for the boards and, for some students, may be the most challenging. Focusing on understanding the mechanisms instead of memorizing the details can make a big difference. Pathophysiology of atherosclerosis and heart failure, mechanism of action of drugs (particularly, physiology interactions) and their adverse effects, ECGs of heart blocks, the cardiac cycle, and the Starling curve are some of the more high-yield topics. Differentiating between systolic and diastolic dysfunction is also very important. Heart murmurs and maneuvers that affect these murmurs have also been high yield and may be asked in a multimedia format.

► Embryology	284
► Anatomy	288
► Physiology	289
► Pathology	302
► Pharmacology	321

► CARDIOVASCULAR—EMBRYOLOGY

Heart morphogenesis First functional organ in vertebrate embryos; beats spontaneously by week 4 of development.

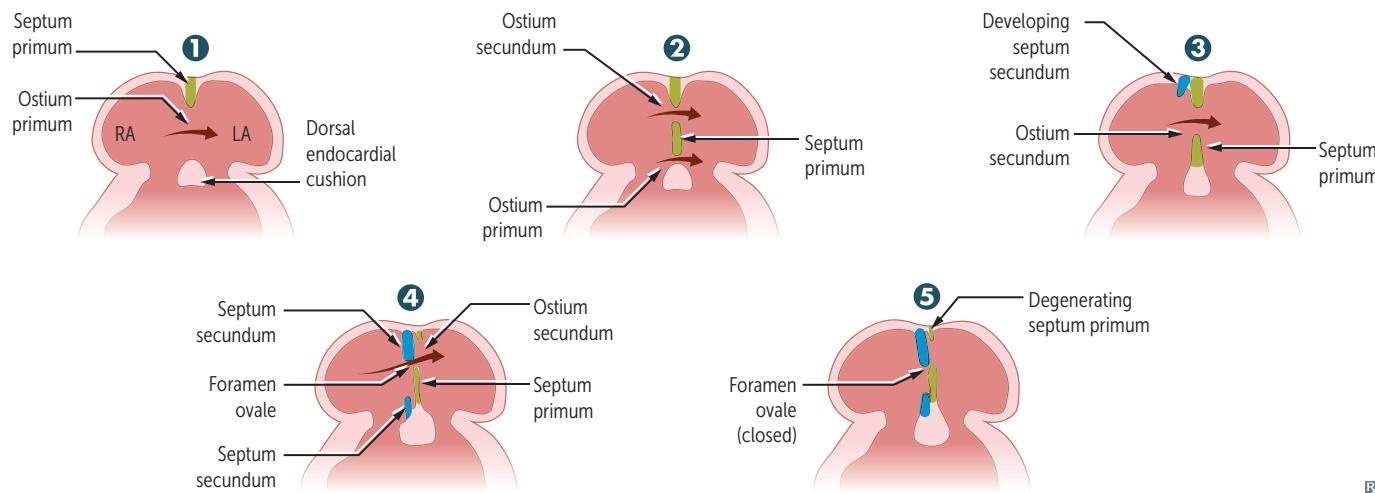
Cardiac looping	Primary heart tube loops to establish left-right polarity; begins in week 4 of development.	Defect in left-right dynein (involved in left-right asymmetry) can lead to dextrocardia, as seen in Kartagener syndrome.
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Septation of the chambers**Atria**

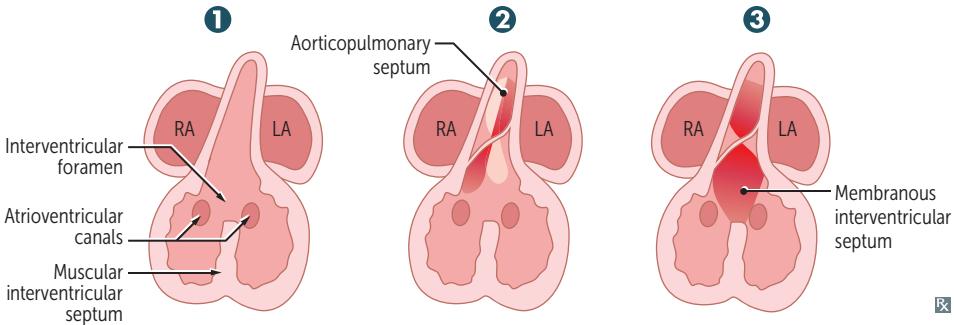
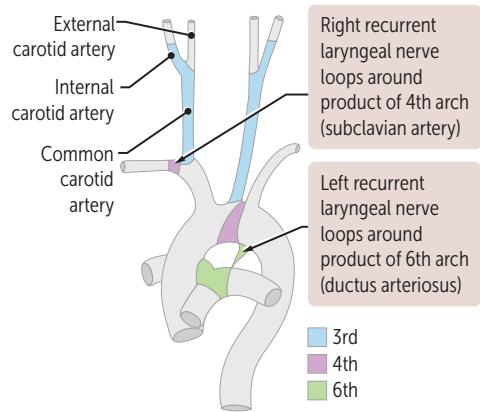
- ① Septum primum grows toward endocardial cushions, narrowing ostium primum.
- ② Ostium secundum forms in septum primum due to cell death (ostium primum regresses).
- ③ Septum secundum develops on the right side of septum primum, as ostium secundum maintains right-to-left shunt.
- ④ Septum secundum expands and covers most of ostium secundum. The residual foramen is the foramen ovale.
- ⑤ Remaining portion of septum primum forms the one-way valve of the foramen ovale.

6. Septum primum closes against septum secundum, sealing the foramen ovale soon after birth because of ↑ LA pressure and ↓ RA pressure.
7. Septum secundum and septum primum fuse during infancy/early childhood, forming the atrial septum.

Patent foramen ovale—caused by failure of septum primum and septum secundum to fuse after birth; most are left untreated. Can lead to paradoxical emboli (venous thromboemboli entering the systemic arterial circulation through right-to-left shunt) as can occur in atrial septal defect (ASD).



Heart morphogenesis (continued)

Ventricles	<p>1 Muscular interventricular septum forms. Opening is called interventricular foramen.</p> <p>2 Aorticopulmonary septum rotates and fuses with muscular ventricular septum to form membranous interventricular septum, closing interventricular foramen.</p> <p>3 Growth of endocardial cushions separates atria from ventricles and contributes to both atrial septation and membranous portion of the interventricular septum.</p>	Ventricular septal defect —most common congenital cardiac anomaly, usually occurs in membranous septum.
		
Outflow tract formation	Neural crest cell migrations → truncal and bulbar ridges that spiral and fuse to form aorticopulmonary septum → ascending aorta and pulmonary trunk.	Conotruncal abnormalities associated with failure of neural crest cells to migrate: <ul style="list-style-type: none"> Transposition of great arteries. Tetralogy of Fallot. Persistent truncus arteriosus.
Valve development	Aortic/pulmonary: derived from endocardial cushions of outflow tract. Mitral/tricuspid: derived from fused endocardial cushions of the AV canal.	Valvular anomalies may be stenotic, regurgitant, atretic (eg, tricuspid atresia), or displaced (eg, Ebstein anomaly).
Aortic arch derivatives	Develop into arterial system.	
1st	Part of maxillary artery (branch of external carotid). 1st arch is maximal .	
2nd	Stapedial artery and hyoid artery . Second = stapedial .	
3rd	Common carotid artery and proximal part of internal carotid artery . C is 3rd letter of alphabet.	
4th	On left, aortic arch; on right, proximal part of right subclavian artery. 4th arch (4 limbs) = systemic.	
6th	Proximal part of pulmonary arteries and (on left only) ductus arteriosus . 6th arch = pulmonary and the pulmonary-to-systemic shunt (ductus arteriosus).	

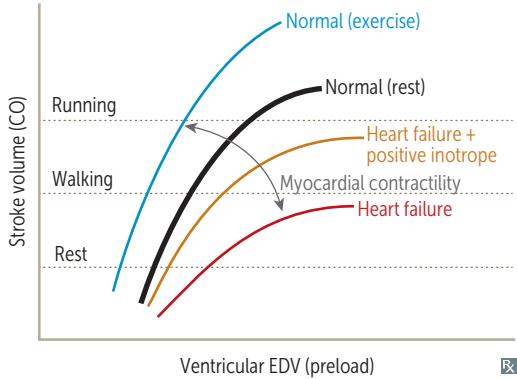
► CARDIOVASCULAR—PHYSIOLOGY

Cardiac output variables

Stroke volume	Stroke Volume affected by Contractility, Afterload, and Preload. ↑ SV with: <ul style="list-style-type: none">■ ↑ Contractility (eg, anxiety, exercise)■ ↑ Preload (eg, early pregnancy)■ ↓ Afterload	SV CAP. Stroke work (SW) is work done by ventricle to eject SV. $SW \propto SV \times MAP$ A failing heart has ↓ SV (systolic and/or diastolic dysfunction).
Contractility	Contractility (and SV) ↑ with: <ul style="list-style-type: none">■ Catecholamine stimulation via β_1 receptor:<ul style="list-style-type: none">■ Activated protein kinase A<ul style="list-style-type: none">→ phospholamban phosphorylation→ active Ca^{2+} ATPase \rightarrow ↑ Ca^{2+} storage in sarcoplasmic reticulum■ Activated protein kinase A \rightarrow Ca^{2+} channel phosphorylation \rightarrow ↑ Ca^{2+} entry \rightarrow ↑ Ca^{2+}-induced Ca^{2+} release■ ↑ intracellular Ca^{2+}■ ↓ extracellular Na^+ (↓ activity of Na^+/Ca^{2+} exchanger)■ Digoxin (blocks Na^+/K^+ pump<ul style="list-style-type: none">→ ↑ intracellular Na^+ \rightarrow ↓ Na^+/Ca^{2+} exchanger activity \rightarrow ↑ intracellular Ca^{2+})	Contractility (and SV) ↓ with: <ul style="list-style-type: none">■ β_1-blockade (↓ cAMP)■ Heart failure (HF) with systolic dysfunction■ Acidosis■ Hypoxia/hypercapnia (↓ Po_2/↑ Pco_2)■ Nondihydropyridine Ca^{2+} channel blockers
Preload	Preload approximated by ventricular end-diastolic volume (EDV); depends on venous tone and circulating blood volume.	Venous vasodilators (eg, nitroglycerin) ↓ preload.
Afterload	Afterload approximated by MAP. ↑ wall tension per Laplace's law \rightarrow ↑ pressure \rightarrow ↑ afterload. LV compensates for ↑ afterload by thickening (hypertrophy) in order to ↓ f_f	

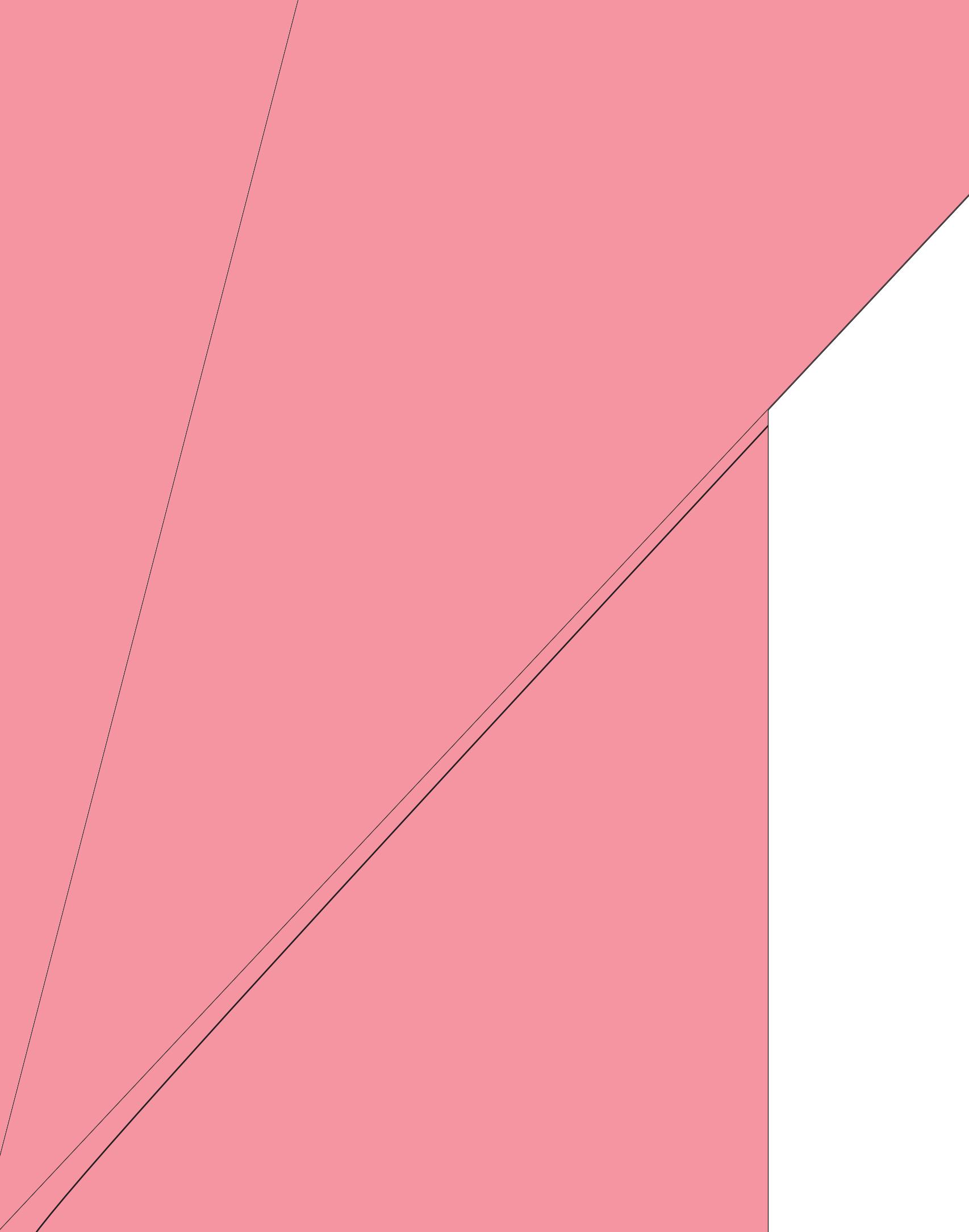
Cardiac output equations

	EQUATION	NOTES
Stroke volume	$SV = EDV - ESV$	$ESV = \text{end-systolic volume}$.
Ejection fraction	$EF = \frac{SV}{EDV} = \frac{EDV - ESV}{EDV}$	EF is an index of ventricular contractility (\downarrow in systolic HF; usually normal in diastolic HF).
Cardiac output	$CO = \dot{Q} = SV \times HR$ Fick principle: $CO = \frac{\text{rate of O}_2 \text{ consumption}}{(\text{arterial O}_2 \text{ content} - \text{venous O}_2 \text{ content})}$	In early stages of exercise, CO maintained by \uparrow HR and \uparrow SV. In later stages, CO maintained by \uparrow HR only (SV plateaus). Diastole is shortened with $\uparrow\uparrow$ HR (eg, ventricular tachycardia) $\rightarrow \downarrow$ diastolic filling time $\rightarrow \downarrow$ SV $\rightarrow \downarrow$ CO.
Pulse pressure	$PP = \text{systolic blood pressure (SBP)} - \text{diastolic blood pressure (DBP)}$	PP directly proportional to SV and inversely proportional to arterial compliance. \uparrow PP in aortic regurgitation, aortic stiffening (isolated systolic hypertension in older adults), obstructive sleep apnea (\uparrow sympathetic tone), high-output state (eg, anemia, hyperthyroidism), exercise (transient). \downarrow PP in aortic stenosis, cardiogenic shock, cardiac tamponade, advanced HF.
Mean arterial pressure	$MAP = CO \times \text{total peripheral resistance (TPR)}$	MAP (at resting HR) = $2/3 DBP + 1/3 SBP = DBP + 1/3 PP$.

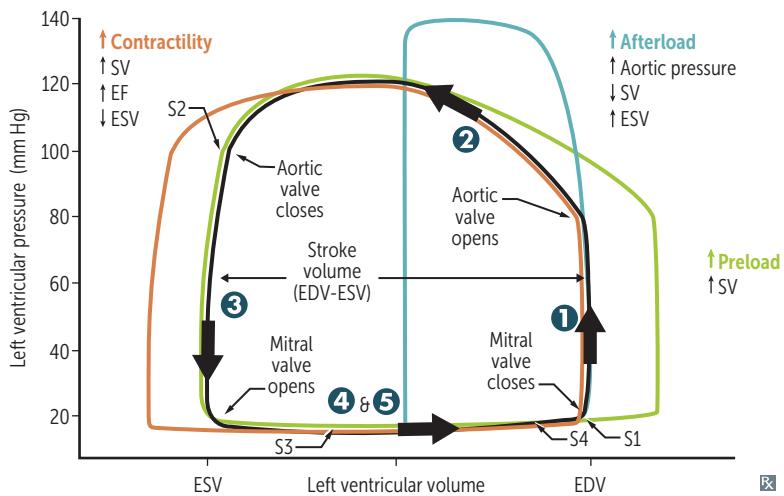
Starling curves

Force of contraction is proportional to end-diastolic length of cardiac muscle fiber (preload).

- \uparrow contractility with catecholamines, positive inotropes (eg, dobutamine, milrinone, digoxin).
- \downarrow contractility with loss of functional myocardium (eg, MI), β -blockers (acutely), nondihydropyridine Ca^{2+} channel blockers, HF.



Pressure-volume loops and cardiac cycle



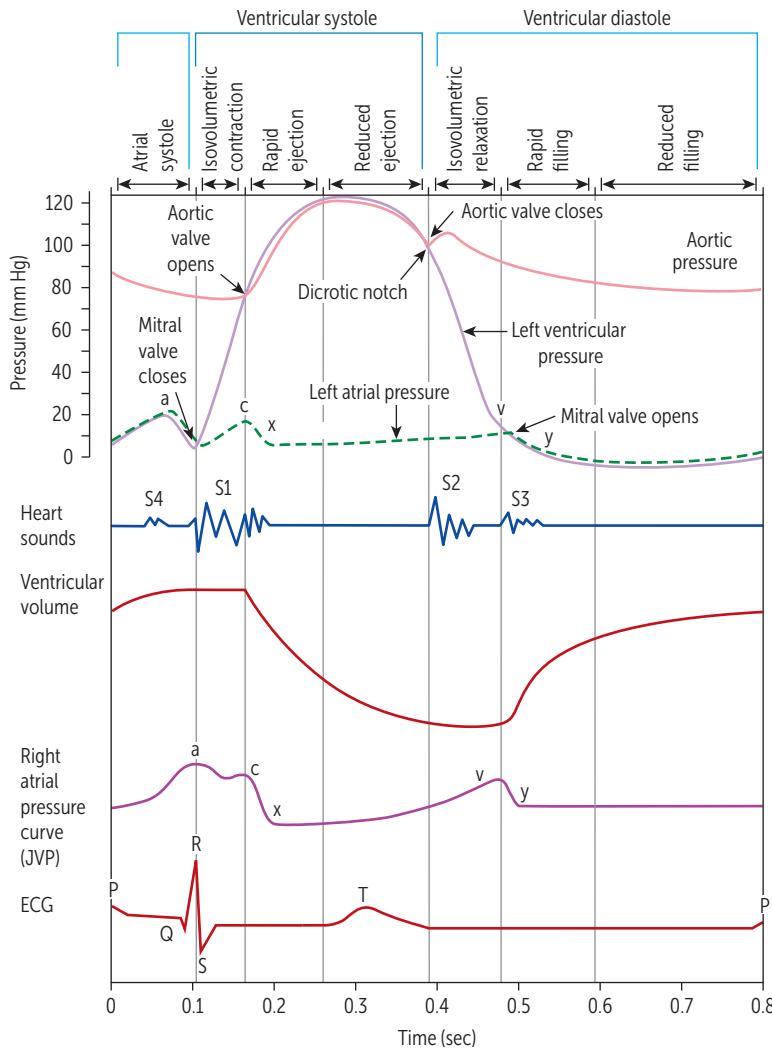
The black loop represents normal cardiac physiology.

Phases—left ventricle:

- ① Isovolumetric contraction—period between mitral valve closing and aortic valve opening; period of highest O₂ consumption
- ② Systolic ejection—period between aortic valve opening and closing
- ③ Isovolumetric relaxation—period between aortic valve closing and mitral valve opening
- ④ Rapid filling—period just after mitral valve opening
- ⑤ Reduced filling—period just before mitral valve closing

Heart sounds:

- S1—mitral and tricuspid valve closure. Loudest at mitral area.
S2—aortic and pulmonary valve closure. Loudest at left upper sternal border.
S3—in early diastole during rapid ventricular filling phase. Best heard at apex with patient in left lateral decubitus position. Associated with ↑ filling pressures (eg, MR, AR, HF, thyrotoxicosis) and more common in dilated ventricles (but can be normal in children, young adults, athletes, and pregnancy). Turbulence caused by blood from LA mixing with ↑ ESV.
S4—in late diastole (“atrial kick”). Turbulence caused by blood entering stiffened LV. Best heard at apex with patient in left lateral decubitus position. High atrial pressure. Associated with ventricular noncompliance (eg, hypertrophy). Considered abnormal if palpable. Common in older adults.

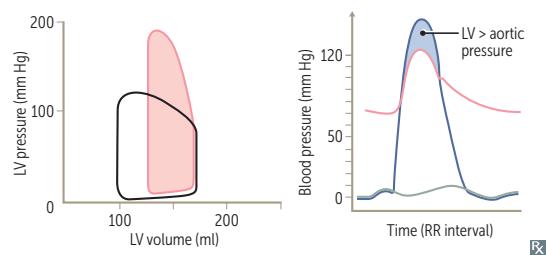


Jugular venous pulse (JVP):

- a wave—atrial contraction. Prominent in AV dissociation (cannon a wave), absent in atrial fibrillation.
- c wave—RV contraction (closed tricuspid valve bulging into atrium).
- x descent—atrial relaxation and downward displacement of closed tricuspid valve during rapid ventricular ejection phase. Reduced or absent in tricuspid regurgitation and right HF because pressure gradients are reduced.
- v wave—↑ RA pressure due to ↑ volume against closed tricuspid valve.
- y descent—RA emptying into RV. Prominent in constrictive pericarditis, absent in cardiac tamponade.

Pressure-volume loops and valvular disease

Aortic stenosis



↑ LV pressure

↑ ESV

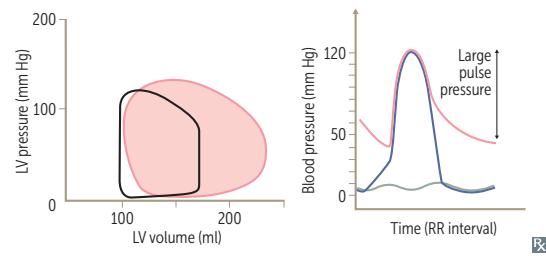
No change in EDV (if mild)

↓ SV

Ventricular hypertrophy → ↓ ventricular compliance → ↑ EDP for given EDV



Aortic regurgitation



No true isovolumetric phase

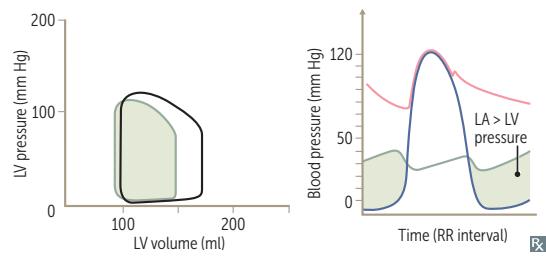
↑ EDV

↑ SV

Loss of dicrotic notch



Mitral stenosis



↑ LA pressure

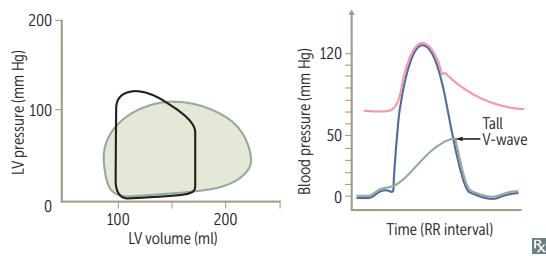
↓ EDV because of impaired ventricular filling

↓ ESV

↓ SV



Mitral regurgitation



No true isovolumetric phase

↓ ESV due to ↓ resistance and

↑ regurgitation into LA during systole

↑ EDV due to ↑ LA volume/pressure from regurgitation → ↑ ventricular filling

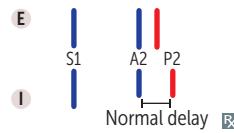
↑ SV (forward flow into systemic circulation plus backflow into LA)



Splitting of S2

Physiologic splitting

Inspiration → drop in intrathoracic pressure
 → ↑ venous return → ↑ RV filling → ↑ RV stroke volume → ↑ RV ejection time
 → delayed closure of pulmonic valve.
 ↓ pulmonary impedance (↑ capacity of the pulmonary circulation) also occurs during inspiration, which contributes to delayed closure of pulmonic valve.

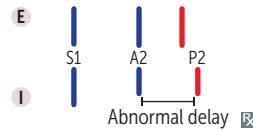


E = Expiration

I = Inspiration

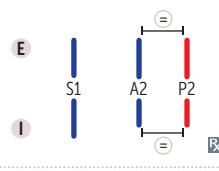
Wide splitting

Seen in conditions that delay RV emptying (eg, pulmonic stenosis, right bundle branch block). Causes delayed pulmonic sound (especially on inspiration). An exaggeration of normal splitting.



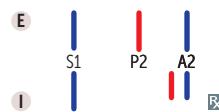
Fixed splitting

Heard in ASD. ASD → left-to-right shunt
 → ↑ RA and RV volumes → ↑ flow through pulmonic valve → delayed pulmonic valve closure (independent of respiration).

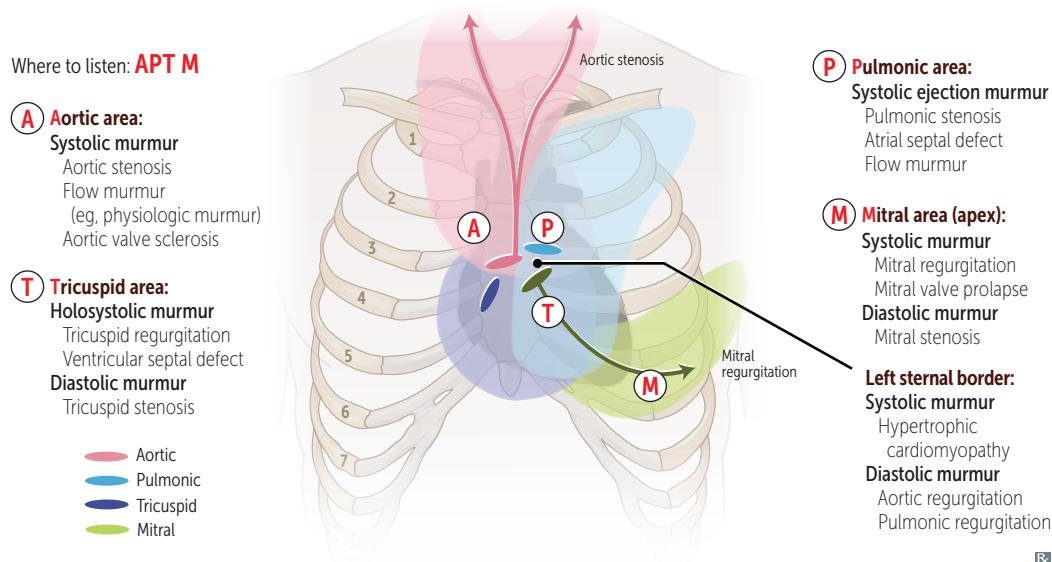


Paradoxical splitting

Heard in conditions that delay aortic valve closure (eg, aortic stenosis, left bundle branch block). Normal order of semilunar valve closure is reversed: in paradoxical splitting P2 occurs before A2. On inspiration, P2 closes later and moves closer to A2, “paradoxically” eliminating the split. On expiration, the split can be heard (opposite to physiologic splitting).

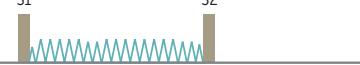
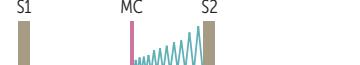
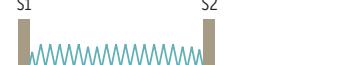
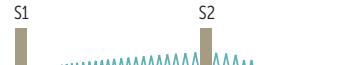


Auscultation of the heart



MANEUVER	CARDIOVASCULAR CHANGES	MURMURS THAT INCREASE WITH MANEUVER	MURMURS THAT DECREASE WITH MANEUVER
Standing, Valsalva (strain phase)	↓ preload (↓ LV volume)	MVP (↓ LV volume) with earlier midsystolic click HCM (↓ LV volume)	Most murmurs (↓ flow through stenotic or regurgitant valve)
Passive leg raise	↑ preload (↑ LV volume)		MVP (↑ LV volume) with later midsystolic click
Squatting	↑ preload, ↑ afterload (↑ LV volume)	Most murmurs (↑ flow through stenotic or regurgitant valve)	HCM (↑ LV volume)
Hand grip	↑↑ afterload → ↑ reverse flow across aortic valve (↑ LV volume)	Most other left-sided murmurs (AR, MR, VSD)	AS (↓ transaortic valve pressure gradient) HCM (↑ LV volume)
Inspiration	↑ venous return to right heart, ↓ venous return to left heart	Most right-sided murmurs	Most left-sided murmurs

Heart murmurs

	AUSCULTATION	CLINICAL ASSOCIATIONS	NOTES
Systolic			
Aortic stenosis	 <p>Crescendo-decrescendo ejection murmur, loudest at heart base, radiates to carotids Soft S2 +/- ejection click “Pulsus parvus et tardus”—weak pulses with delayed peak</p>	<p>In older (>60 years old) patients, most commonly due to age-related calcification In younger patients, most commonly due to early-onset calcification of bicuspid aortic valve</p>	<p>Can lead to Syncope, Angina, Dyspnea on exertion (SAD) LV pressure > aortic pressure during systole</p>
Mitral/tricuspid regurgitation	 <p>Holosystolic, high-pitched “blowing” murmur MR: loudest at apex, radiates toward axilla TR: loudest at tricuspid area</p>	<p>MR: often due to ischemic heart disease (post-MI), MVP, LV dilatation, rheumatic fever TR: often due to RV dilatation Either MR or TR: infective endocarditis</p>	
Mitral valve prolapse	 <p>Late crescendo murmur with midsystolic click (MC) that occurs after carotid pulse Best heard over apex Loudest just before S2</p>	<p>Usually benign, but can predispose to infective endocarditis Can be caused by rheumatic fever, chordae rupture, or myxomatous degeneration (1° or 2° to connective tissue disease)</p>	<p>MC due to sudden tensing of chordae tendineae as mitral leaflets prolapse into LA (chordae cause crescendo with click)</p>
Ventricular septal defect	 <p>Holosystolic, harsh-sounding murmur Loudest at tricuspid area</p>	<p>Congenital</p>	<p>Larger VSDs have lower intensity murmur than smaller VSDs</p>
Diastolic			
Aortic regurgitation	 <p>Early diastolic, decrescendo, high-pitched “blowing” murmur best heard at base (aortic root dilation) or left sternal border (valvular disease)</p>	<p>Causes include BEAR:</p> <ul style="list-style-type: none"> ▪ Bicuspid aortic valve ▪ Endocarditis ▪ Aortic root dilation ▪ Rheumatic fever <p>Wide pulse pressure, pistol shot femoral pulse, pulsing nail bed (Quincke pulse)</p>	<p>Hyperdynamic pulse and head bobbing when severe and chronic Can progress to left HF</p>
Mitral stenosis	 <p>Follows opening snap (OS) Delayed rumbling mid-to-late murmur (↓ interval between S2 and OS correlates with ↑ severity)</p>	<p>Late and highly specific sequelae of rheumatic fever Chronic MS can result in LA dilation and pulmonary congestion, atrial fibrillation, Ortner syndrome, hemoptysis, right HF</p>	<p>OS due to abrupt halt in leaflet motion in diastole after rapid opening due to fusion at leaflet tips LA >> LV pressure during diastole</p>
Continuous			
Patent ductus arteriosus	 <p>Continuous machinelike murmur, best heard at left infraclavicular area  Loudest at S2</p>	<p>Often due to congenital rubella or prematurity</p>	<p>You need a patent for that machine.</p>

Myocardial action potential

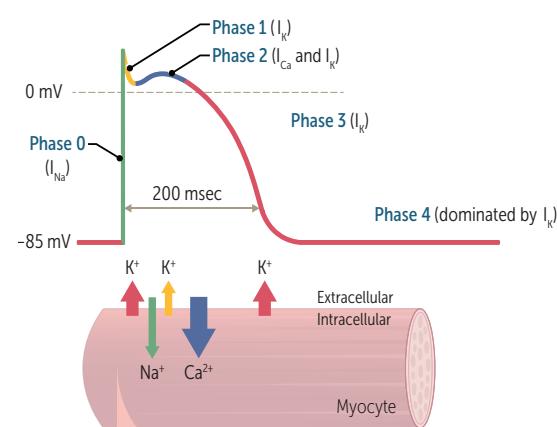
Phase 0 = rapid upstroke and depolarization—voltage-gated Na^+ channels open.

Phase 1 = initial repolarization—inactivation of voltage-gated Na^+ channels. Voltage-gated K^+ channels begin to open.

Phase 2 = plateau (“plat^{two}”)— Ca^{2+} influx through voltage-gated Ca^{2+} channels balances K^+ efflux. Ca^{2+} influx triggers Ca^{2+} release from sarcoplasmic reticulum and myocyte contraction (excitation-contraction coupling).

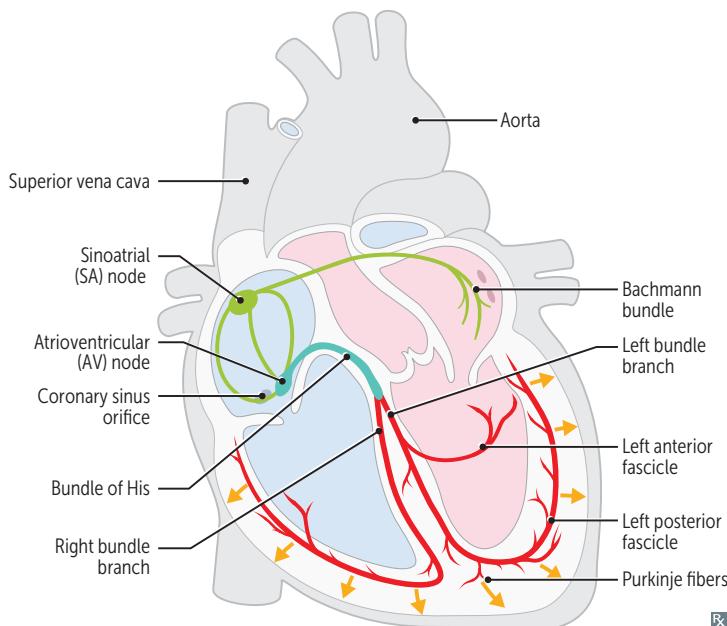
Phase 3 = rapid repolarization—massive K^+ efflux due to opening of voltage-gated slow delayed-rectifier K^+ channels and closure of voltage-gated Ca^{2+} channels.

Phase 4 = resting potential—high K^+ permeability through K^+ channels.

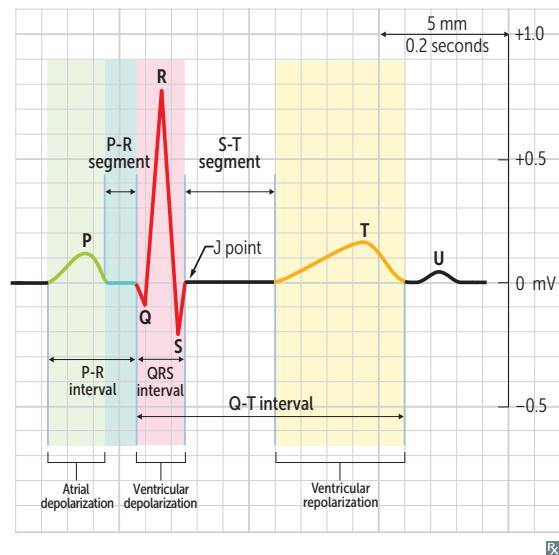


Electrocardiogram

Conduction pathway: SA node → atria
 → AV node → bundle of His → right and left bundle branches → Purkinje fibers
 → ventricles; left bundle branch divides into left anterior and posterior fascicles.
 SA node—located in upper part of crista terminalis near SVC opening; “pacemaker” inherent dominance with slow phase of upstroke.
 AV node—located in interatrial septum near coronary sinus opening. Blood supply usually from RCA. 100-msec delay allows time for ventricular filling.
 Pacemaker rates: SA > AV > bundle of His/Purkinje/ventricles.
 Speed of conduction: **His-Purkinje > Atria > Ventricles > AV node.** **He Parks At Ventura AVenue.**



P wave—atrial depolarization.
 PR interval—time from start of atrial depolarization to start of ventricular depolarization (normally 120-200 msec).
 QRS complex—ventricular depolarization (normally < 100 msec).
 QT interval—ventricular depolarization, mechanical contraction of the ventricles, ventricular repolarization.
 T wave—ventricular repolarization. T-wave inversion may indicate ischemia or recent MI.
 J point—junction between end of QRS complex and start of ST segment.
 ST segment—isoelectric, ventricles depolarized.
 U wave—prominent in hypokalemia (think hyp“U”kalemia), bradycardia.

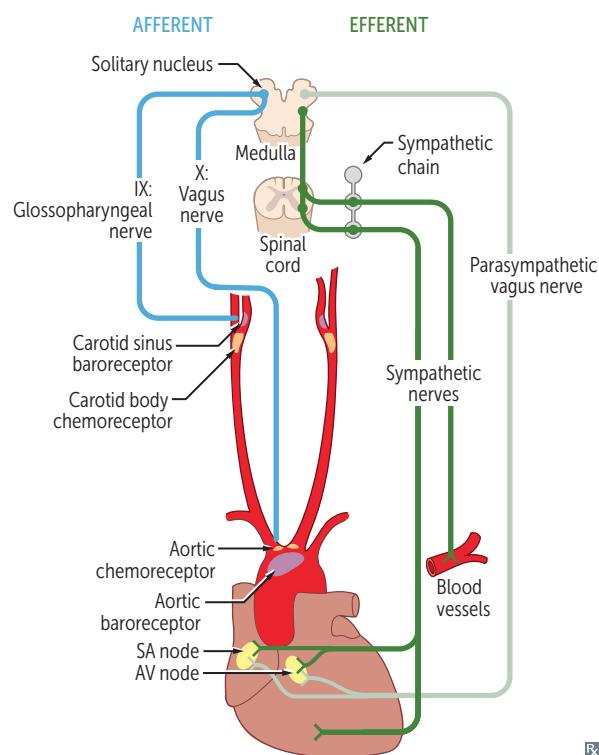


Atrial natriuretic peptide

Released from **atrial myocytes** in response to ↑ blood volume and atrial pressure. Acts via cGMP. Causes vasodilation and ↓ Na⁺ reabsorption at the renal collecting tubule. Dilates afferent renal arterioles and constricts efferent arterioles, promoting diuresis and contributing to “aldosterone escape” mechanism.

B-type (brain) natriuretic peptide

Released from **ventricular myocytes** in response to ↑ tension. Similar physiologic action to ANP, with longer half-life. BNP blood test used for diagnosing HF (very good negative predictive value).

Baroreceptors and chemoreceptors**Receptors:**

- Aortic arch transmits via vagus nerve to solitary nucleus of medulla (responds to changes in BP).
- Carotid sinus (dilated region superior to bifurcation of carotid arteries) transmits via glossopharyngeal nerve to solitary nucleus of medulla (responds to changes in BP).

Chemoreceptors:

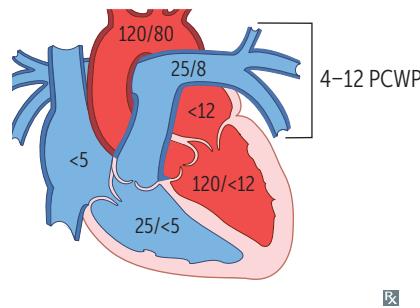
- Peripheral—carotid and aortic bodies are stimulated by ↑ PCO₂, ↓ pH of blood, and ↓ PO₂ (< 60 mm Hg).
- Central—are stimulated by changes in pH and PCO₂ of brain interstitial fluid, which in turn are influenced by arterial CO₂ as H⁺ cannot cross the blood-brain barrier. Do not directly respond to PO₂. Central chemoreceptors become less responsive with chronically ↑ PCO₂ (eg, COPD) → ↑ dependence on peripheral chemoreceptors to detect ↓ O₂ to drive respiration.

Baroreceptors:

- Hypotension—↓ arterial pressure → ↓ stretch → ↓ afferent baroreceptor firing → ↑ efferent sympathetic firing and ↓ efferent parasympathetic stimulation → vasoconstriction, ↑ HR, ↑ contractility, ↑ BP. Important in the response to hypovolemic shock.
- Carotid massage—↑ carotid sinus pressure → ↑ afferent baroreceptor firing → ↑ AV node refractory period → ↓ HR → ↓ CO. Also leads to peripheral vasodilation. Can cause presyncope/syncope. Exaggerated in underlying atherosclerosis, prior neck surgery, older age.
- Component of Cushing reflex (triad of hypertension, bradycardia, and respiratory depression)—↑ intracranial pressure constricts arterioles → cerebral ischemia → ↑ pCO₂ and ↓ pH → central reflex sympathetic ↑ in perfusion pressure (hypertension) → ↑ stretch → peripheral reflex baroreceptor-induced bradycardia.

Normal resting cardiac pressures

Pulmonary capillary wedge pressure (PCWP; in mm Hg) is a good approximation of left atrial pressure, except in mitral stenosis when PCWP > LV end diastolic pressure. PCWP is measured with pulmonary artery catheter (Swan-Ganz catheter).



Rx

Autoregulation

How blood flow to an organ remains constant over a wide range of perfusion pressures.

ORGAN	FACTORS DETERMINING AUTOREGULATION	
Lungs	Hypoxia causes vasoconstriction	The pulmonary vasculature is unique in that alveolar hypoxia causes vasoconstriction so that only well-ventilated areas are perfused. In other organs, hypoxia causes vasodilation
Heart	Local metabolites (vasodilatory): NO, CO ₂ , ↓ O ₂	
Brain	Local metabolites (vasodilatory): CO ₂ (pH)	
Kidneys	Myogenic (stretch-dependent response of afferent arteriole) and tubuloglomerular feedback	
Skeletal muscle	Local metabolites during exercise (vasodilatory): CO ₂ , H ⁺ , Adenosine, Lactate, K ⁺ At rest: sympathetic tone in arteries	CHALK
Skin	Sympathetic vasoconstriction most important mechanism for temperature control	

Capillary fluid exchange

Starling forces determine fluid movement through capillary membranes:

- P_c = capillary hydrostatic pressure—pushes fluid out of capillary
- P_i = interstitial hydrostatic pressure—pushes fluid into capillary
- π_c = plasma oncotic pressure—pulls fluid into capillary
- π_i = interstitial fluid oncotic pressure—pulls fluid out of capillary

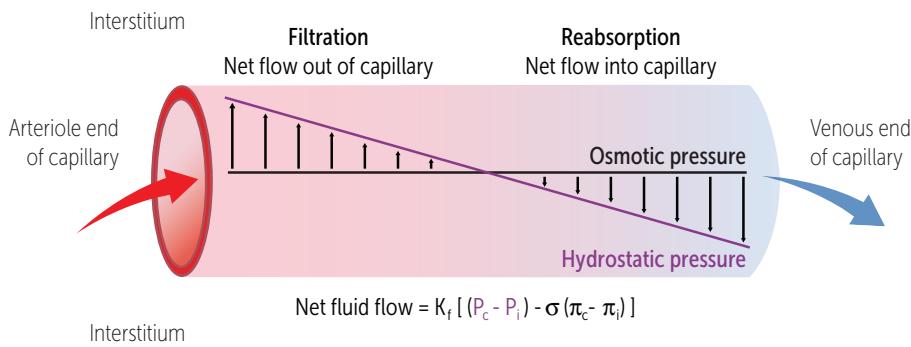
$$J_v = \text{net fluid flow} = K_f [(P_c - P_i) - \sigma(\pi_c - \pi_i)]$$

K_f = capillary permeability to fluid

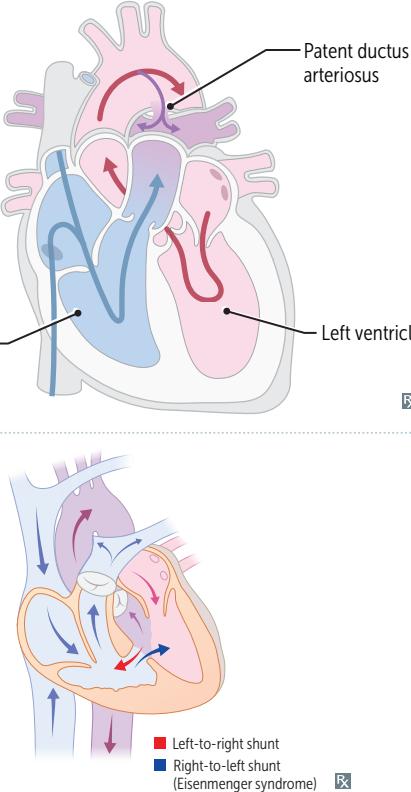
σ = reflection coefficient (measure of capillary impermeability to protein)

Edema—excess fluid outflow into interstitium commonly caused by:

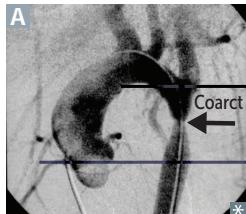
- ↑ capillary pressure ($\uparrow P_c$; eg, HF)
- ↑ capillary permeability ($\uparrow K_f$; eg, toxins, infections, burns)
- ↑ interstitial fluid oncotic pressure ($\uparrow \pi_i$; eg, lymphatic blockage)
- ↓ plasma proteins ($\downarrow \pi_c$; eg, nephrotic syndrome, liver failure, protein malnutrition)



Congenital heart diseases (continued)

LEFT-TO-RIGHT SHUNTS	Acyanotic at presentation; cyanosis may occur years later. Frequency: VSD > ASD > PDA.	Right-to-left shunts: early cyanosis. Left-to-right shunts: “later” cyanosis.
Ventricular septal defect	Asymptomatic at birth, may manifest weeks later or remain asymptomatic throughout life. Most smaller defects self-resolve; larger defects, if left surgically untreated, cause ↑ pulmonary blood flow and LV overload, which may progress to HF.	O ₂ saturation ↑ in RV and pulmonary artery.
Atrial septal defect	Defect in interatrial septum C ; wide, fixed split S2. Ostium secundum defects most common and usually an isolated finding; ostium primum defects rarer and usually occur with other cardiac anomalies. Symptoms range from none to HF. Distinct from patent foramen ovale, which is due to failed fusion.	O ₂ saturation ↑ in RA, RV, and pulmonary artery. May lead to paradoxical emboli (systemic venous emboli use ASD to bypass lungs and become systemic arterial emboli). Associated with Down syndrome.
Patent ductus arteriosus	In fetal period, shunt is right to left (normal). In neonatal period, ↓ pulmonary vascular resistance → shunt becomes left to right → progressive RVH and/or LVH and HF. Associated with a continuous, “machinelike” murmur. Patency is maintained by PGE synthesis and low O ₂ tension. Uncorrected PDA D can eventually result in late cyanosis in the lower extremities (differential cyanosis).	PDA is normal in utero and normally closes only after birth.
Eisenmenger syndrome	Uncorrected left-to-right shunt (VSD, ASD, PDA) → ↑ pulmonary blood flow → pathologic remodeling of vasculature → pulmonary arterial hypertension. RVH occurs to compensate → shunt becomes right to left when RV > LV pressure (see illustration). Causes late cyanosis, clubbing, and polycythemia. Age of onset varies depending on size and severity of initial left-to-right shunt.	 

Coarctation of the aorta



Aortic narrowing **A** near insertion of ductus arteriosus (“juxtaductal”). Associated with bicuspid aortic valve, other heart defects, and Turner syndrome. Hypertension in upper extremities. Lower extremities are cold with weak, delayed pulses (brachiofemoral delay). With age, intercostal arteries enlarge due to collateral circulation; arteries erode ribs → notched appearance on CXR. Complications include HF, ↑ risk of cerebral hemorrhage (berry aneurysms), aortic rupture, and possible infective endocarditis.

Persistent pulmonary hypertension of the newborn

Persistence of ↑ pulmonary vascular resistance after birth. Associated with abnormal development and postpartum adaptation of pulmonary vasculature. Risk factors include aspiration of meconium-stained amniotic fluid and neonatal pneumonia. Leads to right-to-left shunt through foramen ovale and ductus arteriosus. Newborn presents with signs of respiratory distress (eg, tachypnea) and cyanosis. Preductal O₂ saturation is often higher than postductal. Equal pulses (no delay).

Congenital cardiac defect associations

ASSOCIATION	DEFECT
Prenatal alcohol exposure (fetal alcohol syndrome)	VSD, PDA, ASD, tetralogy of Fallot
Congenital rubella	PDA, pulmonary artery stenosis, septal defects
Down syndrome	AV septal defect (endocardial cushion defect), VSD, ASD
Infant of patient with diabetes during pregnancy	Transposition of great arteries, truncus arteriosus, tricuspid atresia, VSD
Marfan syndrome	MVP, thoracic aortic aneurysm and dissection, aortic regurgitation
Prenatal lithium exposure	Ebstein anomaly
Turner syndrome	Bicuspid aortic valve, coarctation of aorta
Williams syndrome	Supravalvular aortic stenosis
22q11 syndromes	Truncus arteriosus, tetralogy of Fallot

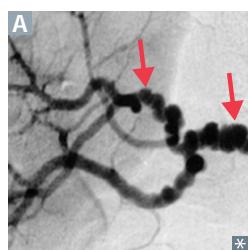
Hypertension

RISK FACTORS

Persistent systolic BP ≥ 130 mm Hg and/or diastolic BP ≥ 80 mm Hg.

↑ age, obesity, diabetes, physical inactivity, high-sodium diet, excess alcohol intake, tobacco smoking, family history; incidence greatest in Black > White > Asian populations.

FEATURES



90% of hypertension is 1° (essential) and related to ↑ CO or ↑ TPR. Remaining 10% mostly 2° to renal/renovascular diseases such as fibromuscular dysplasia (characteristic “string of beads” appearance of renal artery **A**, usually seen in adult females) and atherosclerotic renal artery stenosis, 1° hyperaldosteronism, or obstructive sleep apnea.

Hypertensive urgency—severe (≥ 180/≥ 120 mm Hg) hypertension without acute end-organ damage.

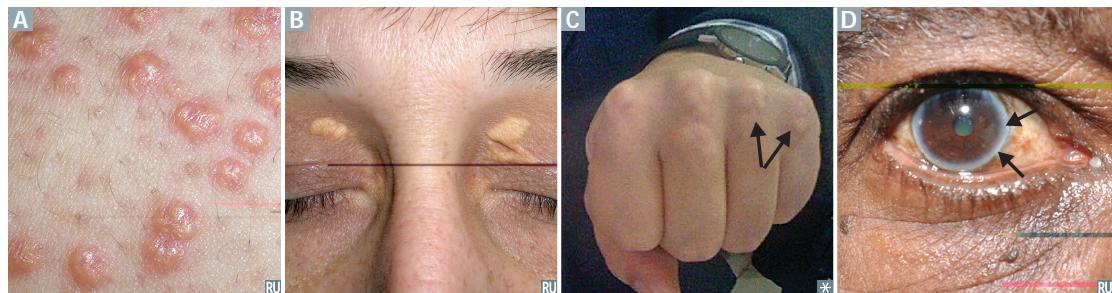
Hypertensive emergency—formerly called malignant hypertension. Severe hypertension with evidence of acute end-organ damage (eg, encephalopathy, stroke, retinal hemorrhages and exudates, papilledema, MI, HF, aortic dissection, kidney injury, microangiopathic hemolytic anemia, eclampsia). Arterioles may show fibrinoid necrosis.

PREDISPOSES TO

CAD, LVH, HF, atrial fibrillation; aortic dissection, aortic aneurysm; stroke; CKD (hypertensive nephropathy); retinopathy.

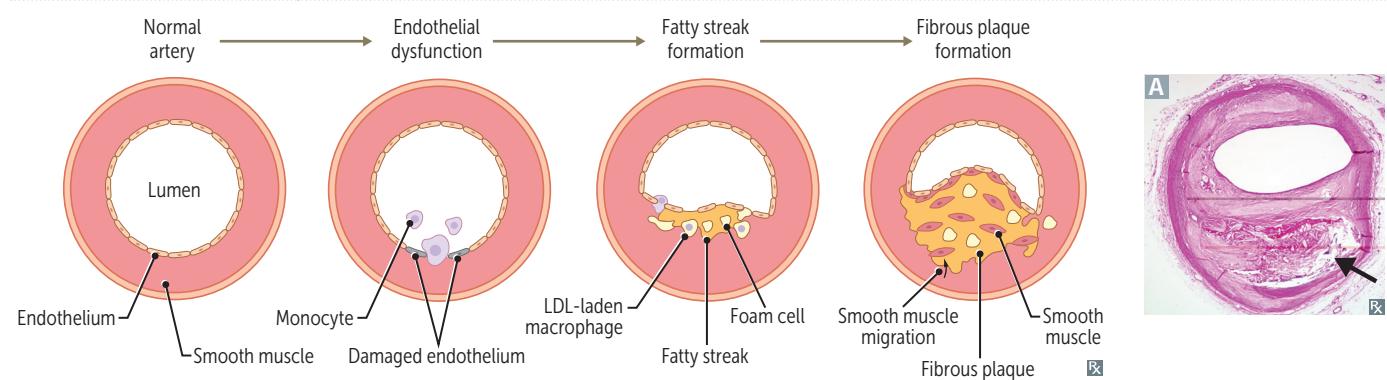
Hyperlipidemia signs

Xanthomas	Plaques or nodules composed of lipid-laden histiocytes in skin A , especially the eyelids (xanthelasma B).
Tendinous xanthoma	Lipid deposit in tendon C , especially Achilles tendon and finger extensors.
Corneal arcus	Lipid deposit in cornea. Common in older adults (arcus senilis D), but appears earlier in life with hypercholesterolemia.



Atherosclerosis

LOCATION	Very common form of arteriosclerosis (hardening of arteries). Disease of elastic arteries and large- and medium-sized muscular arteries; caused by buildup of cholesterol plaques in tunica intima.
RISK FACTORS	Abdominal aorta > coronary artery > popliteal artery > carotid artery > circle of Willis. A copy cat named Willis.
SYMPTOMS	Modifiable: hypertension, tobacco smoking, dyslipidemia (\uparrow LDL, \downarrow HDL), diabetes. Non-modifiable: age, male sex, postmenopausal status, family history.
PROGRESSION	Angina, claudication, but can be asymptomatic.
COMPLICATIONS	Inflammation important in pathogenesis: endothelial cell dysfunction \rightarrow macrophage and LDL accumulation \rightarrow foam cell formation \rightarrow fatty streaks \rightarrow smooth muscle cell migration (involves PDGF and FGF), proliferation, and extracellular matrix deposition \rightarrow fibrous plaque \rightarrow complex atheromas A \rightarrow calcification (calcium content correlates with risk of complications).
	Ischemia, infarction, aneurysm formation, peripheral vascular disease, thrombosis, embolism.



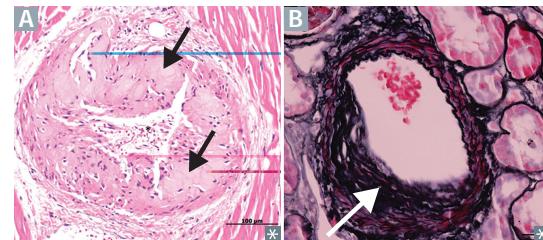
Cholesterol emboli syndrome

Microembolization of cholesterol displaced from atherosclerotic plaques in large arteries (usually the aorta). Results in end-organ damage due to small artery emboli and an inflammatory response (eg, livedo reticularis, digital ischemia [blue toe syndrome], acute renal failure, cerebrovascular accident, gut ischemia). Pulses remain palpable because larger arteries are unaffected. May follow invasive vascular procedures (angiography, angioplasty, endovascular grafting).

Arteriolosclerosis

Common form of arteriosclerosis. Affects small arteries and arterioles. Two types:

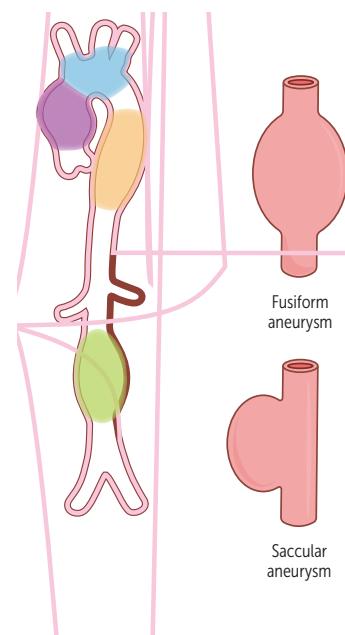
- **Hyaline**—vessel wall thickening 2° to plasma protein leak into subendothelium in hypertension or diabetes mellitus **A**.
- **Hyperplastic**—“onion skinning” **B** in severe hypertension with proliferation of smooth muscle cells.

**Aortic aneurysm**

Localized pathologic dilation of the aorta. May cause abdominal and/or back pain, which is a sign of leaking, dissection, or imminent rupture.

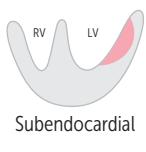
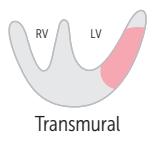
Thoracic aortic aneurysm

Associated with cystic medial degeneration. Risk factors include hypertension, bicuspid aortic valve, connective tissue disease (eg, Marfan syndrome). Also associated with 3° syphilis (obliterative endarteritis of the vasa vasorum). Aortic root dilatation may lead to aortic valve regurgitation.



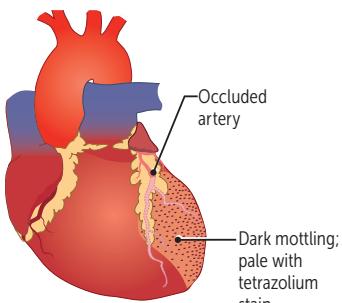
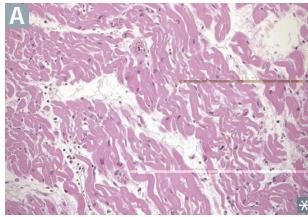
Ischemic heart disease manifestations

Angina	Chest pain due to ischemic myocardium 2° to coronary artery narrowing or spasm; no necrosis.
	<ul style="list-style-type: none"> ▪ Stable—usually 2° to atherosclerosis ($\geq 70\%$ occlusion); exertional chest pain in classic distribution (possibly with ST depression on ECG), resolving with rest or nitroglycerin. ▪ Vasospastic (formerly Prinzmetal or variant)—occurs at rest 2° to coronary artery spasm; transient ST elevation on ECG. Tobacco smoking is a risk factor; hypertension and hypercholesterolemia are not. Triggers include cocaine, alcohol, and triptans. Treat with Ca^{2+} channel blockers, nitrates, and smoking cessation (if applicable). ▪ Unstable—thrombosis with incomplete coronary artery occlusion; $+\text{-}$ ST depression and/or T-wave inversion on ECG but no cardiac biomarker elevation (unlike non-ST-segment elevation MI [NSTEMI]); \uparrow in frequency or intensity of chest pain or any chest pain at rest.

	Stable angina	Unstable angina	NSTEMI	STEMI
PAIN	On exertion	Mild exertion or at rest	At rest	At rest
TROPONIN LEVEL	No elevation	No elevation	Elevated	Elevated
INFARCTION	None	None	 Subendocardial	 Transmural
ECG CHANGES	None	Possible ST depression and/or T-wave inversion	ST depression and/or T-wave inversion	ST elevation
Coronary steal syndrome	Distal to coronary stenosis, vessels are maximally dilated at baseline. Administration of vasodilators (eg, dipyridamole, regadenoson) dilates normal vessels → blood is shunted toward well-perfused areas → ischemia in myocardium perfused by stenosed vessels. Principle behind pharmacologic stress tests with coronary vasodilators.			
Sudden cardiac death	Unexpected death due to cardiac causes within 1 hour of symptom onset, most commonly due to lethal arrhythmia (eg, ventricular fibrillation). Associated with CAD (up to 70% of cases), cardiomyopathy (hypertrophic, dilated), and hereditary channelopathies (eg, long QT syndrome, Brugada syndrome). Prevent with implantable cardioverter-defibrillator.			
Chronic ischemic heart disease	Progressive onset of HF over many years due to chronic ischemic myocardial damage. Myocardial hibernation —potentially reversible LV systolic dysfunction in the setting of chronic ischemia. Contrast with myocardial stunning , a transient LV systolic dysfunction after a brief episode of acute ischemia.			
Myocardial infarction	Most often due to rupture of coronary artery atherosclerotic plaque → acute thrombosis. \uparrow cardiac biomarkers (CK-MB, troponins) are diagnostic.			
	NSTEMI		STEMI	
INFARCT LOCATION	Subendocardial		Transmural	
LAYERS INVOLVED	Subendocardium (inner 1/3) especially vulnerable to ischemia		Full thickness of myocardial wall	
ECG CHANGES	ST-segment depression, T-wave inversion		ST-segment elevation, pathologic Q waves	

Evolution of myocardial infarction

Commonly occluded coronary arteries: LAD > RCA > circumflex.
 Symptoms: diaphoresis, nausea, vomiting, severe retrosternal pain, pain in left arm and/or jaw, shortness of breath, fatigue.

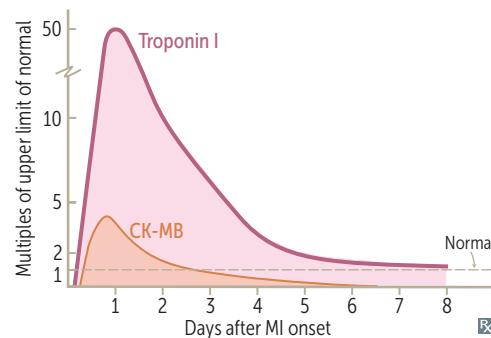
TIME	GROSS	LIGHT MICROSCOPE	COMPLICATIONS
0–24 hours	 <p>Occluded artery Dark mottling; pale with tetrazolium stain</p>	<p>Wavy fibers (0–4 hr), early coagulative necrosis (4–24 hr)</p> <p>A → cell content released into blood; edema, hemorrhage</p> <p>Reperfusion injury → free radicals and ↑ Ca²⁺ influx → hypercontraction of myofibrils (dark eosinophilic stripes)</p> 	Ventricular arrhythmia, HF, cardiogenic shock
1–3 days			

Diagnosis of myocardial infarction

In the first 6 hours, ECG is the gold standard. Cardiac troponin I rises after 4 hours (peaks at 24 hr) and is ↑ for 7–10 days; more specific than other protein markers.

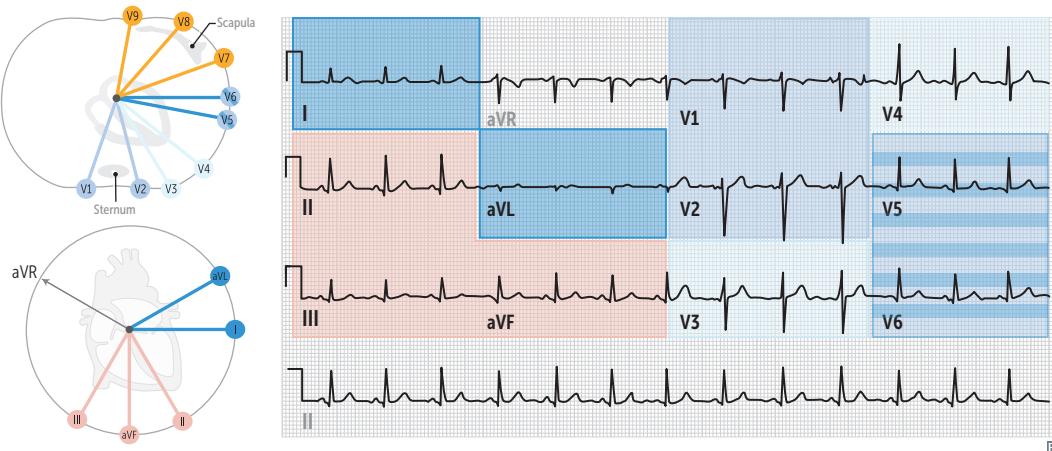
CK-MB increases after 6–12 hours (peaks at 16–24 hr) and is predominantly found in myocardium but can also be released from skeletal muscle. Useful in diagnosing reinfarction following acute MI because levels return to normal after 48 hours.

ECG changes can include ST elevation (STEMI, transmural infarct), ST depression (NSTEMI, subendocardial infarct), hyperacute (peaked) T waves, T-wave inversion, and pathologic Q waves or poor R wave progression (evolving or old transmural infarct).



ECG localization of STEMI

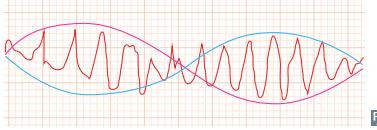
INFARCT LOCATION	LEADS WITH ST-SEGMENT ELEVATIONS OR Q WAVES
Anteroseptal (LAD)	V ₁ –V ₂
Anteroapical (distal LAD)	V ₃ –V ₄
Anterolateral (LAD or LCX)	V ₅ –V ₆
Lateral (LCX)	I, aVL
Inferior (RCA)	II, III, aVF
Posterior (PDA)	V ₇ –V ₉ , ST depression in V ₁ –V ₃ with tall R waves



Narrow complex tachycardias Narrow QRS complex < 120 msec, rapid ventricular activation via normal ventricular conduction system, tachycardia originates within or above AV node (supraventricular arrhythmia).

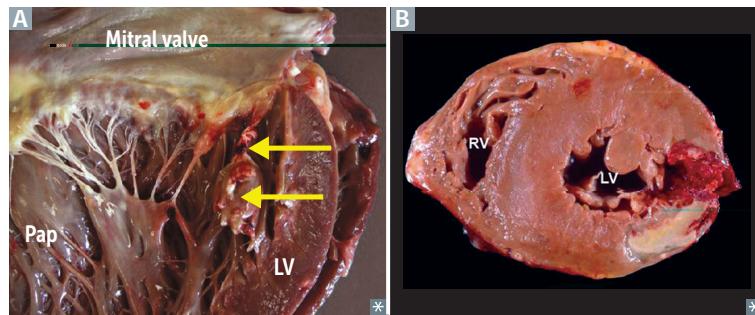
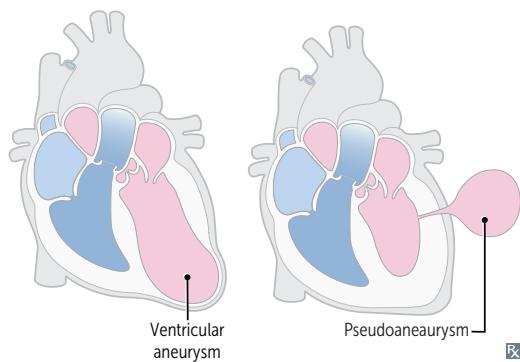
ARRHYTHMIA	DESCRIPTION	ECG FINDINGS
Atrial fibrillation	Irregularly irregular rate and rhythm with no discrete P waves. Arrhythmogenic activity usually originates from automatic foci near pulmonary vein ostia in left atrium. Common risk factors include hypertension and CAD. May predispose to thromboembolic events, particularly stroke. Management: rate and rhythm control, cardioversion. Definitive treatment is ablation of pulmonary vein ostia. Consider anticoagulation based on stroke risk.	
Multifocal atrial tachycardia	Irregularly irregular rate and rhythm with at least 3 distinct P wave morphologies, due to multiple ectopic foci in atria. Associated with underlying conditions such as COPD, pneumonia, HF.	
Atrial flutter	Rapid succession of identical, consecutive atrial depolarization waves causing “sawtooth” appearance of P waves. Arrhythmogenic activity usually originates from reentry circuit around tricuspid annulus in right atrium. Treat like atrial fibrillation +/- catheter ablation of region between tricuspid annulus and IVC.	
Paroxysmal supraventricular tachycardia	Most often due to a reentrant tract between atrium and ventricle, most commonly in AV node. Commonly presents with sudden-onset palpitations, lightheadedness, diaphoresis. Treatment: terminate reentry rhythm by slowing AV node conduction (eg, vagal maneuvers, IV adenosine), electrical cardioversion if hemodynamically unstable. Definitive treatment is catheter ablation of reentry tract.	
Wolff-Parkinson-White syndrome	Most common type of ventricular preexcitation syndrome. Abnormal fast accessory conduction pathway from atria to ventricle (bundle of Kent) bypasses rate-slowness AV node → ventricles partially depolarize earlier → characteristic delta wave with widened QRS complex and shortened PR interval. May result in reentry circuit → supraventricular tachycardia. Treatment: procainamide. Avoid AV nodal blocking drugs.	

Wide complex tachycardias Wide QRS complex \geq 120 msec, slow ventricular activation outside normal ventricular conduction system, tachycardia originates below AV node (ventricular arrhythmia).

ARRHYTHMIA	DESCRIPTION	ECG FINDINGS
Ventricular tachycardia	Typically regular rhythm, rate > 100 . Most commonly due to structural heart disease (eg, cardiomyopathy, scarring after myocardial infarction). High risk of sudden cardiac death.	 Rx
Torsades de pointes	Polymorphic ventricular tachycardia. Shifting sinusoidal waveforms. May progress to ventricular fibrillation. Long QT interval predisposes to torsades de pointes. Caused by drugs, $\downarrow K^+$, $\downarrow Mg^{2+}$, $\downarrow Ca^{2+}$. Torsades de pointes = twisting of the points Treatment: defibrillation for unstable patients, magnesium sulfate for stable patients. Drug-induced long QT (ABCDEF+NO):	 Rx
Ventricular fibrillation	Disorganized rhythm with no identifiable waves. Treatment: fatal without immediate CPR and defibrillation.	 Rx
Hereditary channelopathies	Inherited mutations of cardiac ion channels \rightarrow abnormal myocardial action potential \rightarrow \uparrow risk of ventricular tachyarrhythmias and sudden cardiac death (SCD).	
Brugada syndrome	Autosomal dominant; most commonly due to loss of function mutation of Na^+ channels. \uparrow prevalence in Asian males. ECG pattern of pseudo-right bundle branch block and ST-segment elevations in leads V_1-V_2 . Prevent SCD with ICD.	
Congenital long QT syndrome	Most commonly due to loss of function mutation of K^+ channels (affects repolarization). Includes: ▪ Romano-Ward syndrome —autosomal dominant, pure cardiac phenotype (no deafness). ▪ Jervell and Lange-Nielsen syndrome —autosomal recessive, sensorineural deafness.	
Sick sinus syndrome	Age-related degeneration of SA node. ECG can show bradycardia, sinus pauses, sinus arrest, junctional escape beats.	 Rx

Myocardial infarction complications

COMPLICATION	TIMEFRAME	FINDINGS	NOTES
Cardiac arrhythmia	First few days to several months	Can be supraventricular arrhythmias, ventricular arrhythmias, or conduction blocks.	Due to myocardial death and scarring. Important cause of death before reaching the hospital and within the first 48 hours post-MI.
Peri-infarction pericarditis	1–3 days	Pleuritic chest pain, pericardial friction rub, ECG changes, and/or small pericardial effusion.	Usually self-limited.
Papillary muscle rupture	2–7 days	Can result in acute mitral regurgitation → cardiogenic shock, severe pulmonary edema.	Posteromedial >> anterolateral papillary muscle rupture A , as the posteromedial has single artery blood supply (PDA) whereas anterolateral has dual (LAD, LCX).
Interventricular septal rupture	3–5 days	Symptoms can range from mild to severe with cardiogenic shock and pulmonary edema.	Macrophage-mediated degradation → VSD → ↑ O ₂ saturation and ↑ pressure in RV.
Ventricular pseudoaneurysm	3–14 days	May be asymptomatic. Symptoms may include chest pain, murmur, arrhythmia, syncope, HF, embolus from mural thrombus. Rupture → cardiac tamponade.	Free wall rupture contained by adherent pericardium or scar tissue—does not contain endocardium or myocardium. More likely to rupture than true aneurysm.
Ventricular free wall rupture	5–14 days	Free wall rupture B → cardiac tamponade; acute form usually leads to sudden death.	LV hypertrophy and previous MI protect against free wall rupture.
True ventricular aneurysm	2 weeks to several months	Similar to pseudoaneurysm.	Outward bulge with contraction (“dyskinesia”). Associated with fibrosis.
Postcardiac injury syndrome	Weeks to several months	Fibrinous pericarditis due to autoimmune reaction.	Also called Dressler syndrome. Cardiac antigens released after injury → deposition of immune complexes in pericardium → inflammation.



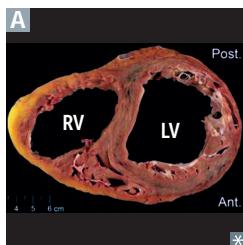
Acute coronary syndrome treatments

Unstable angina/NSTEMI—Anticoagulation (eg, heparin), antiplatelet therapy (eg, aspirin) + ADP receptor inhibitors (eg, clopidogrel), β -blockers, ACE inhibitors, statins. Symptom control with nitroglycerin +/- morphine.

STEMI—In addition to above, reperfusion therapy most important (percutaneous coronary intervention preferred over fibrinolysis). If RV affected (eg, RCA occlusion), support venous return/preload to maintain cardiac output (eg, IV fluids, avoiding nitroglycerin).

Cardiomyopathies

Dilated cardiomyopathy



Most common cardiomyopathy (90% of cases).

Often idiopathic or familial (eg, due to mutation of TTN gene encoding the sarcomeric protein titin). Other etiologies include drugs (eg, alcohol, cocaine, doxorubicin), infection (eg, coxsackie B virus, Chagas disease), ischemia (eg, CAD), systemic conditions (eg, hemochromatosis, sarcoidosis, thyrotoxicosis, wet beriberi), peripartum cardiomyopathy.

Findings: HF, S3, systolic regurgitant murmur, dilated heart on echocardiogram, balloon appearance of heart on CXR.

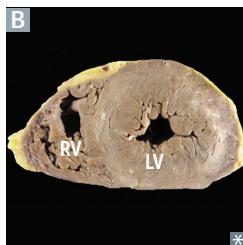
Treatment: Na^+ restriction, ACE inhibitors/ARBs, β -blockers, sacubitril, diuretics, mineralocorticoid receptor blockers (eg, spironolactone), ICD, heart transplant.

Leads to systolic dysfunction.

Displays eccentric hypertrophy **A** (sarcomeres added in series). Compare to athlete's heart, where LV and RV enlargement facilitates \uparrow SV and \uparrow CO.

Stress cardiomyopathy (also called takotsubo cardiomyopathy, broken heart syndrome)—ventricular apical ballooning likely due to \uparrow sympathetic stimulation (eg, stressful situations).

Hypertrophic cardiomyopathy



60–70% of cases are familial, autosomal dominant (most commonly due to mutations in genes encoding sarcomeric proteins, such as myosin binding protein C and β -myosin heavy chain). Causes syncope during exercise and may lead to sudden death (eg, in young athletes) due to ventricular arrhythmia.

Findings: S4, systolic murmur. May see mitral regurgitation due to impaired mitral valve closure.

Treatment: cessation of high-intensity athletics, use of β -blocker or nondihydropyridine Ca^{2+} channel blockers (eg, verapamil). ICD if high risk. Avoid drugs that decrease preload (eg, diuretics, vasodilators).

Diastolic dysfunction ensues.

Displays ventricular concentric hypertrophy (sarcomeres added in parallel) **B**, often septal predominance. Myofibrillar disarray and fibrosis.

Classified as hypertrophic obstructive cardiomyopathy when LV outflow tract is obstructed. Asymmetric septal hypertrophy and systolic anterior motion of mitral valve \rightarrow outflow obstruction \rightarrow dyspnea, possible syncope.

Other causes of concentric LV hypertrophy: chronic HTN, Friedreich ataxia.

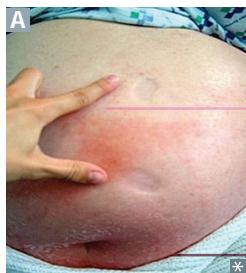
Restrictive/infiltrative cardiomyopathy

Postradiation fibrosis, Löffler endocarditis, Endocardial fibroelastosis (thick fibroelastic tissue in endocardium of young children), Amyloidosis, Sarcoidosis, Hemochromatosis (**PLEASE Help!**).

Diastolic dysfunction ensues. Can have low-voltage ECG despite thick myocardium (especially in amyloidosis).

Löffler endocarditis—associated with hypereosinophilic syndrome; histology shows eosinophilic infiltrates in myocardium.

Heart failure



Clinical syndrome of cardiac pump dysfunction → congestion and low perfusion. Symptoms include dyspnea, orthopnea, fatigue; signs include S3 heart sound, rales, jugular venous distention (JVD), pitting edema **A**.

Systolic dysfunction—heart failure with reduced ejection fraction (HFrEF), ↑ EDV; ↓ contractility often 2° to ischemia/MI or dilated cardiomyopathy.

Diastolic dysfunction—heart failure with preserved ejection fraction (HFpEF), normal EDV; ↓ compliance (↑ EDP) often 2° to myocardial hypertrophy.

Right HF most often results from left HF. Cor pulmonale refers to isolated right HF due to pulmonary cause.

ACE inhibitors, ARBs, angiotensin receptor–neprilysin inhibitors, β-blockers (except in acute decompensated HF), and aldosterone receptor antagonists ↓ mortality in HFrEF. Loop and thiazide diuretics are used mainly for symptomatic relief. Hydralazine with nitrates therapy improves both symptoms and mortality in select patients.

Left heart failure

Orthopnea

Shortness of breath when supine: ↑ venous return from redistribution of blood (immediate gravity effect) exacerbates pulmonary vascular congestion.

Paroxysmal nocturnal dyspnea

Breathless awakening from sleep: ↑ venous return from redistribution of blood, reabsorption of peripheral edema, etc.

Pulmonary edema

↑ pulmonary venous pressure → pulmonary venous distention and transudation of fluid. Presence of hemosiderin-laden macrophages (“HF” cells) in lungs.

Right heart failure

Congestive hepatomegaly

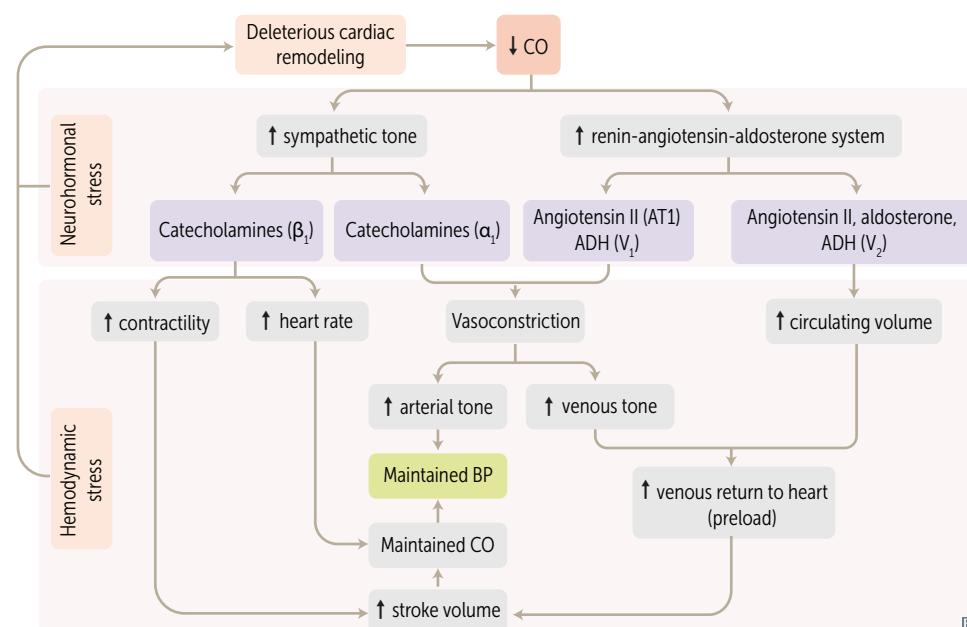
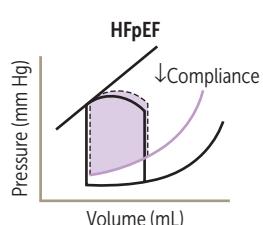
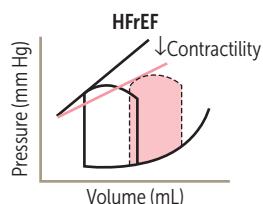
↑ central venous pressure → ↑ resistance to portal flow. Rarely, leads to “cardiac cirrhosis.” Associated with nutmeg liver (mottled appearance) on gross exam.

Jugular venous distention

↑ venous pressure.

Peripheral edema

↑ venous pressure → fluid transudation.



High-output heart failure

Uncommon form of HF characterized by ↑ CO. High-output state is due to ↓ SVR from either vasodilation or arteriovenous shunting. Causes include severe obesity, advanced cirrhosis, severe anemia, hyperthyroidism, wet beriberi, Paget disease of bone.
Presents with symptoms and signs of pulmonary and/or systemic venous congestion.

Shock

Syncope

Transient loss of consciousness caused by a period of ↓ cerebral blood flow. Types:

- Reflex (most common)—vasovagal (common faint), situational (eg, coughing/sneezing, swallowing, defecation, micturition), carotid sinus hypersensitivity.
- Orthostatic—hypovolemia, drugs (eg, antihypertensives), autonomic dysfunction.
- Cardiac—arrhythmias, structural (eg, aortic stenosis, HCM).

Infective endocarditis

Infection of the endocardial surface of the heart, typically involving ≥1 heart valves.

Caused by bacteria >> fungi. Forms:

- **Acute**—classically *S aureus* (high virulence). Large destructive vegetations **A** on previously normal valves. Rapid onset.
- **Subacute**—classically viridans streptococci (low virulence). Smaller vegetations on congenitally abnormal or diseased valves. Sequela of dental procedures. Gradual onset.

Presents with fever (most common), new murmur, vascular and immunologic phenomena.

Vascular phenomena—septic embolism, petechiae, splinter hemorrhages (linear hemorrhagic lesions on nail bed **B**), Janeway lesions (painless, flat, erythematous lesions on palms or soles).

Immunologic phenomena—immune complex deposition, glomerulonephritis, **Osler nodes** (painful ["Ouchy"], raised, violaceous lesions on finger or toe pads **C**), **Roth spots** (Retinal hemorrhagic lesions with pale centers **D**).

Mitral valve (most common) > aortic valve.

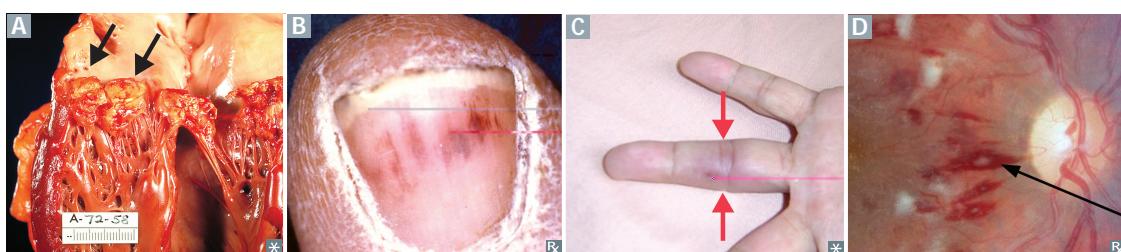
Tricuspid valve involvement is associated with injection **drug** use (don't "tri" **drugs**).

Common associations:

- Prosthetic valves—*S epidermidis*
- GI/GU procedures—*Enterococcus*
- Colon cancer—*S gallolyticus*
- Gram ⊖—**HACEK** organisms (*Haemophilus*, *Aggregatibacter* [formerly *Actinobacillus*], *Cardiobacterium*, *Eikenella*, *Kingella*)
- Culture ⊖—*Coxiella*, *Bartonella*
- Injection drug use—*S aureus*, *Pseudomonas*, *Candida*

Endothelial injury → formation of vegetations consisting of platelets, fibrin, and microbes on heart valves → valve regurgitation, septic embolism (systemic circulation in left-sided endocarditis, pulmonary in right-sided).

Diagnosis requires multiple blood cultures and echocardiography.

**Nonbacterial thrombotic endocarditis**

Also called marantic endocarditis. Rare, noninfective. Vegetations typically arise on mitral or aortic valve and consist of sterile, platelet-rich thrombi that dislodge easily.

Usually asymptomatic until embolism occurs.

Associated with the hypercoagulable state seen in advanced malignancy (especially pancreatic adenocarcinoma) or SLE (called **Libman-Sacks endocarditis** in this setting).

Rheumatic fever

A consequence of pharyngeal infection with group A β -hemolytic streptococci. Late sequelae include **rheumatic heart disease**, which affects heart valves—**mitral > aortic >> tricuspid** (high-pressure valves affected most). Early valvular regurgitation, late valvular stenosis.

Associated with Aschoff bodies (granuloma with giant cells, Anitschkow cells (enlarged macrophages with ovoid, wavy, rodlike nucleus), ↑ anti-streptolysin O (ASO) and ↑ anti-DNase B titers.

Immune mediated (type II hypersensitivity); not a direct effect of bacteria. Antibodies to **M protein** cross-react with self antigens, often **myosin (molecular mimicry)**.

Treatment/prophylaxis: penicillin.

JONES (major criteria):

Joint (migratory polyarthritis)

Heart (carditis)

Nodules in skin (subcutaneous)

Erythema marginatum (evanescent rash with ring margin)

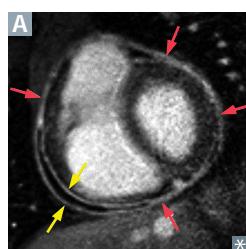
Sydenham chorea (involuntary irregular movements of limbs and face)

Syphilitic heart disease

3° syphilis disrupts the vasa vasorum of the aorta with consequent atrophy of vessel wall and dilation of aorta and valve ring.

May see calcification of aortic root, ascending aortic arch, and thoracic aorta. Leads to “tree bark” appearance of aorta.

Can result in aneurysm of ascending aorta or aortic arch, aortic insufficiency.

Acute pericarditis

Inflammation of the pericardium (red arrows in **A**). Commonly presents with sharp pain, aggravated by inspiration, and relieved by sitting up and leaning forward. Often complicated by pericardial effusion (between yellow arrows in **A**). Presents with friction rub. ECG changes include widespread/diffuse ST-segment elevation and/or PR depression.

Usually idiopathic, but may be due to viral infections (eg, coxsackievirus B), malignancy (metastasis), cardiac surgery, thoracic radiotherapy (early), MI (eg, postcardiac injury syndrome), autoimmune diseases (eg, SLE, rheumatoid arthritis), renal failure (uremia).

Treatment: NSAIDs, colchicine, glucocorticoids, dialysis (uremia).

Constrictive pericarditis

Chronic inflammation of pericardium → pericardial fibrosis +/- calcification → limited space for expansion → ↓ ventricular filling. Usually idiopathic, but may be due to viral infections, cardiac surgery, thoracic radiotherapy (late). TB is the most common cause in resource-limited countries. ↓ EDV → ↓ CO → ↓ venous return. Presents with dyspnea, peripheral edema, jugular venous distention, Kussmaul sign, pulsus paradoxus, pericardial knock.

Kussmaul sign

Paradoxical ↑ in JVP on inspiration (normally, inspiration → negative intrathoracic pressure → ↑ venous return → ↓ JVP). Impaired RV filling → RV cannot accommodate ↑ venous return during inspiration → blood backs up into vena cava → Kussmaul sign. May be seen with constrictive pericarditis, restrictive cardiomyopathy, right HF, massive pulmonary embolism, right atrial or ventricular tumors.

Myocarditis

Inflammation of myocardium. Major cause of SCD in adults < 40 years old. Presentation highly variable, can include dyspnea, chest pain, fever, arrhythmias (persistent tachycardia out of proportion to fever is characteristic). Multiple causes:

- Viral (eg, adenovirus, coxsackie B, parvovirus B19, HIV, HHV-6, COVID-19); lymphocytic infiltrate with focal necrosis highly indicative of viral myocarditis
- Parasitic (eg, *Trypanosoma cruzi*, *Toxoplasma gondii*)
- Bacterial (eg, *Borrelia burgdorferi*, *Mycoplasma pneumoniae*, *Corynebacterium diphtheriae*)
- Toxins (eg, carbon monoxide, black widow venom)
- Rheumatic fever
- Drugs (eg, doxorubicin, cocaine)
- Autoimmune (eg, Kawasaki disease, sarcoidosis, SLE, polymyositis/dermatomyositis)

Complications include sudden death, arrhythmias, heart block, dilated cardiomyopathy, HF, mural thrombus with systemic emboli.

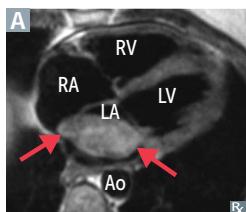
Hereditary hemorrhagic telangiectasia

Also called Osler-Weber-Rendu syndrome. Autosomal dominant disorder of blood vessels. Findings: blanching lesions (telangiectasias) on skin and mucous membranes, recurrent epistaxis, AVMs (eg, brain, lung, liver), GI bleeding, hematuria.

Arteriovenous malformation—abnormal, high-flow connection between artery and vein.

Cardiac tumors

Most common cardiac tumor is a metastasis (eg, melanoma).

Myxomas

Most common 1° cardiac tumor in **adults** (arrows in A). 90% occur in the atria (mostly left atrium). Myxomas are usually described as a “ball valve” obstruction in the left atrium (associated with multiple syncopal episodes). IL-6 production by tumor → constitutional symptoms (eg, fever, weight loss). May auscultate early diastolic “tumor plop” sound (mimics mitral stenosis). Histology: gelatinous material, myxoma cells immersed in glycosaminoglycans.

Adults make 6 myxed drinks.

Rhabdomyomas

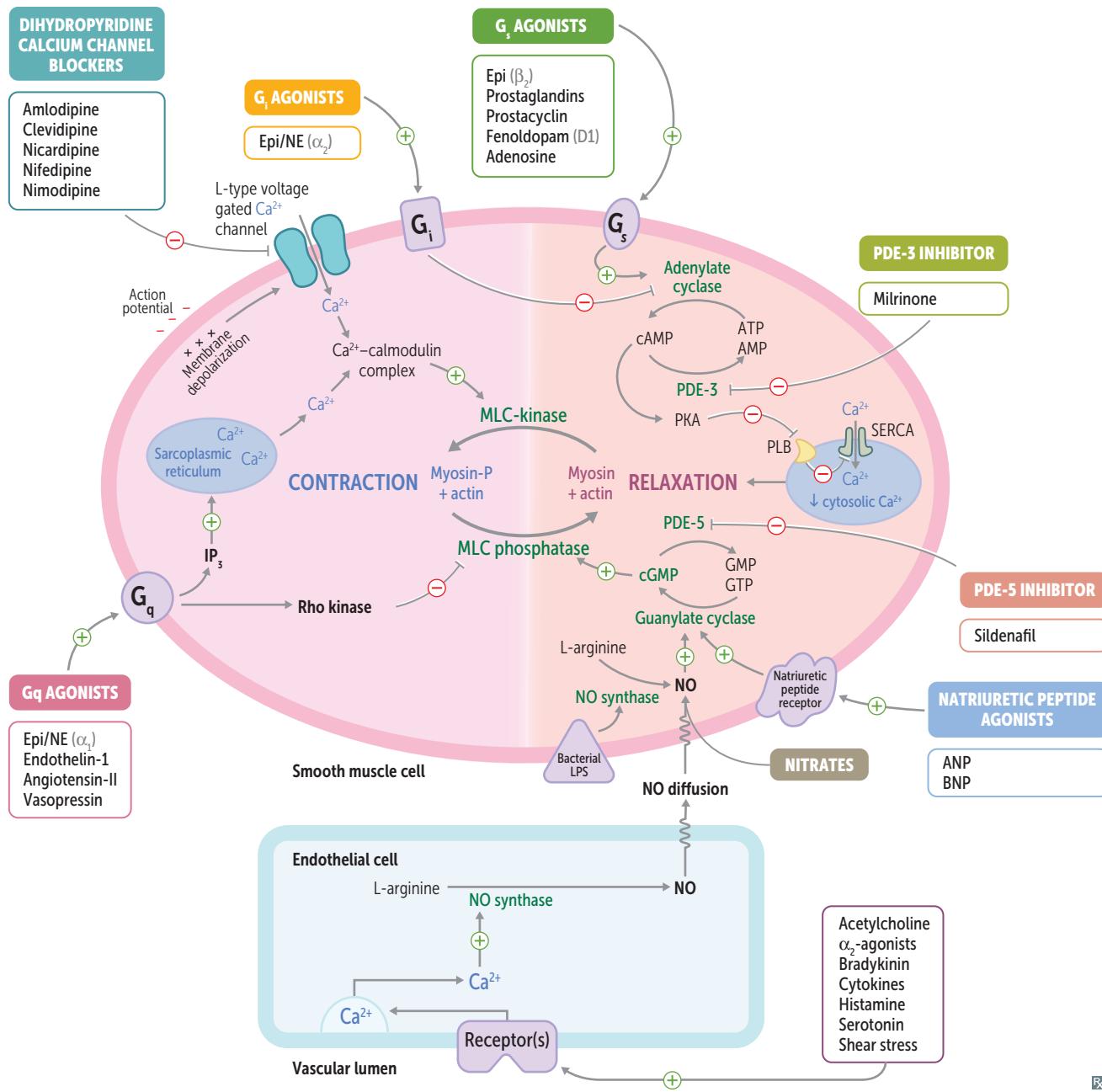
Most frequent 1° cardiac tumor in children (associated with tuberous sclerosis). Histology: hamartomatous growths. More common in the ventricles.

► CARDIOVASCULAR—PHARMACOLOGY

Hypertension treatment

Primary (essential) hypertension	Thiazide diuretics, ACE inhibitors, angiotensin II receptor blockers (ARBs), dihydropyridine Ca ²⁺ channel blockers.	
Hypertension with heart failure	Diuretics, ACE inhibitors/ARBs, β-blockers (compensated HF), aldosterone antagonists.	β-blockers must be used cautiously in decompensated HF and are contraindicated in cardiogenic shock. In HF, ARBs may be combined with the neprilysin inhibitor sacubitril.
Hypertension with diabetes mellitus	ACE inhibitors/ARBs, Ca ²⁺ channel blockers, thiazide diuretics, β-blockers.	ACE inhibitors/ARBs are protective against diabetic nephropathy. β-blockers can mask hypoglycemia symptoms.
Hypertension in asthma	ARBs, Ca ²⁺ channel blockers, thiazide diuretics, cardioselective β-blockers.	Avoid nonselective β-blockers to prevent β ₂ -receptor-induced bronchoconstriction. Avoid ACE inhibitors to prevent confusion between drug or asthma-related cough.
Hypertension in pregnancy	Nifedipine, methyldopa, labetalol, hydralazine.	New moms love hugs.

Cardiovascular agents and molecular targets



Calcium channel blockers	Amlodipine, clevidipine, nicardipine, nifedipine, nimodipine (dihydropyridines, act on vascular smooth muscle); diltiazem, verapamil (nondihydropyridines, act on heart).
MECHANISM	Block voltage-dependent L-type calcium channels of cardiac and smooth muscle → ↓ muscle contractility. Vascular smooth muscle—amlodipine = nifedipine > diltiazem > verapamil. Heart—verapamil > diltiazem > amlodipine = nifedipine.
CLINICAL USE	Dihydropyridines (except nimodipine): hypertension, angina (including vasospastic type), Raynaud phenomenon. Dihydropyridine mainly dilates arteries. Nimodipine: subarachnoid hemorrhage (prevents cerebral vasospasm). Nicardipine, clevidipine: hypertensive urgency or emergency. Nondihydropyridines: hypertension, angina, atrial fibrillation/flutter.
ADVERSE EFFECTS	Gingival hyperplasia. Dihydropyridine: peripheral edema, flushing, dizziness. Nondihydropyridine: cardiac depression, AV block, hyperprolactinemia (verapamil), constipation.

Hydralazine

MECHANISM	↑ cGMP → smooth muscle relaxation. Hydralazine vasodilates arterioles > veins; afterload reduction .
CLINICAL USE	Severe hypertension (particularly acute), HF (with organic nitrate). Safe to use during pregnancy. Frequently coadministered with a β-blocker to prevent reflex tachycardia.
ADVERSE EFFECTS	Compensatory tachycardia (contraindicated in angina/CAD), fluid retention, headache, angina, drug-induced lupus.

Hypertensive emergency

Nitroprusside	Short acting vasodilator (arteries = veins); ↑ cGMP via direct release of NO. Can cause cyanide toxicity (releases cyanide).
Fenoldopam	Dopamine D ₁ receptor agonist—coronary, peripheral, renal, and splanchnic vasodilation. ↓ BP, ↑ natriuresis. Also used postoperatively as an antihypertensive. Can cause hypotension, tachycardia, flushing, headache, nausea.

Nitrates

MECHANISM	Nitroglycerin, isosorbide dinitrate, isosorbide mononitrate.
CLINICAL USE	Vasodilate by ↑ NO in vascular smooth muscle → ↑ in cGMP and smooth muscle relaxation. Dilate veins >> arteries. ↓ preload.
ADVERSE EFFECTS	Angina, acute coronary syndrome, pulmonary edema.
	Reflex tachycardia (treat with β-blockers), methemoglobinemia, hypotension, flushing, headache, “Monday disease” in industrial nitrate exposure: development of tolerance for the vasodilating action during the work week and loss of tolerance over the weekend → tachycardia, dizziness, headache upon reexposure. Contraindicated in right ventricular infarction, hypertrophic cardiomyopathy, and with concurrent PDE-5 inhibitor use.

Antianginal therapy

Goal is reduction of myocardial O₂ consumption (MVO₂) by ↓ 1 or more of the determinants of MVO₂: end-diastolic volume, BP, HR, contractility.

COMPONENT	NITRATES	β-BLOCKERS	NITRATES + β-BLOCKERS
End-diastolic volume	↓	No effect or ↑	No effect or ↓
Blood pressure	↓	↓	↓
Contractility	↑ (reflex response)	↓	Little/no effect
Heart rate	↑ (reflex response)	↓	No effect or ↓
Ejection time	↓	↑	Little/no effect
MVO ₂	↓	↓	↓↓

Verapamil is similar to β-blockers in effect.

Ranolazine

MECHANISM	Inhibits the late phase of inward sodium current thereby reducing diastolic wall tension and oxygen consumption. Does not affect heart rate or blood pressure.
CLINICAL USE	Refractory angina.
ADVERSE EFFECTS	Constipation, dizziness, headache, nausea.

Sacubitril

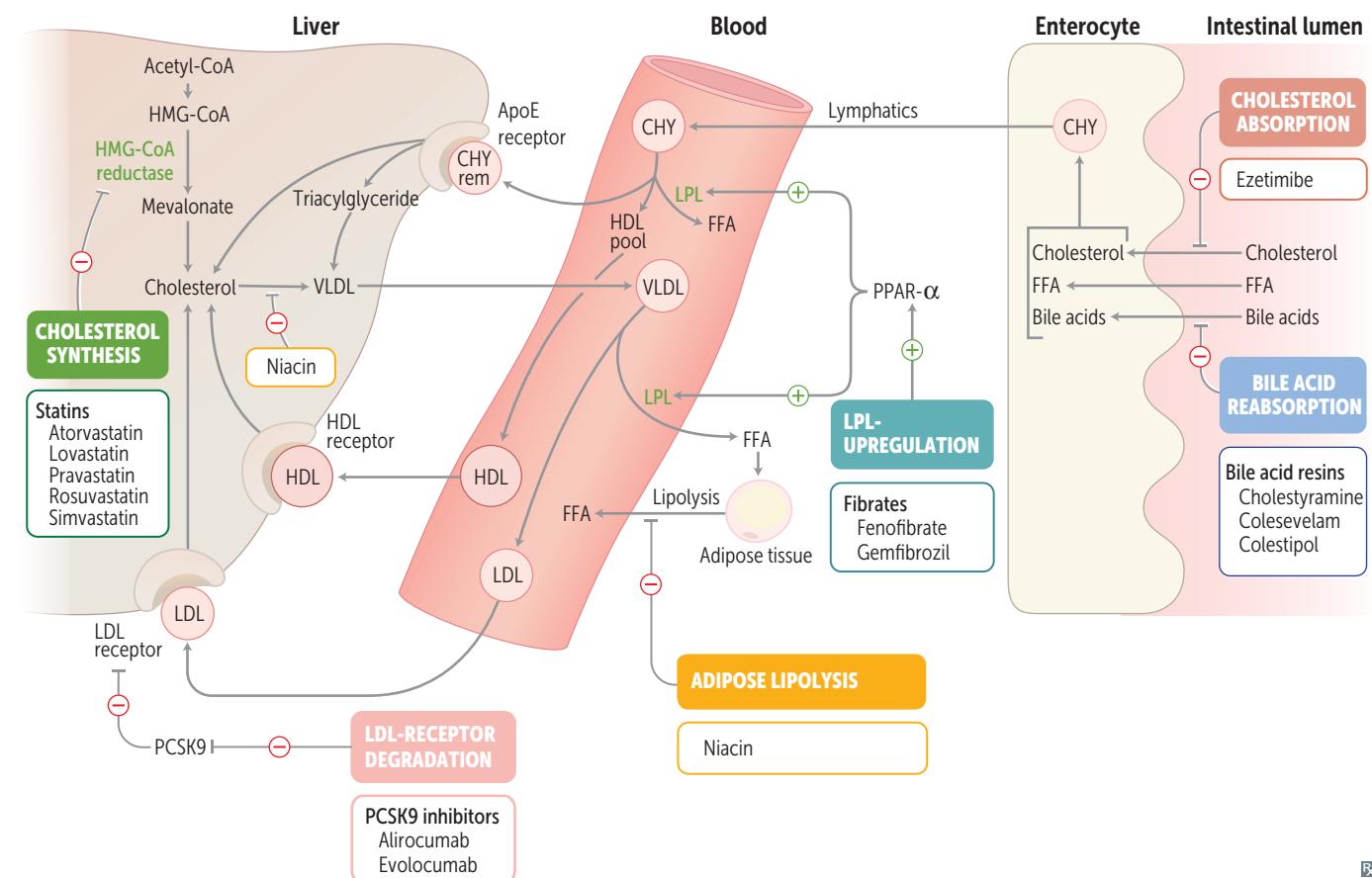
MECHANISM	A neprilysin inhibitor; prevents degradation of bradykinin, natriuretic peptides, angiotensin II, and substance P → ↑ vasodilation, ↓ ECF volume.
CLINICAL USE	Used in combination with valsartan (an ARB) to treat HFrEF.
ADVERSE EFFECTS	Hypotension, hyperkalemia, cough, dizziness; contraindicated with ACE inhibitors due to angioedema (both drugs ↑ bradykinin).

Lipid-lowering agents

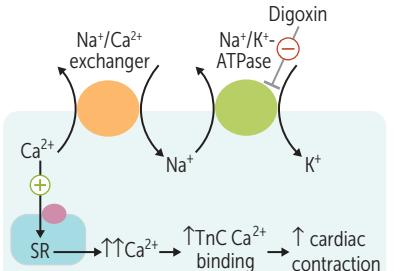
DRUG	LDL	HDL	TRIGLYCERIDES	MECHANISM	ADVERSE EFFECTS
Statins Atorvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin	↓↓	↑	↓	Inhibit HMG-CoA reductase → ↓ cholesterol synthesis; → ↓ intrahepatic cholesterol → ↑ LDL receptor recycling → ↑ LDL catabolism ↓ in mortality in patients with CAD	Hepatotoxicity (↑ LFTs), myopathy (especially when used with fibrates or niacin)
Bile acid resins Cholestyramine, colesevelam, colestipol	↓↓	↑ slightly	↑ slightly	Disrupt enterohepatic bile acid circulation → compensatory ↑ conversion of cholesterol to bile → ↓ intrahepatic cholesterol → ↑ LDL receptor recycling	GI upset, ↓ absorption of other drugs and fat-soluble vitamins
Ezetimibe	↓↓	↑/—	↓/—	Prevents cholesterol absorption at small intestine brush border	Rare ↑ LFTs, diarrhea

Lipid-lowering agents (continued)

DRUG	LDL	HDL	TRIGLYCERIDES	MECHANISM	ADVERSE EFFECTS
Fibrates Fenofibrate, gemfibrozil	↓	↑	↓↓↓	Activate PPAR- α → upregulate LPL → ↑ TG clearance Activate PPAR- α → induce HDL synthesis	Myopathy (↑ risk with statins), cholesterol gallstones (via inhibition of cholesterol 7 α -hydroxylase)
Niacin	↓↓	↑↑	↓	Inhibits lipolysis (hormone- sensitive lipase) in adipose tissue; reduces hepatic VLDL synthesis	Flushed face (prostaglandin mediated; ↓ by NSAIDs or long- term use) Hyperglycemia Hyperuricemia
PCSK9 inhibitors Alirocumab, evolocumab	↓↓↓	↑	↓	Inactivation of LDL-receptor degradation → ↑ removal of LDL from bloodstream	Myalgias, delirium, dementia, other neurocognitive effects
Fish oil and marine omega-3 fatty acids	↑ slightly	↑ slightly	↓ at high doses	Believed to decrease FFA delivery to liver and decrease activity of TG-synthesizing enzymes	Nausea, fishlike taste

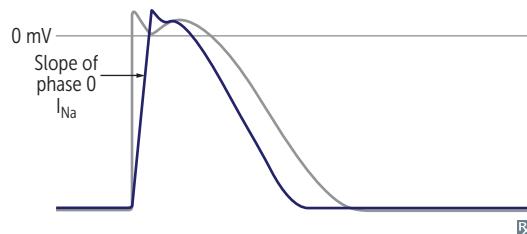
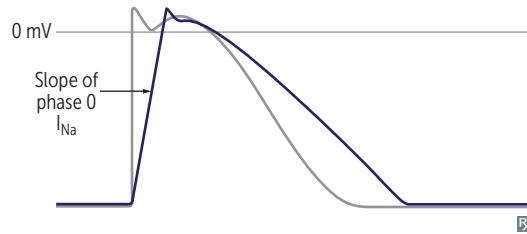


Digoxin

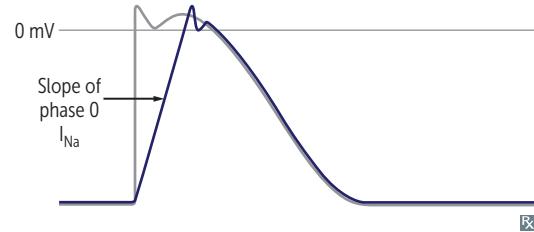
MECHANISM	<p>Direct inhibition of Na^+/K^+-ATPase. → indirect inhibition of $\text{Na}^+/\text{Ca}^{2+}$ exchanger. $\uparrow [\text{Ca}^{2+}]_i \rightarrow$ positive inotropy. Stimulates vagus nerve $\rightarrow \downarrow \text{HR}$.</p> 
CLINICAL USE	HF (\uparrow contractility); atrial fibrillation (\downarrow conduction at AV node and depression of SA node).
ADVERSE EFFECTS	<p>Cholinergic effects (nausea, vomiting, diarrhea), blurry yellow vision (“van Glow”), arrhythmias, AV block.</p> <p>Can lead to hyperkalemia, which indicates poor prognosis.</p> <p>Factors predisposing to toxicity: renal failure (\downarrow excretion), hypokalemia (permissive for digoxin binding at K^+-binding site on Na^+/K^+-ATPase), drugs that displace digoxin from tissue-binding sites, and \downarrow clearance (eg, verapamil, amiodarone, quinidine).</p>
ANTIDOTE	Slowly normalize K^+ , cardiac pacer, anti-digoxin Fab fragments, Mg^{2+} .

Antiarrhythmics—sodium channel blockers (class I)

Class IA	<p>Quinidine, procainamide, disopyramide. “The Queen proclaims Diso’s pyramid.”</p>
MECHANISM	Moderate Na^+ channel blockade. \uparrow AP duration, \uparrow effective refractory period (ERP) in ventricular action potential, \uparrow QT interval, some K^+ channel blocking effects.
CLINICAL USE	Both atrial and ventricular arrhythmias, especially reentrant and ectopic SVT and VT.
ADVERSE EFFECTS	Cinchonism (headache, tinnitus with quinidine), reversible SLE-like syndrome (procainamide), HF (disopyramide), thrombocytopenia, torsades de pointes due to \uparrow QT interval.
Class IB	<p>Lidocaine, phenytoin, mexiletine. “I’d Buy Liddy’s phine Mexican tacos.”</p>
MECHANISM	Weak Na^+ channel blockade. \downarrow AP duration. Preferentially affect ischemic or depolarized Purkinje and ventricular tissue.
CLINICAL USE	Acute ventricular arrhythmias (especially post-MI), digitalis-induced arrhythmias. IB is Best post-MI.
ADVERSE EFFECTS	CNS stimulation/depression, cardiovascular depression.

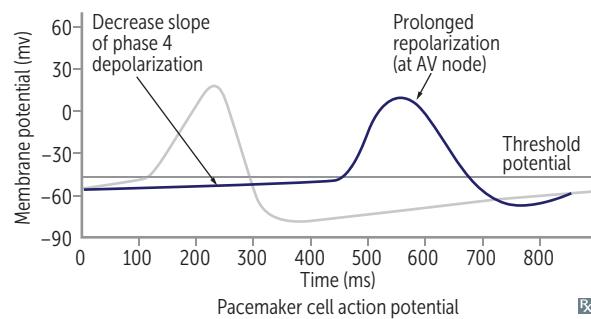


Antiarrhythmics—sodium channel blockers (class I) (continued)

Class IC	Flecainide, propafenone. “Can I have fries, please?”	
MECHANISM	Strong Na^+ channel blockade. Significantly prolongs ERP in AV node and accessory bypass tracts. No effect on ERP in Purkinje and ventricular tissue. Minimal effect on AP duration.	
CLINICAL USE	SVTs, including atrial fibrillation. Only as a last resort in refractory VT.	
ADVERSE EFFECTS	Proarrhythmic, especially post-MI (contraindicated). IC is Contraindicated in structural and ischemic heart disease.	

Antiarrhythmics— β -blockers (class II)

MECHANISM	Decrease SA and AV nodal activity by \downarrow cAMP, $\downarrow \text{Ca}^{2+}$ currents. Suppress abnormal pacemakers by \downarrow slope of phase 4. AV node particularly sensitive— \uparrow PR interval. Esmolol very short acting.
CLINICAL USE	SVT, ventricular rate control for atrial fibrillation and atrial flutter, prevent ventricular arrhythmia post-MI.
ADVERSE EFFECTS	Impotence, exacerbation of COPD and asthma, cardiovascular effects (bradycardia, AV block, HF), CNS effects (sedation, sleep alterations). May mask the signs of hypoglycemia. Metoprolol can cause dyslipidemia. Propranolol can exacerbate vasospasm in vasospastic angina. β -blockers (except the nonselective α - and β -antagonists carvedilol and labetalol) cause unopposed α_1 -agonism if given alone for pheochromocytoma or for cocaine toxicity (unsubstantiated). Treat β -blocker overdose with saline, atropine, glucagon.



Antiarrhythmics—potassium channel blockers (class III)

Amiodarone, Ibutilide, Dofetilide, Sotalol.

AIDS.

MECHANISM

↑ AP duration, ↑ ERP, ↑ QT interval.

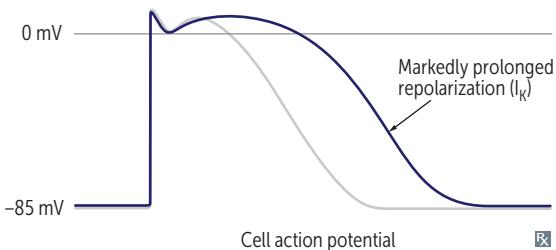
CLINICAL USE

Atrial fibrillation, atrial flutter; ventricular tachycardia (amiodarone, sotalol).

ADVERSE EFFECTS

Sotalol—torsades de pointes, excessive β blockade.
 Ibutilide—torsades de pointes.
 Amiodarone—pulmonary fibrosis, hepatotoxicity, hypothyroidism or hyperthyroidism (amiodarone is 40% iodine by weight), acts as hapten (corneal deposits, blue/gray skin deposits resulting in photodermatitis), neurologic effects, constipation, cardiovascular effects (bradycardia, heart block, HF).

Remember to check PFTs, LFTs, and TFTs when using amiodarone.
 Amiodarone is lipophilic and has class I, II, III, and IV effects.

**Antiarrhythmics—calcium channel blockers (class IV)**

Diltiazem, verapamil.

MECHANISM

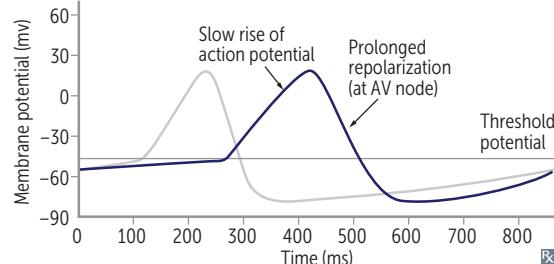
Decrease conduction velocity, ↑ ERP, ↑ PR interval.

CLINICAL USE

Prevention of nodal arrhythmias (eg, SVT), rate control in atrial fibrillation.

ADVERSE EFFECTS

Constipation, flushing, edema, cardiovascular effects (HF, AV block, sinus node depression).

**Other antiarrhythmics**

Adenosine

↑ K⁺ out of cells → hyperpolarizing the cell and ↓ I_{Ca}, decreasing AV node conduction. Drug of choice in diagnosing/terminating certain forms of SVT. Very short acting (~ 15 sec). Effects blunted by theophylline and caffeine (both are adenosine receptor antagonists). Adverse effects include flushing, hypotension, chest pain, sense of impending doom, bronchospasm.

Magnesium

Effective in torsades de pointes and digoxin toxicity.

Ivabradine

MECHANISM

IVabradine prolongs slow depolarization (phase “IV”) by selectively inhibiting “funny” sodium channels (I_f).

CLINICAL USE

Chronic HFrEF.

ADVERSE EFFECTS

Luminous phenomena/visual brightness, hypertension, bradycardia.