Congenital heart defects/diseases

Hereditary and congenital valvular diseases

Pathophysiology of heart failure

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Congenital heart defects/diseases (CHD)

*Emphasis on **hemodynamics**, **fetal–neonatal transition**, and "pattern recognition" across lesions*

Learning objectives

- Explain **fetal circulation** and the **neonatal transition** (changes in PVR/SVR, ductal closure). Explain how fetal→neonatal circulatory transition unmasks many CHDs.
- Classify CHD physiologically into **left-to-right shunts**, **right-to-left shunts**, **obstructive**, and **mixing** lesions, and explain the pathophysiology of each. Predict hemodynamics - whether a lesion causes **cyanosis**, **pulmonary overcirculation**, **heart failure**, or **shock** using pressure/flow logic.
- Recognize "duct-dependent" systemic vs pulmonary blood flow lesions and the consequences of ductal closure. Explain why **prostaglandin E1** can be lifesaving.
- Link lesion anatomy → pressure/flow changes → symptoms (cyanosis, heart failure, shock), key exam findings, and major complications. Describe the mechanisms of **Eisenmenger physiology** and why late cyanosis develops in some acyanotic lesions.

Congenital heart diseases (CHD)

Definition, Epidemiologic context

- structural or functional abnormalities of the heart / great vessels present at birth, arising during embryonic development
- not always clinically manifest immediately
- Incidence: ~8–10 / 1,000 live births, affect ~1% of births in the U.S. (~40,000/year), ≈1 in 4 babies with a heart defect has a critical CHD needing early intervention in the first year.
- Most common congenital malformations/developmental defects.
- Thanks to cardiac surgery and intensive care, most patients now survive into adulthood → growing population of GUCH (grown-up congenital heart disease).

Congenital heart diseases (CHD)

- Influence of genetics vs. environmental factors (e.g. TORCH infections, smoking, alcohol, etc.)
- Varying degree of clinical significance
- ➢ Clinically silent to life-threatening conditions
- Most common CHD:
- ➢ Ventricular septal defect (35.6%), atrial defect (15.4%), patent ductus arteriosus (10.2%)
- ➢ Tetralogy of Fallot (4.4%), transposition of the great arteries (TGA; 3.9%), tricuspid atresia (approx. 1–2%)

TORCH = group of congenital infections (Toxoplasmosis, Others, Rubella, Cytomegalovirus, Herpes simplex)

Hemodynamic classification

Category	Cyanosis	Shunt
Acyanotic with L→R shunt	No	Yes
Cyanotic with R→L shunt	Yes	Yes
Acyanotic without shunt	No	No

Congenital heart diseases (CHD)
Classification

Acyanotic

No shunt

- Aortic stenosis
- Pulmonary artery stenosis*
- Coarctation of the aorta
- Abnormal cardiac position *(ectopia cordis and dextrocardia)*

Left-to-right shunt

- Ventricular septal defect (VSD)
- Atrial septal defect (ASD)
- Patent ductus arteriosus (PDA; ductus arteriosus of Botallo)
- Atrioventricular septal defect (AVSD)
- Partial anomalous pulmonary venous return (PAPVR)
- Lutembacher syndrome

* usually acyanotic, but in severe cases it may lead to cyanosis (if an atrial septal defect is present)

Congenital heart diseases (CHD)
Classification

Cyanotic

Right-to-left shunt

- Tetralogy of Fallot
- Transposition of the great arteries (vessels)
- Ebstein anomaly
- Hypoplastic left heart syndrome
- Pulmonary atresia
- Truncus arteriosus
- Tricuspid atresia
- Single functional ventricle
- Interruption of the aortic arch
- *Eisenmenger syndrome**

** usually not a congenital anomaly, but included in the classification because of the shunt mechanism

A simple diagnostic/physiology framework you repeat throughout

Step 1 — "Where is blood going that it shouldn't?"

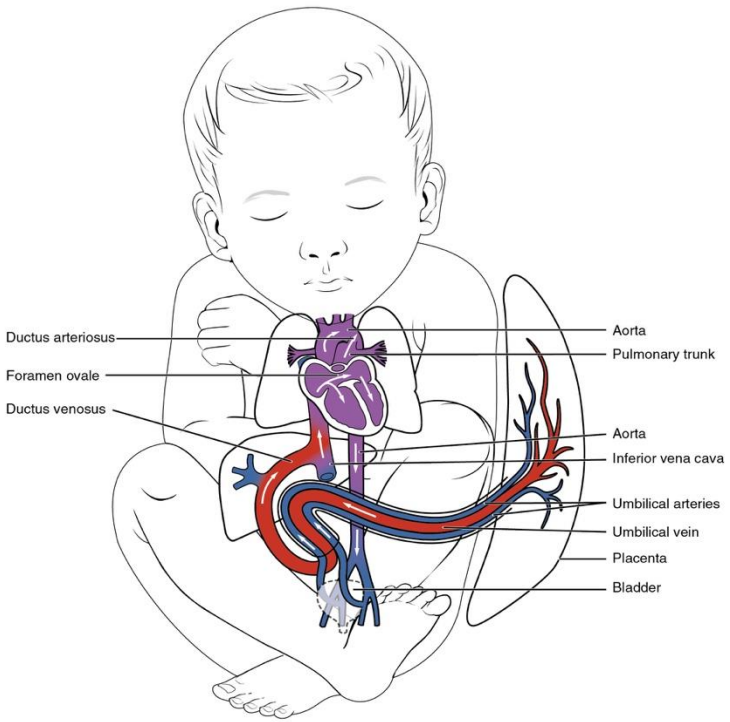
- **Shunt**: L→R or R→L (direction depends on relative pressures/resistances).
- **Obstruction**: outflow limitation → upstream pressure overload, downstream hypoperfusion.
- **Mixing**: parallel circulations or obligatory mixing → systemic oxygen content depends on mixing fraction.

Step 2 — "What happens when PVR falls and the ductus closes?"

- Falling **PVR** after birth **increases L→R shunting** (more pulmonary flow → heart failure over weeks).
- Closing **ductus arteriosus** can cause **shock/collapse** in duct-dependent lesions (hours–days).

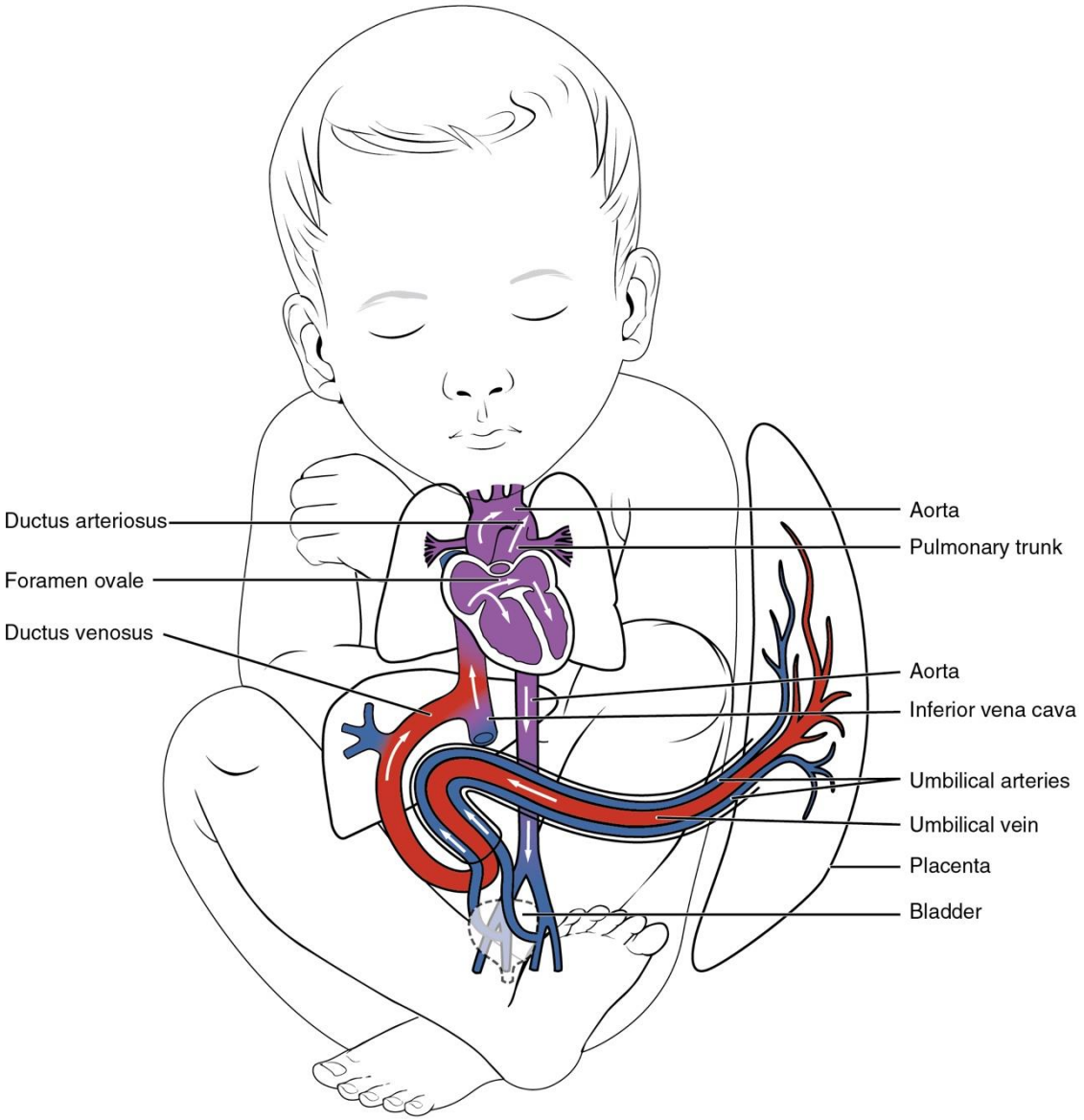
Fetal circulation: high PVR, placenta as oxygenator

- In utero: lungs are fluid-filled → PVR is high → minimal pulmonary blood flow.
- Placenta is the low-resistance oxygenator; umbilical venous blood is the most oxygenated.
- Most RV output bypasses lungs via the ductus arteriosus (DA) into the descending aorta.

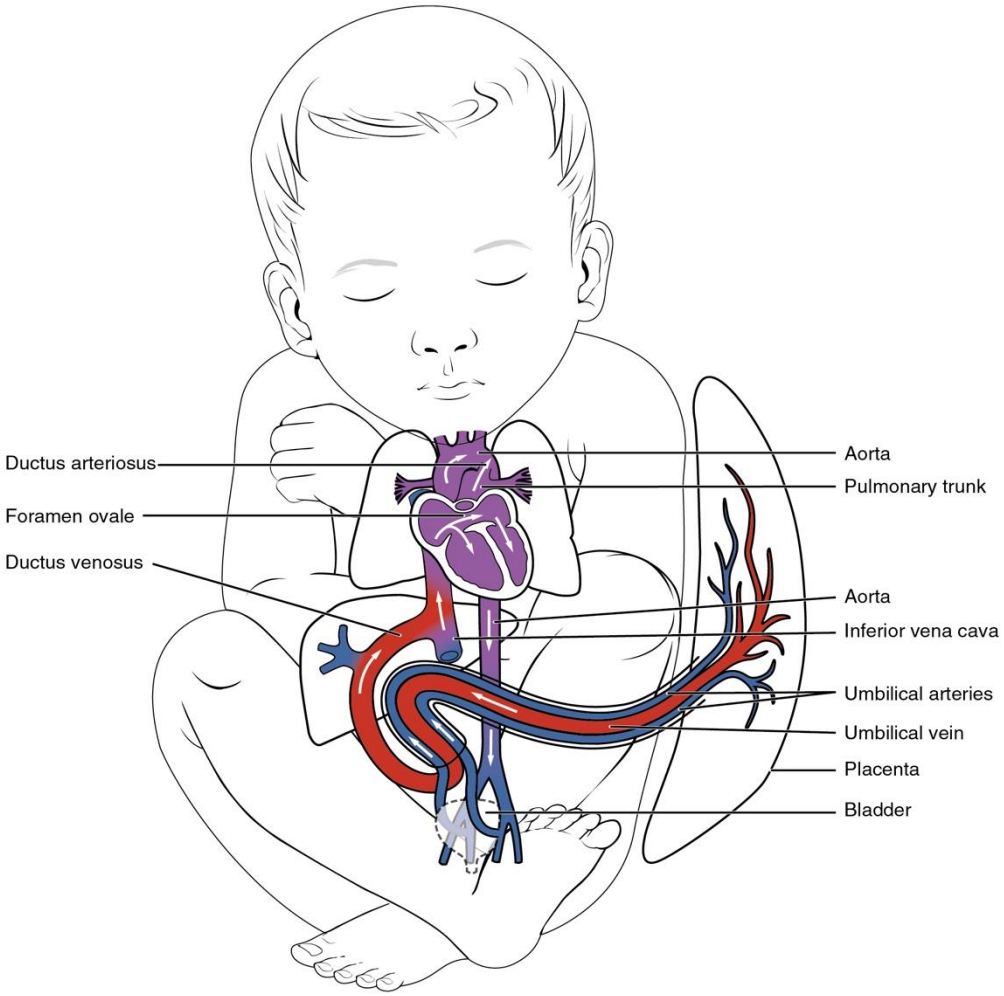


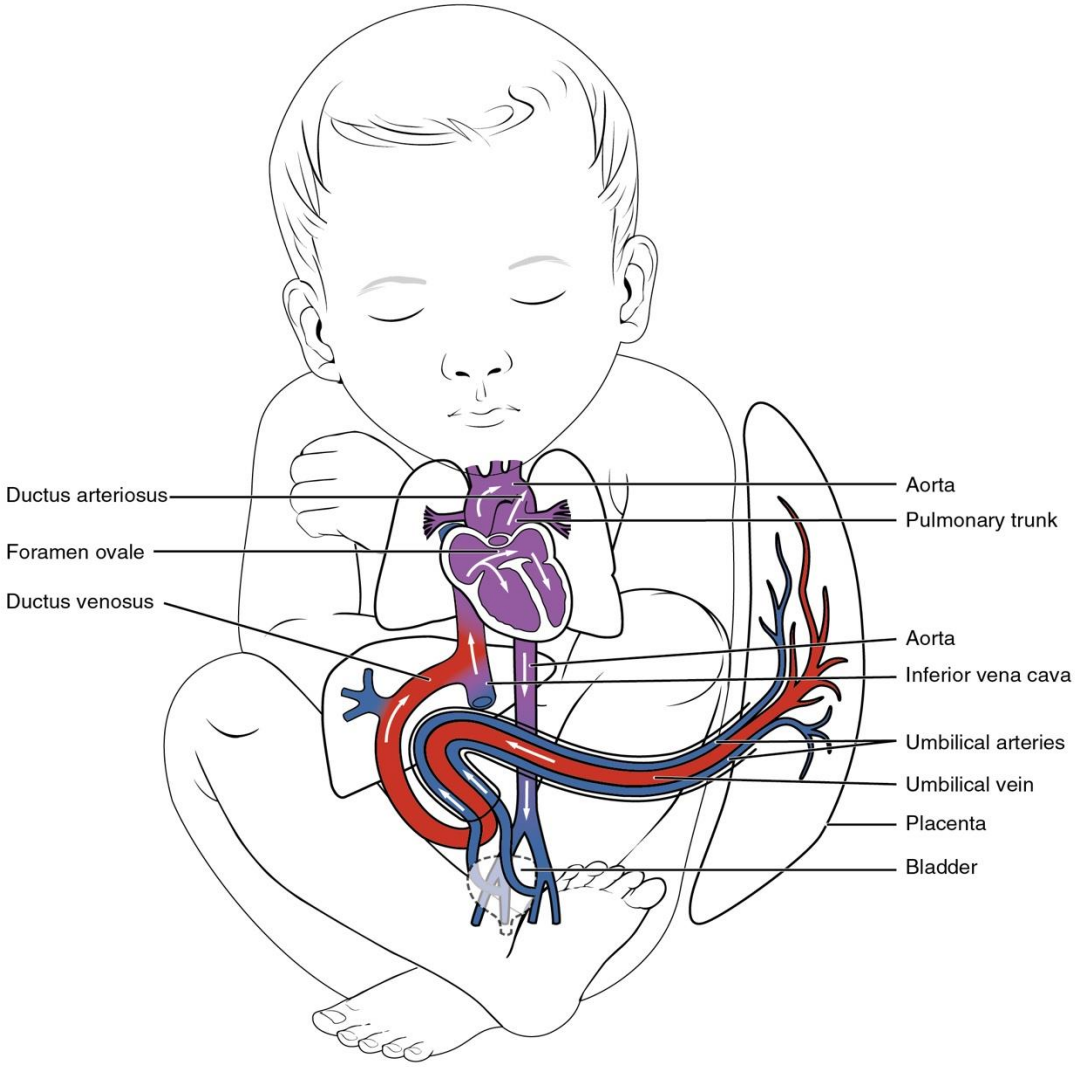
Fetal circulation schematic

Key fetal shunts and their function

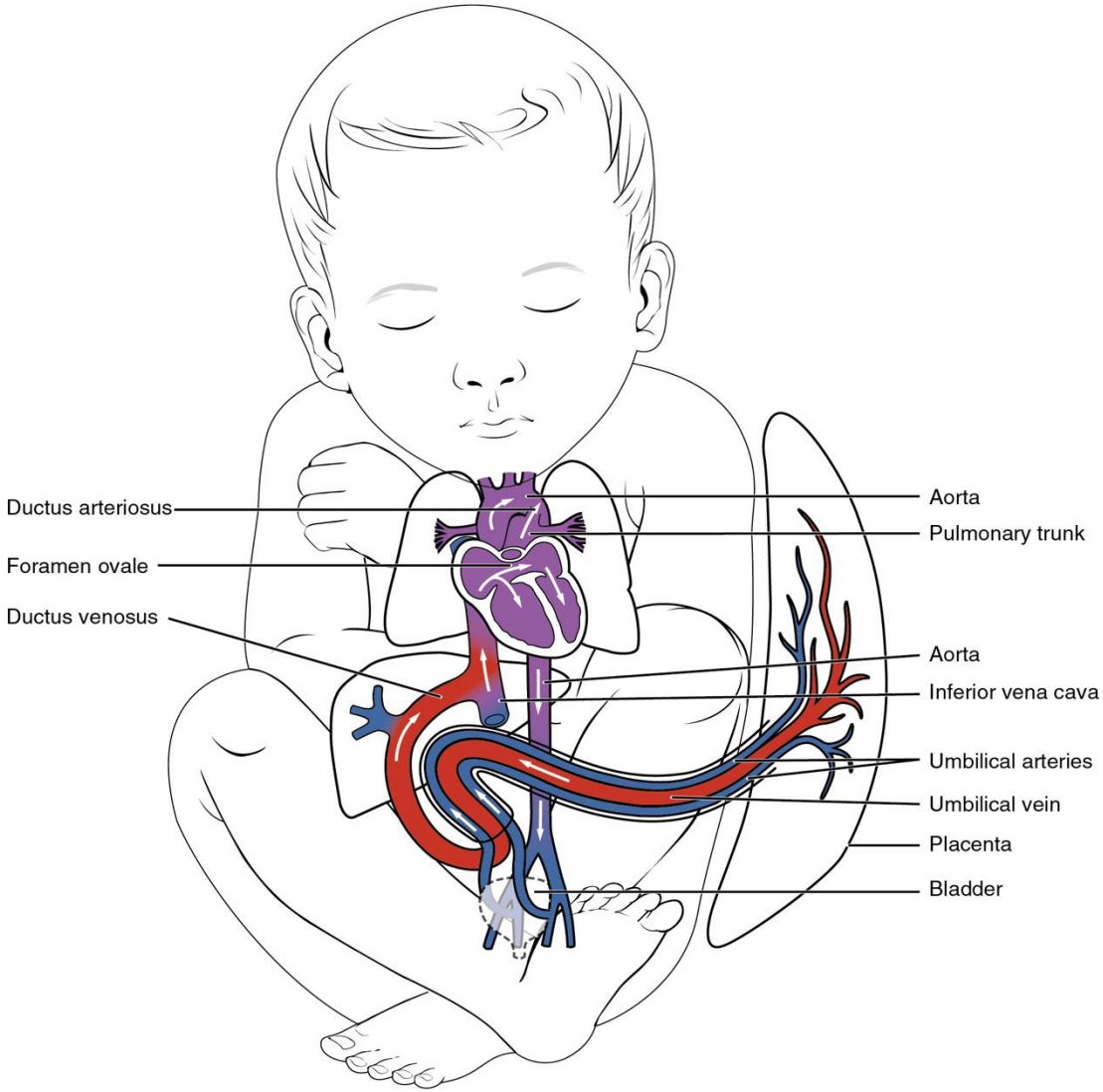


- **Foramen ovale (FO)**: RA→LA stream to supply LV/brain.
  A vital fetal heart structure allowing oxygenated blood to shunt directly from the RA to the LA, bypassing non-functional lungs to supply the LV and brain. In the fetus, this flap-like opening enables high-oxygen blood from the placenta to reach the brain first.





- **Ductus arteriosus (DA)**: PA→aorta (bypasses lungs).
  A vital fetal blood vessel *connecting the main pulmonary artery (PA) directly to the descending aorta,* allowing oxygen-rich blood to bypass non-functional, fluid-filled lungs. It directs RV output to the systemic circulation, closing shortly after birth to become the ligamentum arteriosum.



- **Ductus venosus**: umbilical vein→IVC.

  A vital fetal vascular shunt *connecting the umbilical vein directly to the inferior vena cava (IVC),* allowing oxygenated, nutrient-rich placental blood to bypass the liver and flow to the heart and brain.

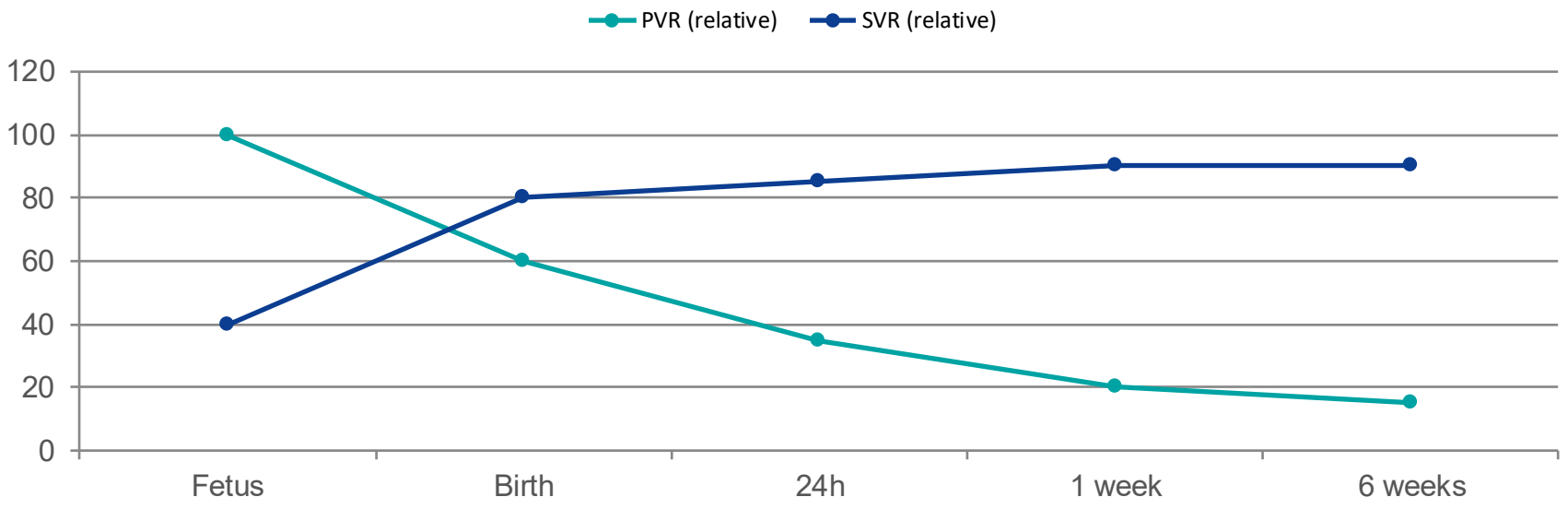
What changes at birth
(the "resistance flip")

- First breaths → **PVR falls sharply**.
- Cord clamping removes placenta → **SVR rises**.
- LA pressure rises; RA pressure falls.
- FO closes functionally due to LA>RA.
- DA constricts with higher O_2 tension + lower prostaglandins.

Birth transition: the resistance flip

Foundation

Key idea: after the first breaths and cord clamping, PVR falls while SVR rises → shunt directions change.



Clinical consequence

- Weeks: falling PVR increases L→R shunts → heart failure
- Days: ductal constriction may unmask duct-dependent lesions → shock/collapse

Fetal circulation → neonatal transition

Fetal circulation essentials

- **High PVR**, **low SVR** (placenta).
- Parallel circulation with three shunts:
  - **Foramen ovale (FO):** RA → LA (bypasses lungs)
  - **Ductus arteriosus (DA):** PA → aorta (bypasses lungs)
  - **Ductus venosus (DV):** umbilical vein → IVC

At birth

- First breaths → **↓PVR** (pulmonary vasodilation).
- Clamping cord → **↑SVR** (placenta removed).
- LA pressure rises → FO functional closure.
- ↑PaO_2 and ↓PGE_2 → DA constriction (functional closure within ~1–2 days; anatomic later).

Closure physiology: FO and DA

- FO closes functionally when LA pressure exceeds RA pressure after PVR falls and pulmonary venous return rises.
- DA constricts in response to increased PaO_2 and reduced prostaglandins; functional closure typically occurs within the first day in term infants.
- Anatomic DA closure completes later (days–weeks); preterm infants often have delayed closure.

Two predictable vulnerability windows

- Hours–days: ductus constricts → duct-dependent lesions can present with sudden cyanosis or shock.
- Weeks: PVR continues to fall → L→R shunts increase → pulmonary overcirculation and heart failure.
- Later months–years: chronic pulmonary overcirculation can remodel pulmonary arterioles → pulmonary hypertension.

"Days = ductus" "Weeks = PVR drop"

The exact timing varies, but the pattern is robust clinically.

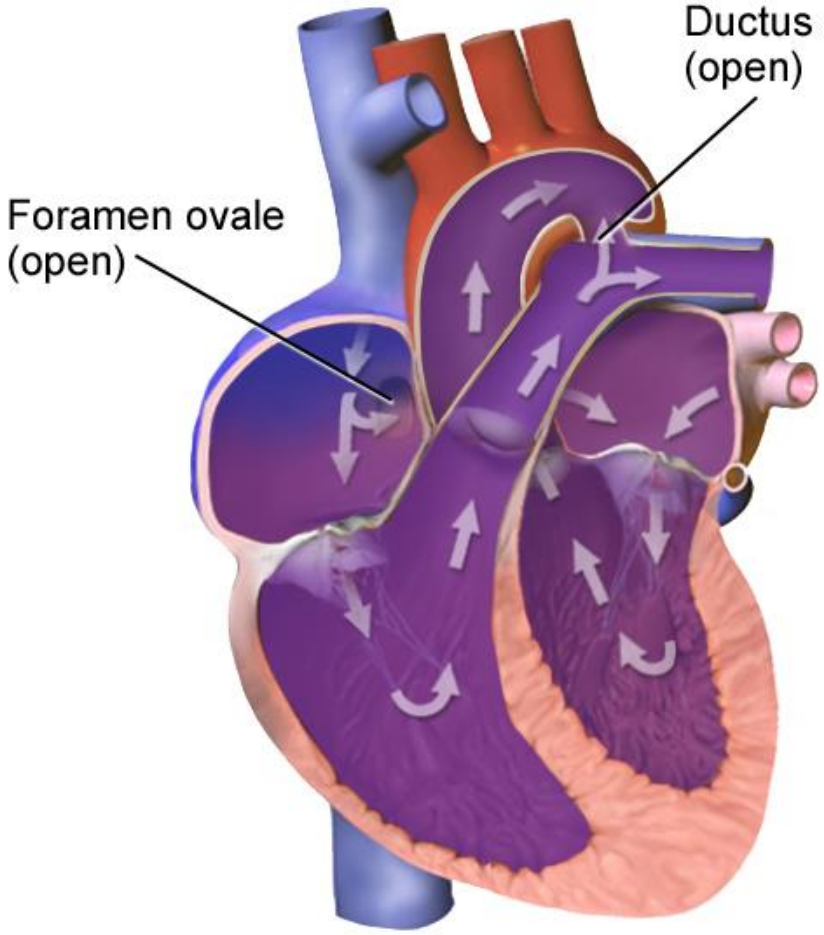
Fetal circulation → neonatal transition

Clinical translation

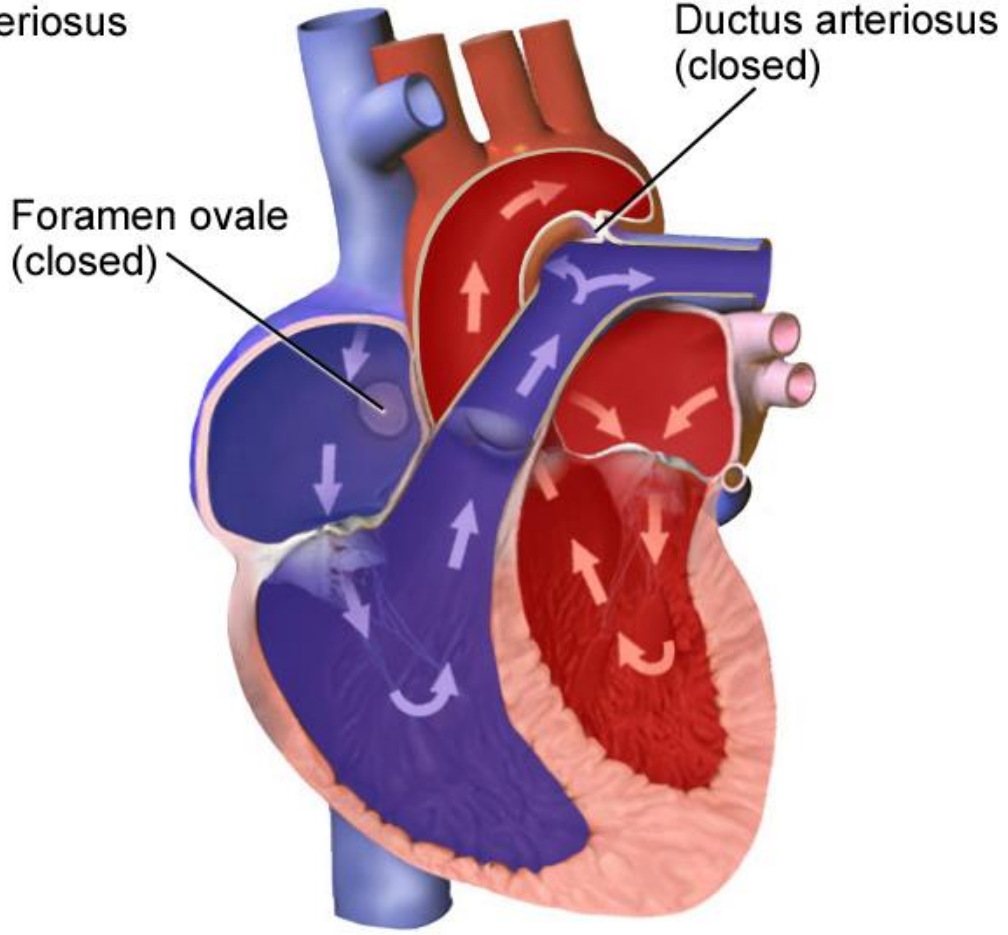
- Lesions that rely on **DA patency** deteriorate when DA closes (often **24–72 hours**):
  - **Systemic outflow obstruction** (e.g., HLHS, critical coarctation, critical AS)
  - **Pulmonary outflow obstruction** (e.g., pulmonary atresia, critical PS)
  - **Parallel circulations needing mixing** (e.g., TGA)

HLHS, hypoplastic left heart syndrome

Fetal Heart



Newborn Heart

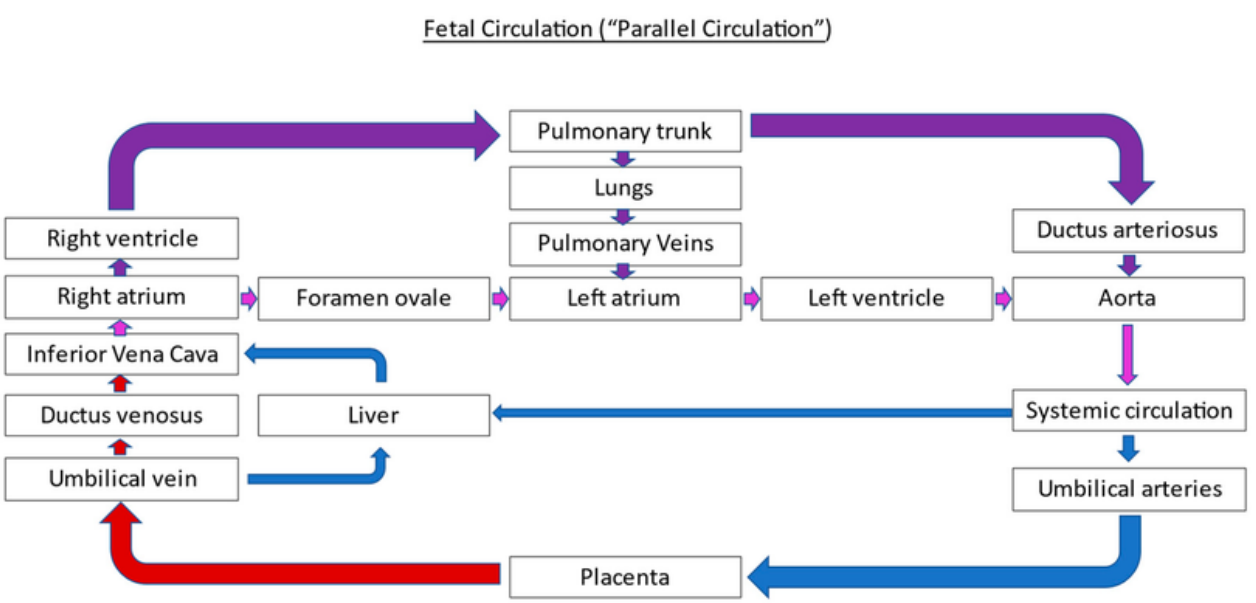


Key postnatal changes

- **FO closes** → atrial septum intact
- **DA closes** → pulmonary & systemic circulations fully separated
- **Pulmonary vascular resistance ↓**, systemic resistance ↑

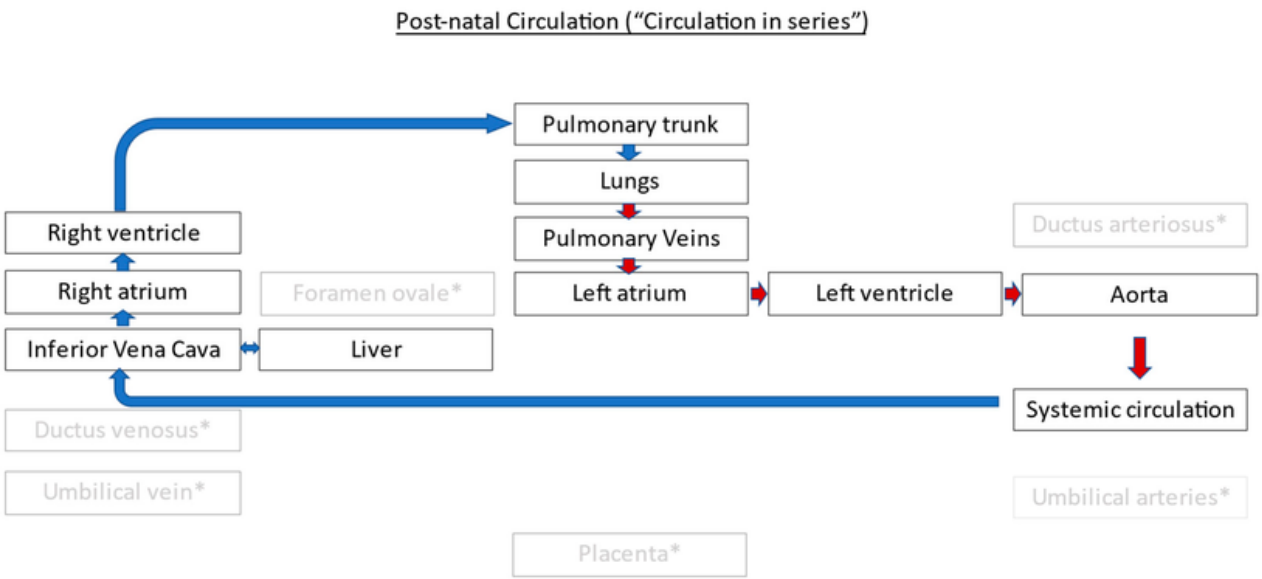
→ circulation becomes **strictly in series**

A



*Fetal circulation is **parallel**, not serial: **FO** shunts oxygenated blood to the left heart, while **DA** bypasses the lungs into the systemic circulation.*

B



*Fetal structures (in gray) disappears after birth

Obstructive lesions: unifying pathophysiology

Obstruction

- Obstruction increases upstream pressure load (hypertrophy) and reduces downstream flow (hypoperfusion).
- Obstruction limits forward flow → pressure overload proximal to obstruction and hypoperfusion distal to it.
- Severe neonatal obstruction may be duct-dependent (systemic or pulmonary flow relies on DA).
- Clinical pattern: cool extremities, weak pulses, poor perfusion, acidosis; murmur may be soft if flow is low.
- Ductal closure can convert “compensated” → **cardiogenic shock**.

- Set up: coarctation = systemic obstruction; pulmonary stenosis/atresia = pulmonary obstruction.

- low flow → quiet murmur; don’t be reassured by a soft auscultation.

Duct-dependent lesions: memorize the two groups

Duct dependence

- Duct-dependent systemic blood flow: HLHS, critical AS, severe coarctation/interrupted arch.
- Duct-dependent pulmonary blood flow: pulmonary atresia, critical PS, severe TOF variants.
- When uncertain in a sick neonate, assume duct-dependence until proven otherwise.

Physiology of decompensation when the ductus closes

Duct dependence

- Systemic duct-dependent lesions: DA closure → Qs↓ → shock, acidosis, end-organ injury.
- Pulmonary duct-dependent lesions: DA closure → Qp↓ → profound cyanosis and hypoxemia.
- Prostaglandin E1 maintains ductal patency and can be life-saving in duct-dependent CHD (the medication's purpose is to restore the bypass pathway until definitive intervention).

“Age of presentation”

- **Hours–days**: duct-dependent lesions, severe obstruction, TGA.
- **Weeks–months**: VSD/PDA/AVSD HF.
- **Years**: ASD, mild obstruction, late Eisenmenger.

atrioventricular septal defect (AVSD)
Transposition of the Great Arteries (TGA)

Volume vs pressure overload *(remodeling logic)*

- **Cyanosis concept**
  - Cyanosis = **arterial desaturation**, usually from **R→L shunt or mixing** (not “lung disease” by default).
- **Pulmonary overcirculation concept**
  - High pulmonary flow → pulmonary venous return ↑ → LA/LV volume overload → HF symptoms.

- **Volume overload** (e.g., L→R shunts) → chamber dilation → increased wall stress → heart failure over time.
- **Pressure overload** (e.g., AS/PS/CoA) → hypertrophy → reduced compliance → limited stroke volume.
- Severe disease can be “quiet” because low flow generates little turbulence (murmur paradox).

Hemodynamics in one line: Q = ΔP / R

- **Shunt magnitude depends on the pressure gradient and the resistance downstream.**
- After birth: decreased PVR lowers downstream resistance → increases L→R shunting (if a connection exists).
- In obstruction: effective resistance rises → flow drops to the downstream bed (hypoperfusion).

- **low systemic flow → acidosis, poor pulses;**
- **high pulmonary flow → tachypnea and poor feeding.**

https://www.merckmanuals.com/professional/pediatrics/perinatal-physiology/perinatal-physiology

Take home message

- Same symptom, different anatomy → physiology helps you triage correctly (cyanosis vs shock vs heart failure).
- Many lesions are silent in utero; presentation begins when PVR changes and the ductus constricts.
- A small set of rules predicts most bedside findings: shunt direction, Qp:Qs balance, and duct dependence.

Qp:Qs is the ratio of pulmonary to systemic blood flow, with a 1:1 ratio indicating balanced circulation. In neonatal congenital heart disease, maintaining this balance is crucial; a ratio >1 indicates excessive pulmonary flow (left-to-right), while <1 indicates inadequate flow (right-to-left). Duct-dependent lesions require a patent ductus arteriosus (PDA) for survival, relying on prostaglandins to prevent closure and maintain necessary pulmonary or systemic perfusion.

Acyanotic CHD without shunt

Acyanotic CHD without shunt

Key features

- No abnormal communication between chambers/vessels
- No mixing of oxygenated and deoxygenated blood
- Systemic arterial oxygen saturation **normal**
- Main problem = **obstruction to blood flow**

Obstruction → ↑ afterload → pressure overload → concentric hypertrophy → eventual dysfunction

Acyanotic CHD without shunt

Classification

Left-sided obstructive lesions

1. Aortic stenosis (valvular, subvalvular, supravalvular)
2. Coarctation of the aorta

Right-sided obstructive lesions

3. Pulmonary stenosis

Acyanotic CHD without shunt

Left-sided obstructive lesions

Aortic stenosis

- Definition: Obstruction to **left ventricular outflow** at:
  - **Valvular** (most common; often bicuspid valve)
  - **Subvalvular** (membrane)
  - **Supravalvular** (e.g., Williams syndrome)

Acyanotic CHD without shunt

Left-sided obstructive lesions

Aortic stenosis

Pathophysiology:

- Narrowed outflow → ↑ LV systolic pressure
- **Pressure overload** of LV
- **Concentric LV hypertrophy**
- Initially preserved cardiac output
- Later:
  - Diastolic dysfunction
  - Myocardial ischemia
  - LV failure
- **No shunt → no cyanosis**

Acyanotic CHD without shunt

Left-sided obstructive lesions

Aortic stenosis

Hemodynamic consequences

- ↑ LV systolic pressure
- Normal or ↓ stroke volume
- ↓ coronary perfusion (esp. during exertion)

Acyanotic CHD without shunt

Left-sided obstructive lesions

Aortic stenosis

Clinical presentation:

- Depends on severity:
  - Asymptomatic (mild)
  - Exertional dyspnea
  - Angina
  - Syncope
  - Sudden cardiac death (rare but exam-favorite)
- **Classic triad (older children/adolescents)**
  1. Chest pain
  2. Syncope
  3. Dyspnea

Acyanotic CHD without shunt

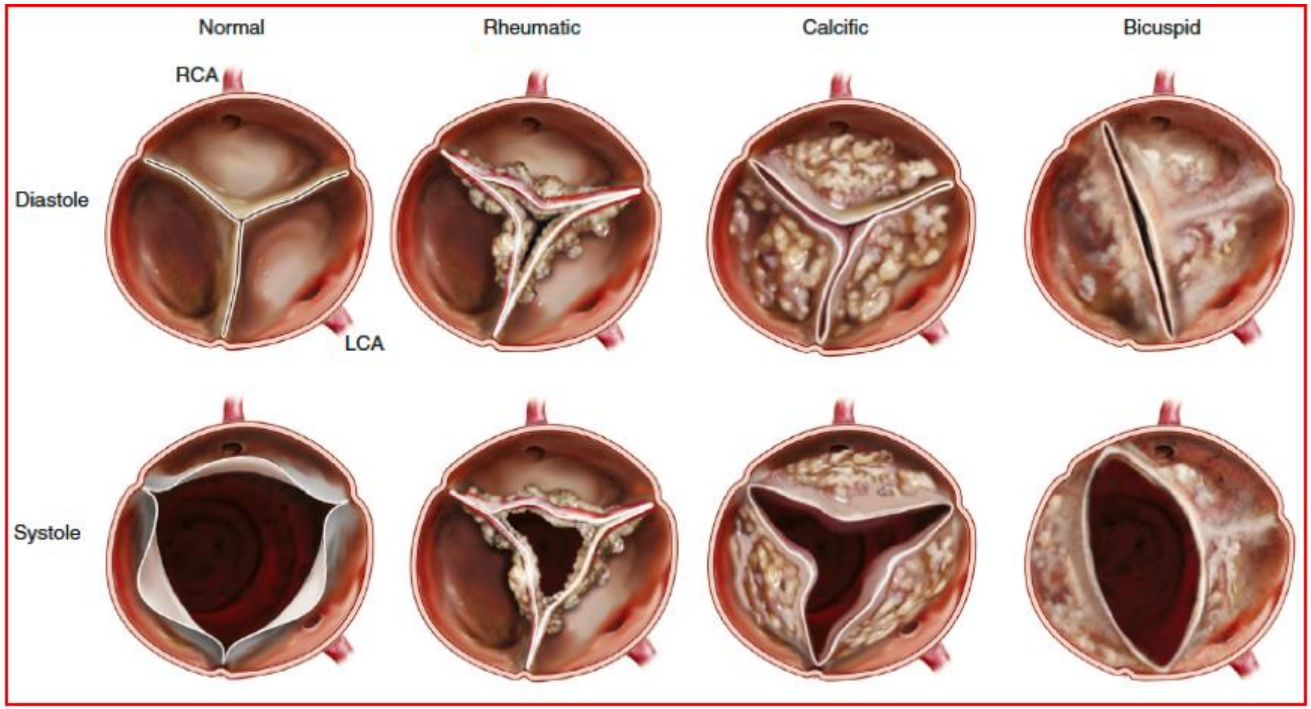
Left-sided obstructive lesions

Aortic stenosis

Physical findings

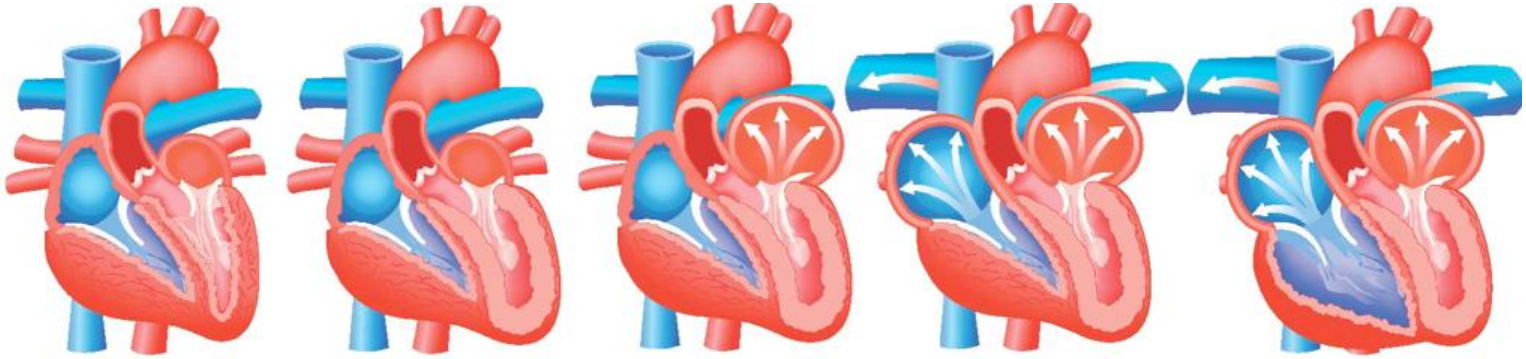
- Harsh **crescendo–decrescendo systolic murmur**
- Right upper sternal border
- Radiates to carotids
- Slow-rising pulse (pulsus parvus et tardus)

- **Pressure overload → concentric hypertrophy**
- Bicuspid aortic valve = common cause
- Risk of **infective endocarditis**



Aortic stenosis etiology: morphology of calcific AS, bicuspid valve, and rheumatic AS (Adapted from C. Otto, Principles of Echocardiography, 2017).

https://recapem.com/wp-content/uploads/2023/07/Aortic-stenosis-etiology.png



Stages/Criteria	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No Cardiac Damage	LV Damage	LA or Mitral Damage	Pulmonary Vasculature or Tricuspid Damage	RV Damage
Echocardiogram		Increased LV Mass Index >115 g/m² (Male) >95 g/m² (Female)	Indexed left atrial volume >34mL/m²	Systolic Pulmonary hypertension ≥60 mmhg	Moderate-Severe right ventricular dysfunction
		E/e' >14	Moderate-Severe mitral regurgitation	Moderate-Severe tricuspid regurgitation	
		LV Ejection Fraction <50%	Atrial Fibrillation		

Cardiac stratification of aortic stenosis based on the extent of cardiac damage. LA, left atrial; LV, left ventricular; RV, right ventricular. PMID: 29020232

https://recapem.com/wp-content/uploads/2023/07/aortic-stenosis-pathophysiology.png

Acyanotic CHD without shunt

Left-sided obstructive lesions

Coarctation of the aorta

Definition:

- Congenital narrowing of the aorta, usually:
  - Just distal to the **left subclavian artery**
  - Near the **ductus arteriosus**

Acyanotic CHD without shunt

Left-sided obstructive lesions

Coarctation of the aorta

Pathophysiology:

- Obstruction to systemic flow (typically near DA insertion)
- ↑ pressure proximal to narrowing
- ↓ pressure distal to narrowing
- LV pressure overload → LV hypertrophy

Hemodynamic consequences:

- **Upper body hypertension**
- **Lower body hypoperfusion**
- Collateral circulation via intercostal arteries

Acyanotic CHD without shunt

Left-sided obstructive lesions

Coarctation of the aorta

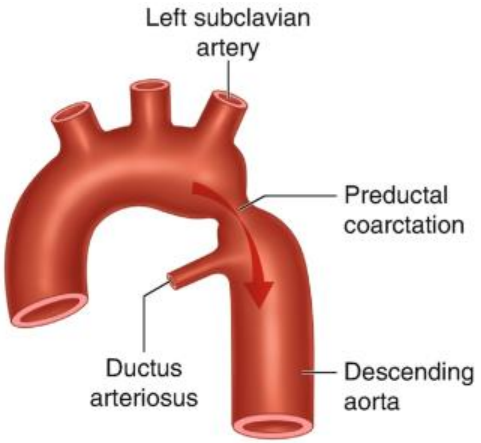
Clinical forms

Infantile (preductal)

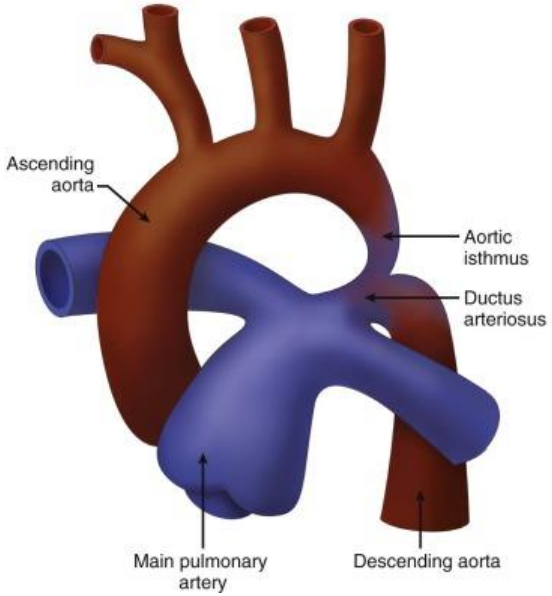
- Severe obstruction
- Duct-dependent systemic circulation
- Heart failure when ductus closes

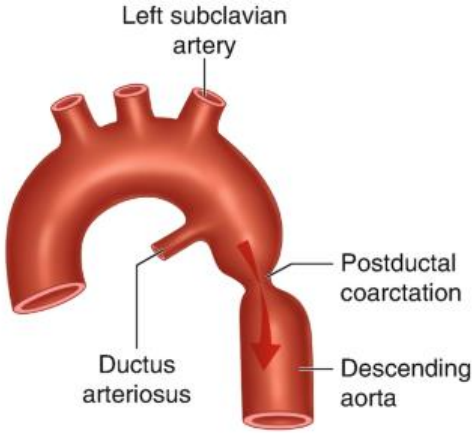
Adult (postductal)

- Often asymptomatic early
- Detected by BP discrepancy



Preductal coarctation





Postductal coarctation

Upravené podľa:
https://media.springernature.com/lw685/springer-static/image/chp%3A10.1007%2F978-3-030-55660-0_20/MediaObjects/331590_1_En_20_Fig9_HTML.png
https://radiologykey.com/wp-content/uploads/2019/09/f020-001-9781416031727.jpg

Acyanotic CHD without shunt

Left-sided obstructive lesions

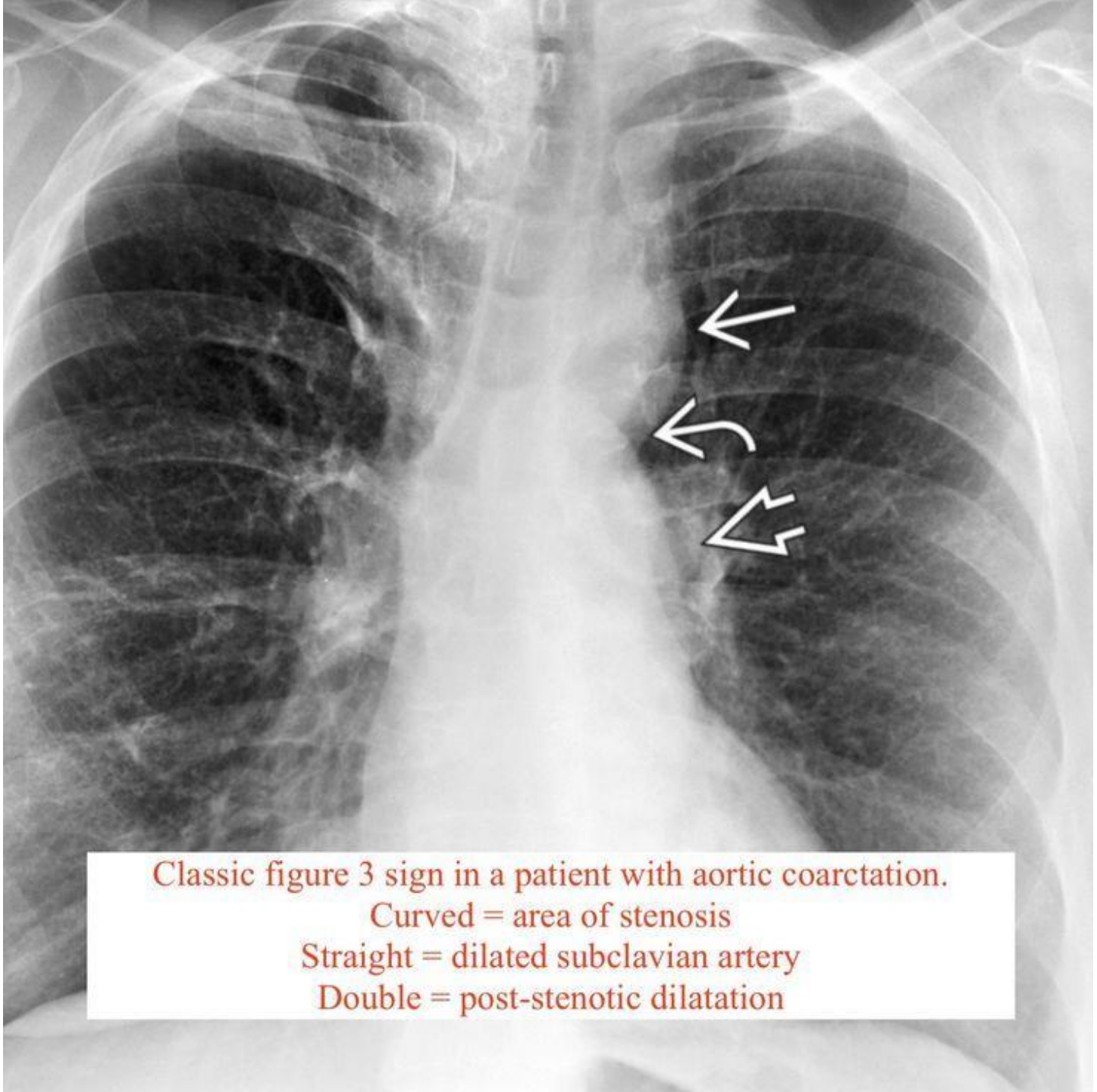
Coarctation of the aorta

Key clinical signs:

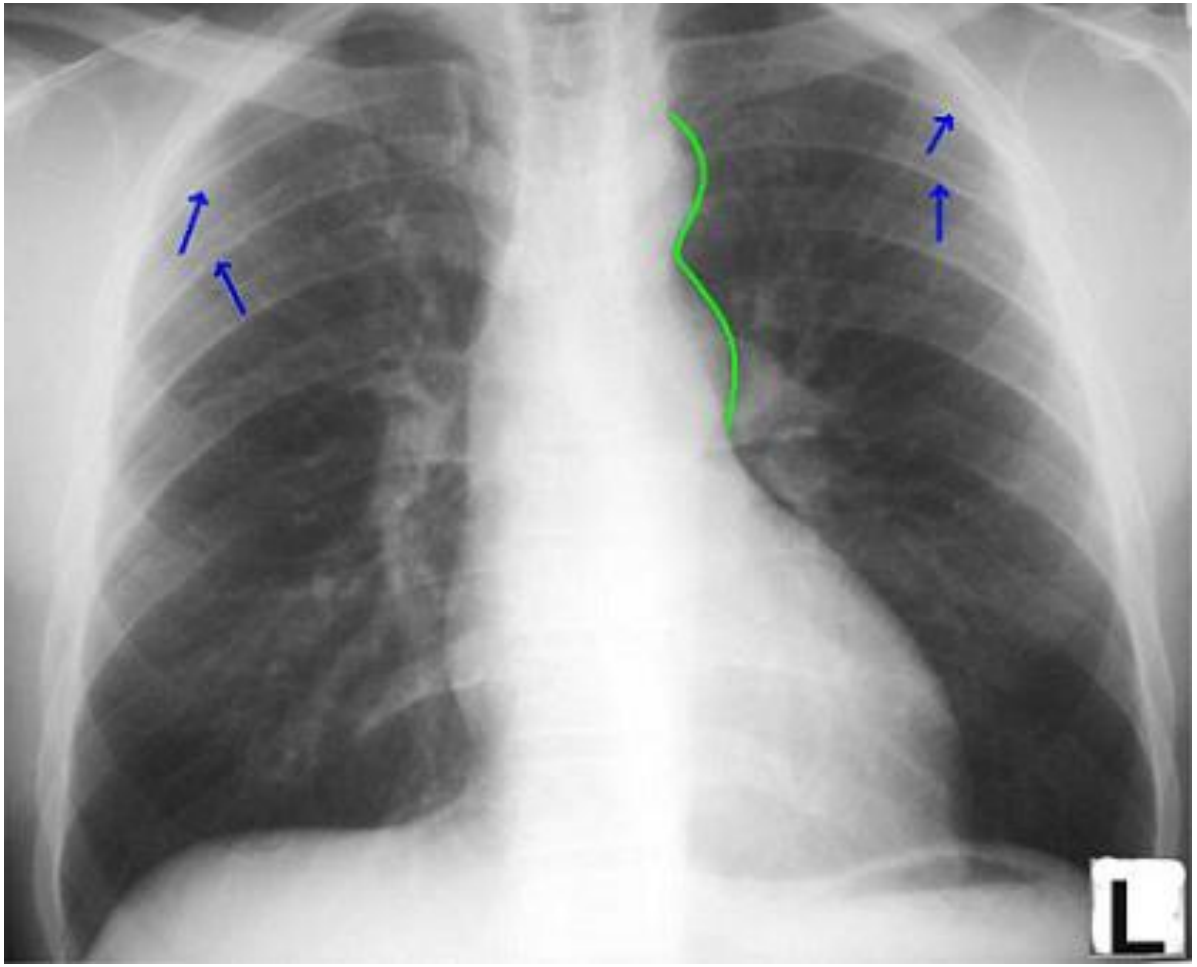
- **BP higher in arms than legs**
- Weak or delayed femoral pulses
- Headache, epistaxis
- Leg fatigue or claudication

Imaging & pathognomonic signs

- Rib notching (collaterals)
- “Figure of 3” sign on chest X-ray



Classic figure 3 sign in a patient with aortic coarctation.
Curved = area of stenosis
Straight = dilated subclavian artery
Double = post-stenotic dilatation



Symptom "3" on X-ray (green line), arrows indicate rib notching (development of collateral circulation)

https://www.wikidoc.org/images/c/cd/COA_x-ray_labeled.jpg

Acyanotic CHD without shunt

Left-sided obstructive lesions

Coarctation of the aorta

Associations:

- Bicuspid aortic valve
- Turner syndrome
- Berry aneurysms (risk of SAH)

Think **coarctation** if:

- Young patient + hypertension
- Weak femoral pulses

Acyanotic CHD without shunt

Right-sided obstructive lesions

Pulmonary stenosis

Definition

- Obstruction to **right ventricular outflow**

Types:

- Valvular (most common)
- Subvalvular
- Supravalvular

Acyanotic CHD without shunt

Right-sided obstructive lesions

Pulmonary stenosis

Pathophysiology:

- RV outflow obstruction
- ↑ RV systolic pressure
- **RV pressure overload**
- RV hypertrophy
- Still **acyanotic** (no shunt)

Acyanotic CHD without shunt

Right-sided obstructive lesions

Pulmonary stenosis

Hemodynamic consequences:

- Reduced pulmonary blood flow
- RV hypertrophy
- Severe cases → RV failure

Pressure overload → concentric RV hypertrophy

Cyanosis only if associated shunt develops (e.g., PFO)

Acyanotic CHD without shunt

Right-sided obstructive lesions

Pulmonary stenosis

Clinical presentation:

- Often asymptomatic (mild)
- Exertional dyspnea
- Fatigue
- Severe neonatal PS → critical illness

Physical findings

- Systolic ejection murmur at left upper sternal border
- Ejection click
- Wide split S2

Acyanotic CHD without shunt

Lesion	Ventricle affected	Overload	Key consequence
Aortic stenosis	LV	Pressure	LV hypertrophy
Coarctation	LV	Pressure	Systemic HTN
Pulmonary stenosis	RV	Pressure	RV hypertrophy

Summary

- Acyanotic non-shunt lesions = **obstructive lesions**
- Main mechanism = **pressure overload**
- Leads to **concentric hypertrophy**
- Oxygenation remains normal
- Symptoms result from ↓ cardiac output or ↑ pressures

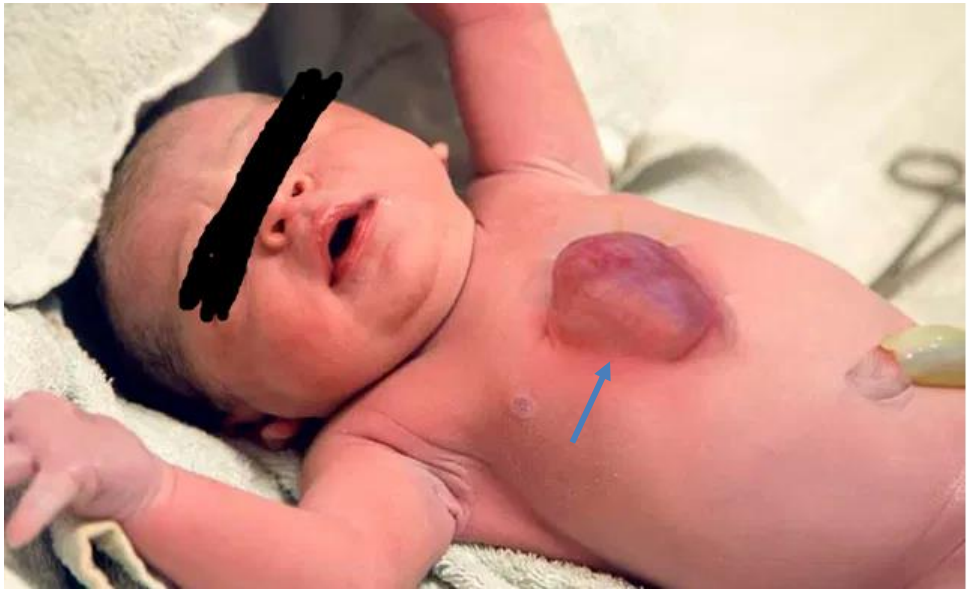
Abnormal positions of the heart

Ectopia cordis

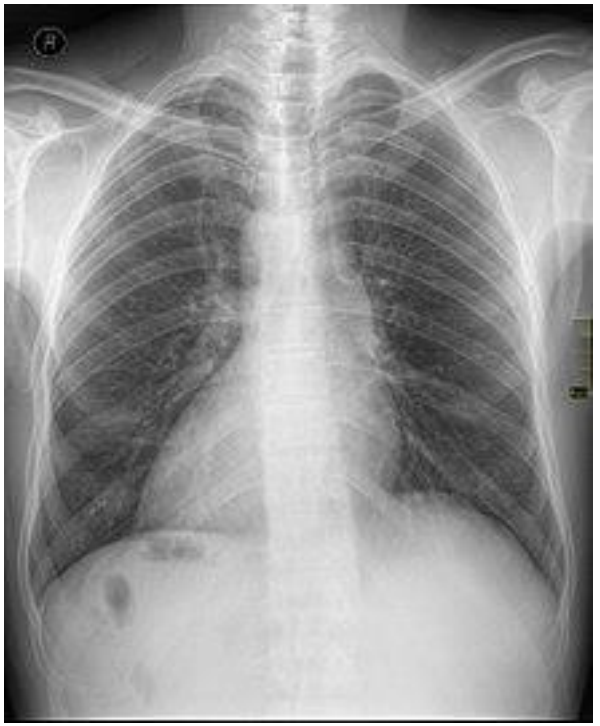
- A rare anomaly in which the heart develops outside the thoracic cavity – 1 in 8,000,000 live births
  - Neck, chest, abdominal cavity
- Prognosis depends mainly on the presence of other congenital malformations (multiple malformations)

Dextrocardia

- A malformation with the apex oriented to the right – 1 in 12,000 live births
- May/may not be a change in organ placement (possibly presence/absence of other CHD)
- Technical dextrocardia – incorrect placement of electrodes on the ECG (left leads above the right ventricle, etc.)



Ectopia cordis



Dextrocardia, situs inversus

https://image.tuasaude.com/media/article/js/ib/tratamento-para-ectopia-cordis_31884.jpg
https://upload.wikimedia.org/wikipedia/commons/thumb/d/d7/Situs_inversus_chest_Nevit.jpg/330px-Situs_inversus_chest_Nevit.jpg

https://www.youtube.com/watch?v=5dOdN6SUBcM

HTTPS://WWW.YOUTUBE.COM/WATCH?V=E9K6UZ1UIDM

Acyanotic CHD: Left-to-right shunts (flow lesions)

Congenital heart diseases (CHD)
Classification

Acyanotic

No shunt

- Aortic stenosis
- Pulmonary artery stenosis*
- Coarctation of the aorta
- Abnormal cardiac position *(ectopia cordis and dextrocardia)*

Left-to-right shunt

- Ventricular septal defect (VSD)
- Atrial septal defect (ASD)
- Patent ductus arteriosus (PDA; ductus arteriosus of Botallo)
- Atrioventricular septal defect (AVSD)
- Partial anomalous pulmonary venous return (PAPVR)
- Lutembacher syndrome

* usually acyanotic, but in severe cases it may lead to cyanosis (if an atrial septal defect is present)

L-R shunt

Unifying mechanism

- Driving force is **pressure gradient**: systemic side > pulmonary side → L→R shunt.
- Consequences depend on **shunt size** and **PVR**.

Why symptoms are delayed in many L→R lesions

- Immediately after birth, **PVR is still relatively high** → less shunt.
- As **PVR falls over weeks**, shunt increases → pulmonary overcirculation → CHF.

- *Oxygenated blood recirculates to lungs → Qp↑ → pulmonary venous return↑.*
- *Downstream effect: LA/LV volume overload (except ASD early, which loads the right heart).*
- *Symptoms emerge as PVR falls: tachypnea, diaphoresis with feeds, poor weight gain, hepatomegaly.*

Pathophysiology sequence

- **Pulmonary overcirculation** → tachypnea, recurrent infections, failure to thrive
- **Volume load**:
  - ASD → **RA/RV dilation**
  - VSD/PDA → **LA/LV dilation**
- Persistent high flow/pressure to lungs → **pulmonary vascular remodeling** → **pulmonary hypertension**
- If pulmonary vascular resistance surpasses systemic: **shunt reversal** → **Eisenmenger** (late cyanosis)

A) ASD

- a CHD characterized by a hole in the wall (septum) between the heart's upper chambers, causing oxygen-rich blood to leak back into the oxygen-poor blood chambers
- Usually small pressure gradient, more a **compliance** issue (LA slightly higher pressure).
- Net L→R occurs because **RV is more compliant** than LV.
- Effects: **RA/RV volume overload**, increased pulmonary flow, fixed split S2.
- Eisenmenger is **uncommon** compared to large VSD/PDA (but possible in large/unrepaired defects).

ASD: why it's often late-presenting

L→R shunts

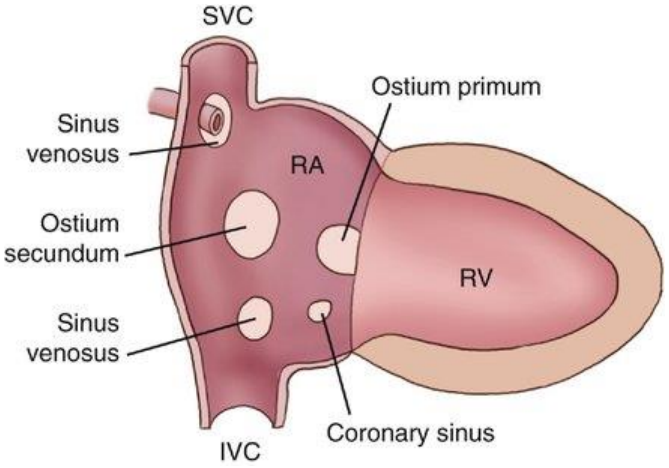
- Usually a low-pressure shunt at atrial level → gradual RV volume overload.
- Fixed split S2: increased RV stroke volume prolongs RV ejection (fixed split S2 is due to persistently increased RV flow, not respiration)
- Pulmonary vascular disease is uncommon in childhood unless defect is large/untreated for years (symptoms often appear with exercise intolerance or arrhythmias later)

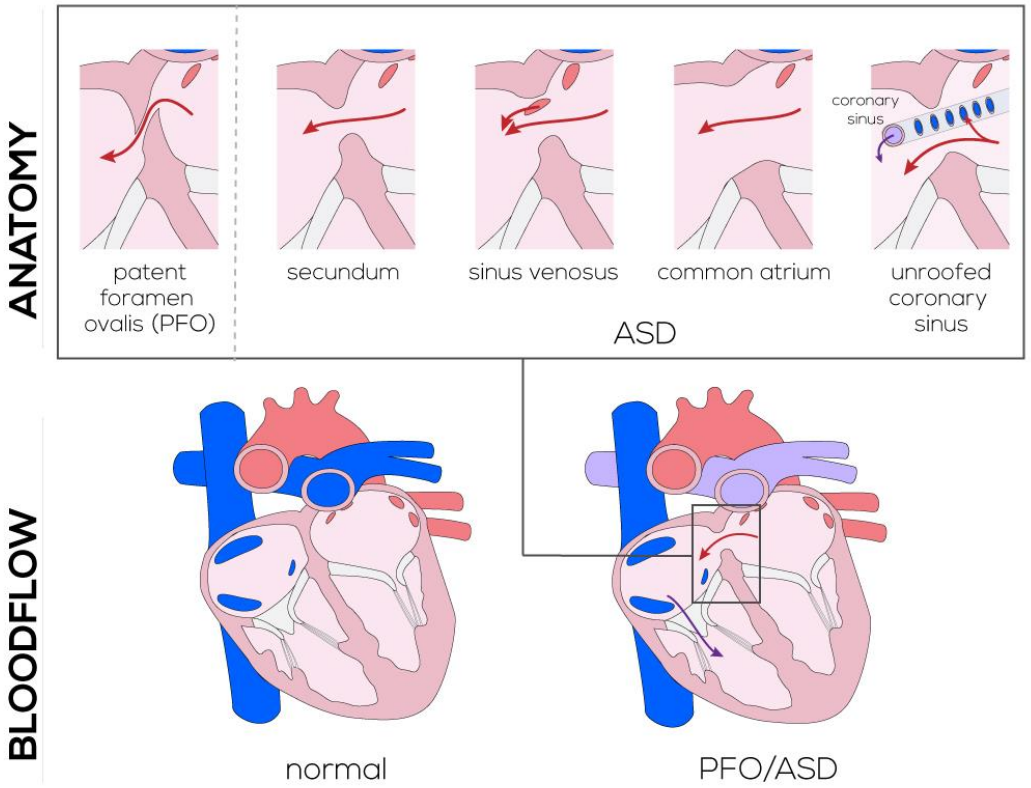
https://www.merckmanuals.com/professional/pediatrics/congenital-cardiovascular-anomalies/atrial-septal-defect-asd

ASD - classification

- According to location and relationship to ostium primum/secundum
- Ostium secundum defect (80%)
- Ostium primum defect (15–20%)
- Sinus venosus defect (5–6%)
- Coronary sinus defect (<1%)

- A defect is considered significant if the ratio Qp/Qs is >1.5





https://radiologykey.com/wp-content/uploads/2016/01/B9781416056690000045_f004-001-9781416056690.jpg
https://www.vhlab.umn.edu/atlas/congenital-defects-tutorial/septal-defects/graphics/ASD-2016.jpg

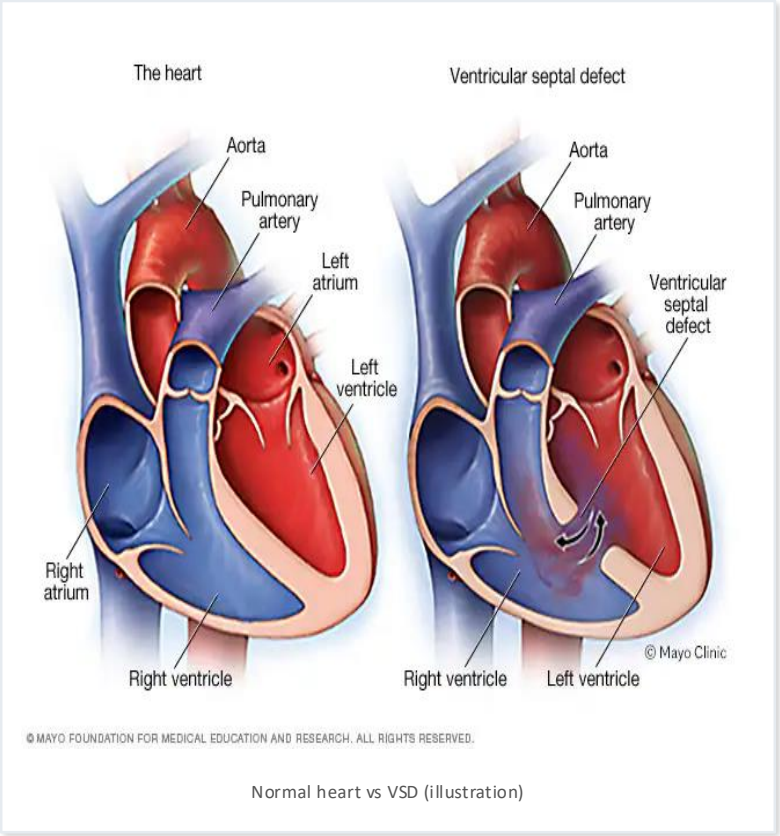
B) VSD

- a defect in the ventricular septum
- the most prevalent congenital cardiac anomaly in children and the second most common heart defect in adults
- **Small VSD:** high velocity jet → loud holosystolic murmur; minimal symptoms.
- **Large VSD:** equalization of LV/RV pressures → large flow driven by relative systemic vs pulmonary resistances.
  - As PVR drops: major L→R → **CHF** (weeks), pulmonary edema.
  - Long term: pulmonary HTN → Eisenmenger.

VSD: timing and the murmur paradox

L→R shunts

- Shunt size depends on VSD size + relative SVR/PVR (downstream resistances).
- Large VSD: early murmur may be soft (low gradient); later, as PVR falls, L→R increases → HF symptoms.
- Chronic large shunt → pulmonary vascular remodeling → pulmonary hypertension → possible Eisenmenger reversal.
- Case: weeks-old infant with HF signs—VSD should be high on the list. The loudness of the murmur does not equal severity -- it correlates with turbulence/gradient.



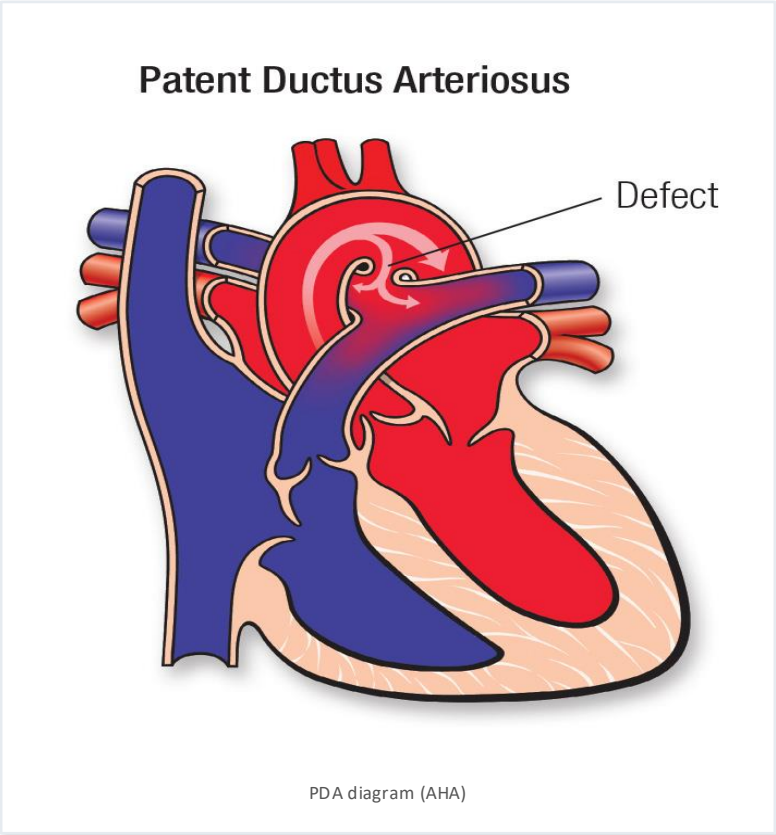
Normal heart vs VSD (illustration)

- *https://www.mayoclinic.org/diseases-conditions/ventricular-septal-defect/multimedia/ventricular-septal-defect/img-20007973*
- *https://www.msdmanuals.com/professional/pediatrics/congenital-cardiovascular-anomalies/ventricular-septal-defect-vsd*

C) PDA

L→R shunts

- Connection between aorta and pulmonary artery persists after birth.
- In term infants, typical direction is L→R: aortic pressure drives flow into PA throughout systole and diastole → "continuous" murmur.
- Large PDA: pulmonary overcirculation + wide pulse pressure; with severe pulmonary HTN, shunt can become bidirectional/R→L (differential cyanosis).
- differential cyanosis concept: lower extremities may be more cyanotic if DA carries desaturated blood into descending aorta
- *neonatal transition: DA normally constricts within the first days of life.*



PDA diagram (AHA)

- *https://www.heart.org/-/media/Images/Health-Topics/Congenital-Heart-Defects/50_1683_42_PDA.jpg*
- *https://www.ncbi.nlm.nih.gov/sites/books/NBK430758/*

PDA: continuous shunt physiology

- After birth aorta pressure > PA pressure → **aorta → PA** shunt.
- "Runoff" lowers diastolic pressure → **wide pulse pressure**, bounding pulses.
- Large PDA → LA/LV volume overload + pulmonary overcirculation.
- Special note: In some lesions, PDA is **beneficial/necessary** (ductal-dependent), not "bad."

D) AVSD

- Atrioventricular Septal Defect (AVSD), or endocardial cushion defect, is a congenital heart condition where holes exist between the heart's atria and ventricles, often accompanied by a single, malformed valve instead of two. It causes oxygen-rich and oxygen-poor blood to mix and forces the heart to work harder.
- Combined atrial + ventricular level communication + AV valve regurgitation → large effective shunt.
- Combined atrial and ventricular level shunting → early large pulmonary overcirculation, early pulmonary HTN.
- High pulmonary blood flow develops early as PVR falls → **early heart failure and pulmonary hypertension risk.**
- Strong association with trisomy 21; recognize because early management hinges on physiology (Qp↑).

Pulmonary hypertension and Eisenmenger: the late flip

L→R shunts

- Chronic Qp↑ injures pulmonary arterioles → vascular remodeling → PVR rises.
- When PVR exceeds SVR, shunt can reverse (R→L) → cyanosis, erythrocytosis, end-organ complications.
- Prevention is timing: close large shunts before irreversible pulmonary vascular disease develops.

- irreversibility - once fixed pulmonary vascular disease is established, closure can be harmful.
- Keep management minimal; focus on pathophysiology and timing of remodeling.

E) Lutembacher syndrome

- a rare, complex cardiac condition characterized by the combination of an atrial septal defect (ASD)—usually congenital—and mitral stenosis (MS), which is typically acquired.
- It causes abnormal blood flow between heart chambers, leading to right heart overload, pulmonary hypertension, and heart failure symptoms.
- Treatment involves surgical or percutaneous closure of the defect and repair of the mitral valve

Eisenmenger syndrome

- **late complication of congenital heart defects with left-to-right shunt, in which irreversible pulmonary hypertension occurs and subsequent reversal of the shunt (right-to-left)**
- **Typically occurs with:**
  - **VSD (most common),**
  - **ASD,**
  - **PDA,**
  - **AV septal defects.**

Eisenmenger syndrome

- 1️⃣ **Initial left-right shunt**
- **After birth, systemic pressure is higher than pulmonary.**
- **Blood flows from the left side of the heart to the right → increased flow through the pulmonary circulation.**
- **The lungs are exposed to:**
- **high flow,**
- **increased pressure,**
- **high shear stress for a long time.**
- 👉 **Clinically: the patient is initially acyanotic.**

- 2️⃣ **Pulmonary vascular remodeling**
- **Chronic overload leads to progressive pulmonary vascular disease:**
- **smooth muscle hypertrophy,**
- **intimal hyperplasia,**
- **fibrosis,**
- **narrowing to obliteration of arterioles.**
- ➡️ **Pulmonary vascular resistance (PVR) increases.**
- **This process is gradually irreversible.**

Eisenmenger syndrome

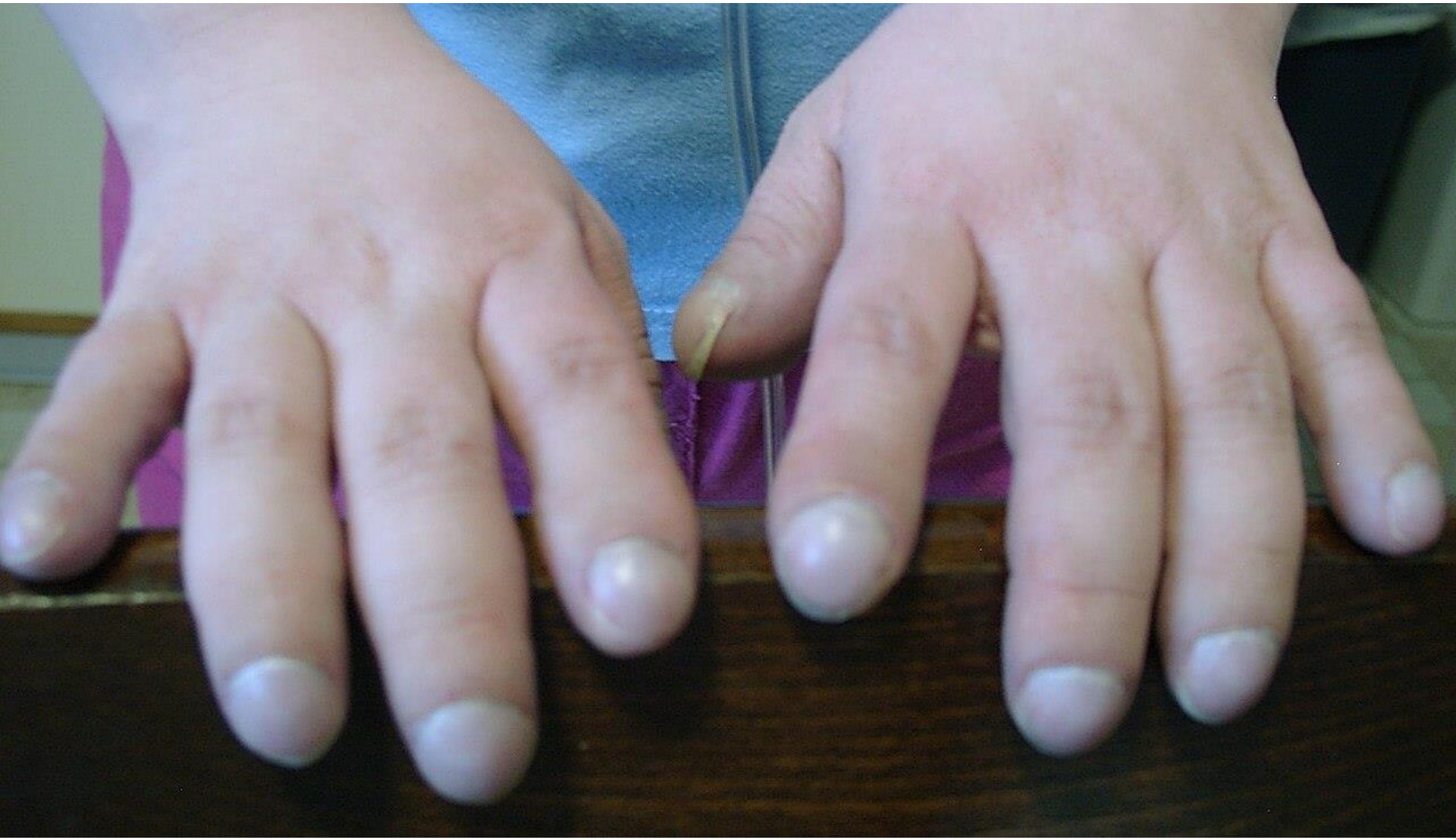
- **3 Development of pulmonary arterial hypertension**
- **PVR approaches systemic resistance.**
- **The pressure in the pulmonary artery increases significantly.**
- **The right ventricle must pump against high resistance →**
- **RV hypertrophy,**
- **later dilation and failure.**

- **4 Reversal of shunt (right to left)**
- **When:**
- **PVR > systemic vascular resistance**
- **→ blood begins to flow from right to left through the original defect.**
- **Consequences:**
- **Deoxygenated blood enters the systemic circulation,**
- **central cyanosis develops = key sign of ES.**

Eisenmenger syndrome

- **Systemic consequences of hypoxemia**
- Chronic hypoxia causes:
- secondary polycythemia (↑ EPO),
- blood hyperviscosity,
- clubbed fingers,
- hemoptysis,
- thromboembolic complications,
- brain abscesses,
- arrhythmias,
- right-sided heart failure.

Eisenmenger syndrome



clubbed fingers

Eisenmenger syndrome

Key pathophysiological points (for exam 💡)

ES = functionally irreparable stage of congenital heart defect

Main mechanism: chronic ↑ pulmonary flow → ↑ PVR → shunt reversal

Cyanosis develops late, not from birth

Surgical correction of the defect is relatively contraindicated at this stage

Cyanotic CHD:
Right-to-left and mixing lesions

Congenital heart diseases (CHD)
Classification

Cyanotic

Right-to-left shunt

- Tetralogy of Fallot
- Transposition of the great arteries (vessels)
- Ebstein anomaly
- Hypoplastic left heart syndrome
- Pulmonary atresia
- Truncus arteriosus
- Tricuspid atresia
- Single functional ventricle
- Interruption of the aortic arch
- *Eisenmenger syndrome**

** usually not a congenital anomaly, but included in the classification because of the shunt mechanism

Cyanosis mechanisms

- **R→L shunt** (deoxygenated blood reaches systemic circulation)
- **Complete mixing** with low systemic saturation (single ventricle physiology, truncus arteriosus)
- **Parallel circuits** without adequate mixing (TGA)

- ***Unifying pathophysiology****: systemic arterial oxygen content reduced by R→L shunting or incomplete mixing; severity depends on mixing sites and relative flows.*

Teaching trick

3 physiologic patterns of cyanosis

Teaching trick: "3 physiologic patterns of cyanosis"

1. **Decreased pulmonary blood flow** (TOF, pulmonary atresia): often darker cyanosis, improves with PGE if ductal flow increases pulmonary perfusion.
2. **Mixing lesions** (truncus, single ventricle): moderate cyanosis + CHF signs.
3. **Parallel circuits** (TGA): profound cyanosis early, minimal murmur, responds to improving mixing.

A) Tetralogy of Fallot (TOF)

- **the model for "decreased pulmonary blood flow"**
- VSD + RVOT obstruction + overriding aorta + RVH
- Key driver: **RVOT obstruction** → R→L across VSD → cyanosis.

TOF dynamic physiology

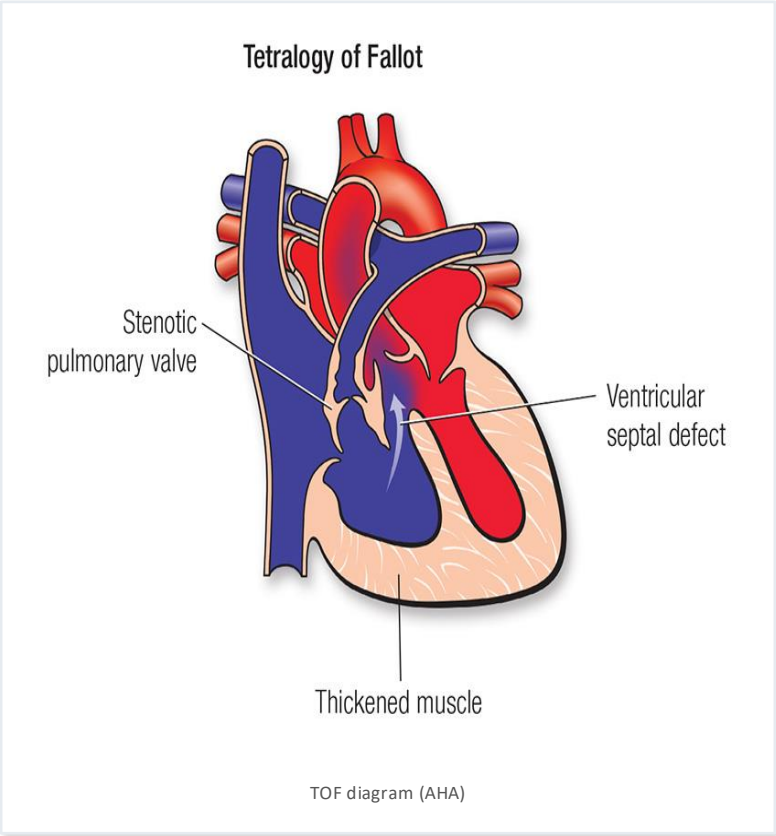
- "Tet spells": sudden ↑R→L shunt due to increased RVOT obstruction or decreased SVR.
- Squatting increases SVR → reduces R→L → improves oxygenation.

right ventricular outflow tract (RVOT) , Right ventricular hypertrophy (RVH)

Tetralogy of Fallot (TOF): R→L driven by RVOT obstruction

Cyanosis

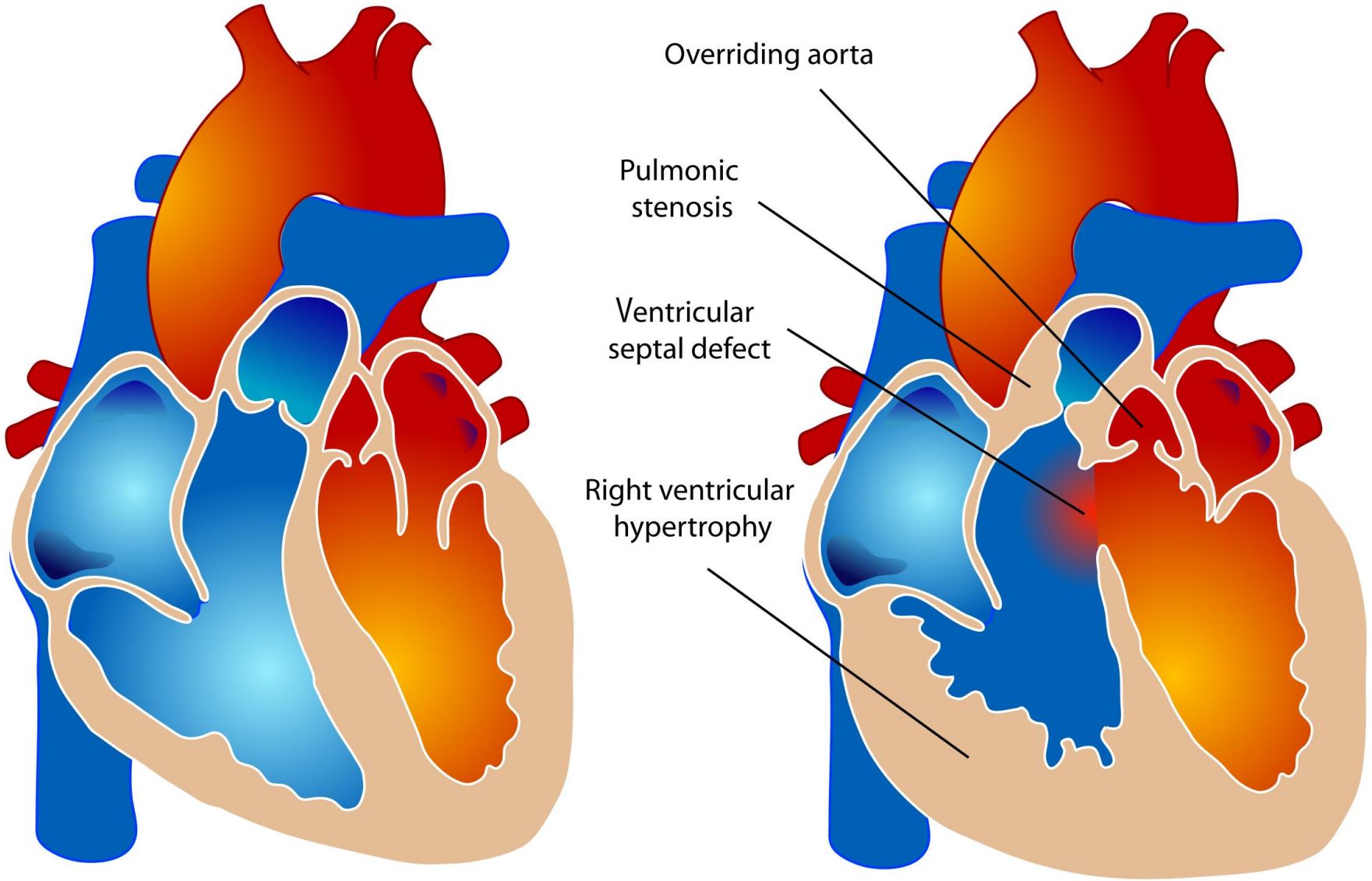
- Core lesions: VSD + RV outflow obstruction + overriding aorta + RV hypertrophy.
- Physiologic driver: RVOT obstruction elevates RV pressure → R→L across VSD (blood takes the VSD shortcut into aorta) → cyanosis.
- Degree of cyanosis tracks RVOT obstruction severity (not VSD size).
- TOF is a prototype for "decreased pulmonary blood flow" cyanotic CHD.



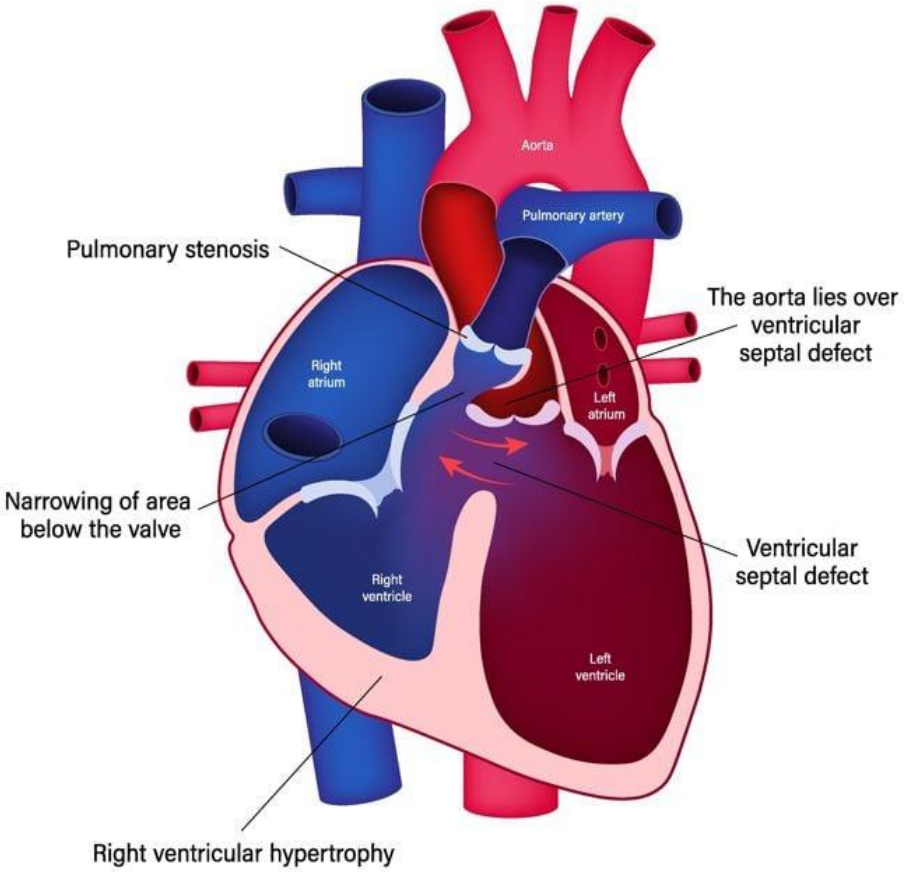
TOF diagram (AHA)

Normal heart

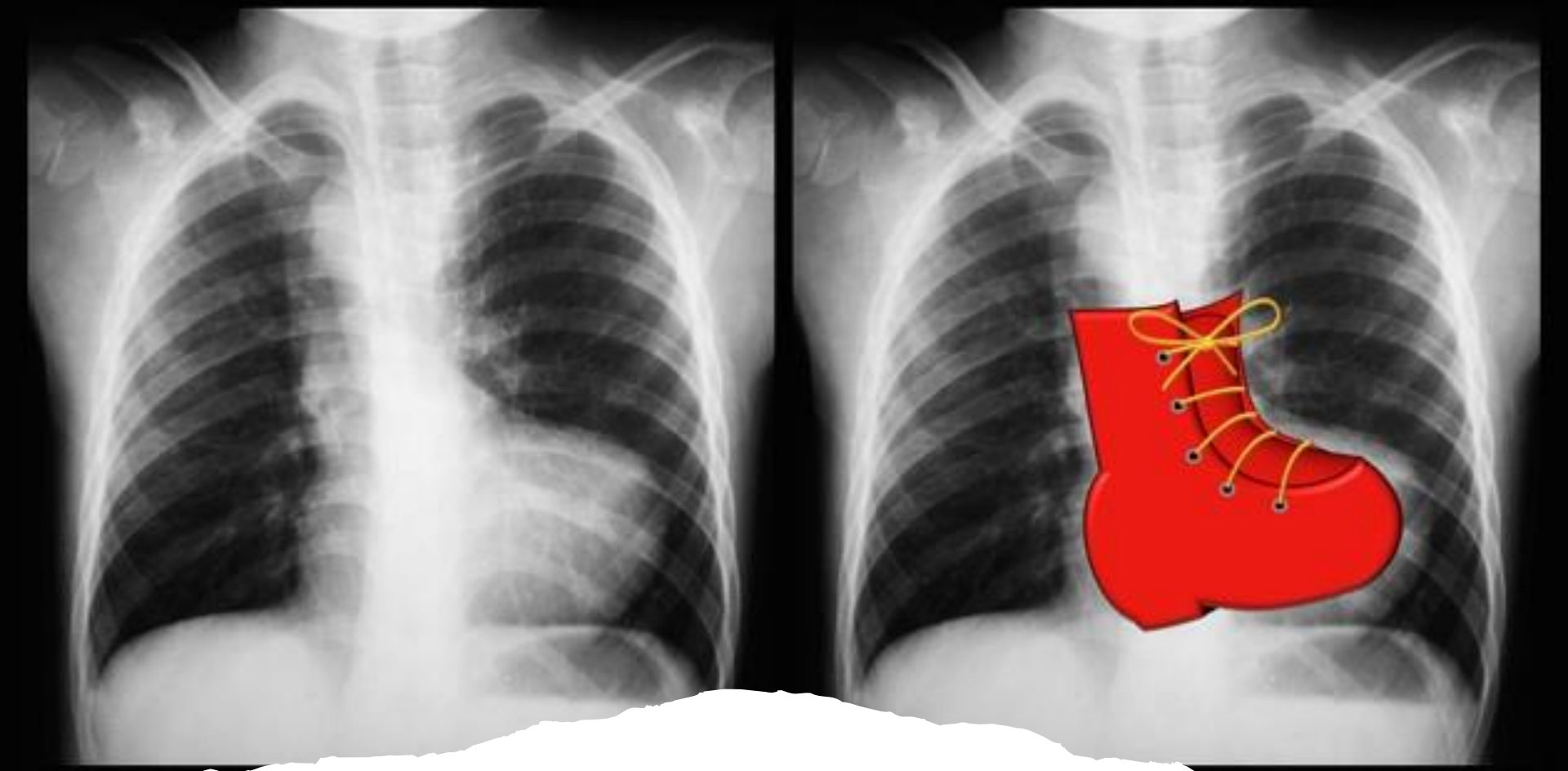
Tetralogy of Fallot



Tetralogy of Fallot



https://www.bhf.org.uk/-/media/images/information-support/conditions/tetralogy-of-fallot/tof-heart-side-2_660x885_noexp.jpg?rev=335333fb3ebf4663818bafadf5ceebf5



Coeur en sabot

TOF “spells” and squatting: SVR as therapy

Cyanosis

- Hypercyanotic spell = acute increase in R→L shunt (often from increased RVOT obstruction and/or decreased SVR).
- Squatting/knee-to-chest increases SVR → promotes L→R across VSD → more pulmonary blood flow → saturation rises.
- A murmur may get softer during a severe spell because RVOT flow decreases.

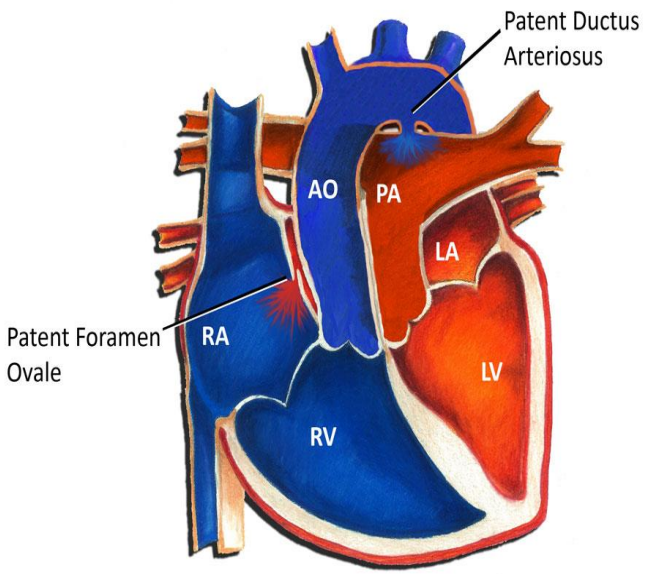
B) Transposition of the great arteries (TGA) — “parallel circulations”

- Aorta from RV; PA from LV → two parallel loops.
- Survival depends on **mixing** at ASD/VSD/PDA.
- As DA closes → less mixing → profound cyanosis and acidosis.
- the ‘problem’ is not pulmonary oxygenation; it’s circuit configuration.

TGA: parallel circuits (mixing is life)

Cyanosis

- In d-TGA: aorta arises from RV; pulmonary artery from LV → two parallel circuits.
- Without mixing (ASD/VSD/PDA), systemic blood recirculates deoxygenated venous blood → profound cyanosis (oxygenated pulmonary venous blood cycles back to lungs unless it can cross to systemic circuit).
- PDA/FO patency is crucial initially, hence the pathophysiology of prostaglandin use.
- Clinical clue: cyanosis with relatively clear lungs and minimal distress early (until decompensates).



TGA diagram (Pediatric Cardiology Associates of Houston)

C) Truncus arteriosus — “one outflow, complete mixing”

- Single arterial trunk supplies systemic + pulmonary.
- Usually large VSD. Oxygenated and deoxygenated blood mix completely → systemic sats moderately low.
- Pulmonary blood flow often excessive → early CHF + pulmonary HTN.

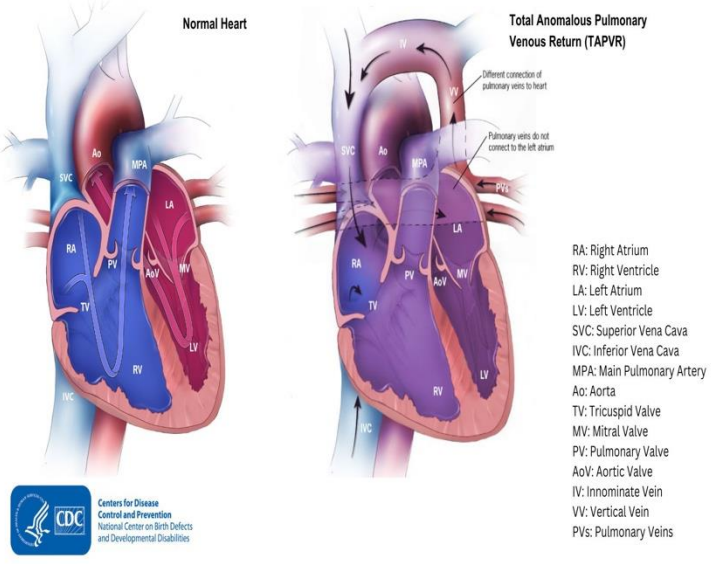
D) Total anomalous pulmonary venous return (TAPVR)

- Pulmonary veins drain to right side; systemic output depends on ASD for blood to reach LA/LV.
- Obstructed TAPVR → pulmonary venous congestion, severe hypoxemia, rapid deterioration.

TAPVR: obligatory mixing; obstruction changes everything

Cyanosis

- Pulmonary veins connect to systemic venous circulation → oxygenated blood returns to RA (mixing mandatory).
- Systemic output requires an atrial-level shunt (ASD/PFO) to reach LA/LV/aorta.
- If venous pathway is obstructed: pulmonary venous congestion → severe hypoxemia + respiratory distress + shock.
- unobstructed vs obstructed TAPVR: obstruction behaves like pulmonary edema clinically.
- why is there cyanosis even though the lungs oxygenate? (oxygenated blood returns to right heart and mixes)



Normal heart vs TAPVR (CDC)

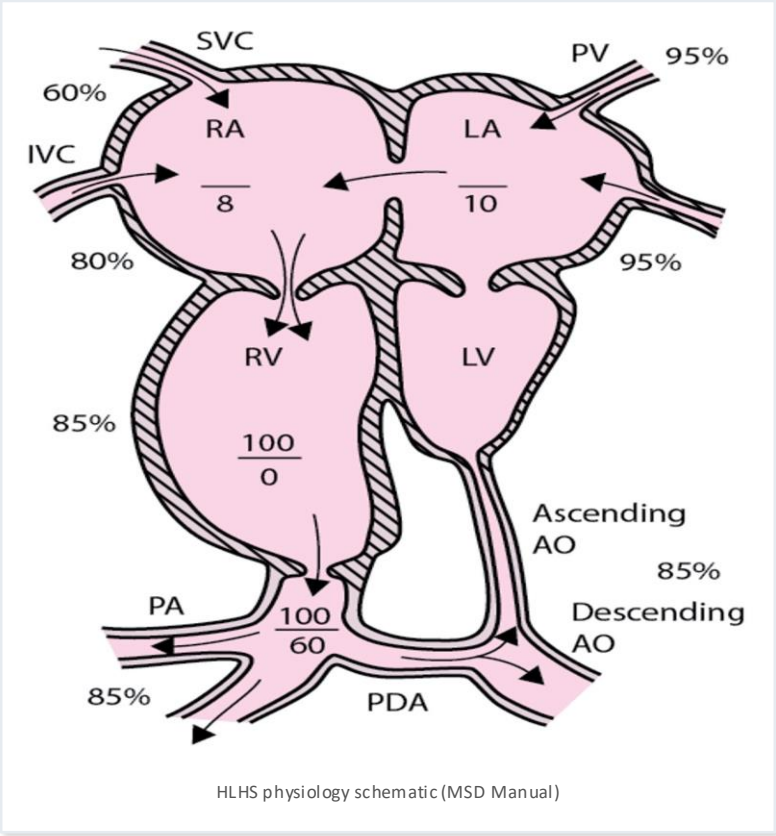
E) Single ventricle / HLHS concept

- In HLHS: LV/aorta inadequate → systemic flow depends on DA (RV → PA → DA → aorta).
- Ductal closure → systemic hypoperfusion/shock.

HLHS: duct-dependent systemic circulation

Mixing

- Underdeveloped left heart cannot support systemic output; RV becomes the effective systemic ventricle.
- Systemic perfusion requires DA (pulmonary artery → aorta) and atrial level mixing.
- DA closure → rapid fall in systemic blood flow → cardiogenic shock and death without intervention.
- RV ejects into PA; DA is the only path to aorta.
- in HLHS, improving saturation is less important than maintaining systemic flow.



HLHS physiology schematic (MSD Manual)

F) Ebstein anomaly

- Definition – rare congenital malformation associated with pathological formation of the tricuspid valve and its location apically to the right ventricle
- Causes - ?, dupl. 15q, anomalies 11q, mutations in MYH7, NKX2.5
- Incidence - 2 – 7 per 100,000/year (2024)
- Pathomechanism
- Faulty delamination of the tricuspid valve from the inteventricular septum -> "apicalization" of the tricuspid valve
- RV divided into two parts
- "Atrialized" RV -> often myopathy, fibrosis -> akinesia, arrhythmias (e.g. Wolff-Parkinson-White syndrome)
- "Functional" RV -> influence of tricuspid regurgitation -> RV remodeling (eccentric hypertrophy) -> smoothing of the ventricular septum -> left ventricular dysfunction
- Frequent presence of shunts -> e.g. foramen ovale -> R-L shunt -> cyanosis (20% fetal death in utero, 45% perinatal mortality)

https://www.youtube.com/watch?v=0Dz1xhMvlQk&t=473s

Physiologic classification (what to predict)

Category	Core problem	Typical timing	Main consequence
L→R shunt	Pulmonary overcirculation	weeks	HF, poor growth
Obstruction	Hypoperfusion / pressure overload	hours–days if severe	shock, acidosis
R→L / decreased Qp	Low pulmonary blood flow	hours–days	cyanosis ± spells
Mixing/parallel	Inadequate mixing	hours–days	cyanosis; depends on mixing sites

Take home message

- CHD symptoms are often **timed** to **ductal closure** (days) or **PVR fall** (weeks).
- Direction of shunt is governed by **pressure and resistance**, not by the label of the defect.
- Cyanosis requires **deoxygenated blood entering systemic circulation**—either by **R→L** or **inadequate mixing**.
- Eisenmenger is not ‘sudden’; it is **pulmonary vascular disease** caused by **chronic high flow/pressure**.

Key takeaways (what to remember)

Summary

- Days = ductus; weeks = falling PVR. Use timing to narrow the differential.
- Always decide: Qp problem? Qs problem? Mixing problem? Often more than one.
- Duct-dependent lesions can crash when DA closes; PGE1 changes physiology by reopening the bypass.
- Saturation is not oxygen delivery—flow (Qs) and hemoglobin matter.

Rapid self-test (5 questions)

Summary

1) Why do large VSDs usually present at 4–8 weeks rather than day 1?

2) In TOF, what changes during a hypercyanotic spell in terms of SVR and shunt direction?

3) Why is mixing mandatory for survival in d-TGA prior to repair?

4) Why can critical obstruction have a soft murmur?

5) Name two duct-dependent systemic flow lesions and two duct-dependent pulmonary flow lesions.

Suggested answers:

1) Early PVR is high; as PVR falls, L→R increases and HF emerges.

2) Often SVR falls and/or RVOT obstruction increases → more R→L; squatting raises SVR and reduces R→L.

3) Parallel circuits require ASD/VSD/PDA for oxygenated blood to reach systemic circulation.

4) Low flow = little turbulence despite severe lesion.

5) Systemic: HLHS, critical AS, severe CoA. Pulmonary: pulmonary atresia, critical PS, severe TOF.

- https://www.merckmanuals.com/professional/pediatrics/perinatal-physiology/perinatal-physiology
- https://pmc.ncbi.nlm.nih.gov/articles/PMC7807827/
- https://pmc.ncbi.nlm.nih.gov/articles/PMC6491149/

Q & A

1. **Why can a large VSD present later than birth?**

   Answer: High neonatal PVR limits L→R shunt initially; as PVR falls, shunt increases → pulmonary overcirculation/CHF.
2. **What physiologic change improves a TOF spell with squatting?**

   Answer: Increased SVR decreases R→L shunt across VSD, improving pulmonary blood flow and oxygenation.
3. **In TGA, why may oxygen have limited effect?**

   Answer: The circuits are parallel; without mixing (ASD/VSD/PDA), oxygenated pulmonary venous blood does not reach systemic circulation.

Q & A

4. **Which lesion most classically causes bounding pulses and wide pulse pressure?**
   Answer: PDA (systemic runoff during diastole).
5. **A 3-day-old develops shock as the DA closes; femoral pulses are weak. Likely physiology?**
   Answer: Ductal-dependent systemic perfusion (critical coarctation or HLHS).
6. **Mechanism of Eisenmenger syndrome in unrepaired large VSD?**
   Answer: Chronic pulmonary overcirculation → pulmonary vascular remodeling → rising PVR → reversal to R→L shunt → cyanosis.

https://www.techmed.sk/auskultacia-srdca-ozvy-selesty/

https://www.techmed.sk/kontinualny-selest/

Pathophysiology of Congenital and Inherited Valve Diseases

Learning objectives

1) Explain how normal valves maintain unidirectional flow and how stenosis vs regurgitation create distinct loading conditions.
2) Predict chamber remodeling and clinical consequences from the lesion's hemodynamics (pressure vs volume overload; atrial vs ventricular effects).
3) Describe key congenital/inherited valve lesions by valve (aortic, mitral, tricuspid, pulmonary) and their developmental/genetic bases.
4) Link molecular/cellular pathways to macroscopic valve dysfunction (calcification, extracellular matrix remodeling, leaflet malformation).
5) Translate physiology into diagnostic logic (why Doppler gradients, valve area surrogates, regurgitant quantification matter).

Physiology

A. Two lesion types, two dominant loading patterns

- **Stenosis = pressure overload** → concentric hypertrophy, higher systolic wall stress, eventual subendocardial ischemia, reduced compliance → diastolic dysfunction.
- **Regurgitation = volume overload** → eccentric remodeling/dilatation, increased stroke volume initially, later reduced forward output and secondary pulmonary venous hypertension.

B. Where the pressure backs up

- Left-sided lesions (mitral/aortic) → pulmonary congestion → pulmonary hypertension (late) → RV strain.
- Right-sided lesions (tricuspid/pulmonary) → systemic venous congestion, hepatomegaly/ascites (late).

C. Why murmurs and timing match physiology

- **Systolic ejection murmur**: semilunar stenosis (AS/PS).
- **Holosystolic regurgitant murmur**: AV valve regurg (MR/TR).
- **Diastolic rumble**: AV stenosis (MS; less “inherited,” but useful comparator).
- **Early diastolic decrescendo**: semilunar regurg (AR/PR).

Key congenital/inherited valve entities to cover

- **Aortic**: BAV → early calcific AS + aortopathy; congenital valvular AS (often bicuspid/unicuspid); supravalvular AS (ELN/Williams spectrum); inherited drivers of calcification (NOTCH1; Lp(a)/OxPL).
- **Mitral**: congenital MS variants (parachute MV, supravalvular ring, cleft in AV canal spectrum); inherited/myxomatous MVP → MR; connective tissue syndromes (e.g., Marfan) → MVP/MR phenotype.
- **Tricuspid**: Ebstein anomaly (delamination failure) → TR + arrhythmias.
- **Pulmonary**: congenital PS (commissural fusion vs dysplastic valve; syndromic associations).

Key prevalence anchors:

- **BAV** is the most common congenital valvular lesion (~0.5–2% of the population). PMC
- **MVP** affects ~2–3% of the general population and is the most common cause of primary MR in many developed settings. MDPI

Key congenital/inherited valve entities to cover

- Congenital + inherited valve disease: structure → flow → remodeling → symptoms
- Focus: aortic + mitral (most common), plus tricuspid/pulmonary exemplars
- For each lesion we will answer:
  - *What is abnormal structurally?*
  - *What does it do to flow?*
  - *How does the heart remodel?*
  - *What complications follow?*

Definitions: “congenital” vs “inherited”

- **Congenital**: present at birth (may manifest later)
- **Inherited**: genetic predisposition/variant → valve malformation or progressive degeneration
- Overlap: many congenital lesions have heritable architecture (e.g., BAV)

➢ *Congenital describes timing; inherited describes etiology. They overlap heavily in valve disease.*

Normal valve function (why valves are “energy savers”)

- Open with minimal gradient; close rapidly to prevent backflow
- Leaflet structure: collagen (strength), elastin (recoil), proteoglycans (viscoelasticity)
- Key cell types: valve endothelial cells + valve interstitial cells (VICs)

➢ *Many diseases are “reversions” to developmental programs: VIC activation → fibrosis/calcification or ECM expansion.*

Stenosis physiology: fixed obstruction

- ↑ velocity through valve → ↑ pressure gradient (Doppler principle)
- Afterload rises → concentric LV hypertrophy (LVOT/aortic)
- Late: diastolic dysfunction → LA pressure ↑ → pulmonary congestion

➢ *we can predict symptoms from physiology: exertional dyspnea and syncope are hemodynamic problems before pump failure.*

Regurgitation physiology: volume overload

- Backward flow each cycle → increased EDV
- Initially ↑ total stroke volume; forward SV may be preserved
- Late: chamber dilation, wall stress ↑, systolic dysfunction

➢ *Regurg lesions are often tolerated for years—until compensation fails.*

Pressure–volume loop intuition

- AS: ↑ systolic pressure, ↓ stroke volume (late), hypertrophy
- AR/MR: ↑ EDV, widened loop, high total stroke volume
- Clinical tie: “silent remodeling” precedes symptoms

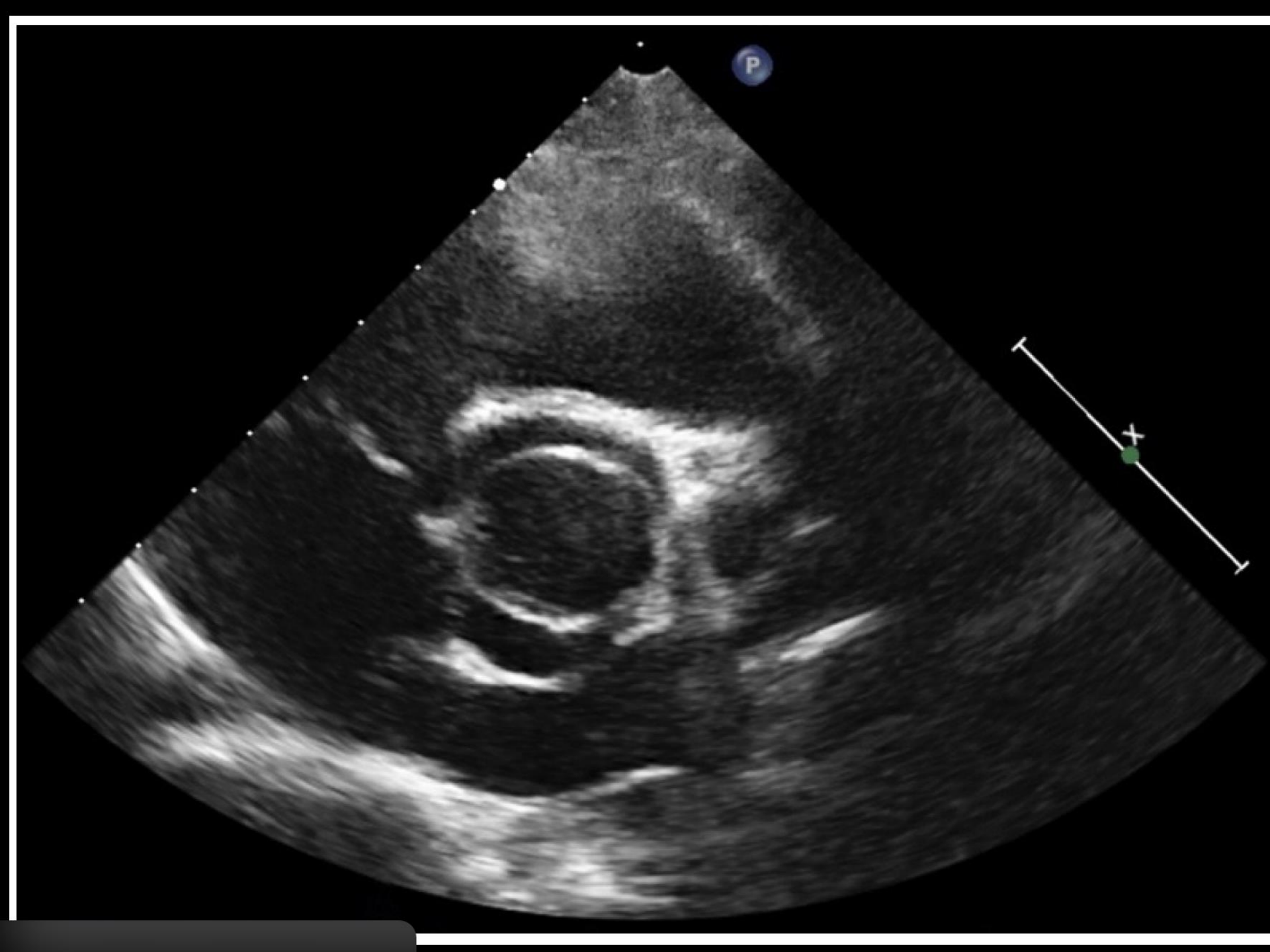
➢ *Even without showing the full loop, emphasize directionality: AS pushes pressure up; regurg pushes volume up.*

AORTIC VALVE
(congenital + inherited pathways)

Bicuspid aortic valve (BAV): why it matters

- Most common congenital valvular lesion (~0.5–2%)
- Abnormal leaflet geometry → eccentric jets + altered wall shear
- Phenotypes: early AS, AR, or mixed; plus ascending aortopathy

➢ *BAV is not just a valve—it's a valve–aorta disease complex. Turbulence and abnormal mechanobiology drive progression.*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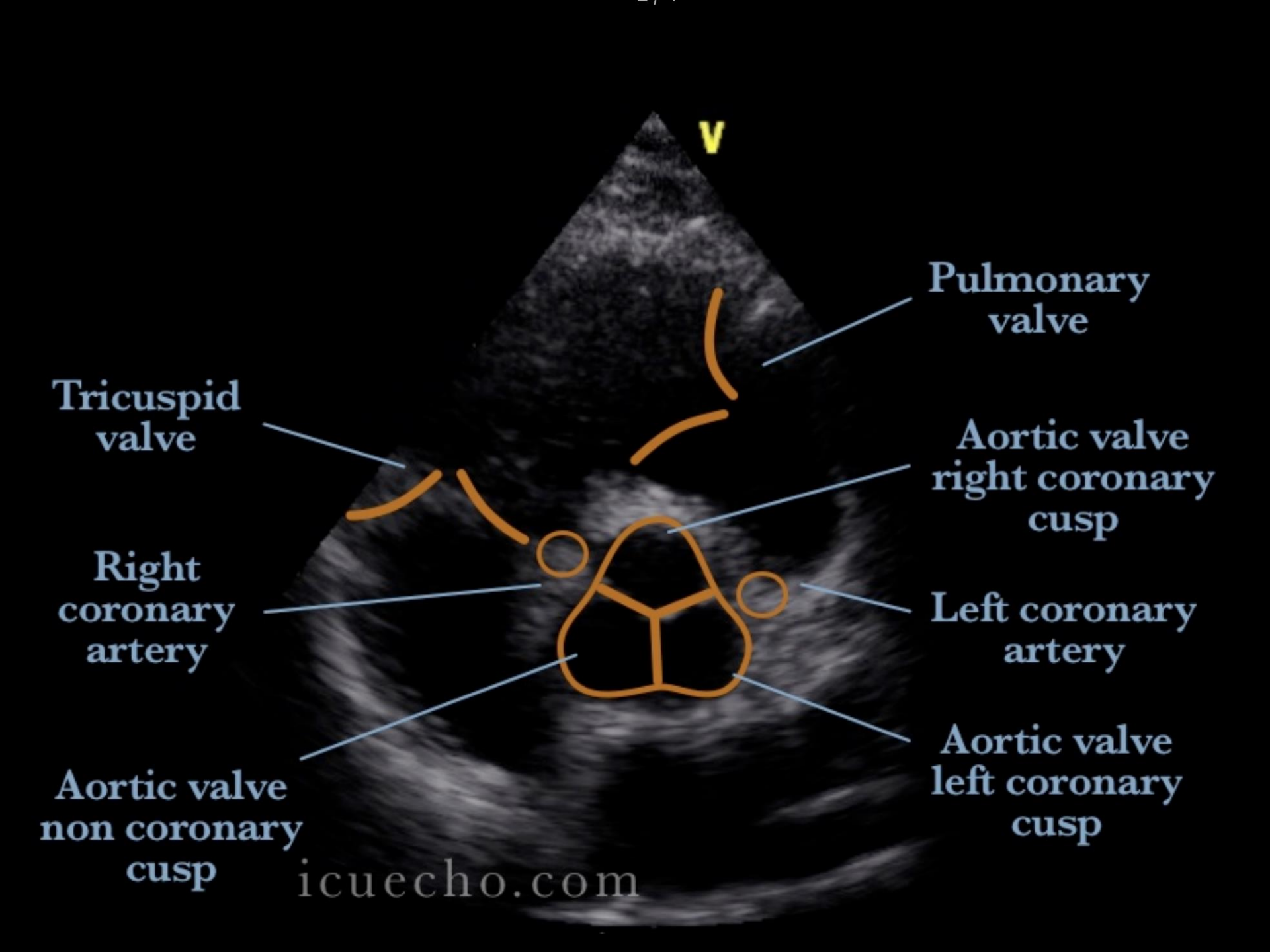

V
Pulmonary valve
Tricuspid valve
Aortic valve right coronary cusp
Right coronary artery
Left coronary artery
Aortic valve non coronary cusp
Aortic valve left coronary cusp
icuecho.com

BAV: progression to calcific AS (mechanobiology)

- Abnormal stress on cusps → endothelial dysfunction
- VIC activation → osteogenic differentiation → calcification
- Result: restricted cusp motion → stenosis

➢ *Calcific aortic valve disease is an active process (not passive "wear and tear"), especially accelerated in BAV.*

Inherited contributors: NOTCH1 and developmental signaling

- NOTCH signaling is central in aortic valve development
- **NOTCH1 mutations**: identified cause of BAV and calcific valve disease
- Concept: impaired protective signaling → VIC activation/calcification

➢ *the principle: disrupted developmental pathways reappear as adult valve disease.*

Inherited contributors: Lp(a) and oxidized phospholipids (OxPL)

- Elevated **Lp(a)** linked to presence/progression of aortic valve calcification
- OxPL carried by Lp(a) promotes VIC osteogenic programs
- Clinical implication: explains “risk beyond LDL”

➢ *Mechanistically: Lp(a) is not just a marker; it transports pro-calcific OxPL that can stimulate calcification biology.*

Congenital valvular aortic stenosis (AVS): the spectrum

- Congenital AVS is a common valve anomaly (not rare)
- Morphology: bicuspid or unicuspid; leaflet thickening/fusion
- Natural history: progressive obstruction → repeated interventions

➢ *In neonates, critical AS is an emergency; in older children it may be silent but still risky due to fixed obstruction.*

Congenital AVS: pathophysiology by age

- Neonate/infant: limited capacity to augment SV → CHF/shock risk
- Older child: compensated obstruction → exertional symptoms later
- Remodeling: hypertrophy + diastolic dysfunction

➢ *fixed obstruction + limited contractile reserve in newborn physiology.*

Supravalvular aortic stenosis (SVAS): “not a valve leaflet problem”

- Narrowing above the valve; often ELN-related arteriopathy
- ELN disruption is a key genetic cause of SVAS
- Hemodynamics: LV pressure overload similar to AS, but lesion location differs
- *CAVE: Students often misclassify SVAS as valvular AS; (emph. on anatomy and the systemic arteriopathy concept)*

MITRAL VALVE (congenital + inherited)

Mitral valve: why AV valves behave differently

- AV valves are tethered by chordae/papillary muscles
- Valve function depends on **ventricle geometry**
- Therefore MR can be “primary” (leaflet/chord) or “secondary” (ventricular)

➢ *Even in congenital/inherited settings, the ventricle–valve apparatus acts as one functional unit.*

Congenital mitral stenosis (CMS): concept

- Structural restriction: small annulus, abnormal chordae, leaflet thickening
- Typical patterns: parachute MV, supravalvular ring (examples)
- Physiology: LA pressure ↑ → pulmonary venous HTN

➢ *CMS is less common than BAV but teaches a classic "upstream pressure" physiology.*

Congenital cleft mitral valve / AV canal spectrum

- Malcoaptation → **primary MR** from birth or childhood
- Volume overload: LA + LV dilation over time
- Clinical: failure to thrive (infants) or exercise intolerance (older)

➢ *regurgitation physiology—especially atrial dilation and pulmonary congestion.*

MVP as an inherited/myxomatous valve disease

- MVP affects ~2–3% of general population
- Pathology: ECM remodeling → leaflet thickening/elongation; annular changes
- Result: MR from malcoaptation; sometimes arrhythmogenic phenotype

➢ *MVP as a structural–biological disease (not just "billowing"). The endpoint is malcoaptation and regurgitation.*

Myxomatous MVP: TGF-β and ECM remodeling

- Myxomatous valves: proteoglycan accumulation + collagen architecture disruption
- TGF-β dysregulation implicated (notably in Marfan-associated MVP)
- Final common pathway: weakened leaflet tissue → prolapse → MR

❖ *Keep it mechanistic: signaling → VIC/myofibroblast activation → matrix changes → leaflet redundancy.*

Connective tissue syndromes and MVP/MR

- Syndromic contexts: Marfan and related connective tissue disorders
- Mechanism: altered fibrillin/ECM signaling → leaflet redundancy + annular changes
- Often coexists with aortic root disease (clinical implication)

➢ *pattern recognition: tall habitus + lens issues + aortic root + MVP → think heritable connective tissue disorders. (Marfan syndrome, Ehlers-Danlos syndromes, Osteogenesis Imperfecta—that impair the body's structural proteins (collagen or elastin))*

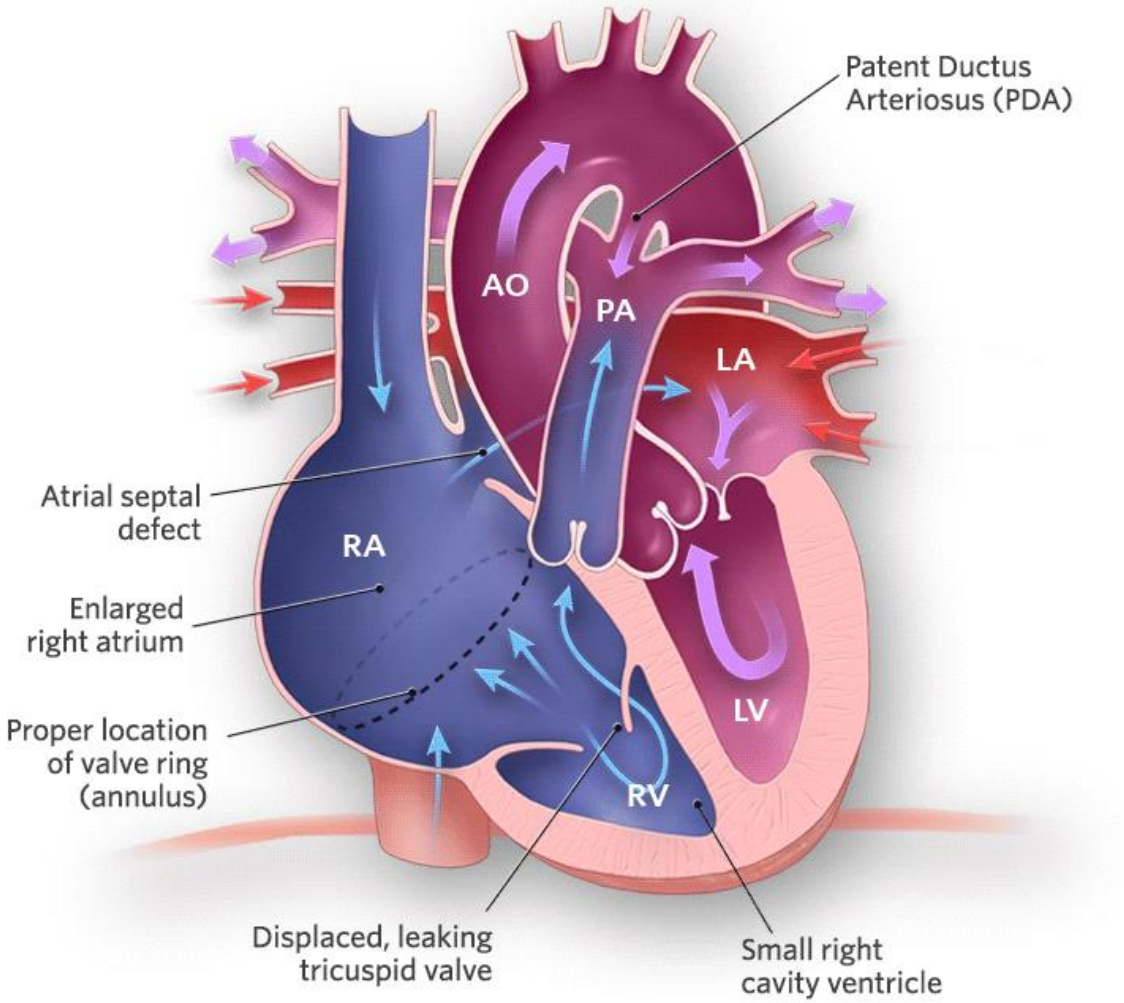
TRICUSPID VALVE: EBSTEIN (congenital exemplar)

Ebstein anomaly: the structural defect

- Apical displacement of tricuspid valve leaflets; “atrialization” of RV
- Failure of normal leaflet delamination during development
- Severe TR common; right atrium dilation

➢ *This is a quintessential developmental malformation producing regurg physiology and arrhythmia risk.*

Ebstein's Anomaly of the Tricuspid Valve

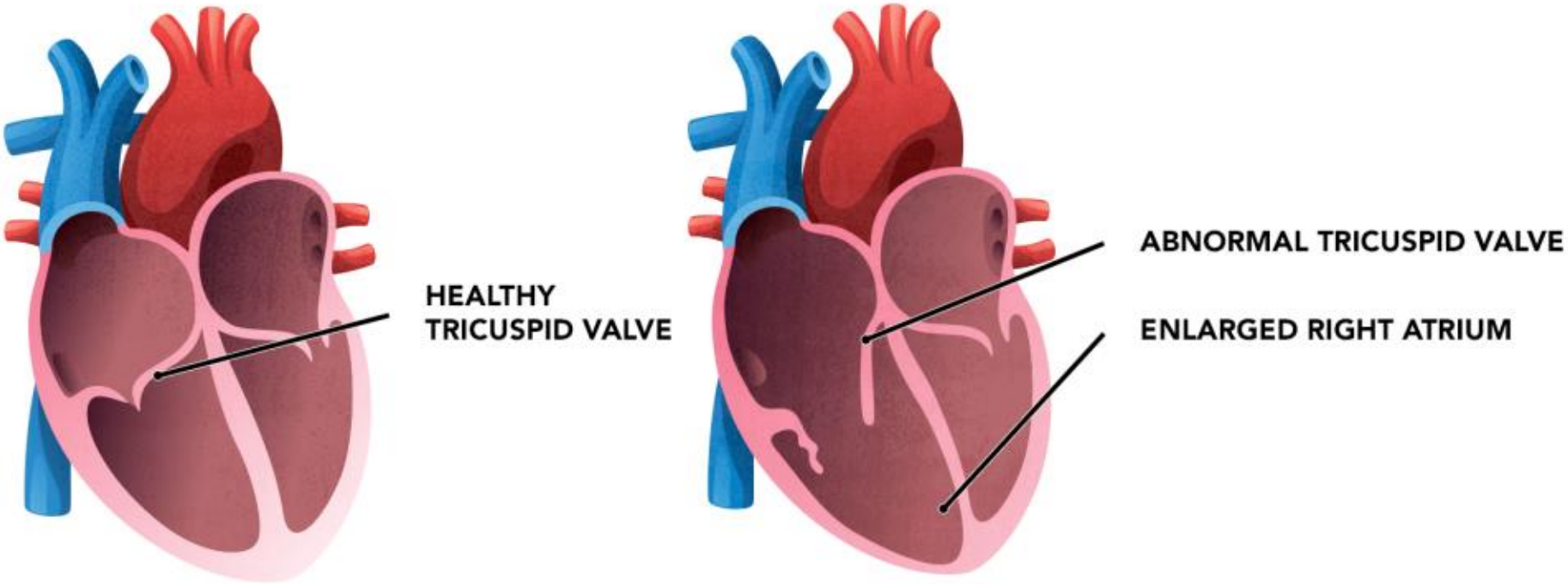


- Oxygen-rich blood
- Oxygen-poor blood
- Mixed blood

AO: Aorta
LA: Left atrium
RA: Right atrium

PA: Pulmonary artery
LV: Left ventricle
RV: Right ventricle

Ebstein's Anomaly



Ebstein physiology: why symptoms vary widely

- TR → RA dilation → atrial arrhythmias
- Reduced effective RV volume → low pulmonary blood flow in severe cases
- Often associated shunts (e.g., ASD/PFO) → cyanosis depending on pressures

➢ *right-sided regurg can produce systemic venous congestion and cyanosis if right-to-left shunting occurs.*

PULMONARY VALVE: CONGENITAL PULMONARY STENOSIS (PS)

Congenital PS: prevalence and types

- PS accounts for ~7–12% of congenital heart disease
- Two main valvular patterns:
  - commissural fusion (doming)
  - dysplastic thickened leaflets (less “doming”)

❖ *Students often assume “stenosis = fused commissures.” Dysplasia is different and affects procedural response.*

PS physiology: RV pressure overload

- RV systolic pressure ↑ → RV hypertrophy
- Severe PS: RV failure; reduced pulmonary flow; exercise intolerance
- Post-stenotic dilation of PA may occur (jet effect)

➢ *Link it directly to AS physiology, but on the right side. Pressure overload physiology is conserved.*

Associated syndromes

- Marfan / Loeys-Dietz / vascular Ehlers-Danlos: aortic root dilatation → AR; MVP/MR.
- Turner syndrome: more common BAV and aortopathy.
- Williams syndrome: supravalvular aortic stenosis.
- Noonan syndrome: PS (dysplastic pulmonary valve).
- 22q11.2 deletion syndrome: more common conotruncal defects; valves may be part of the complex.

CROSS-CUTTING MECHANISMS (ties inherited biology to valve endpoints)

Three final common pathways

- **Calcification** (semilunar valves; often BAV/inherited risk)
- **Fibrosis/scarring** (developmental dysplasia or inflammatory injury)
- **Myxomatous degeneration** (AV valves; MVP phenotype)

➢ No matter the gene/trigger, the valve tends to end in one of these structural endpoints.

Calcification is an active, regulated process

- VIC osteogenic differentiation is a central concept
- Modulated by lipid/oxidative pathways (Lp(a)/OxPL)
- Developmental signaling (NOTCH) can be protective; loss predisposes

➢ *Reinforce: calcification resembles bone-like programs, not simple "deposition."*

Developmental biology: why “valve disease repeats embryology”

- Valve morphogenesis relies on tightly controlled signaling and cell transitions
- Disruption → malformations (congenital) or vulnerability to later degeneration
- Modern reviews integrate congenital, rheumatic, and myxomatous endpoints

❖ *as a conceptual capstone: the adult valve can reactivate developmental/injury programs.*

CLINICAL PHYSIOLOGY IN PRACTICE (diagnostic logic, complications)

Why echocardiography answers physiology questions

- Stenosis: velocities/gradients approximate severity (flow-dependent)
- Regurgitation: quantify jet, vena contracta, regurgitant volume/fraction
- Chamber response (hypertrophy/dilation) is part of severity assessment

➢ *should understand what the echo numbers represent physiologically—pressure drops and backward flow.*

Complications to predict from first principles

- Pressure overload: hypertrophy → ischemia, syncope, HF
- Volume overload: dilation → AF, HF, pulmonary HTN
- Abnormal valves → endocarditis susceptibility (especially turbulent jets)

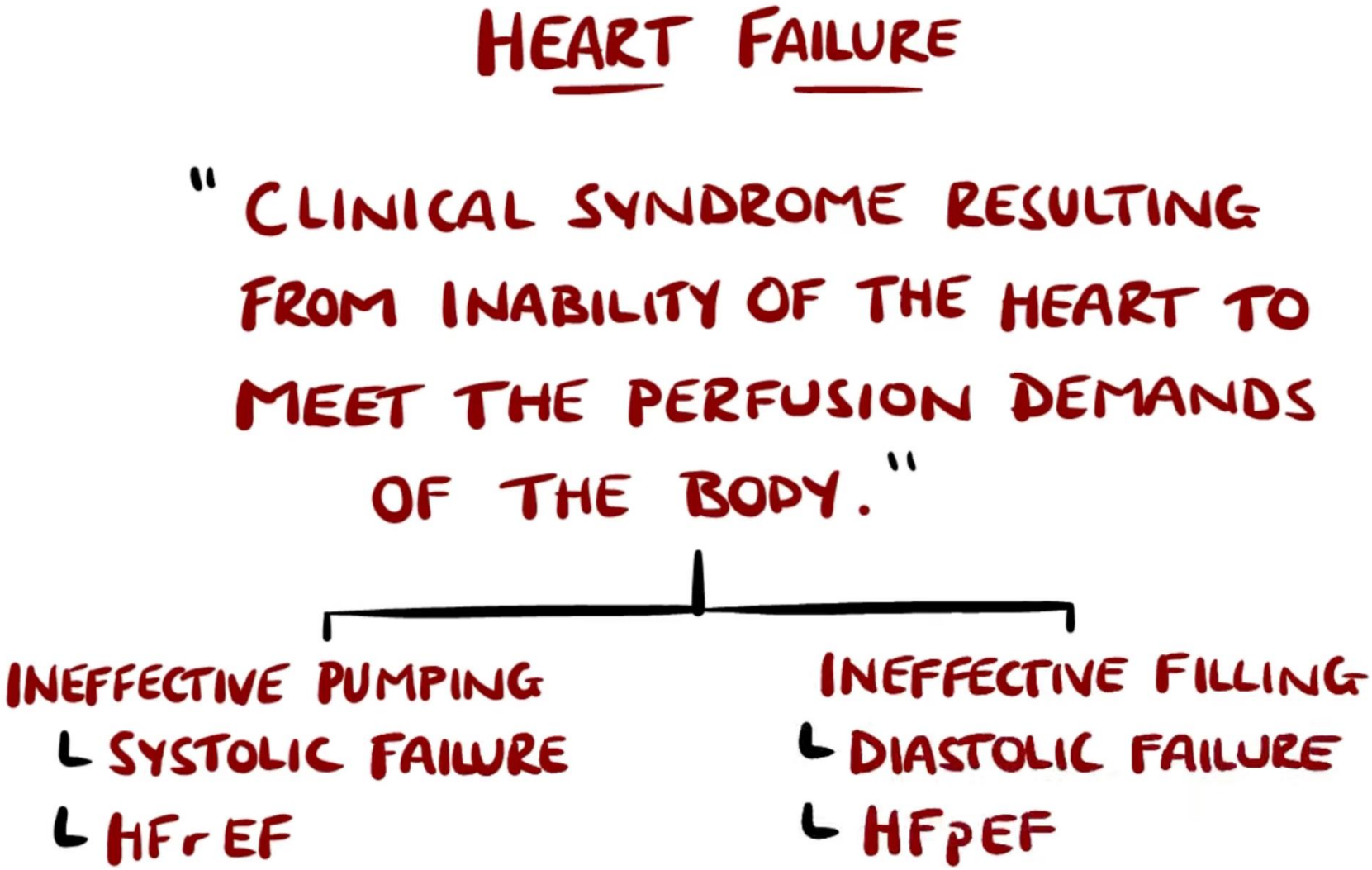
❖ *This is "predictive physiology": once students know lesion type, they can anticipate complications without memorizing lists.*

Summary

- Stenosis = pressure overload; regurg = volume overload
- BAV: common; mechanobiology + genetics (NOTCH1) + calcification pathways (Lp(a)/OxPL)
- MVP: common; myxomatous ECM/TGF-β themes; MR consequences
- Ebstein/PS: developmental malformations → predictable right-sided physiology
- physiology is the organizing principle; genetics and anatomy explain why physiology occurs.

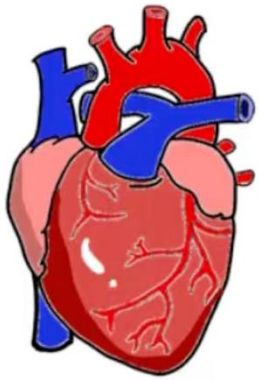
Pathophysiology of heart failure

symptoms/signs due to structural/functional cardiac abnormality causing **low output, high filling pressures, or both**



ACUTE HEART FAILURE

HEART FAILURE – HEART IS UNABLE TO MEET PERFUSION DEMANDS OF THE BODY



ACUTE HEART FAILURE

↳ SUDDEN DETERIORATION IN CARDIAC FUNCTION

PREVIOUSLY HEALTHY
DE NUOVO
ACUTE HEART FAILURE

CHRONIC (BUT STABLE) HEART DISEASE
ACUTE DECOMPENSATED HEART FAILURE

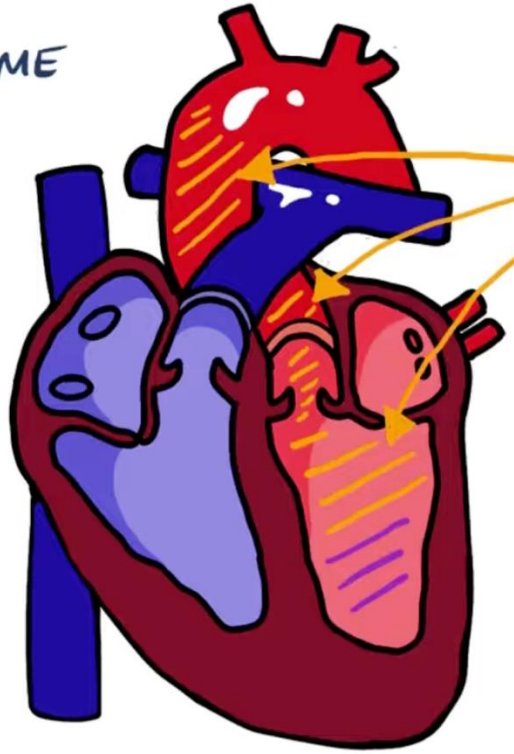
ACUTE HEART FAILURE

CARDIAC OUTPUT:

HEART RATE x STROKE VOLUME

70 BPM x 70 mL

= 4900mL/min



STROKE VOLUME (~70mL)

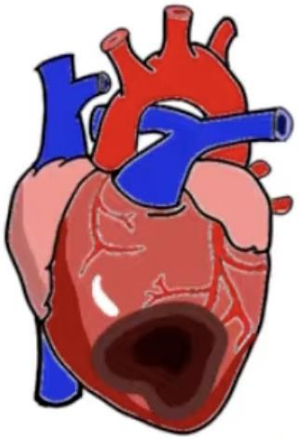
EJECTION FRACTION = STROKE VOLUME (70) / END DIASTOLIC VOLUME (110)

= 64%.

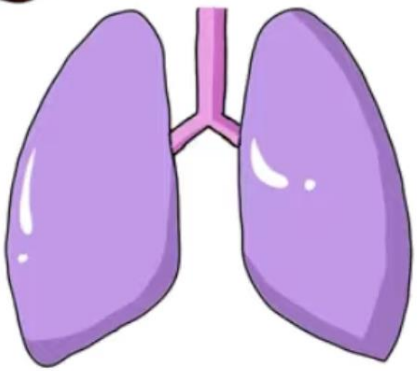
NORMAL RANGE: 55-70%.

ACUTE HEART FAILURE

CAUSES



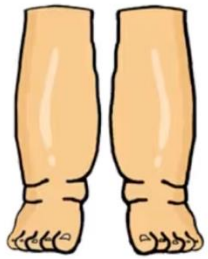
1. MYOCARDIAL INFARCTION
2. ACUTE VALVULOPATHY
   - ↳ MITRAL REGURGITATION
3. ARRHYTHMIAS
   - ↳ VENTRICULAR FIBRILLATION
4. PULMONARY EMBOLISM
5. MYOCARDITIS
6. DRUGS
   - ↳ BETA BLOCKERS + Ca^{2+} CHANNEL BLOCKERS

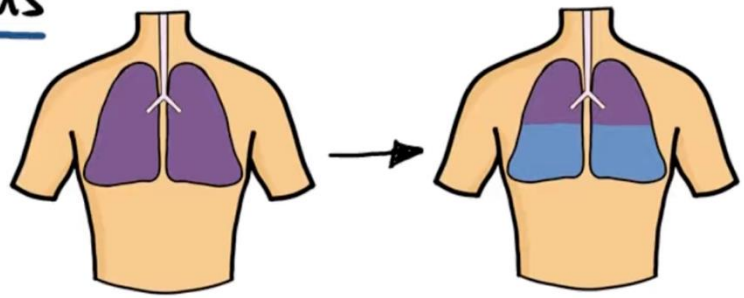


ACUTE HEART FAILURE

SIGNS AND SYMPTOMS

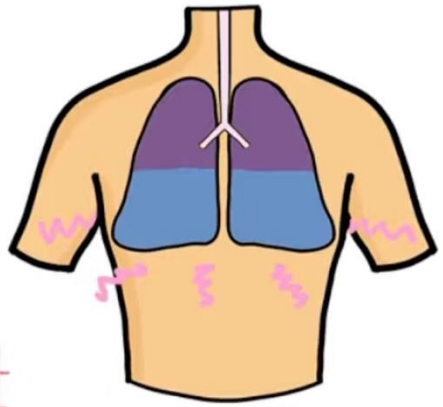
1. SHORTNESS OF BREATH / DYSPNEA
   - ↳ PULMONARY EDEMA
2. CHEST PAIN
3. SWELLING IN PERIPHERIES
   - ↳ JUGULAR VEIN DISTENSION
   - ↳ ACUTE HEPATOMEGALY → PAIN
4. WEAKNESS
5. CYANOSIS





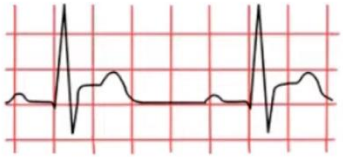
ACUTE HEART FAILURE

DIAGNOSIS



PHYSICAL EXAM:
- CRACKLES AT LUNG BASES
- ADDITIONAL HEART SOUNDS
- JUGULAR VEIN DISTENTION
- PERIPHERIES
- DRUG HISTORY

ECG:
- ISCHEMIA / INFARCTION
- ARRHYTHMIA



LABS:
- TROPONIN
- B-TYPE NATURITIC PEPTIDE (BNP)
- ELECTROLYTES → Na^+ / K^+ / Ca^{2+}

IMAGING:
- CHEST X-RAY
- CARDIAC ULTRASOUND
  - ↳ VOLUMES, EJECTION FRACTION, ANATOMICAL CHANGES

ACUTE HEART FAILURE

TREATMENT

STABILIZE:
- SURGERY (VALVE REPAIR)
- REPERFUSION (MYOCARDIAL INFARCTION)
- OXYGEN
- MEDICATION -
  - DIURETICS
  - IONOTROPES
  - NITRATES
  - PAIN RELIEF
- MECHANICAL ASSIST DEVICE -
  - AORTIC BALLOON PUMP

LONG TERM:
- LIFESTYLE MODIFICATION
- MEDICATION -
  - ACE INHIBITORS / ARBs
  - BETA BLOCKERS
  - STATINS
  - DIURETICS

Classification

- Classifications:
- **Acute vs chronic** HF (tempo matters for compensation).
- **Left vs right** HF (dominant congestion compartment).
- **HFrEF vs HFpEF** (dominant remodeling and loading problem).

❖ Two dominant pathophysiologic “outputs”:

1.Congestion (elevated filling pressures → pulmonary/systemic venous congestion).

2.Hypoperfusion (inadequate forward flow) — often later/advanced HF.

HFrEF

- **(Heart Failure with reduced Ejection Fraction) = heart failure with reduced left ventricular ejection fraction (LVEF) ≤ 40%.**
- Symptoms: Shortness of breath, limited physical fitness, edema.
- Pathophysiology: Impaired systolic function, progressive left ventricular dilation.
- Diagnostics: Echocardiography to measure EF, increased natriuretic peptide levels.
- HFrEF is the main form of chronic heart failure that requires targeted pharmacotherapy.

HFmrEF

- **(Heart Failure with Mildly Reduced Ejection Fraction, or Heart Failure with Mid-Range Ejection Fraction) = a category of heart failure where the LV pumps blood less efficiently, but not as poorly as in HFrEF, with an EF in the range of 40-49% (sometimes specified as 41-49%).**
- It is an intermediate form between HFrEF (heart failure with reduced EF) and HFpEF (heart failure with preserved EF).
- Prevalence: up to 10-20% of heart failure cases
- Treatment includes drugs similar to HFrEF (beta blockers, ACE inhibitors, SGLT2 inhibitors) and diuretics, but more detailed research is still needed on optimal therapy

HFpEF

- **(heart failure with preserved ejection fraction) = the heart muscle contracts normally (EF >50%), but the LV is stiff (diastolic dysfunction), which prevents sufficient filling with blood, leading to increased filling pressure and accumulation of blood in the lungs.**
- Often affects older patients, especially women with AHT, obesity or DM, the risk of death is high, comparable to HFrEF.
- Diagnosis: Problematic, requires ECHOKG to assess function and filling pressures, often accompanied by increased BNP/NT-proBNP values.
- Symptoms: dyspnea on exertion and at rest, fatigue and right ventricular edema.
- Treatment: management of comorbidities (AHT, DM, FiP) and symptomatic treatment, especially diuretics to reduce fluid overload.
- Prognosis: HFpEF is a serious disease with a high rate of rehospitalization. and mortality, up to 65% of patients may die within 5 years of diagnosis.

HFpEF

HFpEF is not just "diastolic HF." It is a multi-organ syndrome, especially in:

- hypertension
- obesity
- type 2 diabetes (T2DM)
- older patients

Mechanisms:

- systemic inflammation (visceral fat)
- endothelial dysfunction
- impaired LV relaxation
- elevated filling pressures even with mild exertion
- pulmonary hypertension

The result is poor exercise tolerance despite a normal ejection fraction.

Classification of HF

A. By ejection fraction

- **HFrEF:** EF < 40% (</=40%)
- **HFmrEF:** EF 40–49% (41-49%)
- **HFpEF:** EF ≥ 50%

➢ **Pathophysiologic differences**

- **HFrEF** = systolic dysfunction → weak contraction
- **HFpEF** = diastolic dysfunction → stiff ventricle, high filling pressures
- **HFmrEF** = transitional phenotype

B. By speed of onset

- **Acute HF** (cardiogenic shock, acute decompensation)
- **Chronic HF** (most common)

C. According to subjective functional load – NYHA I–IV

- **NYHA I–IV (functional classification of heart failure)**

❖ **NYHA I**

- No limitation of physical activity.
- Ordinary activity does not cause dyspnea, fatigue, palpitations, or angina.

❖ **NYHA II**

- Mild limitation of physical activity.
- Comfortable at rest, but ordinary activity causes dyspnea, fatigue, palpitations, or angina.

❖ **NYHA III**

- Marked limitation of physical activity.
- Comfortable at rest, but less-than-ordinary activity provokes symptoms.

❖ **NYHA IV**

- Unable to carry out any physical activity without symptoms.
- Symptoms (dyspnea/fatigue) are present even at rest; they worsen with exertion.

NYHA — Walking on level ground — Stairs

NYHA I

- **Level ground:** No symptoms with normal walking.
- **Stairs:** 1–2 flights without dyspnea/fatigue.

NYHA II

- **Level ground:** Symptoms with fast walking or longer distances.
- **Stairs:** Dyspnea/fatigue after 1–2 flights (especially without stopping).

NYHA III

- **Level ground:** Symptoms even with short walks (tens to a few hundred meters depending on terrain).
- **Stairs:** Symptoms after a few steps or < 1 flight; needs to stop.

NYHA IV

- **Level ground:** Symptoms with minimal exertion (e.g., moving around the apartment) or even at rest.
- **Stairs:** Usually unable; symptoms even at rest (e.g., while dressing).
- **Note:** These are approximate examples; the threshold is individual (age, fitness, COPD, anemia, obesity).

Main pathophysiological mechanisms

A. Reduced cardiac output

HFrEF → ↓ contractility → ↓ CO → activation of compensatory mechanisms.

HFpEF → CO may be normal at rest, but inadequate during exertion because of:

- LV hypertrophy
- myocardial stiffening
- impaired relaxation
- increased LVEDP

B. Elevated filling pressures

Key for the development of dyspnea and congestion.
High LVEDP → transmitted to the LA → to the pulmonary veins → causes pulmonary congestion and dyspnea.

C. Neurohormonal activation – the core of pathophysiology

1. RAAS activation

Renal hypoperfusion → ↑ renin → ↑ angiotensin II → ↑ aldosterone

➡️ vasoconstriction

➡️ Na^+ and water retention

➡️ myocardial hypertrophy and fibrosis

➡️ ventricular remodeling

2. Sympathetic nervous system (SNS)

↑ norepinephrine

➡️ ↑ heart rate, ↑ contractility (beneficial short-term)

➡️ long-term: cardiomyocyte apoptosis, arrhythmias, β-receptor downregulation

3. ADH (vasopressin)

➡️ water retention, hyponatremia, higher filling pressures

4. Inflammatory cytokines

TNF-α, IL-1β, IL-6

➡️ reduce contractility, promote fibrosis

5. Natriuretic peptides (BNP, NT-proBNP) – the only protective system

Act against RAAS and SNS:

➡️ natriuresis

➡️ vasodilation

➡️ antifibrotic effects

In HF they are increased, but their effectiveness is reduced due to receptor resistance.

Remodelation of heart

Long-term overload leads to:

a) Eccentric hypertrophy (volume overload)

- ventricular dilation
- wall thinning
- typical of HFrEF

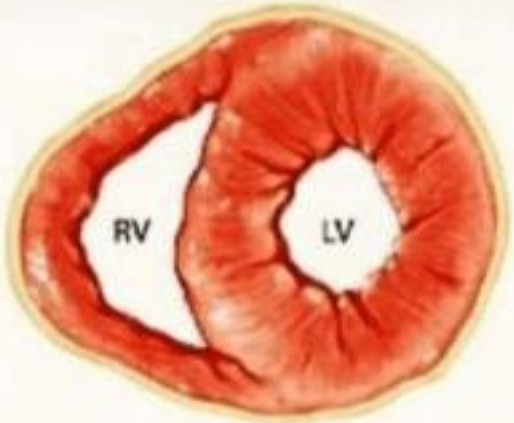
b) Concentric hypertrophy (pressure overload)

- wall thickening
- diastolic dysfunction
- typical of HFpEF (e.g., hypertension)

Mechanisms of remodeling

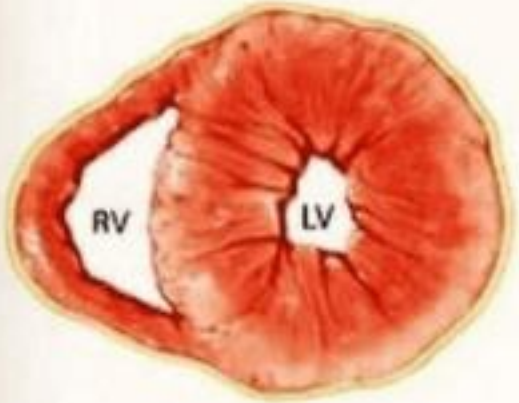
- cardiomyocyte apoptosis
- interstitial fibrosis
- changes in the extracellular matrix
- fibroblast activation

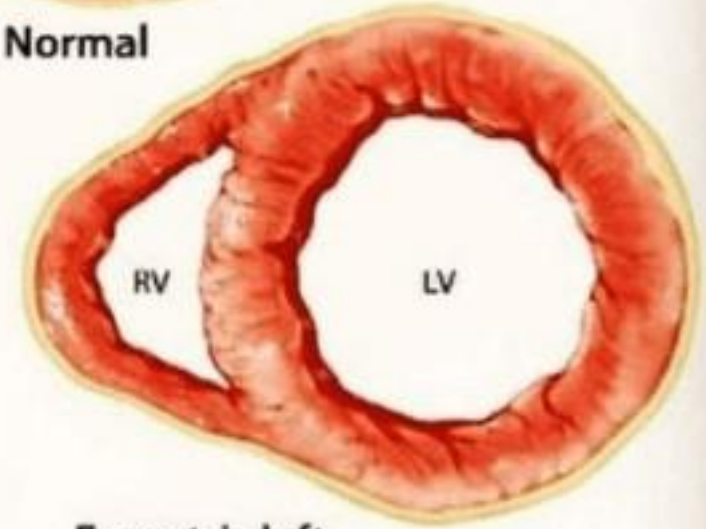
Eccentric and concentric cardiac hypertrophy



@Echo_tips

Normal





Concentric left ventricular hypertrophy

Pressure overload

- Chronic hypertension
- Aortic stenosis

Eccentric left ventricular hypertrophy

Volume overload

- Aortic or mitral regurgitation
- Myocardial infarction
- Dilated cardiomyopathy

https://perfusfind.com/eccentric-and-concentric-cardiac-hypertrophy/

Hemodynamic consequences

1. Forward failure – insufficient output

- fatigue
- muscle weakness
- renal hypoperfusion → RAAS activation

2. Backward failure – congestion

- dyspnea, orthopnea
- lower limb edema
- hepatomegaly
- ascites

Pathophysiology of symptoms

- **Dyspnea**
- pulmonary congestion → transudation of fluid
- reduced lung compliance
- activation of J receptors → sensation of “air hunger”
- **Fatigue**
- low cardiac output (CO)
- reduced perfusion of skeletal muscle
- muscle atrophy and mitochondrial dysfunction (cardiac cachexia)
- **Edema**
- increased venous pressure
- activated RAAS and ADH
- reduced lymphatic drainage
- **Arrhythmias**
- fibrosis
- atrial dilation → atrial fibrillation
- β-receptor downregulation

Cardiogenic shock

- extremely ↓ CO
- systemic vasoconstriction
- elevated lactate
- severe hypoperfusion of kidneys, liver, CNS
- mortality 40–50%

Clinical phenotypes of heart failure (ESC) according to perfusion and congestion

1) ESC "clinical profiles"

The ESC uses bedside stratification of acute heart failure along two axes:

Congestion ("wet" vs "dry")

"wet" = symptoms/signs of fluid overload are present (pulmonary congestion or systemic venous congestion)

"dry" = no significant congestion

Perfusion ("warm" vs "cold")

"warm" = adequate peripheral perfusion

"cold" = hypoperfusion (low output) – clinical signs of "low output"

This yields 4 profiles: **warm–dry, warm–wet, cold–dry, cold–wet.**

2) How to clinically determine congestion and perfusion

2.1 Signs of congestion (“wet”)

- dyspnea, orthopnea, PND
- crackles (rales), pleural effusion
- elevated JVP, hepatojugular reflux
- peripheral edema, ascites, hepatomegaly
- weight gain, oliguria (also with renal venous congestion)

2.2 Signs of hypoperfusion (“cold”)

- cold extremities, mottling, prolonged capillary refill
- hypotension (not required, but common), narrow pulse pressure
- altered mental status, dizziness
- oliguria (from low flow), elevated lactate, metabolic acidosis

Clinical profile of acute HF (ESC)

Clinical profile (ESC)	Congestion	Perfusion	Typical bedside findings	Typical hemodynamics (approx.)	"What I do first" (principle)
Warm–Dry ("warm–dry")	**No**	**Yes**	No orthopnea/crackles, no edema/JVP↑; stable BP; warm extremities; normal capillary refill	**PCWP normal** (≈ ≤18 mmHg), **CI preserved** (≈ ≥2.2 L/min/m²)	Continue/optimize chronic therapy; monitor; **no urgent decongestion**
Warm–Wet ("warm–wet congestion")	**Yes**	**Yes**	Dyspnea, orthopnea, crackles/CXR congestion; JVP↑, edema; warm extremities; BP often normal to high	**PCWP ↑** (≈ >18), **CI preserved** (≈ ≥2.2)	**IV diuretic** (decongestion); if BP is higher consider **vasodilation**; O_2/ventilation as needed
Cold–Dry ("cold–dry")	**No (or minimal)**	**No**	Cold extremities, prolonged capillary refill, weakness, dizziness, oliguria; minimal congestion; BP may be low or normal	Two subtypes: **(A)** PCWP low/normal + **CI ↓**; **(B)** PCWP normal to mildly ↑ + **CI ↓**	Clarify preload: if hypovolemia suspected → **cautious fluid challenge**; otherwise with low output consider **inotrope** and search for the cause
Cold–Wet ("cold–wet")	**Yes**	**No**	Combination: dyspnea/crackles, JVP↑, edema **plus** cold extremities, hypotension/narrow pulse pressure, oliguria, altered mental status, lactate ↑	**PCWP ↑** (≈ >18), **CI ↓** (≈ <2.2)	**Urgent stabilization:** O_2/ventilation; **inotrope** for low output; in hypotensive shock add a **vasopressor**; decongest cautiously; treat trigger (ACS, arrhythmia, mechanical cause); consider **mechanical support**

RAAS in heart failure

- ↓ Renal perfusion → ↑ renin → angiotensin I → angiotensin II
- Vasoconstriction → ↑ afterload
- ↑ Aldosterone → Na^+/water retention → ↑ preload
- ↑ ADH → hyponatremia
- Result: ↑ filling pressures, fibrosis, remodeling

Myocardial remodeling

- ↑ pressure/volume load + RAAS + SNS →
  - Cardiomyocyte hypertrophy
  - Apoptosis
  - Fibroblast activation → fibrosis
- Eccentric hypertrophy → dilation, ↓ EF
- Concentric hypertrophy → stiffening, diastolic dysfunction

RAAS in heart failure

↓ renal perfusion

↓

↑ renin (juxtaglomerular apparatus)

↓

angiotensinogen (liver)

↓

→ angiotensin I → *(ACE in the lungs)*

↓

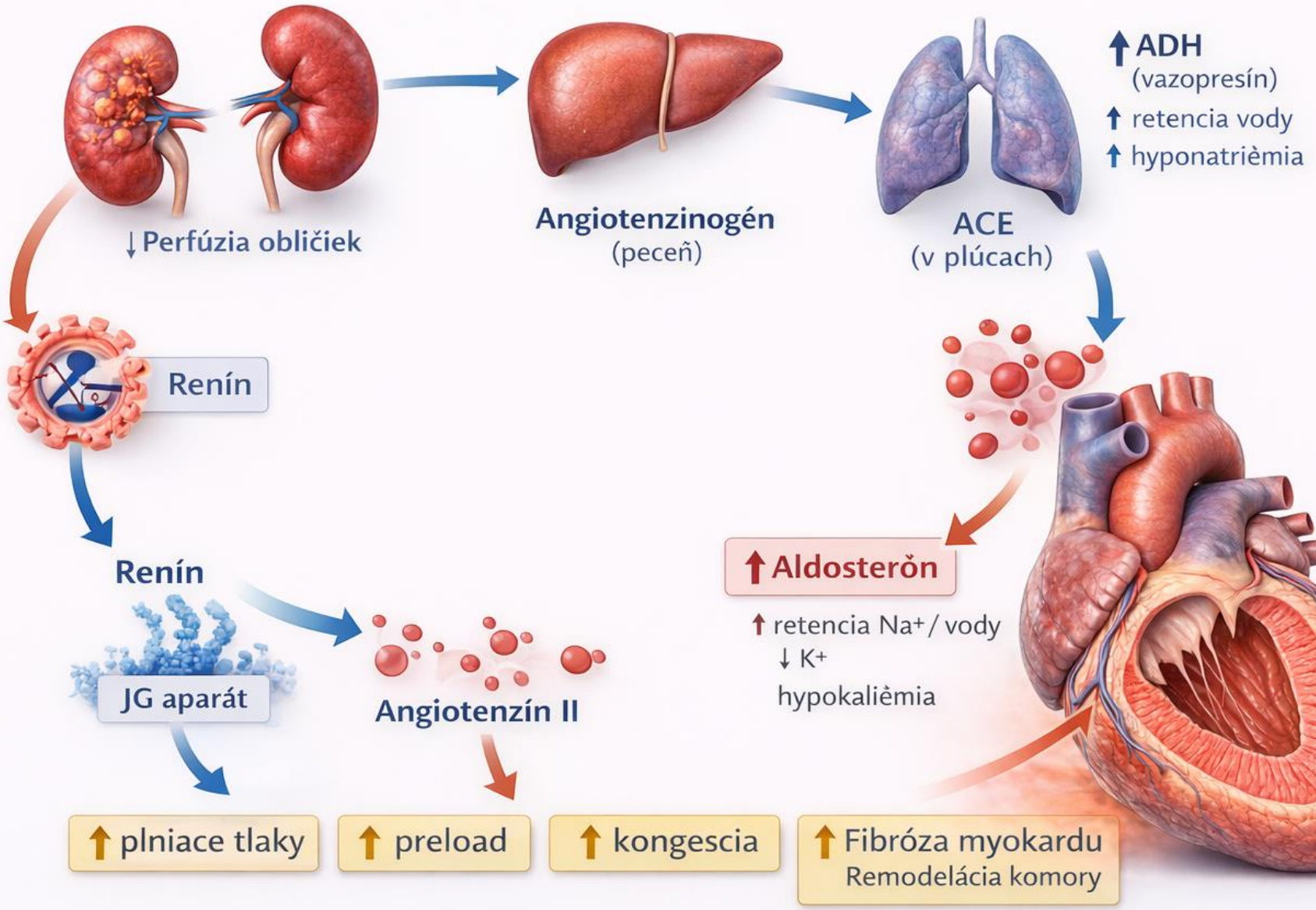
→ angiotensin II →

Effects of angiotensin II:

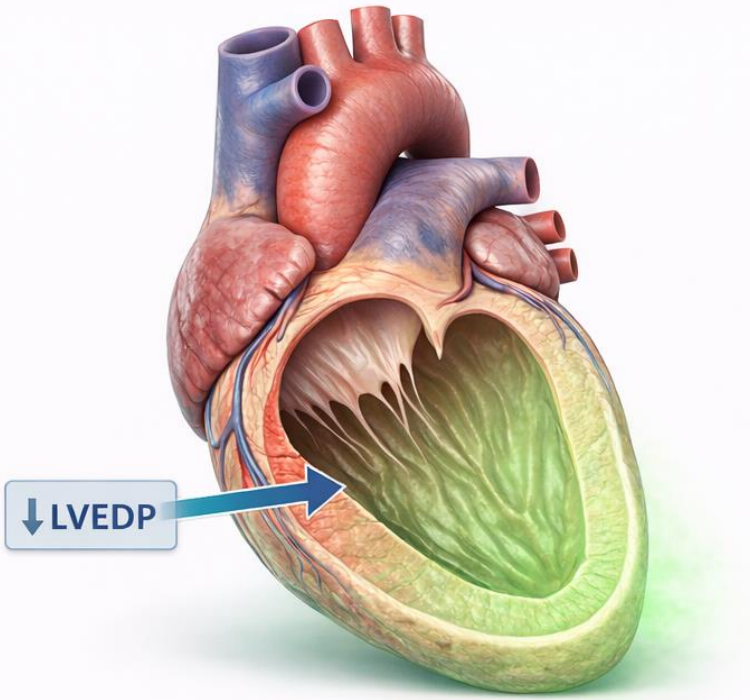
- **Vasoconstriction**
  - ↑ afterload
  - ↑ blood pressure
- **↑ Aldosterone**
  - Na^+/water retention
  - hypokalemia
- **↑ ADH (vasopressin)**
  - water retention
  - hyponatremia

Overall effect: ↑ filling pressures, ↑ preload, ↑ cor ↓ tion, ↑ myocardial fibrosis, ventricular remodeling

RAAS in heart failure



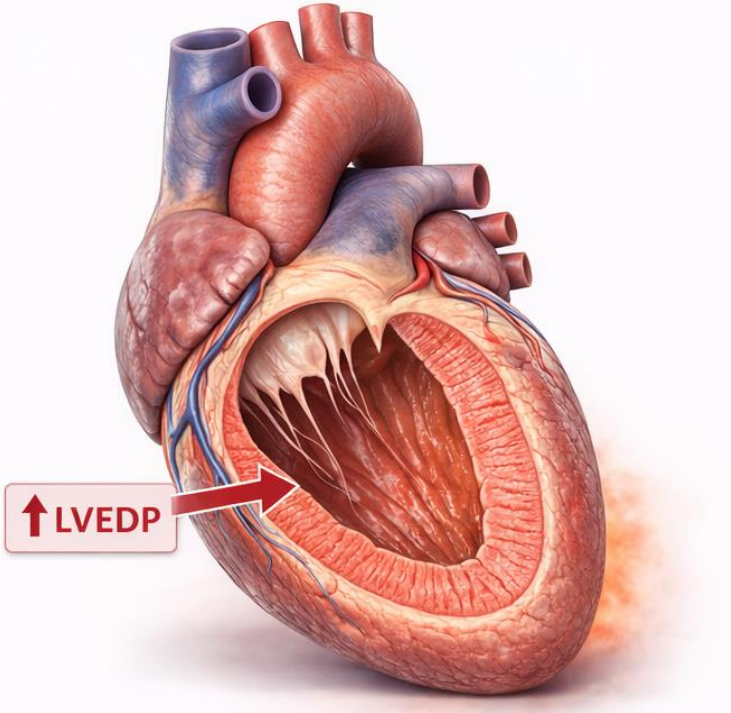
Diastolic dysfunction



Normálna relaxácia ľavej komory (ĽK)

Poddajnost: ↑ dobrá

Normálna diastolická náplň
(nízky plniaci tlak)



Stuhnutosť ľavej komory pri diastolickej dysfunkcii

Poddajnosť: ↓ znížená

- Dilatácia ľavej predsiene
- Plúcna kongescia (↑plniaci tlak)

HFpEF pathophysiology

- Metabolic stress (obesity, type 2 diabetes, hypertension) →
- Systemic inflammation → endothelial dysfunction →
- ↓ NO (nitric oxide) → microvascular ischemia → LV (left ventricular) stiffening
- → ↑ LVEDP (left ventricular end-diastolic pressure), ↑ LA (left atrial) pressure, pulmonary hypertension → exertional dyspnea

HFpEF pathophysiological model

METABOLIC STRESS

(obesity, type 2 diabetes, hypertension, inflammation)

↓

Systemic inflammation and ↑ cytokines

↓

Endothelial dysfunction (NO↓)

↓

↓ Vasodilatory reserve

↓

Microvascular myocardial ischemia

↓

Stiffness + impaired relaxation

↙ ↓ ↘

↑ LVEDP ↑ LA pressure Pulmonary hypertension

Diastolic dysfunction LA dilation ↓ exercise tolerance

and exertional dyspnea

HFpEF = normal EF, but ↑ filling pressures, ↓ compliance

Multisystem disease → treatment goal is ↓ congestion and improved relaxation

Myocardial remodelling *(explains hypertrophy, dilatation, fibrosis)*

- **↑ Load (pressure / volume) + ↑ RAAS + ↑ SNS**

  ↓

  Activation of cardiomyocytes
- **Hypertrophy (compensatory)**
- **Cardiomyocyte apoptosis (harmful)**
- **Fibroblast activation → Interstitial fibrosis**

CHANGES IN LV GEOMETRY (LV geometric change)

- **Eccentric hypertrophy (volume overload)**

  → LV dilatation

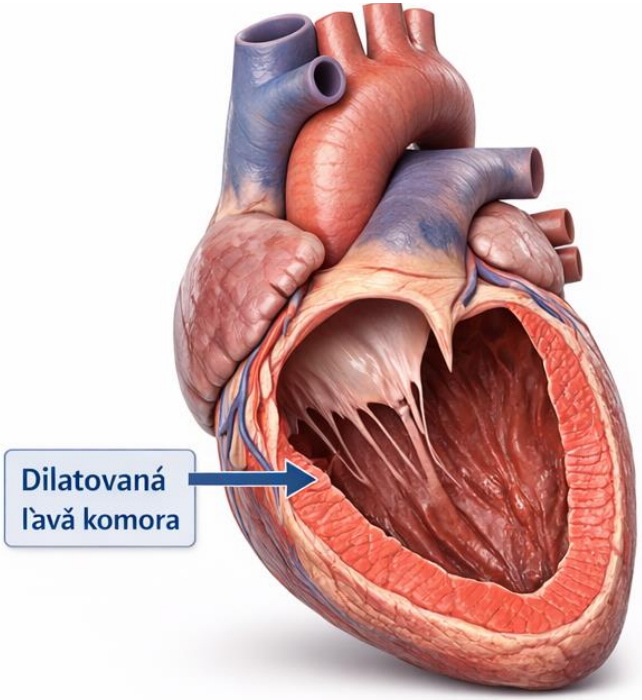
  → ↓ EF
- **Concentric hypertrophy (pressure overload)**

  → LV stiffening

  → diastolic dysfunction

Consequence: progression of **HF**, reduced **CO**, arrhythmias, higher mortality

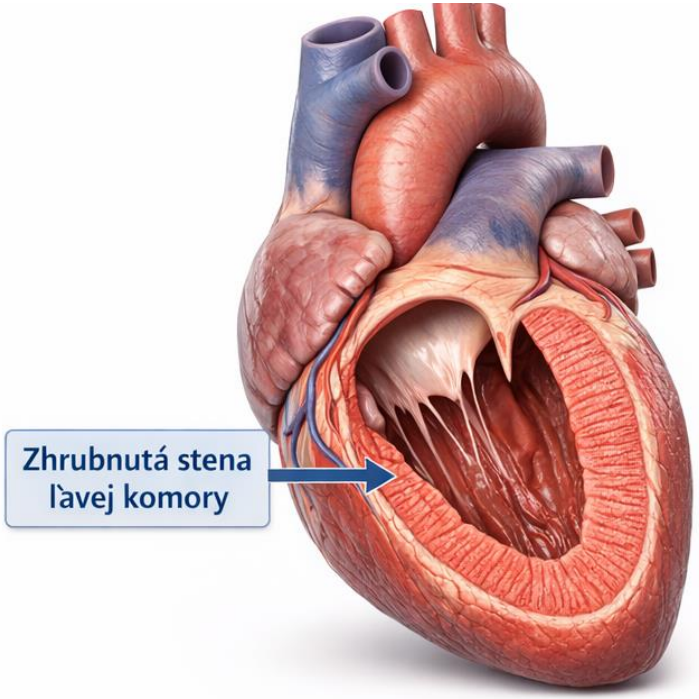
Myocardial remodeling



Eccentrická hypertrofia

(dilatovaná komora)

- Zväčšený objem
- Nízka ejekčná frakcia



Koncentrická hypertrofia

(zhrubnutá stena)

- Zhrubnutá stena
- Diastolická dysfunkcia