

Tetralogy of Fallot

Congenital heart disease: structural anatomy, shunt physiology,
and clinical consequences

A source-grounded pathology lecture

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Learning objectives

- Recognize the four cardinal defects and their common embryologic origin.
- Explain why right ventricular outflow obstruction determines shunt direction.
- Relate characteristic morphology to cyanosis and the clinical spectrum.
- Distinguish tetralogy from VSD alone and other cyanotic shunts.

Tetralogy within congenital heart disease

Congenital cardiac malformations may cause shunting, obstruction, or both.

Congenital

Structural abnormality present at birth.

Shunt

Abnormal communication between cardiac compartments.

Obstruction

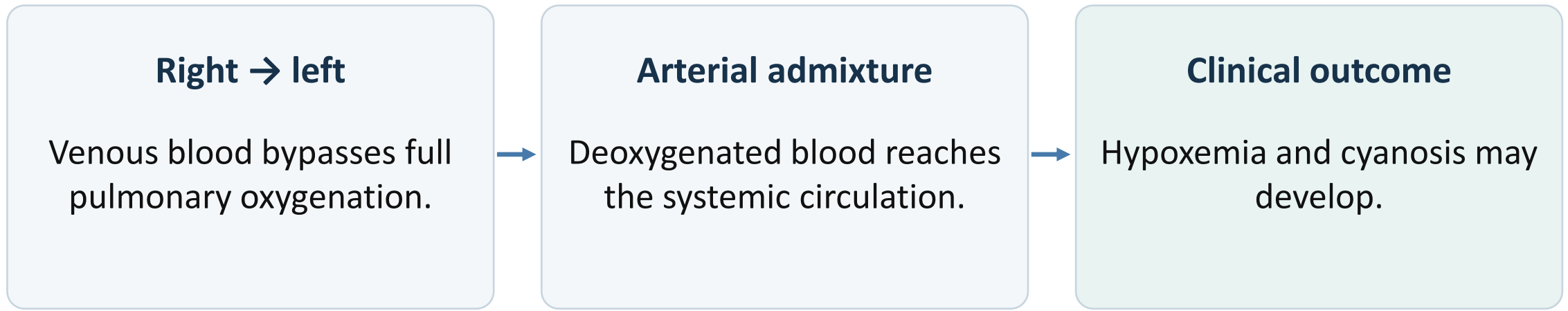
Narrowing of a chamber, valve, or vascular outflow.

Tetralogy

A ventricular shunt combined with pulmonary outflow obstruction.

Why a shunt changes systemic oxygenation

The direction of an abnormal communication governs the clinical consequence.



Shunt physiology: First distinctions

Left-to-right shunt	Right-to-left shunt
Initially no systemic cyanosis	Systemic oxygenation decreases
Pulmonary blood flow increases	Pulmonary circulation is partly bypassed
Pulmonary vascular injury may develop with time	Paradoxical systemic embolism is possible
Typical of isolated VSD/PDA initially	Typical of obstructive severe TOF

The four defining abnormalities

1. Ventricular septal defect

A usually large interventricular communication.

2. RV outflow obstruction

Typically infundibular, sometimes valvular.

3. Overriding aorta

The aortic root straddles the VSD.

4. Right ventricular hypertrophy

Myocardial response to pressure overload.

One embryologic lesion explains three defects

Infundibular septum

Abnormally displaced
anterosuperiorly.



Outflow malalignment

Produces VSD, RVOT
narrowing, and aortic
override.



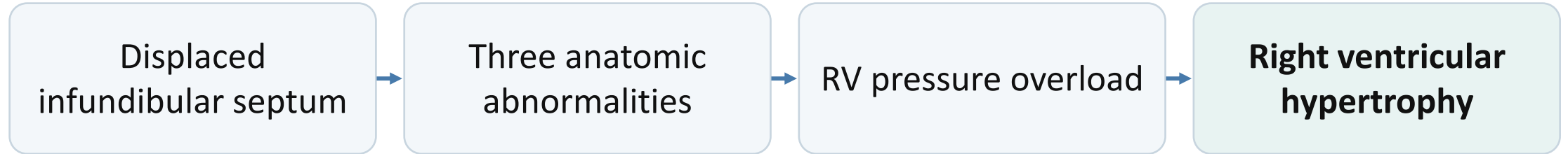
Hemodynamic response

Right ventricular pressure
load causes hypertrophy.

Anterosuperior infundibular displacement

- The primary developmental abnormality involves the infundibular septum.
- Malalignment creates defective ventricular septation.
- Pulmonary outflow caliber is reduced.
- Aortic origin becomes positioned over the septal defect.

Primary malformation versus acquired response



The hypertrophy is a consequence of obstruction—not a fourth independent septation error.

VSD: The intracardiac communication

- A ventricular septal defect creates communication between both ventricles.
- In tetralogy, the opening is usually large.
- Shunting depends on pressure gradients and the outflow obstruction.
- A VSD does not by itself establish the presence of cyanosis.

Overriding aorta: A malaligned outlet

- The aortic valve sits at the superior border of the VSD.
- The root overrides the interventricular opening.
- It is related anatomically to both ventricular chambers.
- Overriding, rather than simple aortic enlargement, is the diagnostic relationship.

RV outflow obstruction: The pivotal lesion

- Most commonly there is narrowing of the infundibulum.
- Pulmonary valvular stenosis may coexist.
- Greater outflow obstruction elevates right ventricular pressure.
- The severity of obstruction determines whether cyanosis is prominent.

Subpulmonic versus pulmonary valve stenosis

Infundibular narrowing	Valvular pulmonary stenosis
Narrowing below the pulmonary valve	Narrowing at the valve
Characteristic dominant TOF site	May accompany the infundibular lesion
Restricts ejection from RV toward pulmonary trunk	Adds further outflow resistance
Direct consequence of malaligned outflow septum	Associated additional narrowing

Right ventricular hypertrophy develops secondarily

RV outflow narrowed

Pulmonary ejection
encounters obstruction.



RV pressure rises

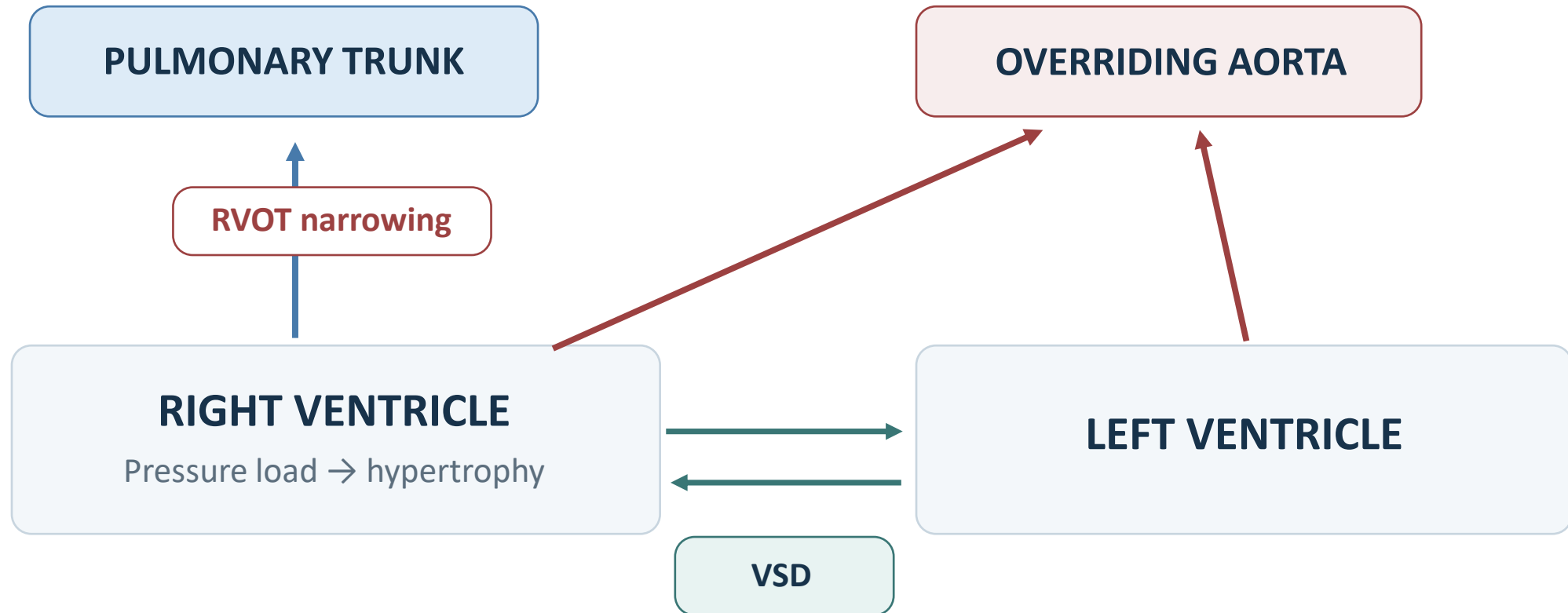
Systolic pressure loading
increases.



Wall thickening

Right ventricular
myocardium hypertrophies.

Tetralogy: The abnormal connections



Right-to-left flow becomes prominent when RV outflow obstruction is severe.

The gross phenotype: Enlarged, boot-shaped heart

- The heart is typically enlarged.
- Marked right ventricular hypertrophy produces the classic boot-shaped outline.
- This external configuration reflects chronic ventricular remodeling.
- The term describes gross shape; It is not a stand-alone diagnosis.

Why the heart becomes boot-shaped

Pulmonary outflow impeded

RV must eject against greater resistance.



RV mass increases

Marked right ventricular hypertrophy develops.



Cardiac contour changes

Enlarged heart assumes a boot-like shape.

Large VSD: Morphology to flow

- The VSD usually lies beneath the overriding aortic valve.
- Its substantial size permits ventricular communication.
- The direction of flow is not fixed across all tetralogy phenotypes.
- Physiology must be interpreted with the degree of pulmonary narrowing.

Aortic override: The superior VSD margin

- The aortic valve forms the superior border of the defect.
- Aortic inflow can be supplied from either ventricular side through the communication.
- This arrangement contributes to systemic admixture when RV pressure is high.
- The aortic relationship is a structural finding, distinct from the direction of shunt.

The outflow narrowing can have two levels

- Infundibular narrowing is the usual dominant obstructive component.
- Additional pulmonary valve stenosis can be present.
- Combined obstruction further limits the RV–pulmonary arterial route.
- Anatomic localization matters when interpreting disease severity.

Pulmonary atresia: The extreme obstructive variant

Pulmonary outlet atretic

Native antegrade pulmonary outflow is severely interrupted.



Alternative blood supply

Patent ductus arteriosus and/or bronchial arteries.



Survival becomes dependent

Pulmonary perfusion requires an alternative route.

Pulmonary atresia and the ductus arteriosus

- Atresia may involve the pulmonary valve and variable portions of pulmonary arteries.
- A patent ductus arteriosus can furnish blood to the pulmonary circulation.
- When this route is critical, loss of ductal patency threatens pulmonary perfusion.
- The defect is more complex than the usual stenotic variant.

Dilated bronchial arteries as an alternate source

- Some atretic forms use dilated bronchial arteries to sustain lung perfusion.
- Bronchial collateral flow may coexist with ductal flow.
- Collateral vessels change the operative anatomy.
- Pulmonary atresia with dilated bronchial arteries as especially complex to repair.

Associated structural findings

Atrial septal defect

May coexist with the ventricular abnormalities.

Aortic insufficiency

May accompany the overriding aortic valve.

Right aortic arch

Reported in about one-quarter of cases.

Pulmonary atresia

A severe variant with alternate pulmonary blood supply.

Right aortic arch: Associated anatomy

- A right aortic arch in approximately 25% of TOF cases.
- This is an associated anatomic variant, not one of the four defining features.
- Its presence reinforces the need to assess the great arteries.
- Do not use an arch variant in isolation to diagnose tetralogy.

The dominant hemodynamic determinant

Pulmonary outflow obstruction

Limits blood exiting RV to the pulmonary circulation.



Right ventricular pressure

Approaches or exceeds left ventricular pressure if severe.



VSD shunt direction

Changes toward right-to-left flow.

Shunting is pressure-dependent—not obligatory

- The VSD provides the potential pathway between ventricles.
- Low RV outflow resistance may permit left-to-right flow.
- Marked RV outflow resistance favors right-to-left flow.
- Consequently, structural tetralogy spans noncyanotic and cyanotic phenotypes.

Mild obstruction: The “pink” phenotype

Modest subpulmonic stenosis

RV outflow remains comparatively accessible.



Possible left-to-right flow

Hemodynamics resemble an isolated VSD.



No obligatory cyanosis

Clinical presentation may be acyanotic.

Severe obstruction: Classic cyanotic tetralogy

Severe RV outflow stenosis

RV pressure
approaches/exceeds LV
pressure.



Right-to-left VSD shunt

Venous blood enters aortic
outflow.



Systemic desaturation

Hypoxemia produces
cyanosis.

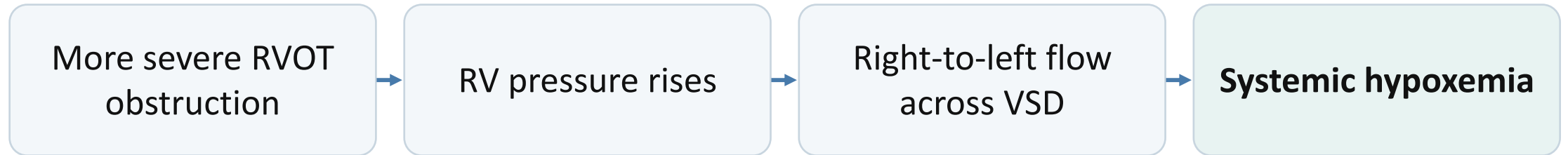
Pink versus classic tetralogy

Milder obstruction (“pink”)	More severe obstruction (classic)
RV–pulmonary outflow relatively preserved	RV–pulmonary outflow markedly impeded
Shunt may be left-to-right	Shunt becomes right-to-left
Cyanosis may be absent	Cyanosis is characteristic
Clinical physiology resembles VSD	Clinical physiology reflects systemic admixture
Same four-defect anatomical framework	Same four-defect anatomical framework

Why cyanosis appears early

- A substantial right-to-left shunt delivers relatively unoxygenated blood to the aorta.
- Pulmonary gas exchange is bypassed by part of the systemic output.
- The systemic arterial oxygen content falls.
- Most infants with TOF become cyanotic at birth or shortly thereafter.

Mechanistic chain from stenosis to cyanosis



The ventricular communication permits the shunt; The obstructive lesion sets its direction.

Hypoxemia and cyanosis are related but distinct

- Hypoxemia: Reduced oxygenation of arterial blood.
- Cyanosis: Visible dusky discoloration of skin or mucous membranes.
- Right-to-left admixture is the shared physiologic cause in severe tetralogy.
- Cyanosis can vary with the severity of outflow obstruction.

Chronic hypoxemia may produce erythrocytosis

- Long-standing right-to-left shunting can sustain systemic hypoxia.
- Hypoxic drive increases circulating red blood cell mass.
- This as polycythemia in cyanotic congenital heart disease.
- It is a consequence of sustained hypoxemia, not a defining cardiac malformation.

Digital clubbing in chronic cyanotic disease

- Prolonged cyanotic congenital heart disease may cause clubbing of fingers and toes.
- The distal digits become enlarged and blunted.
- Bony changes can accompany the soft-tissue alterations.
- The finding indicates a chronic systemic consequence rather than lesion specificity.

Paradoxical embolism: Loss of the pulmonary filter

Systemic venous embolus

Enters the right-sided circulation.



Right-to-left shunt

May bypass pulmonary capillary filtration.



Systemic arterial embolus

Can reach distal organs.

Why pulmonary vascular overload is less typical

- The stenotic pulmonary outlet reduces excessive pressure transmission to the lungs.
- A protective effect on the pulmonary vasculature.
- This contrasts with large uncorrected left-to-right shunts.
- Protection from pulmonary pressure overload does not eliminate systemic cyanosis.

Tetralogy versus a large isolated VSD

Tetralogy of Fallot	Large isolated VSD
VSD plus RV outflow obstruction	Ventricular communication without the TOF tetrad
Severe stenosis can cause early right-to-left shunting	Initial shunting is generally left-to-right
Reduced pressure transmission to lung circulation	Pulmonary overcirculation can cause vascular injury
Marked RVH from outflow pressure load	Cardiac adaptation depends on shunt burden

Why right ventricular failure is uncommon

- Right ventricular hypertrophy reflects pressure load.
- In TOF, some RV blood can exit through the large VSD into the left ventricle/aorta.
- This shunting decompresses the right ventricle.
- Robbins therefore describes overt RV failure as rare in the untreated lesion.

Growth can increase obstruction severity

Child grows

Cardiac mass and dimensions increase.



Pulmonary orifice lags

Obstructed opening fails to enlarge proportionately.



Relative obstruction worsens

Right-to-left shunting may become more important.

Anatomy and physiology need not progress together

- The congenital structural defects are present from birth.
- Their clinical expression depends on the degree of RV outflow narrowing.
- Growth may increase relative obstruction without creating a new defect.
- The same anatomical diagnosis can therefore present differently over time.

Clinical expression follows the obstructive spectrum

Mild RVOT narrowing

VSD-like physiology; Cyanosis may be absent.

Moderate narrowing

Increasing RV load with variable shunt direction.

Severe narrowing

Right-to-left shunt; Classic cyanosis.

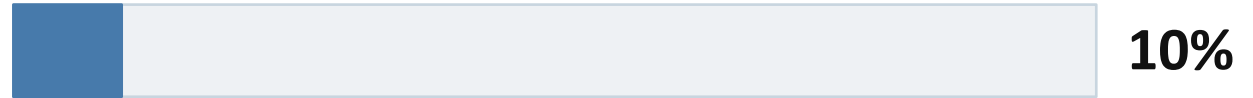
Pulmonary atresia

Survival may require PDA and/or bronchial blood supply.

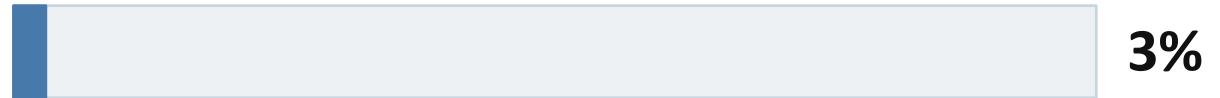
Natural history without repair

Low survival into adulthood among unoperated individuals.

Alive at age 20 years



Alive at age 40 years



Historical textbook figures for untreated TOF; Not contemporary postoperative outcomes.

Survival depends on stenosis severity

- Less severe subpulmonic stenosis may be tolerated longer.
- Marked obstruction leads to early right-to-left shunting and cyanosis.
- Survival estimates for unoperated cohorts should not be applied to repaired patients.
- Marked clinical heterogeneity across the obstructive spectrum.

Surgical repair targets the structural defects

Anatomic disease

VSD, overriding aorta, RVOT obstruction, RVH.



Corrective operation

Addresses the intracardiac defect and RV outflow pathway.



Physiologic goal

Reduce pathological shunting and relieve obstruction.

Why severe variants are harder to repair

- Pulmonary valve and arterial atresia alter the normal outflow route.
- Pulmonary circulation may depend on ductal or bronchial arterial channels.
- Dilated bronchial arteries can complicate reconstruction.
- Robbins specifically highlights these complex anatomic variants.

Tetralogy versus transposition of great arteries

Tetralogy of Fallot	Dextro-transposition (d-TGA)
Malaligned infundibular septum	Abnormal truncal/aortopulmonary septation
VSD with subpulmonic obstruction	Aorta exits RV; Pulmonary artery exits LV
R→L shunt depends on stenosis	Parallel circulations require mixing
Right ventricular hypertrophy from obstruction	Morphologic RV supports systemic circulation

Tetralogy versus Eisenmenger physiology

Tetralogy of Fallot	Eisenmenger syndrome
Congenital pulmonary outflow obstruction	Late pulmonary vascular disease after L→R shunt
R→L shunt may occur early	Shunt reverses after resistance rises
Stenosis limits pulmonary vascular overload	Pulmonary arteriolar remodeling raises resistance
RV hypertrophy is pressure-related	RV hypertrophy reflects pulmonary hypertension

The PDA has opposite roles in different lesions

- An isolated PDA usually produces an initial left-to-right shunt.
- In severe TOF with pulmonary atresia, a PDA may supply vital pulmonary blood flow.
- Thus ductal patency can be undesirable in one context and essential in another.
- Interpret vascular communications using the complete anatomy.

A lesion-based diagnostic reasoning framework

Observed abnormality	Anatomic explanation	Functional consequence
Large VSD	Interventricular communication	Allows pressure-driven shunting
Overriding aorta	Aorta over septal defect	Potential systemic admixture
Subpulmonic stenosis	Narrow infundibulum	RV pressure load; Restricted pulmonary flow
Right ventricular hypertrophy	Secondary wall thickening	Remodeling from pressure load
Pulmonary atresia	Occluded pulmonary outlet	Alternate perfusion needed

Case 1: The acyanotic infant

CLINICAL SCENARIO

An infant has a large ventricular septal communication and aortic override. Subpulmonic narrowing is comparatively mild. The infant has no cyanosis.

What shunt pattern is possible, and how is this phenotype described?

Case 1: Mechanism and interpretation

- Mild subpulmonic obstruction allows a left-to-right VSD shunt.
- Absence of cyanosis does not exclude the anatomic tetrad.
- Robbins calls this pattern “pink tetralogy.”
- As obstruction changes, the direction of shunting can change.

Case 2: Cyanosis soon after birth

CLINICAL SCENARIO

A newborn with a large VSD and overriding aorta develops early cyanosis. Pulmonary outflow is severely narrowed; Right ventricular pressure is high.

Trace the hemodynamic sequence that generates cyanosis.

Case 2: Hemodynamic explanation

- Severe RVOT obstruction raises right ventricular pressure.
- Pressure promotes right-to-left flow across the VSD.
- Venous blood enters the systemic aortic output.
- Systemic arterial hypoxemia becomes clinically apparent as cyanosis.

Case 3: Pulmonary atresia with collaterals

CLINICAL SCENARIO

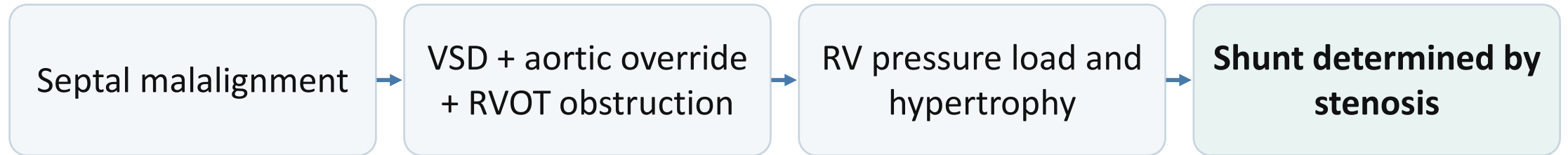
An infant has the usual tetralogy anatomy but also pulmonary valve atresia. The pulmonary circulation depends on a patent ductus and enlarged bronchial arteries.

Why does this variant require special anatomic consideration?

Case 3: Alternative pulmonary perfusion

- Normal forward RV-to-pulmonary arterial flow is interrupted.
- Ductal and bronchial arteries may be necessary to sustain lung blood flow.
- Operative repair must account for these alternate vascular pathways.
- Complete repair is especially complicated in such cases.

Synthesis: One defect cascade, multiple phenotypes



The four anatomic findings are linked; The clinical spectrum is governed largely by RV outflow obstruction.

Morphologic checklist at the specimen level

Feature to identify	Source-described finding
Ventricular septum	Usually large defect
Aortic root	Overriding defect and both ventricles
RV outflow tract	Infundibular narrowing $\pm$ valvular stenosis
Right ventricle	Marked hypertrophy; Boot-shaped heart
Pulmonary arteries	May be atretic in severe variants
Other structures	Possible ASD, aortic insufficiency, right arch

Common reasoning errors

- Treating tetralogy as four unrelated congenital lesions.
- Assuming every VSD causes left-to-right shunting.
- Assuming every TOF infant must be cyanotic regardless of stenosis severity.
- Equating right ventricular hypertrophy with inevitable RV failure.
- Overlooking pulmonary atresia and alternative pulmonary blood supply.

Four findings to retain

Cause

Anterosuperior displacement of the infundibular septum.

Anatomy

VSD, RVOT obstruction, overriding aorta, and RVH.

Physiology

More severe stenosis shifts the VSD shunt right to left.

Consequences

Cyanosis, remodeling, and severity-dependent survival.

Primary source and scope

Primary reference

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026), Chapter 12, pp. 485–490.
- Tetralogy of Fallot section, pp. 489–490; Congenital Heart Disease section, pp. 485–489.

The source conversion references Fig. 12.5; no textbook figure has been reproduced.