

Congenital Heart Disease

Embryogenesis • anatomic malformations • hemodynamic consequences

Pathology lecture | developmental and clinicopathologic foundations

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Learning objectives

Classify congenital lesions

Differentiate septal, obstructive, and abnormal-connection defects

Explain developmental origins

Relate heart fields, neural crest, cushions, and regulatory pathways

Interpret clinical physiology

Predict consequences of shunts, obstruction, and pulmonary remodeling

Congenital heart disease

Structural abnormalities of the heart or great vessels present at birth.

- The umbrella term describes a spectrum, not one clinical syndrome.
- Defects arise chiefly from disturbed cardiovascular morphogenesis.
- Anatomic location and postnatal blood flow jointly determine manifestations.

**Septal
communication**

ASD / VSD

Obstruction

Valves / vessels / chambers

**Abnormal
connections**

Great vessels / coronaries

A developmental disorder with variable severity

Cardiac malformation and clinical presentation are not synonymous.

- The most severe anomalies may preclude intrauterine survival.
- Discrete structural lesions can remain compatible with live birth.
- Clinical consequences may emerge only as circulation changes after delivery.

Before birth

Severe defects may
impair survival

After birth

Previously tolerated
defects may become
symptomatic

The main morphologic categories

Location provides the first useful classification.

- Septal defects: Abnormal communication between chambers.
- Stenotic lesions: Narrowing of valves, vessels, or an entire cardiac chamber.
- Outflow anomalies: Abnormal ventricular–arterial or coronary connections.

Septa

ASD • VSD

Narrowing

Stenosis • hypoplasia

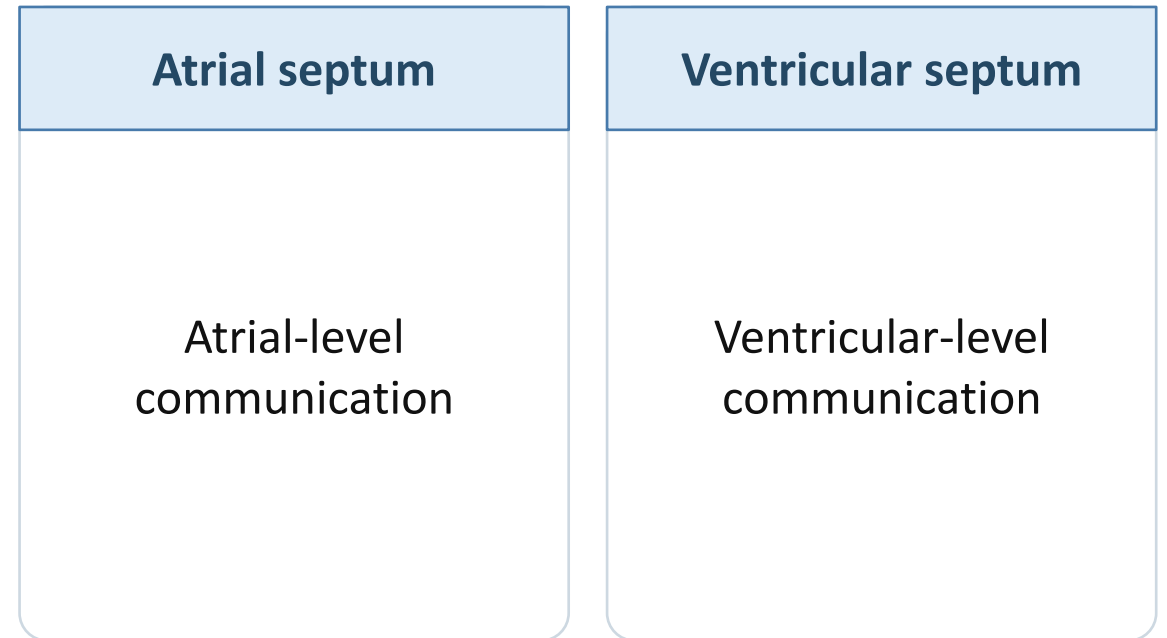
Outflow

Great-artery routing

Septal malformations create communication

An anatomic opening can alter flow before it causes symptoms.

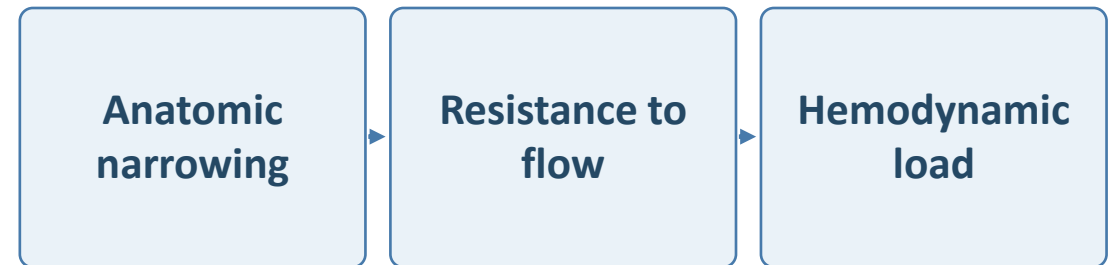
- An atrial septal defect (ASD) joins the atria.
- A ventricular septal defect (VSD) joins the ventricles.
- Physiologic severity depends on more than the mere presence of a hole.



Obstruction spans valves to entire chambers

A narrowed structure restricts forward blood flow.

- Some lesions are localized at a valve or great vessel.
- Hypoplastic left heart is an example involving an underdeveloped cardiac chamber.
- Complete developmental absence of a passage is termed atresia.



Causal sequence / schematic

Abnormal outflow connections

Great-vessel routing can be part of the primary defect.

- The connection of major arteries to ventricles may be abnormal.
- Coronary arteries may also have congenital anomalous origins or courses.
- Describe the connection accurately before predicting its physiology.

Outflow routing

Great arteries
connected
abnormally

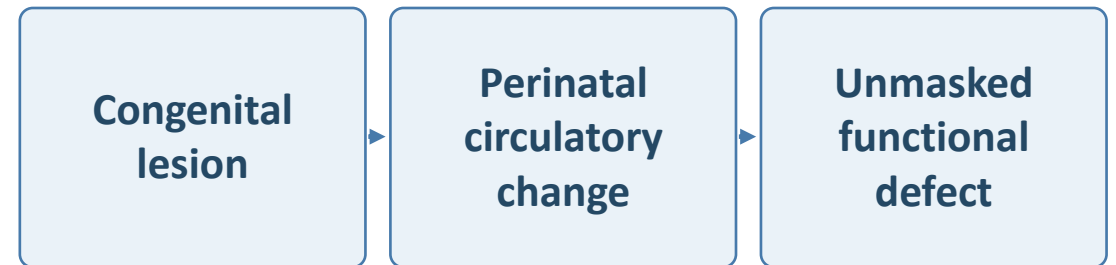
Coronary routing

Anomalous coronary
connections

Why some lesions present after birth

The fetal-to-perinatal circulatory transition changes the consequences of a lesion.

- Anatomic defects are present before clinical signs become obvious.
- Circulatory pressure and flow patterns change around birth.
- A lesion tolerated during fetal life may then become clinically important.

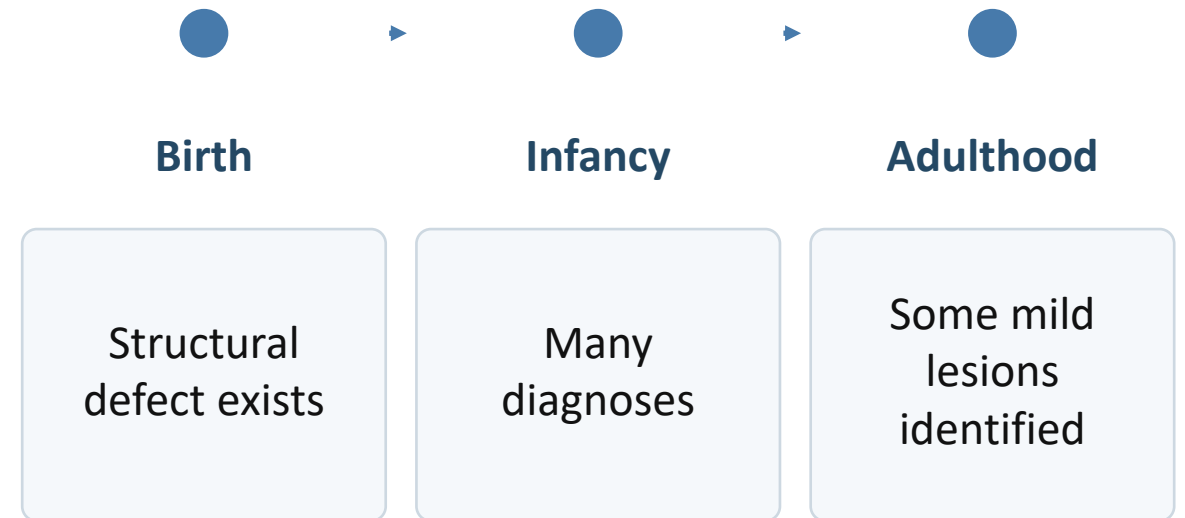


Causal sequence / schematic

Age at recognition is variable

Timing of presentation does not reliably indicate when the defect arose.

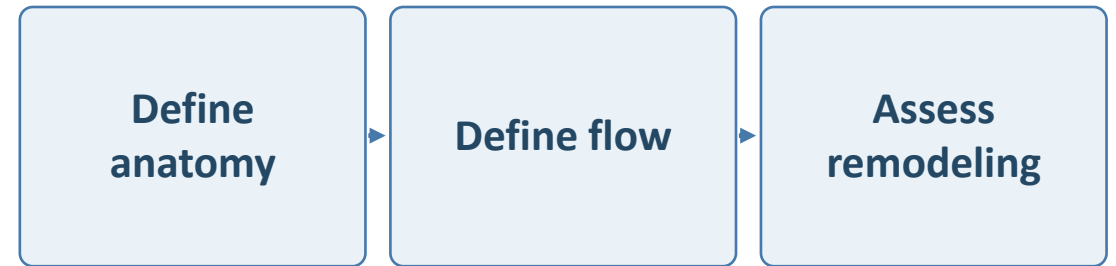
- That about half of CHD is diagnosed during the first year.
- Some mild defects evade recognition until adulthood.
- ASD provides an example of late-recognized congenital disease.



Anatomy and physiology are two separate questions

The same structural category may have different clinical impact.

- First identify the lesion: Communication, obstruction, or anomalous connection.
- Then establish the direction and magnitude of blood flow.
- Finally assess chamber and pulmonary-vascular responses.



Causal sequence / schematic

Incidence depends on case definition

A number is interpretable only after specifying which lesions are counted.

- Routine neonatal echocardiography detects many minor abnormalities.
- Some findings resolve and do not represent a sustained CHD burden.
- Clinical ascertainment yields a different frequency from universal screening.

Screening prevalence

Includes many small,
transient lesions

Significant CHD

Restricted to more
serious
malformations

Small neonatal septal defects may be transient

Detection of an opening is not equivalent to persistent disease.

- Routine neonatal echocardiography identifies small muscular VSDs or ASDs in more than 5% of births.
- These small defects typically close spontaneously during the first year.
- Their inclusion materially inflates the apparent burden of CHD.



Causal sequence / schematic

Bicuspid aortic valve complicates prevalence estimates

Persisting structural variation may remain clinically silent for years.

- Robbins gives an estimated incidence of 1%–2%.
- The valve persists beyond infancy, unlike many tiny neonatal defects.
- Manifestations may be modest and first recognized later in adult life.

Anatomic persistence

Bicuspid morphology
remains

Clinical recognition

May occur much later

Significant CHD: Less than 1% worldwide

More serious cardiovascular malformations remain major birth defects.

- The textbook places worldwide incidence slightly below 1% of live births.
- This estimate explicitly excludes many transiently detected findings.
- Compare frequencies only when case definitions and denominators match.

Significant lesions

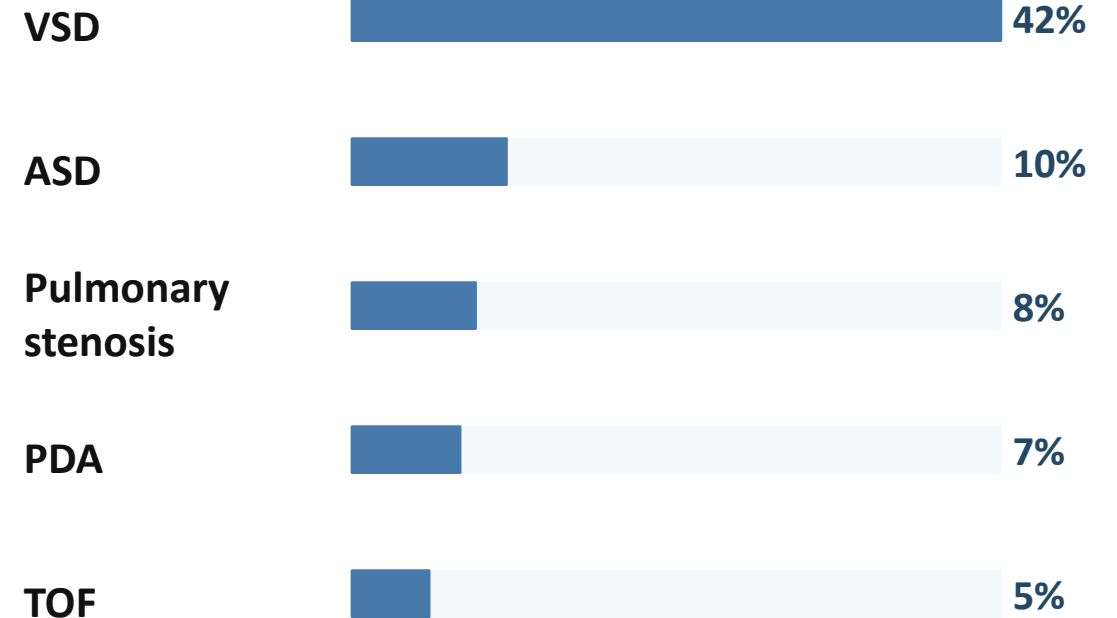
<1% of live births

Textbook estimate; Case definition matters

Most cases occur among a limited set of lesions

Twelve malformations account for approximately 85% of CHD cases in the cited series.

- The distribution is strongly weighted toward septal defects.
- Pulmonary stenosis and patent ductus arteriosus are also common.
- The source table excludes bicuspid aortic valves.



Historical table percentages; Shares are rounded

Frequency table: Common defects

Shares shown here reproduce the Robbins frequency table.

- VSD dominates the observed distribution.
- These are rounded percentages, not individualized risk estimates.

Malformation	Per million	Share (%)
Ventricular septal defect	4482	42
Atrial septal defect	1043	10
Pulmonary stenosis	836	8
Patent ductus arteriosus	781	7
Tetralogy of Fallot	577	5
Coarctation of aorta	492	5

Upper quartile of 44 studies; Historical published compilation

Frequency table: Other listed lesions

Several anatomically distinct abnormalities have similar reported frequencies.

- The frequency table is descriptive, not a severity ranking.
- The reported total is 9757 malformations per million live births across listed entities.

Malformation	Per million	Share (%)
Atrioventricular septal defect	396	4
Aortic stenosis	388	4
Great artery transposition	388	4
Truncus arteriosus	136	1
Total anomalous pulmonary venous connection	120	1
Tricuspid atresia	118	1

Upper quartile of 44 studies; Historical published compilation

A prevalence table is not a clinical prognosis

Frequency, physiological severity, and timing of symptoms differ.

- A relatively common defect may be small or close spontaneously.
- A rarer defect may produce severe neonatal compromise.
- Do not infer outcome from the rank of an anomaly in an incidence table.

Population frequency

How often a lesion is counted

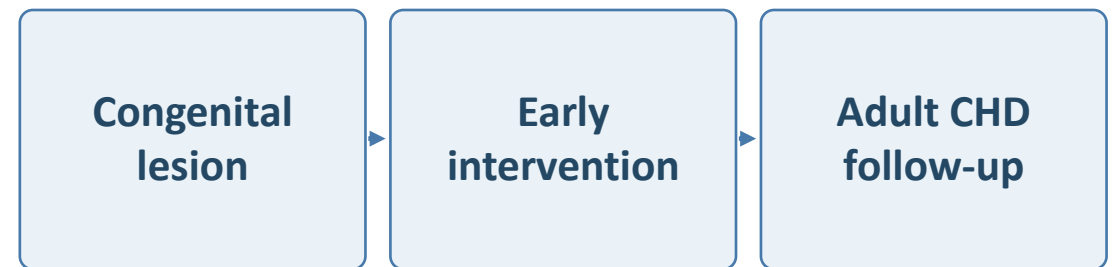
Individual severity

Hemodynamics and associated malformations

Survival into adulthood changes the clinical population

The burden of CHD extends well beyond pediatric cardiology.

- Advances in early repair increase survival with congenital lesions.
- A growing population of adults with CHD.
- Adult follow-up may involve both repaired anatomy and residual physiology.



Causal sequence / schematic

The critical developmental window

Most CHD reflects errors during gestational weeks 3–8.

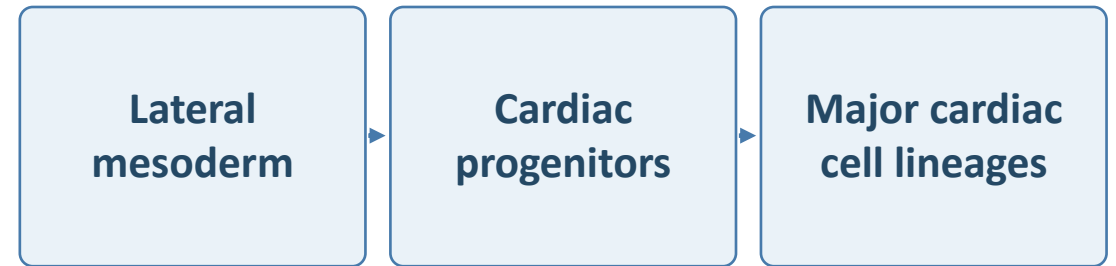
- Major cardiovascular structures form and begin functioning in this interval.
- Errors in migration, remodeling, and septation yield distinct morphologies.
- The timing of an insult affects which structures are vulnerable.



The heart develops from migrating cell populations

Morphogenesis is an orchestrated cellular process, not a simple enlargement.

- Cardiac precursors originate in lateral mesoderm.
- Early cells converge toward the midline in successive heart fields.
- They generate endocardial, myocardial, and smooth-muscle lineages.

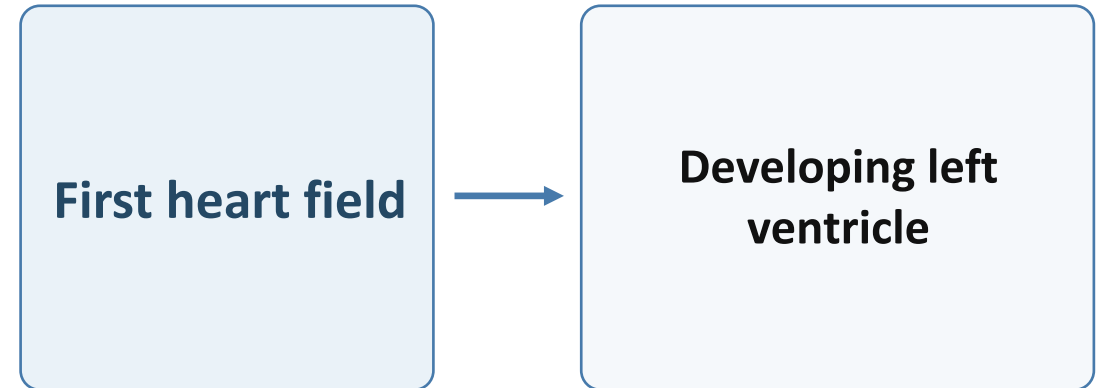


Causal sequence / schematic

The first heart field

One early wave contributes prominently to the developing left ventricle.

- First-wave cardiac precursors reach the midline early.
- Their contribution helps localize potential defects to distinct structures.
- Heart fields are developmental domains rather than adult chambers.



Association in the supplied Robbins table

The second heart field

A later progenitor population contributes to several other regions.

- The second wave contributes to the right ventricle.
- It contributes to the outflow tract and most of the atria.
- Perturbation can thus affect more than one anatomically linked region.

Right ventricle

Second field

Outflow tract

Second field

Most atria

Second field

Heart fields: Complementary anatomic contributions

A discrete heart-field abnormality can have a patterned phenotype.

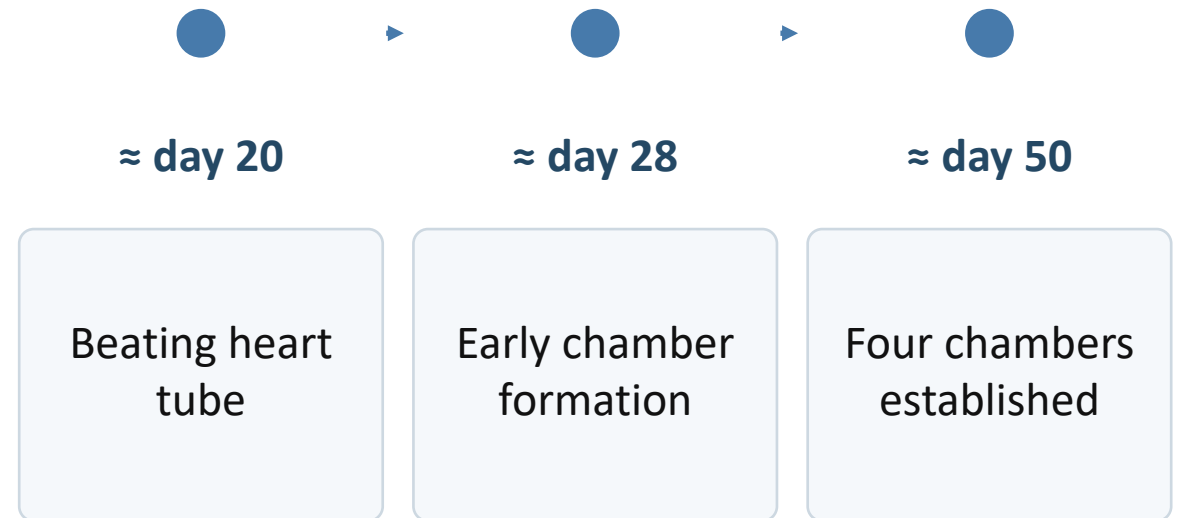
- First heart field: Left ventricular development.
- Second heart field: Right ventricle, outflow tract, and much of the atria.
- A syndrome's distribution may reflect its developmental origin.

First heart field	Second heart field
Primarily developing LV	RV • outflow • much of atria

From cardiac tube to early chambers

The myocardium becomes functional while anatomy is still being established.

- A beating nascent tube by approximately day 20.
- Basic chamber formation begins about eight days later.
- Function and morphogenesis therefore overlap in early development.



Neural crest cells shape the outflow tract

Migrating neural crest derivatives are important for septation and arch formation.

- Cells reach the cardiac outflow during early morphogenesis.
- They help separate aortic and pulmonic outflow tracts.
- They also participate in development of the aortic arch.

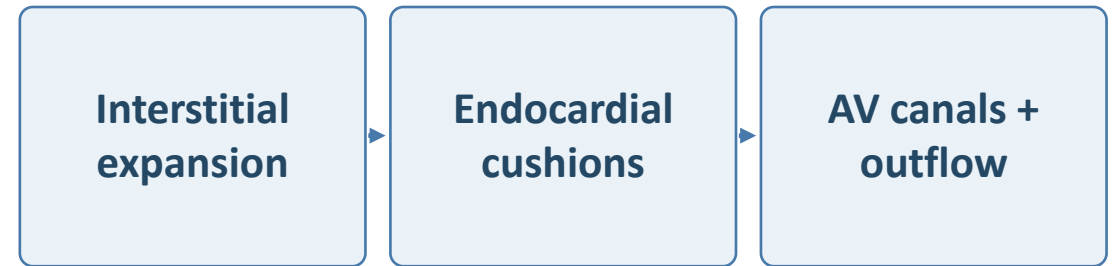


Causal sequence / schematic

Endocardial cushions are major morphogenetic structures

Expanding interstitial connective tissue contributes to valvuloseptal development.

- Definitive endocardial cushions help construct atrioventricular canals.
- They also contribute to outflow tract morphogenesis.
- Impaired cushion formation helps explain certain combined defects.



Causal sequence / schematic

Establishing a four-chambered heart

Septation coordinates the ventricles, atria, and atrioventricular valves.

- This stage at approximately day 50.
- Multiple structures must align and mature together.
- Errors can leave abnormal communications or obstructed pathways.



Why anatomically different defects coexist

Cardiac structures are assembled through overlapping developmental processes.

- Cell migration, tissue growth, and septation are coordinated.
- One disrupted regulatory process may affect several structures.
- Mixed lesions do not necessarily imply separate independent causes.

Cell migration

Regional precursor allocation

Tissue remodeling

Cushions and chamber formation

Septation

Separation of chambers and outflow

Developmental process predicts lesion location

A lesion's location provides mechanistic clues but not a molecular diagnosis.

- Septal abnormalities suggest disturbed separation/remodeling.
- Outflow anomalies may reflect second-field or neural-crest perturbation.
- A precise genotype cannot be inferred from anatomy alone.

Septal region	Outflow region
Partitioning / cushion processes	Second-field / crest processes

Cardiac morphogenesis needs coordinated signaling

No single pathway controls all developmental steps.

- Wnt and Hedgehog signaling.
- VEGF, BMP, TGF- β , fibroblast growth factors, and Notch also participate.
- These signals influence networks of cardiac transcription factors.

Developmental signals

Wnt • Hedgehog • VEGF

Additional signals

BMP • TGF- β • FGF • Notch

Gene regulation

Cardiac transcription programs

Transcription factors convert signals into pattern

Downstream gene control helps determine the right structure in the right place.

- Many inherited CHD mutations affect transcription factors.
- Their activities must be coordinated across progenitor populations.
- Reduced function can disrupt development without complete gene loss.



Causal sequence / schematic

MicroRNAs provide another regulatory layer

Cardiac development depends on carefully controlled expression levels.

- Specific microRNAs help coordinate transcription-factor expression.
- The regulation is temporal and spatial rather than simply on/off.
- Network disruption can produce malformations with variable anatomy.



Causal sequence / schematic

Malformations can arise through different disruptions

The final structure integrates several causal processes.

- Abnormal progenitor migration changes cell allocation.
- Impaired tissue remodeling modifies chambers, cushions, or outflow.
- Perturbed regulatory signals alter the timing and extent of development.

Migration errors

Wrong precursor distribution

Remodeling errors

Altered tissue architecture

Regulatory errors

Mispatterned gene expression

Etiology is both genetic and environmental

Known causal factors explain only a minority of CHD cases.

- Familial variants and chromosome abnormalities are established contributors.
- Embryonic exposures can perturb the same developmental processes.
- Many affected infants have no identifiable specific cause.

Inherited / chromosomal

Gene dosage and variants

Pregnancy exposures

Infection • drugs • metabolism

Most cases

Specific cause remains unknown

Gestational exposures can increase risk

The exposure and the developmental window matter together.

- Congenital rubella is a recognized environmental cause.
- Certain teratogenic agents, including drugs, can disturb development.
- Gestational diabetes is another established association.

Infection

Congenital rubella

Teratogens

Some therapeutic drugs

Metabolic environment

Gestational diabetes

Nutrition can modify developmental risk

Maternal context is relevant to embryonic cardiac formation.

- The Robbins text cites lower CHD incidence with folate supplementation during early pregnancy.
- A risk-modifying association does not specify the cause of an individual lesion.
- Etiologic interpretation must remain multifactorial.

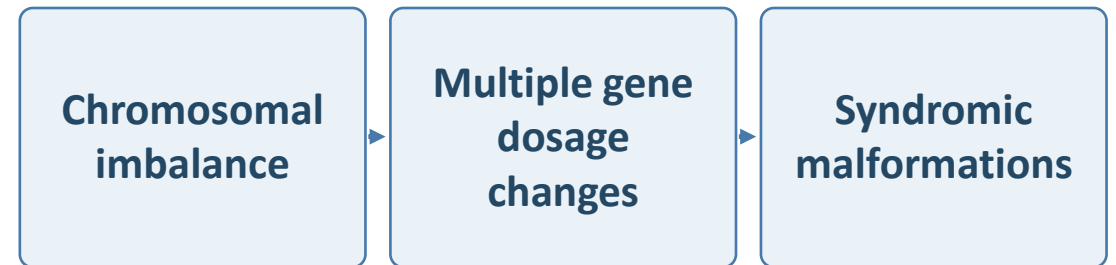


Causal sequence / schematic

Chromosomal disorders can affect cardiac development

Copy-number and chromosome abnormalities can disturb many genes together.

- Several trisomies and monosomy X among CHD associations.
- Cardiac and noncardiac abnormalities may occur together.
- The resulting phenotype reflects dysregulated expression across loci.

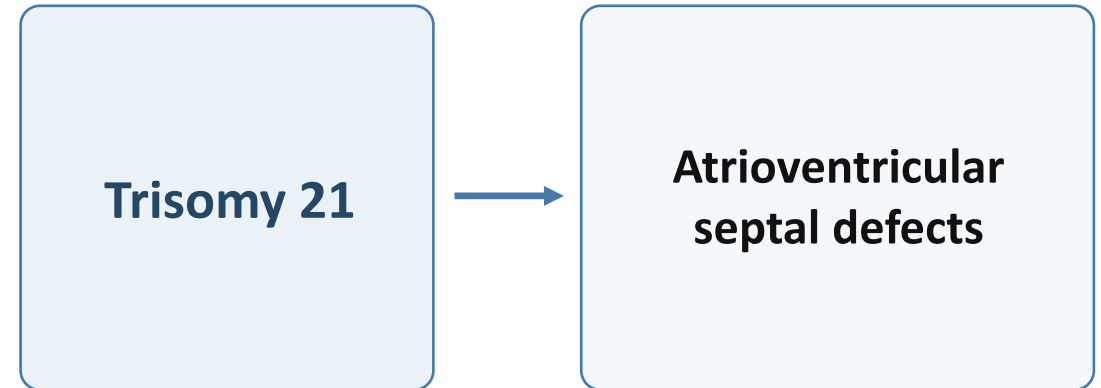


Causal sequence / schematic

Trisomy 21 is a major recognized genetic association

The heart phenotype often involves atrioventricular structures.

- CHD in approximately 40% of patients with Down syndrome.
- Atrioventricular septal structures are frequently affected.
- The developmental pattern is linked to second-field-derived structures.



Association in the supplied Robbins table

Chromosome 22q11.2 deletion links heart and pharyngeal development

DiGeorge syndrome illustrates a syndromic developmental disturbance.

- Development of the fourth branchial arch is affected.
- Third and fourth pharyngeal pouch derivatives may be abnormal.
- Cardiac, thymic, and parathyroid abnormalities can therefore cluster.

Fourth branchial arch

Aortic arch / heart development

Pharyngeal pouches

Thymus and parathyroids

22q11.2 deletion

Multisystem syndrome

TBX1 is a plausible driver within 22q11.2

Its developmental roles connect progenitor expansion with cell migration.

- The deleted segment contains multiple genes, not just TBX1.
- Loss of TBX1 as probably responsible for the cardiac phenotype.
- TBX1 regulates neural-crest migration and second-heart-field expansion.



Causal sequence / schematic

Partial loss of function can be sufficient

Many inherited developmental variants act in heterozygotes.

- An approximate 50% reduction in factor activity can disturb morphogenesis.
- Some genes are dosage-sensitive even when residual activity is present.
- Phenotypic severity need not scale linearly with gene dosage.

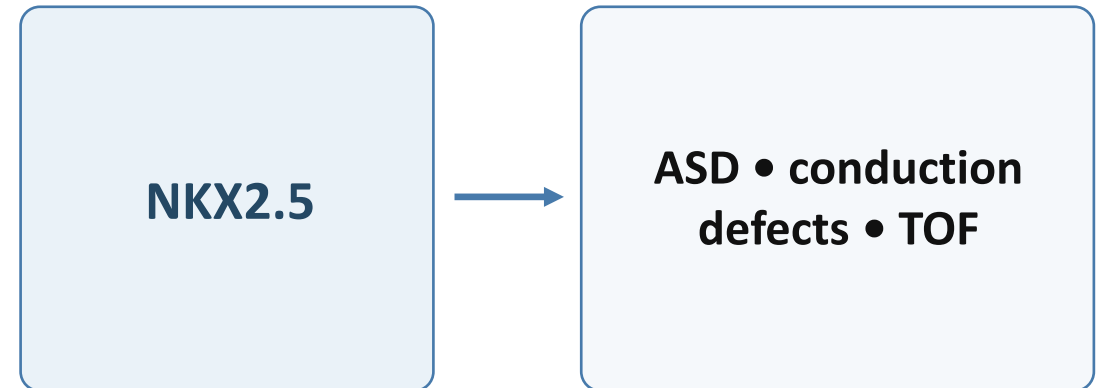


Causal sequence / schematic

NKX2.5 illustrates transcription-factor CHD

Different cardiac phenotypes can arise from variants in one regulator.

- The Robbins table associates NKX2.5 with nonsyndromic ASD or conduction defects.
- The table also lists it among genes associated with tetralogy of Fallot.
- A gene–phenotype relation is not one-to-one.

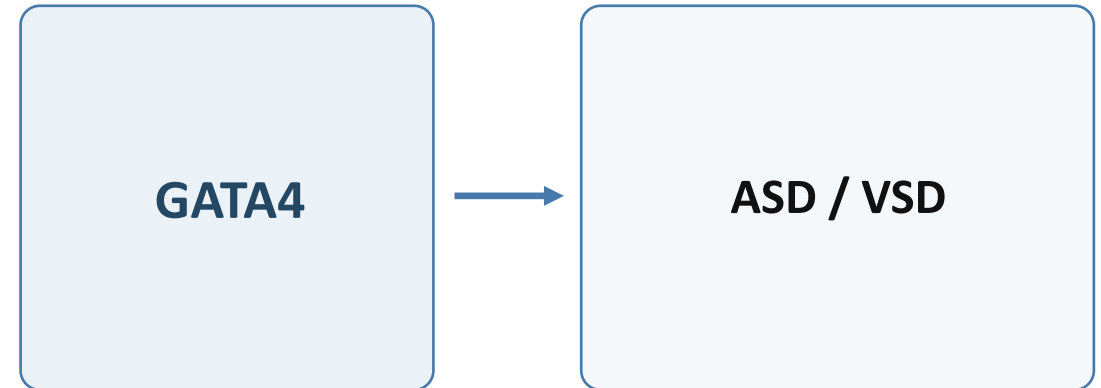


Association in the supplied Robbins table

GATA4 is associated with septal defects

Defects in transcriptional coordination can disrupt atrial or ventricular partitioning.

- GATA4 among genes associated with ASD and VSD.
- It works cooperatively with other cardiac transcription factors.
- The association does not imply that every septal defect has a GATA4 variant.



Association in the supplied Robbins table

Transcription factors act cooperatively

A network model explains shared phenotypes across multiple genes.

- GATA4, TBX5, and NKX2.5 physically interact.
- They co-regulate genes needed for normal cardiac morphogenesis.
- A defect in any member may disrupt the same developmental output.

GATA4

Shared target regulation

TBX5

Shared target regulation

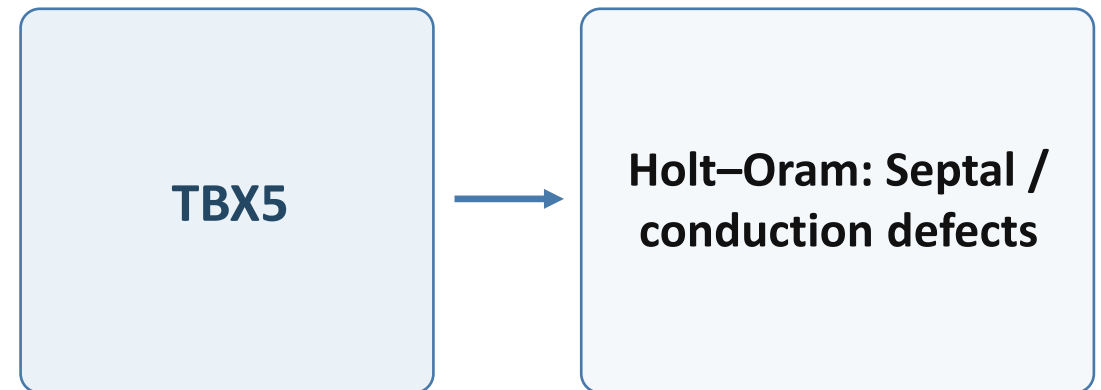
NKX2.5

Shared target regulation

Holt–Oram syndrome illustrates an organ-system link

A cardiac transcription factor can participate in a multisystem syndrome.

- TBX5 is listed as the associated gene.
- The cardiac manifestations include ASD, VSD, or conduction abnormality.
- Associated extracardiac findings help direct etiologic evaluation.



Association in the supplied Robbins table

CHD7 and TFAP2B illustrate diverse gene classes

Congenital cardiac abnormalities are not confined to one pathway.

- CHD7 is associated with CHARGE syndrome and several structural heart lesions.
- TFAP2B is associated with Char syndrome and patent ductus arteriosus.
- Both examples reinforce syndrome-informed interpretation.

CHD7

CHARGE • ASD / VSD
/ PDA

TFAP2B

Char syndrome • PDA

Notch signaling contributes to several defects

Perturbation in one pathway can yield multiple structural phenotypes.

- JAG1 or NOTCH2 with Alagille syndrome.
- Its listed cardiac manifestations include pulmonary artery stenosis or TOF.
- NOTCH1 is mentioned in connection with bicuspid aortic valve.

JAG1 / NOTCH2

Alagille: Pulmonary stenosis / TOF

NOTCH1

Bicuspid aortic valve

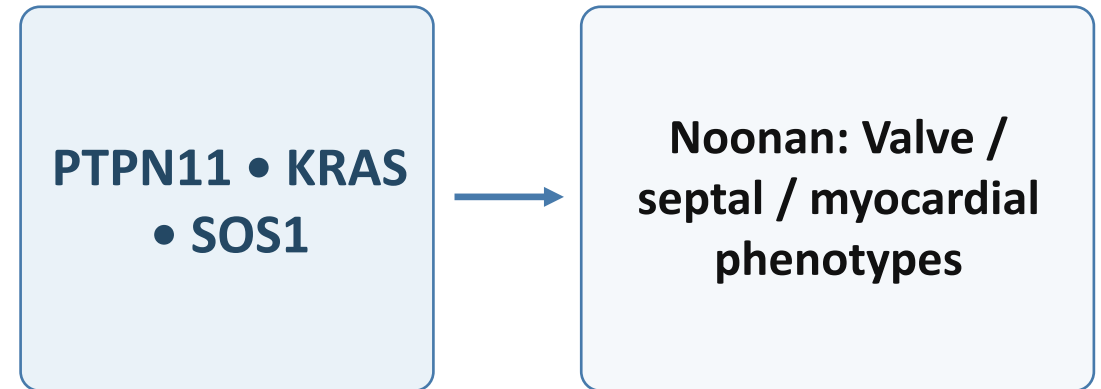
Pathway

Notch signaling

Ras pathway defects provide another mechanism

Congenital malformations may follow altered intracellular signaling.

- PTPN11, KRAS, and SOS1 with Noonan syndrome.
- Reported cardiac manifestations include pulmonary valvular stenosis and VSD.
- Hypertrophic cardiomyopathy may also occur.



Association in the supplied Robbins table

Extracellular matrix signaling can affect the heart

Structural-protein variants may alter both mechanics and signaling.

- Fibrillin mutations underlie Marfan syndrome.
- Fibrillin also restrains TGF- β signaling in the extracellular matrix.
- Excess TGF- β activity contributes to abnormalities in Marfan and Loeys–Dietz syndromes.



Causal sequence / schematic

Genotype does not predict a single phenotype

Robbins cautions that molecular associations are not deterministic.

- Different genes may produce similar cardiac defects.
- The same gene can be associated with more than one lesion.
- Many clinically identical malformations occur sporadically.

Genetic heterogeneity

Different genes →
similar anatomy

Phenotypic variability

One gene → different
manifestations

Most specific causes remain unidentified

Uncertainty is a substantive feature of CHD etiopathogenesis.

- That precise causes are unknown in almost 90% of cases.
- Even known genetic variants show variable nature and severity of defects.
- Gene–environment interactions are proposed as one contributor.

Etiologic uncertainty

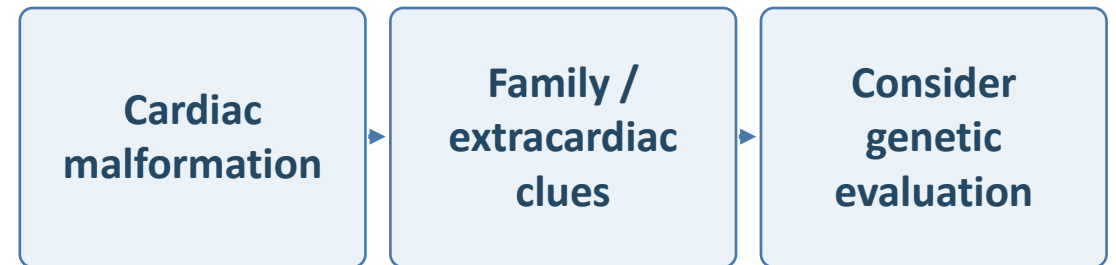
≈90% unexplained

Source estimate; Not an exclusion of genetic influence

When genetic evaluation becomes relevant

Clinical context is more informative than anatomy alone.

- Broader noncardiac syndromic findings raise suspicion for a genetic cause.
- A family history of CHD can also prompt evaluation.
- Genetic-testing guidance as evolving; No universal testing rule is given.



Causal sequence / schematic

Clinical physiology: Shunts and obstruction

Most structural anomalies can be organized by how they disturb blood flow.

- Shunts provide abnormal communication between compartments.
- Obstructive lesions narrow chambers, valves, or vessels.
- Some malformations combine both mechanisms.

Left-to-right

Increased pulmonary flow

Right-to-left

Systemic desaturation

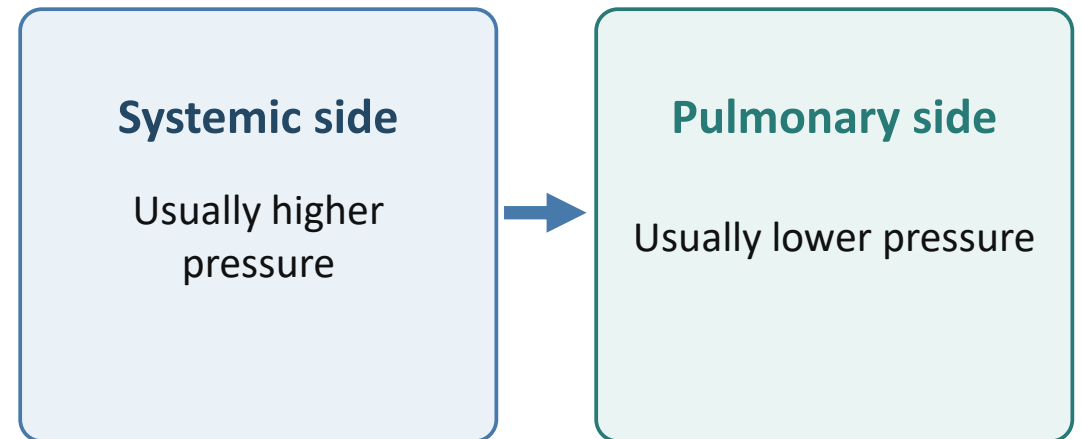
Obstruction

Flow restriction

Shunts are driven by pressure gradients

An abnormal communication allows blood to move between otherwise separated spaces.

- Direction depends on relative pressure and resistance.
- Left-to-right and right-to-left describe flow—not simply the hole's location.
- The same defect can produce different consequences as resistance changes.



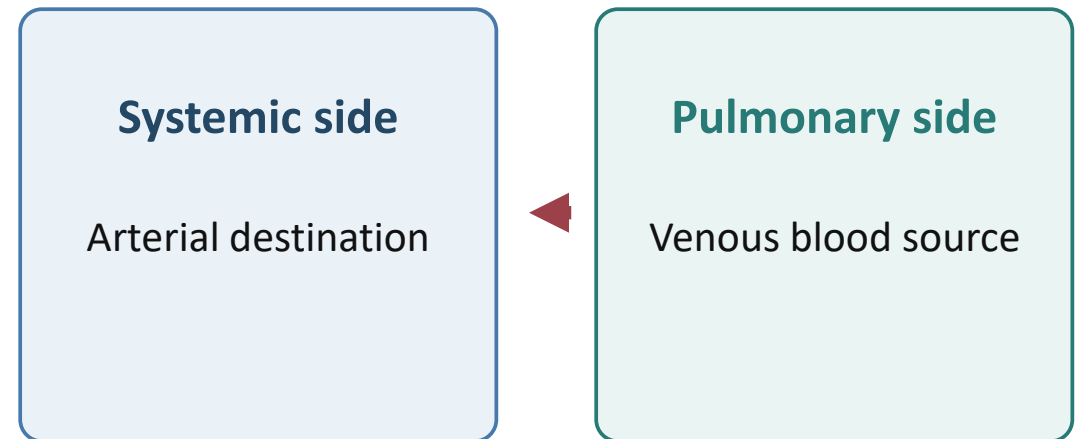
Schematic: Flow direction across an abnormal communication

Direction indicates blood crossing the abnormal communication.

Right-to-left shunts bypass the lungs

Systemic arterial blood receives poorly oxygenated venous blood.

- Blood travels from the right/pulmonary side to the left/systemic side.
- Pulmonary gas-exchange circulation is bypassed in part.
- The direct physiological result is systemic hypoxemia.



Schematic: Flow direction across an abnormal communication

Direction indicates blood crossing the abnormal communication.

Hypoxemia produces central cyanosis

Cyanosis is the clinical expression of an important right-to-left shunt.

- Poorly oxygenated blood enters the systemic arterial supply.
- Dusky discoloration can involve skin and mucous membranes.
- The appearance reflects the physiology, not a unique structural diagnosis.



Causal sequence / schematic

Paradoxical emboli exploit the abnormal pathway

The pulmonary circulation normally filters many venous emboli.

- An embolus in peripheral venous blood may traverse a right-to-left communication.
- It can then enter systemic arterial vessels.
- The embolic pathway is distinct from the cause of cyanosis.



Causal sequence / schematic

Chronic cyanosis produces systemic adaptations

Longstanding oxygen deficiency affects blood and peripheral tissues.

- Polycythemia increases circulating red-cell number.
- Digital clubbing may develop in fingers and toes.
- Hypertrophic osteoarthropathy can include bony change.

Blood

Polycythemia

Digits

Clubbing

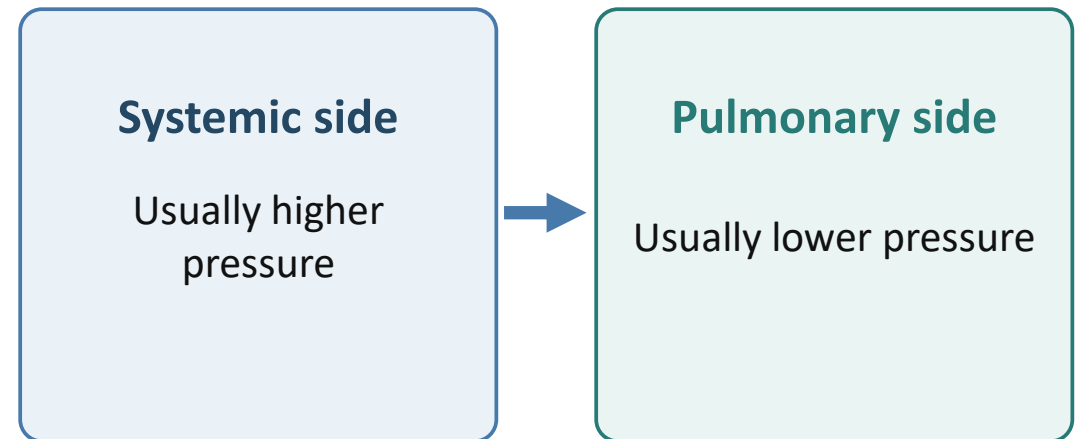
Skeleton

Hypertrophic osteoarthropathy

Left-to-right shunts are initially acyanotic

Blood is directed from systemic toward pulmonary circulation.

- Pulmonary flow increases without initially bypassing lung oxygenation.
- The dominant early problem is increased pulmonary workload.
- Late cyanosis may occur if vascular resistance rises enough to reverse flow.



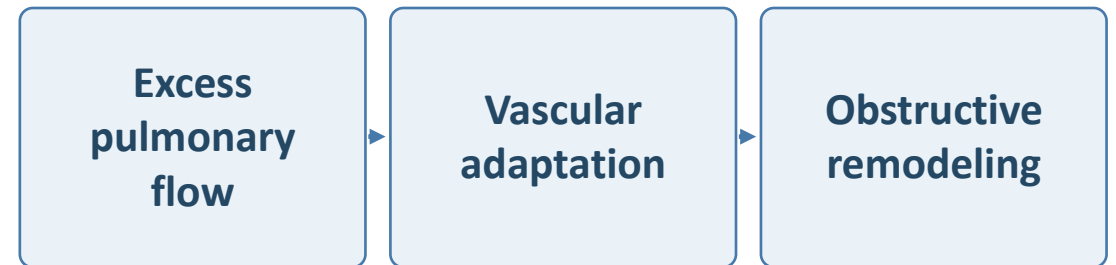
Schematic: Flow direction across an abnormal communication

Direction indicates blood crossing the abnormal communication.

A left-to-right shunt stresses pulmonary vessels

The pulmonary circulation is adapted to low pressure and resistance.

- Prolonged excess flow may increase vascular volume and pressure loads.
- Compensatory vascular changes initially limit distal capillary pressure.
- Persistent overload can lead to progressive obstructive remodeling.



Causal sequence / schematic

Atrial and ventricular-level shunts differ

The site of communication shapes hemodynamic loading.

- ASD typically increases right ventricular and pulmonary outflow volumes.
- VSD and PDA increase pulmonary flow and pressure in the Robbins overview.
- Effect size depends on defect dimensions and position.

ASD	VSD or PDA
Predominantly increased RV / pulmonary flow volume	Increased pulmonary flow and pressure

Size and location determine clinical severity

A shunt can range from incidental to hemodynamically critical.

- Not every communication imposes an equivalent load.
- Some infants remain asymptomatic while others develop severe heart failure.
- Flow and downstream adaptation must be evaluated together.

Small / restrictive lesion

May have few symptoms

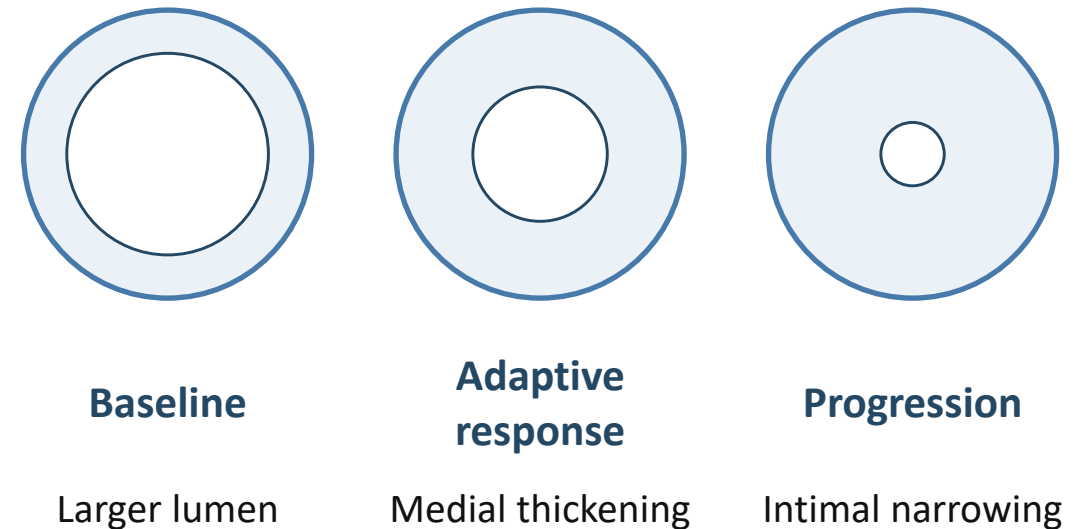
Large / high-flow lesion

May cause serious heart failure

Pulmonary muscular arteries initially respond

The small pulmonary vessels adapt to sustained abnormal pressure.

- Vasoconstriction and medial hypertrophy.
- The response occurs in muscular pulmonary arteries.
- It initially helps protect distal pulmonary capillaries and veins.

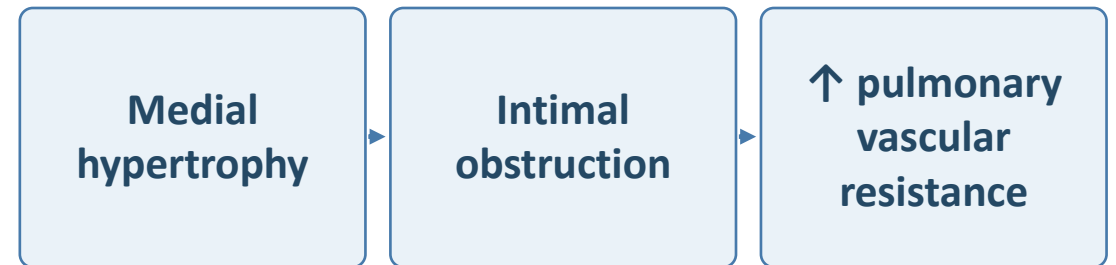


Simplified cross-sectional schematic; Not drawn to scale

Long-standing overload causes fixed vascular lesions

Early functional adaptation can become structural obstruction.

- Persistent pulmonary vasoconstriction promotes obstructive intimal change.
- The vascular pattern resembles systemic hypertensive arteriosclerosis.
- The increased resistance eventually changes shunt physiology.

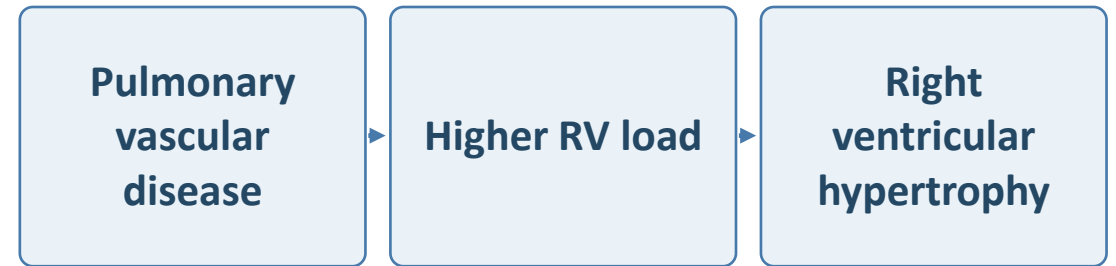


Causal sequence / schematic

Right ventricular hypertrophy reflects pressure loading

The myocardium remodels in response to altered pulmonary hemodynamics.

- Progressive pulmonary vascular resistance raises right-sided load.
- The right ventricle undergoes hypertrophy.
- Cardiac enlargement is thus often secondary to the vascular lesion.

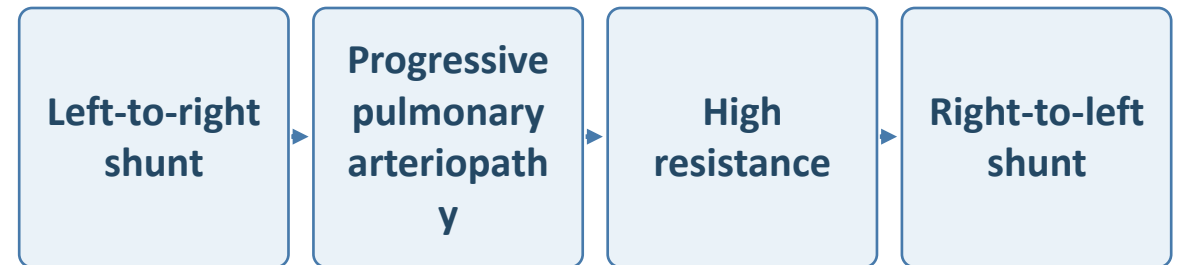


Causal sequence / schematic

Eisenmenger syndrome is a direction reversal

An initially left-to-right shunt can become right-to-left.

- Chronic pulmonary vascular changes elevate resistance toward systemic levels.
- The original shunt direction may reverse.
- Desaturated venous blood then enters the systemic circulation.



Causal sequence / schematic

Late pulmonary vascular disease may be irreversible

The consequences of timing matter for intervention.

- Established irreversible pulmonary hypertension a limit to defect repair.
- Late right heart failure is a major consequence.
- Early closure of significant left-to-right lesions aims to prevent this stage.

**Before fixed
obstruction**

Potential window to
correct shunt

**After irreversible
arteriopathy**

Closure no longer
restores normal
resistance

Obstructive CHD limits flow through a narrowed structure

The impediment may involve chambers, valves, or great vessels.

- Coarctation narrows the aorta.
- Aortic and pulmonary valvular stenoses are additional examples.
- Atresia is complete developmental obstruction.

Great vessel

Coarctation

Valve

Aortic / pulmonary stenosis

Complete blockage

Atresia

Shunt and obstruction can coexist

Mechanisms should not be treated as mutually exclusive classes.

- Tetralogy of Fallot is the Robbins example.
- Pulmonary outflow obstruction coexists with a VSD.
- The combination can support right-to-left flow across the septal defect.



Causal sequence / schematic

Cardiac chambers remodel to the mechanical load

Dilation and hypertrophy are different structural responses.

- Altered flow and pressure commonly cause chamber dilation or hypertrophy.
- Some anomalies cause reduced prenatal chamber growth instead.
- Hypoplasia denotes prenatal underdevelopment; Postnatal loss of mass is atrophy.

Hypertrophy / dilation

Adaptation to
hemodynamic load

Hypoplasia / atrophy

Before-birth
deficiency / postnatal
loss

Pulmonary vascular disease is the turning point

The vascular response can determine the long-term consequences of a defect.

- Shunt anatomy may remain unchanged while pulmonary resistance rises.
- A lesion initially without cyanosis can later cause systemic hypoxemia.
- The downstream pulmonary arteriopathy can become the dominant pathology.

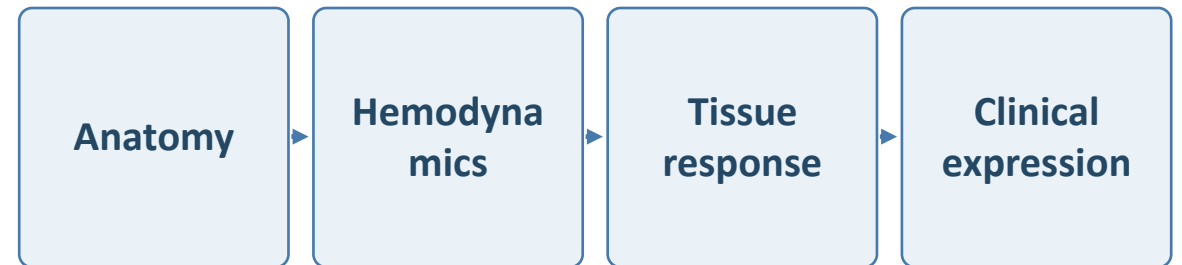


Causal sequence / schematic

A clinical framework for a newly recognized defect

Reason from structure to flow to response.

- Define the anatomic malformation and any associated defects.
- Determine shunt direction or site of obstruction.
- Look for cyanosis, chamber remodeling, and pulmonary vascular disease.

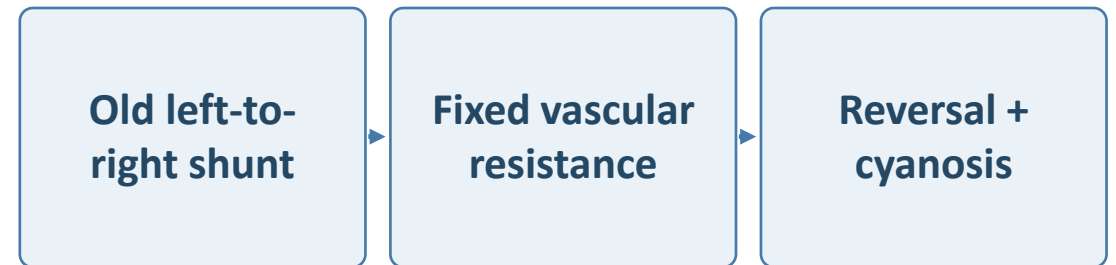


Causal sequence / schematic

Teaching case: Cyanosis after years of a shunt

An unrepaired communication develops a new physiological phenotype.

- Longstanding left-to-right flow increases pulmonary vascular load.
- Pulmonary vascular resistance progressively increases.
- New right-to-left flow suggests Eisenmenger physiology.



Causal sequence / schematic

Teaching case: Congenital lesion plus extracardiac signs

A syndromic pattern changes the etiologic differential.

- A child has an outflow anomaly together with thymic/parathyroid abnormalities.
- The developmental pattern is compatible with a 22q11.2 deletion syndrome.
- TBX1-related disruption is one source-supported mechanistic explanation.



Causal sequence / schematic

Teaching case: Tiny defect on newborn echo

Detected anomaly and persistent CHD burden should be distinguished.

- Routine neonatal imaging identifies a small muscular septal communication.
- Many such findings close in the first year.
- Ascertainment methodology matters when quoting prevalence.



Causal sequence / schematic

Compare the major hemodynamic patterns

A compact differential links physiology to its principal consequence.

- Left-to-right: Pulmonary overcirculation without early cyanosis.
- Right-to-left: Arterial desaturation and potential paradoxical embolism.
- Obstruction: Restricted forward flow and pressure/structural adaptation.

Left-to-right

Pulmonary flow overload

Right-to-left

Systemic hypoxemia

Obstruction

Impaired ejection / passage

Four anchors for understanding CHD

Clinical significance emerges from developmental origin, anatomy, and remodeling.

- Embryogenesis during weeks 3–8 creates structural vulnerability.
- Genetic, chromosomal, and environmental contributors often interact.
- Shunts and obstruction generate distinct but overlapping flow disturbances.
- Pulmonary vascular remodeling can transform long-term prognosis.

Development

Fields • cushions • crest

Etiology

Genes • exposures

Anatomy

Shunts • obstruction

Response

Cardiac / pulmonary remodeling

Primary reading and source limits

Robbins, Cotran & Kumar: Pathologic Basis of Disease

11th edition (2026) • The Heart

Scope

Congenital heart disease: incidence, morphogenesis, etiopathogenesis and physiology.

Evidence caution

Estimates in the textbook reflect the cited underlying studies and definitions.

Individual malformations are developed further in subsequent lectures.