

Carcinoid heart disease

Tumor mediators · endocardial plaques · right-sided valvular dysfunction

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Learning outcomes

Explain how vasoactive products from neuroendocrine tumors reach the endocardium.

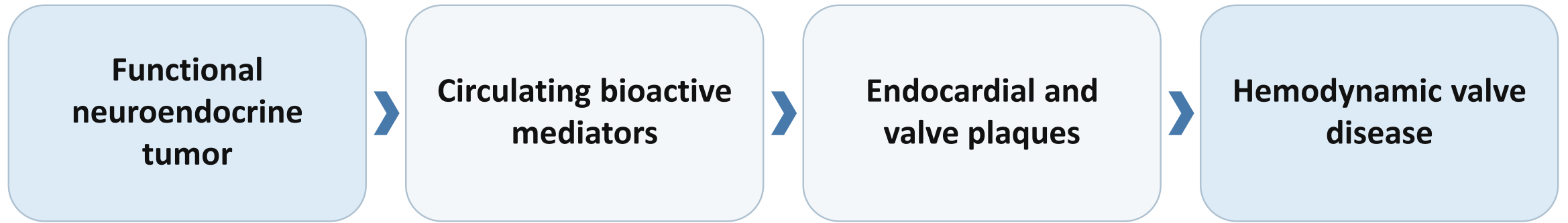
Account for right-sided predominance and identify exceptions.

Recognize the gross and microscopic plaque pattern.

Link tricuspid insufficiency and pulmonary stenosis to altered flow.

Differentiate carcinoid plaques from other valve lesions.

One disease across two organs



Tumor-derived products connect an extracardiac neoplasm to a distinctive cardiac morphology.
The cardiac pathology is not a primary tumor of the heart.

Two related diagnoses—not synonyms

Carcinoid syndrome

Systemic manifestations of circulating tumor products

Flushing, diarrhea, dermatitis,
bronchoconstriction

Carcinoid heart disease

Cardiac manifestation of exposure to tumor products

Glistening endocardial plaques and valve dysfunction

The relevant tumor phenotype is secretory

Neoplasm

Well-differentiated neuroendocrine tumors can release bioactive products.

Functional behavior

Symptoms arise from secreted molecules, not from valve metastasis.

Cardiac outcome

A subset of patients with systemic syndrome develop plaques.

Cardiac involvement is common, not universal

Cardiac manifestations in roughly one-half of patients who develop systemic carcinoid syndrome.

That estimate refers to patients with the systemic syndrome—not every patient with a neuroendocrine tumor.

Cardiac lesions usually appear in the setting of multiple hepatic metastases and sustained mediator access.

The estimate is approximate; It is not a patient-specific prediction.

Digestive neuroendocrine tumor context

Most gastrointestinal neuroendocrine tumors are well differentiated.

The small intestine is an important site of origin.

Some tumors produce vasoactive substances that cause systemic carcinoid syndrome.

Cardiac injury follows mediator exposure rather than direct invasion of the valve.

Terminology

The book notes that “carcinoid” persists in use for many well-differentiated neuroendocrine tumors.

The systemic syndrome is multisystem

Skin

Flushing and dermatitis;
Gastrointestinal source text
also describes sweating.

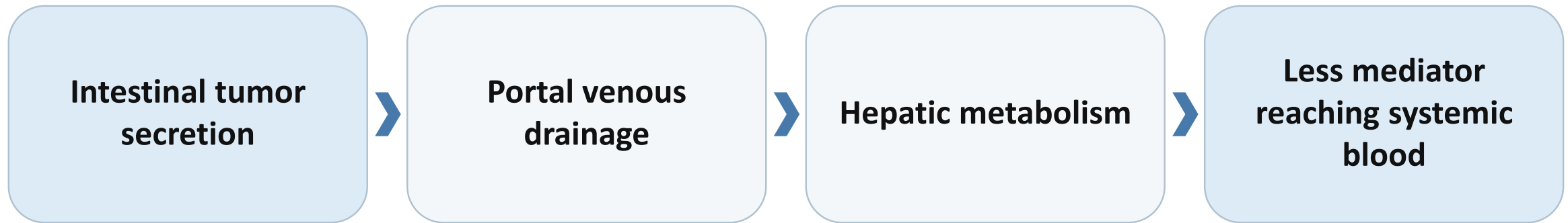
Gut

Diarrhea and colicky
abdominal pain.

Airway

Bronchoconstriction or
bronchospasm.

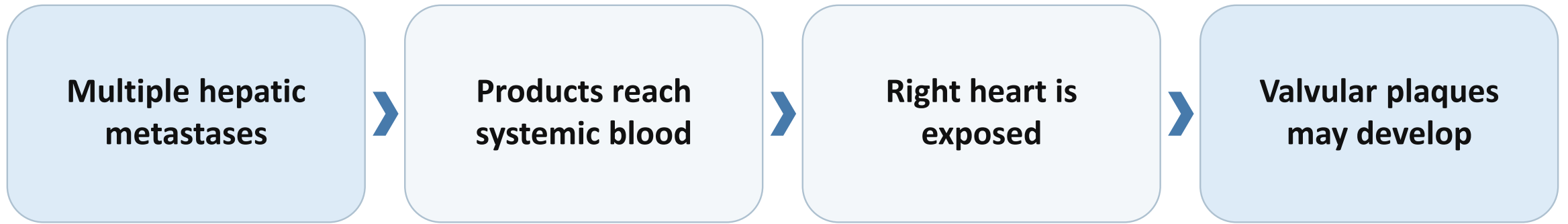
Why many intestinal tumors do not cause the syndrome



The liver normally inactivates circulating products from intestinal tumors.

This first-pass effect explains why secretory capacity alone need not produce the systemic syndrome.

Liver metastases alter the exposure pathway



Cardiac lesions as generally arising after multiple liver metastases.

The qualifying phrase “typically” matters: An anatomic explanation, not an absolute rule.

The first-pass model has two states

Predominantly portal clearance

Secretions enter portal flow.

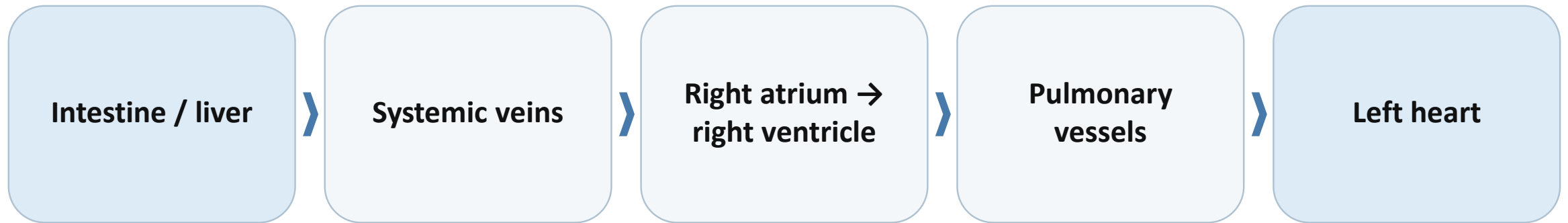
Hepatic degradation limits systemic exposure.

Systemic escape

Extensive hepatic metastases or other bypass routes permit circulation of mediators.

The heart is subsequently exposed.

Follow the blood: Gastrointestinal source to heart



Flow ordering is anatomical; The critical exposures occur in the right heart.
The pulmonary circulation provides a second biochemical barrier.

Why the right heart is most often affected

First contact

The right-sided endocardium is exposed early to products in systemic venous blood.

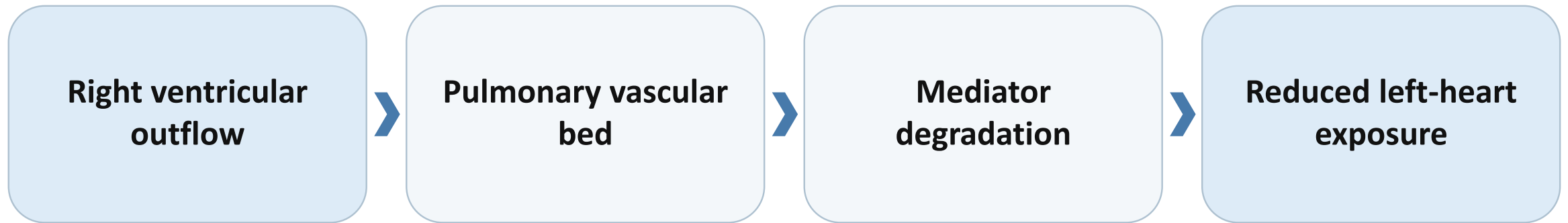
Frequent targets

Right ventricular lining and tricuspid/pulmonary valve surfaces.

Functional pattern

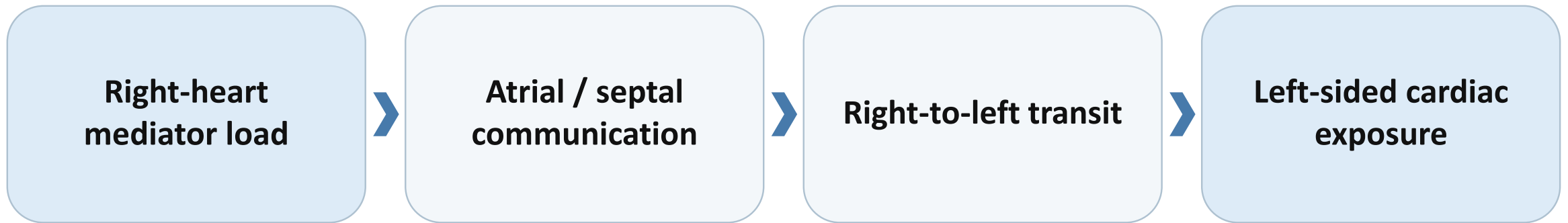
Tricuspid insufficiency with pulmonary stenosis.

Pulmonary inactivation protects the left side



The pulmonary vascular bed provides only partial protection.
Protection is conditional on source and intracardiac flow pathway.

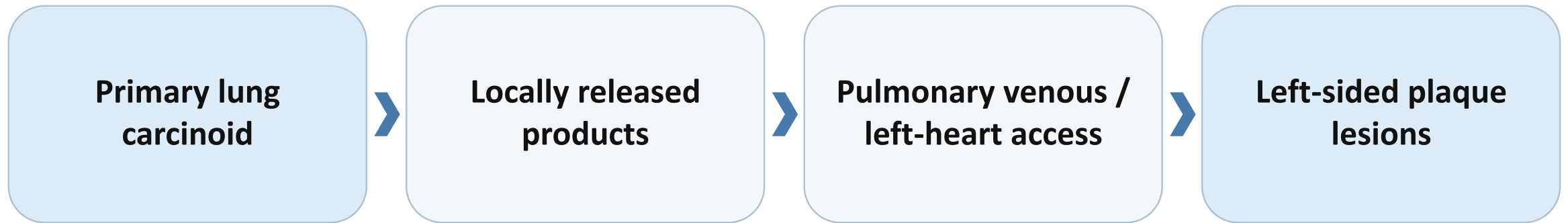
Anatomic exception: Right-to-left shunting



Right-to-left flow across a defect as a route to left-heart plaques.

The defect and direction of flow—not merely the presence of a defect—are crucial.

Primary pulmonary carcinoids can affect the left heart



A pulmonary tumor does not require the same portal-hepatic escape pathway. This exception is explicitly described in the cardiac section.

Right versus left: Mechanisms, not rigid rules

Setting	Exposure logic	Expected cardiac emphasis
GI source with systemic mediators	Systemic venous blood reaches the right heart first	Mainly right heart
Right-to-left intracardiac flow	A portion of mediator-rich blood bypasses pulmonary degradation	Left heart possible
Primary pulmonary carcinoid	Tumor products can reach left cardiac circulation	Left heart possible

The tumor releases several candidate mediators

Amines

Serotonin (5-hydroxytryptamine), histamine.

Peptides / enzymes

Kallikrein, bradykinin, tachykinins.

Lipid mediators

Prostaglandins.

Serotonin: An important signal, not proven sole cause

Serotonin is also named 5-hydroxytryptamine (5-HT).

It among the mediators released by carcinoid tumors.

Higher plasma serotonin correlates with more severe cardiac lesions.

Correlation is not sufficient to establish that serotonin acts alone.

Evidence boundary

The textbook explicitly states that the causal identity among released mediators remains uncertain.

The mediator mechanism remains partly unresolved

Observed

Bioactive products circulate in carcinoid syndrome.

Distinctive endocardial plaques occur.

Serotonin concentrations track severity.

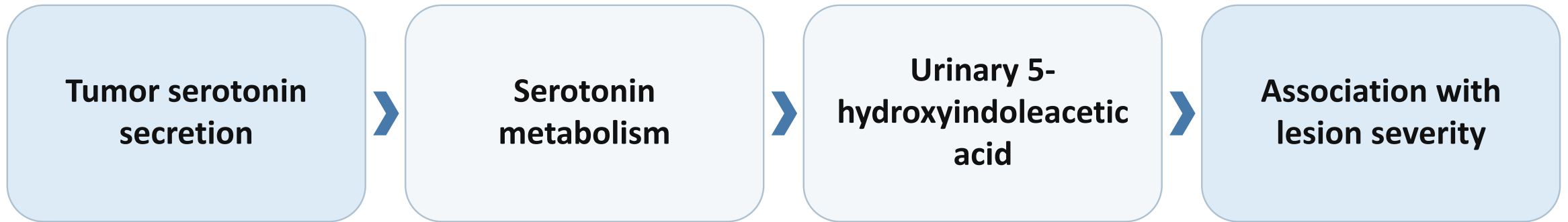
Not established here

Which individual mediator is necessary.

Whether one mediator alone is sufficient.

A fully specified receptor-to-fibrosis pathway.

Urinary 5-HIAA is a serotonin metabolite



5-HIAA means 5-hydroxyindoleacetic acid.

The text states a severity correlation; It does not supply a diagnostic cutoff or performance metric.

A correlation is not a diagnostic criterion

Plasma serotonin

Tracks severity account.

Urinary 5-HIAA

A metabolite whose excretion correlates with severity.

Cardiac morphology

The distinguishing lesion remains a specific endocardial/valvular plaque pattern.

Cardiac injury and systemic symptoms are different readouts

Systemic mediator effects

Flushing; Intestinal hypersecretion;
Bronchoconstriction.

Clinical signs reflect diverse organ responses.

Cardiac tissue response

Plaque-like endocardial thickening.

Valve restriction or loss of competence.

Fenfluramine provides a morphologic analogy

Carcinoid plaques with valve lesions associated with fenfluramine exposure.

Fenfluramine was an appetite suppressant that is no longer marketed.

The drug affects systemic serotonin metabolism.

An analogous lesion supports biologic plausibility but does not prove a unique causal pathway.

Ergot alkaloids are another plaque analogy

Carcinoid-like valvular plaques have also been linked to ergot alkaloids.

The textbook refers to prior ergot use for migraine treatment.

These agents have relationships with serotonin handling.

Morphologic resemblance should not be mistaken for identical clinical exposure patterns.

A left-sided drug-associated analogy

Methysergide / ergotamine

Reported with left-sided plaques after migraine treatment.

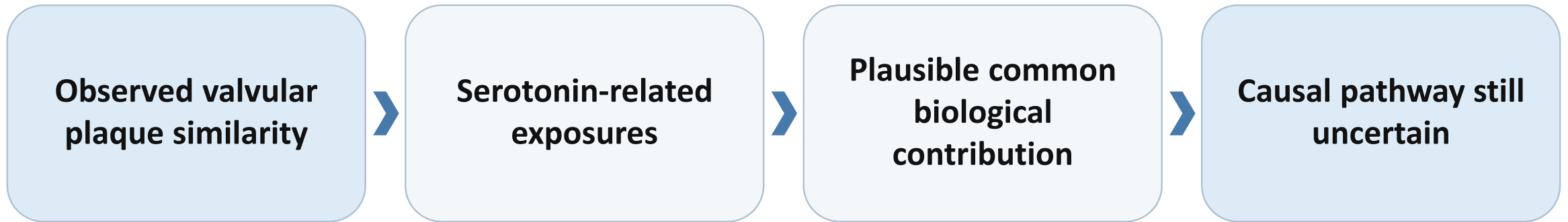
Passage through lung vessels is relevant to their metabolism.

GI carcinoid syndrome

Pulmonary mediator degradation usually limits left-sided lesions.

Right-sided plaque disease predominates.

Shared morphology does not specify molecular causality



Source comparisons are evidence of an association or analogy.

Avoid labeling a hypothetical receptor or molecular intermediate as established fact.

Normal valve function depends on mobile leaflets

Atrioventricular valves

Tricuspid and mitral leaflets close to prevent backflow.

Semilunar valves

Pulmonary and aortic cusps open for ventricular outflow.

Tissue property

Mobility, pliability and structural integrity are required.

Stenosis and insufficiency are different defects

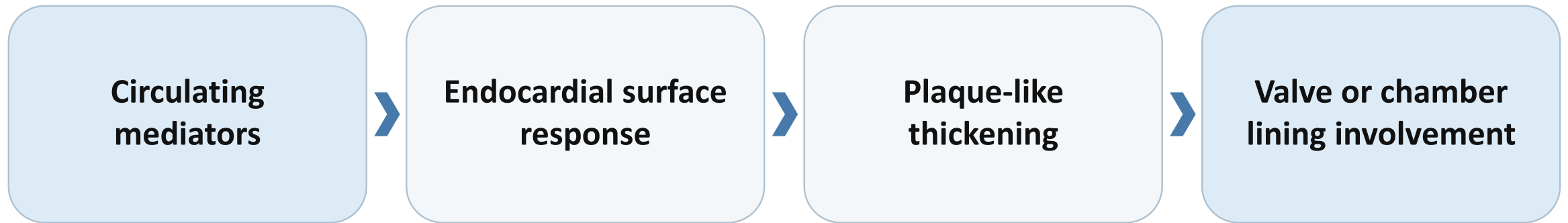
Stenosis: Opening defect

Valve does not open completely.
Forward blood flow is obstructed.

Insufficiency: Closing defect

Valve does not close completely.
Blood regurgitates backward.

Carcinoid plaques are endocardial lesions



The lesion is a surface-associated plaque rather than myocardial replacement.
Both valve leaflets and chamber endocardium may be involved.

Gross morphology: Smooth glistening white plaques

Conceptual depiction — not a gross specimen



Schematic depiction only—not a photograph of a specimen.

The adjective “plaque-like” describes an attached surface thickening.

Right ventricular lining and tricuspid valve

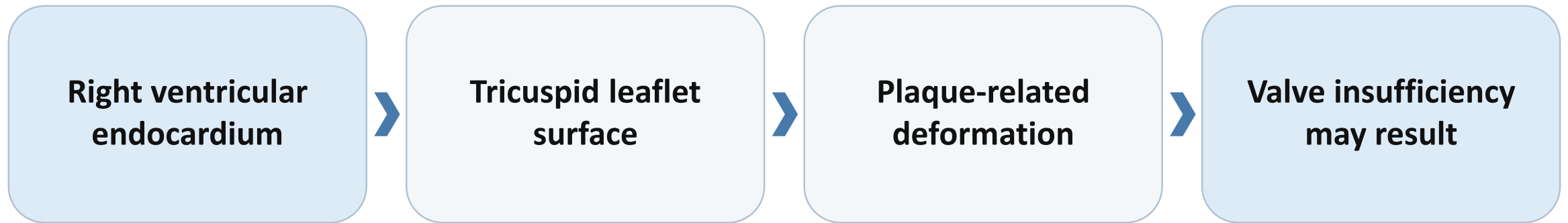


Figure 12.26A depicts the right ventricle and tricuspid valve.

The figure's actual specimen is not reproduced because only its caption is available.

Microscopy: The cellular and matrix components

Cells

Smooth muscle cells are present in the plaques.

Fibrillar component

Relatively sparse collagen fibers.

Dominant extracellular milieu

Matrix rich in acid mucopolysaccharides.

A matrix-rich plaque is not simply dense collagen

Carcinoid plaque

Acid mucopolysaccharide-rich ground substance.

Smooth muscle cells with sparse collagen fibers.

Incorrect oversimplification

“Only dense collagen scar.”

“A destructive inflammatory vegetation.”

Histologic location: Surface over preserved tissue

Plaque: Cells + acid mucopolysaccharide-rich matrix

Underlying endocardial / valvular tissue

Myocardium: Unaffected in illustrated lesion

Schematic cross-section — native editable drawing, not photomicrograph

The source stresses that underlying structures remain intact.

This is a conceptual cross-section; Not original histology.

Movat stain: Which elements are described?

Plaque matrix

Blue-green acid mucopolysaccharide-rich lesion in Fig. 12.26B.

Underlying region

Myocardial elastic tissue appears black in the caption.

Interpretation

Underlying myocardium is unaffected in the illustrated specimen.

Do not equate thickening with tissue destruction

Documented in carcinoid disease

Surface-associated plaque thickening.

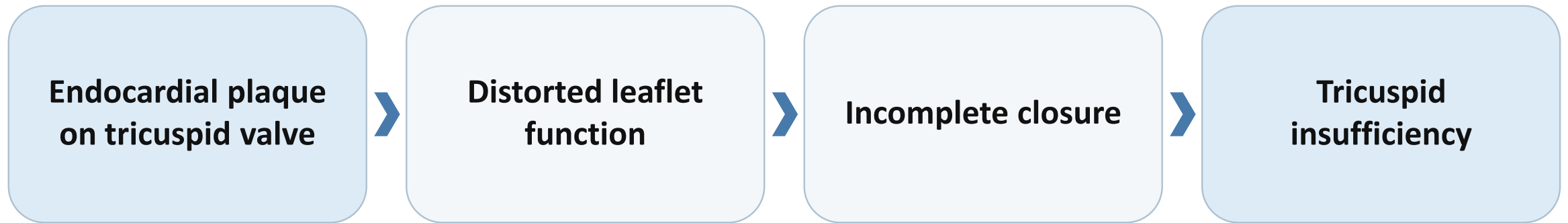
Underlying structures intact.

Different mechanism in IE

Large friable vegetations may accompany injury.

An invasive infection can cause leaflet destruction.

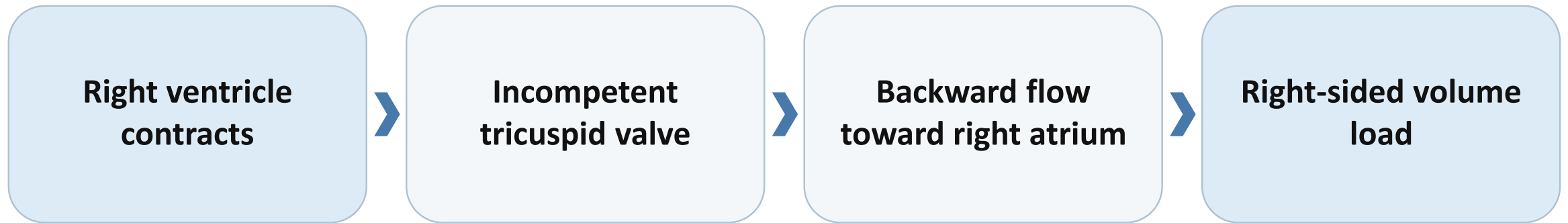
Tricuspid valve: Functional failure



Robbins specifically lists tricuspid insufficiency as typical.

Incomplete closure describes the physiological definition of regurgitation.

Tricuspid insufficiency produces backflow



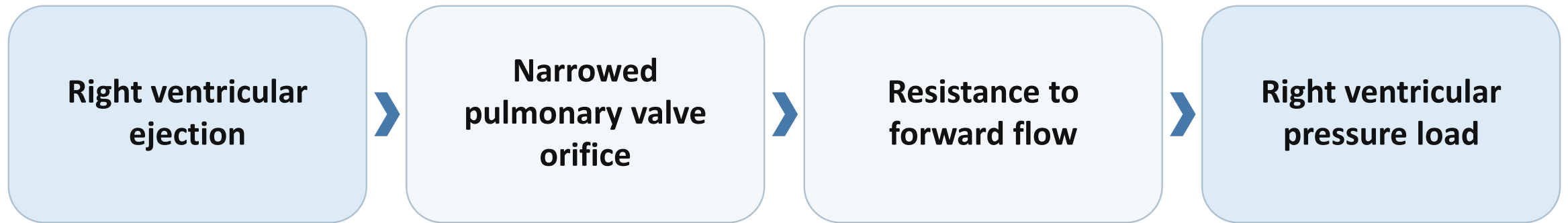
Direction of backflow follows valve anatomy and the generic definition of insufficiency.
Parent cardiac-pathophysiology text links volume overload with chamber dilation.

Pulmonary valve: Obstructed outflow



Robbins specifically lists pulmonary stenosis as typical.
Incomplete opening is the parent chapter definition of stenosis.

Pulmonary stenosis increases outflow resistance



The pressure-load consequence is a physiological interpretation of stenosis. Pressure overload is related to hypertrophy in the parent cardiac section.

Two valves, two flow problems

Valve	Typical disturbance	Direct flow consequence
Tricuspid	Insufficiency	Backflow into right atrium
Pulmonary	Stenosis	Obstruction of forward flow into pulmonary artery
Both involved	Mixed right-sided valve burden	Potential combined volume and pressure loading

Right-heart load can be mixed

Volume component

Tricuspid regurgitation allows return flow toward the right atrium.

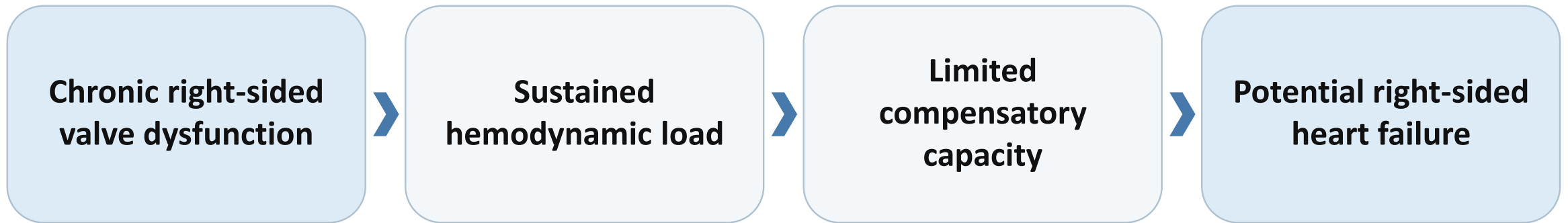
Pressure component

Pulmonary stenosis creates resistance to right ventricular outflow.

Possible adaptation

General ventricular responses include hypertrophy and/or dilation.

Right-heart failure is a possible downstream consequence



Heart failure in terms of inadequate pumping or elevated filling pressures.

The valve-to-heart-failure pathway is clinicopathologic inference; The carcinoid subsection does not quantify it.

Right-sided versus left-sided congestion

Right-heart failure pattern

Engorgement of systemic and portal venous circulations.

Pulmonary congestion is comparatively limited in isolated right-sided failure.

Left-heart failure pattern

Pulmonary venous congestion and edema predominate.

A different hemodynamic site of backlog.

A lesion's layer and function answer different questions

Question	Morphologic answer	Physiologic answer
Where is it?	Valve leaflets and chamber endocardium	Right-sided valves predominate
What is it made of?	Cells, sparse collagen, mucopolysaccharide-rich matrix	—
What does it do?	Thickening / deformation	Tricuspid insufficiency; pulmonary stenosis

Gross plaque and sterile thrombus are not equivalent

Carcinoid plaque

Glistening white endocardial thickening.
Matrix and smooth muscle cells; Deeper tissue intact.

Nonbacterial thrombotic endocarditis

Small sterile bland thrombi attached to valve leaflets.
Loose adherence; Potential embolic source.

Nonbacterial thrombotic endocarditis: Different substrate

Nature

Sterile thrombotic vegetation, not a mucopolysaccharide-rich plaque.

Context

May accompany malignancy or hypercoagulable states.

Consequence

Loose thrombi can embolize even if valve function is little affected.

Libman–Sacks disease adds inflammation

Carcinoid heart disease

Surface plaque with preserved underlying structures.

Bioactive tumor products implicated.

Libman–Sacks endocarditis

Sterile vegetations in lupus.

Immune-complex injury, valvulitis, fibrinoid necrosis.

Infective endocarditis is another distinct process

Carcinoid plaque

Glistening white, plaque-like thickening.
No primary valve infection is invoked in pathogenesis.

Infective endocarditis

Microbe-associated friable vegetations.
Destructive leaflet infection may occur.

Four lesions: Choose by tissue response

Entity	Dominant lesion	Context / distinguishing clue
Carcinoid	Endocardial matrix-rich plaque	Functional NET / carcinoid syndrome
NBTE	Bland thrombotic vegetation	Hypercoagulability; malignancy
Libman–Sacks	Immune valvulitis / sterile vegetation	Systemic lupus erythematosus
Infective endocarditis	Infected, often destructive vegetation	Microbial infection

What a pathologist can infer from the plaque

A smooth white valve or endocardial plaque suggests a surface-deposition / tissue-response process.

A mucopolysaccharide-rich matrix with smooth muscle cells supports the reported carcinoid pattern.

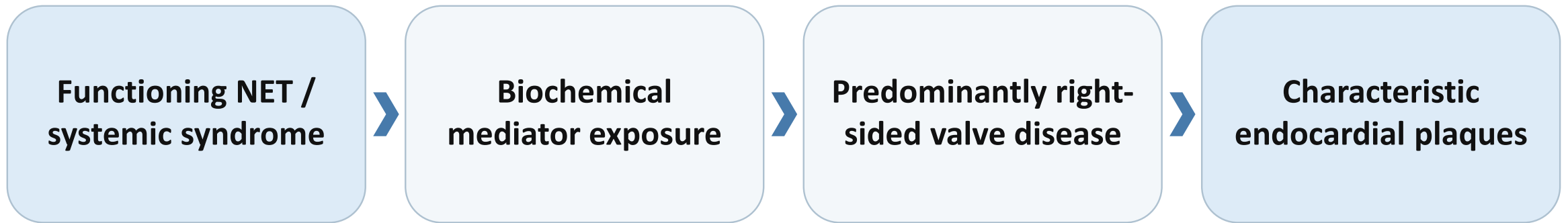
Preservation of deeper structures distinguishes this lesion from destructive processes.

Clinical correlation is needed to connect that morphology to a functional neuroendocrine tumor.

Important limit

A schema or descriptive morphology does not replace a real specimen or full clinical work-up.

Diagnostic synthesis starts with the full phenotype



Each stage adds explanatory support; No single step is an absolute diagnostic requirement in the provided text.

Specific imaging protocols or formal clinical criteria are not provided by the source.

What do serotonin and 5-HIAA tell us?

Supported by Robbins

Plasma serotonin correlates with cardiac lesion severity.

Urinary 5-HIAA excretion also correlates with lesion severity.

Not provided by Robbins passage

Sensitivity or specificity for identifying plaques.

A cutoff that defines cardiac involvement.

Proof of a sole causal mediator.

Avoid five frequent reasoning errors

Do not assume every neuroendocrine tumor produces the systemic syndrome.

Do not assume carcinoid heart disease always affects the left heart or never can.

Do not substitute “dense collagen scar” for the described matrix-rich plaque.

Do not interpret serotonin association as mechanistic proof.

Do not equate carcinoid plaques with cancer-associated NBTE.

Application I: Intestinal tumor with hepatic spread

Hypothetical teaching vignette

A patient has an intestinal neuroendocrine tumor with multiple hepatic metastases, episodic flushing and diarrhea.

Subsequent evaluation detects right-sided valve dysfunction.

Question: Explain the exposure pathway and name the two typical valve defects.

Discuss the inference; The next slide develops the reasoning.

Application I: Connect each observation to a mechanism

Finding	Source-based mechanistic inference
Intestinal secretory tumor	Potential vasoactive mediator source
Multiple liver metastases	Hepatic inactivation barrier may be bypassed
Flushing and diarrhea	Systemic carcinoid syndrome
Right-sided valve lesions	Typical carcinoid cardiac distribution

Application II: Left-sided lesions

Hypothetical teaching vignette

A patient with secretory carcinoid manifestations has a left-sided valve plaque.

A clinician considers a right-to-left intracardiac shunt or a primary pulmonary carcinoid.

Question: Why are these biologically plausible exceptions to the usual sidedness?

Discuss the inference; The next slide develops the reasoning.

Application II: Identify the missing barrier

Right-to-left shunt

Mediator-rich systemic venous blood can pass toward the left side without full pulmonary degradation.

Primary pulmonary source

Secretion occurs within the pulmonary compartment rather than upstream of hepatic first-pass clearance.

Application III: Plaque versus vegetation

Hypothetical teaching vignette

An excised valve shows smooth, glistening white endocardial thickening.

Microscopic description includes acid mucopolysaccharide-rich matrix, smooth muscle cells and preserved deeper structures.

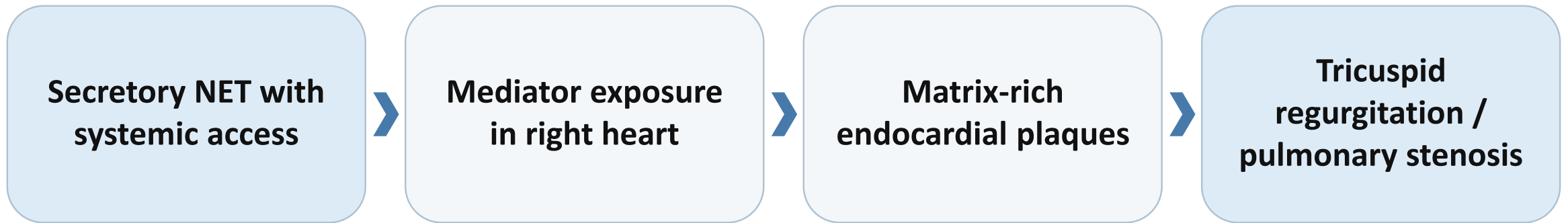
Question: Which lesion pattern is favored, and which common alternatives are morphologically different?

Discuss the inference; The next slide develops the reasoning.

Application III: Decisive tissue features

Feature	Supports carcinoid-type lesion	Argues for another process
Surface appearance	Smooth glistening plaque	Friable vegetation
Composition	Mucopolysaccharide-rich matrix	Bland thrombus or inflammatory necrosis
Deeper structure	Preserved	Destruction in aggressive infection

Reconstruct the full pathophysiology



The causal identity of individual mediators remains uncertain.

Left-sided lesions can occur with altered intracardiac flow or pulmonary origin.

Five defensible conclusions

Carcinoid heart disease is an endocardial and valvular manifestation of circulating tumor products.

Hepatic and pulmonary metabolism explain its common clinical and anatomic pattern.

Plaques are glistening white, matrix-rich, and leave the underlying tissue intact.

Tricuspid insufficiency and pulmonary stenosis are characteristic right-sided effects.

Biomarker association is not proof that serotonin alone causes the lesions.

Primary reading and interpretive boundaries

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026). Chapter 12, “The Heart”: carcinoid heart disease and valvular pathology.

Chapter 17, “The Gastrointestinal Tract”: well-differentiated neuroendocrine tumors and carcinoid syndrome.

Chapter 15, “The Lung”: pulmonary carcinoid tumors and functional secretory manifestations.

Illustrations in this lecture are original editable schematics—not textbook figures or observed specimens.