

Chronic Immune Thrombocytopenic Purpura

Immune platelet clearance • marrow response • clinical and diagnostic pathology

A pathology lecture integrating disease mechanisms with diagnostic reasoning

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Learning objectives

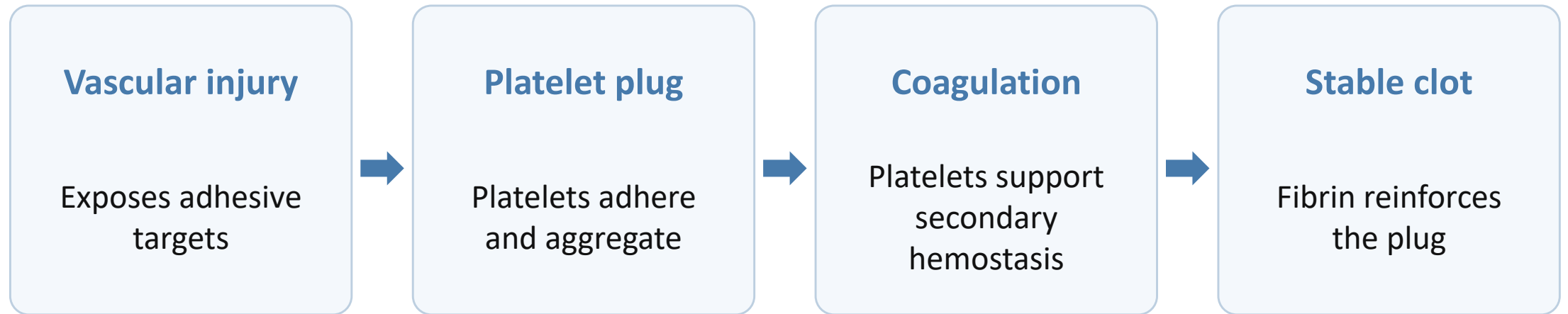
- Explain immune platelet destruction and impaired platelet production in chronic ITP.
- Correlate blood, marrow, and splenic findings with accelerated thrombopoiesis.
- Recognize characteristic bleeding patterns and laboratory findings.
- Differentiate primary ITP from secondary, consumptive, and production disorders.
- Relate treatments to the pathogenetic steps they influence.

Core definition

Autoantibody-mediated platelet destruction

- Chronic ITP is an immune thrombocytopenia dominated by accelerated platelet clearance.
- The disorder may be primary or arise with a recognized associated condition.
- In some patients, antibodies also damage megakaryocytes, reducing platelet production.

Platelets participate in primary hemostasis



A low platelet count chiefly compromises the initial platelet-dependent response.

Why thrombocytopenia bleeds differently

Platelet-number defect

- Small-vessel hemorrhage
- Skin and mucosal bleeding
- Petechiae, purpura, epistaxis

Coagulation-pathway defect

- Typically assessed through PT/PTT
- Abnormalities may prolong clotting assays
- A separate diagnostic pathway

The distinction is conceptual; Bleeding disorders may also overlap.

Platelet counts and bleeding context

Platelet count	Teaching interpretation
<150,000/μL	Usually classified as thrombocytopenia
20,000–50,000/μL	May aggravate bleeding after trauma
<20,000/μL	May be associated with spontaneous bleeding

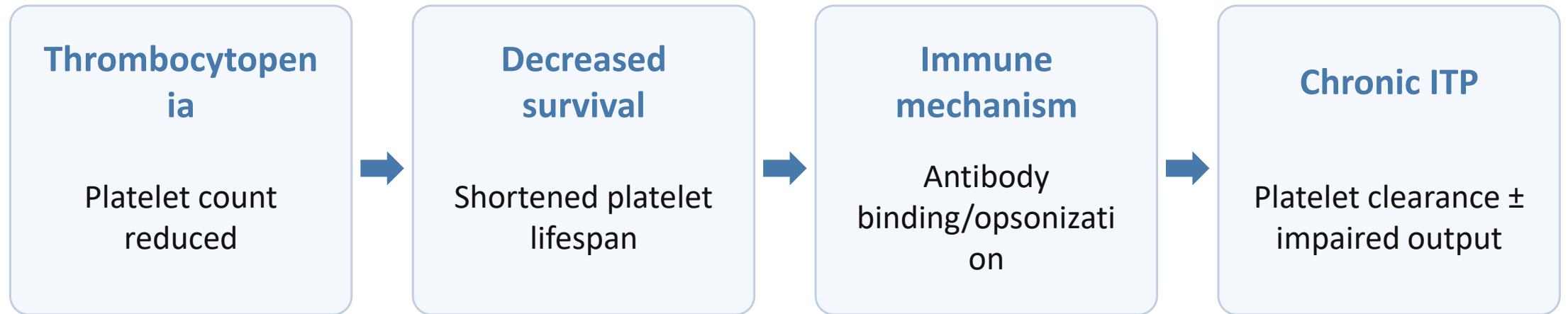
Thresholds describe broad risk patterns, not a patient-specific treatment rule.

Four broad mechanisms of thrombocytopenia

Mechanism	Characteristic process
Reduced production	Bone marrow or megakaryocyte output is impaired
Reduced survival	Immune destruction or nonimmune platelet consumption
Sequestration	Platelets accumulate in an enlarged spleen
Dilution	Massive transfusion decreases platelet concentration

Chronic ITP is primarily a disorder of immune-mediated platelet survival.

Where chronic ITP fits in the differential



Primary versus secondary chronic ITP

Primary ITP

- No identified predisposing disease or exposure
- Diagnosis requires excluding secondary causes
- “Idiopathic” is a historical alternative term

Secondary ITP

- Occurs with another condition or exposure
- Immune mechanism still affects platelets
- Associated disease modifies diagnostic reasoning

Established secondary associations

Systemic lupus erythematosus

Autoimmune disease context can accompany immune platelet loss.

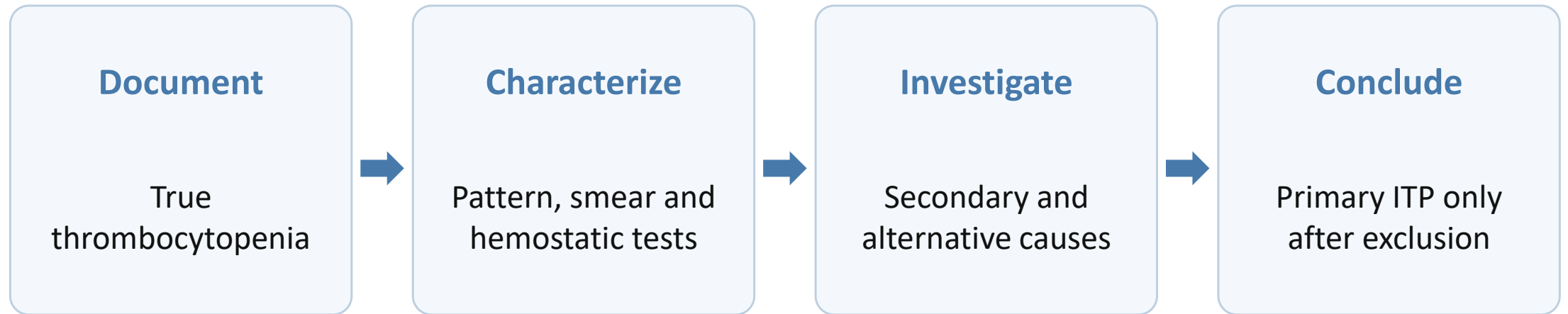
HIV infection

Both immune platelet clearance and impaired megakaryocyte output may occur.

B-cell neoplasms

Chronic lymphocytic leukemia is a specified example.

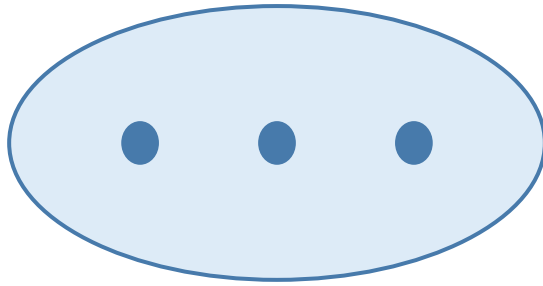
Primary ITP is a diagnosis of exclusion



There is no single positive test that establishes primary ITP.

Platelet membrane glycoproteins are immune targets

Platelet membrane



**Common autoantibody
targets**

Glycoprotein IIb/IIIa

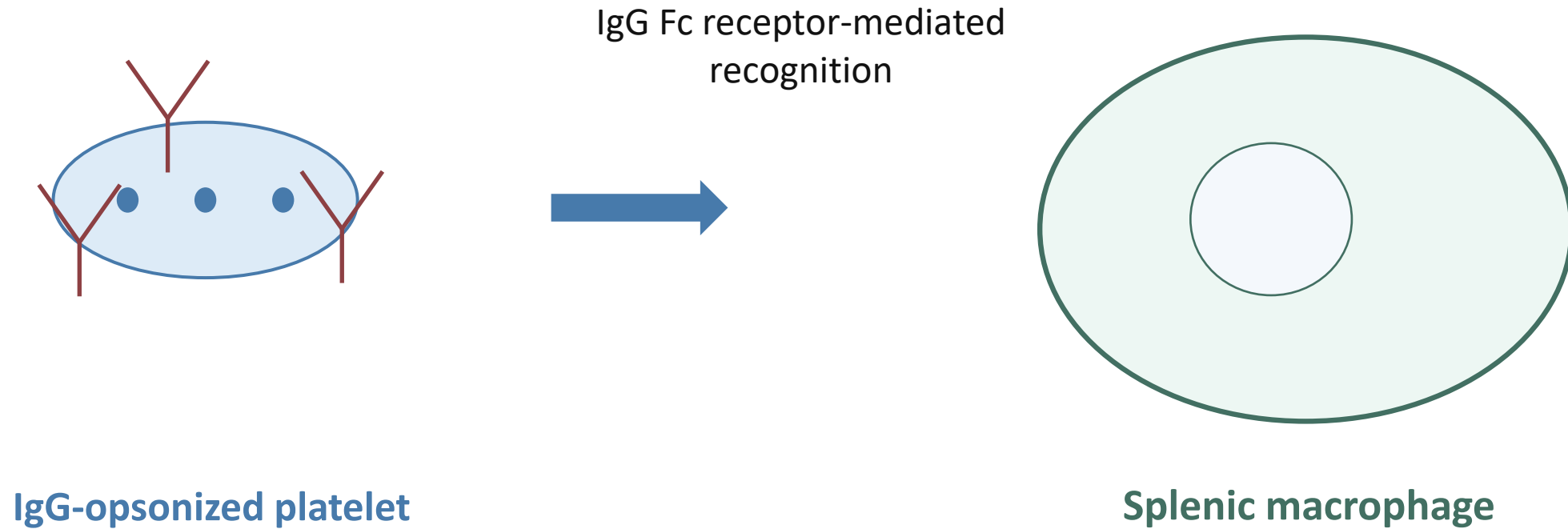
Glycoprotein Ib/IX

The dominant antibody class is IgG

Antiplatelet IgG marks circulating platelets for removal

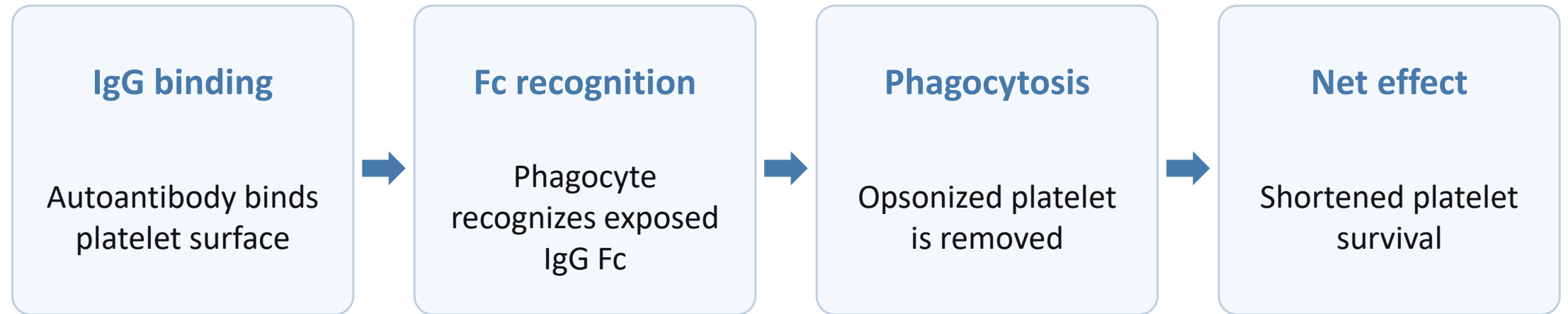
- Autoantibodies commonly bind platelet membrane glycoproteins IIb/IIIa or Ib/IX.
- Antibody-mediated opsonization is the link from autoreactivity to clearance.
- The mechanistic analogy is autoimmune hemolytic anemia.

Fc receptor recognition drives clearance



Schematic — not a microscopy image

Opsonization to platelet removal



The spleen is the principal clearance site

Splenic phagocytes remove opsonized platelets

- Marked platelet improvement after splenectomy provides functional evidence.
- Antibody-coated platelets are cleared through IgG Fc receptor pathways.
- This is accelerated platelet destruction, not primary failure of coagulation.

The spleen has two relevant roles

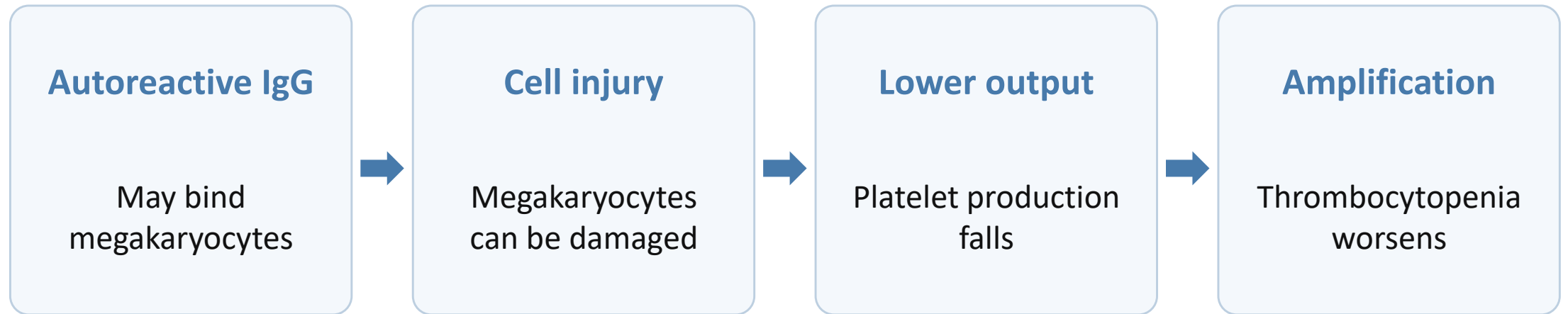
Platelet clearance

- Phagocytes recognize IgG-coated platelets
- Removal reduces platelet survival
- Dominant effect in the pathogenesis

Antibody contribution

- Red pulp contains numerous plasma cells
- Some of the benefit after splenectomy may reflect antibody-source removal
- This is presented as a possible additional mechanism

Some antibodies also affect megakaryocytes



Two interacting causes of the platelet deficit

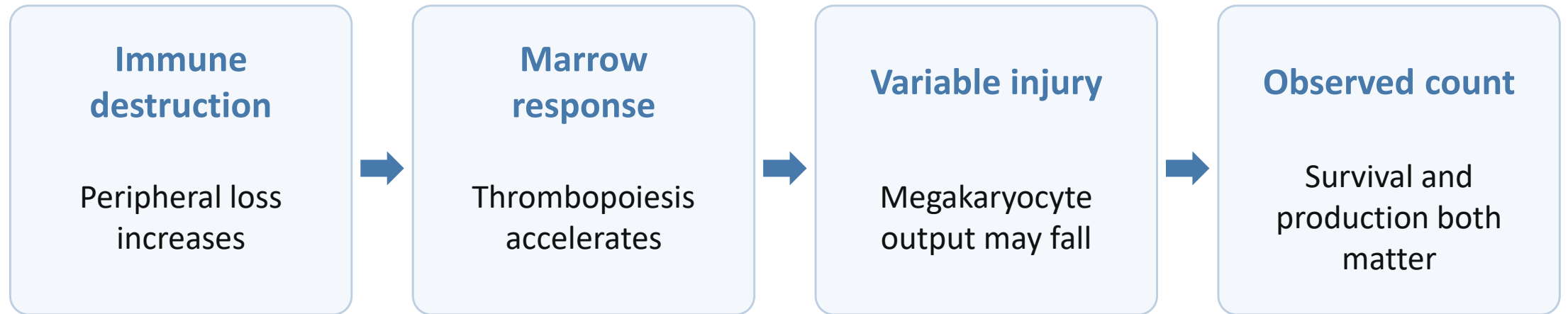
Increased loss

- Platelets opsonized by autoantibodies
- Splenic macrophage uptake
- Shorter circulating survival

Impaired replacement

- Autoantibodies may injure megakaryocytes
- Platelet production may decrease
- Marrow compensation can become inadequate

The net platelet count reflects opposing processes



The blood count is the final balance of clearance and output, not a direct assay of either mechanism.

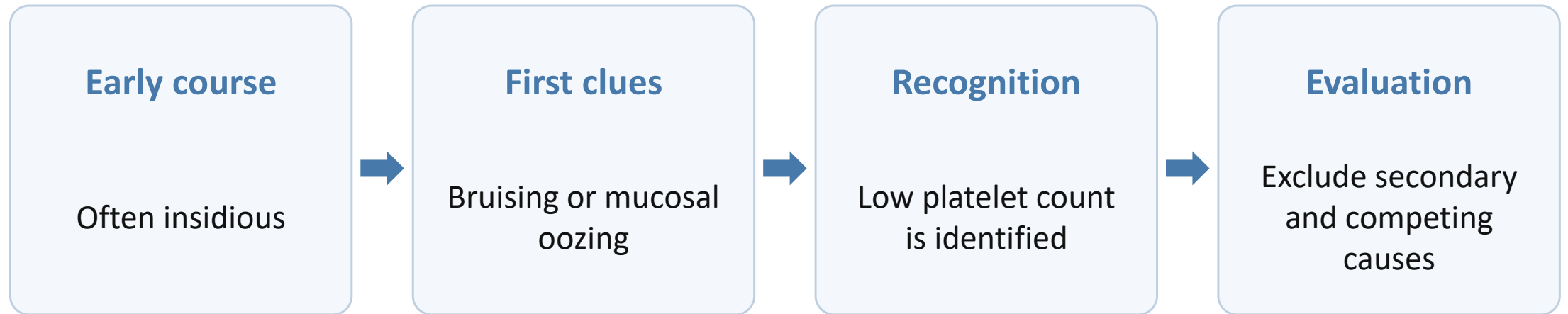
Mechanism: Observation versus inference

Source observation	What it supports	What it does not prove
IgG binding in ~80%	Autoimmunity often detectable	A negative assay excludes ITP
Response to splenectomy	Spleen is major clearance site	Every patient will be cured
Increased marrow megakaryocytes	Compensatory production	A specific histologic diagnosis

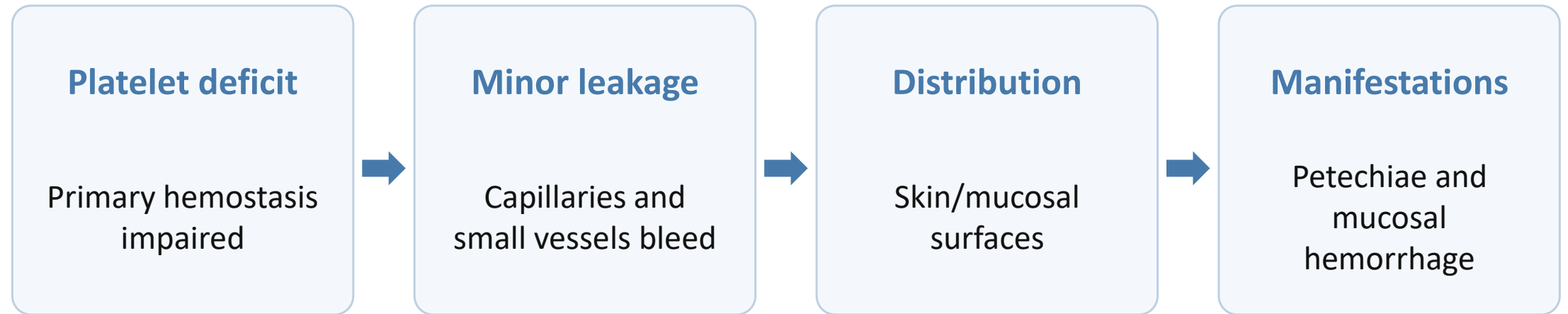
Typical adult presentation

- A predominance in adult women younger than 40 years.
- The reported female-to-male ratio is approximately 3:1.
- This demographic pattern is supportive context, not a diagnostic criterion.
- Neither sex nor age substitutes for demonstrating isolated thrombocytopenia.

Clinical onset and recognition



Why bleeding occurs in small vessels

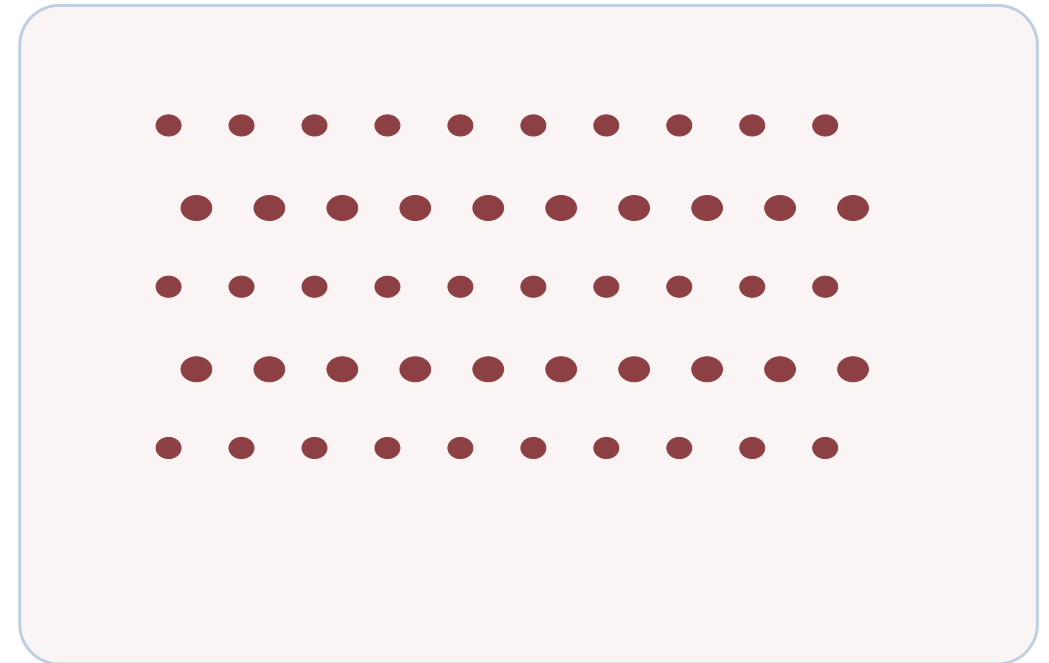


Petechiae can coalesce into larger hemorrhages

Petechiae



Confluent lesions



Schematic pattern only — not a clinical photograph

Dependent areas favor petechiae

Higher local capillary pressure helps explain distribution

- Pinpoint hemorrhages are particularly prominent in dependent skin regions.
- The distribution is a hemodynamic consequence superimposed on platelet deficiency.
- A visible bleeding pattern does not by itself establish the etiology.

Ecchymoses and easy bruising

- Petechiae can become confluent to form ecchymoses.
- Minor trauma may produce bruising out of proportion to the injury.
- Soft-tissue hemorrhage may accompany skin and mucosal bleeding.
- A precise bleeding history should distinguish spontaneous from trauma-related events.

Characteristic mucocutaneous symptoms

Nasal / oral

Epistaxis and gingival bleeding may be early complaints.

Skin

Petechiae, purpura and easy bruising are characteristic.

Soft tissues

Relatively minor trauma may produce clinically evident hemorrhage.

Bleeding may be the first presentation

Gastrointestinal

Melena may be a presenting symptom.

Urinary

Hematuria may disclose the platelet deficit.

Gynecologic

Excessive menstrual flow can be an early clinical clue.

Rare but serious hemorrhage

Intracranial bleeding is a critical complication

- Subarachnoid and intracerebral hemorrhage are described in chronic ITP.
- They may be fatal, although they are rare in treated patients.
- Severity assessment must not be based on the skin findings alone.

Examination: What is typical and atypical?

Compatible with primary ITP

- Mucocutaneous hemorrhage
- Usually normal splenic size
- No expected lymphadenopathy

Suggests a competing diagnosis

- Splenomegaly
- Enlarged lymph nodes
- Clinical context of B-cell neoplasm or systemic illness

Splenomegaly is not expected in primary ITP

An enlarged spleen changes the diagnostic hypothesis

- The spleen as normal-sized in uncomplicated chronic ITP.
- Marked enlargement suggests alternative mechanisms or an associated disorder.
- Hypersplenism and hematologic neoplasms become more relevant.

Lymphadenopathy warrants explanation

Consider secondary ITP or another disease

- Primary chronic ITP ordinarily lacks lymphadenopathy.
- example, a B-cell neoplasm may cause secondary immune thrombocytopenia.
- Physical findings guide selective evaluation rather than confirming ITP.

Morphology involves three compartments

Spleen

Normal-sized; Sinusoidal congestion; Reactive follicles; Occasional megakaryocytes.

Bone marrow

Modest megakaryocytic increase, sometimes immature forms.

Peripheral blood

Thrombocytopenia with some unusually large platelets.

Gross spleen: Usually normal-sized

No characteristic splenic enlargement

- A normal-sized spleen is compatible with immune platelet destruction.
- Increased phagocytic activity does not require gross splenomegaly.
- Organ size alone does not establish or exclude immune clearance.

Microscopic splenic features

Sinusoids

Congestion may be present in the splenic red pulp.

White pulp follicles

Follicular enlargement with prominent reactive germinal centers.

Sinusoidal megakaryocytes

Occasional cells may reflect mild extramedullary hematopoiesis.

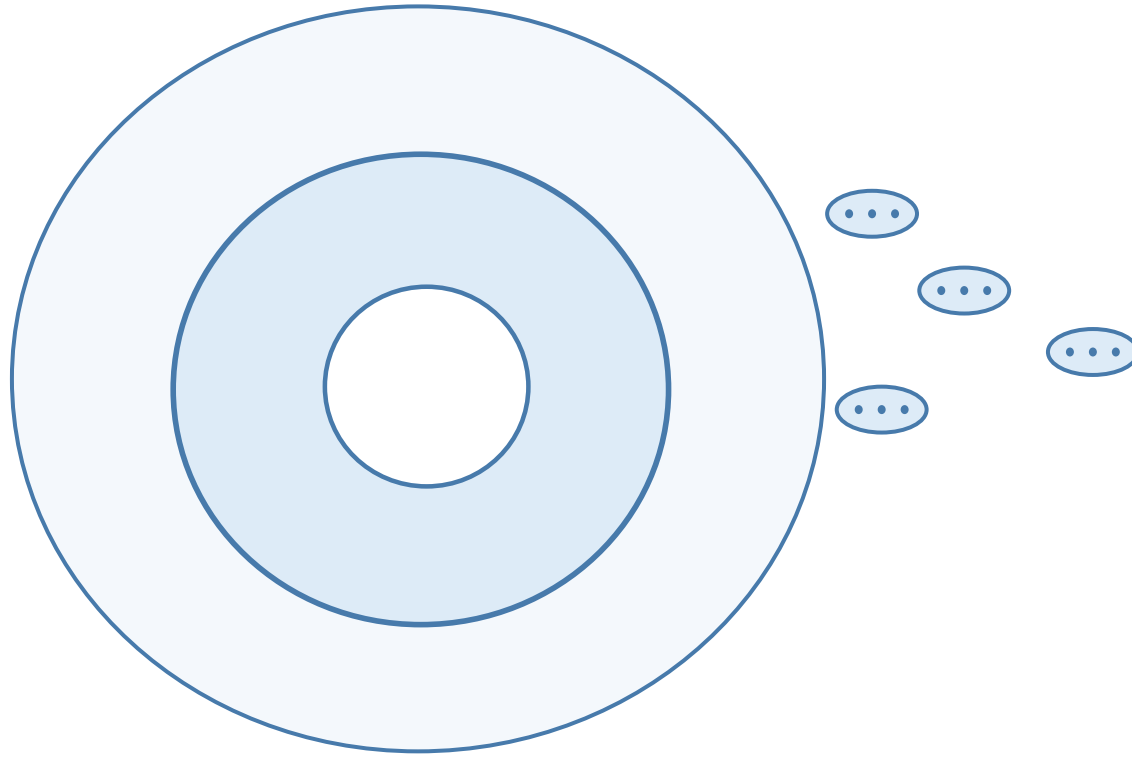
Schematic concept summaries; The textbook findings are not ITP-specific.

Splenic megakaryocytes: A proposed response

A minor extramedullary hematopoietic component is possible

- Scattered megakaryocytes can be found in splenic sinusoids.
- The source proposes elevated thrombopoietin as a possible driver.
- This hypothesis should not be converted into a disease-specific morphologic criterion.

Bone marrow: Compensatory megakaryocytopoiesis



Marrow megakaryocyte

- Modestly increased megakaryocytes
- Some cells show single, large nonlobulated nuclei
- Accelerated thrombopoiesis is not ITP-specific

Immature-appearing megakaryocytes

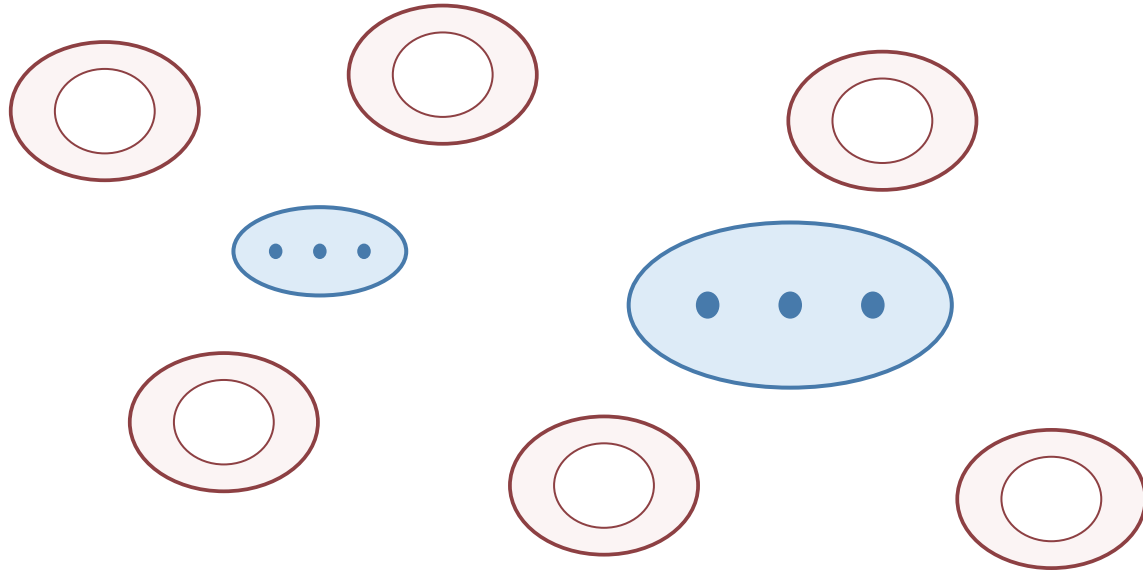
- Some marrow megakaryocytes have large, nonlobulated single nuclei.
- A modest increase in megakaryocyte numbers reflects increased platelet turnover.
- These findings also appear in other causes of accelerated platelet destruction.
- Morphology must be integrated with the clinical and laboratory context.

Marrow morphology is not specific for ITP

Megakaryocytic hyperplasia supports turnover, not etiology

- A similar marrow response can occur in many destructive thrombocytopenias.
- The diagnostic value is often exclusion of marrow failure or another marrow disorder.
- The marrow should not be called pathognomonic for immune thrombocytopenia.

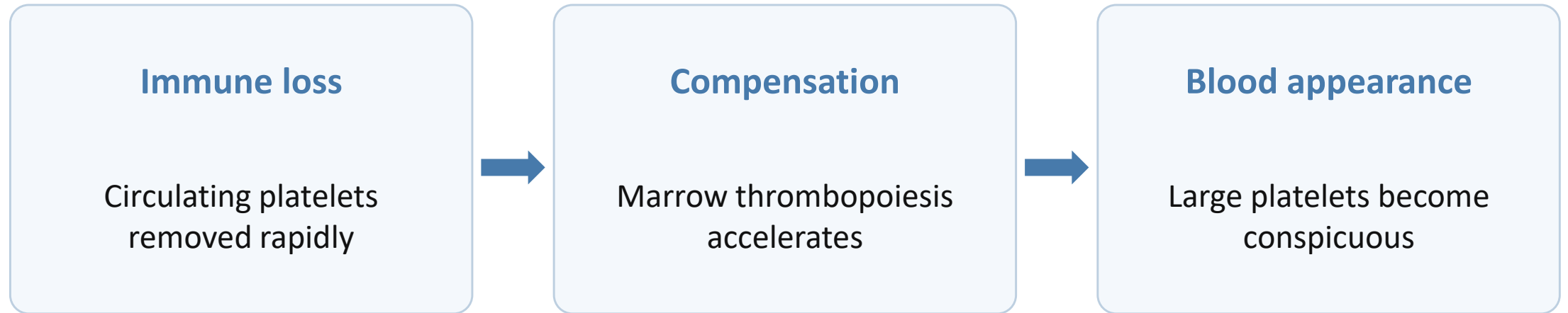
Peripheral blood: Large platelets



Schematic peripheral smear

- Unusually large platelets = megathrombocytes
- Suggest a brisk production response
- Not independently diagnostic of ITP

Why unusually large platelets appear

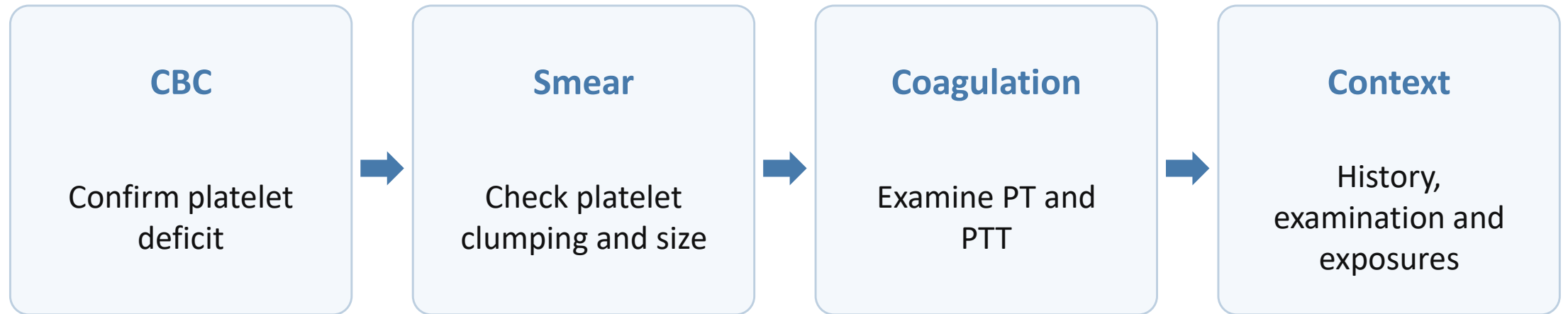


Megathrombocytes are a sign of accelerated platelet production, not a unique ITP marker.

Integrated morphology: Diagnostic meaning

Compartment	Typical observation	Interpretation
Spleen	Normal size, reactive follicles	Compatible but nonspecific
Marrow	Megakaryocytes often increased	Accelerated thrombopoiesis
Peripheral blood	Low count, large platelets	Destruction/compensation pattern

The initial laboratory checkpoint



Exclude artifactual thrombocytopenia

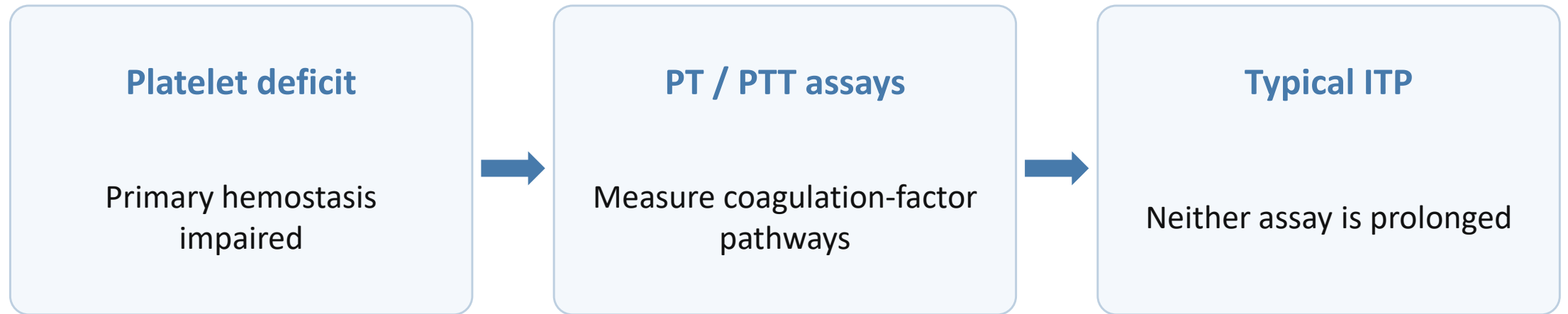
Platelet clumping can produce a falsely low automated count

- Automated platelet counts are performed on anticoagulated blood.
- Peripheral-smear inspection helps detect platelet aggregates.
- A spurious count should not become a diagnosis of ITP.

Expected laboratory constellation

Finding	Textbook pattern	Interpretation
Platelet count	Reduced	Isolated thrombocytopenia
Smear	Often unusually large platelets	Accelerated thrombopoiesis
PT and PTT	Normal	Preserved tested coagulation pathways
Marrow (when examined)	Normal/increased megakaryocytes	Compatible response; Nonspecific

Normal PT/PTT: A mechanistic distinction



Normal PT and PTT do not exclude clinically important platelet-mediated bleeding.

Why platelet autoantibody tests do not confirm ITP

Biologic finding

- Autoantibodies may be shown in plasma or on platelets
- The source reports detection in ~80%

Clinical test limitation

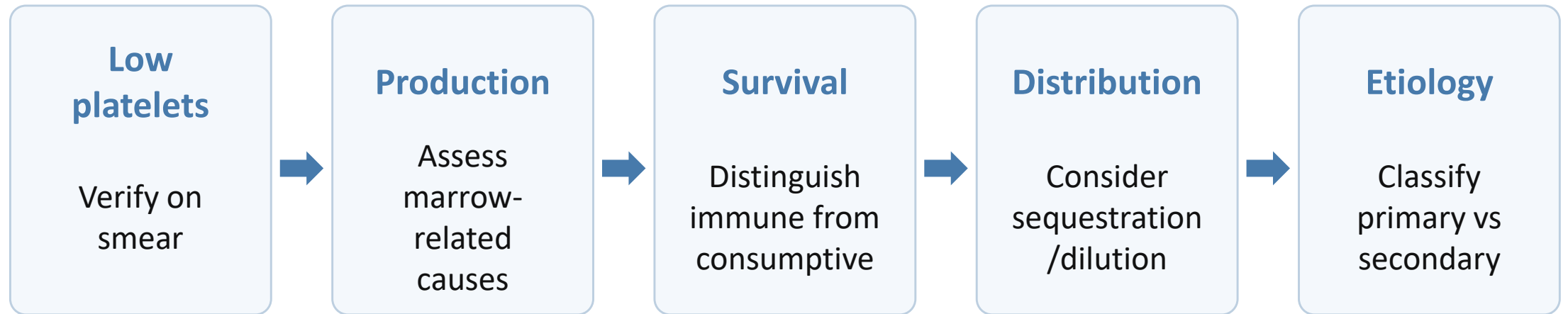
- Sensitivity and specificity are insufficient
- Not clinically useful as a confirmatory test
- Negative or positive tests cannot replace exclusion

The marrow examination has an exclusionary role

Rule out marrow failure or primary marrow pathology

- ITP-associated marrow findings are not specific.
- Aplastic anemia, myelodysplastic disease and marrow infiltration can reduce platelet production.
- Investigate marrow disorders when the clinical picture suggests them.

Diagnostic exclusion is organized by mechanism



Reduced production versus increased destruction

Dimension	Reduced production	Increased destruction
Primary defect	Marrow platelet output	Platelet survival
Examples	Aplasia, leukemia, MDS	ITP; Nonimmune consumption
Marrow clue	Output may be impaired	Often compensatory megakaryocytes
Smear clue	Depends on marrow disorder	Large platelets may appear

Distinguish hypersplenism from primary ITP

Hypersplenism

- Sequestration increases with splenic enlargement
- An enlarged spleen can retain far more circulating platelets
- A distributional mechanism

Primary chronic ITP

- Immune destruction of IgG-coated platelets
- Spleen usually remains normal-sized
- Splenic clearance is not equivalent to hypersplenism

Consumptive thrombocytopenia versus ITP

Feature	Chronic ITP	TMA / DIC
Dominant mechanism	Immune clearance	Excessive consumption
Characteristic context	Isolated platelet deficit	Microvascular thrombi or systemic coagulation
Diagnostic caution	Diagnosis by exclusion	Must not mislabel a dangerous consumption syndrome

Relevant drug-associated thrombocytopenia

Drug-dependent antibodies

Quinine, quinidine and vancomycin are textbook examples.

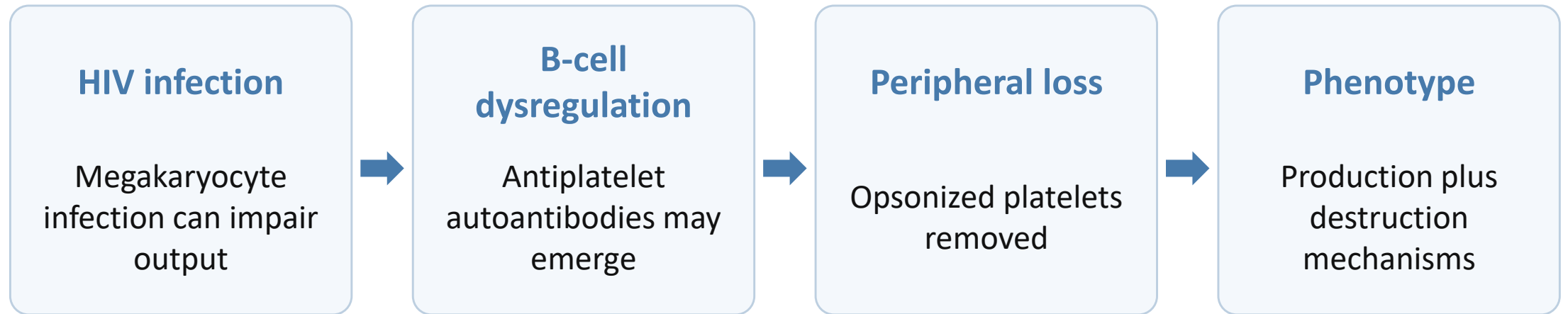
GP1Ib/IIa inhibitors

Drug binding may reveal an immunogenic conformation.

Heparin

Immune HIT has a distinctive platelet-activating, thrombotic phenotype.

HIV-associated platelet loss may be mixed



Chronic versus acute immune thrombocytopenia

Feature	Chronic ITP (textbook)	Acute ITP (textbook)
Typical group	Adult women <40 y	Children, both sexes
Onset	Often insidious	Abrupt, often after viral illness
Course	May persist or relapse	Usually resolves within 6 months
Mechanism	Autoantibody-mediated	Autoantibody-mediated

This reproduces the textbook comparison; It is not a current formal duration-classification rule.

Heparin-induced thrombocytopenia is not chronic ITP

Immune HIT (type II)

- Antibodies recognize heparin–PF4 complexes
- Platelets are activated
- Venous and arterial thrombosis can occur

Chronic ITP

- Antibodies commonly recognize platelet glycoproteins
- Splenic clearance dominates
- Mucocutaneous bleeding is characteristic

TTP is a dangerous alternative diagnosis

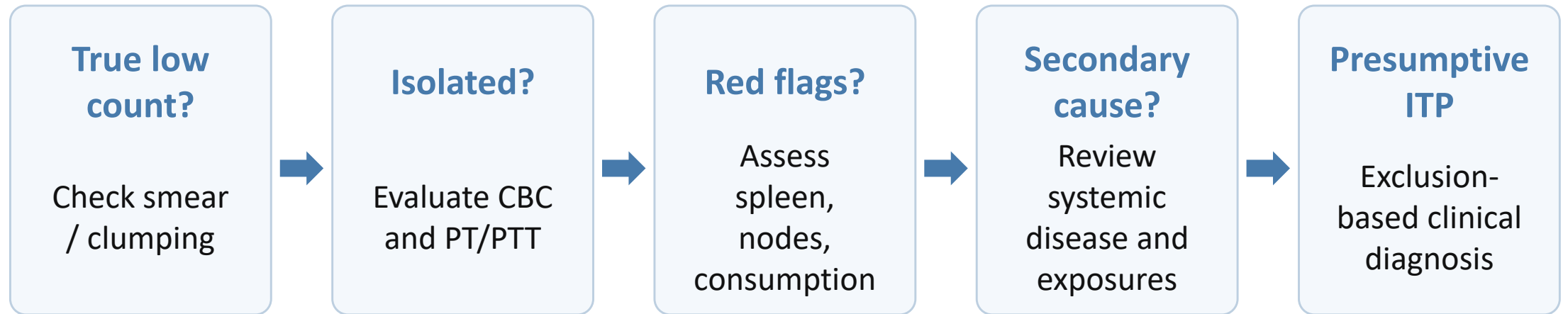
Thrombotic microangiopathy

- Small-vessel platelet thrombi
- Microangiopathic hemolytic anemia is a crucial clue
- Requires urgent disease-specific evaluation

Chronic ITP

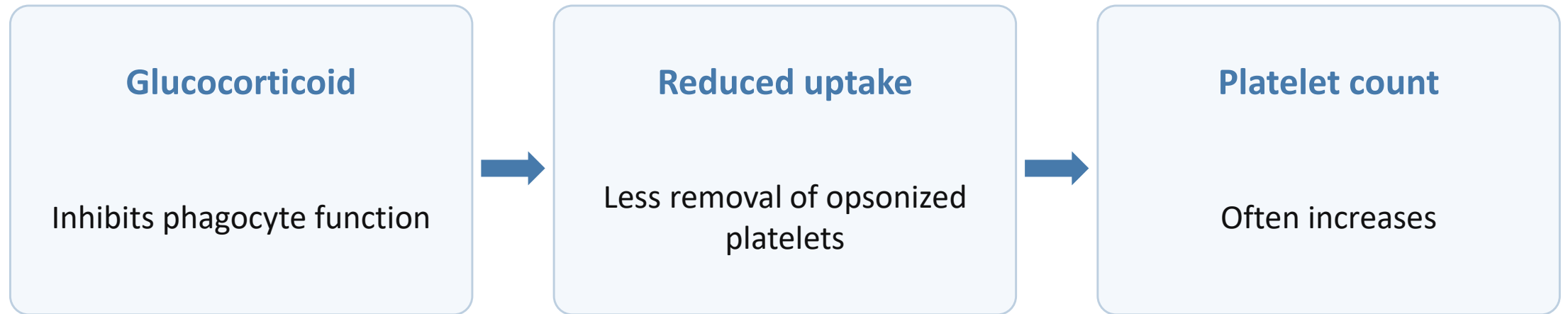
- Predominantly immune platelet clearance
- Typical isolated thrombocytopenia
- No defining microangiopathic hemolysis

Integrated diagnostic reasoning



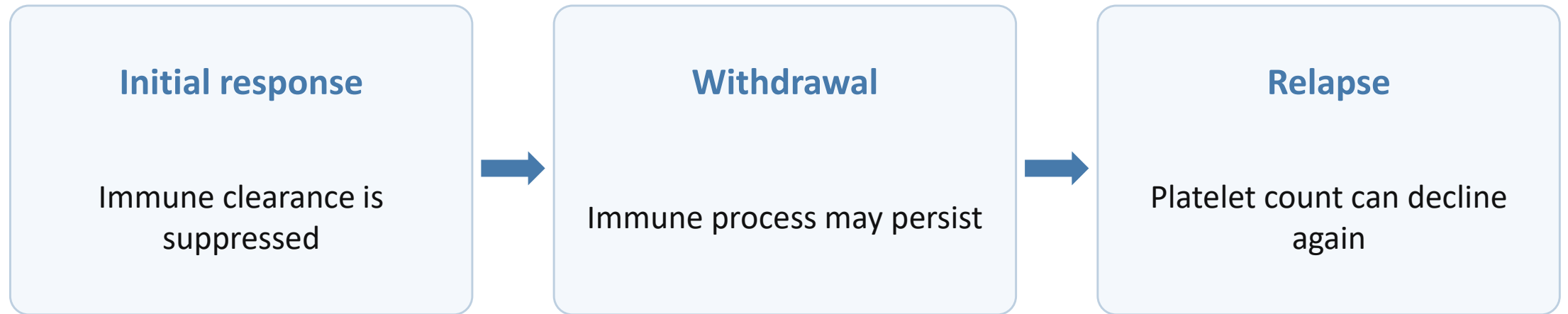
A practical synthesis of the Robbins differential, not an independent guideline algorithm.

Glucocorticoids target platelet clearance



The source reports initial response in almost all patients, with relapse common after withdrawal.

Why relapse after steroid withdrawal matters



An early platelet rise does not ensure durable remission.

Careful observation can be appropriate

Management follows bleeding severity and longitudinal risk

- The textbook permits careful follow-up of some patients with moderately severe thrombocytopenia.
- Some patients may enter spontaneous remission.
- This pathology overview does not define a numerical management threshold or replace clinical guidelines.

Splenectomy: Benefit and trade-off

Mechanistic benefit

- Removes the principal clearance site
- May remove an antibody source
- Platelet count normalizes in about two-thirds of severe cases (textbook)

Important cost

- Increased risk of bacterial sepsis
- Response is not universal
- Treatment decisions require individualized clinical assessment

Immunomodulatory approaches

Intravenous immunoglobulin

An immunomodulatory option described for relapse or splenectomy contraindication.

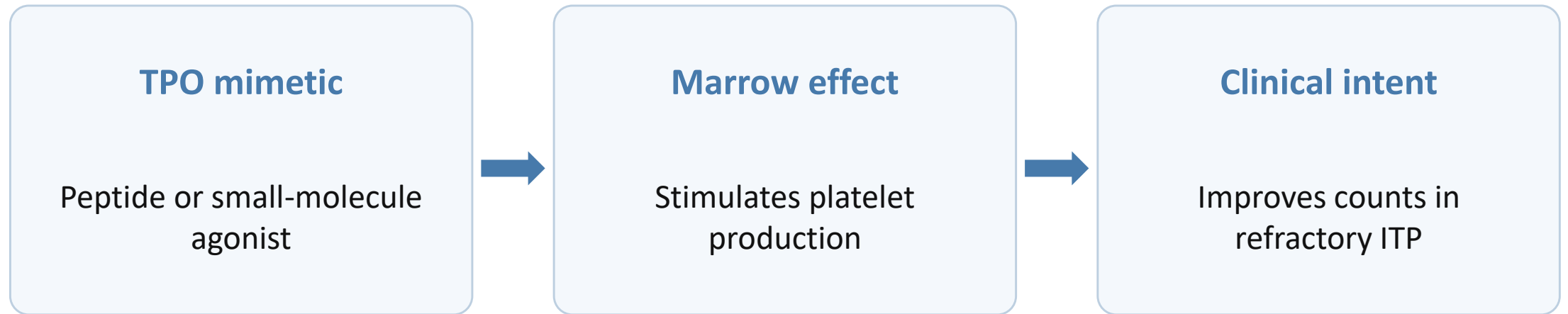
Anti-CD20 antibody

Rituximab targets B cells as an immune-directed strategy.

Treatment context

The source lists these options without presenting a current stepwise guideline.

Thrombopoietin-mimetic therapy



The therapeutic target is platelet production rather than splenic clearance.

Treatments map to distinct pathophysiologic targets

Intervention	Mechanistic focus	Textbook qualification
Glucocorticoids	Phagocyte function	Relapse after withdrawal can occur
Splenectomy	Splenic clearance $\pm$ antibody source	Sepsis risk; Not uniformly effective
IVIG / rituximab	Immune modulation	Options in relapsed or selected patients
TPO mimetics	Platelet production	May help refractory disease

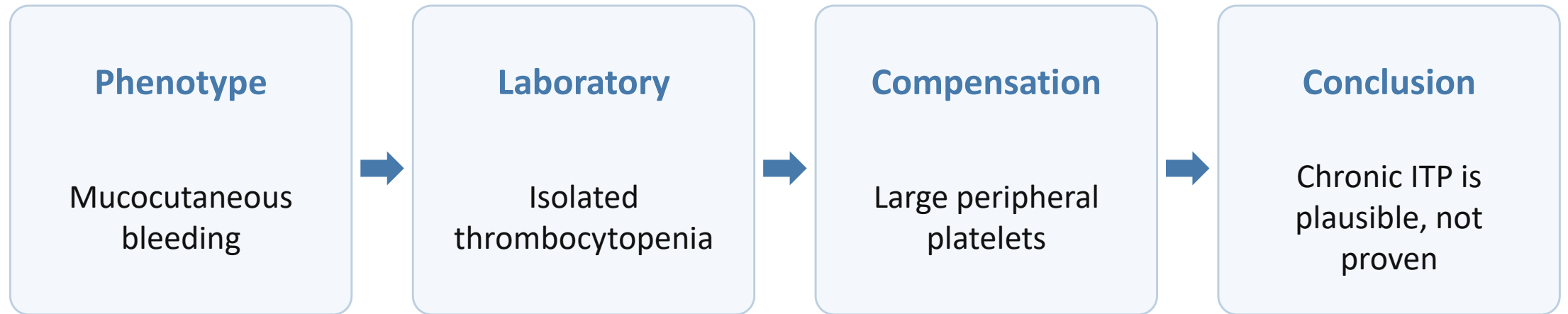
Clinical case A: Isolated platelet loss

- A 32-year-old woman reports months of easy bruising, gingival bleeding and intermittent epistaxis.
- The platelet count is low; Other CBC findings and PT/PTT are not abnormal.
- Peripheral blood shows unusually large platelets.
- There is no splenomegaly or lymphadenopathy.

Clinical question

Which observations support immune platelet destruction, and what still must be excluded?

Case A: Evidence chain



A primary diagnosis requires review of secondary, drug-related, marrow, and consumptive causes.

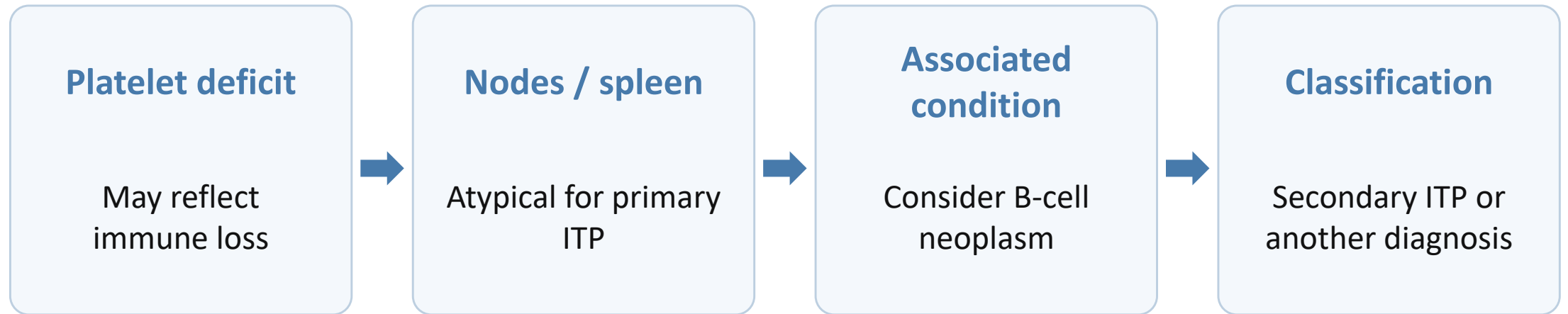
Clinical case B: Diagnostic redirection

- An adult patient has thrombocytopenia together with palpable lymph nodes and splenomegaly.
- The bleeding pattern may resemble immune thrombocytopenia.
- A B-cell neoplasm is one secondary association.
- It is inappropriate to label this uncomplicated primary ITP without further evaluation.

Clinical question

Which examination findings invalidate a simple “primary ITP” shortcut?

Case B: Classify the context



Red flags that change the differential

Finding	Implication
Splenomegaly	Consider sequestration, neoplasm or another disorder
Lymphadenopathy	Consider secondary ITP associated with B-cell disease
Platelet aggregates on smear	Consider spurious thrombocytopenia
Microangiopathic hemolysis	Consider TTP/HUS rather than uncomplicated ITP
Marrow failure pattern	Consider impaired production

Pathology synthesis: Six essential links

Antibody → clearance

IgG-coated platelets are recognized by splenic phagocytes.

Turnover → morphology

Megakaryocytic response and large platelets suggest rapid production.

Platelet loss → bleeding

Skin and mucosal bleeding occur while PT/PTT remain normal.

Primary ITP remains a diagnosis of exclusion; Morphology and antibody testing are not definitive.

Key references and source limits

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026).
- Core source: Chronic Immune Thrombocytopenic Purpura; context: thrombocytopenia and adjacent disorders.
- All diagrams in this presentation are original native PowerPoint schematics, not diagnostic histologic specimens.
- Management content reflects the textbook excerpt, not a separately verified contemporary clinical guideline.