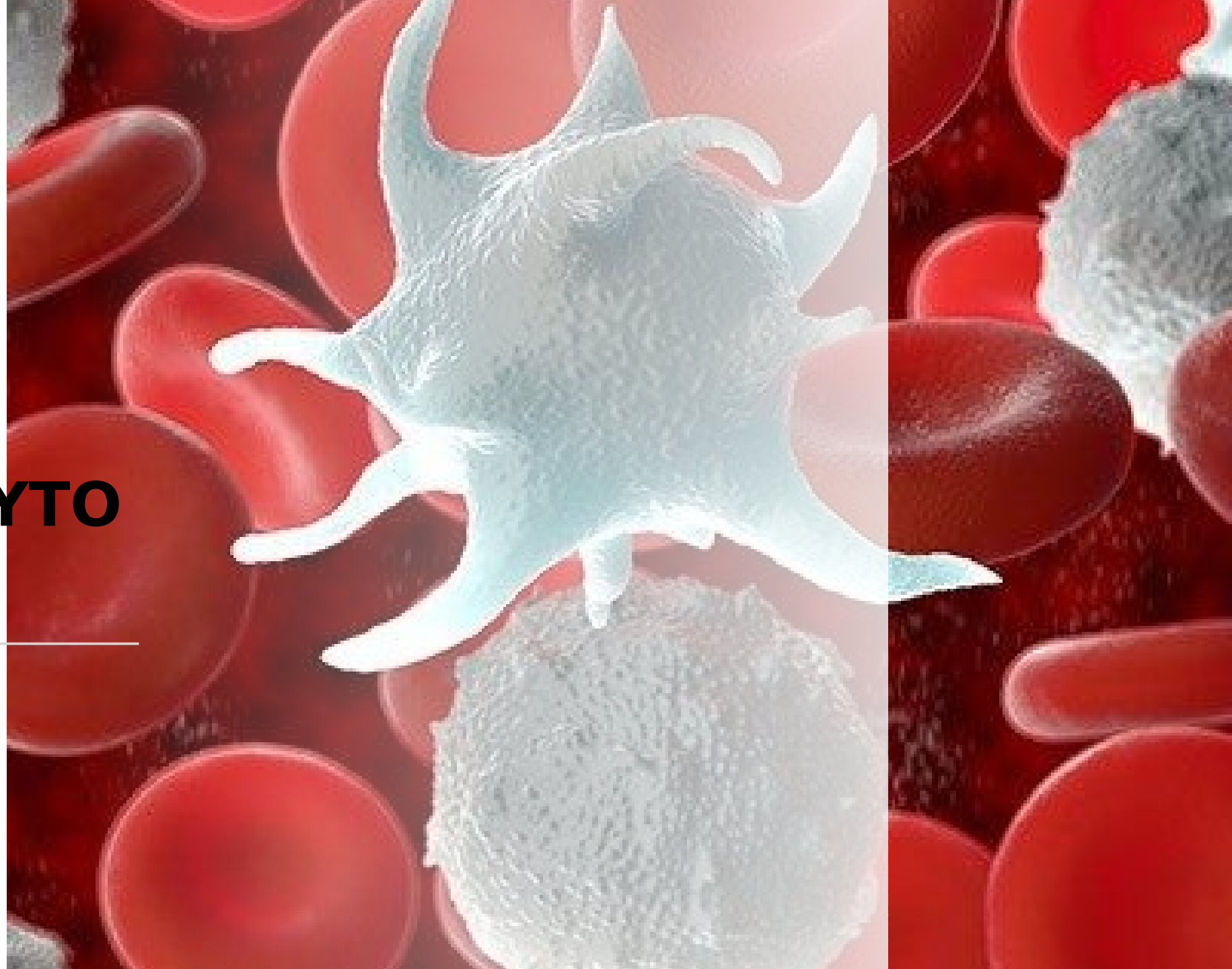
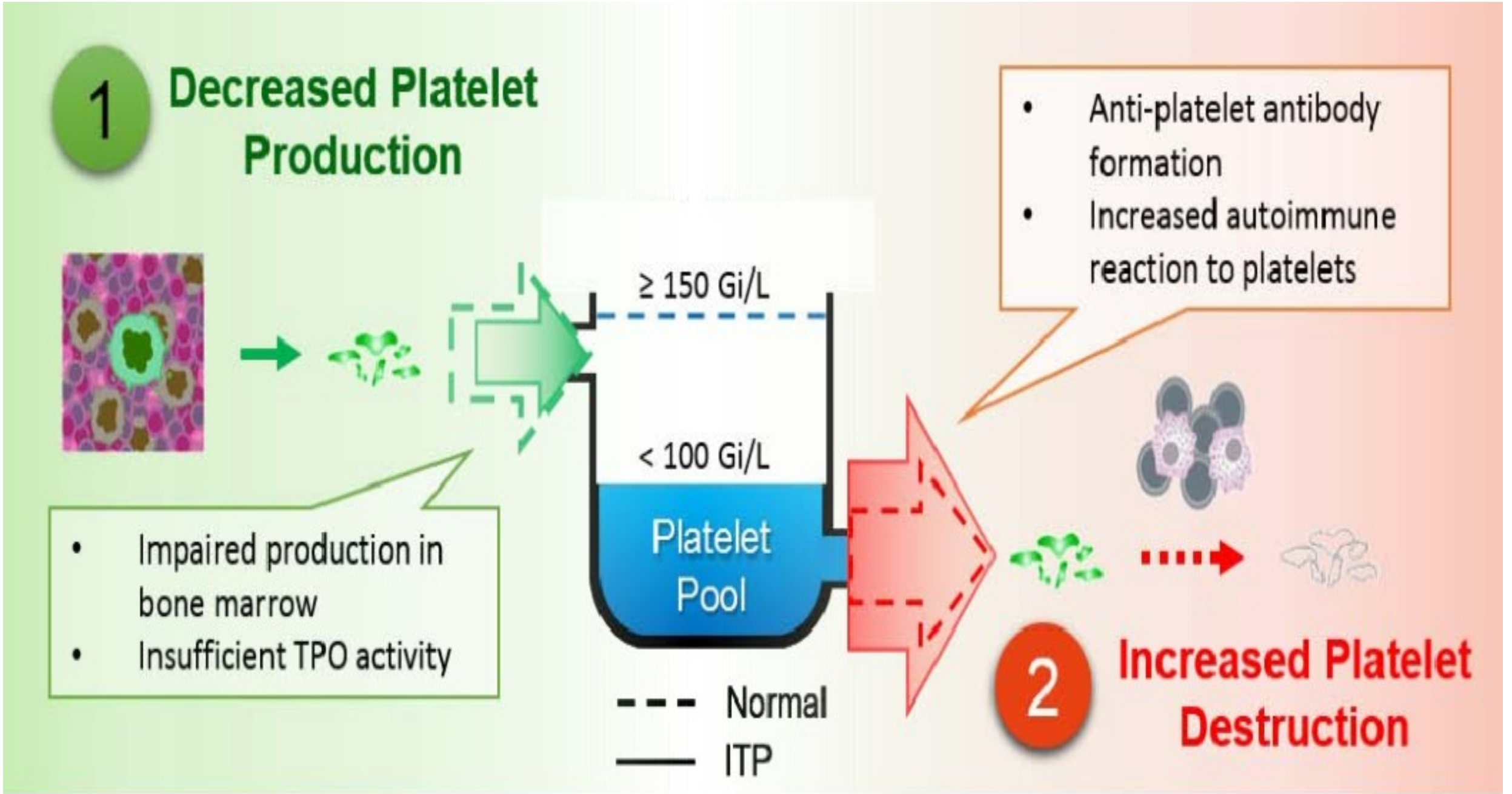
IMMUNE THROMBOCYTO PENIA

DR. FAWAD RAHIM



LEARNING OBJECTIVES

Enumerate	The clinical features of immune thrombocytopenia.
Discuss	The investigations used in the diagnosis of immune thrombocytopenia.
Describe	The first- and second-line management options for immune thrombocytopenia


1
Decreased Platelet Production
• Impaired production in bone marrow
• Insufficient TPO activity
≥ 150 Gi/L
< 100 Gi/L
Platelet Pool
Normal
ITP
• Anti-platelet antibody formation
• Increased autoimmune reaction to platelets
2
Increased Platelet Destruction

IMMUNE THROMBOCYTOPENIA

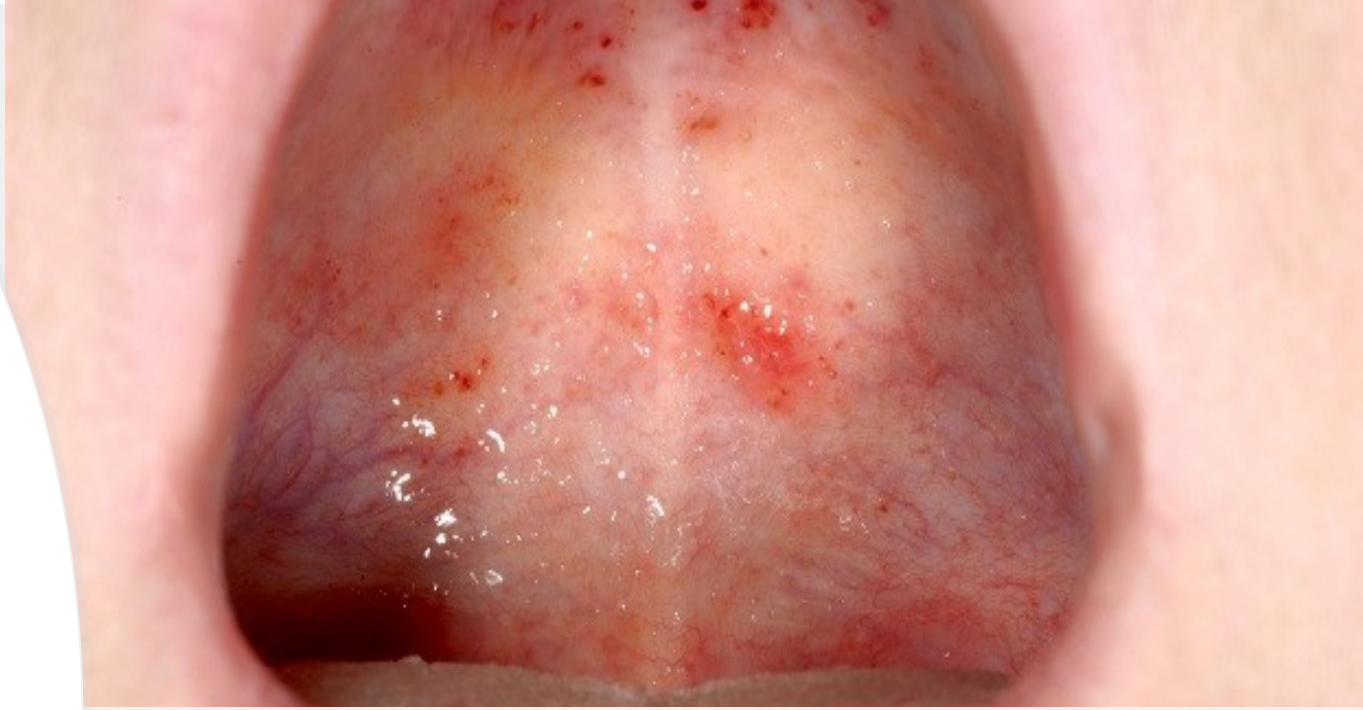
- Reduced platelet lifespan due to antibody-mediated destruction is the predominant hypothesis

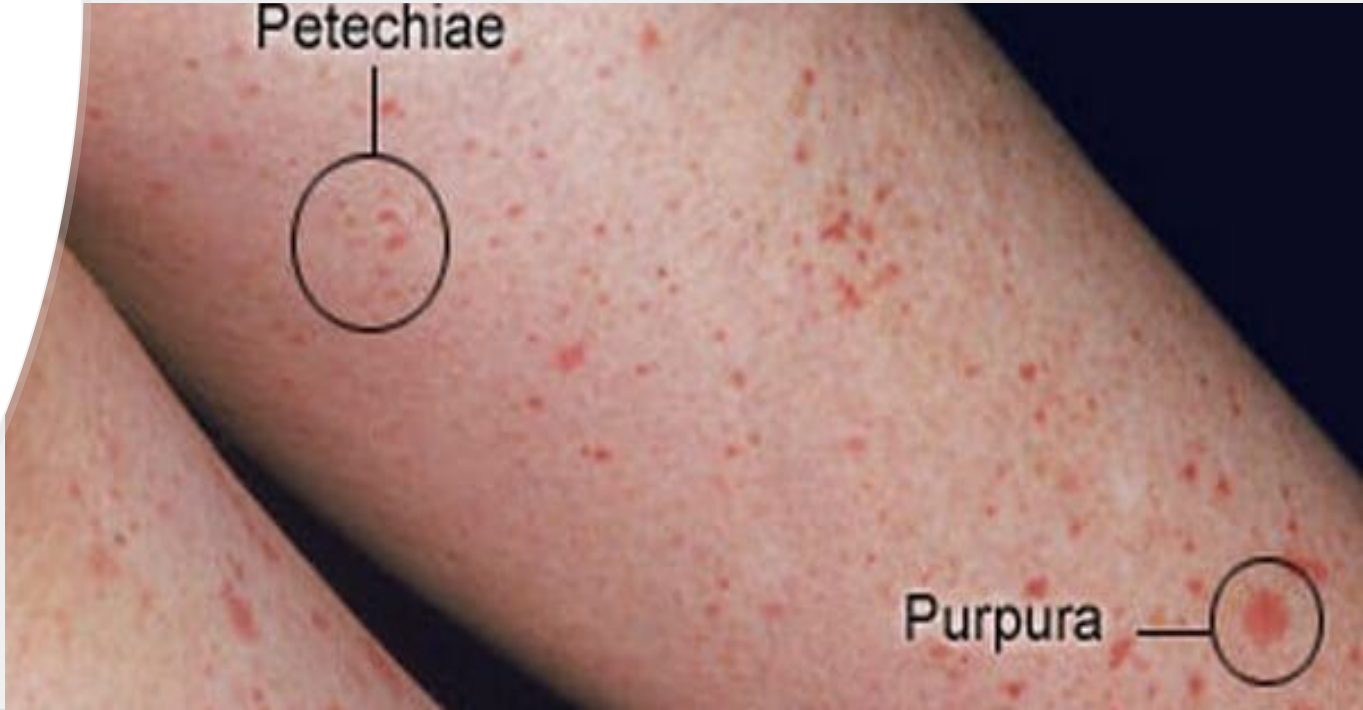
- Primary ITP
- Secondary ITP

Autoimmune Syndromes	Infections	Lymphoid malignancies	Medications / vaccines
• APS • Evans syndrome • IBD • Rheumatoid arthritis • SLE	• CMV • EBV • HCV • Helicobacter pylori • HIV	• Chronic lymphocytic leukemia (CLL) • Lymphoma	• MMR vaccine • Gold • Ipilimumab

CLINICAL FEATURES

- Asymptomatic
- Bleeding : skin or mucous membranes, internal organs
- Severity: Critical, severe and minor





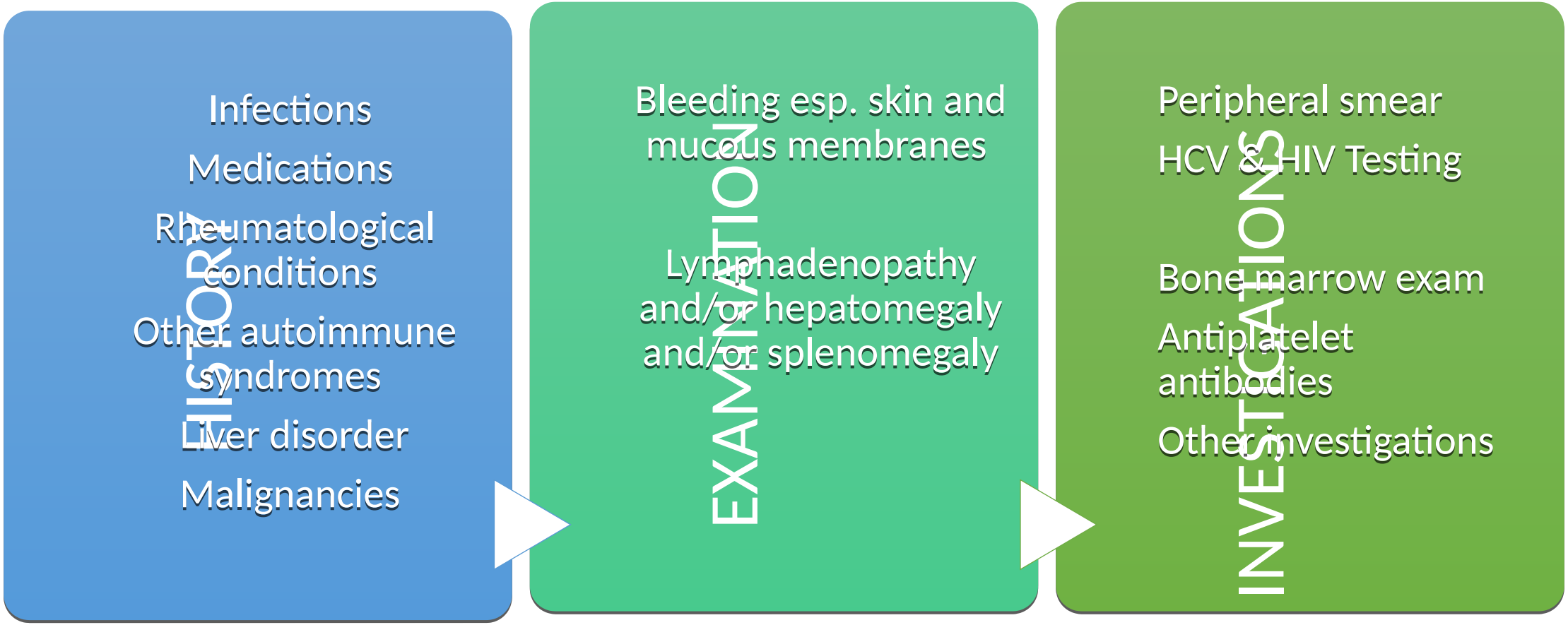
EVALUATION

A diagnosis of exclusion

Major diagnostic concerns in an adult with suspected ITP are twofold:

- Distinguishing ITP from **other causes of thrombocytopenia**, which often have a similar presentation but may require completely different management approaches
- Determining whether the ITP is **primary or secondary** to an underlying condition that might also benefit from treatment

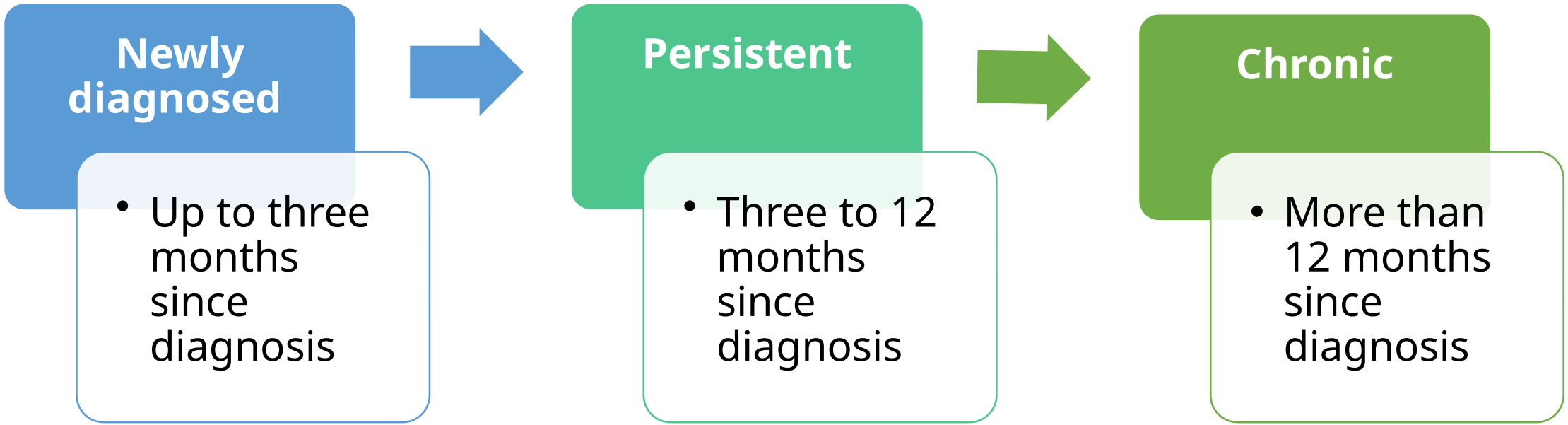
EVALUATION


HISTORY
Infections
Medications
Rheumatological conditions
Other autoimmune syndromes
Liver disorder
Malignancies
EXAMINATION
Bleeding esp. skin and mucous membranes
Lymphadenopathy and/or hepatomegaly and/or splenomegaly
INVESTIGATIONS
Peripheral smear
HCV & HIV Testing
Bone marrow exam
Antiplatelet antibodies
Other investigations

DIAGNOSIS

- Platelet count <100,000/microL without anemia or leukopenia and without another apparent cause

- **Primary** ITP
- **Secondary** ITP


Newly diagnosed
Up to three months since diagnosis
Persistent
Three to 12 months since diagnosis
Chronic
More than 12 months since diagnosis

CRITICAL BLEEDING

Critical anatomical site or hemodynamic instability or respiratory compromise.

Intracranial, intraspinal, intraocular, retroperitoneal, pericardial, or intramuscular bleeding with compartment syndrome.

SEVERE BLEEDING

A fall in hemoglobin of 2 or more g/dL or requires transfusion of 2 or more units of RBCs but does not meet the definition of critical bleeding.

MINOR BLEEDING

Bleeding that does not meet criteria for severe or critical bleeding.

MANAGEMENT

- A diagnosis of ITP does not imply that therapy is always required

- The goal of treatment is to treat or prevent significant bleeding, not to normalize the platelet count.

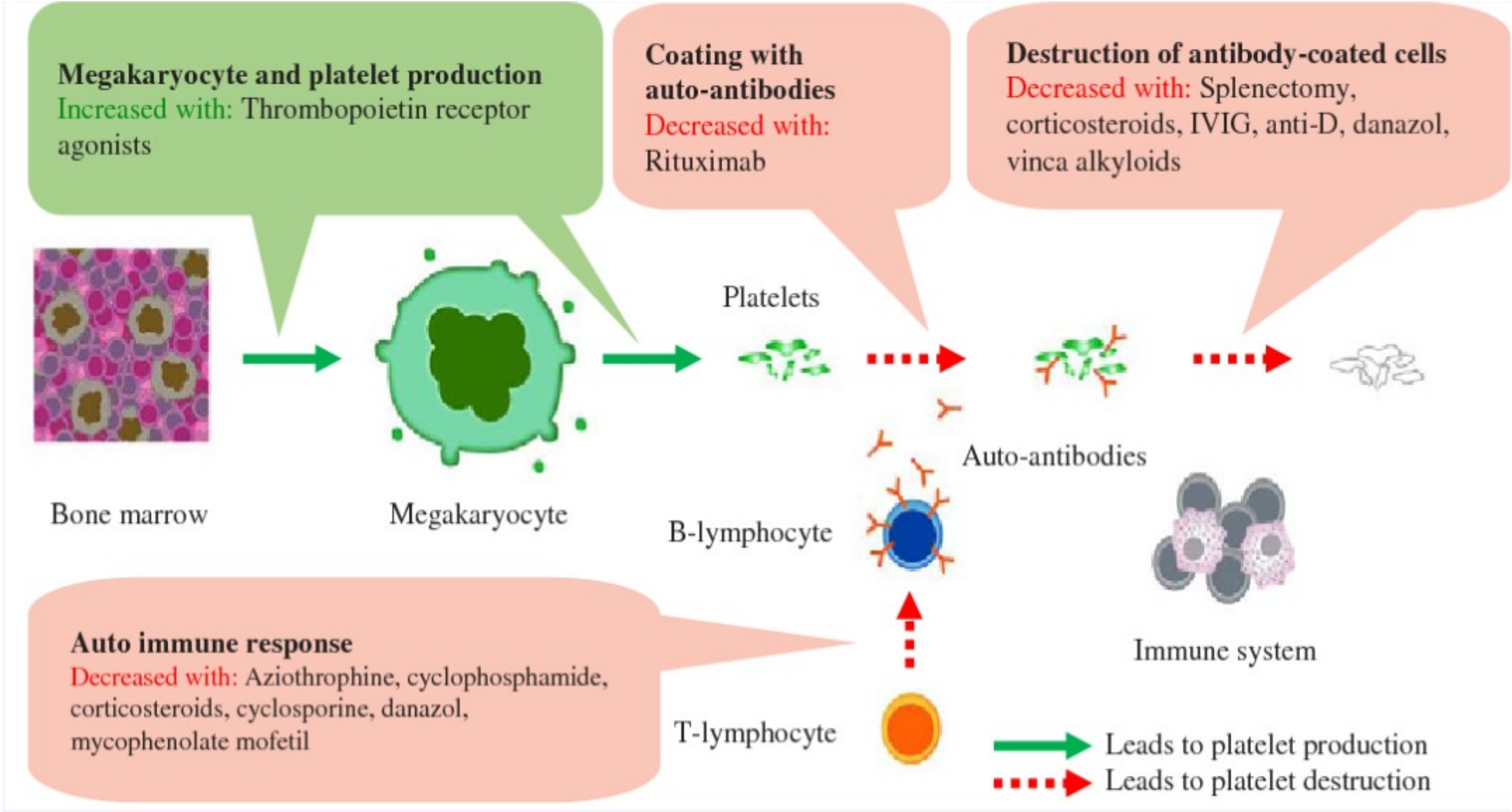
- High risk for bleeding
  - Prior bleeding
  - Platelet count <10,000/microL
  - Older age, especially >60 years

TREATMENT OPTIONS

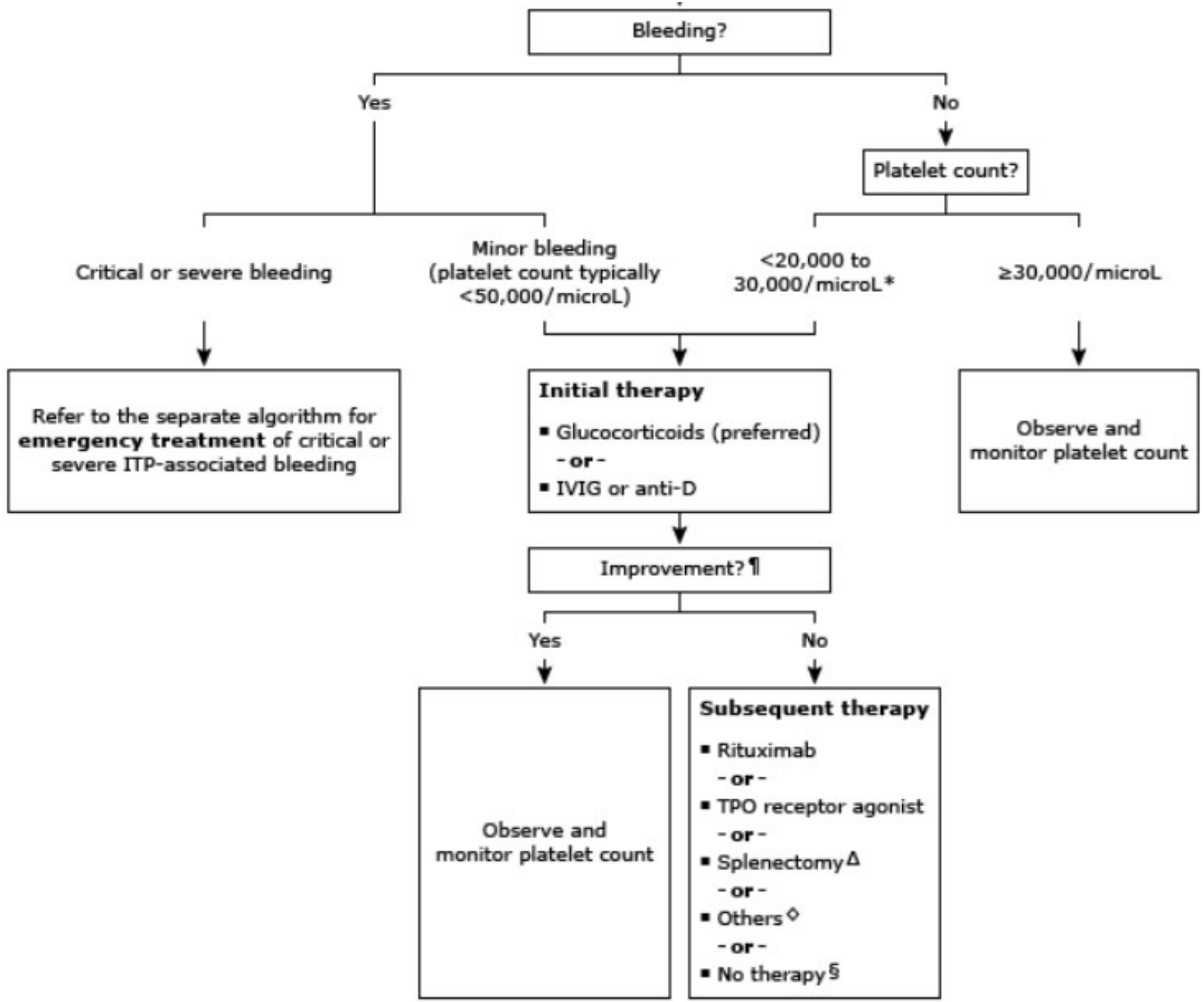
First line : Glucocorticoid, IVIG, Anti-D, Platelets

Second line : Splenectomy, Rituximab, TPO-R agonist

Additional : Fostamatinib, Danazol, Immunosuppressant agents


Megakaryocyte and platelet production
Increased with: Thrombopoietin receptor agonists
Coating with auto-antibodies
Decreased with: Rituximab
Destruction of antibody-coated cells
Decreased with: Splenectomy, corticosteroids, IVIG, anti-D, danazol, vinca alkyloids
Platelets
Bone marrow
Megakaryocyte
Auto-antibodies
B-lymphocyte
Immune system
Auto immune response
Decreased with: Aziothrophine, cyclophosphamide, corticosteroids, cyclosporine, danazol, mycophenolate mofetil
T-lymphocyte
Leads to platelet production
Leads to platelet destruction

	ADVANTAGES	DISADVANTAGES
FIRST LINE		
Glucocorticoids	Effective Oral Inexpensive	May not have durable response Long term adverse effects
IVIG	Rapid	Expensive Adverse effects Short lived action
Anti-D	Rapid	Short lived action Hemolysis Only for Rh+ patients


Bleeding?
Yes
No
Platelet count?
Critical or severe bleeding
Minor bleeding (platelet count typically <50,000/microL)
<20,000 to 30,000/microL*
≥30,000/microL
Refer to the separate algorithm for emergency treatment of critical or severe ITP-associated bleeding
Initial therapy
Glucocorticoids (preferred)
- or -
IVIG or anti-D
Observe and monitor platelet count
Improvement? ¶
Yes
No
Observe and monitor platelet count
Subsequent therapy
Rituximab
- or -
TPO receptor agonist
- or -
Splenectomy Δ
- or -
Others ◇
- or -
No therapy §

WHOM TO TREAT

Presence of bleeding

Platelet count < 30,000

WHOM TO TREAT

All individuals with critical or severe bleeding require treatment to raise the platelet count and stop the bleeding.

Some individuals with minor or no bleeding despite being thrombocytopenic may not require treatment.

Therapy to increase the platelet count is generally not used if the platelet count is >30,000/microL.

HOW TO TREAT

CRITICAL BLEEDING

Typically Plat < 20,000

- PLATELETS
- IVIG + GLUCOCORTICOIDS
- CONTRIBUTORY FACTORS
- OTHER TREATMENTS

SEVERE BLEEDING

Typically Plat < 20,000

- GLUCOCORTICOIDS
- IVIG
- CONTRIBUTORY FACTORS

MINOR BLEEDING

Typically Plat > 50,000

- CONTRIBUTORY FACTORS
- GLUCOCORTICOIDS

SEVERE THROMBOCYTOPENIA WITHOUT BLEEDING

Patients with platelet counts <30,000/microL, and especially those with counts <10,000/microL shall be treated even if they have no bleeding symptoms

Typical initial treatment involves administration of a glucocorticoid

Individuals with platelet counts ≥30,000/microL who are not bleeding are generally not treated to increase platelet count

SECOND LINE TREATMENT

For all patients with persistent ITP who have experienced clinically important bleeding despite first-line therapy with glucocorticoids

Patients with a platelet count <20,000/microL despite initial therapy, even in the absence of bleeding

SECOND LINE TREATMENT OPTIONS

Splenectomy

- Wait for 12 months
- Immunizations

Rituximab

Thrombopoietin receptor agonist (TPO-RA)

- Eltrombopag
- Romiplostim
- Avatrombopag

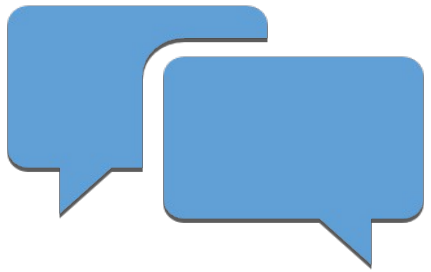
	ADVANTAGES	DISADVANTAGES
SECOND LINE		
Splenectomy	Effective Durable response	Surgical risks Infections
Rituximab	Non-surgical	Expensive Shorter remissions Reactivation of infections Adverse effects
TPO Receptor agonists	Effective Oral No immunosuppression	Expensive Continuous administration

ADDITIONAL OPTIONS

- Fostamatinib
- Danazol
- Immunosuppressive agents
- Intermittent glucocorticoids
- Combination therapy

TO SUMMARIZE…

- A diagnosis of exclusion
- May be secondary to associated condition
- Laboratory diagnosis rely on isolated thrombocytopenia and exclusion of other causes of thrombocytopenia if clinically indicated
- Decision to treat depends on presence of bleeding and platelet count
- Goal of treatment is to prevent / treat bleeding, not to normalize platelet count



Comments

Queries