IMMUNE THROMBOCYTOPENIA (ITP)

TERM DEFINITION

An acquired autoimmune disorder characterized by immune-mediated destruction of otherwise normal platelets.

CLASSIFICATION

ACCORDING TO PRESENCE / ABSENCE OF UNDERLYING DISORDER

PRIMARY
- 80% of cases
- ITP without an obvious initiating or underlying disorder

SECONDARY
- 20% of cases
- ITP associated with an underlying disorder:
  - Autoimmune disease
  - Infection
  - Malignancy
  - Medications
  - Vaccination

ACCORDING TO DURATION

NEWLY DIAGNOSED
- Within 3 months of presentation

PERSISTENT
- 3 to 12 months since diagnosis

CHRONIC
- ITP lasting > 12 months
- 75% of cases of primary ITP assume a chronic course.

ACCORDING TO SEVERITY

SEVERE ITP
- ITP with bleeding symptoms sufficient to require treatment, usually associated with platelet count < 10 x 10^9/L

CLINICAL PEARLS

Patients with ITP are at risk for mucocutaneous bleeding, including petechiae, ecchymoses, oral cavity bleeding and epistaxis.

ITP is associated with fatigue and reduced health-related quality of life.

Only 5% of patients with ITP reported to present with severe bleeding. Intracranial hemorrhage reported in 1.4% of adults.

ITP is often associated with isolated thrombocytopenia but it can occur with other changes in the CBC, especially in secondary ITP.

Clinically important to distinguish between primary ITP and congenital thrombocytopenia as treatment differs between the two conditions.

Clinically important to distinguish between primary and secondary ITP; secondary ITP requires treatment aimed at the underlying cause.

CLINICAL PRESENTATION

PRIMARY ITP
- Often asymptomatic
- May present with mucocutaneous bleeding.

SECONDARY ITP
- Often asymptomatic
- May present with mucocutaneous bleeding.
- May present with symptoms and signs associated with underlying causative condition.

LABS

Perform the following tests in all patients with suspected ITP:
- Complete blood count
- Peripheral smear
- HIV serology, regardless of risk factors*
- HCV serology*

Consider the following tests in selected patients with suspected ITP:
- Quantitative Ig (baseline IgG, IgA and IgM). Low levels may indicate CVID.
- Breath test or the stool antigen test for *H. pylori* infection if patient has abdominal symptoms or is from an endemic region.
- Bone marrow examination in those with abnormal features on physical examination, CBC or peripheral blood smear.

** Positive results used to guide antiviral treatment, which may improve platelet count*

DIAGNOSIS

There is no gold-standard laboratory test for ITP. ***ITP is a diagnosis of exclusion.*** The most compelling evidence supporting a diagnosis of ITP is a platelet response to ITP-specific therapy.

Thrombocytopenia

- **Pseudo-thrombocytopenia**
- **Real thrombocytopenia**
  - **↑ Consumption / Destruction**
    - Thrombotic microangiopathy
    - Gestational thrombocytopenia
    - Antiphospholipid syndrome
    - Medication effect
    - Infection
  - **↓ Production**
    - Bone marrow disease
    - Ethanol abuse
    - Familial thrombocytopenia
    - Medication
    - Infection
  - **Sequestration**
    - Portal hypertension
    - Hypersplenism

TREATMENT PRINCIPLES

WHEN TO TREAT

In general, treatment is started in patients with newly diagnosed ITP when/if their platelets fall below 20-30 x 10^9/L

WHERE TO TREAT

Individuals with newly diagnosed ITP and platelet counts <10 x 10^9/L are typically hospitalized.

Consider hospitalizing patients with newly diagnosed ITP and a platelet count of < 20 x 10^9/L, who are asymptomatic or have minor mucocutaneous bleeding.

HOW TO TREAT

In ***nonemergency setting***, patients with newly diagnosed ITP and bleeding should receive corticosteroids.

Emergency treatment of ITP (life-threatening bleeding or for those requiring rapid increase in platelet counts):

Management of bleeding may require platelet transfusions in combination with high doses of parenteral corticosteroids (methylprednisolone 1 g intravenously daily for 2 to 3 days) supplemented with IVIG (1 g/kg for 1 to 2 days).

In ***secondary ITP***, treat the underlying condition.

GOAL OF TREATMENT

Maintain a hemostatic platelet count while minimizing the toxicity of therapy.

MEDICATIONS

FIRST LINE

Corticosteroids are the the first-line treatment of choice. Options include one of the following:

- Prednisone 0.5-2 mg/kg/day
- Dexamethasone (40 mg/day for 4 days)

If responsive (for example, achieving platelet count > 50 x 10^9/L), prednisio(ao)ne should be tapered with the goal of discontinuing treatment by 6 weeks.

ITP is a chronic disease. ***Most adult patients (about 75%) relapse upon cessation of corticosteroid treatment.***

SECOND LINE

No optimal single second-line treatment for all patients.

3 options:
- TPO-RA (eltrombopag or romiplostim) - preferred over rituximab
- Rituximab - preferred over splenectomy
- Splenectomy (delay for > 1 year)

40%-60% reported responses to these therapies.

THIRD LINE

- Immunosuppressive agents, cyclosporine A, cyclophosphamide, mycophenolate mofetil
- Dapsone
- Danazol
- Fostamatinib

	Time to initial response	Time to peak response
Prednisone	4-14 days	7-28 days
Dexamethasone	2-14 days	4-28 days
IVIG	1-3 days	2-7 days
Rituximab	7-56 days	14-180 days
Eltrombopag	7-28 days	14-90 days

HISTORY OF MEDICINE

Before platelets were identified, the identification of ITP was based exclusively on the presence of purpura in an otherwise healthy individual.

In **1735**, Paul Gottleib Werlhof of Hanover, a poet, composer and linguist, and physician to George II of England in his German States, described the first classic case of ITP (*Morbus Maculosus Haemorrhagicus*) and the disease was thus also known as Werlhof's Disease.

In **1882**, the Italian pathologist Giulio Bizzozero of Turin demonstrated that platelets were an independent cell line with the specialized function of hemostasis.

In **1883**, Krauss in Germany called attention to the fact that platelets were diminished during the active phase of the purpura and increased when the hemorrhages ceased. Georges Hayem in Paris performed the first actual count of platelets in a patient with purpura in 1889.

NOTES

ATTRIBUTIONS
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The Blood Project
ENCYCLOPEDIA OF BLOOD