Diagnosis, Epidemiology and Patient Characteristics of Immune Thrombocytopenia

Maria L Lozano

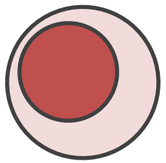
Hospital Morales Meseguer, University of Murcia, Spain

Disclosures

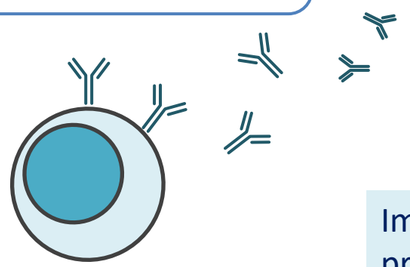
Research support/PI	Amgen; Fujimori Kogyo Co
Speaker's fees	Sobi; Grifols
Scientific advisory board	Amgen; Novartis, Argenx, Sobi, Sanofi, Grifols

ITP is driven by immune dysregulation affecting both platelet destruction and production[1–3]

Antigen-dependent
CD4+ T cell recruitment and
inflammatory cytokine production



Loss of immune tolerance

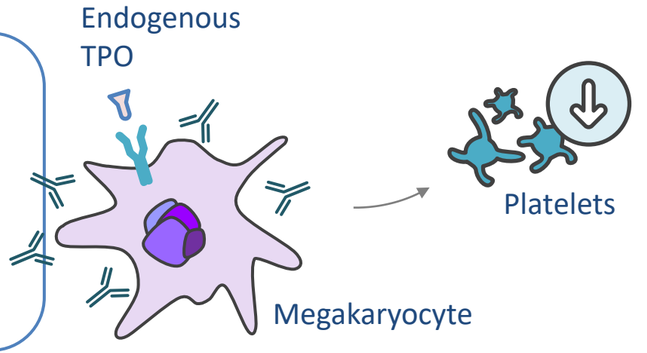


Autoantibody production
by **B-cell activation**

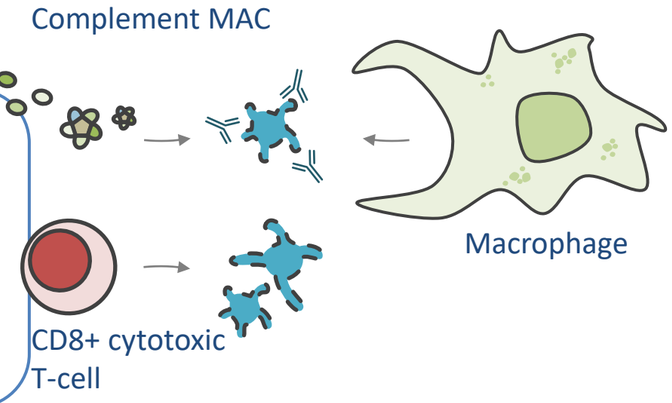
Autoantibodies
bind to platelets and megakaryocytes

Imbalanced inflammatory core with ↑ proinflammatory (Th17, Th1) and deficient regulation (↓Treg and Breg)
→supports thrombo-inflammation

Reduced platelet production by inhibition/impaired maturation of megakaryocytes



Platelet destruction by T-cells, macrophages, and complement

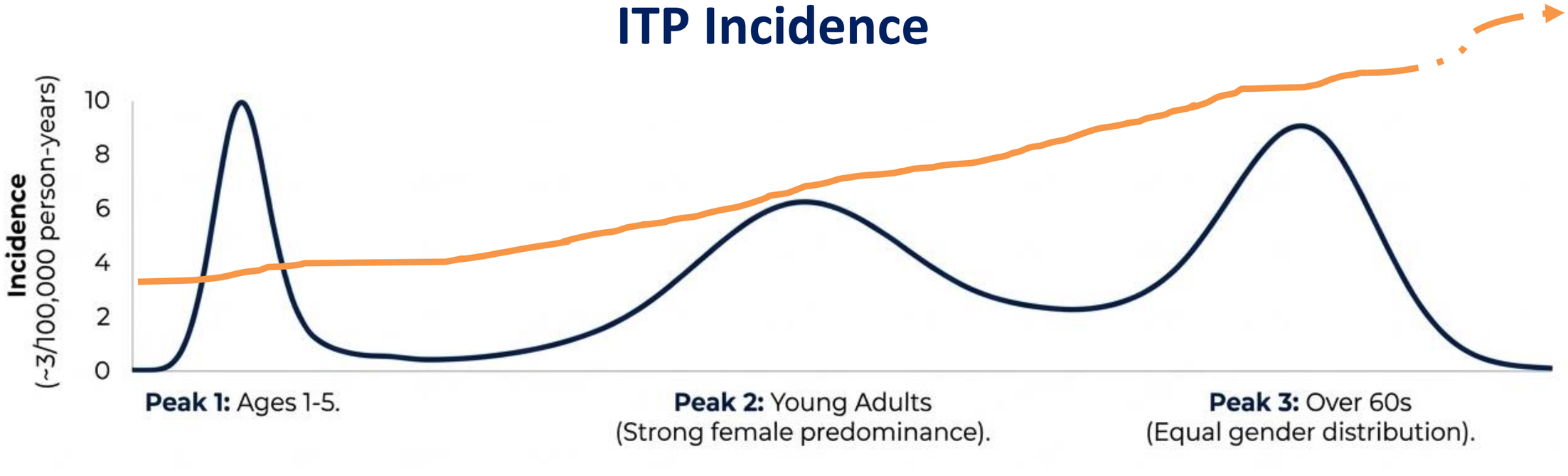


ITP is characterised by consistently low platelet counts (<100 ×10^9/L)[4,5]

CD, cluster of differentiation; ITP, immune thrombocytopenia; MAC, membrane attack complex; TPO, thrombopoietin.

1. Kistanguri & McCrae. *Hematol Oncol Clin North Am* 2013 **2.** Cooper & Ghanima. *N Engl J Med* 2019 **3.** Provan & Semple. *EBioMedicine* 2022
4. Neunert et al. *Blood Adv* 2019 **5.** Matzdorff et al. *Oncol Res Treat* 2023;suppl.

ITP Incidence

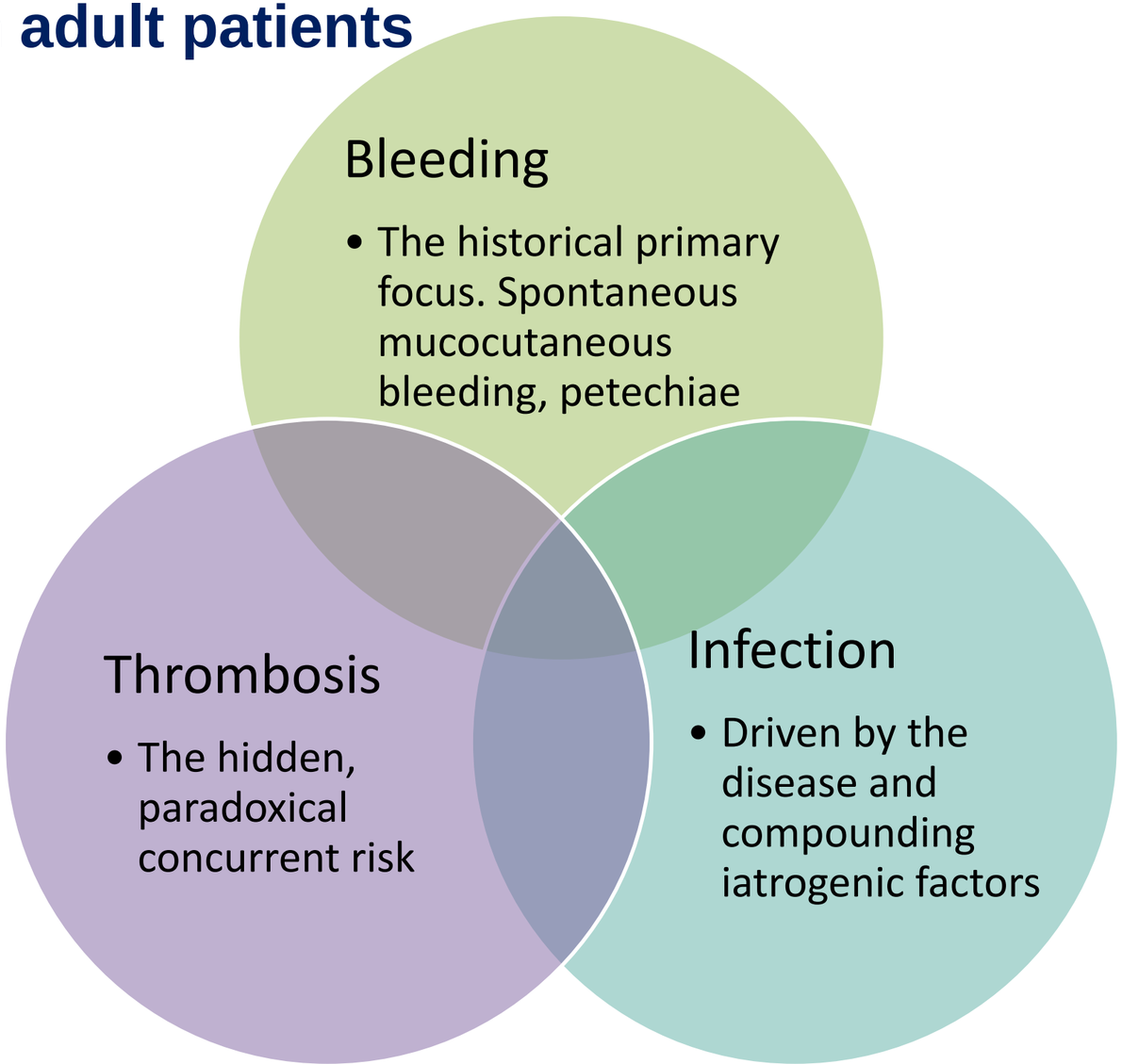


Different disease trajectories	
Pediatric	**Adult**
Onset: Acute, often post-viral	**Onset:** Insidious, autoimmune
Spontaneous Remission: High, >60% within months	**Spontaneous Remission:** Low
Chronicity Rate: ≈35.7%	**Chronicity Rate:** 60-66.7%
Comorbidities: Rare	**Impact:** Severe fatigue, frequent compounding comorbidities

The overall **prevalence** is significantly higher in adults (up to 23.6 per 100,000) than in children (4.6 per 100,000) due to the high rate of chronification in older populations

Schoonen WM, et al. Br J Haematol 2009; 145: 235-244; Yong M, et al. Br J Haematol 2010; 149: 855-864; Feudjo-Tepie M.A., et al. Blood 2007; 110: 3202

The visible burden in ITP extends far beyond haemorrhage. Infection and thrombosis are as frequent as severe bleeding and represent the primary causes of mortality in adult patients



Moulis G, et al. Rev Med Interne. 2021;42:11-15

Bleeding

Magnitude: 70% rate of bleeding at initial diagnosis (predominantly mucocutaneous)

Clinical context: Severe bleeding (hematuria, gastrointestinal) is rare (6%); intracraneal haemorrhage is exceptionally rare: <1% per year

Predisposing factors:

-Platelet counts < $10x10^9$/l

-Medications: Anticoagulants, NSAIDs, SRIs

-Patient demographics and comorbidities: Age > 60 yrs, hypertension, peptic ulcer, history of major bleeding

Infection

Magnitude: ≈15% 1-year hospital consultation risk for chronic patients (dominated by lung infections)

Clinical context: Dominated by lung infections (35%-45%)

Predisposing factors:

-Age >60 years

-Male sex

-Chronic lung disease as well as chronic kidney disease

-Exposure to corticosteroids (prednisone equivalent > 5 mg/day) and to rituximab

Thrombosis

Magnitude: Incidence of arterial thrombosis of 1.5/100 patient-years, and 0.7/100 patient-years for venous thrombosis

Clinical context: Mortality rates (1-year and 5-year) after a venous or an arterial thrombosis are similar to mortality rates after a hospital contact for bleeding

Predisposing factors:

-Cardiovascular risk factors

-Antiphospholipid antibodies

-Splenectomy

-Corticosteroids

-Intravenous immunoglobulin

-Thrombopoietin receptor agonists

Moulis G, et al. Rev Med Interne. 2021;42:11-15; Cooper N, et al. Am J Hematol 2021;96:188-198; Garabet L, et al. Br J Haematol. 2026 Apr 9. doi: 10.1111/bjh.70474. Epub ahead of print.

Infection

Magnitude: ≈15% 1-year hospital consultation risk for chronic patients

Clinical context: Dominated by lung infections (35%-45%)

Predisposing factors:

-Age >60 years

-Male sex

-Chronic lung disease as well as chronic kidney disease

-Exposure to corticosteroids (prednisone equivalent > 5 mg/day) and to rituximab

Moulis G, et al. Rev Med Interne. 2021;42:11-15; Cooper N, et al. Am J Hematol 2021;96:188-198; Garabet L, et al. Br J Haematol. 2026 Apr 9. doi: 10.1111/bjh.70474. Epub ahead of print.

Bleeding

Magnitude: 70% rate of bleeding at initial diagnosis (predominantly mucocutaneous)

Clinical context: Severe bleeding (hematuria, gastrointestinal) is rare (6%); intracraneal haemorrhage is exceptionally rare: <1% per year

Predisposing factors:

-Platelet counts < 10x109/l

-Medications: Anticoagulants, NSAIDs, SRIs

-Patient demographics and comorbidities: Age > 60 yrs, hypertension, peptic ulcer, history of major bleeding

Infection

Magnitude: ≈15% 1-year hospital consultation risk for chronic patients (dominated by lung infections)

Clinical context: Dominated by lung infections (35%-45%)

Predisposing factors:

-Age >60 years

-Male sex

-Chronic lung disease as well as chronic kidney disease

-Exposure to corticosteroids (prednisone equivalent > 5 mg/day) and to rituximab

Thrombosis

Magnitude: Incidence of arterial thrombosis of 1.5/100 patient-years, and 0.7/100 patient-years for venous thrombosis

Clinical context: Mortality rates (1-year and 5-year) after a venous or an arterial thrombosis are similar to mortality rates after a hospital contact for bleeding

Predisposing factors:

-Cardiovascular risk factors

-Antiphospholipid antibodies

-Splenectomy

-Corticosteroids

-Intravenous immunoglobulin

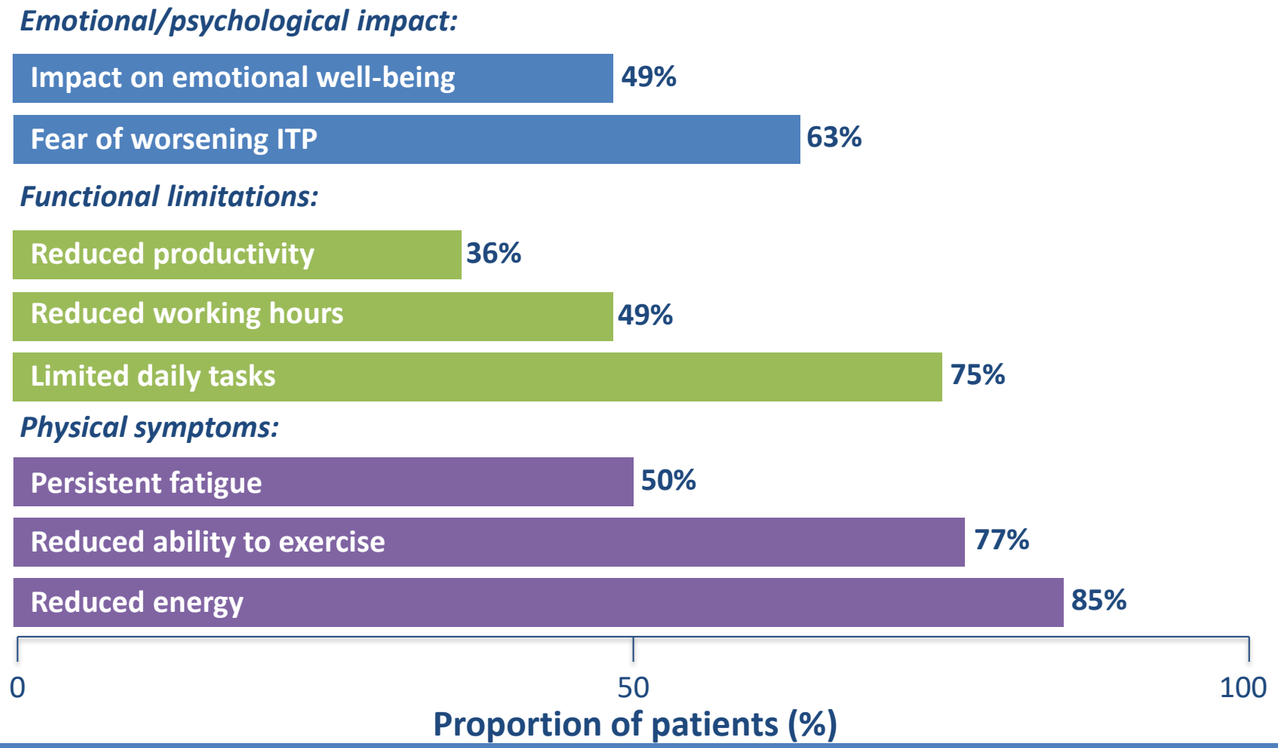
-Thrombopoietin receptor agonists

Moulis G, et al. Rev Med Interne. 2021;42:11-15; Cooper N, et al. Am J Hematol 2021;96:188-198; Garabet L, et al. Br J Haematol. 2026 Apr 9. doi: 10.1111/bjh.70474. Epub ahead of print.

The invisible burden: ITP has a substantial impact on patients' daily activities and emotional well-being[1]

The global ITP World Impact Survey (**I-WISh**) study assessed the **impact of ITP on HRQoL** and productivity from **patient and physician perspectives**[1]

Patient perspectives (n=1,507)



Physician perspectives (n=472)

reported that ITP symptoms **reduced patient HRQoL**

reported that ITP-related fatigue **substantially reduced HRQoL**

PROs capture **dimensions of disease impact** that may be **underestimated by platelet counts or bleeding scores**[1,2]

HRQoL, health-related quality of life; ITP, immune thrombocytopenia; PRO, patient-reported outcome.

1. Cooper et al. *Am J Haematol* 2021a **2.** Cooper et al. *Am J Haematol* 2021b.

ITP as a syndromic syndrome: Increased susceptibility for autoimmune diseases, malignancies, immunodeficiencies, and other systemic diseases

2.09% of Patients with Primary ITP develop systemic Lupus Erythematosus (SLE)

- Female patients **(RR 4.29)** and those presenting with positive ANA titers **(RR 26.29)** constitute the highest risk cohort
- Other Autoimmune diseases
  - Frequent co-occurrence of Hashimoto´s and Grave´s diseases
  - Shared pathophysiology: Antiphospholipid Syndrome and Evans syndrome

6.60x HR Leukemia; **9.73xHR** Lymphoma

- The highest risk for leukemia is observed in the 1st year following ITP diagnosis, but risk persists long-term.
- Elevated risk spans accross both Hodgkin´s and non-Hodgkin´s variants

Systemic Organ Comorbidities (Metabolic & Renal)

- Diabetes **(RR 1.73)** (a 73% increased incidence compared to the general population)
- Renal failure **(RR 2.05)** (more than double the risk compared to non-ITP cohorts)

Association with Immunodeficiencies

- Strong association with Common Variable Immunodeficiency (CVID)
- Suggests that ITP is often an early clinical manifestation of broader aberrant immune surveillance

Enger C, et al. Int J Hematol. 2010;92:289-95; Schifferli A, et al. Front Med (Lausanne). 2021;8:613192; Pamuk ON, et al. Autoimmun Rev. 2023;22:103297; Mannering N, et al. Haematologica. 2025;110:2764-2773

ITP continues to be a Diagnosis of Exclusion in a Patient with Platelet Counts < $100x10^9$/L. No single confirmatory test exist

Mandatory Workup

- Detailed Patient History
- Complete Blood Count (CBC) with reticulocytes
- Peripheral blood smear
- Immunoglobulin levels (IgG, IgA, IgM)
- Viral serology (HIV, HBV, HCV)

Contextual Utility

- *H. pylori* screening (especially in endemic regions or symptomatic patients)
- Anti-glycoprotein antibody assays (high specificity, low sensitivity; useful for "ruling in" but not ruling out)
- Bone marrow examination (Suspicion of additional disease, or refractoriness to treatments.)
- Genetic evaluation of inherited thrombocytopenia or primary immunodeficiencies (11% of patients diagnosed with Chronic ITP carry a pathogenic (or likely pathogenic) variant primarily linked to underlying platelet disorders, or primary immunodeficiencies)
- Pregnancy test (females of childbearing age)
- Antinuclear antibodies (ANA) and direct antiglobulin test (autoimmune diseases; Evans syndrome)
- Antithyroid antibodies, thyroid function (frequent co-occurrence of thyroid disease)
- Antiphospholipid antibodies (assess thrombotic predisposition)
- PCR for parvovirus, EBV, or CMV (rule out viral disease)

Not Recommended

- Platelet-associated total IgG (PAIgG)
- Serum complement
- Bleeding time

Provan D, et al. Blood Adv. 2019;3:3780-3817; Gafter-Gvili A. Eur J Intern Med. 2023;108:18-24; Matzdorff A, et al. Oncol Res Treat. 2023;46 Suppl 2:5-44; Martínez-Carballeira D, et al. Hematol Rep. 2024;16:204-219

The Challenge of Misdiagnosis in ITP

McMaster Registry

15.1% of patients initially diagnosed with primary ITP are subsequently reclassified

- Primary ITP → another diagnosis: **12.2%**
- Other thrombocytopenias → primary ITP: **3.1%**

Challenging cases of adults with thrombocytopenia (70.8% changes in diagnosis)

- **38.5%** of presumed primary ITP became secondary ITP.
- **34.6%** of presumed primary ITP became non-ITP thrombocytopenia.
- **35%** of presumed non-ITP cases were eventually classified as primary ITP.
- More than half of patients with an initially unknown diagnosis were finally classified as primary ITP.

Most frequent alternative diagnoses

- Myelodysplastic syndromes
- Inherited thrombocytopenias
- Liver disease/hypersplenism
- Pseudothrombocytopenia
- Drug-induced thrombocytopenia
- Pregnancy-related thrombocytopenia
- Autoimmune diseases (APS, Evans syndrome)
- Chronic infections (particularly HCV)

Arnold DM, et al. Blood Adv. 2017;1:2414-2420; Gabe C, et al. TH Open. 2023;7:e105-e109

The unfulfilled Promise of Additional Tests: No reliable biomarkers have been validated for routine clinical practice

Proteomics

- Haptoglobin isoforms, HSPA6, ITGB3, YWHAH
- Purely experimental; lacks robust standardisation and diverse cohort validation

Genetics & Epigenetics

- Functional SNPs, DNA methylation patterns
- Association remain correlative; fundamentally lacking translational proof for diagnostic application

miRNAs

- Regulators of immune dysregulation and megakaryocytic failure
- Potential role in ITP pathogenesis; not yet validated as reliable diagnostic or prognostic biomarkers

Platelet indices

- Immature platelet fraction (IPF), Thrombopoietin (TPO) levels
- High diagnostic overlap; unable to distinguish between destructive vs. hypoproductive thrombocytopenia in individual patients

Liu Z,et al. Br J Haematol. 2026,. doi: 10.1111/bjh.70485. Epub ahead of print; Zhou X, et al. Mol Biol Rep. 2025;52:257; Patidar P, et al. Thromb J. 2026;24:25; Boura-Theodorou A, et al. Proteomes. 2026;14:12

Refraiming ITP as a Complex Immune Syndrome

Understanding the disease

- ITP is not a single disorder
- Heterogeneous immune mechanism
- Dynamic evolution over time
- Distinct endotypes likely exist

What matters to patients

- The burden extends beyond platelet counts
- Bleeding remains important, but is only one component
- Infection, thrombosis, fatigue and treatment toxicity drive morbidity
- Systemic comorbidities and immune dysregulation influence long-term outcomes

Implications

- Diagnosis of exclusion: better diagnostic tools and biomarkers are needed
- Treatment success should go beyond increasing platelet counts, and towards restoration of homeostasis
- Need for therapies to target specific underlying immune defects and help minimize cumulative toxicity