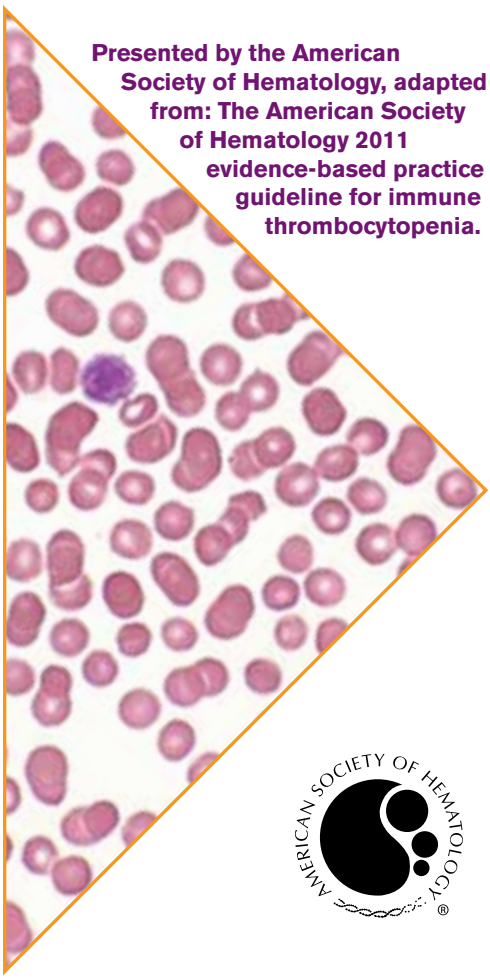
QUICK REFERENCE

2011 Clinical Practice Guideline on the Evaluation and Management of Immune Thrombocytopenia (ITP)



Presented by the American Society of Hematology, adapted from: The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia.

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DIAGNOSIS of ITP

1. Necessary Evaluation

- **History:** Isolated bleeding symptoms consistent with thrombocytopenia without constitutional symptoms (e.g. significant weight loss, bone pain, night sweats).
- **Physical examination:** Bleeding symptoms in the absence of hepatosplenomegaly, lymphadenopathy, or stigmata of congenital conditions.
- **Complete blood count:** Isolated thrombocytopenia (platelet count <100 x 10^9/L). Anemia only if due to significant bleeding—otherwise normal red cell indices, white blood cell count and differential.
- **Peripheral blood smear:** Identified platelets should be normal to large in size. Red and white blood cell morphology should be normal.

2. Bone Marrow Evaluation

- Bone marrow examination is unnecessary in patients with the typical features of ITP outlined above, irrespective of the age of the patient.
- Bone marrow examination is felt to be unnecessary in children with typical ITP prior to initiation of treatment with corticosteroids, prior to splenectomy, or in patients who fail intravenous immunoglobulin (IVIg) therapy.
- The presence of abnormalities in the history, physical examination, or the complete blood count and peripheral blood smear should be further investigated, e.g. with a bone marrow examination or other appropriate investigations, before the diagnosis of ITP is made.

3. Additional Evaluations

- All adult patients with newly diagnosed ITP should undergo testing for HIV and HCV.
- There is insufficient evidence to support the routine use of anti-platelet, antiphospholipid, and anti-nuclear antibodies, thrombopoietin levels, or platelet parameters obtained on automated analyzers in the evaluation of patients with suspected ITP.

MANAGEMENT of ITP

The goal of all treatment strategies for ITP is to achieve a platelet count that is associated with adequate hemostasis, rather than a normal platelet count. The decision to treat should involve a discussion with the patient and consideration of the severity of bleeding, anticipated surgical procedures, medication side effects, and health-related quality of life.

I. Initial Management of ITP

1. Assessment of Disease Status:

- What bleeding is the patient experiencing?
  - Determine the timing, location, and severity of bleeding symptoms.
  - Does this patient have any additional risk factors for bleeding such as use of antithrombotic agents or high-risk occupation?
- Is a surgical procedure anticipated?
- Is this patient likely to comply with recommended treatments?
- Is the bleeding experienced by this patient interfering with his or her daily activities or causing significant anxiety?

2. General Considerations for Initial Management:

- The majority of patients with no bleeding or mild bleeding (defined here as skin manifestations only, such as petechiae and bruising) can be treated with observation alone regardless of platelet count.
- First-line treatment includes observation, corticosteroids, IVIg, or anti-D immunoglobulin (anti-D).
- Anti-D should be used with caution given recent FDA warnings of severe hemolysis. It is therefore not advised in patients with bleeding causing a decline in hemoglobin, or those with evidence of autoimmune hemolysis.

3. Special Considerations for Adults and Children:

Adults:

- Consider treatment for patients with a platelet count < 30 x 10^9/L.
- Longer courses of corticosteroids are preferred over shorter courses of corticosteroids or IVIg.
- IVIg may be used in conjunction with corticosteroids if a more rapid increase in platelet count is required.
- Either IVIg (1g/kg for one dose, repeated as necessary) or anti-D (in appropriate patients) may be used as a first-line treatment if corticosteroids are contraindicated.

Children:

- A single dose of IVIg (0.8-1.0 g/kg) or a short course of corticosteroids should be used as first-line treatment.
- IVIg should be used instead of corticosteroids if a more rapid increase in platelet count is required.
- There is no evidence to support using corticosteroids for longer courses compared to very brief courses.
- Anti-D may be considered for first-line therapy in Rh+ non-splenectomized children with recognition of the risks outlined above.

II. Subsequent Management of ITP

1. Assessment of Disease Status:

- What bleeding is the patient experiencing? Determine the timing, location, and severity of bleeding symptoms.
- Does this patient have a change in history or physical examination that requires evaluation for another diagnosis that could be causing thrombocytopenia?
- Does this patient have any contraindications to splenectomy?
- How is the diagnosis of ITP affecting the patient's ability to work, go to school, or participate in activities?
- Does the patient respond intermittently to his or her current drug therapy?
- Is the patient experiencing side effects from chronic medication use?
- How is the patient coping psychologically with having a low platelet count?

2. General Considerations for Subsequent Management:

- Adults who have a platelet count > 30 x 10^9/L and are asymptomatic following splenectomy do not require further therapy.
- In children, splenectomy or other interventions with potentially serious complications should be delayed for at least 12 months, unless warranted by severe disease unresponsive to other measures or due to quality of life considerations.
- If previous treatment with corticosteroids, IVIg, or anti-D has been successful, these options may be used as needed to prevent bleeding.
- If previous treatment with corticosteroids, IVIg, or anti-D has been unsuccessful, subsequent treatment may include splenectomy, rituximab, thrombopoietin receptor agonists, or more potent immunosuppression.

3. Special Considerations for Children and Adults:*

	Children	Adults
Splenectomy	Recommended for children with significant or persistent bleeding and lack of response or intolerance of other therapies such as corticosteroids, IVIg, and anti-D, and/or who have a need for improved quality of life.	Recommended for adults who have failed corticosteroid therapy, with similar efficacy with open or laparoscopic procedures.
Rituximab	May be considered for children with ITP who have significant ongoing bleeding and/or have a need for improved quality of life despite conventional treatment. Also may be considered as an alternative to splenectomy in children with chronic ITP or as therapy in those who have failed splenectomy.	May be considered for adults at risk of bleeding who have failed one line of therapy such as corticosteroids, IVIg, or splenectomy.
Thrombopoietin Receptor Agonists	Studies are ongoing, but there are no published data to guide the use of these agents in children.	Recommended for adults at risk of bleeding who relapse after splenectomy or who have a contraindication to splenectomy and who have failed at least one other therapy. These agents may also be considered for adults at risk of bleeding who have failed one line of therapy such as corticosteroids or IVIg and who have not undergone splenectomy.
High-Dose Dexamethasone	May be considered for children or adolescents with ITP who have significant ongoing bleeding and/or have a need for improved quality of life despite conventional treatment. Also may be considered as an alternative to splenectomy in children with chronic ITP or in those who have failed splenectomy.	No comment in current guidelines.
Immunosuppression	Multiple agents have been reported; however data for any one specific agent remain insufficient for specific recommendations.	Multiple agents have been reported; however data for any one specific agent remain insufficient for specific recommendations.

*Of the pharmacologic options listed above, the thrombopoietin receptor agonists have FDA approval in adults with chronic ITP who have an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Dexamethasone has FDA approval for treatment of ITP in adults. All other therapies are considered off-label use.

Further CONSIDERATIONS

1. Special Considerations for Secondary ITP:

Secondary ITP (HIV- associated):

- Treatment of the underlying HIV infection with antiviral therapy should be considered prior to other treatment options unless the patient has clinically significant bleeding.
- IVIg, corticosteroids, or anti-D may be used initially for patients requiring further therapy.
- Splenectomy is considered preferable to other agents in symptomatic patients who have failed initial drug therapy.

Secondary ITP (HCV- associated):

- Antiviral therapy should be considered in the absence of contraindications, but the platelet count should be closely monitored in these situations due to a risk of worsening thrombocytopenia attributable to interferon.
- If treatment is required, the initial management should be with IVIg.

Secondary ITP (*H. pylori*- associated):

- Routine testing for *H.pylori* is not recommended in asymptomatic children with unresolved ITP.
- Screening for *H.pylori* should be considered in adults for whom eradication therapy would be undertaken if testing were positive.
- Eradication therapy for *H.pylori* should be administered to patients who are found to have infection.

2. MMR-related ITP:

- Children with a history of ITP who are not immunized should receive their scheduled first MMR vaccine.
- In children with either non-vaccine or vaccine-related ITP who have already received their first dose of MMR vaccine, vaccine titers can be checked. If the child displays full immunity, no further MMR vaccine should be given. If the child does not have adequate immunity, then the child should be re-immunized at the recommended age.

3. ITP in Pregnancy:

- Pregnant patients requiring treatment should receive either corticosteroids or IVIg.
- For pregnant women with ITP, the mode of delivery should be based on obstetric indications.

This document summarizes the recommendations from: Neunert C, Lim W, Crowther M, Cohen A, Solberg L, and Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190-4207.

The American Society of Hematology (ASH) published a landmark paper in 1996 designed to assist clinicians in the management of Immune Thrombocytopenia (ITP). Since then, there have been numerous advances in the management of ITP mandating an update to the published guidelines. The guideline update uses an evidence-based approach, interpretation, and presentation of the available evidence and provides treatment recommendations using the GRADE system.

Use of the terminology "Immune Thrombocytopenia" in the title of the quick reference guide as well as the guideline is referenced in the 2011 ITP Guideline publication as follows: "The disease and its most widely accepted abbreviation, ITP, has variably been defined as 'immune thrombocytopenic purpura,' 'idiopathic thrombocytopenic purpura' and most recently, 'immune thrombocytopenia.'"

Background Image: Peripheral smear in a patient with ITP showing an almost total absence of platelets. A large, young platelet is seen in the center of the smear. From the ASH Image Bank, courtesy of John Lazarchick, MD.

Guidelines provide the practitioner with clear principles and strategies for quality patient care and do not establish a fixed set of rules that preempt physician judgment.

For further information, please see the complete guidelines located at *www.hematology.org/practiceguidelines*. You may also contact the ASH Government Relations & Practice Department at (202)776-0544.

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