HEMATO-ONCOLOGY

DEPARTMENT

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American Society of Hematology

Clinical guideline update on "Immune thrombocytopenia: an evidence based practice guideline developed by the American Society of Hematology"

Cindy Neunert, Wendy Lim, Mark Crowther, Alan Cohen, Lawrence Solberg, Jr. and Mark Crowther

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PRACTICE GUIDELINE

BASED ON EVIDENCE

GRADE SYSTEM

- The GRADE system provides a score for a recommendation of **1A, 1B, 1C, 2A, 2B or 2C**.
- The numerical value indicates the strength of the recommendation
  - 1 indicating a high degree of confidence that the desirable outcomes of an intervention exceed the undesirable effects (or vice versa) in most patient populations.
  - 2 indicates a lower degree of confidence that the desirable outcomes outweigh undesirable outcomes (or vice versa) evidence.

GRADE SYSTEM

- A score of "**A**" suggests the recommendation is supported by consistent evidence from *randomized controlled trials (RCTs) or exceptionally strong observational studies*.
- A score of "**B**" suggests the recommendation is supported by *RCTs with important limitations* or *strong evidence from observational studies*
- A score of "**C**" indicates evidence derived from *RCTs with serious flaws, weaker observational studies or indirect evidence*.

1. DEFINITION

- The International Working Group (IWG) also defines ITP as
  - Newly diagnosed (diagnosis to 3 months),
  - Persistent (3 to 12 months from diagnosis)
  - Chronic (lasting for more than 12 months)
- The IWG proposed
  - Complete response (CR) is defined as a platelet count $\geq$ 100 x 109/L
  - Response (R) is defined as a *platelet count* $\geq$*30* but <100 x 109/L and *a doubling from baseline*.

1. DEFINITION

- Corticosteroid dependence is defined as the *need for ongoing or repeated administration of corticosteroids* to maintain a platelet count in excess of 30 x 109/L and/or to avoid bleeding.

2. DIAGNOSIS OF ITP

- We recommend:
  - Bone marrow examination is unnecessary in children and adolescents with the typical features of ITP (Grade 1B).
  - Bone marrow examination is *not necessary in children who fail IVIg therapy* (Grade 1B).

2. DIAGNOSIS OF ITP

- We suggest:
  - Bone marrow examination is also not necessary in similar patients prior to initiation of treatment with corticosteroids or prior to splenectomy (Grade 2C).
  - Testing for ANA is not necessary in the evaluation of children and adolescents with suspected ITP (Grade 2C)

3.INITIAL MANAGEMENT OF ITP

We recommend:

- Children with **no bleeding or mild bleeding** (defined as skin manifestations, such as bruising and petechiae only) be managed with **observation** alone regardless of platelet count (Grade 1B).

3.INITIAL MANAGEMENT OF ITP

Table 8. Grade of severity and management of patients with ITP

Bleeding/quality of life	Management approach
Grade 1. Minor bleeding, few petechiae (≤ 100 total) and/or ≤ 5 small bruises (≤ 3-cm diameter); no mucosal bleeding	Consent for observation
Grade 2. Mild bleeding, many petechiae (> 100 total) and/or > 5 large bruises (> 3-cm diameter); no mucosal bleeding	Consent for observation or for treatment in selected children
Grade 3. Moderate bleeding, overt mucosal bleeding, troublesome lifestyle	Intervention to reach grade 1/2 in selected children
Grade 4. Mucosal bleeding or suspected internal hemorrhage	Intervention

Modified from Buchanan and Adix[181]; Bolton-Maggs and Moon[174]; Imbach et al.[171]

Initial pharmacological management of pediatric ITP

- We recommend:
  - A single dose of IVIg (0.8 to 1 g/kg) or a short course of corticosteroids be used as first line treatment (Grade 1B).
  - IVIg can be used if a more rapid increase in the platelet count is desired (Grade1B).
  - Anti-D therapy is not advised in children with a hemoglobin concentration that is decreased
- **We suggest:** A single dose of anti-D can be used as first line treatment in Rh+, nonsplenectomized children requiring treatment (Grade 2B).

5.Children who are treatment non-responders

Appropriate "second line" treatments for pediatric ITP

- We suggest:
  - Rituximab be **considered** for ITP who have significant ongoing bleeding despite treatment with IVIg, anti-D or conventional doses of corticosteroids (Grade 2C).
  - Rituximab may also be **considered as an alternative to splenectomy** with **chronic ITP *or*** in patients who **do not respond favorably to splenectomy** (Grade 2C).

5.Children who are treatment non-responders

- High-dose dexamethasone may be considered for children or adolescents with ITP who have significant ongoing bleeding despite treatment with IVIg, anti-D or conventional doses of corticosteroids. (Grade 2C)
- High-dose dexamethasone may also be considered as an **alternative to splenectomy** in chronic ITP or in patients who do not respond favorably to splenectomy (Grade 2C).

5.Children who are treatment non-responders

Splenectomy for persistent or chronic ITP or ITP unresponsive to initial measures

- We recommend:
  - Splenectomy for chronic or persistent ITP with significant or persistent bleeding, AND lack of responsiveness or intolerance of other therapies such as corticosteroids, IVIg and anti-D and/or who have a need for improved quality of life (Grade 1B).

- We suggest:
  - Splenectomy or other interventions with potentially serious complications be delayed for at least 12 months, unless accompanied by severe disease defined by the IWG as unresponsive to other measures or other quality of life considerations (Grade 2C)

H pylori testing in children with persistent or chronic ITP

- We recommend: Against routine testing for H. pylori in children with chronic ITP (Grade 1B).

6.Management of MMR- associated ITP

- We recommend:
  - Children with a history of ITP who are unimmunized receive their scheduled first MMR vaccine (Grade 1B).
  - 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.
    - full immunity (90-95% of children): no further MMR vaccine.
    - unadequate immunity: re-immunized with MMR vaccine at the recommended age (Grade 1B).

6.Management of MMR-associated ITP

- The incidence of MMR vaccine – associated ITP to be 0.87 to 4 /100,000
- The incidence of ITP following natural measles or rubella infection ranges from 6 to 1200/ 100,000 cases.

→ the risk of developing ITP is higher following natural infection with these viruses, justifying vaccination

FOR YOUR ATTENTION