THE AMERICAN SOCIETY OF HEMATOLOGY 2011 EVIDENCE-BASED PRACTICE GUIDELINE FOR IMMUNE THROMBOCYTOPENIA


SSH Beirut, September 10, 2011
Methodology

Development of a background consisting of recommendations on Nomenclature, diagnosis, and response criteria

Creation of focused clinical questions that form the basis for the Systematic literature review

Establishment of evidence tables and the development of recommendations using the GRADE methodology
Introduction

- Immune thrombocytopenia (ITP) is characterized by isolated thrombocytopenia in the absence of identifiable and specific precipitants.

- The ASH published a comprehensive guideline about the management of this disorder in 1996.

- Given the recent advances in the definition and management of ITP, an update of these guidelines is required.
Introduction

- In this paper, the authors performed a comprehensive literature review and presented the evidence using the GRADE system.

- Recommendations are provided for primary and selected secondary forms of ITP.

- A lack of good quality evidence was noted in the following areas: management of bleeding, second-line therapies in children and adults, timing of splenectomy, and platelet threshold at which interventions should be initiated.
Nomenclature and Diagnosis

- ITP is an **autoimmune** disorder characterized by the immunologic destruction of otherwise normal platelets.

- Can occur in isolation (**primary**) or in association with other disorders (**secondary**).
## Nomenclature and Diagnosis

<table>
<thead>
<tr>
<th>Table 2. Causes of secondary ITP</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Antiphospholipid syndrome</td>
</tr>
<tr>
<td>• Autoimmune thrombocytopenia (eg, Evans syndrome)</td>
</tr>
<tr>
<td>• Common variable immune deficiency</td>
</tr>
<tr>
<td>• Drug administration side effect</td>
</tr>
<tr>
<td>• Infection with cytomegalovirus, <em>Helicobacter pylori</em>, hepatitis C, human immunodeficiency virus, varicella zoster</td>
</tr>
<tr>
<td>• Lymphoproliferative disorders</td>
</tr>
<tr>
<td>• Bone marrow transplantation side effect</td>
</tr>
<tr>
<td>• Vaccination side effect</td>
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<tr>
<td>• Systemic lupus erythematosus</td>
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</tbody>
</table>

Evans syndrome is associated with autoimmune thrombocytopenia with coincident hemolytic anemia.
Immune Thrombocytopenia

- Autoantibody to platelets, initially a “a plasma factor” documented by Harrigton
- Increased platelet turnover
- Increased platelet production
ITP in Childhood

Key Features

- Same frequency for males and females
- Common from 1-9 years of age
- Peak age 2-5 years
- Seasonal winter and fall > spring > summer
- Rapid and sudden onset of bruises/ petechiae
- Immune trigger: “primed” by infection, bites (insect), drug allergies, immunizations
Pathogenesis of Epitope Spread in Immune Thrombocytopenic Purpura
<p>| Common Laboratory Tests obtained in the Thrombocytopenic Patient at Presentation |
|---|---|
| Complete Blood Count and Differential Review Smear | Rule Out: Multi-lineage Involvement Leukemia or Aplastic/ Myelodysplasia Evaluate Platelet Size (giant or ‘dust-like’) |
| Reticulocyte Count | Hemolytic Disease or Chronic Blood Loss |
| Red Cell Blood Type, Rh, antibody screen | Possible Anti-D antibody Treatment Autoimmune Hemolytic Disease |
| Chemistry Panel | Eliminate systematic disease i.e.. HUS, Hepatitis, Hemolyas, Occult malignancy with elevated LDH or Uric acid |
| DIC Screen | Sepsis, Kasabach Merrit Syndrome |
| Quantitative Immunological | Rule Out: Common Variable Immune Deficiency, Wiskott-Aldrich |
| Viral Titers/ PCR | Torch titers for infants, CMV, EBV for older children |
| Collagen Vascular Panel ( ANA, anti-DNA) | Older patients especially those with more chronic onset |</p>
<table>
<thead>
<tr>
<th>History and Physical Findings <strong>Not Consistent with ITP of Childhood</strong></th>
<th>Alternative Diagnosis</th>
</tr>
</thead>
</table>
| Thrombocytopenia present from birth | Amegakaryocytosis  
Primary Thrombocytopenia  
Giant Platelet Syndrome |
| Weight Loss and Recurrent Fevers  
Bloody Diarrhea | Malignancy, Immune Deficiencies  
Wiskott Aldrich |
| Recurrent Infections and Failure to Thrive  
History or Presence of Jaundice | Primary Immune disorder, HIV  
Autoimmune Hemolytic Disease  
Hepatitis, Cirrhosis with Splenomegaly |
| Splenomegaly, lymphadenopathy | Autoimmune Lymphoproliferative Syndrome (ALPS), Primary Immune Disorders, Gauchers, Malignancies, Hypersplenism syndromes |
| Forearm or hand anomalies | Thrombocytopenia Absent Radii (TAR)  
Fanconi’s Syndrome |
| Malar Rash, Dermatomyocytis Polymyocytis, Eczema  
Cardiac Malformations with or without DiGeorge syndrome | Collagen Vascular Panel, Wiskott Aldrich  
Chromosome 22 microdeletions with large platelets, with or without Evans Syndrome |
<table>
<thead>
<tr>
<th>Treatment for Acute ITP Patients</th>
<th>Corticosteroids (4mg/kg/day 1-7)</th>
<th>IV Immunoglobulin (1-2 gm s/kg)</th>
<th>Anti-D Immunoglobulin (75 μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response&gt;20,000 At 48 hours</td>
<td>60-70 % of Patients</td>
<td>70-80 % of Patients</td>
<td>77 % of Patients</td>
</tr>
<tr>
<td>Common Side Effects</td>
<td>Weight gain, irritability,</td>
<td>Post infusion headache, vomiting,</td>
<td>Hemolysis, chills, fever,</td>
</tr>
<tr>
<td></td>
<td>hypertension, stomach pain,</td>
<td>allergic reactions, fever,</td>
<td>headache</td>
</tr>
<tr>
<td></td>
<td>hyperglycemia</td>
<td>chills</td>
<td></td>
</tr>
<tr>
<td>Rare but Severe Reactions</td>
<td>Gastric ulcer, reflux, bleeding,</td>
<td>Anaphylaxis, aseptic meningitis,</td>
<td>Massive hemolysis with</td>
</tr>
<tr>
<td></td>
<td>hypertension, induced ICH</td>
<td>renal failure</td>
<td>associated back pain mysigia,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>anemia</td>
</tr>
<tr>
<td>Duration of initial response (days)</td>
<td>Wide range of response after 30 days of wearing from initial dose to 0</td>
<td>21-72 days with platelet count greater than 20,000/mm³</td>
<td>21-48 days based on the 75 μg/kg dose</td>
</tr>
</tbody>
</table>
Nomenclature and Diagnosis

- Primary ITP was defined by the IWG as a platelet count <100,000 /L, in the absence of other causes or disorders associated with thrombocytopenia.

- Cutpoint was based on three things:

  1. 100,000<Plt<150,000: <6.9 % chance of having persistent thrombocytopenia.
  2. non-Western ethnicities, normal plt counts can be lower.
  3. to reduce concern over “mild” physiologic thrombocytopenia of pregnancy.
Nomenclature and Diagnosis

Primary ITP

Newly Diagnosed: from Dx to 3 months.
Persistent: 3-12 months after Dx
Chronic: >12 months from Dx.
Still Defining …

- **Severe ITP**: Clinically relevant bleeding, defined as bleeding at presentation requiring treatment, or new bleeding symptoms requiring new interventions or increasing drug doses.

- **Refractory ITP**: presence of severe ITP after splenectomy.

- **Non-splenectomized patients**: defined as responders or non-responders to various drug therapies.
# Nomenclature and Diagnosis

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response (CR)</td>
<td>A platelet count ≥ 100 × 10^9/L measured on 2 occasions &gt; 7 days apart and the absence of bleeding.</td>
</tr>
<tr>
<td>Response (R)</td>
<td>A platelet count ≥ 30 × 10^9/L and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions &gt; 7 days apart and the absence of bleeding.</td>
</tr>
<tr>
<td>No response (NR)</td>
<td>A platelet count &lt; 30 × 10^9/L or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.</td>
</tr>
<tr>
<td>Loss of complete response</td>
<td>A platelet count &lt; 100 × 10^9/L measured on 2 occasions more than a day apart and/or the presence of bleeding.</td>
</tr>
<tr>
<td>Loss of response</td>
<td>A platelet count &lt; 30 × 10^9/L or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.</td>
</tr>
</tbody>
</table>

*Based on the recommendations of the International Working Group.*
Table 4. Definitions of time to and duration of response, and the time to initial and peak response for different ITP treatments*

<table>
<thead>
<tr>
<th>Expected time to response</th>
<th>Treatment type</th>
<th>Initial response, days</th>
<th>Peak response, days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anti-D</td>
<td>1-3</td>
<td>3-7</td>
</tr>
<tr>
<td></td>
<td>Azathioprine</td>
<td>30-90</td>
<td>30-180</td>
</tr>
<tr>
<td></td>
<td>Danazol</td>
<td>14-90</td>
<td>28-180</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>2-14</td>
<td>4-28</td>
</tr>
<tr>
<td></td>
<td>Eltrombopag</td>
<td>7-28</td>
<td>14-90</td>
</tr>
<tr>
<td></td>
<td>IVIg</td>
<td>1-3</td>
<td>2-7</td>
</tr>
<tr>
<td></td>
<td>Prednisone</td>
<td>4-14</td>
<td>7-28</td>
</tr>
<tr>
<td></td>
<td>Rituximab</td>
<td>7-56</td>
<td>14-180</td>
</tr>
<tr>
<td></td>
<td>Romiplostim</td>
<td>5-14</td>
<td>14-60</td>
</tr>
<tr>
<td></td>
<td>Splenectomy</td>
<td>1-56</td>
<td>7-56</td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
<td>7-14</td>
<td>7-42</td>
</tr>
<tr>
<td></td>
<td>Vincristine</td>
<td>7-14</td>
<td>7-42</td>
</tr>
</tbody>
</table>

*Adapted from the International Working Group.7
GRADING the evidence

Grades
Recommendation
Assessment
Development
Evaluation
GRADING the evidence

- Provides the score for a recommendation of 1A, 1B, 1C, 2A, 2B, 2C.

- 1: high degree of confidence that the desirable outcomes of an intervention exceed the undesirable effects ("we recommend")

- 2: a lesser degree of evidence that the desirable outcomes outweigh the undesirable effects ("we suggest")
GRADING the evidence

- **A**: Supported by consistent evidence by RCTs, or exceptionally strong observational studies.

- **B**: Supported by RCTs with important limitations or strong evidence from observational studies.

- **C**: Derived from RCTs with serious flaws, weaker observational studies, or indirect evidence.
Methodology

- The authors began their recommendations with the ASH 1996 guidelines.

- They searched the EMBASE and MEDLINE databases from 1996 to December 2009 for each of the clinical questions.

- When a systematic review or meta-analysis was found, the authors searched for subsequently published studies and updated the evidence.
Methodology

- If a systematic review was not available, the authors searched for RCTs.

- If neither was found the authors searched for rigorous cohort studies or case control studies.

- Confined to 50 patients for adult series and 25 patients for pediatric series.
Methodology

- Grades of recommendations were proposed by a principal nominated author for that area.

- They were then vetted in a series of teleconferences involving the authors of the guideline.

- An external panel was convened to ensure that all pertinent articles were identified and accurately assessed, and to determine whether all clinically relevant areas with evidence were assessed, and to determine whether the guideline was concise and well-organized.

Underwent peer review process.
Section 1: ITP in children

3 yr old girl presents with 24 hr history of bruising and petechiae. PE is notable for few areas of petechiae and several small bruises to her arms and legs. CBC reveals a platelet count of 8000, and smear shows few large platelets.

Are there additional tests that can help confirm the diagnosis of ITP in this patient?
1.1 Diagnosis of ITP

- BM examination is not necessary in
  1) children and adolescents with the typical features of ITP (Grade 1B).
  2) children and adolescents who fail IVIg therapy (Grade 1B).
  3) similar patients before steroid initiation or before splenectomy (Grade 2C).

- Testing for antinuclear antibodies is not necessary in children and adolescents with suspected ITP (Grade 2C).
1.2 Initial management of ITP

3 yr old girl presents with 24 hr history of bruising and petechiae. PE is notable for few areas of petechiae and several small bruises to her arms and legs. CBC reveals a platelet count of 8000, and smear shows few large platelets.

Do you treat this child with medication at this time?
Children with no bleeding or mild bleeding (defined as skin manifestations only, such as bruising and petechiae) can be managed with observation alone regardless of platelet count (Grade 1B).
1.2 Initial management of ITP

The child develops an episode of epistaxis that lasts about 15 minutes. You make the decision to treat based on the bleeding.

What medication do you treat with at this time?
1.2 Initial management of ITP

- A single dose of **IVIg** (0.8 to 1g/kg) or a short course of **corticosteroids** to be used as first line treatment (Grade 1B).

- IVIg can be used if a more rapid increase in the platelet count is desired (Grade 1B).
1.2 Initial management of ITP

- Anti-D therapy is not advised in children with a Hb concentration that is decreased because of bleeding or with evidence of autoimmune hemolysis (Grade 1C).

- A single dose of anti-D can be used as first line treatment in Rh positive, non-splenectomized children requiring treatment (Grade 2B).
2.1 Appropriate second line treatments for pediatric ITP

A 6 year old child was diagnosed with ITP 6 months ago and continues to have a platelet count of 20,000. The child has had no response to IVIg or anti D, and has recently had a decline in response to steroids. She suffers from troublesome recurrent epistaxis.

What treatments should be considered for children who are unresponsive to initial treatment and/or who have persistent or chronic ITP?
Appropriate second line treatments for pediatric ITP

- If previous treatment with corticosteroids, IVIg, or anti-D have been successful, these agents may be used again to prevent bleeding especially during the first 12 months.

- List of agents expanding: MMF, Danazol, Interferon, Azathioprine, cyclosporine … But data is insufficient to make recommendations about any of these agents (alone or in combination).
2.1 Appropriate second-line treatments for pediatric ITP

- **Rituximab** can be considered for children and adolescents with ITP who have significant ongoing bleeding despite first line treatment (Grade 2C).

- **Rituximab** may be considered as an alternative to splenectomy in children and adolescents with chronic ITP or those who don’t respond favorably to splenectomy (Grade 2C).
2.1 Appropriate second-line treatments for pediatric ITP

- High dose dexamethasone may be considered in children and adolescents who have significant ongoing bleeding despite first line treatment (Grade 2C).

- High dose dexamethasone may be considered as an alternative to splenectomy in chronic ITP or in patients who do not respond favorably to splenectomy (Grade 2C).
2.2 Splenectomy

- The 1996 ASH guideline considered splenectomy to be an effective therapy for chronic and persistent ITP in children and adolescents.

- Data insufficient to make recommendations regarding indications and timing.

- Studies continue to show a sustained response rate of 70-80%.
2.2 Splenectomy

- Splenectomy for persistent or chronic ITP who have significant or persistent bleeding, and lack or responsiveness or intolerance to other therapy (Grade 1 B).

- Splenectomy be delayed for at least 12 months, unless accompanied by severe disease as defined by the IWG as unresponsive to other measures or other quality of life considerations (Grade 2C).
2.3 *H Pylori* testing

- One RCT investigating the role of *H Pylori* eradication in children with chronic ITP (55 children).

- The prevalence of *H Pylori* was not different than that in healthy Thai children.

- The primary end point was achieved in 12% of the treatment group and 13% in the placebo group.
2.3 *H Pylori* testing

- Authors recommend **against routine testing** for *H Pylori* in children with chronic ITP (Grade 1 B).
15 m old child presents with 24 hr history of bruising and petechiae. The child received an MMR vaccination 2 weeks earlier. PE is remarkable for several areas of scattered petechiae and several small bruises. Plt count 8000.

What do you tell the mother about future vaccinations?
MMR-associated ITP

- Eleven studies reported the prevalence of MMR-associated ITP to be 0.87-4 cases per 100,000

- ITP following natural measles or rubella ranges from 6 to 1200 cases per 100,000

- MMR vaccination or re-vaccination in children with ITP did not lead to the recurrence of the thrombocytopenia.
MMR-associated ITP

- Children with a history of ITP who are unimmunized receive their scheduled MMR vaccine (grade 1B).

- In children with ITP (vaccine or non-vaccine related) who received their first dose, vaccine titers can be checked and re-vaccination given accordingly (grade 1B).
A previously healthy 28 year old woman presents with isolated mucosal hemorrhage. A CBC showed a platelet count of 9000.

What testing is required to confirm the diagnosis of ITP?
4.1 Initial diagnosis of ITP

- Testing patients for HCV and HIV (grade 1 B).

- Further investigations are required if there are other abnormalities in the blood count or peripheral blood smear (grade 2 C).

- A bone marrow examination is unnecessary irrespective of age in patients presenting with typical ITP (grade 2C).
The patient is concerned about her bleeding and has learned from the internet that a low platelet count is associated with a risk of bleeding. When is treatment indicated for newly diagnosed ITP?
Treatment of newly diagnosed adult ITP

- Treatment should be administered for newly diagnosed adult patients with a platelet count of less than 30,000 (grade 2C).
Given her degree of thrombocytopenia, recurrent mucosal hemorrhage and level of concern, you recommend treatment.

What is suitable first line treatment for newly diagnosed ITP?
First line treatment for newly diagnosed adult ITP

- Longer courses of corticosteroids are preferred over shorter courses of corticosteroids or IVIg (grade 2B).

- IVIg is to be used with steroids when a more rapid increase in plt count is needed (grade 2B).

- Either IVIg or anti-D can be used when steroids are contraindicated (grade 2C).
Section 2: ITP in the adult

Patient’s plt count increases to more than 100,000. Three months after stopping steroids, the patient develops epistaxis, mucosal bleeding and...

What is the most appropriate next therapy?
Second line treatment

- **Splenectomy** for patients who have failed corticosteroid therapy (grade 1B).

- **Thrombopoietin receptor agonists** for patients at risk of bleeding who relapse after splenectomy OR who have a contraindication to splenectomy and who have failed at least on other therapy (grade 1B).
Second line treatment

- **Thrombopoietin receptor agonists** may be considered for patients at risk of bleeding who have failed one line of therapy and who have not had a splenectomy (grade 2C).

- **Rituximab** may be considered for patients at risk of bleeding who have failed one line of therapy (grade 2C).
After a successful splenectomy, the patient achieves a stable plt count of 50-60,000.

When is treatment indicated for ITP after splenectomy?
Adult refractory ITP after splenectomy

- Against further treatment in asymptomatic patients after splenectomy who have platelet counts >30,000.
Secondary ITP

You are following a patient who was referred because he was being treated for hepatitis C infection, and on his last routine CBC he was noted to have a plt count of 30,000.

How should ITP be managed in the background of HCV?
HCV associated ITP

- Antiviral therapy should be considered in the absence of contraindications (grade 2C).

- If treatment for ITP is required, the initial treatment should be IVIg (grade 2C).
HIV-associated ITP

- Treatment of the HIV infection with anti-viral therapy should be considered before other treatment options unless the patient has clinically significant bleeding complications (grade 1A).

- Initial treatment should consist of corticosteroids, IVIg, or anti-D (grade 2C), and splenectomy in case of failure of the above (grade 2C).
H pylori associated ITP

- Eradication therapy should be administered in patients who are found to have H pylori infection (based on urea breath tests, stool antigen tests, or endoscopic biopsies) (grade 1B).

- Screening for H pylori should be considered in patients with ITP in whom eradication therapy would be used if positive (grade 2C).
A well known chronic ITP patient is brought to the hospital after being involved in an accident. His level of consciousness is impaired and a CT scan demonstrates an intracranial hemorrhage.

In addition to standard life-saving measures, what treatment should be considered in patients with ITP who have life-, limb-, or sight threatening hemorrhage?
Emergency Management of ITP

- IVIg has proven to have the most rapid onset of action and should be used with corticosteroids (grade 2B).

- Physicians may wish to try treatments with evidence limited to case reports but which in theory may be more rapidly acting.
Platelet transfusions

- Ranging from q 30 min- q 8 hrs.

- Usually used in conjunction with a continuous infusion of IVIg.

- These report either a rapid reduction in bleeding and/or an improvement in the platelet count.

- The effect on the platelet count is short-lived.
Recombinant Factor VII

- Has been used in several patients with ITP who were either bleeding or undergoing surgery.

- In all 18 cases reported, the bleeding stopped but 3 patients died.

- Care must be taken because of risk of thrombosis.
Anti-fibrinolytic agents

- Are discussed in case reports as an adjunct treatment for bleeding in thrombocytopenic patients, but their efficacy is unproved.
Emergent splenectomy

- In truly life-threatening bleeding, emergent splenectomy has been reported.

- This treatment should be considered heroic given the dangers of unplanned surgery, lack of immunization, risk of surgical bleeding, and risk of managing bleeding while preparing a patient for major abdominal surgery.
Guideline was developed to provide practicing clinicians with evidence based guidance for the management of ITP.

The authors support the further standardization of the terminology for ITP.

The authors were unable to make specific recommendations in some key areas: acute bleeding, patients who have failed first line therapy, and specific platelet thresholds at which treatment should be initiated.
Table 1. Summary of recommendations

Section 1: ITP in children
Case 1: newly diagnosed ITP in children

Diagnosis of ITP
1.1.A. 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).
1.1.B. We suggest:
- Bone marrow examination is also not necessary in similar patients prior to initiation of treatment with corticosteroids or before splenectomy (grade 2C).
- Testing for antinuclear antibodies is not necessary in the evaluation of children and adolescents with suspected ITP (grade 2C).

Initial management of ITP
1.2.A. We recommend:
- Children with no bleeding or mild bleeding (defined as skin manifestations only, such as bruising and petechiae) be managed with observation alone regardless of platelet count (grade 1B).

Initial pharmacologic management of pediatric ITP
1.3.A. We recommend:
- For pediatric patients requiring treatment, a single dose of IVIg (0.8-1 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 (grade 1B).
- Anti-D therapy is not advised in children with a hemoglobin concentration that is decreased due to bleeding, or with evidence of autoimmune hemolysis (grade 1C).
1.3.B. We suggest:
- A single dose of anti-D can be used as first-line treatment in Rh-positive, nonsplenectomized children requiring treatment (grade 2B).

Case 2: children who are treatment nonresponders

Appropriate second-line treatments for pediatric ITP
2.1.A. We suggest:
- Rituximab 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).
- Rituximab may also be considered as an alternative to splenectomy in children and adolescents with chronic ITP or in patients who do not respond favorably to splenectomy (grade 2C).
- 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 children and adolescents with chronic ITP or in patients who do not respond favorably to splenectomy (grade 2C).

Splenectomy for persistent or chronic ITP or ITP unresponsive to initial measures
2.2.A. We recommend:
- Splenectomy for children and adolescents with chronic or persistent ITP who have 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).
2.2.B. 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 International Working Group as unresponsive to other measures or other quality of life considerations (grade 2C).

H pylori testing in children with persistent or chronic ITP
2.3.A. We recommend:
- Against routine testing for H pylori in children with chronic ITP (grade 1B).
Case 4: newly diagnosed ITP in the adult

Initial diagnosis of ITP

4.1. A. We recommend:
- Testing patients for HCV and HIV (grade 1B).

4.1.B. We suggest:
- Further investigations if there are abnormalities (other than thrombocytopenia and perhaps findings of iron deficiency) in the blood count or smear (grade 2C).
- A bone marrow examination is not necessary irrespective of age in patients presenting with typical ITP (grade 2C).

Treatment of newly diagnosed adult ITP

4.2. A. We suggest:
- Treatment be administered for newly diagnosed patients with a platelet count < 30 × 10^9/L (grade 2C).

First-line treatment of adult ITP

4.3. A. We suggest:
- Longer courses of corticosteroids are preferred over shorter courses of corticosteroids or IVIg as first-line treatment (grade 2B).
- IVIg be used with corticosteroids when a more rapid increase in platelet count is required (grade 2B).
- Either IVIg or anti-D (in appropriate patients) be used as a first-line treatment if corticosteroids are contraindicated (grade 2C).
- If IVIg is used, the dose should initially be 1 g/kg as a one-time dose. This dosage may be repeated if necessary (grade 2B).

Treatment of patients who are unresponsive to or relapse after initial corticosteroid therapy

4.4. A. We recommend:
- Splenectomy for patients who have failed corticosteroid therapy (grade 1B).
- Thrombopoietin receptor agonists for patients at risk of bleeding who relapse after splenectomy or who have a contraindication to splenectomy and who have failed at least one other therapy (grade 1B).

4.4.B. We suggest:
- Thrombopoietin receptor agonists may be considered for patients at risk of bleeding who have failed one line of therapy such as corticosteroids or IVIg and who have not had splenectomy (grade 2C).
- Rituximab may be considered for patients at risk of bleeding who have failed one line of therapy such as corticosteroids, IVIg, or splenectomy (grade 2C).

Laparoscopic versus open splenectomy and vaccination prior to splenectomy

4.5. A. We recommend:
- That for medically suitable patients, both laparoscopic and open splenectomy offer similar efficacy (grade 1C).

Case 5: treatment of adult ITP after splenectomy

Treatment of ITP after splenectomy

5.1. A. We recommend:
- Against further treatment in asymptomatic patients after splenectomy who have platelet counts > 30 × 10^9/L (grade 1C).
Case 6: Treatment of ITP in pregnancy

Management of ITP during pregnancy

6.1. We recommend:
- Pregnant patients requiring treatment receive either corticosteroids or IVlg (grade 1C).

Treatment of ITP during labor and delivery

6.2. We suggest:
- For pregnant women with ITP, the mode of delivery should be based on obstetric indications (grade 2C).

Case 7: Treatment of specific forms of secondary ITP

Management of secondary ITP, HCV-associated

7.1. We suggest:
- In patients with secondary ITP due to HCV infection, antiviral therapy should be considered in the absence of contraindications (grade 2C). However, the platelet count should be closely monitored due to a risk of worsening thrombocytopenia attributable to interferon.
- If treatment for ITP is required, the initial treatment should be IVlg (grade 2C).

Management of secondary ITP, HIV-associated

7.2. We recommend:
- For patients with secondary ITP due to HIV, treatment of the HIV infection with antiviral therapy should be considered before other treatment options unless the patient has clinical significant bleeding complications (grade 1A).
- If treatment for ITP is required, initial treatment should consist of corticosteroids, IVlg, or anti-D (grade 2C) and splenectomy in preference to other agents in symptomatic patients who fail corticosteroids, IVlg, or anti-D (grade 2C).

Management of secondary ITP, *H pylori*-associated

7.3. We recommend:
- That eradication therapy be administered in patients who are found to have *H pylori* infection (based on urea breath tests, stool antigen tests, or endoscopic biopsies) (grade 1B).

7.3. We suggest:
- Screening for *H pylori* be considered in patients with ITP in whom eradication therapy would be used if testing is positive (grade 2C).
Thank You