Thrombocytopenia

By:

Sonephet SAYSOULIGNO. MD
Pediatric Hemato-Oncologist
Hematology department
National Children Hospital, Vientiane, Lao PDR

I. Increased Platelet Destruction

A. Immune thrombocytopenias

B. Nonimmune thrombocytopenias

II. Disorders of Platelet Distribution or Pooling

A. Hypersplenism (e.g., portal hypertension, Gaucher disease, cyanotic congenital heart disease, neoplastic, infectious)

B. Hypothermia

III. Decreased Platelet Production – Deficient Thrombopoiesis (decreased or absent megakaryocytes in the marrow – amegakaryocytic thrombocytopenia)

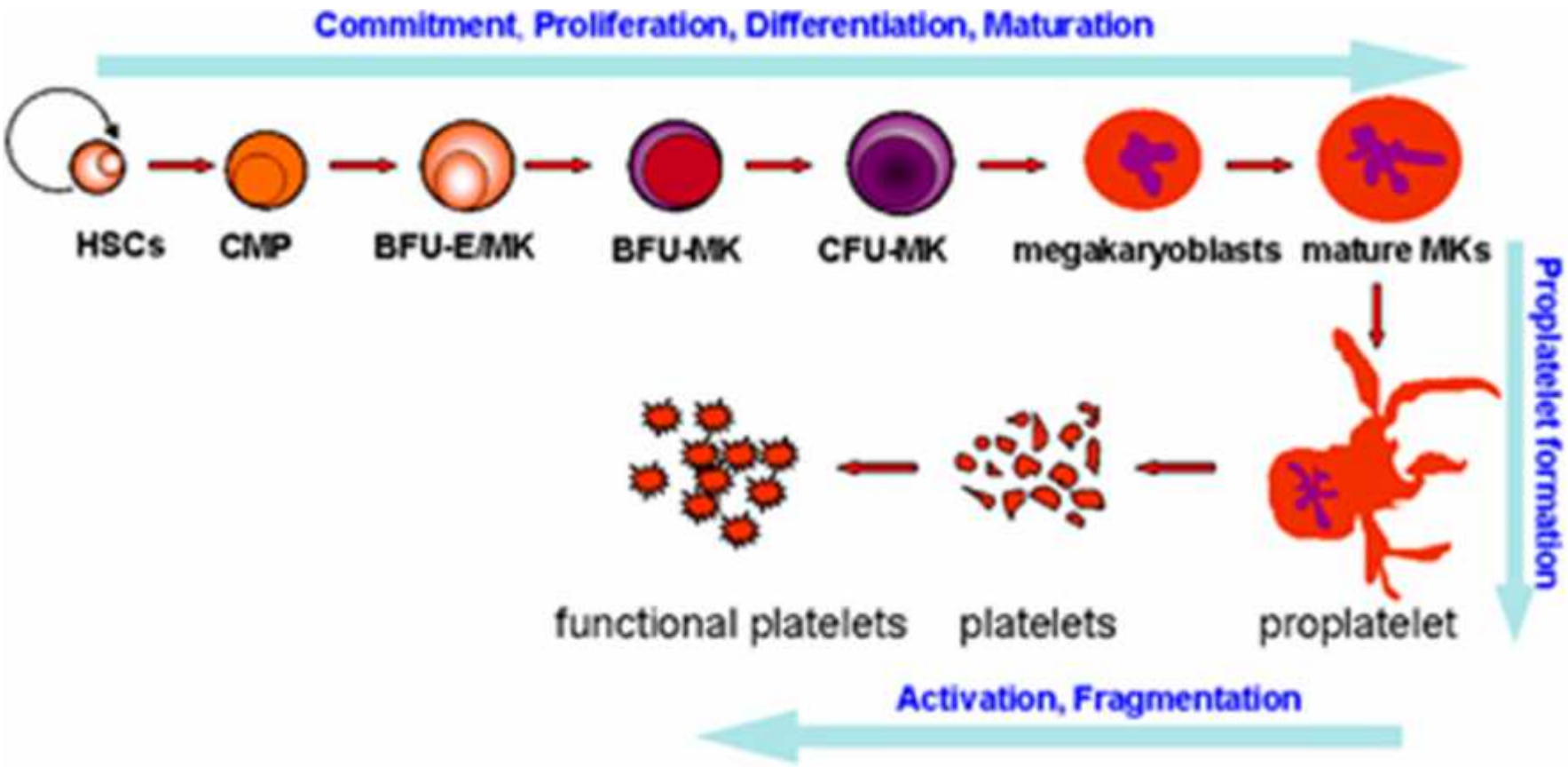
A. Hypoplasia or suppression of megakaryocytes

B. Marrow infiltrative processes

IV. Pseudothrombocytopenia

Table 12-2 Pathophysiological Classification of Thrombocytopenic States

I. **Increased Platelet Destruction** (normal or increased megakaryocytes in the marrow – megakaryocytic thrombocytopenia)
   A. Immune thrombocytopenias
      1. Idiopathic
         a. Immune (idiopathic) thrombocytopenic purpura
      2. Secondary
         a. Infection induced (e.g., viral – HIV, CMV, EBV, varicella, rubella, rubeola, mumps, measles, pertussis, hepatitis, parvovirus B19; bacterial – tuberculosis, typhoid)
         b. Drug-induced (see Table 12-10)
         c. Post-transfusion purpura
         d. Autoimmune hemolytic anemia (Evans syndrome)
         e. Systemic lupus erythematosus
         f. Hyperthyroidism
         g. Lymphoproliferative disorders
      3. Neonatal immune thrombocytopenias
         a. Neonatal autoimmune thrombocytopenia
         b. Neonatal alloimmune thrombocytopenia
         c. Erythroblastosis fetalis–Rh incompatibility
   B. Nonimmune thrombocytopenias
      1. Due to platelet consumption
         a. Microangiopathic hemolytic anemia: hemolytic-uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), hematopoietic stem cell transplantation (HSCT) associated microangiopathy
         b. Disseminated intravascular coagulation
         c. Virus-associated hemophagocytic syndrome
         d. Kasabach–Merritt syndrome (giant hemangioma)
         e. Cyanotic heart disease


Commitment, Proliferation, Differentiation, Maturation
HSCs
CMP
BFU-E/MK
BFU-MK
CFU-MK
megakaryoblasts
mature MKs
Proplatelet formation
functional platelets
platelets
proplatelet
Activation, Fragmentation

Immune thrombocytopenia (ITP)

20/4/58

- Immune thrombocytopenia (ITP)- isolated, immune-mediated thrombocytopenia (peripheral blood platelet count <100,000/microL).
- It is an acquired and most commonly benign disorder.
- ITP - idiopathic thrombocytopenic purpura or immune thrombocytopenic purpura.
- Now: Immune ThrombocytoPenia "ITP", while acknowledging the immune-mediated mechanism of the disorder, and that many patients have little or no signs of purpura or bleeding.

The international working group

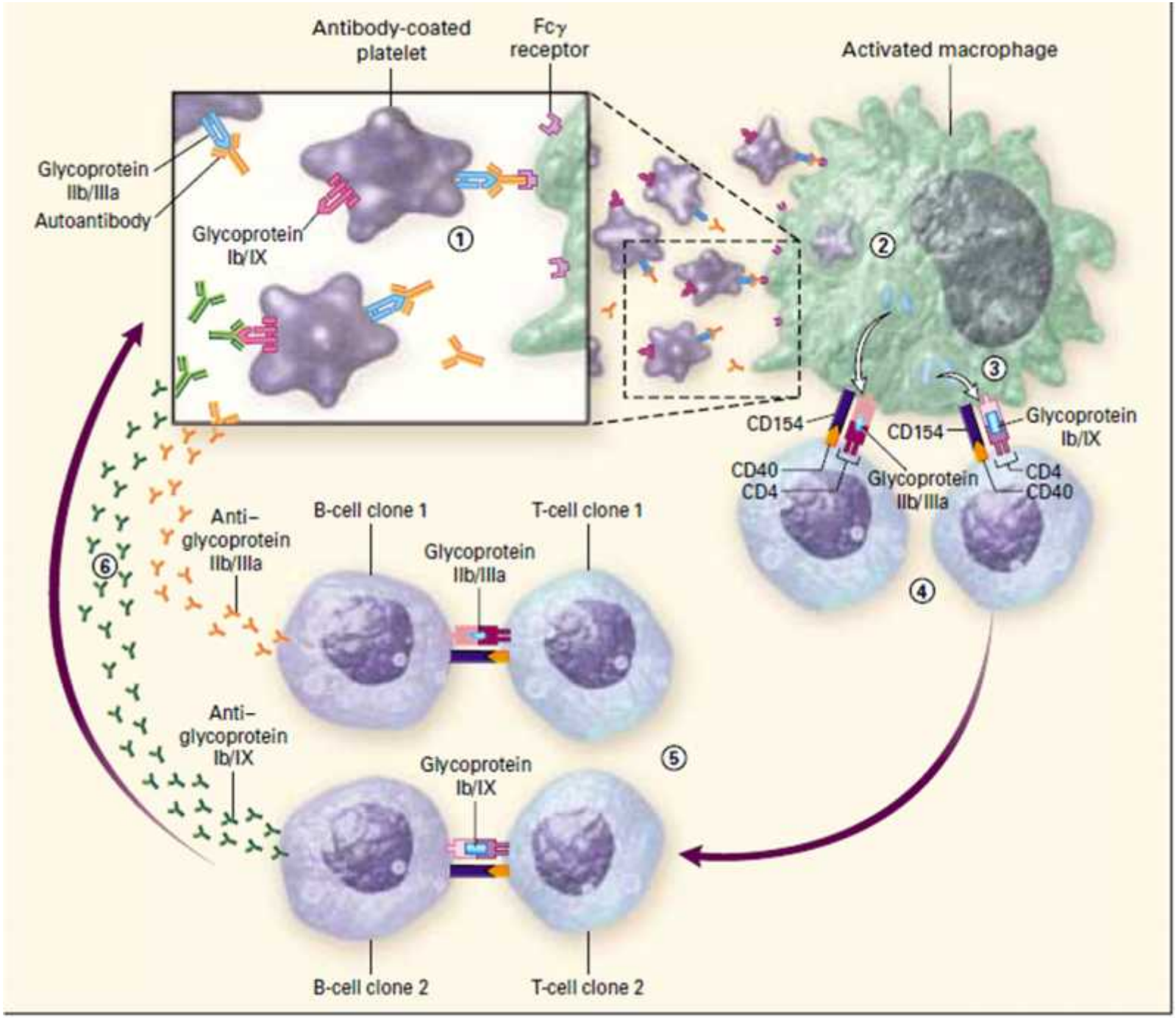
- Primary ITP: Defined as isolated thrombocytopenia (immunemediated) in the absence of underlying disorders that may be associated with thrombocytopenia. It is a diagnosis of exclusion.

- Secondary ITP: A specific etiology for thrombocytopenia is identified [e.g. , systemic lupus erythematosus (SLE), HIV, drugs].

- immune-mediated mechanism of the disorder.
- The antibody coated platelets are removed following binding to Fc receptors on macrophages.
- Incidence 1-6.4 cases/100,000, (4.8 , 1-4yr: Nordic country)
- Age 2-5 yr

UpToDate

Pathogenesis of ITP



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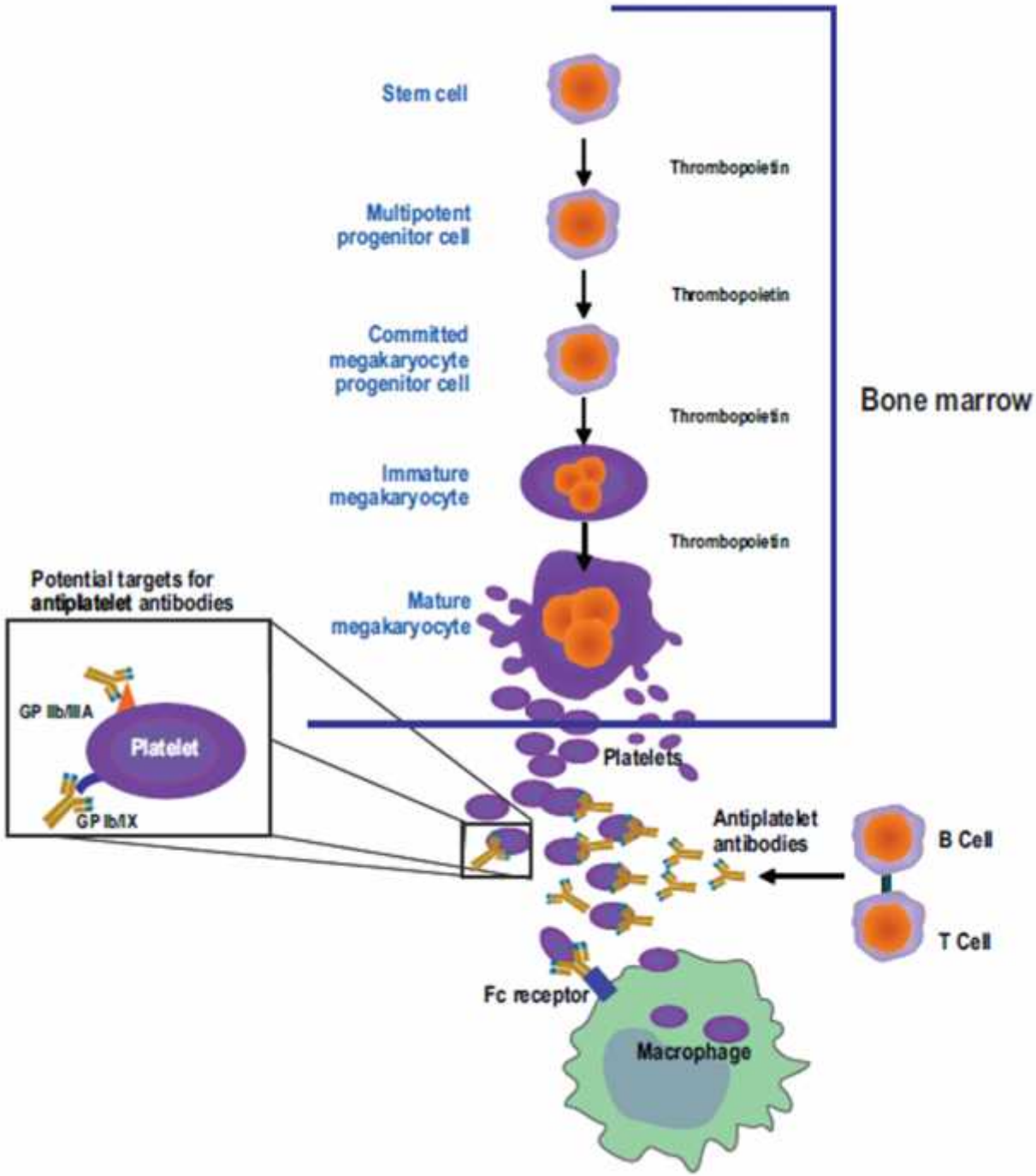
Stem cell
Thrombopoietin
Multipotent progenitor cell
Thrombopoietin
Committed megakaryocyte progenitor cell
Thrombopoietin
Immature megakaryocyte
Thrombopoietin
Mature megakaryocyte
Bone marrow
Platelets
Potential targets for antiplatelet antibodies
GP IIb/IIIA
Platelet
GP Ib/IX
Antiplatelet antibodies
B Cell
T Cell
Fc receptor
Macrophage

- History of viral infection 60%
- 6 weeks after measles, mumps, and rubella (MMR) vaccination(2.6/100,00 doses)
- family history of thrombocytopenia- very few children with ITP(inherited non-immune thrombocytopenia).
- Drug-induced thrombocytopenia is rare in children.

Table 12-10 Drugs Proven or Suspected to Induce Drug-dependent Antibody-mediated Immune Thrombocytopenia

Anti-inflammatory
- Acetaminophen
- Acetylsalicylic acid
- Diclofenac
- Ibuprofen
- Indomethacin
- Meclofenamate
- Mefenamic acid
- Naproxen
- Oxyphenbutazone
- Phenylbutazone
- Piroxicam
- Sodium-p-amino salicylic acid
- Sulfasalzine
- Sulindac
- Tolmetin

Antibiotics
- Antituberculous drugs
  - Ethambutol
  - Isoniazid
  - Para-aminosalicylic acid (PAS)
  - Rifampin
  - Streptomycin
- Penicillin group
  - Ampicillin
  - Methicillin
  - Penicillin
  - Mezlocillin
  - Piperacillin
- Cephalosporin
  - Cefamandole
  - Cefotetan
  - Ceftazidime
  - Cephalothin
- Sulfonamides
  - Sulfamethoxazole
  - Sulfamethoxypyridazine
  - Sulfisoxazole
- Other antibiotics
  - Amphotericin B
  - Ciprofloxacin
  - Clarithromycin
  - Fluconazole
  - Gentamicin
  - Indinavir
  - Nalidixic acid

Anticonvulsants, Sedatives and Antidepressants
- Amitriptyline
- Carbamazepine
- Desipramine
- Diazepam
- Doxepin
- Haloperidol
- Imipramine
- Lithium
- Mianserin
- Phenytoin
- Valproic acid

Cardiac and Antihypertensive Drugs
- Acetazolamide
- Amiodarone
- Alprenolol
- Captopril
- Chlorothiazide
- Chlorthalidone
- Digoxin
- Digitoxin
- Furosemide
- Hydrochlorothiazide
- α-methyldopa
- Oxprenolol
- Procainamide
- Spironolactone

H_2-antagonists
- Cimetidine
- Ranitidine

Cinchona Alkaloids
- Quinidine
- Quinine

Miscellaneous
- Antazoline
- Chlorpheniramine
- Chlorpropamide
- Danazol
- Desferrioxamine
- Diethylstilbestrol
- Etretinate
- Glibenclamide
- Gold salts
- Heparin
- Interferon-α

Clinical manifestation

In a large registry study of children with newly diagnosed ITP, the following bleeding manifestations were reported:

- Cutaneous (petechiae, purpura, or bruising) – 86%
- Oral – 19%
- Nasal – 20%
- No bleeding – 9%
- Menstrual, gastrointestinal, or urinary bleeding < 3%.
- No patients were observed to have conjunctival or retinal hemorrhages.

UpToDate

- On physical examination: no significant enlargement of lymph nodes, liver, or spleen, although the spleen may be slightly enlarged in 10% of cases.

- If one or more of these findings are present, another diagnosis should be strongly considered

- Serious hemorrhage — about 3%

- Intercontinental Childhood ITP Study Group (ICIS):

- 863 patients.
  - 2.9 % had severe bleeding at diagnosis: epistaxis, gastrointestinal bleeding, and/or intracranial hemorrhage (ICH)
  - 86% had platelet counts ≤20,000/microL.

In the Nordic registry of 501 patients:

- 15 patients (3%) had severe hemorrhage, consisting of profound epistaxis and/or gastrointestinal bleeding that required blood transfusions.

- 3 cases Plt between 16,000 and 24,000 microL.

- Intracranial hemorrhage (ICH) is the most serious consequence of thrombocytopenia.

- The incidence of ICH is 0.1 to 0.8 percent

- > 90 % of ICHs in children with ITP are supratentoria

Table 12-8 Characteristics of ICH in ITP

Incidence:	0.2–0.8%
Age:	13 months–16 years
Platelet count:	<20,000 in 90% of cases <10,000 in 75% of cases
Interval between diagnosis of ITP and ICH:	At presentation (25% of cases) <1 week (45% of cases) week–6 months (25% of cases) Greater than 6 months (30%)

Identifiable risk factors for ICH include:

- Head injuries (33%) (versus 1% in ITP without ICH)
- Hematuria (22%) (versus 0% in ITP without ICH)
- Hemorrhage more than petechiae and bruises (63%) (versus 44% in ITP without ICH)
- AV malformation
- Aspirin treatment

Site of ICH

- Intracerebral (77% of cases) – 87% supratentorial; 13% posterior fossa
- Subdural hematoma (23% of cases)

Prior Treatment

- 70% had prior treatment

Survival

- 75% survive, but 1/3 have neurologic sequelae

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Primary ITP is categorized into 3 phases

- Newly diagnosed ITP – ITP < 3months from diagnosis
- Persistent ITP – Ongoing ITP between 3 - 12 months from the initial diagnosis
- Chronic ITP – ITP lasting for > 12 months
- Recurrent ITP : return of thrombocytopenia/symptoms after at least 3 mo of remission
- Refractory ITP: Child with ITP who has failed first line therapy as well as splenectomy, and continues to experience clinically significant bleeding.

- The presentations of newly diagnosed, persistent, and chronic ITP are similar.

- However, chronic ITP are older
  - less severe thrombocytopenia at the initial diagnosis
  - less likely to have a history of a prior infection or vaccination.

Table 12-9 Features of Newly Diagnosed and Chronic ITP

Feature	Newly Diagnosed	Chronic
Age	Children 2–6 years old	Adults
Sex distribution	Equal	Female:male = 2:1
Preceding infection	~80%	Unusual
Seasonal predilection	Springtime	None
Associated autoimmunity	Uncommon	More common
Onset	Acute	Insidious
Platelet count	$<20{,}000/mm^3$	$<20{,}000–80{,}000/mm^3$
Eosinophilia-lymphocytosis	Not uncommon	Rare
IgA/IgG levels	Normal	Infrequently low
Duration	2–8 weeks	1 to many years
Prognosis	Spontaneous remission in 70–80% of cases	Ongoing thrombocytopenia with occasional remission

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DIAGNOSIS

The diagnosis of ITP is based upon the following criteria:

- Platelet count <100,000/microL (often <20,000/microL).
- Normal wbc, red cell

- No abnormalities on the peripheral blood smear. (no evidence of hemolysis or of blast cells).

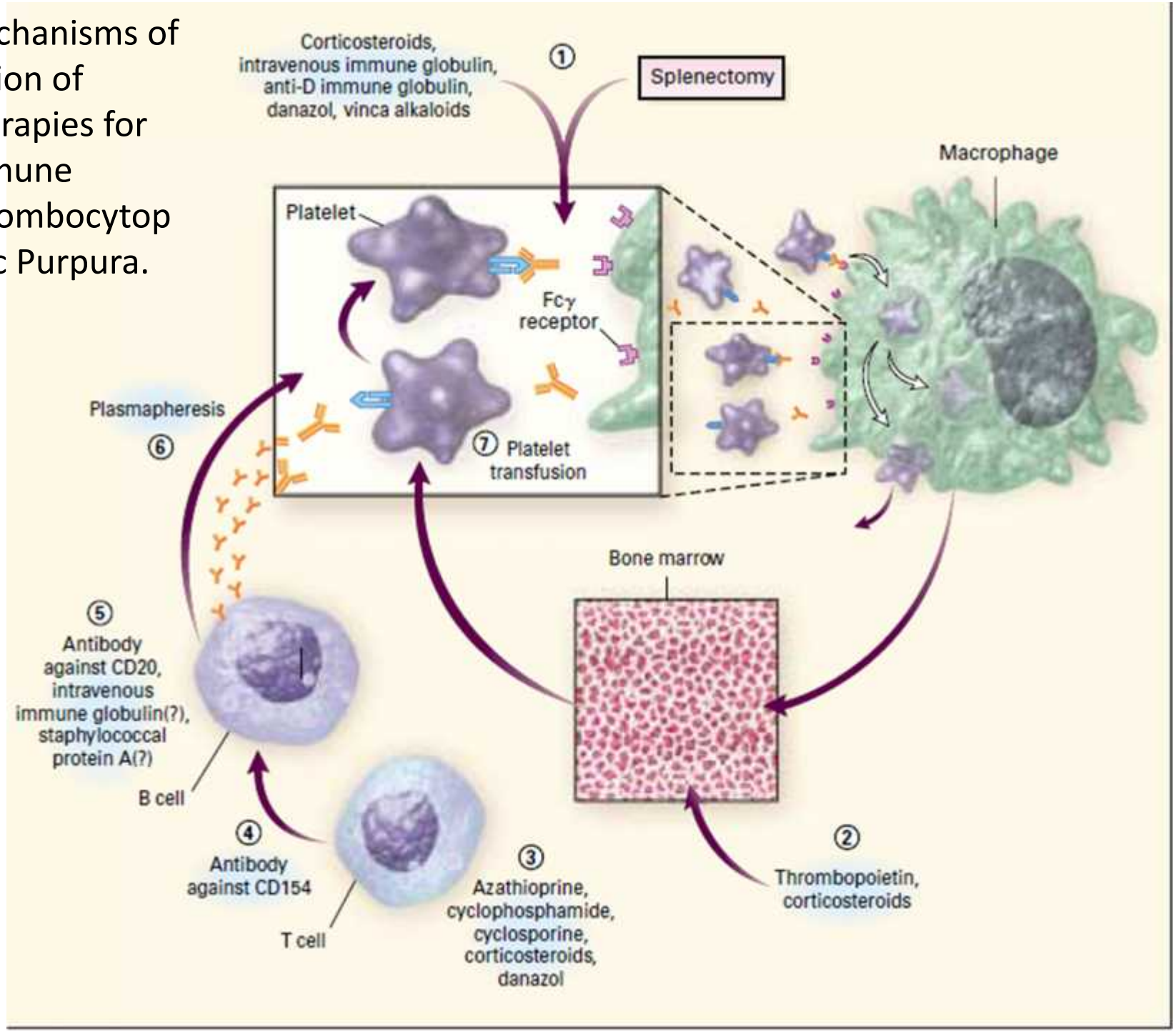
- No clinically apparent associated conditions that may cause thrombocytopenia, after a thorough history and physical examination.

DIAGNOSIS

- It is a diagnosis of exclusion, other causes of thrombocytopenia must be ruled out.

Treatment

Mechanisms of Action of Therapies for Immune Thrombocytopenic Purpura.



- Approximately 50 - 70% of children recover within 3 months with or without treatment:(platelet count >150,000/microL).

The Nordic registry. 6 months follow-up data were available for 409 patients. The following findings were noted:

- A platelet count >20,000/microL at 1 month 92%.
- Complete remission (platelet count >150,000/microL) 50 % <1 month, 68% 3 months, and 75% six months.
- 25 % had platelet counts <150,000/microL six months after presentation.

Treatment

First line therapy: Newly diagnosed ITP

1. Corticosteroid
2. IVIG
3. Anti-D

Second line therapy: if not response to first line

1. Dexamethasone
2. Pulse methylprednisolone
3. Rituximab
4. Immunosuppresive drug
5. TPO receptor agonist

First line therapy

	dose	Response rate %	Duration to response (d)	Side effect
IVIG	0.8-1g/kg (1-2d)	>80	1-2	headache
prednisolone	1-2mg/kg/d (14d) 4mg/kg/d (3-4d)	<75	2-7	Behavior change Abdominal pain Hyperglycemia Hypertension Avascular necrosis
Anti-D	50-75 μg/kg	55-77	3-7	Hemolysis Headache Diziness Nausea chill

Second line therapy

	doses	Response rate %	Duration to response (d)	Side effect
Dexamethasone	28mg/m²/d 3d	80	3	Behavior change
Methylprednisolone	30mg/kg/d (3d) 20mg/kg/d (4d) Max 1g	60-100	1	Behavior change Abdominal pain Weigh gain Hyperglycemia Hypertension Avascular necrosis
Rituximab	375mg/m²/week, 4weeks	31-79	2-3 weeks	Fever Rash Joint pain Serum sickness Steven-Johnson

Life threatening bleeding

- Headache
- N/V
- Conscious change
- History of head trauma, aspirin, NSAIDs
- Massive GI bleeding
- Severse anemia
- Hypotension

- MRI emergency

Management

- Pulse methylprednisolone 30mg/kg/d, (Max 1g/d) 1-3days
- And IVIG 1g/kg
- And Plt concentrate 2-4 unit/m^2/t or iv continue 0.5-1unit/m^2/h

Chronic ITP

- 20%, 1/3 spontaneous recovery(several months, years)
- w/u for SLE, HIV
- Corticosteroid short course
- Methylprednisolone 15-30mg/m^2/d, 3days
- Or IVIG 400-500mg/kg/d, 2d or 800mg/kg/d, 1d

splenectomy

- Age> 5yrs
- Chronic ITP> 1yr
- Not responded for medical treatment
- ↓bleedinng 60-90%

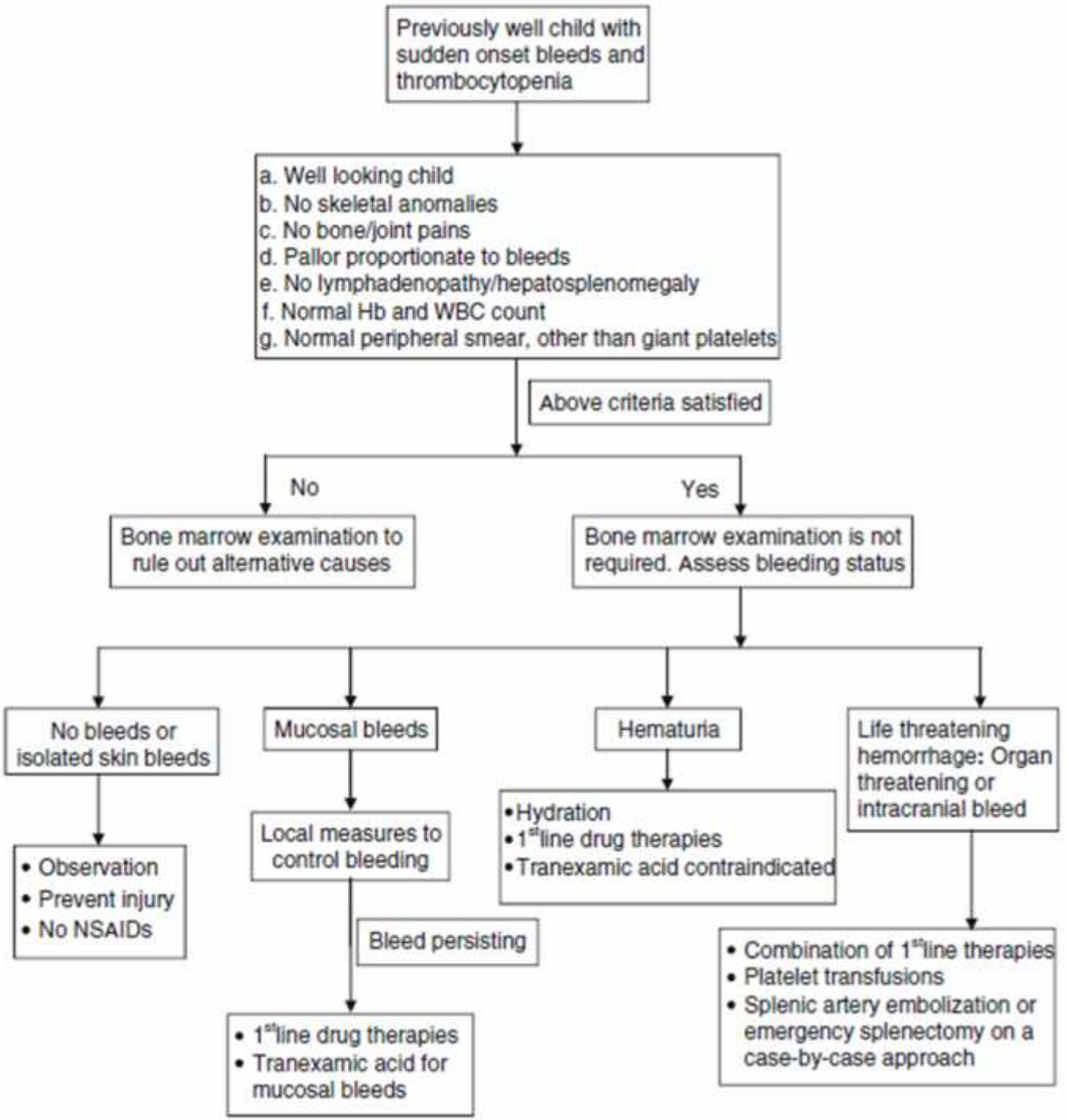
Refractory chronic ITP

- Frequent bleeding after splenectomy

  - Rituximab, 30%

  - Thrombopoietin receptor agonist

Fig. 1 Approach to a child with suspected ITP



CLINICAL AND LABORATORY OBSERVATIONS

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Newly Diagnosed Immune Thrombocytopenic Purpura in Childhood: Successful Implementation of a Limited Intervention Strategy in the Setting of Pediatric Emergency Care

Barbara Rohmer[1], Frédéric V. Valla, MD[1,2], Frédéric Baleydier, MD, PhD[1,3,4], Valérie Launay, MD[1,2], Florence Dommange-Romero, MD[1,3], and Corinne Pondarré, MD, PhD[1,3,4,5]

Immune thrombocytopenic purpura is a bleeding disorder for which management remains mainly guided by platelet counts. Pediatric hematologists and emergency physicians collaborated to set up a limited intervention strategy, focusing on clinical bleeding severity irrespective of platelet counts, starting in the emergency room. We report how this strategy was safely applied for 106 consecutive children admitted for newly diagnosed immune thrombocytopenic purpura. *(J Pediatr 2015;166:480-2).*

All pediatric hematologists agree with the rapid initiation of therapy for immune thrombocytopenic purpura (ITP) with life-threatening bleeding. For the child with only minor or mild bleeds, there is wide disagreement about whether intervention with medication is necessary.[1-5] Guidelines from the French Society of Pediatric Hematology and Immunology recommended in 2007 to sys-

severe hemorrhage (activities/sport and medication restrictions). They were told to watch for mucosal or extensive bleeding. Children with minor and mild bleeds were permitted to go to school. Initial information was provided by a pediatric emergency physician, but parents were given a 24-hour contact pediatric hematologist's name and phone number.

January 2008 to January 2012

106, admitted at the Pediatric Emergency Department in Lyon, France, with newly diagnosed ITP

- Male>female, mean age =5.3 years(5 months to 17 years).
- 10< 1 year.
- 20 >10 years .

Table I. Patients groups and treatment protocol according to bleeding symptoms

	Group A Minor bleeding	Group B Mild bleeding	Group C Moderate bleeding	Group D Severe or life threatening bleeding
Buchanan score	0/1/2	3	3	4/5
Symptoms	Isolated skin bleeding or Skin bleeds with minor epistaxis (≤2 within last 48 h)	Mild mucosal bleeding (recurrent epistaxis >3 within last 48 h, oropharyngeal blood blisters, gum bleeding)	Moderate mucosal bleeding (active gingival bleeding, active epistaxis hematuria, metrorrhagia, melena, rectorrhagia, hematemesis) + No acute anemia requiring transfusion	Severe mucosal or internal bleeding, intracranial bleeding, life threatening hemorrhage or Acute anemia requiring transfusion
Treatment	Watchful waiting	Corticosteroids (Prednisone, 4 d, 4 mg/kg/d)	Corticosteroids and immunoglobulins (Prednisone,4 d, 4 mg/kg/d + immunoglobulins 0.8 g/kg/d, 1 d)	Platelet and red cell transfusion + Corticosteroids and immunoglobulins (Prednisone, 4 mg/kg/d more than 4 d + immunoglobulins 0.8 g/kg/d, more than 1 d) ± Surgical procedure
Supportive strategy	Counseling of parents and children, including available therapies and reasons for choosing wait and watch approach, medication and sport restrictions, and minimizing the number of blood counts. Careful observation to appreciate bleeding tendency. School attendance. Home return (except if psychosocial issues).		Hospital admission until resolution of bleeding	Intensive care unit admission

Management of immune thrombocytopenia (ITP) in newly-diagnosed children, by bleeding severity

Grade (international consensus report)[1]	Bleeding severity	Clinical symptoms	Suggested management approach
Grade I	Minor/minimal	Few petechiae (≤100 total) and/or ≤5 small bruises (≤3 cm in diameter)	Observation (or occasionally pharmacologic treatment in selected children, based on multiple considerations*)
Grade II	Mild	Many petechiae (>100 total) and/or >5 large bruises (>3 cm in diameter)	Observation, OR pharmacologic treatment in selected children*
Grade III	Moderate	Mucosal bleeding ("wet purpura") that does not require immediate medical attention or supervision, such as brief epistaxis, intermittent gum bleeding, menorrhagia, and/or a lifestyle that increases bleeding risks	Pharmacologic treatment in most children,* with a goal of reducing the bleeding symptoms. We suggest IVIG• or anti-D•Δ in patients who require a rapid increase in platelets; otherwise, a short course of glucocorticoids is an acceptable alternative.
Grade IV	Severe	Mucosal bleeding or suspected internal hemorrhage that requires immediate medical attention (such as hemorrhage in the brain, lung, muscle or joint, or melena)	Pharmacologic treatment, usually including IVIG or anti-DΔ with IV glucocorticoids because these agents increase platelet counts more rapidly than glucocorticoids alone
	Life-threatening	Documented intracranial hemorrhage or life-threatening or fatal hemorrhage in any site	Platelet transfusion and aggressive pharmacologic treatment (usually with three or four agents; see topic text)

This approach to grading bleeding severity in children with ITP is based on the international consensus report.[1] Suggested management reflects our practice, and is consistent with guidelines from the American Society of Hematology (ASH).[2]

IVIG: intravenous immunoglobulin G; Anti-D: anti-Rho (D) immunoglobulin.

* For patients with mild or moderate bleeding, the decision to begin pharmacologic intervention may include considerations of platelet count, risk factors for significant bleeding (eg, head trauma or anticipated procedure), a high level of lifestyle activity, recent use of non-steroidal anti-inflammatory drugs (NSAIDs), an underlying condition that increases the risk of thrombocytopenia or bleeding, quality of life, and/or reliability of medical follow-up (see topic text).

• In our practice, for patients treated with IVIG or anti-D, we also co-administer a single dose of methylprednisolone 30 mg/kg (up to 1 gram maximum) to minimize side effects and increase efficacy.

Δ Anti-D is contraindicated in patients who are Rh-negative or splenectomized because it is not effective in these groups. Anti-D also should not be used in patients with a positive direct antiglobulin test (DAT, also known as a direct Coombs test), unless this result is attributable to recent administration of anti-D. Anti-D should be used with care in patients with substantial comorbidities or who have evidence of anemia or hemolysis.

Table II. Clinical presentation in relation to platelet count at diagnosis, treatment, and outcome

Group	A	B	A + B	C	D	Total
Buchanan	0-1-2	3		3	4-5	
Patients	63	37	100	5	1	106
Average platelet count in G/L*	18.4	5.8	13.7	10	17	13.5
Platelet count <10 G/L	32	32	64	3	0	67
Treatment (In **bold**, according to protocol. In *italic*, protocol violation)						
Watchful waiting (children with platelet count <10)	**59 (30)**	*4 (3)*	63 (33)			63
GC (platelet count <10)		**30 (28)**	30 (28)			30
Immunoglobulins (platelet count <10)	*3 (2) (-head injury -former hemolytic anemia -age <1 y)*	*2 (2) (age <1 y)*	*5 (3)*	*1*		6
GC + immunoglobulins (platelet count <10)	*1 (urgent skin surgery)*	*1 (expected poor treatment adherence)*	*2*	**4 (3)**	**1**	7
Number of children requiring a treatment episode after initial diagnostic period	11	7	18	0	0	18
Disease duration†						
<3 mo	31	24	55	3	1	59
Between 3 and 6 mo	17	3	20	0	0	20
Between 6 and 12 mo	2	2	4	0	0	4
More than 12 mo	12	4	16	1	0	17
Unknown (lost to follow-up)	1	4	5	1	0	6
Remission‡						
Remission at 6 mo (%)	77%	81%	78%	75%	100%	79%
Remission at 12 mo (%)	80%	87%	83%			83%
Dead	0	0	0	0	0	0

GC, gluco-corticosteroids.
*G/L: 1×10^9/L
†Disease duration: duration of thrombocytopenia <100 G/L.
‡Remission rate was evaluated for 100 children, as 6 children were lost to follow-up after 1-6 mo.

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

Table 3. Definitions of response to treatment by ITP*

Complete response (CR)	A platelet count ≥ 100×10^9/L measured on 2 occasions > 7 days apart and the absence of bleeding.
Response (R)	A platelet count ≥ 30×10^9/L and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart and the absence of bleeding.
No response (NR)	A platelet count < 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.
Loss of complete response	A platelet count < 100×10^9/L measured on 2 occasions more than a day apart and/or the presence of bleeding.
Loss of response	A platelet count < 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.

*Based on the recommendations of the International Working Group.[7]

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Table 4. Definitions of time to and duration of response, and the time to initial and peak response for different ITP treatments*

Time to response	From start of treatment until either complete response or response		
Duration of response	Time from complete response or response until loss of complete response or response Measured as the proportion of the cumulative time spent in complete response or response during the period under examination as well as the total time observed from which the proportion is derived		
Expected time to response	**Treatment type**	**Initial response, days**	**Peak response, days**
	Anti-D	1-3	3-7
	Azathioprine	30-90	30-180
	Danazol	14-90	28-180
	Dexamethasone	2-14	4-28
	Eltrombopag	7-28	14-90
	IVIg	1-3	2-7
	Prednisone	4-14	7-28
	Rituximab	7-56	14-180
	Romiplostim	5-14	14-60
	Splenectomy	1-56	7-56
	Vinblastine	7-14	7-42
	Vincristine	7-14	7-42

*Adapted from the International Working Group.[7]

Indian J Pediatr. 2014 Oct;81(10):1033-41. doi: 10.1007/s12098-013-1217-2. Epub 2013 Oct 5.

Newly diagnosed immune thrombocytopenia: update on diagnosis and management.

Bansal D[1], Rajendran A, Singhi S.

Author information

Abstract

Immune thrombocytopenia (ITP) continues to intrigue pediatricians and hematologists alike. Patients can have a dramatic presentation with wide-spread bleeds over a few days. There is an aura and fear of intra-cranial hemorrhage that drives the physician to recommend and the patient's family to accept drug treatment. Difference of opinion among physicians in the recommendations for treatment is not uncommon, even though recent evidence-based guidelines recommend a conservative, observation-based approach for the majority of patients with newly diagnosed childhood ITP. It is important to note that a specific 'platelet cut-off count', is no longer suggested as an indication by itself to recommend drug therapy. The manuscript is an update on newly diagnosed ITP in children. Recent changes in definitions and recommendations for treatment are highlighted. Pros and cons of 1st line drugs, including corticosteroids, intravenous immunoglobulin and anti-D are listed. Adjunctive therapies for the management of epistaxis and menorrhagia are described. Role of splenic artery embolization and emergency splenectomy in the backdrop of severe thrombocytopenia is discussed. Realistic case scenarios, common errors and frequently asked questions are included for a practical and easy reading.

PMID: 24091868 [PubMed - in process]

Table 2 First-line drugs for treatment of ITP [4, 9]

	Intravenous immunoglobulin	Anti-D	Corticosteroids[a]
Dose	1. Traditional dose: 2 g/kg divided over 2–5 d 2. Low dose: 0.8–1.0 g/kg single dose	50–75 μg/kg short i.v infusion	**Oral prednisolone** 1. Traditional regimen: 2 mg/kg/d in 3 divided doses (max: 60–80 mg/d) for~21 d 2. 4 mg/kg/d×7 d; tapered and stopped by day 21 3. 2 mg/kg/d×14 d; tapered and stopped by day 21 4. 4 mg/kg/d in 3–4 divided doses for 4 d with no tapering (max: 180 mg/d) **Methyl prednisolone** • 30 mg/kg/d (max : 1 g/d) IV or PO for 3 d
Common adverse effects	Fever, flu-like symptoms, headache[5], mild hemolytic anemia and neutropenia	Fever, chills[b], nausea and vomiting, fall in hemoglobin[c]	Hyperglycemia, gastritis, hypertension, behavioral changes, fluid retention, weight gain
Rare adverse events	Aseptic meningitis (10 %), anaphylaxis, renal failure, risk of viral transmission	Massive IV hemolysis, secondary renal failure	
Advantages	Rapid increase in platelet counts	Less expensive than IVIg, shorter infusion	Not a blood product, low cost
Disadvantages	Long duration of infusion, cost, hospitalization, a blood product	Cannot be used in Rh negative or splenectomized individuals	Bone marrow examination suggested prior to steroids (not mandatory)
Efficacy (%)	70–80	70–80	60–70
Approximate cost of therapy for a 15 kg child	0.8 g/kg: Rs. 17,250 to 62,500 (5 g vial: Rs. 5750 to 25,000)	Rs. 15,000 (300 μg vial: Rs. 4990)	Oral prednisolone: Rs. 200 Methyl prednisolone: Rs. 2000

[a] Irrespective of platelet count, oral steroids should not be continued for >2–3 wk, even at low doses—to avoid toxic effects. [5] May result in suspicion of intracranial bleed and need for CT head to rule it out

[b] Infusion related side effects can be ameliorated with acetaminophen/ steroid premedication

[c] Obligatory hemolysis is inevitable with an average decline in Hb of 0.5–1 g/dL; most cases of hemolysis do not require medical intervention

- Spontaneous recovery
- Minor bleeding = observe