

Pediatric Cytopenia and Abnormal Bleeding

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Objectives

1. Identify and evaluate common cytopenias
2. Define abnormal bleeding and when to refer a patient for evaluation of a bleeding disorder



Definitions

- Know if your lab uses Pediatric Reference Ranges
- Anemia

Normal values for hematologic parameters in children

Age	Hemoglobin (g/dL)		Hematocrit (%)		MCV (fL)		RDW (%)	
	Lower limit	Upper limit	Lower limit	Upper limit	Lower limit	Upper limit	Lower limit	Upper limit
6 months to <2 years*	11.0 ^f	13.5	31	42	73	85	12.3	15.6
2 to 6 years	11.0 ^f	13.7	34	44	75	86	12.0	14.6
6 to 12 years	11.2	14.5	35	44	78	90	11.9	13.8
12 to <18 years								
Female	11.4	14.7	36	46	80	96	11.9	14.6
Male	12.4	16.4	40	51	80	96	11.9	13.7

1. Brugnara C, Oski FA, Nathan DG. Diagnostic approach to the anemic patient. In: Nathan and Oski's Hematology and Oncology of Infancy and Childhood, 8th ed, Orkin S, Nathan D, Ginsburg D, et al (Eds), Elsevier 2015. p.293



Anemia

- Case: 3 yo girl comes for a well-child check-up, thriving, without complaints and you obtain a routine hemoglobin check. The results come back with hemoglobin of 8 g/dL
- What next?
- Obtain a full CBC with a retic count



Anemia

- Mean corpuscular volume (MCV)
 - Microcytic
- Iron deficiency
 - Ferritin
 - Iron studies
- Thalassemia
 - Review newborn screen results
 - Hemoglobin electrophoresis
- Chronic inflammation
 - CRP
 - Ferritin



Anemia

- Mean corpuscular volume (MCV)
 - Microcytic
 - Iron deficiency
 - Thalassemia
 - Anemia of chronic inflammation
- Iron deficiency
 - Ferritin
 - Iron studies
- Trial of oral iron therapy
 - 3-4 mg/Kg/day divided BID
- If starting hemoglobin <8 g/dL will repeat CBC and retic in 1 week
- If starting hemoglobin >8 will follow-up in 1 month with repeat CBC and retic
- Once all RBC indices normal (hemoglobin, MCV) then will treat for an additional 2 months of iron until ferritin normalized
- Treatment directed at etiology (i.e. diet, heavy menstrual bleeding)
- Send patient to ED if:
 - Symptomatic anemia
- Refer to Hematology if:
 - Not responding to iron regimen
 - Etiology of iron deficiency not clear
 - Etiology of iron deficiency related to other hematologic concern



Anemia

- Mean corpuscular volume (MCV)
 - Microcytic
 - Iron deficiency
 - Thalassemia
 - Anemia of chronic inflammation
- Thalassemia
 - Review newborn screen results
 - Hemoglobin electrophoresis
- State assigned Hemoglobinopathy Educator
 - Reviews results with family
- Send patient to ED if:
 - Symptomatic anemia
- Refer to Hematology if:
 - Multiple or complex hemoglobinopathies
 - Sickle Cell, Sickle-Hemoglobin C, Sickle-Beta thalassemia, homozygous hemoglobin C, Hemoglobin D



Anemia

- Mean corpuscular volume (MCV)
 - Microcytic
 - Iron deficiency
 - Thalassemia
 - Anemia of chronic inflammation
 - Chronic inflammation
 - CRP
 - Ferritin
- Iron will not help and may add to inflammation
 - Determining cause of inflammation based on history and exam and refer based on this



Anemia

- Mean corpuscular volume (MCV)
 - Normocytic
- Reticulocyte count
 - Normal or low – infection (bacterial, viral, sepsis in general), chronic inflammation, drugs
 - Elevated – blood loss, hemolysis
 - Hemolysis – ↑LDH, ↓haptoglobin and ↑indirect/unconjugated bilirubin
- Refer to hematology
 - Normocytic anemia that persists for >6-8 weeks
 - Worsening normocytic anemia without identifiable cause
 - Any concern for hemolytic process



Anemia

- Mean corpuscular volume (MCV)
 - Macrocytic
- Reticulocyte count
 - Elevated reticulocyte can increase MCV
- Thyroid disease, Vitamin B12/Folate deficiencies, Drugs (antiepileptics), liver disease
- Refer to hematology
 - No identifiable cause including above work-up normal



Definitions

- Neutropenia and Infectious Risks
- 1000 – 1500: None
- 500 – 1000: Minimal – Mild
- 250 – 500: Moderate – Severe
(skin, mucous membranes)
- < 250: Severe
(sepsis, pneumonia, abscesses)



Neutropenia

- Case: 3 yo boy comes for an Emergency Room follow-up visit. He was in the ER with fever, rhinorrhea, cough. Was found to have human metapneumovirus with clear chest xray. Sent home with supportive care. He is doing overall better with no fever, but still with cough and persistent rhinorrhea and now with rash. You opt to get a CBC with diff with the only abnormality being an ANC of 550 cells/mcL.
- What next?



Neutropenia

- History and Physical Exam are most helpful
 - Asymptomatic – no history of recurrent infections, no fever, no growth abnormalities
 - Common symptoms present – post-viral recent or current history of cough, rhinorrhea, +/- fever, viral rash
- Repeat CBC in 1-2 months or sooner if any clinical changes
 - Anticipatory guidance for fever to families – go to ER to be evaluated
- Refer to hematology
 - Neutropenia persists beyond 2 months – at least 2 CBC with persistent neutropenia
 - Additional history or exam concerns



Neutropenia

- History and Physical Exam are most helpful
 - Symptomatic – fever without obvious source, limb pain, bleeding or petechial rash, recurrent bacterial infections (sinusitis, skin, pneumonia), unexplained weight loss, night sweats, organomegaly, unexplained lymphadenopathy, family history of recurrent infections or neutropenia, poor growth parameters, dysmorphic features (albinism, café-au-lait spots, abnormal thumbs, abnormal hair or nails), other cytopenias present*
- Additional labs to consider
 - Uric acid, LDH, other infectious etiologies (EBV, CMV, HIV) pending additional history
- Refer to hematology
 - Call Hem/Onc on-call to discuss this patient to determine timing of referral



Definitions

- Thrombocytopenia
- Normal 150 K/mcL – 450 K/mcL
- Increased risk of bleeding when <50 K/mcL
- Increases risk of spontaneous bleeding when <20 K/mcL
 - Except in cases consistent with immune thrombocytopenia purpura (ITP)



Thrombocytopenia

- Case: 13 yo boy comes for routine check-up, has been well with no complaints. Only new history is that he now eats a vegan diet. No exam findings of concern. You decide to get a CBC and only abnormality is a platelet count of 4 K/mcL.
- What next?



Thrombocytopenia

- Mean Platelet Volume (MPV)
 - Increased (>10) – think about peripheral destruction
 - Decreased (<5) – Wiskcote Aldrich syndrome
- Immature platelet fraction (IPF)
 - Increased – think about peripheral destruction/consumption
 - Low or normal – think about myelosuppression



Thrombocytopenia

- History and Physical Exam are most helpful
 - Asymptomatic – no bleeding, no fever, no growth abnormalities
 - Common symptoms present – post-viral recent or current history of cough, rhinorrhea, +/- fever, viral rash
- If completely asymptomatic – consider repeating within a few days to week
- Repeat CBC in 1-2 months or sooner if any clinical changes
 - Anticipatory guidance for bleeding to families – increased bruising, petechiae, prolonged >15 min
- Refer to hematology
 - Thrombocytopenia persists – at least 2 CBCs with persistent thrombocytopenia
 - Platelet count <20 K/mcL
 - Thrombocytopenia with bleeding symptoms
 - Additional history or exam concerns





Acute Immune Thrombocytopenia (ITP) Clinical Practice Guidelines

Introduction

Immune thrombocytopenia is the most common cause of symptomatic thrombocytopenia in children. ITP is characterized by isolated thrombocytopenia often occurring in the absence of identifiable and specific precipitants.

*The following guidelines are based on **clear evidence of ITP** from history, physical exam, and CBC with differential and without the following clinical or laboratory findings: fever, weight loss, bone pain, limp, joint pain or arthritis, jaundice, mouth sores, recurrent infections, hepatomegaly, splenomegaly, lymphadenopathy, skeletal or soft-tissue morphologic abnormalities, non-petechial rash, family history of low platelets or bleeding disorders, and other cytopenias (other than anemia explained by presentation) and/or abnormalities on the peripheral smear.





Acute Immune Thrombocytopenia (ITP) Clinical Practice Guidelines

Guidelines for Assessment

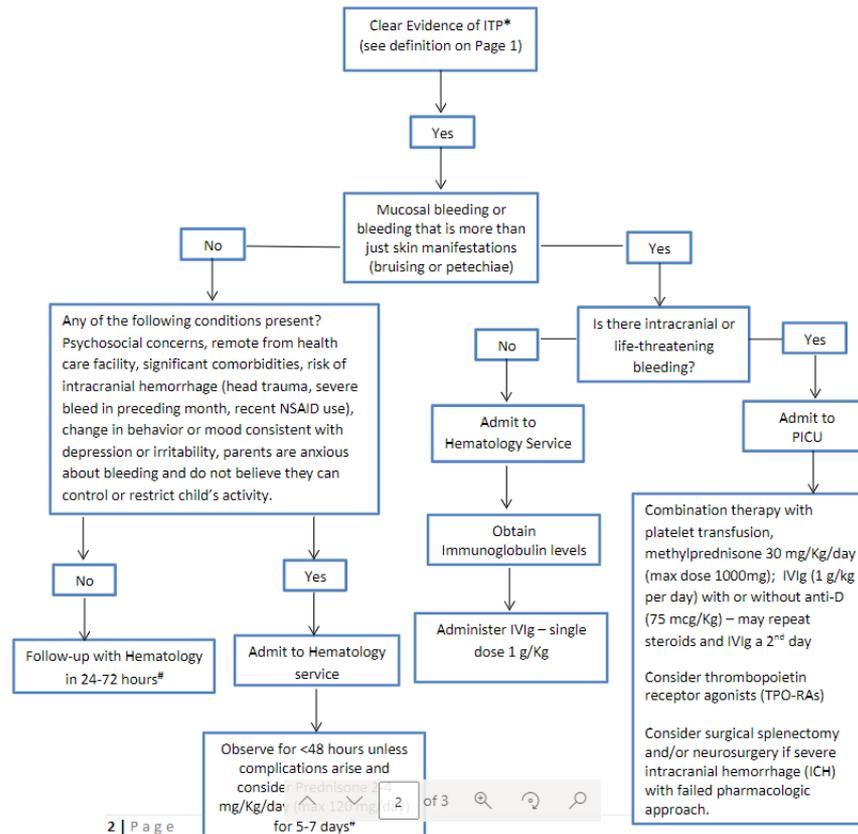
1. Laboratory testing to obtain at presentation
 - a. CBC with differential
2. Laboratory testing not necessary at presentation
 - a. Reticulocyte count
 - b. Rh blood typing
 - c. Direct antiglobulin (Coomb's) test (DAT)
 - d. Anti-nuclear antibody (ANA)
 - e. Complement level
 - f. Antiphospholipid antibodies
 - g. Thrombopoietin level
 - h. Immunoglobulin A, G, M levels¹
 - i. Bone marrow aspirate or biopsy
 - j. Helicobacter pylori testing
 - k. Hepatitis B or C testing
 - l. Viral testing including: EBV, CMV, HIV, parvovirus
 - m. Thyroid function testing

¹Recommended prior to IVIG therapy



Acute Immune Thrombocytopenia (ITP) Clinical Practice Guidelines

Management of ITP



Acute Immune Thrombocytopenia (ITP) Clinical Practice Guidelines

- <https://akronchildrens.sharepoint.com/sites/mykidsnet-mytools-clinicalpathways/Shared Documents/Forms/AllItems.aspx?id=%2Fsites%2Fmykidsnet-mytools-clinicalpathways%2FShared Documents%2F%28ITP%29 Clinical Practice Guidelines May 2021%2Epdf&parent=%2Fsites%2Fmykidsnet-mytools-clinicalpathways%2FShared Documents>

Abnormal Bleeding

- Recommend utilization of Bleeding Assessment Tools or Centers for Disease Control Guidance
 - Most useful in young adult women or older
 - In young children consider these tools and/or assessing family history utilizing similar questions to determine need for referral



Pediatric Bleeding Questionnaire

Score \ Symptom	-1	0	1	2	3	4
Epistaxis	-	No or trivial (≤ 5 per year)	> 5 per year OR > 10 minutes duration	Consultation only	Packing, cauterization or antifibrinolytics	Blood transfusion, replacement therapy or desmopressin
Cutaneous	-	No or trivial (≤ 1 cm)	> 1 cm AND no trauma	Consultation only	-	-
Minor wounds	-	No or trivial (≤ 5 per year)	> 5 per year OR > 5 minutes duration	Consultation only or Steri-strips	Surgical hemostasis or antifibrinolytics	Blood transfusion, replacement therapy or desmopressin
Oral cavity	-	No	Reported at least once	Consultation only	Surgical hemostasis or antifibrinolytics	Blood transfusion, replacement therapy or desmopressin
Gastrointestinal tract	-	No	Identified cause	Consultation or spontaneous	Surgical hemostasis, antifibrinolytics, blood transfusion, replacement therapy or desmopressin	-
Tooth extraction	No bleeding in at least 2 extractions	None done or no bleeding in 1 extraction	Reported, no consultation	Consultation only	Resuturing, repacking or antifibrinolytics	Blood transfusion, replacement therapy or desmopressin
Surgery	No bleeding in at least 2 surgeries	None done or no bleeding in 1	Reported, no consultation	Consultation only	Surgical hemostasis or antifibrinolytics	Blood transfusion, replacement therapy or desmopressin
Menorrhagia	-	No	Reported or consultation only	Antifibrinolytics or contraceptive pill use	D&C or iron therapy	Blood transfusion, replacement therapy, desmopressin or hysterectomy
Post-partum	No bleeding in at least 2 deliveries	No deliveries or no bleeding in 1 delivery	Reported or consultation only	D&C, iron therapy or antifibrinolytics	Blood transfusion, replacement therapy or desmopressin	-
Muscle hematoma	-	Never	Post-trauma, no therapy	Spontaneous, no therapy	Spontaneous or traumatic, requiring replacement therapy or desmopressin	Spontaneous or traumatic, requiring surgical intervention or blood transfusion
Hemarthrosis	-	Never	Post-trauma, no therapy	Spontaneous, no therapy	Spontaneous or traumatic, requiring replacement therapy or desmopressin	Spontaneous or traumatic, requiring surgical intervention or blood transfusion
Central nervous system	-	Never	-	-	Subdural, any intervention	Intracerebral, any intervention
Other *	-	No	Reported	Consultation only	Surgical hemostasis, antifibrinolytics or iron therapy	Blood transfusion, replacement therapy or desmopressin



Pediatric Bleeding Assessment

- “Other” category are: umbilical stump bleeding, cephalohematoma, post-circumcision bleeding, post-venipuncture bleeding, and macroscopic hematuria
- Refer to hematology
 - For score of >3
- [Microsoft Word - PBQ.doc \(wfh.org\)](#)



Screening Tool for Identifying Women with Menorrhagia for Testing and Evaluation for Underlying Bleeding Disorders

Instructions: Circle the appropriate response for each of the eight (8) questions below.

1. **How many days did your period usually last, from the time bleeding began until it completely stopped?**
 - i. Less than 7 days
 - ii. Greater than or equal to 7 days
 - iii. Don't know
2. **How often did you experience a sensation of "flooding" or "gushing" during your period?**
 - i. Never, rarely, or some periods
 - ii. Every or most periods
 - iii. Don't know
3. **During your period did you ever have bleeding where you would bleed through a tampon or napkin in 2 hours or less?**
 - i. Never, rarely, or some periods
 - ii. Every or most periods
 - iii. Don't know
4. **Have you ever been treated for anemia?**
 - i. No
 - ii. Yes
 - iii. Don't know
5. **Has anyone in your family ever been diagnosed with a bleeding disorder?**
 - i. No
 - ii. Yes
 - iii. Don't know
6. **Have you ever had a tooth extracted or had dental surgery?**
 - i. No (If no, go to question 7)
 - ii. Yes
 - iii. Don't know

a. Did you have a problem with bleeding after tooth extraction or dental surgery?

 - i. No
 - ii. Yes
 - iii. Don't know

7. **Have you ever had surgery other than dental surgery?**
 - i. No (If no, go to question 8)
 - ii. Yes
 - iii. Don't know

a. Did you have bleeding problems after surgery?

 - i. No
 - ii. Yes
 - iii. Don't know
8. **Have you ever been pregnant?**
 - i. No
 - ii. Yes
 - iii. Don't know

a. Have you ever had a bleeding problem following delivery or after a miscarriage?

 - i. No
 - ii. Yes
 - iii. Don't know

How to Use the Screening Tool

The screening tool is considered to be positive if 1 of the following 4 criteria were met:

1. The duration of menses was greater than or equal to 7 days **and** the woman reported either "flooding" or bleeding through a tampon or napkin in 2 hours or less with most periods;
2. A history of treatment of anemia;
3. A family history of a diagnosed bleeding disorder; or
4. A history of excessive bleeding with tooth extraction, delivery or miscarriage, or surgery

Sources:

Philipp CS, Faiz A, Dowling NF, et al. Development of a screening tool for identifying women with menorrhagia for hemostatic evaluation. *Am J Obstet Gynecol* 2008; 163:e1-163.e8.

Philipp CS, Faiz A, Heit JA, et al. Evaluation of a screening tool for bleeding disorders in a US multisite cohort of women with menorrhagia. *Am J Obstet Gynecol* 2011; 204:209.e1-7.

National Center on Birth Defects and Developmental Disabilities
Division of Blood Disorders



[NCDBBB Fact Sheet. \(cdc.gov\)](https://www.cdc.gov)



Akron Children's Hospital

Thank you

