A Practical Approach to Anemia in the Pediatric Patient

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Objectives

• List the most common causes of anemia in children and adolescents.
• Recognize that certain types of anemia are more common in certain age groups.
• Generate a differential diagnosis based on, age, MCV and clinical history.
• Select appropriate lab tests to begin a workup of anemia.

Anemia

• Use common sense, and think in global terms
  • RBCs being lost?
    • GI bleeding, menstrual loss (both often with Fe deficiency)
  • RBCs being made appropriately and then destroyed?
    • AIHA (elevated bili & retic, classic w/ hemolysis)
    • Hypersplenism (?liver dz w/ portal hypertension)
Anemia
- RBCs not being made?
  - Fe deficiency – not enough substrate; low retic
  - Transient erythroblastopenia of childhood (TEC) – transient marrow shut-off; zero retic
  - Marrow infiltration (other counts likely to be affected)
  - Aplastic anemia (WBC, plt also low; possible increased MCV)

Anemia
- RBCs not being made correctly, thus being destroyed?
  - Hereditary spherocytosis (elevated bili & retic)
  - RBCs made with wrong Hgb/enzyme defect, thus hemolyzing?
  - Sickle cell, thalassemia, G6PD

Anemia
- Similarly, think about what’s common, given the age and clinical presentation
  - Infants <12mos
    - Fe def is exceedingly RARE; think physiologic nadir if near 2 mos, ABO/Rh incompatibility if newborn, congenital anemia, G6PD def, α thal trait, leukemia (unlikely to present w/ isolated anemia)
Anemia

- Toddlers – many more possibilities
  - Fe def very common, TEC, Diamond-Blackfan Anemia, HS, previously undiagnosed sickle cell, α thal trait, G6PD def, HUS, leukemia

Anemia

- School age
  - Fe def possible, HS, α thal trait, AIHA, HUS, leukemia, GI blood loss
- Later school age/adolescent
  - Fe def common in menstruating ♀ (think twice about Fe def in males), AIHA, GI blood loss, leukemia

Hemoglobin values vary with age

<table>
<thead>
<tr>
<th>Age</th>
<th>Hb (gm/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn (cord blood)</td>
<td>13.8-20.0</td>
</tr>
<tr>
<td>Infancy 2-3 months</td>
<td>9.0 (term)</td>
</tr>
<tr>
<td>3-6 months</td>
<td>8.5 (low birth wt.)</td>
</tr>
<tr>
<td>6-12 months</td>
<td>9.5</td>
</tr>
<tr>
<td>Child 12-24 months</td>
<td>10.5</td>
</tr>
<tr>
<td>&gt; 24 months</td>
<td>11.5</td>
</tr>
<tr>
<td>Adolescence &gt; 13 years</td>
<td>12.0 (female)</td>
</tr>
<tr>
<td></td>
<td>13.5 (male)</td>
</tr>
</tbody>
</table>
Anemia

- Use the entire history and physical to your advantage
  - Diet, pica behaviors, living situation, family ethnicity & surgeries, frequent moves, neonatal history, menstrual history, viral history, GI blood loss, medications
  - Vitals, color, organomegaly, nodes

Anemia

- Labs
  - Hgb – how low?
  - Indices (MCV, particularly in comparison to Hgb, MCHC) and smear
  - Retic count!

- Others as indicated
  - Fe studies – Fe, TIBC, ferritin
  - Bili
  - Coomb’s
  - Lead level
  - Hgb electrophoresis
  - Osmotic fragility
**Differential Diagnosis of Anemia**

- **Divide into groups by size of cell (MCV)**

<table>
<thead>
<tr>
<th>Microcytic</th>
<th>Normocytic</th>
<th>Macrocytic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe-def.</td>
<td>Acute blood loss</td>
<td>Newborn</td>
</tr>
<tr>
<td>Thalassemia</td>
<td>Liver disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td>Sideroblastic</td>
<td>Renal disease</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Lead toxicity</td>
<td>Infiltrated marrow</td>
<td>Splenectomy</td>
</tr>
<tr>
<td>Hgb E</td>
<td>TEC</td>
<td>Trisomy 21</td>
</tr>
<tr>
<td>Inborn errors</td>
<td>Connective tissue</td>
<td>Reticulocytosis</td>
</tr>
<tr>
<td>Copper def.</td>
<td>Aplastic Anemia</td>
<td>Aplastic Anemia/MDS</td>
</tr>
<tr>
<td>Atransferrinemia</td>
<td>Infection</td>
<td>Vit B12/Folate</td>
</tr>
</tbody>
</table>

**Differential Diagnosis of Anemia**

- **Consider increased destruction versus decreased production based on reticulocyte count**

- **Production**
  - Dietary (Fe, B12, Folate)
  - Aplastic Anemia
  - Diamond-Blackfan
  - TEC
  - Bone Marrow infiltrate

- **Destruction**
  - Hemoglobin defects
  - Enzyme defects
  - Membrane defects
  - Immune-mediated

19 mo old male noted by his grandmother to be pale and fussy. Described as very picky, his diet is mainly string cheese, mac & cheese and milk. The child appears in no distress. He is slightly tachycardic with normal heart rhythm, no gallop, +systolic murmur, normal BP and good peripheral perfusion. CBC shows Hb=5.0 gm/dl, MCV 52fL, retic 1.6%.

What is the most appropriate clinical management?

1) Refer immediately to the closest hospital for 10cc/kg PRBC transfusion.
2) Schedule a slow transfusion with 5cc/kg of PRBC then start supplementation with oral iron.
3) Start the patient on a daily children’s chewable vitamin with Fe.
4) Obtain nutrition consult and start oral Fe at 3-6 mg/kg elemental Fe daily.
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Iron Deficiency Anemia

- Toddlers and adolescent females particularly susceptible
- Anemia of varying degree (can be severe), with low RBC and MCV and inadequate reticulocytosis (↓substrate)
- ↓Fe, ↑TIBC, nl to ↓ferritin

Iron Deficiency Anemia

- Treat with oral iron
  - 3-6 mg elemental Fe/kg/day in divided doses
  - 325 mg qd-bid (adolescents)
- Recheck CBC, retic in 2-3 wks
- No change - ↑ '?compliance, wrong dx (thal trait)
- If no obvious dietary or menstrual hx to explain the Fe deficiency, rule out occult GI blood loss
Which of the following sets of labs are consistent with iron deficiency anemia?

1) ↑RDW, ↓RBC#, ↑MCV
2) Normal RDW, ↑RBC#, ↓MCV
3) ↑RDW, ↓RBC#, ↓MCV

Thal trait vs. Fe-deficiency

- Remember, in thalassemia trait, all red cells are very small (↓MCV), but they're all the same size (nl RDW), and there is no production problem (nl to ↑RBC). There is marked discrepancy between Hgb value and MCV, whereas in Fe-def, these two values tend to go down at a similar rate.
The kicker – Fe-def and thal trait can coexist, so your history becomes very critical. Outside of the newborn period, electrophoresis is not particularly helpful.

A previously healthy 19 month old male gradually develops anorexia with decreased activity. Hgb 5.1 gm/dL, retic <0.1%, WBC 4,500, platelets 440,000, MCV 80. The most likely diagnosis is:

1) Iron deficiency anemia
2) Leukemia
3) Transient erythroblastopenia of childhood (TEC)
4) Diamond-Blackfan anemia
5) None of the above
Transient Erythroblastopenia of Childhood (TEC)

- Transient, self-limited red cell aplasia (in contrast to DBA) that typically lasts for a few weeks
- Age: 1-4 years
- Low Hgb 3-9 gm/dl, nearly absent retic count, normal MCV
- Mild neutropenia noted in some series
- Typical clinical course: anemia of 1-2 months’ duration, followed by complete recovery
- Treatment does not affect time to recovery.

Diamond Blackfan Anemia

- Progressive normochromic, macrocytic anemia in infancy or early childhood (90% diagnosed by age 1)
- 30-50% of patients with DBA have associated congenital abnormalities:
  - Craniofacial abnormalities
  - Neck anomalies
  - Thumb abnormalities
  - Genitourinary malformations
  - Pre- and postnatal growth failure

- Reticulocytopenia and elevated erythrocyte ADA
- Normal cellularity of the bone marrow with markedly decreased or absent erythroid precursors
- Treatment: Steroids, blood transfusions, stem cell transplant
A two-year-old girl who had prolonged neonatal jaundice is found to have a palpable spleen tip and the following lab data: Hb 10.0, retic 5.6%, WBC 6,000, platelets 320,000, MCHC 37, MCV 82, RDW 19. Which of the following will help in the diagnosis?

1) Osmotic fragility
2) Review of the peripheral blood smear
3) Careful family history
4) Review of peripheral blood smear of parents
5) All of the above

Hereditary Spherocytosis

- Common inherited hemolytic anemia, arising from defect in RBC skeletal membrane protein; nondeformable spherocytes are destroyed in spleen
- Varying anemia with ↑bili & retic, and ↑MCHC (due to relative cellular dehydration)
- Close attn to family history, patient’s and sibs’ neonatal histories (75% autosomal dominant)
Hereditary Spherocytosis

- Chronic stable hemolysis with exacerbations, often post-viral (watch out for parvo); may require transfusion
- Osmotic fragility test for diagnosis (tough when young; can test parents)
- No therapy needed unless h/o frequent, severe hemolysis → splenectomy (try to wait till age 5)
- Should be on folic acid supplement

Hereditary spherocytosis may be associated with all of the following except:

1) Low Hemoglobin
2) Increased MCHC
3) Low MCHC
4) Splenomegaly
5) Worsening anemia during parvovirus B19 infection
2 y/o boy who is allergic to PCN and cephalosporins presents with pallor, irritability 1 week after being treated for otitis. Child’s family is from Persia. Exam is notable for mild pallor with olive complexion. Hgb 6.2, MCV 82, retic 6.8%. Which of the following is false regarding this boy’s likely diagnosis?

1) Inheritance is X-linked.
2) Most cases are characterized by chronic mild hemolysis.
3) Only viral illnesses are known to precipitate hemolysis.
4) Hemolysis is intravascular.
5) Enzyme levels are variable over time.

9 year old male presents with history of fatigue, pallor and mild jaundice. He has recently been treated for pneumonia. Peripheral smear shows RBC agglutination. The most likely diagnosis is:

1) G6PD deficiency
2) Warm IgG autoimmune hemolytic anemia
3) Thalassemia
4) Cold IgM autoimmune hemolytic anemia
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Autoimmune Hemolytic Anemia

- Any age pt, but more common in school age +
- Normocytic anemia, sometimes dramatic, with ↑ bilirubin & reticulocytes + Direct Coomb’s (presence of Abs on RBCs)
- Possible viral hx
- Likely pallor due to abrupt onset; splenomegaly

Autoimmune Hemolytic Anemia

- Needs a peds hematologist
- Complex mgmt: steroids, IVIG, immunosuppressives, splenectomy, difficult transfusions; if lucky, resolves spontaneously
### Intravascular vs. Extravascular

<table>
<thead>
<tr>
<th>Intravascular</th>
<th>Extravascular</th>
</tr>
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<tbody>
<tr>
<td>AHTR</td>
<td>AIHA</td>
</tr>
<tr>
<td>Severe burns</td>
<td>DHTRA</td>
</tr>
<tr>
<td>Severe microangiopathy</td>
<td>Hemoglobinopathies</td>
</tr>
<tr>
<td>G6PD</td>
<td>HS</td>
</tr>
<tr>
<td>DIC</td>
<td>Hypersplenism</td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
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### Warm vs. Cold

<table>
<thead>
<tr>
<th>Warm</th>
<th>Cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>IgM</td>
</tr>
<tr>
<td>Coomb’s: IgG +/- complement</td>
<td>Coomb’s: complement only</td>
</tr>
<tr>
<td>Spleen</td>
<td>Liver</td>
</tr>
<tr>
<td>Bad</td>
<td>Good</td>
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