Anemia and Transfusion in Children
Anemia

- Defined by age-specific norms
- **History:** fatigue, pica, nutrition, growth, medications, blood loss, ethnicity, FH of splenectomy, cholecystectomy
- **PE:** vital signs, pallor, murmur, icterus, hepatosplenomegaly, systemic illness
- **Initial labs:** CBC, indices, retic count, blood smear, stool guiac, UA, bilirubin, BUN
Fig. 20.1 Oxygen dissociation curve showing the left shift of fetal haemoglobin compared with adult haemoglobin. Fetal haemoglobin has a higher affinity for oxygen.

Fig. 20.2 Changes in haemoglobin concentration with age, showing that the haemoglobin is high at birth and falls to its lowest level at 2–3 months of age.
# Normal Values

<table>
<thead>
<tr>
<th></th>
<th>HCT</th>
<th>WBC</th>
<th>PLTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>50-35%</td>
<td>18K</td>
<td>150-350K</td>
</tr>
<tr>
<td>Child</td>
<td>35-40%</td>
<td>4-15K</td>
<td>150-350K</td>
</tr>
<tr>
<td>Teen</td>
<td>40-45%</td>
<td>5-10K</td>
<td>150-350K</td>
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</table>
Fig. 20.3 Causes of anaemia in infants and children beyond the neonatal period.

**CAUSES OF ANAEMIA IN INFANTS AND CHILDREN**

- **Deficiency of haemopoietic factors**
  - Nutritional iron deficiency
  - Folate or, very rarely, B₁₂ deficiency
  - Excess tea ingestion

- **Disorder of haemoglobin synthesis**
  - Haemoglobinopathies – sickle cell, thalassaemia

- **Haemolysis**
  - Red cell enzyme deficiency – G6PD, pyruvate kinase
  - Red cell membrane defects – spherocytosis
  - Autoimmune haemolytic anaemia

- **Blood loss**
  - Gastrointestinal – gastro-oesophageal reflux, Meckel’s diverticulum, cow’s milk protein intolerance
  - Parasites – hookworm
  - Menstruation in adolescent females
  - Epistaxis
  - Iatrogenic – excessive venesection in infants
  - Bleeding disorders – haemophilia, von Willebrand’s disease (epistaxis, menorrhagia)

- **Bone marrow failure**
  - Aplastic anaemia – Fanconi’s
  - Acquired red cell aplasia – Diamond-Blackfan
  - Transient erythroblastopenia of childhood (TEC)

- **Infection/inflammation/chronic illness**
  - Malabsorption syndromes e.g. coeliac disease
  - Chronic inflammatory disorders e.g. juvenile idiopathic arthritis
  - Organ failure e.g. renal failure
  - Chronic infection
  - Malignant disease
  - Lead poisoning
# Anemia: Classification

<table>
<thead>
<tr>
<th>Retic Count</th>
<th>MCV Low</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Fe defic</td>
<td>Chronic Disease</td>
<td>Folic/B12 Defic</td>
</tr>
<tr>
<td></td>
<td>Pb, Al, Cu defic</td>
<td>JRA</td>
<td>Aplasia</td>
</tr>
<tr>
<td>Normal</td>
<td>Thal Trait</td>
<td>Acute Bleeding</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>Thalass- emia</td>
<td>Hemolysis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hgb C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Case History

- **History:** Tuana, a 2-yr-old Vietnamese child, was noted to be very pale when seen in the ER for a URI. CBC showed Hgb5.0, MCV 55, retics 1%, smear hypochromic, microcytic.
- **Diet:** fussy eater, no meat, cow’s milk 3 pints/day, eating soil when playing outside.
- **Rx:** Replacing some of the milk with iron-rich non-meat foods + oral iron raised her Hgb to 7.5 in 10 days.
• What are the most common pediatric problems affecting their red blood cells?
• What are the diagnostic and therapeutic options and what is their rationale?
• What are the current guidelines for transfusing children?
Mentzer Index

- MCV/RBC $> 13.5$ = Iron Deficiency
- MCV/RBC $< 11.5$ = Thal Minor
Iron Deficiency

• Maternal reserves last about 4 months
• Infants especially premies are at greater risk because of their rapid growth
• 50% of the iron is absorbed from maternal milk but only 10% from cow’s milk
• Infant formula and cereals must be fortified
• Vitamin C enhances, tea slows, absorption
Dietary Iron Sources

- **High in iron:** red meat, liver, kidney, oily fish (sardines)
- **Average iron:** beans, peas, fortified cereals, dark green veggies, nuts
- **Foods to avoid:** excess cow’s milk, tea, high-fiber (phytates inhibit absorption)
IRON REQUIREMENTS DURING CHILDHOOD

Term newborn
Body stores: 250 mg
- 75% in blood
- 25% in ferritin
and haemosiderin

Adult
Body stores: 4–5 g

Growth

Elemental iron requirement
1 mg/kg per day

Iron intake:
Breast milk: 1.5 mg/L, 50% absorbed
Infant formula: 5–9 mg/L, 10% absorbed
Cow's milk: 0.5 mg/L, 10% absorbed
Mixed diet: 4–9 mg/day, 10–15% absorbed
Iron Deficiency

- **Lab**: Hypochromic/microcytic anemia
- Low serum ferritin (total body stores)
- Low iron, transferrin, high TIBC
- **Therapy**: Give with meals, vitamin C
- **Children**: 6mg Fe/kg/day divided bid
- **Infants**: 3mg Fe /kg/day divided bid
- Give liquid iron through straw/dropper
Fig. 20.6 Investigations in iron deficiency. (Adapted from Nathan D G, Oski S H, Hematology of Infancy and Childhood, Saunders, Philadelphia, 1993.)
Hemolytic Anemia

- Increased RBC turnover
- **Causes:** membrane disorders, enzyme deficiencies, immune destruction, hemoglobinopathies, DIC, HUS
- **Clinical:** ethnicity, neonatal jaundice, drug- or infection-induced, h/o transfusions, FH
- **Labs:** indirect bili, retics high, haptoglobin (low), PK/G6PD (low), osmotic fragility (high), CT (+ve), Hgb EPS (SSD, Thal)
Fig. 20.7
Diagnostic approach to haemolytic anaemias.

- **Intracorpuscular**
  - Inherited problem with red cells
  - Haemoglobinopathies (e.g., sickle cell disease, thalassemia)
  - Red cell membrane defects (e.g., hereditary spherocytosis)
  - Red cell enzyme defect (e.g., G6PD deficiency, pyruvate kinase deficiency)

- **Red cell morphology**
  - Fragments: Indicates cell destruction
  - Spherocytes: Indicates red cell deformation

- **Fragments**
  - Positive: Indicates presence of fragmented red cells
  - Negative: Indicates absence of fragmented red cells

- **Direct antiglobulin test**
  - Negative: Indicates absence of antibody against red cells
  - Positive: Indicates presence of antibody against red cells

- **Extracorpuscular**
  - Acquired problem outside red cells
  - Parasites, e.g., malaria
  - Bacterial toxins
  - Flow disturbance, e.g., valve prosthesis

- **Autoimmune haemolytic anaemia**
  - Cold – viral
  - Warm – auto-immune

- **Other**
  - Liver and renal failure
Case History

- **History**: Shamorrow, a 9-year-old girl with known SSD, presented with worsening chest pain for 6 hrs; **PE**: T39.7, labored breathing, reduced breath sounds both bases;

- **Labs**: Hgb 5.6gm, arterial PO2 70, CXR bilateral basal basal consolidation; BC negative

- **Management**: O² by CPAP, ceftriaxone + zithromycin, exchange transfusion x 1, opiate analgesics. Good recovery
Sickle Cell Disease

- Homozygous SS state from 2 beta-globin chains having a single amino acid substitution (glutamine for valine)
- 1 in 12 African Americans carries trait; the trait rarely causes symptoms
- SS hemoglobin molecule is deformed by deoxygenation, cold, dehydration, acidosis and stress of all kinds
Sickle Cell Disease

• **Dx:** newborn screening; sickledex and sickle prep may give false negative result;

• **Complications:** pain, sequestration, aplasia, sepsis, osteomyelitis, priapism, acute chest syndrome, gall stones, delayed puberty, cardiac, renal disease

• **Pain crises:** hydration, oxygenation, warmth, NSAIDS, opiates, transfusion, exchange tx, systemic antibiotics;
### Clinical Manifestations of Sickle Cell Disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>Moderate (usually Hb 6-8 g/dl) with clinically detectable jaundice from chronic haemolysis</td>
</tr>
<tr>
<td>Painful crises</td>
<td>Vaso-occlusive crises causing pain may affect all organs of the body with varying frequency and severity. A common mode of presentation in late infancy is hand-foot syndrome, in which there is dactylitis with swelling and pain of the fingers and feet from vaso-occlusion (Fig. 20.12). The bones of the limbs and spine are common sites, whereas cerebral and pulmonary infarction are uncommon but more serious. The commonest presentation of cerebral infarction is acute hemiparesis from blockage of the medium to large arteries, unlike vaso-occlusion in the small vessels elsewhere in the body. Vascular necrosis of the femoral heads may also occur.</td>
</tr>
</tbody>
</table>
| Other crises       | Associated with a further drop in the haemoglobin level:  
|                    | 1. Haemolytic crises  
|                    | 2. Aplastic crises, where the haemoglobin can fall precipitously, are most often caused by parvovirus infection  
|                    | 3. Sequestration crises, with accumulation of sickled cells, can cause marked, sudden splenic enlargement, abdominal pain and circulatory collapse |
| Infection          | Autosplenectomy, due to splenic infarction during infancy, markedly increases the susceptibility to infection from encapsulated organisms such as pneumococci and *Haemophilus influenzae*. There is also an increased incidence of osteomyelitis caused by *Salmonella* and other organisms. The risk of overwhelming sepsis is most common in early childhood. |
| Priapism           | Needs to be treated promptly with exchange transfusion, as it may lead to fibrosis of the corpora cavernosa and subsequent erectile dysfunction |
| Splenomegaly       | Common in young children, but becomes less frequent in older children |
| Long-term problems | Short stature and delayed puberty  
|                    | Adenotonsillar hypertrophy causing sleep apnoea syndrome leading to nocturnal hypoxaemia, which can cause vaso-occlusive crises  
|                    | Cardiac enlargement from chronic anaemia  
|                    | Heart failure from uncorrected anaemia  
|                    | Renal dysfunction – may result in enuresis because of failure to concentrate urine  
|                    | Gallstones – due to excessive bilirubin production  
|                    | Leg ulcers |
SSD: Preventing Infection

- Parental education the most important
- Penecillin prophylaxis: newborn until aged 6
- Continue indefinitely after splenectomy
- Pneumococcal vaccine at 2 and 5 years + conjugate vaccine
- Meningococcal vaccine at 2 years
- Hepatitis vaccine x 3
- Ensure Hib series is completed
**CLINICAL FEATURES AND COMPLICATIONS OF β-THALASSAEMIA MAJOR**

**Pallor**

**Jaundice**

**Bossing of the skull**

**Maxillary overgrowth**

**Splenomegaly**

**Need for repeated blood transfusions**

Complications shown in Figure 20.17

**Fig. 20.16** Facies in β-thalassaemia showing maxillary overgrowth and skull bossing.

**Fig. 20.17** Complications of multiple blood transfusions.

- **Iron deposition – the most important**
- **Heart – cardiomyopathy**
- **Liver – cirrhosis**
- **Pancreas – diabetes**
- **Endocrine gland – failure**
- **Skin – hyperpigmentation**

- **Antibody formation – now uncommon**
  - Red cell antibodies
  - HLA antibodies

- **Infection – now rare**
  - Hepatitis (blood is now screened for hepatitis B and C)
  - HIV infection (blood is now screened)
  - Malaria

- **Venous access**
  - Multiple infusions and blood samples
Fig. 20.14 Ethnic origin of patients with thalassaemia.
Bone Marrow Disorders

• Transient Suppression (Parvovirus, CMV, EBV, HHV-6)
• Aplastic/Hypoplastic States - Blackfan-Diamond, Fanconi, TEC
• Myelodysplasia
• Malignant Infiltration
Transfusion in Children
Blood Volume (ml/kg)

- Pre-terms: 100
- Term: 85
- 12 months: 70
- 3 years: 75
- 6 years: 80
- 8 years - adult: 70-90
Red Cell Transfusion

- **Indications:** Acute blood loss (10-15%), improving oxygenation, volume expansion
  Packed RBC: HCT 60-70%; always type & crossmatch if poss, otherwise O negative;
- 10 ml/kg, slower after acute vol depletion
- Filter leucodepletion: Reduces risk of CMV infection (>99%), sensitization reactions
- Radiation (25 Gy): prevents lymphocyte engraftment, GVHD
- Washing: prevents urticarial and febrile reactions
Platelet Transfusion

- **Indication**: Severe thrombocytopenia not due to increased destruction
- Platelet count <10K; <50K before surgery
- Pooled concentrates: 8-10 donors
- Single-donor: pheresis product for allo-immunized non-responding patients
- 2 units of platelets per 10 kg body weight will raise platelet count to 60K
- Washing or WBC depletion reduces platelet content markedly
Other Transfusion Products

- **FFP**: contains all factors except platelets
- Anticoagulant factors AT3, Pr C, S
- DIC, HUS, liver failure, Vit K deficiency
- 15 ml/kg; not to simply expand volume
- **Cryoprecipitate**: VWD, uremia, fibrinogen and factor XIII deficiency
- Monoclonal VIII and IX: derived from pooled human blood, being replaced by (more expensive) recombinant factors
Complications of Transfusions

- Acute hemolytic reactions: most often major blood group incompatibility; signs of shock, DIC, hemoglobinuria, Coombs Test positive
- Delayed hemolysis: minor RBC antigens
- Febrile non-hemolytic: transfused WBC antigens; premedicate with antipyretics, steroids, antihistamines; leuko-deplete next time
- Urticaria: reaction to donor proteins; wash unit for transfusion next time
- Infection: CMV, hepatitis, HIV, sepsis
Ruby Red

- Her body fragrant from alveolar showers,
- floats forth our curvy spheroid Ruby Red;
- her cheeks aglow with O2’s heartening powers,
- she charts her course for that far capillary bed.
- The rosy roller rides the aortic road,
- unmindful of her distant splenic fate,
- through arteriolar backwoods bears her load -
- the wastrel CO2 recoils too late.
- But macrocytic changes lie ahead,
- and days of crenation speedily ensue;
- she’s targeted for pyknosis, so ‘tis said;
- our once pink heroine fades a warning blue.
- And so poor Ruby meets her final test,
- in gentle hemolysis rolled to rest.