Diploma in Child Health
HAEMATOLOGY LECTURE
UCT School of Child and Adolescent Health 2008

A Davidson, F Desai, M Hendricks
Haematology - Oncology Service
Red Cross Children’s Hospital
STRUCTURE OF THIS MODULE

■ UTILISE ONLINE LECTURE MATERIAL
  ■ Study Lecture Notes
  ■ Try to Solve Cases
  ■ Use References

■ ATTEND INTERACTIVE TEACHING SESSION
  ■ Come to the Lecture if possible

■ AT THE BEDSIDE
  ■ Utilise this approach in the clinical setting
Anaemia in Childhood

A Davidson, F Desai, M Hendricks
Red Cross Children’s Hospital
ANAEMIA

Simple:
- only the RBC’s are involved.

Complex:
- other cell lines such as white cells or platelets are involved. Suggests BM infiltration or hypoplasia. Refer to Paediatric Haematologist for Bone Marrow Aspiration.
<table>
<thead>
<tr>
<th>Age</th>
<th>Hb g/dl</th>
<th>MCV fl</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 2 weeks</td>
<td>14.0</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>6 weeks</td>
<td>9.5</td>
<td>80-96</td>
</tr>
<tr>
<td>3 months</td>
<td>10.0</td>
<td>72-96</td>
</tr>
<tr>
<td>6 - 18 months</td>
<td>11.0</td>
<td>70-96</td>
</tr>
<tr>
<td>18 - 48 months</td>
<td>11.5</td>
<td>75-96</td>
</tr>
<tr>
<td>4 - 12 years</td>
<td>11.5</td>
<td>76-96</td>
</tr>
<tr>
<td>&gt; 12 years</td>
<td>12-14</td>
<td>78-96</td>
</tr>
</tbody>
</table>
What Kind of Anaemia is it and what is the Cause?

- Low MCV
  - Microcytic hypochromic anaemia
  - Fe Deficiency is the most likely

- High MCV
  - Macrocytic anaemia
  - Rare ... Folate or B12 deficiency are the commonest causes
What Kind of Anaemia is it and what is the Cause?

- Normal MCV
  - Normocytic anaemia

- High Reticulocyte count
  - Blood loss
  - Haemolysis

- Low Reticulocyte count
  - Marrow hypoplasia
  - Chronic disease
ANAEMIA

Low Hb only

MCV

LOW

High

NORMAL

Clinical setting Raised RDW

↓ Folate / B12

Retics ↑

Retics ↓

↓ Iron

Yes

NO

Other Eg. Thal

Low Hb AND Low WCC or Plts

Marrow suppression / infiltration

Aplastic Anaemia Acute Infection Disseminated TB Malignancy

Normal

Chronic Inflammation Renal disease Parvovirus infection

↓ Iron and folate

Haemolysis

Urine dipstix Smear Coombs Bilirubin

Acute Blood loss

Coombs +

Auto- or Iso-Immune

Hb or Enzyme abn

Coombs -
MICROCYTIC HYPOCHROMIC ANAEMIA

- Commonest anaemia in childhood
- Often an incidental pick up
- Usually due to Fe deficiency
Causes of Iron Deficiency

- Inadequate Intake
- Increased Demand
- Blood Loss
- Impaired Absorption

MICROCYTIC ANAEMIA
Dietary Iron in Infants

- Requirements: 1mg/kg/day full term infants
  2mg/kg/day low birthweight babies

- Breast and unfortified cows milk equally low in iron (0.5 -1.5mg/l) but infants absorb 49% of iron from breast milk and only 10% from cows milk.
Increased Iron Demand

- Children are particularly susceptible during periods of rapid growth.

- At risk are:
  - Low birth weight babies
  - Premature Infants
  - Twins
  - Adolescents

MICROCYTIC ANAEMIA
Blood Loss - Sites

- GIT
- Nose: Recurrent Epistaxis
- Uterus: Menorrhagia in adolescent girls
- Kidney: Haematuria
- Lungs: Idiopathic pulmonary heamosiderosis

MICROCYTIC ANAEMIA
Blood Loss from Gut

- Often occult

Causes include:
- Gastritis - drug ingestion e.g. aspirin
- Milk Allergy
- Intestinal parasites e.g. Trichuris
- Anatomic GIT lesions e.g. hiatus hernia, Meckel’s diverticulum, varices
- Inflammatory Bowel Disease

MICROCYTIC ANAEMIA
Impaired Absorption

- Rare cause of Iron deficiency in children

- May result from:
  - Malabsorption syndromes
  - Severe prolonged diarrhoea
  - Inflammatory bowel disease

MICROCYTIC ANAEMIA
Haematologic Findings in Iron Deficiency

- **Hb:** Low
- **RBC Indices:**
  - Low MCV
  - Wide red cell distribution width (RDW)
- **Blood Smear:** Hypochromia, microcytosis
The blood smear shows iron deficiency anemia with microcytic and hypochromic red cells.
Therapeutic Trial of Oral Iron

- Provided examination reveals only pallor and no other abnormality:
  - Check the diet is adequate
  - Look for stool occult blood loss
  - Treat with Iron (elemental Fe 3mg/kg/day)

MICROCYTIC ANAEMIA
Response to Iron Therapy

- Subjective improvement
- Reticulocytosis
  - 5-10% maximal at 5 -10 days
- Hb Rise
  - from about 5 days

MICROCYTIC ANAEMIA
Haemoglobin Rise

- The more severe the anaemia the greater the daily increment
  
- 0.25 - 0.4 g/dl/day from 5 to 18 days
  
- Thereafter 0.1 g/dl/day
  
- By 18 days Hb reaches midway between initial and normal Hb
Management Iron Deficiency

- Continue iron therapy at full dose until Hb is normal.
- Then continue at full dose for a further 6 weeks to replenish iron stores.
Poor Response to Iron

- Is the child iron deficient?
- Do iron studies
Iron Studies in Iron Deficiency

- Low serum ferritin (reflects body iron stores)
  This is the most reliable and easily available test.
- Low serum iron and percentage iron saturation
- Elevated free erythrocyte protoporphyrin

MICROCYTIC ANAEMIA
Poor Response to Iron

LOW FERRITIN

- Check compliance.
- Check the dose and the product.
- Look for occult blood loss.
What is Appropriate Iron Therapy?

- Recommended: Oral ferrous iron  
  e.g. ferrous gluconate 3-6mg/kg/day

- Enteric coated tablets and sustained release capsules should be avoided in children. They ensure transit of iron beyond the site of maximum absorption.
Poor Response to Iron

NORMAL OR HIGH FERRITIN

- The diagnosis of iron deficiency is wrong

- Other causes of microcytic anaemia:
  Thalassaemia trait
  Chronic inflammatory disease
  Sideroblastic Anaemia
  Lead poisoning
  Copper Deficiency

MICROCYTIC ANAEMIA
NORMOCYTIC ANAEMIA

- High Reticulocyte count
  - Blood loss
  - Haemolysis

- Low or Normal Reticulocyte count
  - Marrow hypoplasia
  - Chronic disease
Congenital Haemolytic Anaemia

- Membrane anomalies
  - Hereditary Spherocytosis, Elliptocytosis

- RBC Enzyme Deficiencies
  - G6PD or PK deficiency

- Haemoglobinopathies
  - Thalassaemia or Sickle Cell Syndromes

NORMOCYTIC ANAEMIA
The blood smears show hereditary elliptocytosis with numerous elliptocytes and smaller numbers of ovalocytes (A), and hereditary spherocytosis with numerous spherocytes (C).
The blood smears show acute haemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficiency, with a bite cell (A) and blister and contracted cells (B).
Thalassaemia

The typical facies of a Thalassaemia patient. The malar prominence is the result of extramedullary haematopoiesis.
The blood smear shows sickle cell anaemia with numerous sickle cells and as well as a nucleated red cell.
Acquired Haemolytic Anaemia

- Isoimmune
  - Haemolytic disease of newborn
  - Incompatible blood transfusion

- Autoimmune
  - Idiopathic
  - Infections
  - Collagen diseases
  - Malignancy
Clinical Features of Haemolysis

- Pallor and Jaundice
- Splenomegaly
- Dark urine

- Check family history for anaemia, jaundice or gallstones

NORMOCYTIC ANAEMIA
Laboratory Features of Haemolysis

- **Serum**
  - Unconjugated Hyperbilirubinaemia
  - Elevated Lactic Dehydrogenase
  - Decreased Haptoglobin

- **Urine**
  - Urobilin
Haemolytic Anaemia: Establishing the Cause

- Coombs Test
  - if negative excludes acquired causes.

- Blood Smear
  - look for spherocytes, sickle cells.

- Haemoglobin Electrophoresis
  - RBC enzyme assays and osmotic fragility.

NORMOCYTIC ANAEMIA
Anaemia of Chronic Disease

- Infections
  - Bronchiectasis  TB  HIV

- Renal Disease

- Chronic Inflammatory Disease

NORMOCYTIC ANAEMIA
MACROCYTIC ANAEMIA

- Folate Deficiency
  - Severe malnutrition
  - Goats milk
  - Drugs e.g. cotrimoxazole, anticonvulsants

- B12 Deficiency
  - Pernicious anaemia
  - Blind loops and Short bowel syndrome
  - Isolated B12 Malabsorption
The blood smear shows macrocytic anaemia with anisocytosis, macrocytosis and a hypersegmented neutrophil.
MACROCYTIC ANAEMIA

- Do Folate and Vitamin B12.
- Refer patients with low Serum B12 to a haematologist.
IN CONCLUSION

- Anaemia is a symptom and not a diagnosis
- Find and treat the cause
- Shot Gun Therapy (Iron, folate, B12 and blood transfusion) is wrong

*The correct diagnosis is delayed*
ANAEMIA CLINICAL CASES
THANDI  Aged 8 years

- History: Fatigue and recurrent nose bleeds for 4 weeks.
- Examination: Pale with purpura.
  No adenopathy or hepatosplenomegaly.
- FBC: Hb 7.2  MCV 85  Plts 80  WCC 2.1  Retics 0.1%.
  Differential: N 80%  M 10%  E 2%

- What type of anaemia is this?
- What is the differential diagnosis?
- What investigation is essential?
CLINICAL CASES

XOLA  Aged 8 years

- History: Noted to be pale when he presented with a URTI.
- Examination: Wt 20kg. Systems normal.
- FBC: Hb 6  MCV 68  RDW 24  WBC 12  Plt 250  Normal diff.
- Iron deficiency suspected ...
  treated with Fe Gluconate (20mg elemental Fe for 4 weeks)
- Repeat FBC: Hb 6.8  MCV 68.
- Stool occult blood negative X 2. Taking medication properly.

What is the most likely cause of the poor response?
How would you handle the problem?
THEO  Aged 5 years

- History: Presented with tiredness.
- Examination: Pale, not jaundiced. 2cm splenomegaly.
- FBC: Hb 7  MCV 65  RDW 12.
- Treated with iron. No response after three weeks.
- Repeat FBC: Hb 7  MCV 65  Retics 5%.
- Stool occult blood negative. Serum ferritin normal.

Does he have iron deficiency?
How would you investigate further?
CLINICAL CASES

CINDY  Aged 10 years

- History: Presented with epigastric pain and lethargy.
- FBC: Hb 6  MCV 60  RDW 26.

What type of anaemia is this?
What are the possible causes in this child?
What investigations would you do?
CLINICAL CASES

SINOXOLO  Aged 6 years

- Transfused on two occasions for recurring anaemia. Now presents with symptoms of cardiac failure.
- Examination: Below 3rd centile for height and weight.
  - Generalised adenopathy and enlarged parotids.
  - Pulse 150 reg. Cardiomegaly with signs of CCF.
  - Dull to percussion left lower lobe with bronchial breathing.
  - 4cm firm liver and 2cm firm spleen.
- FBC: Hb 3.2  MCV 88  WBC 5.2  Plt 250  Retics 0.1%.

**What type of anaemia is this? What are the possible causes?**
**How would you investigate further?**
WENDY  Aged 8 years

- Presented in a rural town with acute abdominal pain.
- Diagnosis: Acute Appendicitis ... Uninflamed appendix removed.
- 24 hours later noted to be pale and jaundiced.
- FBC: Hb 3.2  MCV 90  Retics 10%.
- Chemistry: Total BRN 70 Conjugated BRN 10.

- *What is in the differential diagnosis?*
- *What investigations would you do?*
CLINICAL CASES

STEPHEN  Aged 18 months

- Apathetic and eating poorly for a month.
- FBC:  Hb 5.4  MCV 102  WBC 12.1  Plt 200.

- What type of anaemia is this?
- What investigations would you do?
Investigating Bleeding Disorders in Childhood

A Davidson, F Desai, M Hendricks
Red Cross Children’s Hospital
The History
Four important Questions

- Is the child a bleeder?
- What type of bleeding is it?
- How severe is the disorder?
- Is it inherited?
Is The Child a Bleeder?

- Bruises at abnormal sites
- Any spontaneous bleeding
- Bleeding disproportionate to degree of trauma
- Prolonged bleeding from cuts
- Haemorrhage following dental extraction / surgery
Types of Bleeding

Thrombocytopenia
- Epistaxis
- Mucus Membranes
- Petechiae
- Small bruises
- GIT
- Menorrhagia

Coagulation defect
- Deep seated haematomas
- Haemarthrosis
- Renal
Screening Tests For Bleeding Disorders

- Platelet Count
- INR
- PTT
- Bleeding Time
## Causes of Thrombocytopenia

<table>
<thead>
<tr>
<th>Diminished Production</th>
<th>Peripheral Consumption</th>
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<tbody>
<tr>
<td>Aplastic Anaemia</td>
<td>ITP</td>
</tr>
<tr>
<td>Marrow Infiltration</td>
<td>Drug Induced</td>
</tr>
<tr>
<td>Selective Depression (Drugs)</td>
<td>DIC</td>
</tr>
<tr>
<td></td>
<td>Cavernous Haemangioma</td>
</tr>
<tr>
<td></td>
<td>Massive Blood Transfusion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelet Sequestration</th>
<th>Ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersplenism</td>
<td>Thrombopoiesis</td>
</tr>
<tr>
<td></td>
<td>B12 or Folate Deficiency</td>
</tr>
</tbody>
</table>

- **Diminished Production:** Aplastic Anaemia, Marrow Infiltration, Selective Depression (Drugs)
- **Peripheral Consumption:** ITP, Drug Induced, DIC, Cavernous Haemangioma, Massive Blood Transfusion
- **Platelet Sequestration:** Hypersplenism
- **Ineffective Thrombopoiesis:** B12 or Folate Deficiency
Congenital Disorders of Platelet Function

- Thrombasthaenia
- Storage pool disease
- Abnormal release mechanism
- Bernard-Soulier Syndrome

⇒ Suspect when platelet count is normal and bleeding time prolonged. Same situation in vWD but PTT usually also prolonged
Acquired Disorders Causing Defective Platelet Function

- Scurvy
- Uraemia
- Drugs
  - e.g. Aspirin, Antihistaminics, Cephalosporins, Penicillins
- Collagen Disorders
- MDS and Leukaemia
- Hypothyroidism
- Viral infections
CLOTTING CASCADES

INTRINSIC

CONTACT ACTIVATION

EXTRINSIC

TISSUE THROMBOPLASTIN

INR

PTT

COMMON

X

V

Prothrombin

Fibrinogen

FIBRIN
Assessment of Coagulation

**INR Normal / PTT Prolonged**
- Haemophilia A or B
- von Willebrand Disease

⇒ Do Factor VIII Levels ... if normal check Factor IX

**INR Prolonged / PTT Prolonged**
- Liver Disease
- Vitamin K Deficiency
- Haemorrhagic disease of the Newborn
- DIC
Assessment of Coagulation

Normal PTT with Prolonged INR
Factor VII Deficiency

⇒ Very Rare
Haemophilia

- Incidence +/- 1 in 5000 males
- Haemophilia A 80-85%
- Haemophilia B 10-15%
- Sex-linked inheritance
- High spontaneous mutation rate = 20-30%
- DNA-based analysis of factor VIII is available to characterise genotype of carriers and affected males
## Relationship of Factor Levels to Severity of Clinical manifestations of Hemophilia A and B

<table>
<thead>
<tr>
<th>Type</th>
<th>% Factor VIII/IX</th>
<th>Type of Haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>&lt;1</td>
<td>Spontaneous; Haemarthroses and deep tissue haemorrhages</td>
</tr>
<tr>
<td>Moderate</td>
<td>1-5</td>
<td>Gross bleeding following mild to haemarthrosis; seldom spontaneous haemorrhage</td>
</tr>
<tr>
<td>Mild</td>
<td>5-20</td>
<td>Severe haemorrhage only following moderate to severe trauma or surgery</td>
</tr>
<tr>
<td>High-risk carrier females</td>
<td>30-50</td>
<td>Gynaecologic and obstetric hemorrhage</td>
</tr>
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</table>
Von Willebrand Disease

- 1% of population

- Disorder of protein (von Willebrand factor)
  - Responsible for adherence of platelets to damaged endothelium

- First described by Erik von Willebrand in 1925

- Pattern:
  - Mucocutaneous bleeding
  - Post-traumatic and post-surgical bleeding

- Heterozygous disorder (variety of genetic defects)
  - Usually autosomal dominant

- Lab Workup: Prolonged BT
  - Prolonged PTT
  - Decreased vWF
  - Decreased VIII

- Spectrum: Type I (mild AD … 65-80%) to Type III (severe AR)
Laboratory investigations must be assessed in their clinical context.

Negative laboratory results in the face of a severe clinical history of bleeding means that the patient has not been fully investigated.

Remember Factor XIII deficiency and recheck for vWD.
BLEEDING DISORDER
CLINICAL CASES
SIVIWE  Aged 6 years

- Presents with recurrent bruising on the shins.
- Grandmother had severe epistaxis at the age of 50.

*How likely is this to be a bleeding disorder?*
*What points are important in the history?*
*What screening tests would you do?*
CLINICAL CASES

- MARIA  Aged 3 years
  - 3 day history of fever and vomiting.
  - Investigations:  Hb 8  MCV 80  WCC 20  Plt 85.
    \[\text{INR 2.1  PTT 48  Fibrinogen 0.9.}\]
  - What is the likely diagnosis?
  - What is the appropriate management?
TIMMY  Aged 5 months

- 3 month history of jaundice and pale stools.
- Investigations: Hb 9  MCV 80  WCC 10  Plt 120.
  INR 1.8  PTT 55  Fibrinogen 1.1.

- What is the likely diagnosis?
- What tests would confirm the diagnosis?
NELISWA  Aged 3 years

- Recent URTI. One day history of petechiae and purpura.
- Examination: Well looking child. Multiple petechiae.
  No nodes or spleen.
- Investigations: Hb 11.5  WCC 7  Plt 4.

What is the likely diagnosis?
What is the most important investigation to confirm this?
What other investigations should be done?
CLINICAL CASES

NELISWA
Aged 3 years
NELISWA
Aged 3 years

This bone marrow slide shows increased megakaryocytes ...

One is undergoing cytoplasmic budding
MICHAEL  Aged 5 years

- Swollen left knee following trauma.
- Seen in SOPD – blood aspirated. Treated with antibiotics.
- Returned 3 weeks later: Left knee still swollen, tender, ↓ROM.
- Aspirated again – blood.
- Investigations: Hb 10  MCV 86  Plt 444  INR 1  PTT 80.4.

- What is the likely diagnosis?
- What is the inheritance of this condition?
- What investigations are required to prove the diagnosis?
Acute haemarthrosis.
CLINICAL CASES

- MICHAEL  Aged 5 years
CLINICAL CASES

SARAH  Aged 2 years

- Seen at Trauma Unit.
- Ongoing bleeding from laceration on the tongue.
- Examination: Pale. Bruise on forehead.
  - Bleeding laceration on tongue.
- Investigations: Hb 7.9  MCV 69  Plt 400  INR 1  PTT 50.

- What is the likely diagnosis?
- What is the inheritance of this condition?
- What investigations are required to prove the diagnosis?
CLINICAL CASES

JAMIE  Aged 21 months

- Oozing from a small cut in the mouth for 3 days.
- Seen by GP – treated with an adrenaline injection.
- Examination: Pale. Bleeding from a 1cm laceration on palate.
- Investigations: Hb 10  MCV 70  Plt 381  INR 1  PTT 30.

- What is the differential diagnosis?
- What tests should be done?
REFERENCES
References


References

