

Slide 3 - April 2008 / Cycle 32

ERYTHROPOIESIS AND GENERAL ASPECTS OF ANAEMIA

Please read this bit first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT00025**.

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

FORWARD

This clinical page may not exactly match the slide due to the need to vary the clinical descriptions for CPD purposes.

Scanned and edited from Essential Haematology by Hoffman, Pettit and Moss. Blackwell (2001).

Reticulocyte count.

The normal count is 0.5 – 2.5%, and the absolute count $25-125 \times 10^9 / l$. This should rise in anaemia because of erythropoietin increase and be higher the more severe the anaemia. This is particularly so when there has been time for erythroid hyperplasia to develop in the marrow as in chronic haemolysis. After an acute major haemorrhage, there is an erythropoietin response in 6h, the reticulocyte count rises within 2-3 days, reaches a maximum in 6-10 days and remains raised until the haemoglobin returns to the normal level. If the reticulocyte count is not raised in an anaemic patient this suggests impaired marrow function or lack of erythropoietin stimulus (Table 2.4.).

Blood film.

It is essential to examine the blood film in all cases of anaemia. Abnormal red cell morphology (Fig. 2.15) or red cell inclusions (Fig. 2.16) may suggest a particular diagnosis. When causes of both microcytosis and macrocytosis are present, e.g. mixed iron and folate or B₁₂ deficiency, the indices may be normal but the blood film reveals a 'diporphic' appearance (a dual population of large, well haemoglobinized cells and small, hypochromic cells). During the blood film examination the white cell differential count is performed, platelet number and morphology



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are assessed and the presence or absence of abnormal cells, e.g. normoblasts, granulocyte precursors or blast cells, is noted.

Table 2.4. Factors impairing the normal reticulocyte response to anaemia.

Marrow diseases, e.g. hypoplasia, infiltration by carcinoma, lymphoma, myeloma, acute leukaemia, tuberculosis

Deficiency of iron, vitamin B₁₂ or folate

Lack of erythropoietin, e.g. renal disease

Reduced tissue O₂ consumption, e.g. myxoedema, protein deficiency

Ineffective erythropoietin, e.g. thalassaemia major, megaloblastic anaemia, myelodysplasia, myelofibrosis, congenital, dyserythropoetic anaemia

Chronic inflammatory or malignant disease



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Red cell abnormality	Causes	Red cell abnormality	Causes
 Normal		 Microspherocyte	Hereditary spherocytosis, autoimmune haemolytic anaemia, septicaemia
 Macrocyte	Liver disease, alcoholism. Oval in megaloblastic anaemia	 Fragments	DIC, microangiopathy, HUS, TTP, burns, cardiac valves
 Target cell	Iron deficiency, liver disease, haemoglobinopathies, post-splenectomy	 Elliptocyte	Hereditary elliptocytosis
 Stomatocyte	Liver disease, alcoholism	 Tear drop poikilocyte	Myelofibrosis, extramedullary haemopoiesis
 Pencil cell	Iron deficiency	 Basket cell	Oxidant damage—e.g. G6PD deficiency, unstable haemoglobin
 Echinocyte	Liver disease, post-splenectomy	 Sickle cell	Sickle cell anaemia
 Acanthocyte	Liver disease, abetalipoproteinaemia, renal failure	 Microcyte	Iron deficiency, haemoglobinopathy

Fig. 2.15. Some of the more frequent variations in size (anisocytosis) and shape (poikilocytosis) that may be found in different anaemias. DIC - disseminated intravascular coagulopathy; G6PD - glucose-6-phosphate dehydrogenase; HUS - haemolytic uraemic syndrome; TTP - thrombotic thrombocytopenic purpura.

Bone marrow examination.

This may be performed by aspiration or trephine biopsy (Fig. 2.17). During bone marrow aspiration a needle is inserted into the marrow and a liquid sample of marrow is sucked into a syringe. This is then spread on a slide for microscopy and stained by the usual Romanowsky technique. A great deal of morphological information can be obtained by examining aspirate slides. The detail of the developing cells can be examined (e.g. normoblastic or megaloblastic), the proportion of the different cell lines assessed (myeloid : erythroid ratio) and the presence of cells foreign to the marrow (e.g. secondary carcinoma) observed. The cellularity of the marrow can also be viewed provided fragments are obtained. An iron stain is performed routinely so that the amount of iron in reticuloendothelial stores (macrophages) and as fine granules ('sideotic' granules) in the developing erythroblasts can be assessed.

An aspirate sample may also be used for a number of other specialized investigations (Table 2.5.).

A trephine biopsy provides a solid core of bone including marrow and is examined as a histological specimen after fixation in formalin, decalcification and sectioning. It is less valuable than aspiration when individual cell detail is to be examined but provides panoramic views of the marrow from which overall marrow architecture, cellularity and presence of fibrosis or abnormal infiltrates can be reliably determined.

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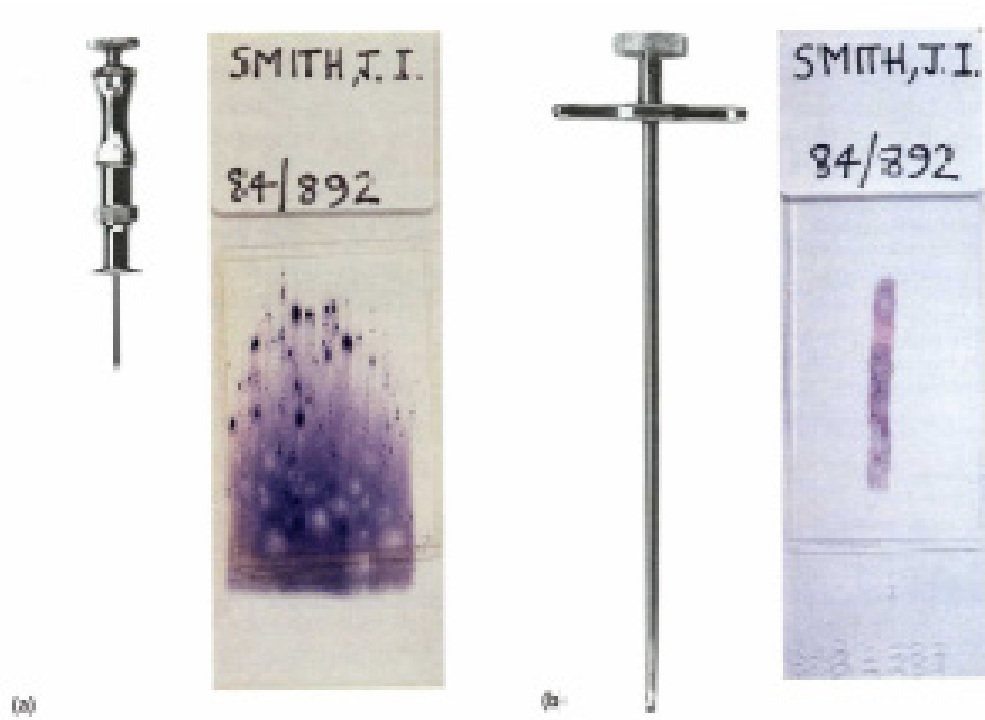


Fig. 2.17 (a) The Salah bone marrow aspiration needle and a smear made from a bone marrow aspirate.
(b) The Jamshidi bone marrow trephine needle and normal trephine section.

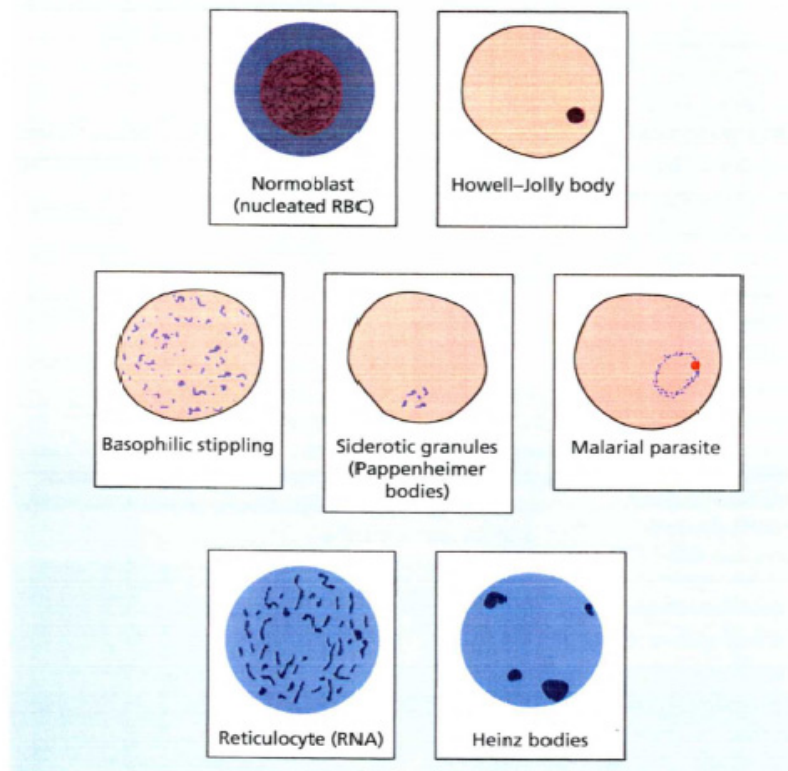


Fig. 2.16. Red blood cell (RBC) inclusions which may be seen in the peripheral blood film in various conditions. The reticulocyte RNA and Heinz bodies are only demonstrated by supravital staining, e.g. with new methylene blue. Heinz bodies are oxidized denatured haemoglobin. Siderotic granules (Pappenheimer bodies) contain iron. They are purple on conventional staining but blue with Perl's stain. The Howell-Jolly body is a DNA remnant. Basophilic stippling is denatured RNA.

Table 2.5. Comparison of bone marrow aspiration and trephine biopsy

	Aspiration	Trephine
Site	Posterior iliac crest or sternum (tibia in infants)	Posterior iliac crest
Stains	Romanowsky; Perl's reaction (for iron)	Haematoxylin and eosins; reticullin (silver stain)
Result available	1 – 2 h	1 -7 days (according to decalcification method)
Main indications	Investigation of anaemia, pancytopenia, Suspected leukaemia or myeloma, neutropenia Thrombocytopenia, etc.	Indication for additional trephine : suspicion of polycythaemia vera, myelofibrosis and other myeloproliferative disorders, aplastic anaemia, malignant lymphoma, secondary carcinoma, cases of splenomegaly or pyrexia of undetermined cause. Any case where aspiration gives a 'dry' tap.
Special tests	Cytogenetics, microbiological culture, biochemical Analysis, immunological and cytochemical markers, Immunoglobulin or T-cell receptor gene, DNA or RNA analysis for gene abnormalities, progenitor cell Culture.	Immunophenotyping

CPD Questions.



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1. Poikilocytosis is a variation in red cell size. True or false ?
2. Describe the Romanowsky technique in detail.



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