

## Recent advances in haematology

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Haematology is a diverse specialty embracing clinical and laboratory aspects of adult and paediatric disease, both malignant and non-malignant. We describe here some of the progress that has been made in diagnostic and therapeutic strategies. Molecular advances are continuing at a phenomenal rate (exceeding the rate of progress in therapeutics), offering highly sensitive methods for disease detection and, in some disorders, prospects of cure through gene therapy.

### Methods

We used information from recent key meetings, including those of the British Society for Haematology and the American Society of Hematology; leading articles in major haematology journals; and discussion with colleagues. The choice of topics covered is largely personal, and owing to space restrictions we have not included every "advance" within the specialty.

### Anaemias

Distinguishing between anaemia due to iron deficiency and anaemia of chronic disease is a difficult but common problem in medical practice. Anaemia of chronic disease is complex and involves inflammatory cytokines,<sup>1</sup> reduced marrow response to erythropoietin, reduced red cell life span, and impaired reuse of iron.<sup>2</sup> In typical, uncomplicated iron deficiency anaemia the haemoglobin concentration, mean cell volume, and serum ferritin and iron concentrations are reduced with raised total iron binding capacity; unfortunately cases are often not typical, and the results of these tests may seem conflicting. Furthermore, if a patient with anaemia of chronic disease is also iron deficient, the parameters for diagnosing iron deficiency are altered, making the diagnosis difficult; often a bone marrow aspirate, stained for iron, is the only method for accurately assessing iron status. This is expensive, time consuming, and unpleasant for the patient. Recently the serum transferrin receptor assay has been developed, enabling more accurate assessment of iron status in this group of patients.

Serum ferritin, a 480 kDa multisubunit protein, represents the body's iron storage pool. A reduced serum ferritin concentration generally indicates depletion of the iron stores. Ferritin, however, is an "acute phase protein," whose concentration is raised in inflammatory disorders; in a patient with, for example, active rheumatoid disease the ferritin concentration may be normal (or even raised) even if the patient is

### Recent advances

Iron deficiency anaemia can now be distinguished from anaemia of chronic disease by using serum transferrin receptor assays

A recently discovered human herpesvirus may have a role in development of myeloma

Additional thrombotic risk factors—for example, factor V and prothrombin gene mutations, hyperhomocysteinaemia—have been identified

Newly designed DNA probe arrays have the potential to allow rapid automated detection of mutations

Antisense therapy, ribozyme technology, and other novel treatment methods are being developed

truly iron deficient. The transferrin receptor assay aims to distinguish clearly between simple iron deficiency and anaemia of chronic disease in most cases.

How does the transferrin receptor assay work? Transferrin is a protein that carries plasma iron. Cells that require iron express the transferrin receptor on the cell surface.<sup>3</sup> The receptor binds plasma transferrin with bound iron atoms, after which the transferrin receptor-transferrin complex is internalised (Fig 1). After unloading the iron atoms, the transferrin receptor-transferrin complex moves back to the cell surface and dissociates, leaving transferrin free to pick up further iron atoms. In iron deficiency anaemia the number of transferrin receptors increases (is upregulated),<sup>4</sup> whereas in anaemia of chronic disease the number of transferrin receptors remains normal. Assays for transferrin receptors may be performed on serum with an enzyme linked immunosorbent assay (ELISA), allowing large numbers of samples to be batch tested. According to available data, the test seems as reliable as testing bone marrow aspirate for diagnosing iron deficiency and should be valuable in patients with rheumatology disorders and others with inflammatory disorders.

### Haemophilia

Haemophilia A (Factor VIII deficiency) and B (Factor IX deficiency, Christmas disease) are X-linked bleeding

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