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Management of iron deficiency in anaemia

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Iron deficiency anaemia affects about 10% of the world's population. There is a finely balanced relationship in humans between iron availability in the diet and iron requirements, with regulation of iron absorption being the key to control of body iron levels. Iron is normally rigorously conserved. The outward limb of the main internal circuit delivers iron via the plasma transport protein, transferrin, to red cell precursors in the bone marrow, where it is used for synthesis of haemoglobin: about two-thirds of the normal adult body iron content of 3-4g is in circulating red cells. In the return circuit, worn out red cells are engulfed by macrophages, where iron is released from haemoglobin either back to plasma transferrin, or to an intracellular iron storage protein, ferritin. Iron deficiency may result from loss of haemoglobin iron from this circuit (by abnormal bleeding), or from failure of iron absorption to keep pace with increased physiological iron requirements (e.g. of growth, menstruation or pregnancy). In addition, functional iron deficiency may develop despite normal, or even increased, total body iron, when demand for iron by the bone marrow exceeds the rate at which iron can be recirculated. This is seen most frequently in inflammatory diseases, where iron diversion to macrophage iron stores contributes to the 'anaemia of chronic disorders'. These different clinical circumstances each require their own approach to management.

A high prevalence of iron deficiency may justify prophylactic approaches, including food iron fortification (whether directed to the whole population or targeted to those at high risk, e.g. infants), or iron therapy (e.g. in pregnancy). With food iron fortification, the mechanisms of iron absorption become an important consideration. Non-haem iron must be presented to the gut mucosa in an available form: the presence of dietary 'promotors' (e.g. ascorbic acid) and 'inhibitors' (e.g. phytate) determines the solubility of non-haem iron in the gut lumen. The physiological basis of transport across cell membranes is finally yielding to molecular analysis: reduction to ferrous iron may be a necessary initial step at the mucosal cell membrane, and candidate transporter proteins are being identified. Haem iron, by contrast, is relatively well absorbed via specific mucosal receptors—lack of haem iron and of meat-derived promotors of non-haem iron absorption underlie the increased risk of iron deficiency in vegetarians. The potential risk to patients with genetic haemochromatosis has to be balanced against the potential benefits. This is one reason why food iron fortification has been withdrawn in Sweden (Olsson et al, 1997). In pregnancy, particularly the last trimester, dietary iron absorption cannot keep pace with the demands of the growing fetus. However, oral iron supplementation has remained controversial, despite evidence that iron deficiency anaemia is associated with premature labour.

Simple ferrous salts remain the basis of individual iron therapy: gastro-intestinal side effects have led to the promotion of alternatives, e.g. slow release preparations (where lack of toxicity is associated with release of iron beyond the site of maximum absorption in the duodenum), or more recently a gastric delivery system using a buoyant capsule matrix. Parenteral iron is associated with more severe adverse reactions, and its use has been restricted to occasional patients with continuing rapid blood loss. More recently, the problem of functional iron deficiency restricting the response to recombinant erythropoietin treatment in chronic renal failure (where there are continuing blood losses through dialysis, and iron absorption may be sub-optimal) has reawakened interest in the use of intravenous iron supplements (Druëke et al, 1997).

Druëke, T.B., Barany, P., Cazzola, M. et al (1997). Management of iron deficiency in renal anemia: guidelines for the optimal therapeutic approach in erythropoietin-treated patients. Clin. Nephrol. 48: 1–8.

Olsson, K.S., Vaisanen, M., Konar, J. Bruce, A. (1997). The effect of withdrawal of food iron fortification in Sweden as studied with phlebotomy in subjects with genetic hemochromatosis. Eur. J. Clin. Nutr. 51: 782–6.