How is IDA picked up and managed by primary care?

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- The incidence (of anaemia) in patients with colorectal cancer (CRC) was 39%
- There is a strong correlation between anaemia and CRC
- Haemoglobin level is an independent marker of risk for CRC.
- A low baseline Hb level was associated with a higher response to the iron supplementation

The prevalence of anaemia rises above the age of 65 years with the condition being more common in males than females (Guralnik et al, 2004). In this group approximately one third is associated with nutrient deficiency, a third without nutrient deficiency and the final third is of unknown aetiology (NHANES III phase 2). This final group generally will have low levels of inflammatory mediators (a marker of anaemia of chronic disease [ACD]). Anaemia in these patients is frequently a result of reduced erythropoietin production (Ferrucci et al, 2007). The production of erythropoietin appears to tire with age.

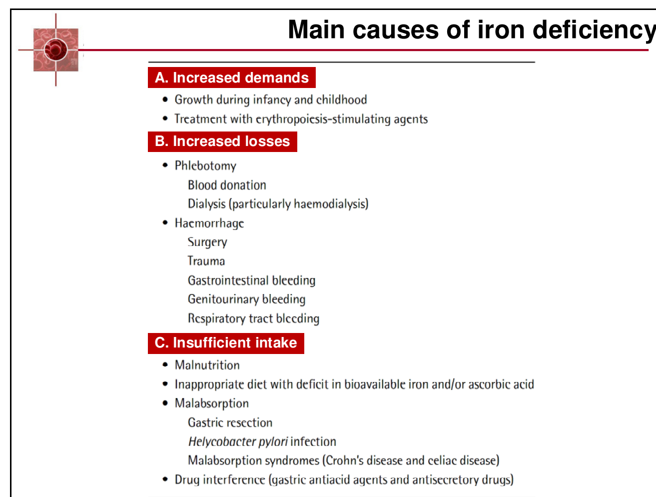
The importance of pre-operative assessment that includes anaemic status is emphasised by Wu et al (2007) who found a level of 42.8% in patients over 65 years undergoing non-cardiac surgical procedures. The European cancer anaemia survey (Ludwig et al, 2004) found levels of anaemia ranging from 29% (breast) to 53% (leukaemia). The incidence in patients with colorectal cancer (CRC) was 39%.

There is a strong correlation between anaemia and CRC. Sadahiro et al (1998) reported 23% of patients had anaemia and 40% were iron deficient (ID). In 2005 Beale et al reported that 41% of patients with CRC had IDA and that 61% of patients were iron deficient. In 2006 Prutki et al reported levels of 70% with 80% of patients having a low serum ferritin and 40% with low ferritin or low mean corpuscular volume (MCV). More recently in the UK Hamilton et al (2008) published a case-control study which concluded that haemoglobin level (Hb) is an independent marker of risk for CRC.

The prevalence of anaemia in inflammatory bowel disease (IBD) is also high, 6 – 73% (Gisbert & Gomollón, 2008). This was a systematic review and the prevalence in individual studies depended on the year of publication, environment (hospital or primary care), type of IBD (Crohn's disease or ulcerative colitis) and definition of anaemia. The same analysis revealed a mean prevalence of ID of 45% (range 36 – 75%).

The delays and accountability for diagnosis and treatment in care pathways are cause for concern. With the endeavour of seeking a solution a study was undertaken in Spain to see if the use of a haemoglobin meter (HemoCue®) could reduce diagnostic delays. Results of venous and capillary samples were compared with blood laboratory standard tests. The results were highly encouraging (Munoz et al, 2005) with only one false negative. It was suggested that the use of such 'office/consulting room' based testing could eliminate those who are non-anaemic. Those identified as anaemic could then have an appropriate laboratory appraisal for anaemia. This saves time and is 'cost-saving' to the healthcare system (NB Dr Gozzard indicated 250,000 tests being undertaken by the laboratory at his hospital of which 50% were provoked by GPs; there could be a substantial cost saving to the NHS.) The downside of 'in office' testing is that ID (per se) will not be detected if it is not reflected in the Hb level.

The main causes of ID are well documented (see figure for summary; Munoz et al 2008).



Pertinent to gastroenterology is the impact on the absorption of iron caused by Helicobacter Pylori infection. It is suggested that the bacteria secrete hepcidin mimetics thereby reducing iron uptake by enterocytes.

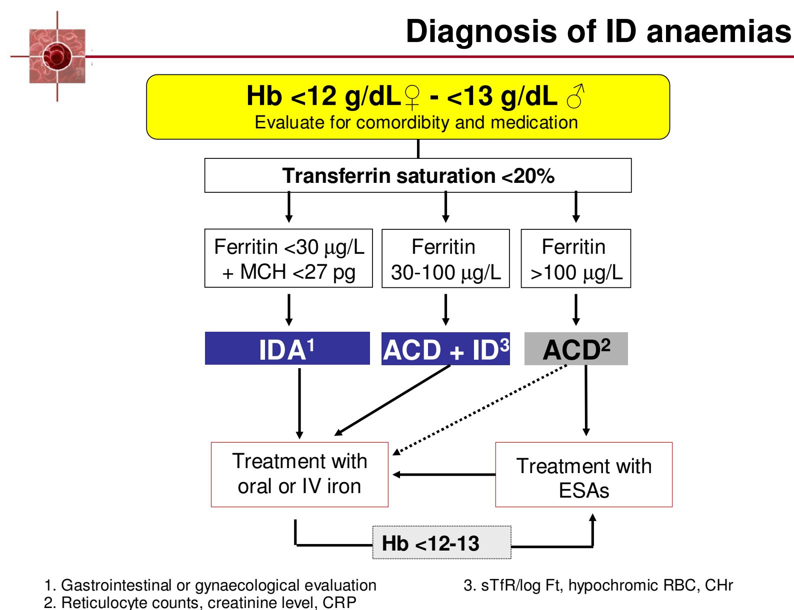
With regard to diagnosing IDA it was suggested that tests should address:

- Adequacy of stored iron?
- Adequacy of iron delivered for erythropoiesis?
- Integrity of the blood cells

The potential shortfalls of using mean corpuscular volume (MCV) as a parameter were highlighted:

- If the MCV is low it is a strong indicator of ID
- If it is high it is a reasonable indicator of B12 or folate deficiency
- If normal it could be interpreted as absence of anaemia or it may reflect ID and folate or B12 deficiency; the MCV can also be normal in patients with ACD

An alternative approach was suggested (see figure; Muñoz et al 2009a). This is based on an algorithm which is informed by Hb, transferrin saturation, ferritin and mean corpuscular haemoglobin levels and which will provide differential diagnosis.



To correct ID and IDA intravenous (IV) iron is a valuable treatment. When given to three different cohorts of patients with ID (CRC, hysterectomy and hip/knee replacement) the mean increase in Hb level following a mean dose of 1200mg of IV iron was 20g/l after 4 weeks. However, the response varied according to the cohort. The mean Hb increase was 30g/l in the hysterectomy group, 18g/l in the arthroplasty group and 9g/l in the CRC group. The suggested rationale for the differences reflects that in the hysterectomy group the underlying cause was ID, whereas in the arthroplasty group there was associated ACD and in the CRC group there was a mixed aetiology of ID and ACD plus continual blood loss. It was noted across the groups, and overall, that a low baseline Hb level was associated with a higher response to the iron supplementation (Muñoz et al 2009b).

The benefits of high doses (total dose infusion) have been highlighted in a study by García-Ere et al, 2009. The impact of administering multiple doses of IV iron (300 mg/session) was compared with high doses, 500 mg or more/session in 47 patients with IDA caused by a variety of conditions. It was found that patients receiving the higher dose administration achieved similar post-treatment Hb levels (increase in Hb of 20g/l or Hb ≥ 120g/l) but much more rapidly (21 vs 39 days). The higher dose was also associated with higher ferritin levels (271 vs 116µg/l). These results endorse the use of total dose infusion regimens and may explain the benefit of administering high doses of IV iron to patients with ACD. In these patients iron is delivered in a ferric form into the plasma. It is postulated that whilst the marrow requires 20–30mg/day for erythropoiesis, according to data from in vitro studies, approximately 45mg of iron can be sustained in the plasma after the administration of 1000mg IV iron, meanwhile, the iron overload of the macrophages in the reticulo-endothelial system may causes a 'by-pass' of the hepcidin block allowing a flow to the marrow, transported by transferrin, to sustain the erythropoiesis.