A comprehensive guide to the management of anaemia

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A systematic approach to evaluation and investigation is key to the successful management of anaemia. Our drug review considers the various oral and parenteral treatments available.

Anaemia continues to be a significant health problem, occurring in 12 per cent of the population of developed countries. Severe anaemia, as described in the past, is rare in UK practice nowadays, but mild to moderate forms are common and require thoughtful, systematic evaluation and initial investigation in primary care. A simple approach to understanding and classifying anaemia is presented here to help physicians achieve effective diagnosis, management and triage of anaemias encountered in clinical practice.

Management principles
Anaemia is a sign of an underlying condition and not a complete diagnosis in itself. Appropriate evaluation, investigation and management of anaemia are based on a systematic approach. Accurate diagnosis of iron-deficiency anaemia, for example, can be a key finding in identifying adult patients with a possible diagnosis of bowel cancer.

Any condition that can impair the production, or increase the rate of destruction, or loss of erythrocytes can result in anaemia if the bone marrow is not able to compensate for the rate of loss of red blood cells (RBCs). This situation can arise in nutritional deficiencies, systemic disease, primary bone marrow disorders, autoimmune conditions, primary abnormalities of erythrocytes and blood loss.

The ease with which deficiency anaemia – iron, folate and vitamin B12 – can be corrected may tempt empirical therapy or self-treatment, which can lead to significant diagnostic errors. Wherever possible the clinician should aim to understand the cause of anaemia in a given individual rather than resort to empiricism that may lead to missed or delayed diagnosis in many cases.

In the UK advice on possible causation and further investigation and/or referral of unexplained or atypical anaemias can always be obtained through local haematology departments.

Pathogenesis of anaemia
The basic mechanisms of anaemia can be summarised as:
- Impaired ability of the bone marrow to produce sufficient numbers of RBCs
- Accelerated destruction or loss of RBCs
• combinations of both the above.

In Western populations anaemia is considered to be present when the haemoglobin level is less than 130g/L in males and 115g/L in females.

Mean cell volume (MCV) – a measure of average RBC size (normal range 78–98fl) – is used to classify anaemia and thus determine further investigation and management. This represents a functional approach to dealing with anaemia in primary care. Table 1 illustrates the causes of anaemia classified by the MCV.

Low MCV – hypochromic microcytic anaemia
Anaemia in this form arises from impaired haemoglobin synthesis and is a result of reduced production of either haem or globin.
• Decreased haem synthesis is seen in:
  – Iron deficiency. The commonest worldwide cause of anaemia and is due to iron losses exceeding intake.
  – Chronic disorders. Chronic infectious or inflammatory diseases or cancer can also cause anaemia by impairing the utilisation of available iron. Paradoxically, in many of these conditions stored iron is increased. There is also impaired responsiveness to erythropoietin (EPO), the hormone that stimulates RBC production. Variable degrees of reduction in the MCV result, causing confusion with iron deficiency.
• Disorders of impaired globin synthesis: alpha- and beta-thalassaemia syndromes resulting from inherited disorders of globin synthesis. Homozygous forms result in serious, transfusion-dependent congenital anaemia. Heterozygous “trait” forms typically produce microcytosis with or without anaemia – mild degrees of anaemia are more typically associated with the beta-thalassaemia trait.
**Haemoglobinopathies** A variety of amino acid changes in the haemoglobin molecule are recognised, most commonly haemoglobins S, C and E. Some of these can present with a microcytic anaemia. However, their presence is usually apparent because of other clinical problems in addition to anaemia, such as painful crisis in sickle cell anaemia. (See haemolytic anaemias below for further details.)

**Sideroblastic anaemias** are rare disorders of haem synthesis that can result in microcytic anaemia. Lead poisoning can also be a cause. Most commonly found in adults, sideroblastic anaemia is a form of myelodysplastic syndrome.

**Raised MCV – macrocytic anaemias**
The macrocytic anaemias are usually subclassified as megaloblastic and non-megaloblastic based on findings from bone marrow examination.

**Megaloblastic anaemias** occur whenever there is a significant deficiency of key substrates in the DNA synthetic pathways. Peripheral blood macrocytosis (increased MCV) results, together with varying degrees of anaemia. These anaemias occur in deficiencies of cobalamin (vitamin B₁₂, e.g. pernicious anaemia) and folate, and associated with drug therapy that interferes with nucleic acid metabolism, e.g. antineoplastic agents – hydroxycarbamide, methotrexate and azathioprine. Excessive alcohol intake can occasionally produce megaloblastic changes on its own; these are usually associated with nutritional deficiency of folic acid.

**Macrocytic anaemias without megaloblastic marrow changes**
Excess alcohol intake is a common cause, although macrocytosis without anaemia is the more frequent manifestation. Co-existent nutritional deficiency of folic acid may also be a contributing factor in some cases. Liver disease, drug therapy (anticonvulsants or chemotherapy), thyroid disease (thyrotoxicosis or myxoedema).
and aplastic anaemia (a rare condition of failure of all marrow elements) may also be responsible, and some forms of myelodysplastic syndrome may present with an isolated macrocytic anaemia.

**Normal MCV – normocytic anaemias**

Anaemia in this form is very common with many causes, including those that can cause microcytic chronic-disorder anaemias. The most important cause of acute-onset normocytic anaemia is acute blood loss, and this must always be considered in initial clinical assessment of anaemia as well as other causes. Additional possible causes include EPO deficiency (associated with chronic renal dysfunction) and reduced responsiveness to EPO.

**Haemolytic anaemias**

Haemolytic anaemias result from increased red cell destruction; the lifespan of circulating RBCs is reduced, and these may present with low, normal or raised levels of MCV. The rate of RBC destruction exceeds the ability of the bone marrow to compensate, and worsening, sometimes life-threatening, anaemia may ensue.

In haemolytic anaemias serum bilirubin levels are often, but not always, raised due to increased breakdown of haemoglobin. Other markers of haemolysis include a raised lactate dehydrogenase (LDH) and an increased number of early red cells (reticulocytes) in the peripheral blood.

The types of haemolytic anaemias encountered in UK practice are listed in Table 2.

**Dilutional anaemia (pseudoanaemias)**

An increase in plasma volume will result in reduced haemoglobin concentration, haematocrit and RBC count without any decrease in the patient’s total RBC mass. For example, in pregnancy the haemoglobin level can fall as low as about 100g/L (physiologic anaemia of pregnancy). No treatment is required. Hyperviscosity syndromes such as myeloma or Waldenström’s macroglobulinaemia can lead to a similar problem.

**Clinical manifestations of anaemia**

Specific signs and symptoms of anaemia vary widely (see Table 3), even in patients with the same degree of anaemia. Key factors that influence anaemic symptoms include the degree of anaemia, rapidity of its onset and co-morbidity such as cardiac failure. Compensatory mechanisms often limit symptoms in anaemia with a chronic onset: slowly developing or longstanding anaemia can be asymptomatic even with surprisingly low haemoglobin levels. Where patients are well adapted to their anaemia there is no clinical urgency to normalise the haemoglobin level – in older patients rapid correction of chronic anaemia by transfusion can be potentially harmful as such an approach can result in cardiac failure.

There are no reliable clinical findings. Pallor may occur, and jaundice may be seen in haemolytic anaemia. Specific features in the clinical history or physical signs may point towards a specific cause for the anaemia. Classical signs of iron deficiency such as koilonychia or oesophageal webs are nowadays extremely rare in UK clinical practice.

**Clinical evaluation of anaemia**

The physician needs to determine the likely cause of the anaemia and the extent to which investigation and treatment are warranted for the individual patient – for example, in very frail or elderly patients with significant co-morbidity invasive investigations for blood loss or other pathology are unlikely to prove beneficial either to the patient or the NHS.

<table>
<thead>
<tr>
<th>Microcytic anaemias (low MCV)</th>
<th>Common</th>
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<tr>
<td>• iron-deficiency anaemia (~60%)</td>
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<td>• anaemia of chronic disorders (~20–30%)</td>
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<td>• haemoglobinopathies</td>
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<td>– thalassaemias</td>
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<td>– haemoglobin E trait and haemoglobin E disease</td>
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<tr>
<td>Rare</td>
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<tr>
<td>• paroxysmal nocturnal haemoglobinuria</td>
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<tr>
<td>• atransferrinaemia</td>
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<td>• antibodies to the transferrin receptor</td>
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<td>• aluminium intoxication</td>
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<td>• sideroblastic anaemias</td>
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<table>
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<tr>
<th>Macrocytic anaemias (high MCV)</th>
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<td>• (chronic) alcohol excess*</td>
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<td>• vitamin B₁₂ or folate deficiency</td>
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<td>• drug intake</td>
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<td>• haemolysis</td>
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<td>• liver disease</td>
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<td>• myelodysplastic syndromes</td>
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<td>• thyroid disease</td>
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<td>• unexplained/“idiopathic”</td>
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<tr>
<td>Rare</td>
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<tr>
<td>• hypoplastic and aplastic anaemia</td>
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<th>Normocytic anaemias (normal MCV)</th>
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<td>• acute blood loss</td>
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<td>• anaemia of renal failure</td>
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<td>• anaemia of chronic disorders</td>
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<td>• haemolytic anaemia</td>
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<td>• anaemia of liver disease (multifactorial)</td>
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<td>• anaemia of endocrine disease</td>
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<tr>
<td>• early iron-deficiency anaemia</td>
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<tr>
<td>• mixed iron and vitamin B₁₂/folate deficiency (masked megaloblastic anaemia)</td>
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<tr>
<td>• structural variant haemoglobinopathies including haemoglobins S, C and D</td>
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<tr>
<td>Rare</td>
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<tr>
<td>• hypoplastic and aplastic anaemia</td>
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*macrocytosis without anaemia is a very common indicator of excess alcohol intake

Table 1. Causes of micro-, macro- and normocytic anaemias
Haemolytic anaemias due to intrinsic RBC defects
- haemoglobinopathies
  - sickle-cell disease (SS, SC, SB)
  - major and intermediate thalassaemia (α and β)
- RBC membrane defects
  - hereditary spherocytosis
- RBC enzyme deficiencies
  - paroxysmal nocturnal haemoglobinuria

Haemolytic anaemias due to abnormalities extrinsic to RBCs
- autoimmune haemolytic anaemia
- microangiopathic haemolysis
- hypersplenism
- oxidative haemolysis

Table 2. Classification of haemolytic anaemias

A further key step in the clinical evaluation of anaemia is to look at other results generated in the full blood count, specifically the white cell and platelet counts. The presence of significant abnormalities may be suggestive of, for example, drug toxicity, bone marrow pathology or an underlying autoimmune condition. Discussion of these abnormalities is beyond the scope of this article but the physician is reminded of their relevance as part of anaemia evaluation.

The most practical approach is to base initial assessment of anaemia on the MCV (see Figure 1). The most practical ‘second-stage’ diagnostically helpful tests are serum ferritin, serum vitamin B₁₂ and folate assays (or red cell folate). The use of serum iron and total iron binding capacity in the diagnosis of iron deficiency should be discouraged – it is no longer reliable and has been superseded by serum ferritin.

Screening for thalassaemia trait should also be considered in patients with Mediterranean, African, Middle Eastern or Far Eastern ethnicity or ancestry – it should also be considered where investigation does not clearly identify iron deficiency. Thalassaemia-trait patients do not benefit from iron supplementation – unless they are shown to be iron deficient.

Once the likely mechanism for a given case is identified, further referral and/or investigation should then be directed to find the likely underlying cause. In public health terms clear and prompt identification of iron deficiency in older adults represents a key step in identification of those at risk of colorectal cancer.

Identification of iron-deficiency anaemia is a clear indication that iron loss exceeds intake and, in UK practice, invariably is an indication of chronic blood loss. The clinical history will normally identify overt bleeding whether gynaecological, genitourinary or gastrointestinal. Chronic GI bleeding may be undetected by the patient and missed on history taking.

The British Society of Gastroenterology provides guidelines on the management of iron-deficiency anaemia.¹ Key practice points in these guidelines include the following statements:
- faecal occult blood testing is of no value to further investigation of iron-deficiency anaemia
- upper and lower GI investigation should be considered in all postmenopausal females and all male patients where iron-deficiency anaemia has been confirmed unless there is a history of significant, overt non-GI blood loss
- all patients should be screened for coeliac disease
- in patients aged >50 or with marked anaemia or a significant family history of colorectal carcinoma, lower GI investigation should still be considered even if coeliac disease is found
- only postmenopausal women and men aged >50 years should have investigation of iron deficiency without anaemia.

Treatment for anaemia
Iron deficiency – oral replacement

The treatment of choice for iron-deficiency anaemia is an oral preparation (see prescribing points). The most cost-effective approach is ferrous sulphate 200mg twice daily, or three times daily if tolerated. Other commonly used ferrous salts, eg gluconate and fumarate, have similar rates of absorption, differing principally in the amount of elemental iron released. Patients unable to tolerate ferrous sulphate may try other ferrous salts.

Complete correction of chronic anaemia is seldom urgent. Red cell transfusion is not indicated as standard treatment of chronically deficient patients. However, supportive transfusion of 2 units of RBCs may be helpful where anaemic symptoms or effects are severe and need to be managed pending a response to supplementation.

Slow-release and enteric-coated preparations are promoted as producing fewer side-effects and only require once-daily administration. However, they dissolve slowly and can bypass the proximal small bowel where most absorption takes place. There is no evidence that they are worth the extra cost and they may be significantly less effective. A poor response to therapy with slow-release iron cannot then be reliably interpreted clinically.

Iron absorption occurs best under conditions of low pH in the proximal small bowel such as one hour before meals or at bedtime. Medication that decreases acid secretion reduces absorption, as does food intake. GI side-effects are unfortunately common and troublesome (see Table 4). They include nausea,
epigastric colic and reflux, and reflect the amount of ionised iron delivered to the stomach and proximal small bowel. Pragmatically, because side-effects are minimised, the clinical recommendation is that iron supplements are taken after meals. Vitamin C enhances iron absorption but is of no therapeutic value since increased absorption is generally associated with increased side-effects, therein reducing adherence – so, for iron deficiency simple iron salts are the mainstay and gold standard for treatment.

Lower GI side-effects are reported in about 25 per cent of patients but are not necessarily a reflection of iron dosage. Constipation usually responds to dietary fibre or a stool softener.

Iron treatment must continue for three months after normalisation of haemoglobin to replenish stores – failure to do this is a common error of omission in practice and can lead to subsequent confusion in follow-up. It is also the case that patients commonly become less adherent with continued iron supplementation simply because they feel better and have not been made aware of the importance of continued treatment to replace iron stores.

Parenteral preparations (such as parenteral iron) may be used to replenish iron stores rapidly and effectively. Parenteral iron does not produce a faster haemoglobin response than adequately absorbed oral iron.

**Parenteral iron**

In the past the risks of anaphylaxis from iron dextran infusions limited the use of intravenous iron – newer intravenous iron preparations described below have minimal risk. With the newer intravenous iron preparations outlined below, intramuscular administration can no longer be clinically recommended – it is painful and causes permanent skin discolouration.

A potential advantage of calculated intravenous iron infusions is that elements of uncertainty about administered dosage and adherence are eliminated – a fact that can be of great help in the setting of recurrent anaemia. There are also situations when it is helpful to replace iron stores quickly such as before childbirth or surgery – optimising body iron stores preoperatively is also a valuable strategy to minimise the use of donor blood in elective surgery.

Evolution in these areas of clinical practice will thus likely result in increased use of intravenous iron for specific clinical situations. As a principle, however, parenteral iron should never be initiated by primary care in the absence of agreement from a relevant specialist in secondary care that it is clinically indicated.

Parenteral iron is indicated where there is documented malabsorption, genuine intolerance to oral preparations or continuing blood loss. Specific indications also include iron deficiency associated with active inflammatory bowel disease, in patients on renal dialysis (combined with erythropoietins), and in specific groups with chemotherapy-induced anaemia (see NICE TA142); provided it is with the exception of patients on renal dialysis. There is an increased risk of infection with parenteral iron therapy due to the utilisation by bacteria of iron as a growth factor. Iron infusions should therefore be avoided in acute or chronic infection.

Parenteral iron preparations available in the UK include the following:

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<th>Acute-onset anaemia</th>
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<tr>
<td>• fatigue</td>
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<td>• generalised weakness</td>
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<td>• loss of stamina</td>
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<td>• acute dyspnoea</td>
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<td>• syncope</td>
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<tr>
<th>Chronic anaemia</th>
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<tr>
<td>• weakness, fatigue, lethargy</td>
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<tr>
<td>• palpitations</td>
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<tr>
<td>• dyspnoea or orthopnoea</td>
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<tr>
<td>• orthostatic light-headedness</td>
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<tr>
<td>• new onset or worsening of angina</td>
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<td>• new onset or worsening of claudication</td>
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<th>Physical signs</th>
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<tr>
<td>• pallor of skin and mucosal surfaces</td>
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<td>• resting or orthostatic tachycardia</td>
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<td>• parasternal systolic ejection flow murmur</td>
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<tr>
<th>Vitamin B&lt;sub&gt;12&lt;/sub&gt; deficiency</th>
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<tr>
<td>• glossitis</td>
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<tr>
<td>• peripheral neuropathy</td>
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<tr>
<td>• combination of motor (upper and lower motor neurone type) and sensory deficits</td>
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<tr>
<th>Haemolytic anaemias</th>
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<tr>
<td>• jaundice</td>
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<tr>
<td>• splenomegaly</td>
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<tr>
<td>• evidence/history of splenectomy or cholecystectomy</td>
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<tr>
<td>• leg ulcers</td>
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<td>• shortened digits in sickle cell disease</td>
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<tr>
<th>Iron deficiency</th>
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<td>• angular cheilosis</td>
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<tr>
<td>• glossitis</td>
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<td>• koilonychia</td>
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**Table 3. Symptoms and signs of anaemias**

- Iron dextran (CosmoFer) is given by slow IV infusion over several hours and carries a small risk (0.7 per cent) of anaphylaxis. It has the advantage of requiring only one or two doses to replace iron stores.

- Iron sucrose complex (Venofer) has a very low incidence of serious adverse reactions (0.03 per cent). The total dose is calculated with a standard formula. Its disadvantage is that replacement involves a series of infusions, typically twice a week for one to five weeks depending on the level of anaemia and patient weight.

- Ferric carboxymaltose (Ferinject) is not associated with severe allergic reactions and the total required dose can be administered in one to two 15-minute intravenous infusions 500–1000mg a week apart. It is, however, more expensive than the other preparations, but the fact that it can be administered as a short single infusion will go some way to offsetting the increased drug cost.

- Iron isomaltoside (Monofer) can be administered in either one
Complete clinical evaluation

FBC and blood film evaluation

MCV

MCV, MCH low

Assess iron stores – measure serum ferritin

Test for Hb disorder

Signs of inflammation, raised ESR or C-reactive protein

MCV normal

Reticulocyte count

Low

High

Anaemia of chronic disease

Renal failure, primary bone marrow disease, chronic disease, early Fe deficiency

Haemolysis, bleeding

MCV raised

Assess vitamin B₁₂, folate, thyroid and liver function, protein, reticulocyte count

Any indication for bone marrow?*

Appropriate diagnosis, plan further investigations and start treatment

Oral ferrous sulphate 200mg 3 times daily

Folate supplementation, specific Rx for each symptom, eg pain relief in sickle cell disease

Treat inflammation, consider EPO

EPO therapy according to underlying problem

Folate supplementation, specific Rx as per diagnosis

im or sc vitamin B₁₂ – often lifelong, oral folate replacement

Rx as per diagnosis

*eg pancytopenia, raised MCV with normal B₁₂, folate, etc, may signify primary bone marrow failure

*whether this is done simultaneously with requesting a ferritin level will depend on the ethnic background of the patient and/or local haematology guidance/advice

Figure 1. Evaluation and management of anaemia (FBC = full blood count; MCH = mean corpuscular haemoglobin; MCV = mean cell volume)
**Iron**
- nausea and epigastric pain (dose related)
- altered bowel habit – constipation or diarrhoea
- may exacerbate symptoms in inflammatory bowel disease
- severe constipation (rarely leading to bowel obstruction secondary to faecal impaction in older people)
- acute overdosage – nausea, vomiting, diarrhoea, GI bleeding, hypotension and coma
- acute hypersensitivity
  - anaphylaxis with iron dextran
  - painful local lymphadenopathy
  - flu-like symptoms

**Vitamin \(B_{12}\) (hydroxocobalamín)**
- rare
  - itching, rashes
  - fever, chills
  - hypokalaemia in severely deficient patients (needs monitoring for the early part of the treatment)
- very rare
  - acneform or bullous eruptions
  - anaphylaxis

**Folate**
- rashes and allergic reactions
- may worsen neurological symptoms or mask latent vitamin \(B_{12}\) deficiency

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<tr>
<th>Side-effects of treatments for anaemia</th>
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**Vitamin \(B_{12}\) or cobalamin deficiency**
Nowadays, most patients with vitamin \(B_{12}\) or cobalamin deficiency rarely present with the classical florid manifestations described in textbooks; emergency treatment is thus rarely required.

Initial treatment of vitamin \(B_{12}\) deficiency aims to correct the anaemia and resolve neurological abnormalities where present; it will treat the deficiency and replenish stores. In acute forms of presentation blood transfusion should be avoided as it risks exacerbating reversible cardiac dysfunction present in acute megaloblastic anaemia.

Because the disorder is caused by cobalamin malabsorption in the great majority of cases, parenteral cobalamin supplementation (hydroxocobalamín) is given intramuscularly. After injection, significant amounts of the vitamin (up to 80 per cent) are excreted in the urine; therefore, initial therapy should be with several large doses of cobalamin. Injections given on alternate days replenish stores more rapidly than daily injections, although there is no evidence that any one established regimen works better than others.

Patients with pernicious anaemia need lifelong therapy. Hence all younger patients should be confirmed to have pernicious anaemia as opposed to a reversible cause such as malabsorption.

It is not clear whether large or more frequent doses of hydroxocobalamín are needed in patients with neurological damage. In these patients, the same schedule of cobalamin as detailed above is usually sufficient, but longer courses are frequently given.

In severe vitamin \(B_{12}\) deficiency, regular monitoring of serum potassium is recommended during initial therapy as hypokalaemia can occur, and potassium supplementation is recommended for hypokalaemic patients. Co-existent iron deficiency or marginal bone marrow iron stores can limit recovery and should be treated with 200mg ferrous sulphate three times a day.

Lifelong vitamin \(B_{12}\) replacement therapy is required in pernicious anaemia, achieved by administration of 1mg hydroxocobalamín every three months. Thyroid function tests are also recommended annually in these patients because of an association with other autoimmune disorders such as hypothyroidism.

An oral preparation of vitamin \(B_{12}\) cyanocobalamín, is available and is effective, but requires larger doses and is significantly more expensive than available intramuscular forms. Such an approach may, however, be recommended in vegetarians who develop dietary vitamin \(B_{12}\) deficiency.

**Folic acid deficiency**
In contrast to vitamin \(B_{12}\) deficiency, folate deficiency is usually treated with oral replacement. Folate absorption occurs throughout the small intestine. Megaloblastic anaemia from folic acid deficiency responds readily to 5mg folic acid daily, except in situations of severe malabsorption where a larger dose may be needed. Replenishment of folate stores can be achieved within several weeks of oral therapy.

In general, maintenance therapy is not indicated except in patients on long-term haemodialysis and those with disorders of increased cellular turnover, such as chronic haemolytic states. Such patients should be advised about the necessity of lifelong therapy.

The clinical response in folic acid deficiency is very similar to that seen with vitamin \(B_{12}\) deficiency. No significant primary toxicity from folate treatment has been reported. There is concern about the use of folate in vitamin \(B_{12}\)-deficient patients

**Prescribing points – folate replacement**
- rule out presence of vitamin \(B_{12}\) deficiency before starting therapy
- initial treatment – 5mg daily until correction of anaemia
- only patients with chronic haemolysis or increased cell turnover disorders need long-term therapy
- all patients should be investigated for causes of folate deficiency
- check for response in 5–7 days and in severe cases check for evidence of response in 48–72 hours by reticulocyte count
Anaemia

Advances in anaemia treatment
EPO is produced in the kidneys and regulates RBC production. Its gene was cloned in 1988 and recombinant forms (epoetin) became available for clinical use in 1990. EPO is now established as the standard therapy for anaemia in patients on renal dialysis (supported by folic acid supplementation and intravenous iron to overcome a functional iron deficiency) and patients with established chronic renal failure who are not on dialysis. There are NICE guidelines for its use in adult patients with haemoglobin levels <11g/dl.¹

EPO use is also recognised as effective in managing:
- therapy-related anaemia of HIV patients
- cancer-related anaemia in non-myeloid malignancies.

There is also growing evidence for the use of EPO in anaemia of chronic disease, myelodysplastic syndromes and other conditions. Although there may be concern about increased drug costs with EPO, these have to be balanced with potential improvements in clinical outcomes, less need for expensive and potentially hazardous donor blood and a reduction in hospital stay and other therapeutic dependencies.

Conclusion
Anaemia remains a significant public health problem and is a pointer to an underlying disease in most patients. Simple, inexpensive measures, such as iron replacement, continue to represent the only treatments needed for patients shown to be deficient in these factors. Treatment in primary care must be complemented by a systematic, clinically focussed approach to anaemia evaluation to achieve optimum and timely referral for investigative procedures such as GI endoscopy, for example, when iron-deficiency anaemia is identified.

Indeed the British Society of Gastroenterology has suggested some basic quality standards for iron deficiency:
- all patients with iron-deficiency anaemia should be screened for coeliac disease
- all patients (other than menstruating women) with iron-deficiency anaemia and no obvious cause should have both an upper GI endoscopy and either colonoscopy or radiological imaging (unless carcinoma or coeliac disease is found)

Prescribing points – vitamin B₁₂ therapy

- initial treatment is with 1mg im injections of hydroxocobalamin given three times a week for two weeks
- maintenance is with 1mg injections at three-monthly intervals for life in pernicious anaemia
- all patients with pernicious anaemia need therapy for life – because of this all younger patients should be confirmed to have pernicious anaemia and not a reversible cause like malabsorption
- the clinical response to therapy is usually marked – an immediate sense of well-being, rapid reversal of pancytopenia and mucosal changes, bone marrow reverting to normal in 24 hours, and a brisk reticulocytosis seen as early as after day 3 of treatment
- disappearance of macrocytic red cells and correction of the MCV may take several weeks

- all patients receive appropriate iron replacement
- all those not responding to treatment should be considered for further investigation
- in all patients being investigated for iron-deficiency anaemia, reasonable evidence of iron-deficiency anaemia should be documented by appropriate Hb, MCH and MCV or ferritin values, or there should be an explanation of why iron deficiency is suspected in patients not showing typical blood test results.

These form a useful template for audit in primary care – particularly in relation to the common problem of iron deficiency. They focus on the importance of simple diagnostic tests available to primary care coupled with systematic clinical assessment to determine the appropriate next steps in further investigation.

Anaemia is a common finding in practice. A systematic approach to determining the likely cause is a core skill in primary care; the finding of anaemia and its significance for the individual patient combine to determine the next stages and extent of further investigation – getting this process right has profound implications for the cost-effectiveness and management of NHS resources. The approach outlined in this review aims to equip the busy primary-care clinician with the skills to achieve this objective.

References

Declaration of interests
None to declare.

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