



IRON, FOLATE AND VITAMIN B12 DEFICIENCY ANAEMIAS

Top tips for MURs

- Assess whether the patient has Iron Deficiency Anaemia (IDA), vitamin B12 or folate deficiency anaemia; counsel patient on the reason for taking replacement therapy
 - Counsel patients on common side effects (see overleaf) and signs and symptoms of complications that need referral (see red flags below)
- For patients receiving treatment for IDA:**
- Stress the importance of adherence – if left untreated iron deficiency anaemia (IDA) can reduce the body's immunity and may lead to other complications such as tachycardia, heart failure or restless leg syndrome¹
 - Advise patients about safe storage of iron tablets; accidental overdose in children may be life-threatening²
 - Advise that there is better absorption when iron supplements are taken on an empty stomach. If patients have gastrointestinal side effects then they can be advised to take their iron tablets with or after food.
 - Check the patient has been monitored – a Full Blood Count (FBC) should be taken 2-4 weeks after diagnosis and monitored every 3 months for the first year, then rechecked annually²
 - * Advise the patient that oral absorption of iron is reduced by certain medications e.g. antacids (see drug interactions section)
 - Advise the patient that certain foods and drinks can reduce the absorption of iron e.g. foods containing calcium, tannins (e.g. tea, coffee, cocoa) and phytates (found in cereal grains, legumes, nuts and seeds)²
 - Consider whether other medications may be causing the anaemia (e.g. NSAIDs / Aspirin)
- For patients receiving treatment for Vitamin B12/ Folate deficiency anaemia:**
- Stress the importance of adherence – untreated anaemia can cause cardiopulmonary complications, neurological changes (e.g. neuropathy, visual disturbances) and neural tube defects in the foetus³. If neurological problems develop, they can be irreversible.
 - Initially, FBC and reticulocyte count should be performed after 10 days and after 8 weeks. On-going monitoring for vitamin B12 or folate deficiency is generally regarded as unnecessary unless symptoms reoccur or lack of compliance is suspected³.
 - Advise patients receiving replacement therapy with oral vitamin B12 and folic acid that absorption may be reduced by other medications (see drug interactions section)
 - Consider whether other medications may be causing the underlying vitamin B12 deficiency, e.g. colchicine, neomycin, metformin and anticonvulsants or long-term use of drugs that reduce gastric acid production e.g. PPIs/ H2 receptor antagonists
 - Consider whether other medications may be causing the underlying folate deficiency, e.g. anticonvulsants, nitrofurantoin, alcohol or medicines which reduce the absorption of folate e.g. colestyramine, sulfasalazine and methotrexate. Trimethoprim may also exacerbate pre-existing folate deficiency, although it is not the cause of folate deficiency anaemia³
 - Report any relevant adverse drug reactions to the yellow card scheme

Pathophysiology of IDA

Iron deficiency anaemia (IDA) occurs when the body's iron demand is not met by iron absorption from the diet, leading to a reduction in red blood cell production². This may occur as a result of gastrointestinal causes, for example due to NSAIDs/aspirin use, gynaecological causes such as menstruation or pregnancy, or malabsorption, for example due to coeliac disease or Helicobacter pylori infection. Common symptoms include fatigue, pallor, dyspnoea and palpitations². Treatment should only occur in the presence of demonstrable iron-deficiency states, after investigations to exclude serious underlying causes such as carcinoma or gastric erosion⁴.

Pathophysiology of vitamin B12 and folate deficiency anaemias

Vitamin B12 or folate deficiency are the most common causes of megaloblastic anaemia, characterized by the formation of abnormally large red blood cells with defects in DNA synthesis. Vitamin B12 deficiency is commonly caused by the autoimmune disorder 'pernicious anaemia', which results in the reduction of intrinsic factor, which is essential for absorption of vitamin B12. Other causes of vitamin B12 deficiency include gastric causes, inadequate dietary intake (e.g. vegan diet), intestinal malabsorption (e.g. Crohn's disease) or drugs (e.g. colchicine). Folate deficiency can occur due to dietary deficiency, malabsorption, pregnancy, malignancy, blood disorders, inflammation or drugs. Common symptoms of anaemia include fatigue, dyspnoea, palpitations, headaches, tinnitus or anorexia. Patients with vitamin B12 deficiency may experience neurological symptoms such as numbness or visual disturbances, whereas patients with folate deficiency may report peripheral neuropathy symptoms or psychiatric disturbance e.g. depression³.

How do drugs used to treat or prevent anaemia work?

Iron supplements	For treatment of IDA, iron supplements are used as replacement therapy and treatment is continued for 3 months once haemoglobin concentration and red cell indices are normal. An ongoing prophylactic dose (e.g. one tablet daily) may be used in patients at high risk of IDA.
Folic acid	Folate replacement therapy is usually recommended for 4 months (unless the underlying cause is persistent). ³
Vitamin B 12 (Hydroxocobalamin injections / cyanocobalamin tablets)	Intramuscular hydroxocobalamin is preferred as replacement therapy, as it is retained in the body for longer and can be given at intervals of up to 3 months ³ . Management depends on whether patients have neurological involvement.





Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 or more days)
- Counsel patient on healthy eating, exercise & weight loss (if BMI > 25kg/m²) – reduce saturated fat and salt intake, increase oily fish intake, complete a minimum of 30 minutes moderate intensity physical activity, five times a week Reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Advise patients who smoke the benefits of stopping smoking and how to access pharmacy smoking cessation services or 'Help Me Quit' resources
- Counsel the patient on good sources of foods to address the relevant deficiency (see table):

Iron Deficient Anaemia	Folate deficiency	Vitamin B12 deficiency
Dark-green vegetables (e.g. kale), iron-fortified bread or cereals, brown rice, pulses and beans, meat, fish and tofu, eggs, dried fruit such as dried apricots, prunes and raisins ²	Broccoli, brussel sprouts, asparagus, peas, chickpeas and brown rice ³	Meat, salmon, cod, eggs and dairy products. For vegans / vegetarians: fortified foods e.g. fortified soy products, yeast extract (Marmite®), fortified breakfast cereals and breads ^{3,1}

Red flags that need referral

- Signs of gastrointestinal bleeding – hematemesis (blood in vomit) or melaena (the passage of black, tarry or sticky stools –although darkened stools may be a side effect of iron therapy (**see common side effects below**))
- Any unintended weight loss or persistent vomiting
- New or persistent symptoms despite treatment

What are the common side effects to look out for?

Drug	Common side effects	Recommendation
Iron supplements	Gastrointestinal adverse effects e.g. epigastric pain, heartburn, nausea	May diminish over time. Gastrointestinal side effects may be dose related, therefore reducing the dose may reduce side effects. Advise patients to take iron with or after food. If problematic, refer to prescriber for an alternative iron salt; ferrous gluconate contains less elemental iron and may induce fewer side effects.
	Change in bowel habit – constipation, faecal impaction, diarrhoea, change in stool colour	If patient presents with constipation or faecal impaction, advise on a high fibre diet and consider the use of laxatives. Offer reassurance to patients with darkened stools that this is a common side effect (but see red flags sections to distinguish from malaena) ²
Folic acid	Gastrointestinal disturbances	Refer to prescriber if problematic.
Vitamin B12 (Hydroxocobalamin injections / cyanocobalamin tablets)	Nausea, headache, dizziness, fever, hot flushes, pruritis and injection-site reactions ^{3,4}	Refer to prescriber if problematic.

Potential serious drug interactions?

Medicines used for anaemia can interact with other medications - **See BNF Appendix1: Interactions for more details**

- Iron supplements: absorption can be reduced by thyroid hormones, zinc and magnesium-containing antacids and calcium salts, recommend to take at least 4 hours apart⁴
- Folic acid: absorption reduced by antacids (SpC recommends to take at least 2 hours apart), sulfasalazine, antiepileptics and cytotoxics⁴
- Vitamin B12: blood levels of hydroxocobalamin may be reduced by concurrent administration of oral contraceptives, although this is unlikely to have clinical significance³
- Oral vitamin B12 absorption may be reduced by 4-aminosalicylic acid, colchicine, biguanides, neomycin, colestyramine, potassium chloride, methyl dopa and cimetidine³

Where can you find more information?

1. NHS Choices <http://www.nhs.uk/pages/home.aspx>
2. CKS: NICE Clinical Knowledge Summaries Anaemia – iron deficiency <https://cks.nice.org.uk/anaemia-iron-deficiency>
3. CKS: NICE Clinical Knowledge Summaries <https://cks.nice.org.uk/anaemia-b12-and-folate-deficiency>
4. BNF: subsections 9.1 Anaemias and some other blood disorders
5. WCPPE e-learning programme: Biochemistry, available on the WCPPE website: <https://www.wcppe.org.uk/>

