

1. Anaemia: overview

(Based on NICE 2015, NG12, Lancet 2016;387:907, BMJ 2012;344:d79530 BJGP 2018; DOI:https://doi.org/10.3399/bjgp18X698357)

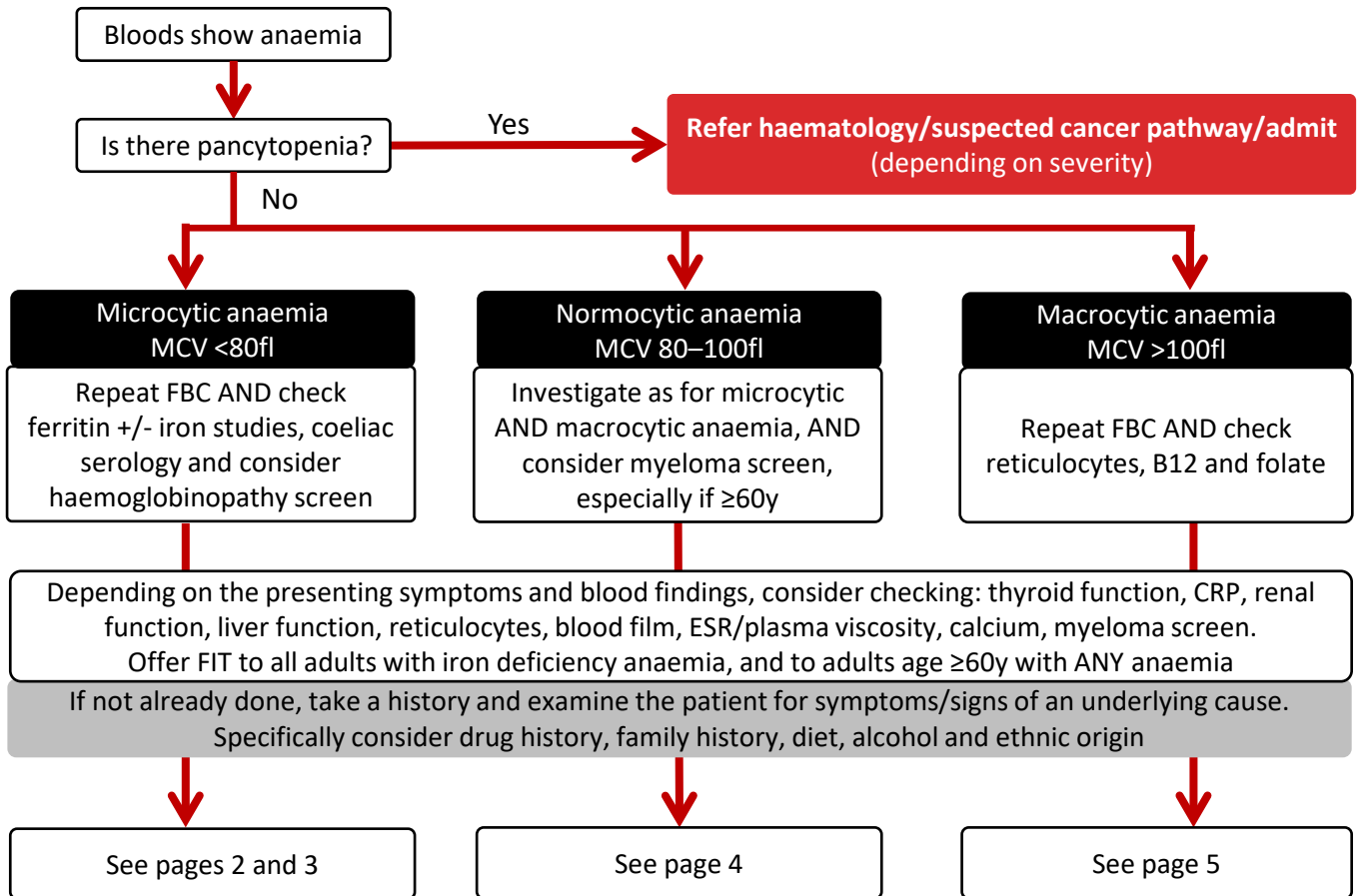


Red Whale

GEMS
Guidelines & Evidence Made Simple

This GEMS relates to those with an anaemia suitable for investigation in primary care: if haemoglobin very low/pancytopenia/symptomatic, use clinical judgement about urgent investigation/referral/admission

Anaemia is not a standalone condition – it is a sign of underlying pathology. Assess for a cause



Symptoms/signs of anaemia

Any anaemia: pallor, fatigue, dyspnoea, headache, tachycardia, systolic murmur, vertigo, syncope, haemodynamic instability, angina.

Specific features of iron deficiency:

- Dry rough skin, dry damaged hair, alopecia, koilonychia (spoon-shaped fingernails), loss of tongue papillae, atrophic glossitis.
- May also have restless legs syndrome or Plummer-Vinson syndrome (dysphagia, iron deficiency anaemia and oesophageal webs).

NICE suspected cancer guidance referral criteria for anaemia (NICE NG12 (updated 2023, NICE 2023, DG56))/ ACPGBI/BSG FIT testing for people with symptoms/signs of possible colorectal cancer (Gut 2022;71:1939):

All adults with iron deficiency anaemia
≥60y with ANY anaemia (even in absence of iron deficiency)

Offer faecal immunochemical test (FIT)
Refer on suspected cancer pathway if positive
(≥10mcgHb/g)

≥55y with upper abdominal pain and low haemoglobin
(type of anaemia not specified)

Consider non-urgent direct-access OGD

Women ≥55y with visible haematuria and anaemia
(type of anaemia not specified)

Consider direct-access gynae USS

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature. The information presented herein should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular, we suggest you carefully consider the specific facts, circumstances and medical history of any patient, and recommendations of the relevant regulatory authorities. We also suggest that you check drug doses, potential side-effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages. July 2024. For full references see the relevant Red Whale articles.

2. Microcytic anaemia

(Based on Lancet 2016;387:907, BMJ 2017;357:j2513, NEJM 2019;381:1148, <https://nhsbt.dbe.blob.core.windows.net/umbraco-assets-corp/14681/bolton-anaemia-management-in-primary-care-pathway-final-december-2015.pdf>)



Red Whale

GEMS
Guidelines & Evidence Made Simple

This GEMS relates to those with an anaemia suitable for investigation in primary care: if haemoglobin very low/pancytopenia/symptomatic, use clinical judgement about urgent investigation/referral/admission

Anaemia is not a standalone condition – it is a sign of underlying pathology. Assess for a cause

Bloods show a microcytic anaemia: **check haematinics**

Ferritin low

Ferritin normal/raised

Iron deficiency anaemia
(see page 3 for management)

Look for possible causes:

- **Blood loss:** upper GI or colorectal cancers, gastric ulcer, angiodysplasia, inflammatory bowel disease, gynae blood loss, surgery, haematuria, epistaxis, haemoptysis, drugs (NSAIDs, aspirin, anticoagulation), parasites
- **Malabsorption:** coeliac disease, gastric bypass surgery, gastrectomy, *H. pylori*, drugs, e.g. PPIs
- **Poor dietary intake**
- **Rare genetic defects**
- **Physiological causes:** infancy, teenage girls, pregnancy, regular blood donation, elite athletes

Functional iron deficiency/ anaemia of chronic disease
(adequate iron stores but body unable to use them)

Iron studies show:

- Ferritin: raised
- Serum iron: low
- Transferrin/TIBC: low
- Unsaturated iron-binding capacity: low/normal
- Transferrin saturation: low

Possible causes:

- CKD, heart failure
- Liver disease
- Rheumatoid arthritis
- Cancer
- Acute/chronic inflammation
- Chronic infection

Haematological

- **Consider screening for haemoglobinopathies**

Possible causes:

- Thalassaemia trait
- Sideroblastic anaemia
- Sickle cell anaemia

Beware dual pathology: iron deficiency anaemia and anaemia of chronic disease may coexist (e.g. rheumatoid arthritis and a new colorectal cancer). Unpicking this can be tricky – see page 3 for more information

Why is there an anaemia?

Review the notes:

- Why were the bloods done in the first place? Any red flags in the history? Any other blood abnormalities?

Review medications:

- Any antiplatelets, anticoagulation, NSAIDs, SSRIs? Are they on a PPI?

Review the patient:

- Are they symptomatic of the anaemia? Any decompensation, e.g. decompensated heart failure?
- Do they have any symptoms which may signify an underlying cause?
- Dipstick urine: any non-visible haematuria?
- Offer a FIT (NICE 2021, NG12, NICE 2017, DG30 ACPGBI/BSG Gut 2022:71:1939).
- Check bloods for coeliac serology.

Microcytosis WITHOUT anaemia

Microcytosis WITHOUT anaemia could be an indicator for underlying cancer (BJGP 2020;70(696):e457).

- This was particularly the case for men $\geq 40y$ and both sexes $\geq 70y$.
- Commonest cancers were colorectal, lung and kidney. Stomach cancer and lymphoma were also seen.

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature. The information presented herein should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular, we suggest you carefully consider the specific facts, circumstances and medical history of any patient, and recommendations of the relevant regulatory authorities. We also suggest that you check drug doses, potential side-effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages. July 2024. For full references see the relevant Red Whale articles.

3. Managing iron deficiency anaemia

(Based on Lancet 2016;387:907, NEJM 2019;381:1148, BNF accessed July 2023, <https://nhs.uk/medicines/iron-supplements/> (management-in-primary-care-pathway- final-december-2015.pdf))



This GEMS relates to those with an anaemia suitable for investigation in primary care: if haemoglobin very low/pancytopenia/symptomatic, use clinical judgement about urgent investigation/referral/admission

Anaemia is not a standalone condition – it is a sign of underlying pathology. Assess for a cause

Treatment of an iron deficiency anaemia

This section discusses treatment of the anaemia; remember to look for and treat the underlying cause.

Oral iron:

- Replace with oral tablets, e.g. ferrous sulphate 200mg/fumarate 210mg/gluconate 600mg ONCE daily.
- Take on an empty stomach. Absorption can be reduced by:
 - Taking iron with food (reduces absorption by up to 40%; does also reduce side-effects).
 - Taking iron with a cup of tea (reduces absorption by up to 90%!) (it's the tea, not the milk, that does it!).
 - Taking other medications at the same time as taking iron (e.g. antacids).

Use parenteral iron if:

- Unable to tolerate oral iron. **Daily or alternate-day iron?**
- Impaired GI absorption. The BNF states that for the treatment of iron deficiency anaemia, ferrous (sulphate, fumarate or gluconate) should be given ONCE a day, and be reduced to every other day if not tolerated.
- On haemodialysis.
- Functional iron deficiency.

How long to give oral iron for and when to retest

Give oral iron for 4w, then recheck FBC

(Historically, when ferrous was prescribed 2–3x/d, we would expect 10–20g/l increase over 4w)

Ensure cause has been investigated

If Hb improved/normalised after 4w:
continue iron replacement for 2–4m, then recheck Hb.
If Hb normalised at this stage: continue iron replacement for 3m.
(Lancet suggests monthly FBC, ferritin and iron studies)

If Hb remains low after 4w, with iron deficiency picture:
check adherence and how taking (see above regarding absorption).
Refer for parenteral iron.

After treatment and resolution of the anaemia, check bloods to monitor for any recurrence.

The Lancet suggests check FBC, ferritin and iron studies every month for 3 months, and then 3 monthly for 1y.

Identifying a true iron deficiency in the presence of an anaemia of chronic disease

People with an anaemia of chronic disease may ALSO have an iron deficiency anaemia, and this can be tricky to unpick. Here are some pointers (NEJM 2019;381:1148):

- Try and identify blood loss:
 - Occult, e.g. GI tract (consider a FIT test), consider dipping a urine. Refer as appropriate.
 - Secondary to a procedure/operation.
- Consider a therapeutic trial of oral/intravenous iron:
 - Oral iron is less readily absorbed in those with anaemia of chronic disease; IV iron may be better.
 - With IV iron replacement, partial haemoglobin correction occurs within 4w and levels off by 8w.

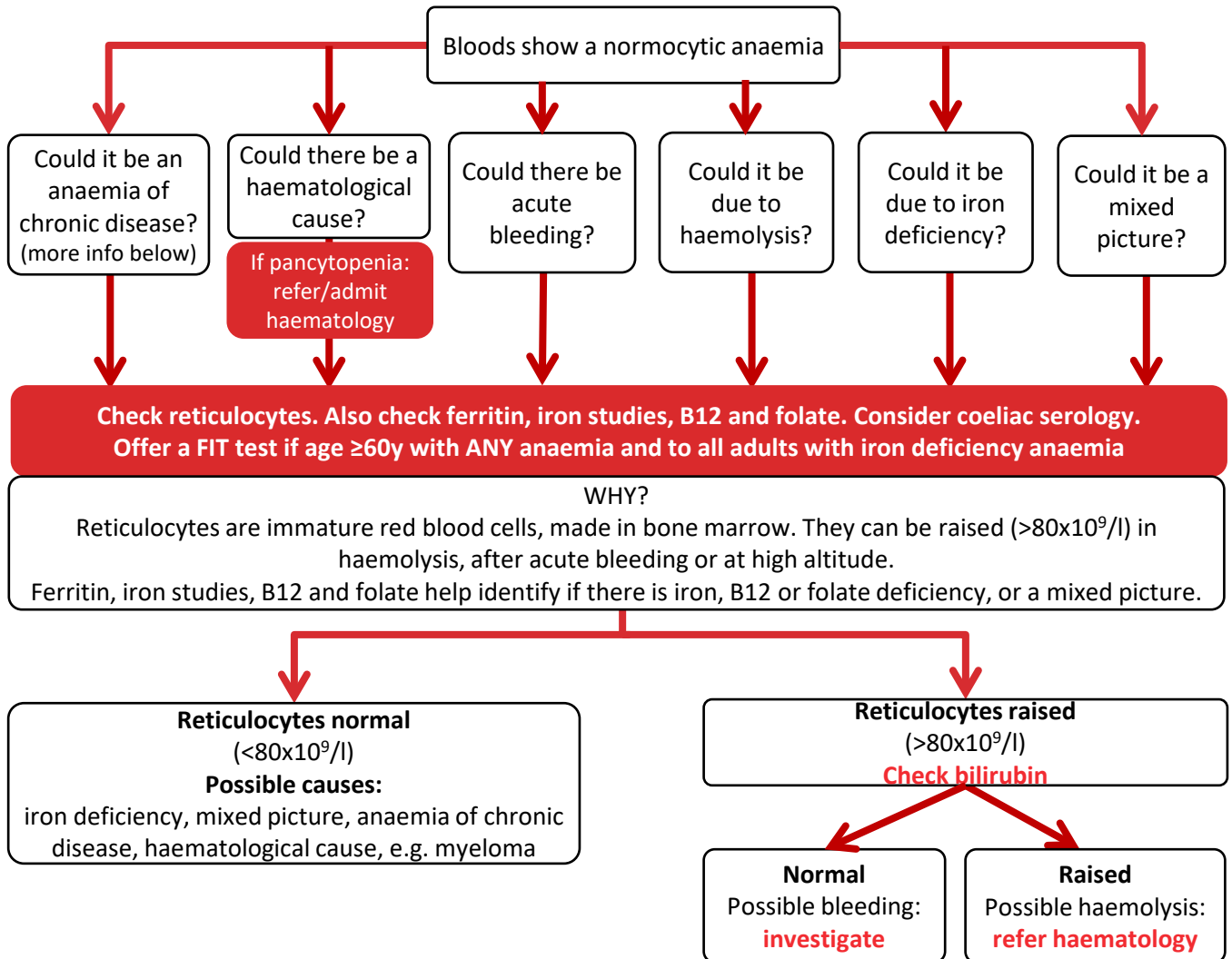
4. Normocytic anaemia

(Based on Lancet 2016;387:907, NEJM 2019;381:1148, <https://nhsbt.dbe.blob.core.windows.net/umbraco-assets-corp/14681/bolton-anaemia-management-in-primary-care-pathway-final-december-2015.pdf>)



This GEMS relates to those with an anaemia suitable for investigation in primary care: if haemoglobin very low/pancytopenia/symptomatic, use clinical judgement about urgent investigation/referral/admission

Anaemia is not a standalone condition – it is a sign of underlying pathology. Assess for a cause



Why is there an anaemia?

Review the notes:

- Any underlying conditions which may be responsible for an anaemia of chronic disease?
- Any history of haemolysis/haematological conditions? Any history of recent bleeding?
- Any symptoms/signs that would fit with iron/B12/folate deficiency? (see 'why is there an anaemia?' on pages 2 and 5)

Anaemia of chronic disease

- Consider if a normocytic normochromic anaemia AND evidence of systemic inflammation (raised ESR/CRP) AND haematinics compatible with anaemia of chronic disease (see p2).
- Usually a mild or moderate anaemia (70–120g/l) which occurs because there is decreased erythrocyte production and lifespan (reduced by 25%).
- Can occur in systemic inflammatory conditions (e.g. rheumatoid arthritis, SLE, IBD), chronic disease (e.g. CKD, heart failure, COPD, cystic fibrosis), chronic infection (e.g. TB), acquired immunodeficiency syndrome, cancer (e.g. ovarian, lung, lymphoma).

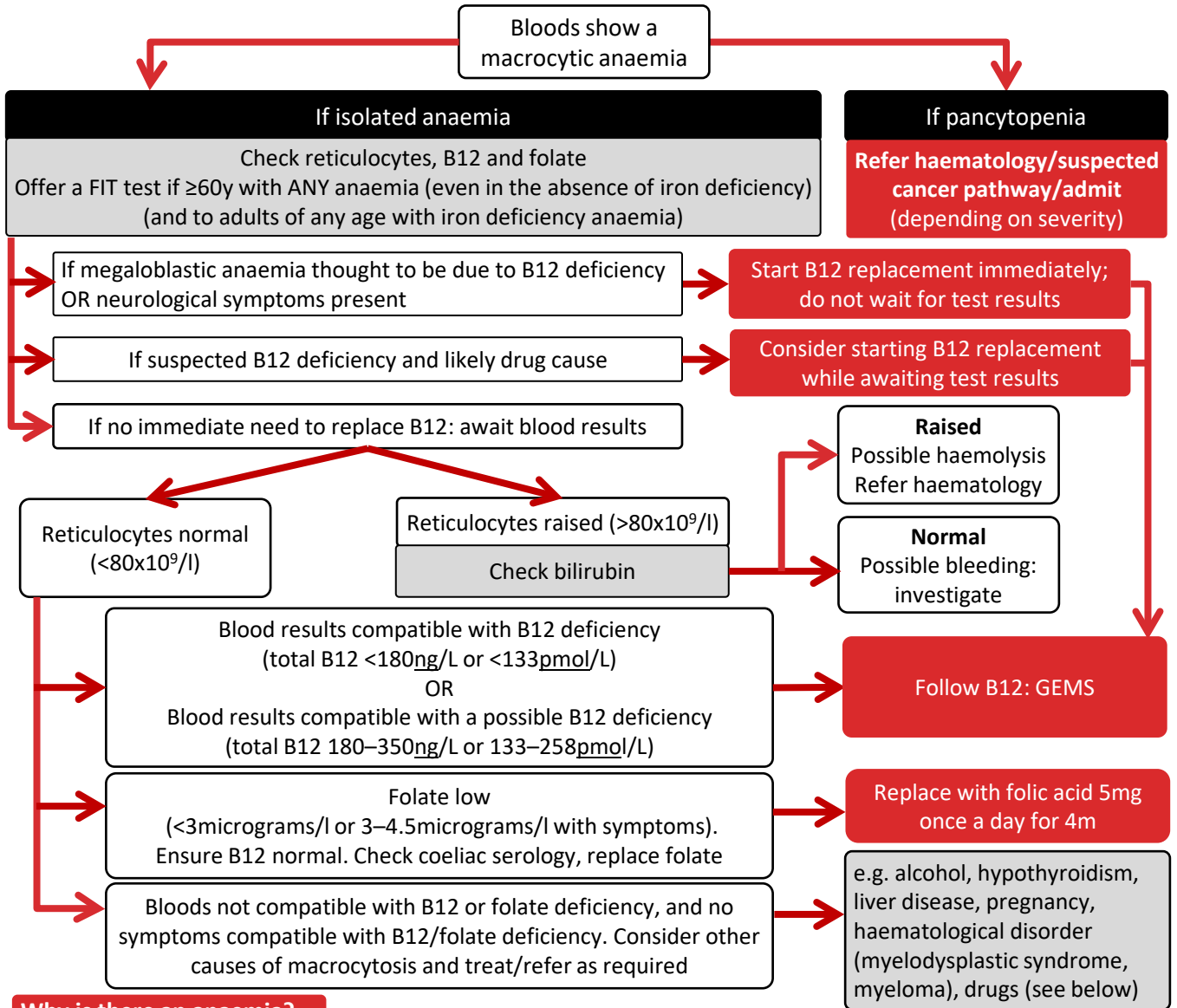
5. Macrocytic anaemia

(Based on NICE 2024, NG239, BJH 2014;166:496, NEJM 2013;368:149,BNF, accessed Nov 2020, <https://nhs.uk/medicines/umbraco-assets-corp/14681/bolton-anaemia-management-in-primary-care-pathway-final-december-2015.pdf>)



This GEMS relates to those with an anaemia suitable for investigation in primary care: if haemoglobin very low/pancytopenia/symptomatic, use clinical judgement about urgent investigation/referral/admission

Anaemia is not a standalone condition – it is a sign of underlying pathology. Assess for a cause



Why is there an anaemia?

Review the notes:

- Why were the bloods done? Any red flags in the history? Any other blood abnormalities?
- Any risk factors for B12 (+/- folate) deficiency, e.g. dietary deficiency, gastrointestinal surgery, abdominal/pelvic radiotherapy, atrophic gastritis, an autoimmune condition or family history of B12 deficiency/autoimmune condition.

Review medications (NICE 2024, NG239, BJH 2014;166:496, Oxford Handbook of Clinical Medicine, 10th Edition, 2017):

- Are they on azathioprine or hydroxyurea?
- Methotrexate, anticonvulsants and trimethoprim can cause a folate deficiency.
- Metformin, PPIs, colchicine, H2-receptor antagonists, phenobarbital, pregabalin, primidone, topiramate and recreational nitrous oxide use are associated with B12 deficiency.

Review the patient:

- Are they symptomatic of the anaemia? Any decompensation, e.g. decompensated heart failure?
- Do they have any symptoms that may signify an underlying cause?

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature. The information presented herein should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular, we suggest you carefully consider the specific facts, circumstances and medical history of any patient, and recommendations of the relevant regulatory authorities. We also suggest that you check drug doses, potential side-effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages. July 2024. For full references see the relevant Red Whale articles.