

Investigation and Management of the Adult Patient with Anaemia

Microcytic Anaemia

STEP 1

- Full Blood Picture Test

STEP 2

- Iron studies, including ferritin and transferrin saturation (TSAT)
- CRP

STEP 3

- Correct anaemia
- Investigate cause if unknown
(unless further investigation not in patient's best interests)

STEP 4

- Monitor response to replacement therapy
- Treat disease causing the anaemia

* **MCV < 76fl or MCH < 27pg**
Microcytic anaemia

* Normal range values may differ between hospital laboratories

Se ferritin < 30 ug/L when CRP < 30 mg/l
Se ferritin < 100 ug/L when CRP > 30 mg/l
or TSAT < 20%

Manage as IRON DEFICIENCY ANAEMIA
Discuss management of anaemia with an Obstetrician if pregnant

Ferritin > 70 ug/L, CRP normal or increased and TSAT > 20%

IRON DEFICIENCY ANAEMIA

- Start oral iron therapy to normalise Hb and replenish iron stores
Start with parenteral iron therapy if:
 - History of oral iron intolerance or poor compliance
 - Impaired gastrointestinal absorption
 - Haemodialysis
 - Major surgery must take place in < 3 weeks
- Review history & examination for source of chronic bleeding
Refer to Gastroenterologist if
 - Adult male
 - Postmenopausal female
 - Premenopausal female with gastro-intestinal symptoms or bleeding

Refer to Gynaecologist if

- Post menopausal bleeding
- Menorrhagia

MICROCYTIC ANAEMIA UNLIKELY TO BE DUE TO IRON DEFICIENCY

Assess for:

- Acute or chronic inflammatory disease
- Chronic infection
- Malignancy
- Liver disease

Check differential white cell count (WCC), liver function tests (LFTS)

Refer to a Haematologist if:

- Thalassaemia or sideroblastic anaemia suspected
or
- Cause of anaemia is unknown

IRON DEFICIENCY ANAEMIA

Check full blood picture (FBP) after 2-4 weeks of iron therapy
If Hb has improved (10-20g/L increase):

- Check if Hb normalised after 2-4 months iron therapy
- Continue iron therapy for another 3 months to replenish iron stores

If no improvement, consider:

- Switch to intravenous iron therapy

ANAEMIA OF CHRONIC DISEASE

A diagnosis of exclusion
Unresponsive to parenteral iron unless iron deficiency also present

Treat and monitor the underlying cause

Investigation and Management of the Adult Patient with Anaemia

GUIDANCE ON THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA

Iron deficiency anaemia is the most prevalent cause of anaemia. It can be due to blood loss, impaired iron absorption or failure to utilise iron stores.

1. Have a high index of suspicion for iron deficiency anaemia in patients with:

- Chronic gastro-intestinal symptoms or evidence of chronic bleeding from gastro-intestinal tract
- Acute or chronic inflammatory bowel disease or malabsorption
- Malignancy
- Menorrhagia
- Recent pregnancy

2. Investigate the cause of anaemia promptly unless the aetiology is already known or further investigations are not in the patient's best interests (e.g. palliative care patient).

Anaemia should be investigated more urgently in men with a haemoglobin concentration < 120 g/L and in women with a haemoglobin concentration < 100 g/L, because such low levels of Hb may be indicative of serious disease.

3. Once iron deficiency has been detected treatment should not be delayed

- **Oral iron therapy** is the treatment of choice in most cases, **even if temporary discontinuation for 1 week is indicated to facilitate colonoscopy**
- Prescribe ferrous sulphate 200mg twice or three times a day (at least 6hr apart), preferably between meals, if tolerated

- If nausea, abdominal pain, constipation or diarrhoea occur, advise ferrous sulphate be taken with food, reduce daily dose of ferrous sulphate or change to ferrous gluconate 600 mg twice a day
- Haemoglobin (Hb) should rise by 20 g/L every 3-4 weeks and be within normal range after 2-4 months of iron therapy
- Continue oral iron therapy for 3 months after Hb has returned to normal range, to replenish iron stores.
- Measure Hb every 3 months for a year, then monitor annually, prescribing additional iron therapy as required

Intravenous iron therapy is indicated if:

- Oral iron therapy has failed or was not tolerated by patient
- History of malabsorption or chronic inflammatory bowel disease
- Functional iron deficiency - e.g. chronic kidney disease (CKD) on haemodialysis
- Major surgery must proceed in less than 3 weeks time

Normocytic anaemia can be due to CKD or anaemia of chronic disease but may also be a sign of early iron deficiency anaemia.

- ** In CKD treat as iron deficiency anaemia if transferrin saturation (TSAT) is less than 20% AND ferritin is less than 100 ug/L. Measure **both** of these parameters to assess iron deficiency and response to replacement therapy.

Iron should be administered intravenously for patients on haemodialysis, unless this route is contraindicated.

Consult with patient's Nephrologist about addition of Erythropoiesis-Stimulating Agent (ESA) if inadequate response in Hb with iron therapy alone.

Macrocytic anaemia is most commonly due to excessive alcohol intake, folate and / or vitamin B12 deficiency but may also occur with myelodysplasia, myeloma, cytotoxic drug therapy and following gastrectomy or terminal ileum resection

- Do not delay replacement therapy with folic acid and / or vitamin B12. Investigate cause, if unknown.
- Ensure that vitamin B12 therapy is commenced with folic acid when both nutritional deficiencies exist, to avoid neurological complications.

Anaemia prior to scheduled major surgery whether mild or severe, is an independent risk factor for postoperative major morbidity and mortality. Major surgery should therefore be delayed until anaemia is corrected, if it is in the patient's best interests.

References

World Health Organisation. Worldwide Prevalence of Anaemia 1993-2005. WHO 2008.

Cook J. Diagnosis and Management of Iron Deficiency Anaemia. Best Practice Research and Clinical Haematology 2005; 18: 319-32.

Goddard AF, James MW, McIntyre AS, Scott BB, on behalf of the British Society of Gastroenterology, Guidelines for the management of iron deficiency anaemia. GUT 2011; 60: 1309 - 1316

Goodnough LT, Maniatis A, Earnshaw P et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines BJA 2011; 106: 13-22

Hoffbrand AV, Moss PAH, Pettit JE. Essential Haematology 2006, Blackwell Publishing Ed. Musallam et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. www.thelancet.com October 2011.

**National Institute for Clinical Excellence, Anaemia management in people with chronic kidney disease. June 2015 cks.nice.org.uk/anaemia-iron-deficiency

NHS Clinical Knowledge Summaries Anaemia - iron deficiency, February 2013 cks.nice.org.uk/anaemia-iron-deficiency.

***NHS Clinical Knowledge Summaries, Anaemia - vitamin B12 and folate deficiency, July 2015 cks.nice.org.uk/anaemia-b12-and-folate-deficiency

S Pavord, B Myers, S Robinson et al, on behalf of the British Committee for Standards in Haematology, UK Guidelines on the management of iron deficiency in pregnancy July 2011. www.bcshguidelines.com.

Investigation and Management of the Adult Patient with Anaemia

Normocytic Anaemia

STEP 1

- Full Blood Picture Test

STEP 2

- Iron studies, including ferritin and TSAT
- Check folate and vitamin B12 levels
- Urea, creatinine, eGFR

STEP 3

- Correct anaemia
- Investigate cause if unknown

STEP 4

- Monitor response to replacement therapy
- Treat disease causing the anaemia (if appropriate)

*** MCV 76 - 100 fl
MCH 27-32pg
Normocytic anaemia**

* Normal range values may differ between hospital laboratories

Ferritin < 30 ug/L when CRP < 30 mg/L
 Ferritin < 100 ug/L when CRP > 30 mg/L
 TSAT < 20%
 Normal eGFR and blood creatinine

Treat as IRON DEFICIENCY ANAEMIA
 See STEP 3 for microcytic anaemia

Ferritin < 100 ug/L **and** TSAT < 20% **
 Normal vitamin B12 level
 Low or normal folate level

Elevated blood creatinine, eGFR < 60 ml/min

Consider CHRONIC KIDNEY DISEASE

Ferritin > 30 ug/L and TSAT > 20%

Normal folate and vitamin B12 levels
 Normal renal function (eGFR > 60 ml/min)
 Go to STEP 3

CHRONIC KIDNEY DISEASE

Refer to a Nephrologist if new diagnosis or deterioration of renal function

Treat as IRON DEFICIENCY ANAEMIA
 See STEP 3 for microcytic anaemia
 Seek advice from a Nephrologist or a Haematologist

NORMOCYTIC ANAEMIA OF UNKNOWN CAUSE

Assess for:

- Acute or chronic inflammatory disease
- Chronic infection
- Malignancy
- Liver disease

Check differential WCC & LFTs

If cause still unknown refer to a Haematologist

CHRONIC KIDNEY DISEASE

Continue oral iron if Hb has improved by 10-20 g/L after 2-4 weeks. Aim for:

- Hb > 110 g/L
- TSAT > 20%
- Ferritin greater than 100 ug/L but less than 800 ug/L**

Offer intravenous iron If:

- No improvement in Hb
- Intolerant of oral iron
- On regular haemodialysis

Discuss addition of § ESA with patient's Nephrologist

Treat concurrent folate deficiency

ANAEMIA OF CHRONIC DISEASE

A diagnosis of exclusion, unresponsive to parenteral iron

Iron deficiency may also be present

Monitor and treat the underlying cause

Investigation and Management of the Adult Patient with Anaemia

Macrocytic anaemia

STEP 1

- Full Blood Picture Test

Refer to a Haematologist if haemolysis detected in FBP (confirmed on repeat FBP)

* **MCV > 100 fl or MCH > 32 pg**

* Normal range values may differ between hospital laboratories

STEP 2

- Check folate and vitamin B12 levels
- Urea, creatinine, eGFR
- Liver function tests

Low folate and / or low vitamin B12 level
FOLATE AND / OR VITAMIN B12 DEFICIENCY
*** Seek urgent advice from a Haematologist if neurological symptoms secondary to folate or vitamin B12 deficiency or if patient is pregnant

Normal renal function, folate and vitamin B12 levels
Go to STEP 3

STEP 3

- Correct anaemia
- Investigate cause if unknown

FOLATE DEFICIENCY

- Start oral folic acid 5 mg daily
If co-existing vitamin B12 deficiency start vitamin B12 injections at same time to avoid neurological complications
- Assess for cause - poor diet, liver disease, alcohol misuse, gastro-intestinal surgery, recent pregnancy, chronic inflammatory disease (e.g. Crohn's disease or TB), malignancy and drug therapy (e.g. anticonvulsants)

VITAMIN B12 DEFICIENCY

- Hydroxocobalamin intramuscular injections:
1 mg alternate days for 2 weeks, then 1 mg every 3 months for life
- Investigate for possible cause, e.g.
 - Malabsorption
 - Post gastrectomy
 - Terminal ileum disease or resection

MACROCYTIC ANAEMIA OF UNKNOWN CAUSE

Investigate for possible cause:

- Liver disease
- Alcohol misuse
- Hypothyroidism
- Drug causes e.g. cytotoxics

If myelodysplasia or myeloma suspected or if cause of anaemia still unknown refer to a Haematologist

STEP 4

- Monitor response to replacement therapy
- Treat disease causing the anaemia (if appropriate)

FOLATE DEFICIENCY

Monitor Hb and reticulocyte count

- after 10 days for response
- after 8 weeks to check if Hb has returned to normal range
- after 4 months course completed

VITAMIN B12 DEFICIENCY

Monitor Hb and reticulocyte count

- after 10 days for response
- after 8 weeks to check if Hb has returned to normal range

MACROCYTIC ANAEMIA not due to folate or vitamin B12 deficiency

Monitor Hb

Treat and monitor cause if identified