Clinical Guideline: Investigation and Management of Anaemia within DBTH

Last Update: July 2021
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Introduction
This clinical guideline is for the investigation and management of anaemia, including blood product prescription. It provides quick reference information based on contemporary guidelines and will help to align clinical practice in-line with national guidance.

Acknowledgements: Some of the tables were uses from the guidelines Anaemia: When to suspect and how to interpret the results. Clinical Focus in Primary Care. 2016, 9(2): 60–74 with permission from Dr.K.Pendry.

References
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JPAC Handbook of Transfusion Medicine. 2015. Available at https://www.transfusionguidelines.org/transfusion-handbook
Alimam S, Allard S, Pendry K. Anaemia: When to suspect and how to interpret the results. Clinical Focus in Primary Care. 2016, 9(2): 60–74
Medlock R, Sorour Y. Interpretation and action for low serum vitamin B12 level. 2014. Internal DBTH Pathology Guideline.
Devalia V, Hamilton S, Molloy A. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. British Journal of Haematology. 2014, 4 (166): 496-513
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1.

Blood Transfusion for Stable Anaemia

Stable anaemia is defined as no active haemorrhage. For major haemorrhage, please see the major haemorrhage protocol (***link here***).

1) Identify and treat the cause for anaemia

a. Optimal patient management of anaemia requires identification and treatment of the underlying cause
b. Blood transfusion can often be avoided through diagnostic workup (See below)

2) Use restrictive transfusion thresholds

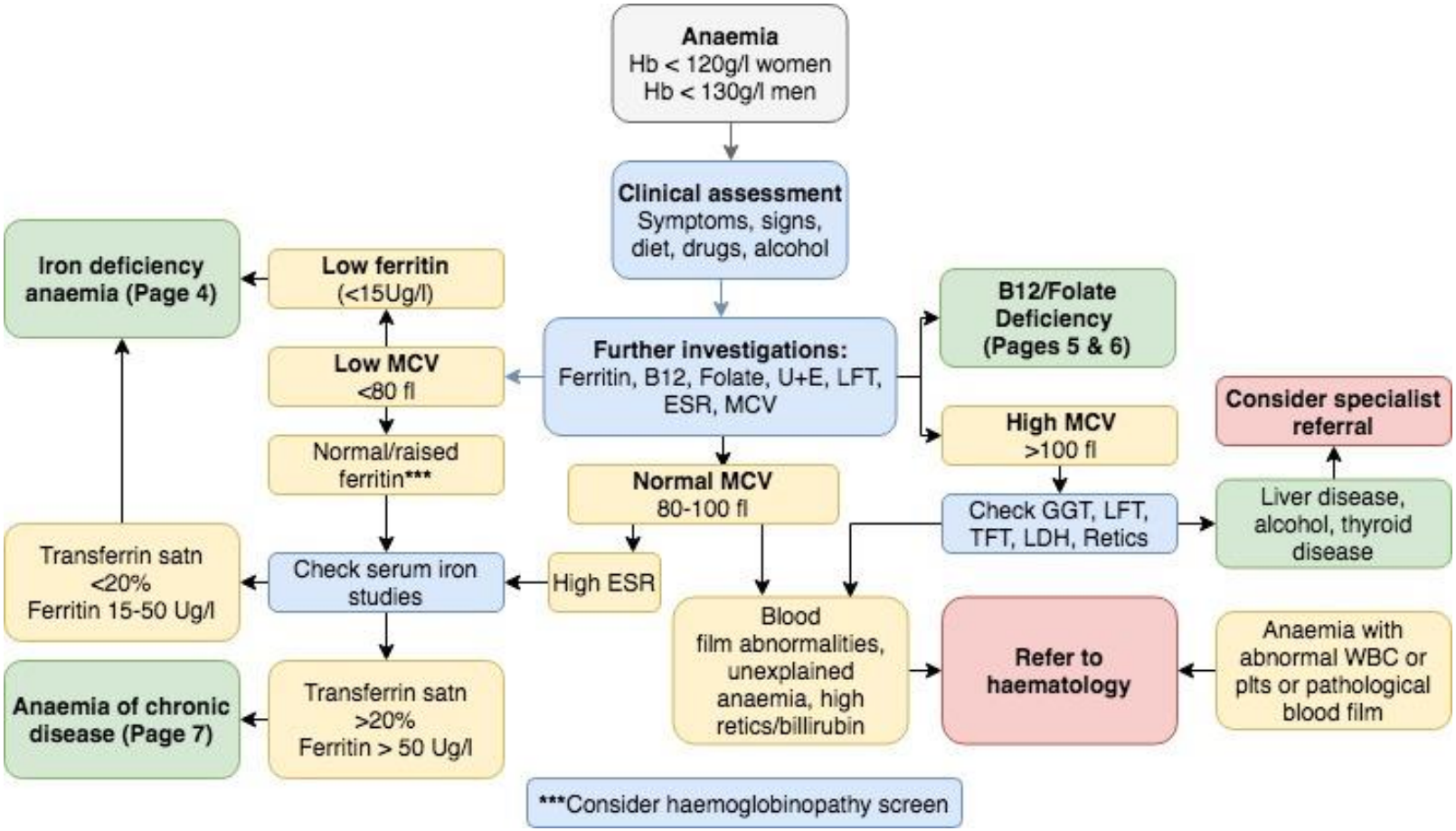
a. Restrictive thresholds reduce morbidity and protect patients from exposure to blood products
b. Always transfuse if symptomatic in addition to treatment of the underlying cause
c. If no active bleeding and a reversible cause is identified, prescribe the minimum number of units to achieve a target Haemoglobin level.
d. Assume an increment of 10g/L per unit for a 70kg adult.

Red cell transfusion thresholds		
R1	Acute Bleeding	Once normovolaemia achieved, frequent measurement of Hb should be used – see suggested thresholds below
R2	Stable Anaemia (No active bleeding)	Hb <70 g/l Use a target Hb of 70-90g/L
R3	Stable Anaemia & ischaemic heart disease	Hb <80g/l Use a target Hb of 80-100g/L
R4	Transfusion dependent anaemia (e.g. MDS)	Maintain an Hb which prevents symptoms. Suggest an initial threshold of 80g/L then adjust as required.
R5	Radiotherapy	Limited data for maintaining Hb of 110g/L.

3) Don’t give unit two without review

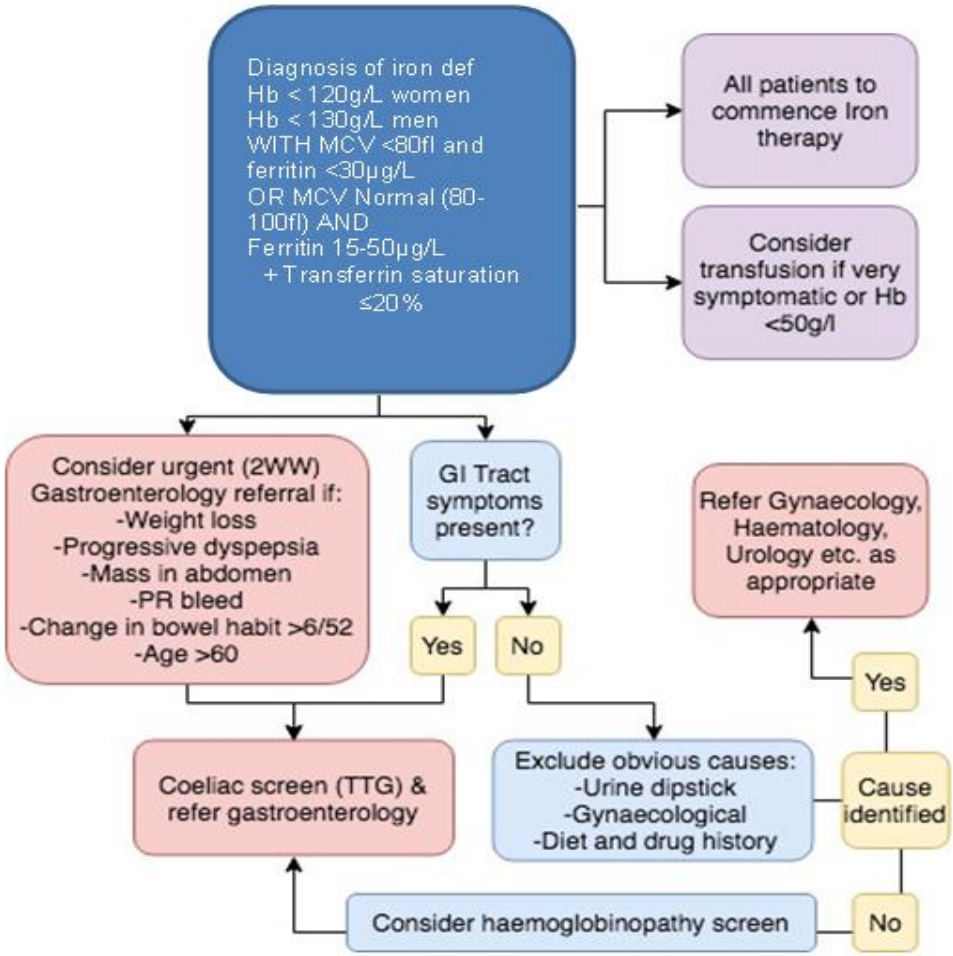
a. Clinically reassess your patient after each unit transfused, and check a haemoglobin level
    i. Is your patient still symptomatic?
    ii. Is further transfusion appropriate?
b. Only order one unit at a time for non-bleeding patients
c. Document patient consent and the reason for transfusion

Diagnostic approach to the patient with anaemia



- All patients should have FBC, U+E, LFT, B12, Folate, Ferritin checked within the last 4 weeks
- Turn-around time for add-on haematinics is 2 hours

Iron Deficiency Anaemia



Investigation of Iron Deficiency Anaemia

- Consider aspirin / NSAIDs as cause but investigate all IDA.
- Do a urine dipstick in all patients; 1% of have a renal malignancy.

Treatment of Iron Deficiency Anaemia

Oral Iron Therapy

- Patients should be advised to take iron on an empty stomach, prior to usual medications. Use the maximum tolerated dose.

Drug	Initial dose	Frequency
Ferrous Sulphate	200mg	OD to TDS
Ferrous Fumarate	210mg	

- Patients should be counselled regarding diet including details of iron rich food sources. Consider providing written information: https://www.bda.uk.com/foodfacts/iron_food_fact_sheet.pdf

IV Iron Therapy

- IV iron should be used in patients who fail to respond to oral iron, or are intolerant of oral iron.
- Consider first line if:
  - History of oral iron intolerance or poor compliance
  - Impaired gastrointestinal absorption (Metastatic Carcinoma, IBD and Duodenal pathology)
  - Major surgery planned within 3 weeks
  - Patients on Haemodialysis

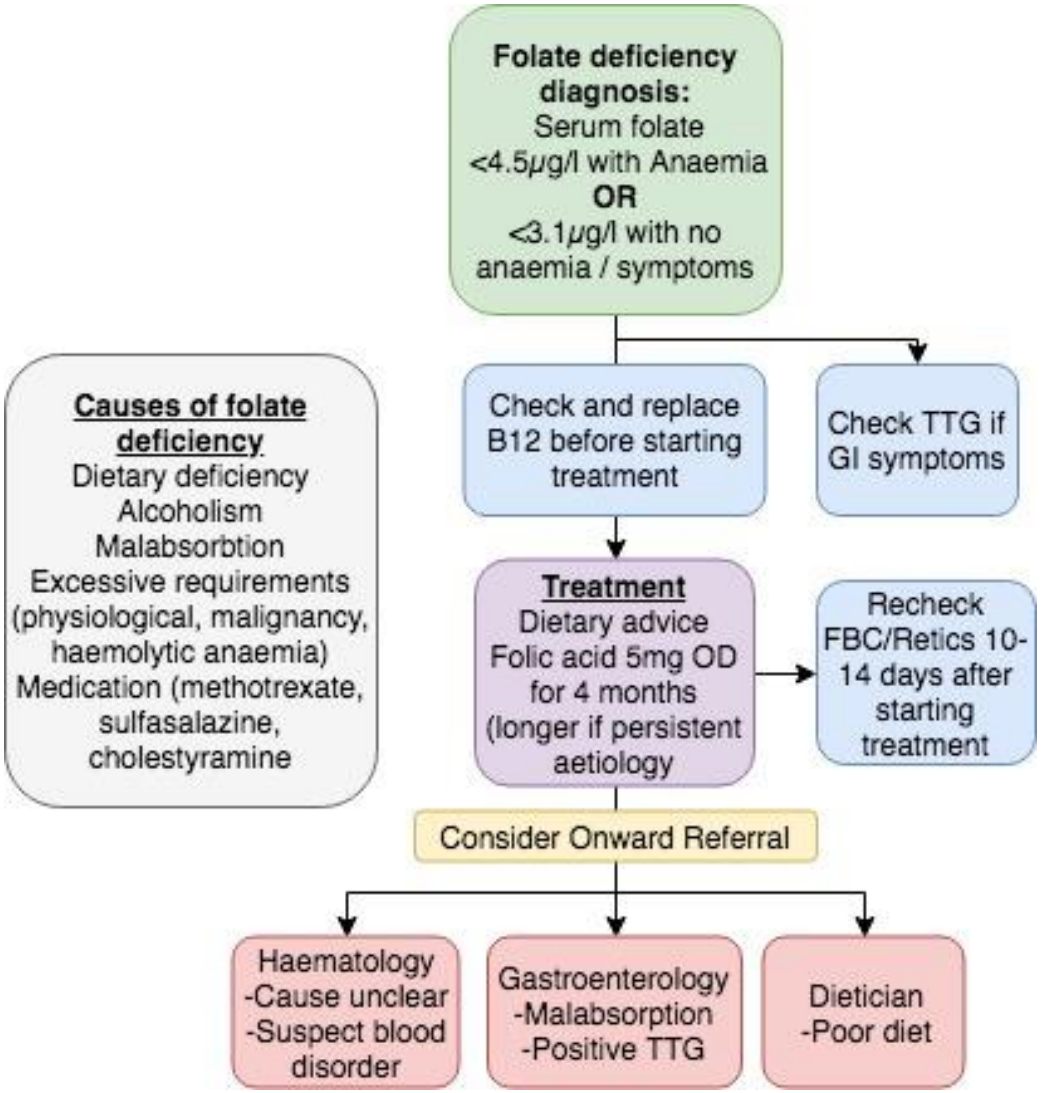
Blood Transfusion

- Blood transfusion should be reserved for those with risk of further bleeding, imminent cardiac compromise or disabling symptoms requiring immediate attention. Give alongside iron therapy

Follow-up

1. Check FBC after 10 days to check treatment response
2. Check FBC at 12 weeks to confirm resolution of anaemia
3. Check FBC / Ferritin on completion of treatment
4. Continue Iron supplementation 3 months after normalisation of Hb to replenish Iron stores.

Folate Deficiency Anaemia



Treatment of Folate Deficiency Anaemia

Give information on natural sources of folate, including Leafy / green vegetables, Brown rice and chickpeas. Consider providing written information:
https://www.bda.uk.com/foodfacts/FolicAcid.pdf

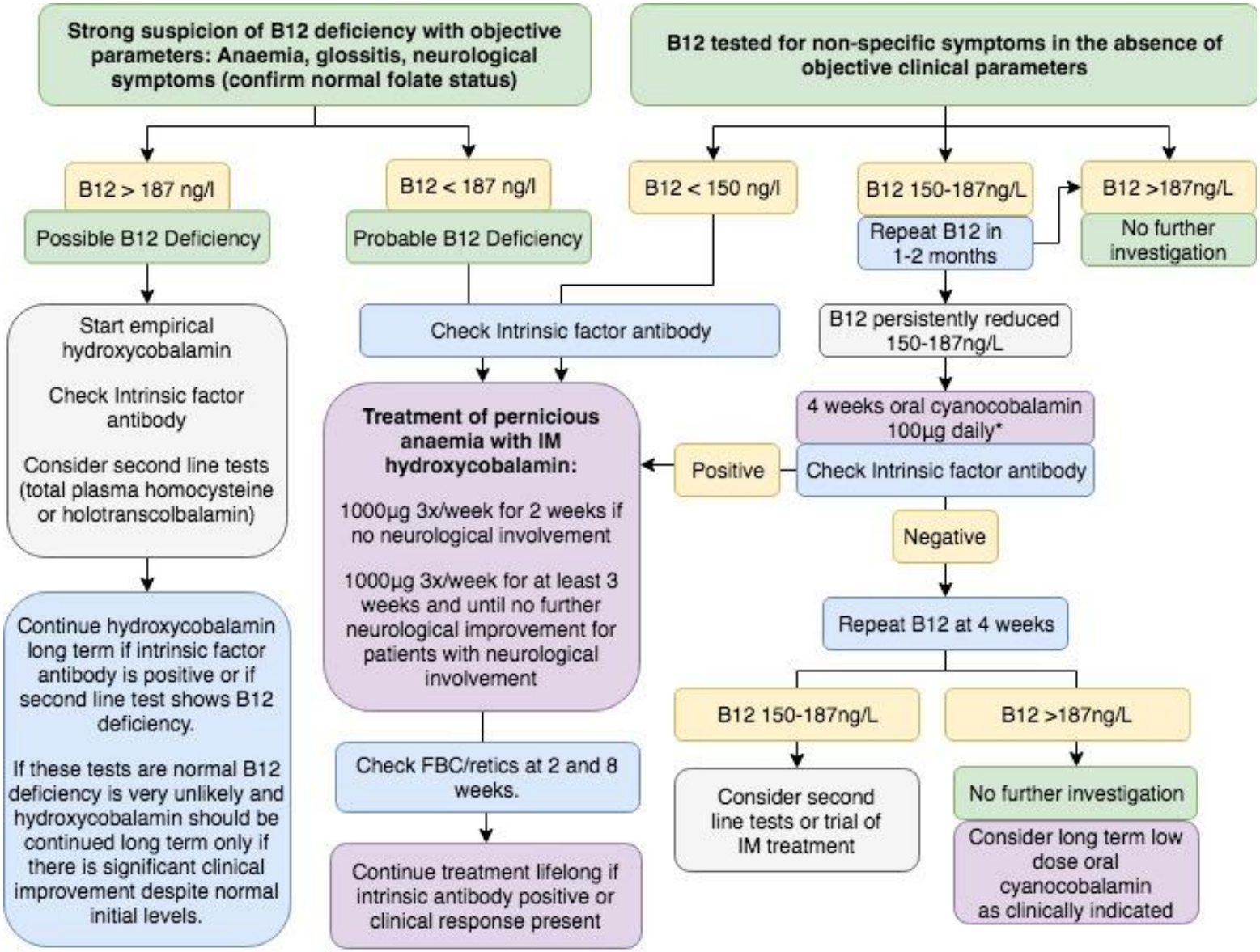
Offer daily oral folic acid for 3 months after Hb normalised, or longer if the underlying cause is persistent

Follow up

FBC and reticulocyte count should be checked:

5. After 10 days to check response to treatment (Rise in FBC, normalisation of reticulocyte count)
6. After 8 weeks to confirm normal blood count
7. On completion of treatment to confirm response

B12 Deficiency Anaemia 1



Consider dietary and malabsorptive causes in all patients.

Coeliac serology and referral to gastroenterology may be appropriate if malabsorption, mixed anaemia or GI tract symptoms are present.

Give all patients information on dietary sources of B12, e.g. fortified foods (some soy products, and some breakfast cereals and breads), meat, eggs, and dairy products. Consider providing a written information leaflet: https://ods.od.nih.gov/pdf/factsheets/VitaminB12-Consumer.pdf

B12 Deficiency Anaemia 2

Interpretation of B12 Results

- The interpretation of serum B12 relies heavily on the clinical picture as there is no gold standard test to define B12 deficiency.
- Neurological presentation (peripheral neuropathy, sub-acute combined degeneration of the cord) may occur in the absence of haematological changes, and early treatment is
- essential to avoid permanent neurological disability
- Low B12 levels of uncertain significance may occur with non-specific symptoms and no anaemia (tiredness, neuro-psychiatric, and blood done for "screening")
- Patients with strong clinical features of B12 deficiency may have serum B12 levels that lie within the reference range (false normal B12 level).
- Serum B12 levels should be measured concurrently with folate levels given the biochemical pathways and clinical picture of these deficiencies are similar.
- Raised MCV, oval macrocytes and hypersegmented neutrophils may be helpful in confirming B12 deficiency.
- The absence of a raised MCV does not exclude B12 deficiency- neurological impairment can occur with a normal MCV in 25% of cases.
- When treating with oral cyanocobalamin the patient should be counselled to report any symptoms of neuropathy immediately. If neuropathy occurs then treat as pernicious anaemia
- There is no need to repeat the B12 assay while the patient is on parenteral B12 supplement. The effects should be assessed by FBC only.

SPECIAL GROUPS:

Metformin

- Metformin is associated with reduced serum B12 levels.
- No specific recommendations for monitoring or treatment can be made

Oral contraceptives and HRT

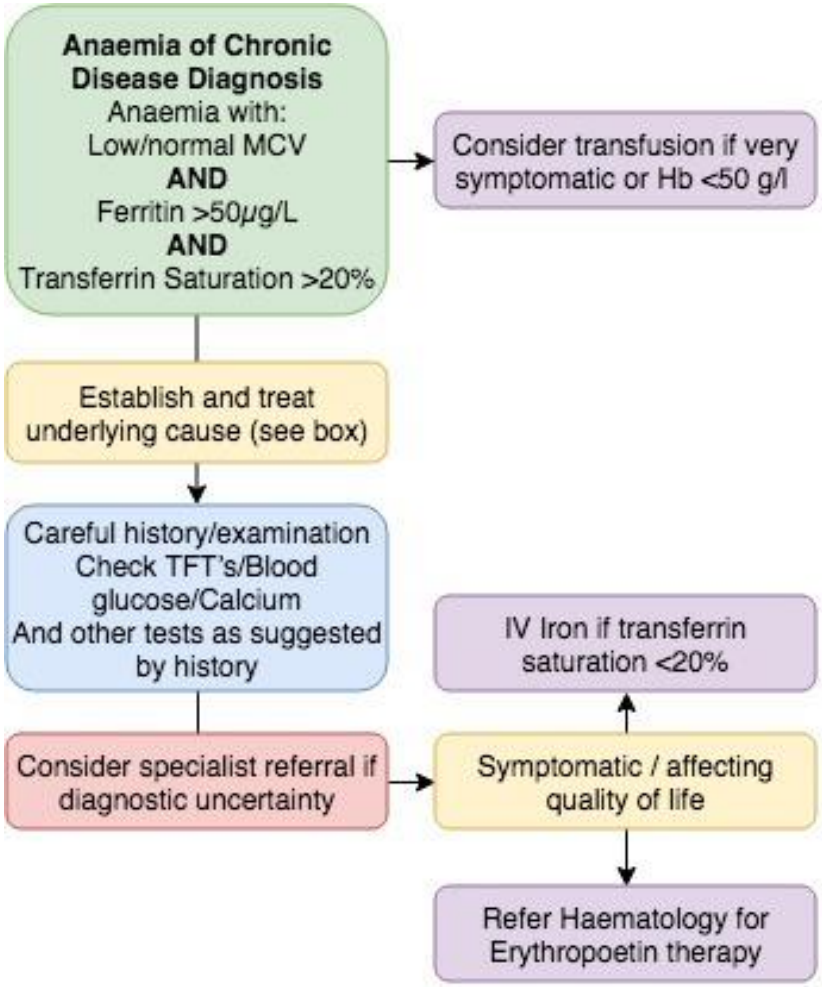
- These agents also cause a reduction in serum B12 levels, but may not be significant in low dose contraceptives and HRT.
- Women with borderline results (150-187ng/L) do not require further investigation and should be advised to review their intake of B12 rich foods

Pregnancy

- During pregnancy B12 level is usually lower than normal and testing should be discouraged unless there a clinical suspicion.
- In the presence of strong clinical suspicion, anti-intrinsic factor antibodies should be checked and treat as pernicious anaemia if positive.
- If a low B12 result has been found in the presence of negative anti-IFAB, but with strong clinical suspicion of deficiency, in order to limit extensive investigation with resultant anxiety
- and to treat potential fetal deficiency, three injections of hydroxocobalamin are suggested to cover the pregnancy, with serum B12 levels being checked 2 months post-partum to ensure resolution to normal levels.

Source: Medlock R, Sorour Y. Interpretation and action for low serum vitamin B12 level. 2014. Internal DBTH Pathology Guideline.

Anaemia of Chronic Disease



Causes of Anaemia of Chronic disease

- Chronic infection (e.g., tuberculosis, chronic fungal infections, hepatitis, osteomyelitis, HIV)

- Acute infection (e.g., pneumonia, pyelonephritis, endocarditis, cellulitis, and soft tissue infections)

-Chronic diseases (e.g., chronic kidney disease, diabetes mellitus, congestive heart failure, major recent thrombosis, chronic pulmonary disease)

-Malignancy (e.g., lymphoma, renal cell carcinoma, multiple myeloma)

-Collagen vascular and autoimmune disorders (e.g., rheumatoid arthritis, SLE, dermatomyositis, giant cell arteritis, polymyalgia rheumatica, scleroderma, inflammatory bowel disease)

-Critical illness and major trauma.

Definition

Anaemia due to an inflammation-mediated reduction in RBC production and survival. Characterised by mild to moderate anaemia that is either normocytic normochromic or microcytic hypochromic with normal RBC morphology. Ferritin and transferrin saturation are elevated.

Clinical Assessment

- History of an autoimmune, malignant, or infectious disorder, or of recent major surgery, trauma, or critical illness.
- Bleeding is rare and alternative diagnoses should be considered.

Investigations

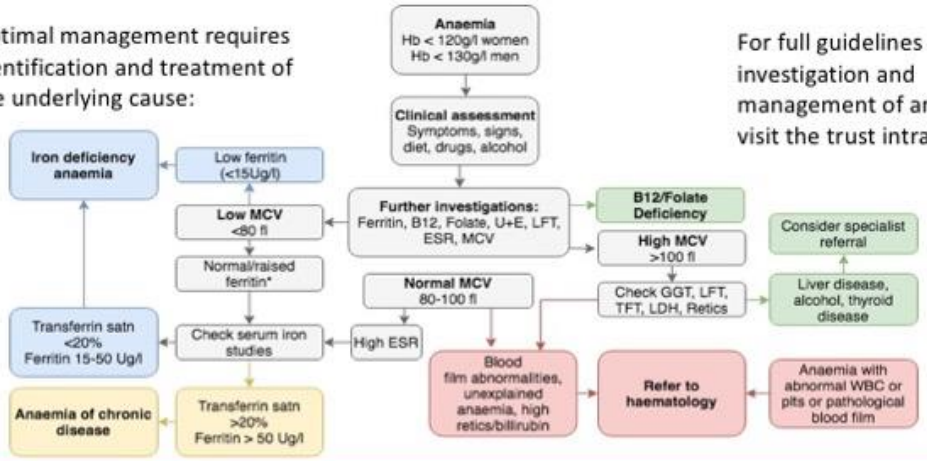
- FBC, blood film, reticulocyte count, ferritin, serum iron studies, CRP/ ESR, creatinine, LDH, and liver function tests.
- Exclude alternate causes of anaemia (Iron, B12, Folate deficiency)
- Consider haematology referral following initial workup to assist in diagnosis and management

Better blood transfusion for patients with stable anaemia

NHS
Doncaster and Bassetlaw Teaching Hospitals
NHS Foundation Trust

1) Identify and treat the cause for anaemia

Optimal management requires identification and treatment of the underlying cause:



For full guidelines on the investigation and management of anaemia, visit the trust intranet

2) Use restrictive transfusion thresholds

Red cell transfusion thresholds		
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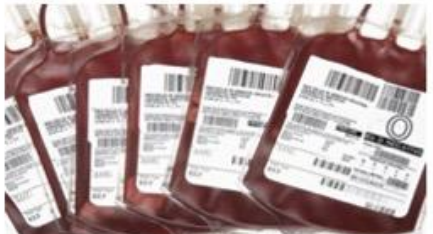
- Restrictive thresholds reduce morbidity
- Transfuse in addition to treatment of the underlying cause
- If no bleeding and reversible cause identified, use the minimum number of units to achieve a target Hb.
- Assume an increment of 10g/L per unit for a 70kg adult.

3) Don't give unit two without review

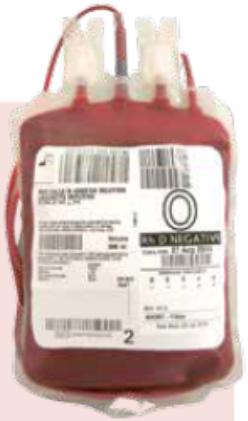
- Reassess your patient after each unit transfused
  - ✓ **Is your patient still symptomatic?**
  - ✓ **Is further transfusion appropriate?**
- Only order one unit at a time for non-bleeding patients
- Document patient consent and the reason for transfusion



NHS
Blood and Transplant

SINGLE Unit Blood Transfusions reduce the risk of an adverse reaction

Don't give unit two without review



Before you transfuse your patient:

- What is your patient's current haemoglobin level?
- What is your patient's target haemoglobin level and would this be achieved by transfusing one unit?

Each unit transfused is an independent clinical decision

Clinically re-assess your patient after each unit is transfused.

✓ Is your patient still symptomatic?

✓ Is further transfusion appropriate?

Only order one unit at a time for non-bleeding patients.

Document the reason for the transfusion.[1]

Further copies are available from NHSBT.CustomerService@nhsbt.nhs.uk

1. *British Committee for Standards in Haematology: Addendum to the Guideline on the Administration of Blood Components. 2012*