Information for Clinicians

Biochemistry department

Ferritin interpretation – a guide for GPs (Non-pregnant adults)

Background

Ferritin is a surrogate measure of body iron stores. In health, the value is directly proportional to the level of iron stores, however in some circumstances, for example in patients with co-existent inflammatory disorders, ferritin may be within the normal or elevated range even when iron stores are absent. This means that a low ferritin does suggest deficiency but above this threshold clinical evaluation and context is always required.

The current laboratory assay for Ferritin is calibrated to the WHO international reference standard.

Low Ferritin

With Anaemia

In many cases, ferritin will have been requested due to finding anaemia. The investigation of anaemia includes assessment of possible iron deficiency anaemia as a differential, **with the first line test being ferritin**.

Anaemia is defined as:
- In adult men Hb below 130 g/L.
- In non-pregnant adult women Hb below 120 g/L

Please note different ranges are applied in pregnancy.

Anaemia with low ferritin (<11 ug/L in women, <24 ug/L in men) confirms iron deficiency anaemia (IDA). Post-menopausal women may have a slightly higher lower limit of normal but assay specific ranges are not available.
Comprehensive guidelines are available via NICE Clinical Knowledge Summaries:
Anaemia - iron deficiency | Health topics A to Z | CKS | NICE

Ferritin thresholds vary according to the local laboratory and there is debate within the literature regarding where the appropriate thresholds should be placed.

The local lower limits to define iron deficiency are based on the assay specific lower limit of normal and are fairly robust. Low iron stores slightly above these thresholds may still warrant investigation if anaemia is present.

Most would consider that there is an indeterminate range where inflammation or conditions that increase Ferritin should be excluded. We would suggest that 11-100 ug/L in women and 24-100ug/L in men is the range where inflammation, infection or influence from malignancy, renal, liver and heart failure should be excluded.

Not every patient requires investigation of ferritin in the indeterminate range; this level can be interpreted as normal where there are no reasons for an acute phase reaction. However, it is important to consider the patient's history and current status to ensure that cases of iron deficiency are not missed. **Where there is doubt, Transferrin Saturation should be tested. Transferrin saturations below 16% indicate iron deficiency.**

Causes of raised ferritin levels include:

- Acute or chronic inflammation.
- CKD
- Heart failure
- Liver disease
- Excessive alcohol intake
- Malignancy
- Hyperthyroidism

Initial investigations

The flow chart below is a guide based on the British Society for Haematology best practice guide.

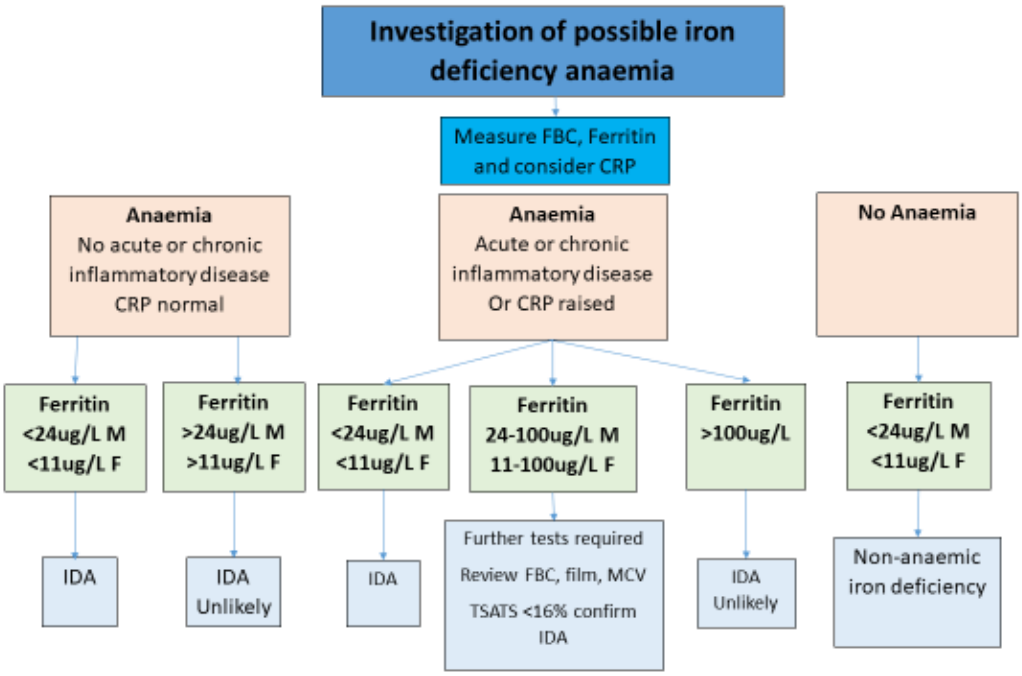


Figure 1 Investigation of possible iron deficiency anaemia

Non-Anaemic iron deficiency

Non-anaemic iron deficiency is relatively common. It can present with non-specific symptoms such as:

- Fatigue
- Poor attention or memory loss
- Sore tongue
- Poor condition of skin, nails or hair including hair loss
- Delayed wound healing
- Restless legs syndrome

The overall prevalence of significant underlying GI pathology, and in particular of GI malignancy, is low in Non-Anaemic Iron Deficiency (NAID). In the absence of other pointers, GI investigation generally is not warranted in premenopausal women since the cause is likely to be menstrual blood loss and/or recent pregnancy. The threshold for investigation of NAID should however be low in men, postmenopausal women, and those with GI symptoms or a family history of GI pathology (British Society Gastroenterology).

It is also important to highlight that where there are red flag symptoms, a referral should not be delayed. Waiting for haemoglobin to drop below a normal value in patients with iron deficiency can cause a delay in diagnosis. Low ferritin is usually first to appear and is very sensitive to detect iron deficiency. In the context of worrying

symptoms, it should be investigated at an early stage rather than waiting for anaemia to develop.

There is no consensus on the treatment of iron deficiency in the absence of anaemia, but there is evidence for some degree of symptomatic improvement, particularly for fatigue.

Patients should be monitored for development of anaemia (3-6 monthly) and the underlying cause should be identified.

Iron supplementation is often associated with side effects so it makes sense to only treat those with symptoms. Asymptomatic individuals should be directed to iron rich foods.

GP consultation for low ferritin

Iron deficiency is often multifactorial and some causes are serious, therefore a careful evaluation is required, looking for symptoms of anaemia and possible causes (see below). Where there is a young and/or overtly well individual, concurrent CRP is not required, but especially in an older population or where there are co-morbidities, a CRP may also help with interpretation of ferritin. Where there is doubt, Transferrin Saturation can help define if iron deficiency is present when less than 16%.

Causes of Iron deficiency

- **Dietary deficiency** — e.g. plant based diets or where requirements exceed intake (young and old)
- **Malabsorption** — e.g. coeliac disease, inflammatory bowel disease, gastrectomy, or *Helicobacter pylori* infection.
- **Increased loss** — chronic blood loss, especially GI or gynae
  - In adult men and postmenopausal women, GI blood loss is the most common cause of iron deficiency anaemia. It can be caused by aspirin or NSAIDs, colonic carcinoma, gastric carcinoma, benign gastric ulceration, and angiodysplasia.
  - Menstruation is the most common cause of iron deficiency anaemia in premenopausal women.
- **Increased requirement** — physiological iron requirements are three times higher in pregnancy than they are in menstruating women, with increasing demand as pregnancy advances.
- **Other causes** — these include blood donation, self-harm, haematuria (rare), nosebleeds (rare), and medication.

Iron deficiency anaemia confirmed

For all people with iron deficiency anaemia:

- Screen for coeliac disease
- Test the urine for blood
- Offer faecal immunochemical testing (FIT) to guide referral of suspected colorectal cancer in adults as per guidelines
- Consider stool examination to detect parasites, if appropriate from the person's travel history

If no obvious cause, appropriate further investigation is generally guided by the person's age and sex.

It is usually unnecessary to further investigate the following groups of people prior to treatment:

- Otherwise healthy young people in whom history clearly suggests a cause — for example, regular blood donors.
- Menstruating young women with no history of gastrointestinal symptoms or family history of colorectal cancer.
- People who are terminally ill or unable to undergo invasive investigations
- People who refuse further investigations.

Treatment of iron deficiency anaemia in the community

- Referrals should be according to NICE guidance and based on presentation: Scenario: Management | Management | Anaemia - iron deficiency | CKS | NICE
- Address any underlying causes that can be managed in primary care (for example treat menorrhagia or stop nonsteroidal anti-inflammatory drugs)
- If dietary deficiency of iron is thought to be a contributory cause of iron deficiency anaemia, advise the person to maintain an adequate balanced intake of iron-rich foods

Dietary iron

- Iron exists in two forms known as haem and non-haem. Haem iron is found in animal tissue (meat) and is the most easily absorbed by the body. Non-haem iron is found in vegetables, beans, pulses and grains and is less easily absorbed by the body.
- Good sources of haem iron are: red meats such as beef, lamb and liver*, some fish and shellfish*. White meat such as chicken and turkey contain smaller quantities of haem iron. . (*avoid during pregnancy).
- Good sources of non-haem iron are: fortified breakfast cereals or bread, dark green leafy vegetables such as watercress, beans, dried fruit, nuts and soya products, e.g. tofu
- See iron sources and daily requirements below

Improving the absorption of iron

- Consuming haem iron (e.g. red meat) at the same time as non-haem iron (e.g. cabbage) can increase the absorption of non-haem iron.
- Vitamin C also helps to increase the absorption of iron.
- Absorption of iron is reduced by: fizzy drinks, large quantities of milk and dairy foods, tea and coffee and having too many high fibre cereals. Antacid medication for indigestion also reduces absorption.

Iron rich foods

Recommended daily amounts of iron are:

- **Adult men 8.7 mg a day or 29 points**
- **Premenopausal women 14.8 mg or 49 points**
- **Post-menopausal women 8.7 mg or 29 points**

Food type	Amount	Points
Black pudding	75g	30
Kidney (lambs)	80g	29
Kidney (chicken)	70g	26
Liver pate	Starter size	15
Beef stew	Casserole portion	10
Beef burger	78g	6
Bacon	2 slices	1
Pork sausages	2	3
Chicken breast	1	1
Ham	3 slices	2
Mussels	25g	23
Smoked salmon	100g	3
Branflakes	portion	24
Special K	portion	23
Weetabix	portion x2	15
Muesli	portion	9
Lentils	2 tbs	9
Baked beans	2 tbs	6
Kidney beans	2 tbs	4
Chickpeas	2tbs	4
Kale	90g	6
Spinach	80g	4
Broccoli	85g	2
Peas	100g	2
Dried figs	4 figs	11
Eggs	1 fried	4
Roasted cashew nuts	25g bag	5

Oral treatment

- **Prescribe** all people with iron deficiency anaemia one tablet daily of oral ferrous sulfate, ferrous fumarate, or ferrous gluconate
    - If this is not tolerated, reduce the dose to one tablet on alternate days, offer laxatives as required, suggest taking after meals or consider alternative oral preparations.
    - If at least two oral preparations have not been tolerated consider Ferric Maltol (third line agent due to cost, see BSW guide BSW-Pathway-for-use-of-ferric-maltol-Ferraccru-Feb2022v1.1.pdf)
    - Consider parenteral iron if unable to tolerate oral iron (usually oral options should be exhausted including two iron supplements and ferric Maltol) or if after 1 month anaemia is worsening or after a 3-6 month course anaemia is not improving (see below).
    - Do not wait for investigations to be carried out before prescribing iron supplements.

- **Monitoring** – timelines vary in guidelines.
  NICE & British Society of Gastroenterologists suggest rechecking FBC within 4 weeks to assess the person's response. Hb should rise by about 20 g/L over 3–4 weeks.
  Some primary care experts say checking after 3 months is acceptable (AAFP).
    - If there is a lack of response, refer to secondary care
    - If there is a response, check FBC at 3-6 months to ensure that the haemoglobin level has returned to normal.
- Once haemoglobin concentration and red cell indices are normal:
    - Continue iron treatment for 3 months to aid replenishment of iron stores, and then stop.
    - Then monitor the person's full blood count periodically — for example, at 3, 6, 12, and 24 months.
- If haemoglobin or red cell indices drop below normal, prescribe iron supplements.
    - Further investigation is only necessary if haemoglobin or red cell indices cannot be maintained this way or if there is any evidence of an active undiagnosed pathology (for example ongoing weight loss or chronic unexplained diarrhoea, persistently elevated inflammatory markers and the persistence or recurrence of IDA).
    - Consider an ongoing prophylactic dose in people who are at particular risk of iron deficiency anaemia.

Raised Ferritin

The primary care population is predominantly a well patient population, thereby reducing (although not eliminating) the effect of other conditions on ferritin values. Major studies of raised ferritin values in primary care have been reported. Due to it being an acute phase protein, other causes of a raised level should be considered, but only a minority of subjects with elevated ferritin are homozygotes for C282Y in the *HFE* gene (Adams *et al*, 2005).

The commonest causes of raised ferritin without iron overload relate to inflammatory disorders, malignancy, chronic alcohol consumption, liver disease or metabolic abnormalities. Rarer causes for raised ferritin can be seen in Rheumatological conditions, Porphyria Cutanea Tarda and genetic causes.

GP consultation for raised ferritin

A clinical history and examination, together with a few simple investigations, will often reveal the probable underlying cause.

In particular, patients should be questioned about alcohol intake and other risk factors for liver disease, transfusion history or oral iron supplementation, family history of iron overload and the presence or absence of diabetes mellitus, obesity and hypertension, history of early cataracts (associated with genetic causes), as well as for symptoms and signs that may point to an underlying inflammatory or malignant disorder.

Initial investigations

Initial tests should include:

- Full blood count
- Repeat Ferritin
- Transferrin saturation (iron studies)
- Renal and Liver function tests (with viral hepatitis serology if LFTs are abnormal)
- C-reactive protein
- If possible metabolic syndrome, consider HbA1c & Lipids

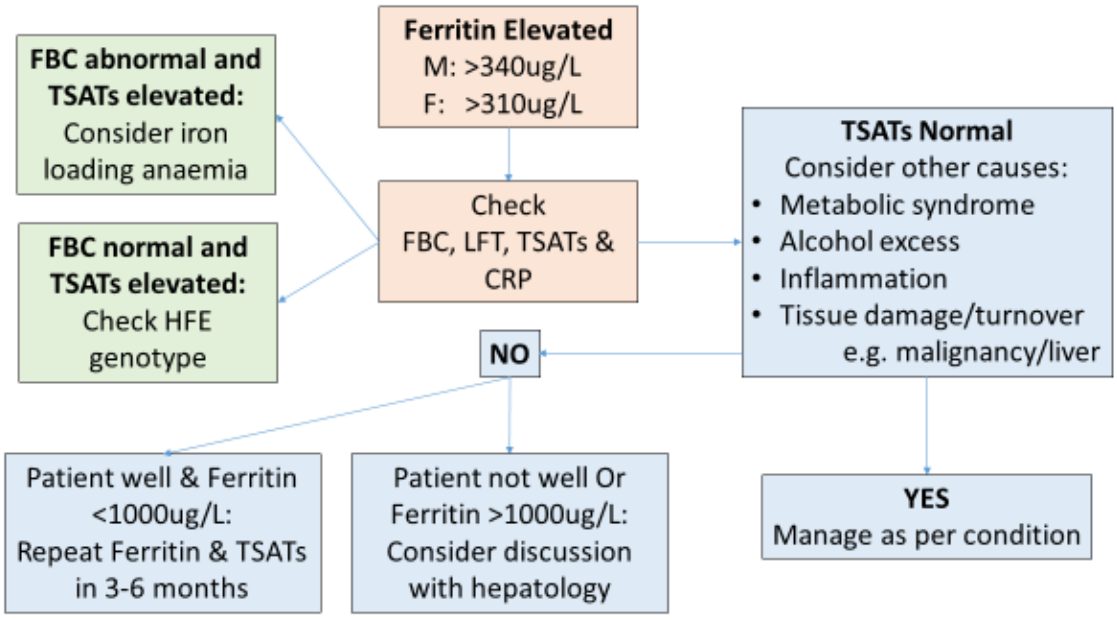


Figure 2 Investigation of elevated ferritin

Cases of haemochromatosis confirmed by HFE genotype should have a liver ultrasound arranged and onward referral to gastroenterology.

References

1. Guideline for the laboratory diagnosis of iron deficiency in adults (excluding pregnancy) and children. Andrew Fletcher et al. A British Society for Haematology Good Practice Paper 24 October 2021

2. British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults. Jonathon Snook et al. Gut 2021 Nov;70(11):2030-2051

3. Non-anaemic iron deficiency Shalini Balendran, Cecily Forsyth Aust Prescr. 2021 Dec 1;44(6):193–196.

4. NICE Clinical Knowledge summaries Iron deficiency Anaemia

5. Iron deficiency anaemia: Evaluation and management. American Academy of Family Physicians 2012; 87 (2): 98-104. M. Short

6. Milton Keynes University hospital Good sources of iron

7. Haemochromatosis and iron-overload screening in a racially diverse population. Adams et al. N Engl J Med 2005

Amendment History

Issue	Status	Date	Reason for Change	Authorised

Document Control Information

Consultation Schedule

Name and Title of Individual	Date Consulted
Jennifer Page	October 2024
Sue Scott	October 2024
GHFT haematology and Biochemistry	February 2025
SFT Haematology and Biochemistry	February 2025
NBT Haematology and Biochemistry	February 2025
UHBW Haematology and Biochemistry	February 2025

The following people have submitted responses to the consultation process:

Name and Title of Individual	Date Responded

Name of Committee/s (if applicable)	Date of Committee

Ratification Assurance Statement

Dear Dr Jennifer Page

Please review the following information to support the ratification of the below named document.

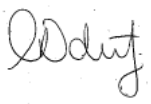
Name of Guideline: Ferritin interpretation – a guide for GP's

Name of author: Moya O'Doherty

Job Title: Consultant Biochemist

I, the above named author, confirm that:

- The Guideline presented for ratification describes best practise known to me at the time of the development of the guideline.
- I will bring to the attention of my clinical director or line manger any information which may affect the validity of this Guideline as soon as this becomes known to me;
- I have undertaken appropriate consultation on this Guideline and have considered all responses.
- I acknowledge that the policy will be kept under review, and that I may be asked to refine the guideline. If no interim changes are required it will then be formally reviewed on its documented review date.

Signature of Author:  **Date:** 11/03/2025

Name of Person Ratifying this Guideline: Jennifer Page

Job Title: Consultant Haematologist

Signature:  **Date:** 17/03/2025

To the person approving this Guideline:

Please ensure this page has been completed correctly, then print, sign and **post this page only** to: Director's Office, Wolfson Centre (D1), Royal United Hospital

The **whole guideline** must be sent electronically to: ruh-tr.policies@nhs.net