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Iron Matters
Highlights of a Clinical Webcast Series

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Iron deficiency is common in patients with heart failure, chronic kidney disease, GI disorders and restless leg syndrome, as well as in pregnant women and in surgical patients. A recent series of webcasts, convened by specialist physician Dr Sarah Bell, was held over eight weeks discussing the importance of iron replacement in these groups. The webinar series was sponsored by Aspen New Zealand and this review covers the highlights.

IRON – THE BASICS

Nicola Eaddy, Haematologist at Auckland City Hospital and LabPlus

Iron is essential for oxygen transport, DNA synthesis and electron transport. Excess free iron, however, can produce free radicals therefore tight control is important.

Iron regulation

The body needs approximately 20 mg of iron each day to form RBC. Plasma contains only 2-4 mg of iron, therefore turnover occurs every few hours. Macrophages deliver 20-25 mg of iron per day to the plasma by salvaging aging RBC. Diet provides 1-2 mg per day of iron. Surplus iron is stored as ferritin in the liver, heart and spleen. Regulation of iron occurs between absorption, recycling and release of iron stores, and the unregulated loss via skin and blood.

Absorption of dietary iron

Ascorbate and citrate solubilise iron and increase its absorption. Inhibitors of iron absorption include phytates, polyphenols, calcium and some proteins and medicines that decrease gastric acid.

Ferroportin and hepcidin

Ferroportin moves iron across cells to the plasma where it is transported by transferrin.

Hepcidin is critically important in iron regulation and it mediates ACD by interacting with ferroportin; inflammation induces hepcidin, causing inhibition of ferroportin to limit iron for pathogens. Hepcidin also increases in iron overload. Conversely, erythropoietic demand decreases hepcidin to increase iron availability.

Blood tests to assess iron status

A request for iron studies includes:

1. Serum iron
2. Serum transferrin
3. Transferrin saturation
4. Serum ferritin

Serum iron

Serum iron measures circulating iron, most of which is bound to transferrin. Iron is low in ID, ACD and inflammation and it fluctuates with diet and due to diurnal variation. A low serum iron in isolation is **NOT** diagnostic of ID.

A low serum iron by itself is not diagnostic for iron deficiency

Abbreviations used in this review

ACD = anaemia of chronic disease
BMI = body mass index
CKD = chronic kidney disease
CHr = reticulocyte haemoglobin content
CNS = central nervous system
CSF = cerebrospinal fluid
DHB = district health board
DMPA = depot medroxyprogesterone acetate
DNA = deoxyribonucleic acid
EPO = erythropoietin
ESA = erythropoietin stimulating agents
ESKD = end-stage renal disease
FBC = full blood count
GI = gastrointestinal
GFR = glomerular filtration rate
Hb = haemoglobin
HFmrEF = heart failure with mid-range ejection fraction
HFpEF = heart failure with preserved ejection fraction
HFrEF = heart failure with reduced ejection fraction
HHT = hereditary haemorrhagic telangiectasia
IBD = inflammatory bowel disease
ID = iron deficiency
IDA = iron deficiency anaemia
IUGR = intrauterine growth restriction
IV = intravenous
LVEF = left ventricular ejection fraction
MI = myocardial infarction
MRI = magnetic resonance imaging
NNT = number needed to treat
NSAID = non-steroidal anti-inflammatory drugs
NYHA = New York Heart Association
OGD = oesophago-gastro-duodenoscopy
OSA = obstructive sleep apnoea
OTC = over-the-counter
PLM = periodic limb movement in sleep
PPIs = proton pump inhibitors
PTH = parathyroid hormone
QoL = quality of life
RBC = red blood cells
RCT = randomised controlled trial
RET-He = reticulocyte haemoglobin content
RLS = restless leg syndrome
sTFR = soluble transferrin receptor
T2D = type 2 diabetes
TIBC = total iron binding capacity
TSAT = transferrin saturation
VO_2 max = volume of oxygen maximum

Serum transferrin

Serum transferrin has a high rate of turnover and it is increased in ID, pregnancy and with oral contraceptive use and decreased with ACD, inflammation, cancers, iron overload and protein malnutrition. Serum transferrin can be reported as TIBC (transferrin mg/dL x 1.389).

Transferrin saturation

Transferrin saturation represents the percentage of binding sites (transferrin) occupied by iron. Normal values are 25-45%, but in ID binding capacity is increased resulting in lower saturation (< 19% cut-off).

Serum ferritin

Ferritin is an acute phase reactant that protects against oxidative stress and inflammation. Serum ferritin reflects total iron storage, i.e. 1 ng/mL approximately equals 10 mg stored iron.

- Serum ferritin < 15 ng/mL is 99% specific for ID but only 57% sensitive
- Serum ferritin < 30 ng/mL is 92% specific and 98% sensitive*

*Studies conducted in pregnant women from Malawi

Serum ferritin can increase independently of iron status in inflammation, infection, liver disease, heart failure and cancer.

Additional tests following iron studies to confirm iron deficiency

The soluble transferrin receptor (sTFR) assay may be useful if iron studies are inconclusive. Erythrocytes in the bone marrow increase transferrin receptor numbers in ID. sTFR correlates with the erythropoietic rate and is increased in ID and is usually normal in ACD, although it may be increased in functional ID (see definitions) or due to ESA use or haemolysis.

In patients with ACD and a raised sTFR, a trial of iron replacement may be considered

Reticulocyte haemoglobin content (CHr or RET-He) is routinely performed in renal patients. This estimates the haemoglobin content of RBC and is not influenced by inflammation. A CHr can be rapidly performed and may help to predict which patients will respond to iron. Patients with haemoglobinopathies should not be tested for CHr.

Bone marrow stain is a qualitative assessment of iron in the bone marrow that is the gold standard for assessing iron stores.

Definitions
Absolute iron deficiency = Absence of (or severely reduced) storage iron in the monocyte-macrophage system
Functional iron deficiency = Barely adequate iron stores for normal haematopoiesis, but the iron is not available for RBC production.

Iron deficiency

People with high iron requirements are at risk of ID include:

- Infants, young children and adolescents
- Women, particularly those who are menstruating, pregnant or postpartum
- Vegans, vegetarians or those who donate blood regularly
- Endurance athletes

ID is masked by co-morbidities. Potential causes of ID include low iron intake, reduced absorption, e.g. PPIs, gastrointestinal blood loss, e.g. anticoagulants, peptic ulcers, cancer, CKD and obesity.

Progressive iron depletion

The first stage of ID is iron depletion, without anaemia, as labile stores are sufficient to maintain RBC haemoglobin. Patients with very-low ferritin may develop symptoms.

The second stage is normocytic and normochromic anaemia. Patients often have a normal reticulocyte count but low serum ferritin and serum iron, increased transferrin/TIBC and low transferrin saturation.

Severe anaemia is hypochromic and microcytic and the reticulocyte count will be low.

Functional iron deficiency

There are two types of functional iron deficiency: ACD/inflammation and ESA. ACD functional iron deficiency is caused by hepcidin blocking the release of iron into circulation. Common causes include infection, malignancy and long-term conditions, e.g. diabetes, and bariatric surgery.

ACD should be suspected in patients with a low transferrin saturation and a normal or elevated ferritin. Management of ACD iron deficiency is treatment of the underlying condition.

Renal or cancer patients who are taking ESA can be diagnosed with ID if they have a normal or elevated ferritin (100-500 ng/mL) and a transferrin saturation < 20%. These patients benefit from iron supplementation.

Testing for iron deficiency

ID can be diagnosed following a history, examination, FBC (including RBC indices) and a serum ferritin alone for a classic presentation, but for other patients the panel of iron studies is recommended. A suggested testing algorithm is presented in **Figure 1** and **Table 1** provides guidance on interpreting results.

Figure 1: Suggested testing algorithm for suspected ID, adapted from Eaddy (2021)

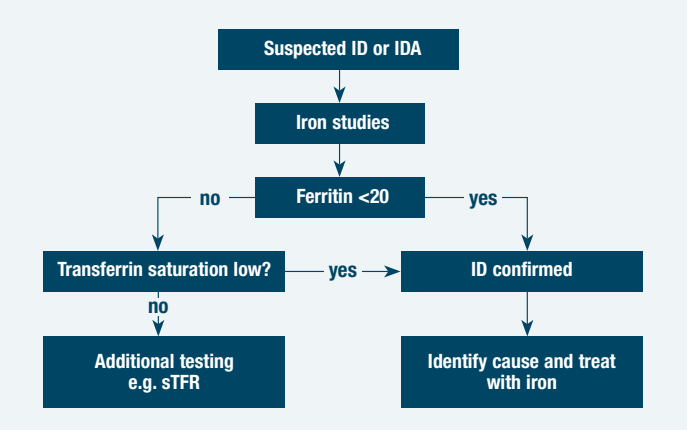

Table 1: Interpretation of iron studies adapted from LabPLUS (2009)[1]

	Normal	Iron deficiency	Anaemia of chronic disease	Iron overload	Liver disease
Serum iron	Normal	Decreased	Decreased	Increased	Increased or normal
TIBC	Normal	Increased	Normal or decreased	Decreased	Decreased or normal
Saturation	Normal	Decreased	Decreased usually	Increased	Normal
Ferritin	Normal	Decreased	Normal or increased	Increased	Increased
StfR	Normal	Increased	Normal or slightly increased	Normal	Normal

Treatment of iron deficiency

ID is generally treated with oral iron salts. Evidence shows that lower doses are more effective and high doses can cause adverse effects. Alternate day dosing has been shown to increase absorption, however, these studies were conducted in non-anaemic patients.

Reasons for treatment failure may include non-compliance, misdiagnosis, co-existing conditions, e.g. folate or vitamin B12 deficiency, malabsorption, e.g. rapid GI transport, concurrent use of antacids, congenital defect, or ongoing blood loss.

IV iron

IV iron is subsidised for patients who are intolerant or unresponsive to oral iron. Patients who are likely to benefit from IV iron include those with:

- Reduced iron absorption capacity
- Severe anaemia
- High hepcidin due to inflammation
- A need to recover rapidly
- Renal disease who are taking ESA
- Inflammatory bowel diseases

Iron overload

Iron overload may be caused by transfusions or supplements, increased absorption due to hereditary haemochromatosis, ineffective erythropoiesis, e.g. thalassemia, sideroblastic anaemias, liver disease and rarely genetic mutations affecting absorption.

Clinical signs of iron overload include chronic liver disease, cardiac enlargement, heart failure, conduction defects, diabetes, hypogonadism and hyperpigmentation.

Testing for iron overload

In most patients, request an FBC with RBC indices, plus iron studies. A family history of iron overload means genetic testing is appropriate alongside iron studies. A CRP test may determine if inflammation is contributing.

An algorithm for investigating suspected iron overload is presented in **Figure 2**.

TAKE-HOME MESSAGES

- A low serum iron is not diagnostic for iron deficiency
- The sTFR assay may be helpful if there is concurrent inflammation in a diagnosis of iron deficiency
- Consider trialling oral iron on alternate days or reducing the dose to reduce toxicity
- If the transferrin saturation is low – iron overload is unlikely.

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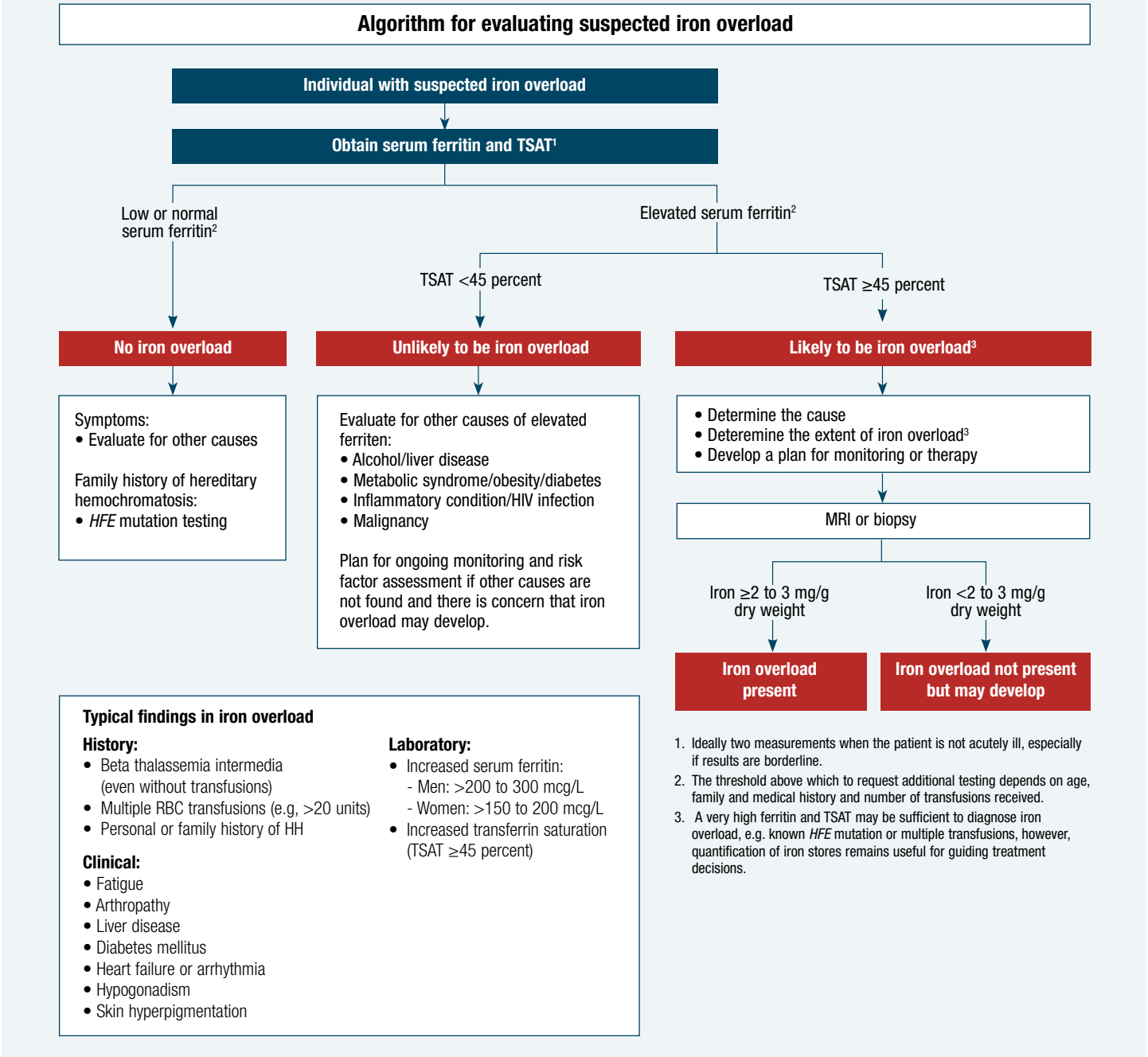
Figure 2: Investigation of suspected iron overload, adapted from Bacon et al (2021).[2]



IRON IN CHRONIC KIDNEY DISEASE

Hari Talreja, Renal Physician/ Nephrologist at Counties Manukau Health

Reviewing erythropoiesis, anaemia and CKD

Hypoxia is the main driver of erythropoiesis and it may be caused by low oxygen, low RBCs or increased oxygen demand. Hypoxia causes the kidney to release EPO which stimulates the bone marrow to produce more RBC.

Anaemia in CKD is associated with an increased risk of cardiovascular events, mortality and progression to ESKD.[1–3]

The prevalence of anaemia in people without CKD is approximately 6.3% compared to 15.4% in people with CKD.[4] The likelihood of anaemia increases when GFR is < 60 mL/min/1.73m^2.[5,6] In patients with stage 4 and 5 CKD the prevalence of anaemia is > 50%.[4]

ID is a major cause of anaemia in non-dialysis CKD. Iron transport is disrupted in CKD as inflammation upregulates hepcidin. EPO production also decreases as CKD progresses and uraemic toxins cause erythropoietin resistance. Toxins may also reduce RBC survival by > 50%.

In dialysis patients, absolute ID is indicated by TSAT < 20% and serum ferritin < 100 ng/L. Functional ID is characterised by TSAT < 20% and a serum ferritin 100-800 ng/L. Reticulo-endothelial blockade by hepcidin needs to be distinguished from functional ID as the TSAT and ferritin may be similar. Patients with functional ID have increased haemoglobin following iron supplementation but this does not occur in reticulo-endothelial blockade.

Case study 1 - CKD patient not on dialysis

An active 75-year-old male with worsening lack of energy and reduced exercise tolerance. He has stage 3 CKD, T2D and hypertension. Heart rate and blood pressure are normal with no evidence of hypervolaemia, although he is slightly pale. Laboratory testing reveals:[6]

- Serum creatinine 182 umol/L
- eGFR 35 mL/min1.73m^2
- uACR 100 mg/mmol
- **Hb 95 g/L**
- **TSAT 15%**
- **Ferritin 90 ug/L**
- Folate and vitamin B12 are normal

The question is whether the patient has absolute ID or if functional ID. Absolute ID is diagnosed due to ferritin < 100 µg/L and TSAT < 20%. In this situation, all correctable causes of anaemia should be addressed first. After receiving oral or IV iron, ESA may be appropriate if the haemoglobin is < 100 g/L.[6] This approach is extended by the FIND-CKD study showing that high-dose IV iron (target 400-600 ug/L) resulted in more patients avoiding EPO treatment than treating with oral iron or IV iron with a low ferritin target (100-200 ug/L) without an increase in adverse effects.[7]

CONCLUSIONS FOR CASE STUDY 1

- ID (absolute or functional) is common in patients with anaemia and CKD
- ID should be assessed and corrected before considering ESA
- IV iron is more efficacious than oral iron in increasing Hb in iron-deficient patients with CKD
- Serum ferritin levels ≥ 800 µg/L are not associated with an increased risk of adverse events
- When prescribing IV iron in non-haemodialysis CKD, consider high-dose, low frequency IV as the treatment of choice

Case study 2 - CKD patient on haemodialysis

A 65-year-old male with ESKD has been receiving haemodialysis for 1 year. Progressive lethargy and tiredness have developed recently. He has a history of GI bleeds and is taking a PPI, 3 antihypertensives, a statin and EPO (5000 units/week). Heart rate and blood pressure are normal and he has a mild pallor. Laboratory testing reveals:

- **Hgb 95 g/L**
- **TSAT 15%**
- **Ferritin 150 µg/L**
- PTH 41 pmol/L*
- Folate and vitamin B12 are normal

*PTH is often high in dialysis patients which may reduce their response to EPO.

Dialysis management avoids high hb (135 g/L) levels with ESA agents due to stroke and thrombosis risk.[8–11] The treatment options are low-dose or high-dose IV iron given proactively or reactively. The PIVOTAL study found that high-dose IV iron targeting ferritin > 70 µg/L and TSAT > 40% resulted in a 3% reduction in absolute risk of death and cardiovascular events (NNT=33).[12]

CONCLUSIONS FOR CASE STUDY 2

- High dose IV iron (proactive) is associated with improved survival and fewer cardiovascular events than low dose IV iron (reactive)
- High dose IV iron is associated with better QoL and fewer transfusions
- There are no safety concerns about high dose IV iron
- Consider targeting a higher ferritin and TSAT

Case study 3 - CKD patient with heart failure

A 60-year-old male with progressive fatigue and reduced exercise tolerance has hypertension, T2D and an MI 3 years ago. HFrEF-LVEF 30%, NYHA class II/III and CKD stage 3. Mild pedal oedema and pallor are present. Laboratory testing reveals:

- S Cr 170 µmol/L
- eGFR 37 mL/min1.73m^2
- uACR 2.5 mg/mmol
- **Hb 100 g/L**
- **TSAT 17%**
- **Ferritin 80 µg/L**
- Folate and Vit B12 normal

International guidelines recommend IV iron for patients with symptomatic heart failure, CKD, ID and TSAT < 20%.[6,13,14]

CONCLUSIONS FOR CASE STUDY 3

- IV iron reduces HF symptoms and improves exercise capacity
- Guidelines recommend IV iron for patients with heart failure
- In combined CKD and heart failure, be aggressive in treating ID

Haemoglobin targets in CKD

For many patients with anaemia and CKD a Hb target of 100-115 g/L is recommended.[15] A target > 130 g/L is not recommended due to the increased mortality and morbidity risk.[15] In dialysis with anaemia secondary to CKD, an ESA may prevent haemoglobin dropping below 100 g/L and avoid the need for transfusions.[15]

TAKE-HOME MESSAGES

- Anaemia and ID are common in CKD and multiply all adverse outcomes
- Guidelines recommend iron repletion prior to ESA and ensuring ID is treated in anaemic patients
- There is no harm associated with a high ferritin/TSAT over a longer period of time
- IV iron provides a timely and effective correction of low ferritin/TSAT levels; oral iron is not as effective as IV iron
- IV iron lowers the need for ESA and blood transfusions

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TREATING PERIOPERATIVE ANAEMIA

Kerry Gunn, Anaesthesiologist, Department of Anaesthesia and Perioperative Medicine, Auckland City Hospital

A 1999 study showed that a restrictive red cell transfusion strategy was associated with better outcomes for critically ill patients, compared with a liberal strategy.[1] This result has been repeated in a range of procedures and it is now accepted that there is no post-operative benefit in liberal transfusion strategies and it is acceptable to allow Hb to fall to 80 g/L before administering transfusions.[2,3]

Managing preoperative anaemia

Anaemia in surgical patients is common and ranges from 6% in males aged 18-29 years to 48% in males aged over 70 years, and 29% in females aged 18-29 years to 43% in females aged over 70 years.[4] Mixed or inflammatory anaemia becomes more common in older patients.

Preoperative anaemia is a mortality predictor (OR=2.43, $P<0.0001$), similar to significant renal dysfunction and age > 70 years.[5] This risk is partially because patients with preoperative anaemia are five to seven times more likely to receive a transfusion than non-anaemic patients.

Preoperative IV iron

Ferric carboxymaltose (Ferinject®) given IV is the single most effective intervention for improving a patient's haemopoietic ability prior to surgery, thereby reducing both the likelihood of perioperative transfusion and IDA.

A loss of 500-1000 mL of blood equates to a 250-500 mg loss of iron. This cannot be regained postoperatively via absorption, therefore IV iron is the only logical way to replete the patient's iron stores.

Oral iron post discharge is not an effective perioperative intervention because absorption of oral iron is inhibited by hepcidin blockade due to surgical stress.[6]

Effective blood management

Perioperative blood management is based on:

1. Optimising red cell mass, e.g. IV iron
2. Minimising blood loss and bleeding, e.g. improving surgical techniques
3. Harnessing and optimising the physiological reserve of anaemia, e.g. restrictive transfusion strategies

The use of preoperative IV iron in Auckland DHB has reduced surgical transfusion rates from approximately 40% to approximately 10%.

Guideline recommendations

A management algorithm[7] for patients undergoing blood loss surgery is provided in **Figure 1**; similar recommendations are provided by the National Institute for Health and Care Excellence (NICE).[8] Special Authority funding criteria for IV ferric carboxymaltose reflect Figure 1.

1. ID may be present in the elderly or patients with inflammation with ferritin 60–100 mcg/L.
2. Patients without a clear physiological explanation for ID (especially men and postmenopausal women) should undergo gastroscopy/colonoscopy to exclude GI bleeding.
3. CRP may be normal in the presence of chronic disease and inflammation.
4. Consider thalassaemia if MCH or MCV is low and not explained by ID, or if long standing. Check B12/folate if macrocytic or if there are risk factors for deficiency or if anaemia is unexplained. Consider blood loss or haemolysis if reticulocyte count is increased.

An orthopaedic study demonstrated an approximate 10 g/L rise in post-operative Hb when Figure 1 was implemented and this was associated with a reduction in the number of blood transfusions ($P<0.001$).[9] A similar result was found in patients undergoing bowel surgery where Hb levels continued to rise at week four, compared to usual care, where Hb levels remained static.[10]

Conclusions

Preoperative IV iron in patients with low ferritin:

- Elevates Hb levels relatively quickly, e.g. 4 weeks
- Reduces hospital transfusions
- Elevates post-operative ferritin and post-discharge increases in Hb

The challenge of process

The ideal time to deliver IV iron is from 4 to 6 weeks prior to the surgery. This requires communication between secondary and primary care. Primary care can be reassured that IV infusions of ferric carboxymaltose are associated with low rates of mild adverse reactions. There is some concern, however, that IV iron is associated with an increased risk of infection,[11] although this was not observed in the PREVENTT study.

The PREVENTT study

PREVENTT enrolled more than 400 patients with anaemia who were undergoing laparotomy. A single dose of IV iron resulted in an approximate 10 g/L increase in Hb eight weeks after surgery and this was maintained at six months.[12] The unexpected outcome was the similar transfusion rate between the treatment and the placebo arms.[12] This might be explained by the relatively short time period between the infusion and surgery, i.e. 14-15 days.[12] PREVENTT also did not detect a difference in adverse outcomes, length of hospital stay or change in QoL between the treatment and the placebo arms.[12] There were, however, fewer unplanned readmissions and post-operative infections in the treatment arm.[12]

The PREVENTT study limits the totality of enthusiasm for giving all patients with anaemia preoperative IV iron because the benefits of doing so may not be as great as thought. It is possible that the iron dosing may need to be increased for some patients and IV iron may need to be given earlier. PREVENTT is being repeated in other groups, e.g. cardiac patients, and these results are awaited. Current guidelines are unchanged following PREVENTT.

It is hoped that future studies will also elucidate whether preoperative iron helps to improve VO_2 max, thereby contributing to a faster recovery from surgery.

TAKE-HOME MESSAGES

- Iron deficiency is common in surgery
  - It is often mild but ferritin levels often not assessed
- Treatment with IV iron is effective
- Raising Hb levels reduces transfusion rates
- Normalising iron stores may have additional benefits
- IV iron is safe

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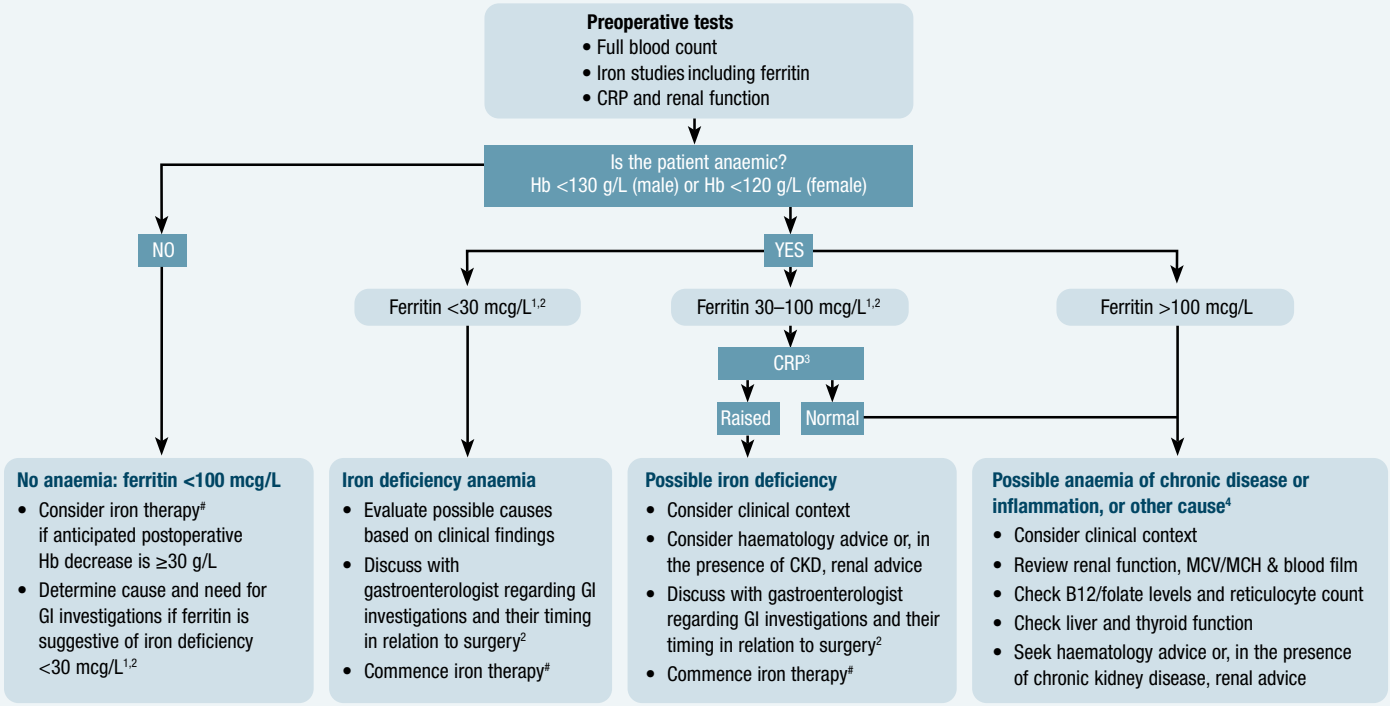
Figure 1: Preoperative haemoglobin assessment and optimisation algorithm for patients where > 500 mL of blood loss is anticipated, adapted from the National Blood Authority (2012)[7]



1. Iron deficiency may be present in the elderly or patients with inflammation with ferritin 60–100 mcg/L.
2. Patients without a clear physiological explanation for iron deficiency (especially men and postmenopausal women) should undergo gastroscopy/colonoscopy to exclude GI bleeding.
3. CRP may be normal in the presence of chronic disease and inflammation.
4. Consider thalassaemia if MCH or MCV is low and not explained by iron deficiency, or if long standing. Check B12/folate if macrocytic or if there are risk factors for deficiency or if anaemia is unexplained. Consider blood loss or haemolysis if reticulocyte count is increased.

Oral iron in divided daily doses and evaluate response after 1 month. IV iron if oral iron is contraindicated, not tolerated or ineffective and consider if rapid iron repletion is important, e.g. < 2 months to non-deferrable surgery.

IRON DEFICIENCY AND THE GASTROINTESTINAL TRACT

Kumudith Ekanayaka, Consultant Gastroenterologist and General Physician, Middlemore Hospital

Iron absorption

A healthy GI tract helps to maintain iron homeostasis. The GI tract is adaptive and its ability to absorb nutrients may change with age and in response to diet, environment, pregnancy and disease.

On average 20-30 mg/day of iron is ingested and approximately 1 mg/day needs to be absorbed to account for normal losses. Most iron is absorbed in the proximal small intestine across the intestinal villi and ferrous iron (Fe^{2+}) is absorbed better than ferric iron (Fe^{3+}). Regulation of iron absorption occurs via a mucosal block, a store regulator and feedback from erythropoiesis.

Identifying GI causes of iron deficiency

If a patient is iron deficient it is important to consider where the iron is being lost and which investigations can confirm this.

GI symptoms may be upper intestinal, e.g. vomiting, dysphagia, lower intestinal, e.g. changes in bowel habit, or constitutional, e.g. anorexia and weight loss. Red flags requiring urgent follow-up include unexplained weight loss, older age of onset, family history of cancer, severe unremitting symptoms, rectal bleeding or nocturnal symptoms.

The patient's history

Factors that should be noted in the history of a patient with ID include:

- Diet, e.g. vegetarianism or veganism may contribute to ID
- Surgical history, e.g. bariatric surgery can result in malabsorption
- Medical history, e.g. previous peptic ulcers may explain occult blood loss
- Medicine history, e.g. aspirin or NSAID use can cause blood loss
- Social history, e.g. alcohol misuse can cause portal hypertension
- Family history, e.g. colorectal cancer or IBD

The examination

The patient should be examined for signs of ID and IDA, e.g. pallor, tachycardia or hypotension, lymphadenopathy, cardiac causes, e.g. aortic stenosis, abdominal pathology, e.g. masses or portal hypertension, and rectal bleeding and pathology.

Gastrointestinal causes of iron deficiency

The common GI causes of ID are outlined below and **Table 1** provides signs of ID with a GI cause.

Coeliac disease

Coeliac disease occurs in 1% of the population.[1] It manifests as an immune-mediated enteropathy defined by characteristic changes on histology.[1] Patients with Coeliac disease may have low bone density, deficiencies in iron, folate and B12, dermatitis, and other skin conditions and immune diseases.[2]

ID in Coeliac disease results from impaired iron absorption due to villous atrophy with occult bleeding potentially contributing. Patients take six to 12 months to recover. In 102 patients with Coeliac disease, 69% had anaemia.[3] In 200 patients with anaemia, 5% were diagnosed with Coeliac disease.[4]

Bariatric surgery

ID following bariatric surgery may occur because iron needs to be conjugated with vitamin C, amino acids or sugars for absorption and to protect the GI tract. Bariatric surgery reduces gastric acid availability and lesions are also a source of blood loss.

ID rates following bariatric surgery range from 12% to 47%.[5] However, one study found that 51% of patients were iron deficient over a ten-year period, with 6.7% requiring IV iron (preferred to oral iron).[5,6] There is little difference in the rates of deficiency between types of surgery.[7]

Portal hypertension

Portal hypertension may develop due to liver cirrhosis increasing hepatic vascular resistance. Oesophageal, gastric and duodenal varices or pulmonary hypertensive gastropathy may result with potentially fatal blood loss. Management involves treating or removing the underlying cause and GI complications can be treated with ligation or beta-blockers.

Crohn's disease

Crohn's disease may occur anywhere in the GI tract, but most often in the distal small intestine and the proximal colon. Crohn's is discontinuous with transmural involvement. ID may occur due to impaired absorption or blood loss in colonic disease.

Ulcerative colitis

Ulcerative colitis involves the mucosal layer of the large intestine. The distribution of the disease is 45% rectosigmoid, 35% distal to splenic flexure and 20% pancolitis. Iron absorption is not impaired in ulcerative colitis, but blood loss from ulcerations can cause ID and anaemia.

Gastrointestinal cancer

All GI cancers are associated with ID and anaemia; the prevalence is 50-60% in patients with colorectal cancer. Larger tumours and right-sided tumours (which may be diagnosed later) are more strongly associated with ID and anaemia. Malignant polyps are more likely to lose blood than benign polyps.

Who to investigate

A gastroscopy, usually paired with a colonoscopy, a Coeliac screen, urine test and possibly a chest X-ray are routinely requested in secondary care for patients with any of the following characteristics:

- Male
- Female > 45 years
- Symptomatic
- Premenopausal with symptoms of the upper or lower GI tract or who are recurrently iron deficient despite optimal treatment

Gastroscopy

Duodenal biopsies are performed for all iron deficient patients undergoing gastroscopy to rule out Coeliac disease. This procedure can also detect oesophagitis, ulcers, angiodysplasia and portal hypertension.

Colonoscopy

Biopsies are performed during coloscopy in the ileum and colon to detect Crohn's disease, tumours, IBD, microscopic colitis, diverticular disease and haemorrhoids.

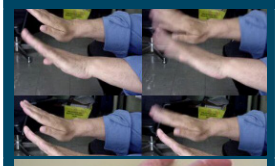
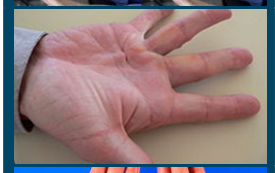
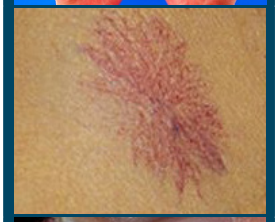
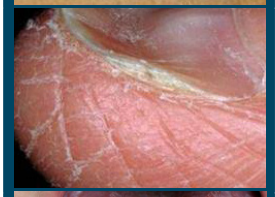
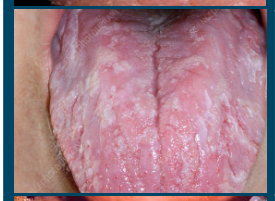
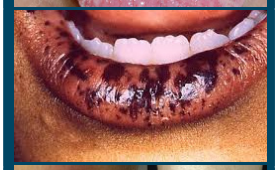
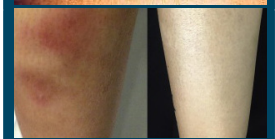
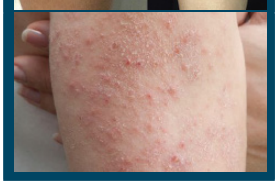
Urgent endoscopy is beneficial in unstable GI bleeds and injections of adrenalin can tamponade bleeding. Thermal therapies may be delivered by endoscope and endoclips and banding mechanisms may also be used.

Wireless capsule endoscopy (Pillcam) may be used if findings from gastroscopy and endoscopy are absent. This technique has a high yield compared to other endoscopic techniques. The risk using Pillcam is that strictures or obstructions may cause pill retention.

TAKE-HOME MESSAGES

- Iron deficiency is common
- There are multiple gastrointestinal causes
- It is very important to take a good history and to perform a thorough investigation
- There are multiple modalities of investigations

Table 1: Signs of iron deficiency with a gastrointestinal cause

Signs of iron deficiency		Underlying GI cause
	Asterixis	Portal hypertension
	Dupytrons contracture	Portal hypertension
	Palmar erythema	Portal hypertension
	Spider naevi	Portal hypertension
	Koilonychia	Malnutrition GI blood loss Worms GI malignancy Coeliac disease
	Glossitis	Coeliac disease
	Peutz-Jehgers syndrome	Autosomal dominant inherited disorder characterised by GI hamartomatous polyps
	Erythema nodusum	Ulcerative colitis Chron's disease
	Dermatitis herpetiformis	Coeliac disease

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IV IRON AND HEART FAILURE – WHAT'S ALL THE FUSS ABOUT?

Nicky Edwards, consultant cardiologist, Green Lane Cardiovascular Service, Auckland

The burden of heart failure

Heart failure occurs in approximately 5.5% of the NZ population aged over 50 years and the prevalence is higher in Māori and Pacific peoples. Heart failure is the leading cause of hospitalisation in people aged over 65 years and causes 45% of NZ cardiovascular deaths. The average duration of first hospitalisation for heart failure is one week and costs approximately $17,000. Within 3 years of being diagnosed with heart failure, 34% of patients with NYHA I/II and 42% of those with NYHA III/IV are dead.

Causes of heart failure

Heart failure is the end product of multiple causes, e.g. cardiac remodelling following myocardial infarction, atrial fibrillation, valve disease, hypertension or alcohol or drug misuse. Heart failure is classified as:

- HFrEF - ejection fraction is < 35-40%
- HFmrEF - ejection fraction is 40-49%
- HFpEF - ejection fraction is normal (55-65%) but the heart is stiff and inefficient.

Treatments and prognosis for heart failure

Heart failure is associated with worse long-term survival after five years than most common cancers.[1] The increased range of treatments for heart failure is, however, resulting in a better prognosis for many patients.

Iron and heart failure

Iron deficiency in heart failure is defined as ferritin < 100 µg/L or ferritin 100-299 µg/L and TSAT < 20%.[2]

Ferritin levels may be close to normal in people with heart failure and ID because ferritin is an acute phase protein and heart failure is an inflammatory condition. Interpreting ferritin levels in patients with heart failure is therefore challenging and using the TSAT is helpful.

The prevalence of ID is 50% across all types and stages of heart failure.[2]

The pathophysiology of iron deficiency

ID in heart failure may be caused by:[3]

- Reduced uptake from the GI tract due to oedema
- Reduced iron stores due to inflammation and renal disease
- Iron loss, e.g. the use of antiplatelet medicines

Functional ID resulting from systemic inflammation due to hepcidin blockade is the most common cause of ID in heart failure. Absolute ID may also occur where iron stores are depleted through impaired intake and iron loss.

Iron is a key micronutrient

Iron is critically important for oxygen delivery and cellular metabolism and a lack of it can cause mitochondrial dysfunction, oxidative stress, apoptosis and reduced myocardial efficiency.[4] The functional consequences of ID in heart failure are reductions in exercise capacity and QoL that contribute to worse outcomes.[5]

Iron replacement in heart failure treatment

The IV route is the preferred method for administering iron to patients with heart failure; absorption of oral iron is poor in heart failure.

Oral iron is not effective in heart failure

The IRONOUT study found that high dose oral iron did not improve VO_2 max in patients with HFrEF at 16 weeks and > 60% of patients had adverse effects.[6] Furthermore, there is no data showing that oral iron is effective in patients with heart failure.

IV iron is recommended

The Australian and New Zealand and European guidelines recommend that **patients with HFrEF and persistent symptoms undergo iron studies and IV iron be considered if ferritin < 100 µg/L or ferritin 100-299 µg/L and TSAT < 20%.**[7,8]

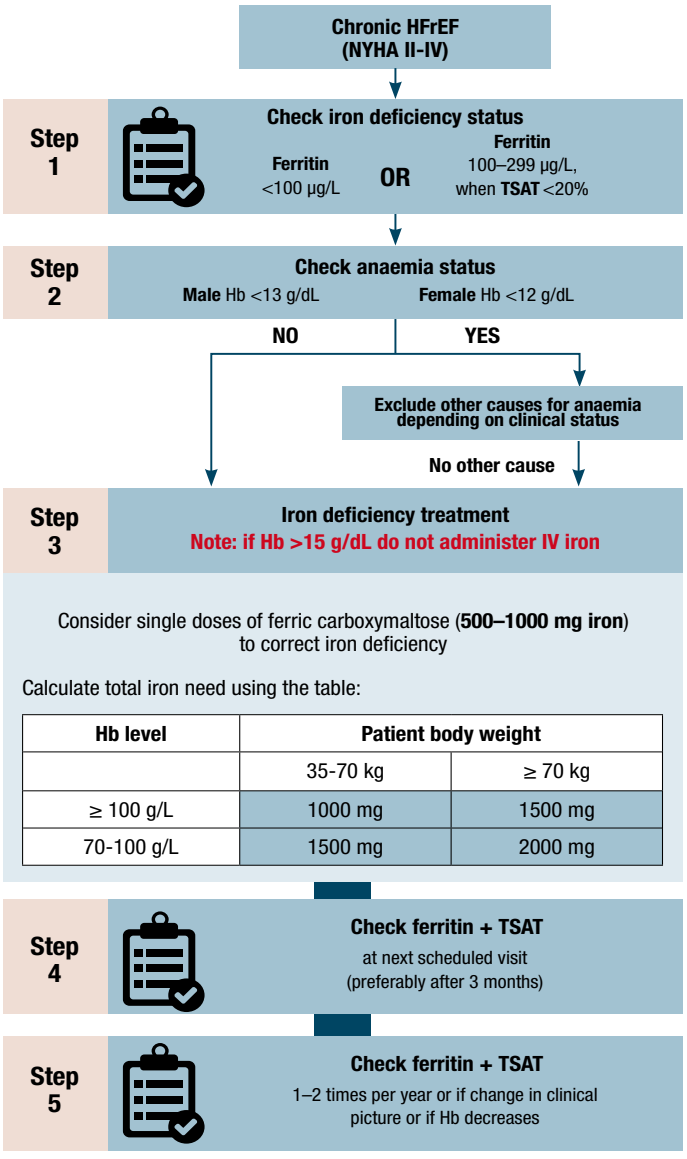
The guideline recommendations are based on a meta-analysis that found IV ferric carboxymaltose in heart failure was consistently associated with improvements in QoL and exercise capacity and delays in hospitalisation and CV mortality.[9]

The AFFIRM-AHF study found that in patients admitted to hospital with HFrEF < 50% and serum ferritin < 100 µg/L or serum ferritin 100-299 µg/L and TSAT < 20%, IV iron resulted in fewer hospitalisations at one year, compared to placebo.[10] Fewer hospitalisations represents improvements in QoL and functionality for patients.

IV iron – Ferinject®

The advantages of ferric carboxymaltose over iron sucrose are that larger doses can be given with less injections and that increases in haemoglobin are sustained for longer. The adverse effect rate is less than 1%. Iron stores are increased after approximately two weeks of the infusion. IDA is part of the Special Authority criteria for Ferinject, however, funding is available if patients have symptomatic heart failure following the recommendation of a specialist. Delivery of Ferinject occurs as a slow push (100mg/min, i.e. 2 mL) or a diluted infusion over 15 minutes with a 30 minute observation period. The patient's iron stores are checked after approximately one month and in some cases a second infusion may be appropriate in six months. A management algorithm is provided in **Figure 1**.

Figure 1: Algorithm for screening, testing, diagnosing, treating and follow-up of patients with heart failure and ID, adapted from McDonagh *et al* (2018)[11]



Hb level	Patient body weight	
	35-70 kg	≥ 70 kg
≥ 100 g/L	1000 mg	1500 mg
70-100 g/L	1500 mg	2000 mg

TAKE-HOME MESSAGES

- Iron deficiency is common in heart failure and occurs in 30-50% of patients, regardless of heart failure severity
- Monitoring of ferritin and TSAT is recommended for all patients with heart failure – haemoglobin is not the key
- Iron deficiency is associated with reductions in exercise capacity, physical wellbeing and poorer clinical outcomes and death, independently of haemoglobin levels
- Oral iron has limited efficacy; do not use it
- The data for the benefits of IV iron in heart failure is growing in terms of exercise capacity, QoL, ejection fraction and hospitalisation.

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IRON IN PREGNANCY: REPLENISHING FOR TWO

Ian Kando, obstetric medicine specialist and clinical lead in obstetric medicine at Auckland City Hospital

ID is often under recognised as a pathological state. IDA is the end-stage complication of iron deficiency. Both ID and IDA are common in pregnancy. During pregnancy, an increase in plasma cell volume occurs that is larger than the corresponding increase in red cell mass, resulting in haemodilution. This can make it difficult to differentiate pathological anaemia from physiological adaption.

Defining anaemia in pregnancy

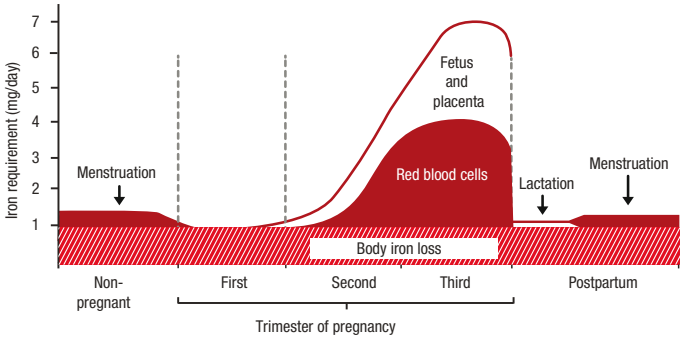
There is lack of consensus for a Hb threshold to define anaemia during pregnancy. Some district health boards currently define anaemia in pregnancy as an Hb count $\leq$ 100 g/L; international guidelines cite $\leq$ 110 g/L during pregnancy and $\leq$ 100 g/L postpartum. This inconsistency is due to two factors: the absence of prospective studies to show that anaemia *per se* is directly linked to increased maternal or neonatal risk and the recognition that polycythaemia can be associated with adverse outcomes in pregnancy.

Iron requirements during pregnancy

Serum ferritin is a good marker of iron status during pregnancy. Ferritin is initially high in early gestation in response to reduced erythropoietin activity, but progressively drops to nearly 50% of the pre-pregnancy level, reaching a nadir by 28 weeks' gestation. In routine clinical practice, screening for ID and IDA with a full blood count and ferritin is performed around 24 to 26 weeks' gestation in anticipation of this nadir.

Iron requirement throughout pregnancy is not uniform (**Figure 1**). Prior to pregnancy iron is lost through menstruation. During the first trimester iron requirements are low due to the cessation of menstruation. In the second and third trimester iron requirements increase substantially due to fetal, placental and maternal (red cell mass) demand. Lactation and resumption of menstruation drive postpartum iron requirements.

Figure 1: Estimated daily iron requirements during pregnancy in a 55 kg woman, adapted from Bothwell (2000)[1]



IDA and adverse outcomes

The maternal risks of IDA include cardiovascular strain, postpartum haemorrhage and peripartum blood transfusion. The fetal risks of IDA include IUGR and preterm delivery.

ID during pregnancy may reduce QoL due to physical and mental fatigue, dyspnoea, headache, restless legs, pica, cold intolerance and hair loss. For the infant, maternal ID can also led to poor infant weight gain, reduced immune function, learning and cognition deficits and behavioural issues. There is evidence that providing small doses of supplemental iron from 20 weeks' gestation in women with anaemia in early pregnancy, reduces the risk of adverse perinatal outcomes.

Treating iron deficiency during pregnancy

There is debate about whether to be proactive or reactive in the treatment of ID during pregnancy. The considerations that influence treatment decisions include:

1. Treatment compliance
2. Potential adverse effects of treatment
3. The unpredictability of pregnancy, e.g. the risk of preterm birth or haemorrhage

When to check ferritin levels

Although not universal practice, ferritin should be considered at the first antenatal booking to determine the need and timing for supplementation. A baseline ferritin $\geq$ 70 µmol/L in the first trimester, that is not due to infection or inflammation, suggests supplementation may not be required during pregnancy.

Consideration for early iron supplementation should be given to women with risk factors such as low intake of red meat, nutritional disorders, high intake of calcium, tea or coffee, malabsorption, menorrhagia, blood donation, immigration from overseas and short inter-pregnancy intervals.[2]

Treatment options

It is difficult to increase iron levels through diet alone as 25% of haem iron is absorbed from meat (e.g. 0.5 mg iron absorbed from 150 gm of lean beef) and only 5% of non-haem iron is absorbed from non-meat sources (e.g. 0.1 mg iron absorbed from 1 cup of spinach).

Despite the different options and formulations of oral iron supplement, approximately 25% of elemental iron is absorbed. Absorption can be promoted or inhibited by dietary factors.

The ability to absorb iron increases as a woman's iron requirements increases beyond 20 weeks of gestation. If a woman is iron deficient at booking, however, it is likely that she will benefit from earlier supplementation due to her iron deficit state.

Maternal iron loss can occur following delivery. Approximately 250 mg and 500 mg of iron is lost through a vaginal delivery and caesarean section respectively. Supplementation is the most effective way to replace this loss.

Oral iron can be less effective if there is concurrent infection or inflammation because of hepcidin production which blocks iron absorption. In this situation, wait for the inflammation to settle or consider IV iron. Providing too much oral iron can also increase the hepcidin block on iron absorption.

How often and how much?

Low-dose oral iron (200-300 mg) causes less GI adverse effects and is absorbed better than high-dose oral iron (> 400 mg). Compliance is better with a low-dose regimen.

Once daily dosing is associated with better compliance, however, this may increase hepcidin production which decreases absorption. In non-pregnant patients, alternative day or third day dosing is associated with better iron absorption. The recommended options are:

1. Once daily low-dose oral iron if compliance is an issue.
2. Low-dose oral iron on alternate days if adverse effects are a concern.

Intravenous iron

Figure 2 shows where ferric carboxymaltose is recommended to prevent IDA in women who:

- Present late in pregnancy
- Have severe ID or IDA
- Are intolerant to oral iron

Postpartum IV iron is given to ID women especially if haemorrhage has occurred. IV iron is generally not recommended during the first trimester due to a lack of safety data. Following IV iron a haemoglobin rise of 15-22 g/L/week occurs for two weeks with a 7-16 g/L/week increase thereafter.

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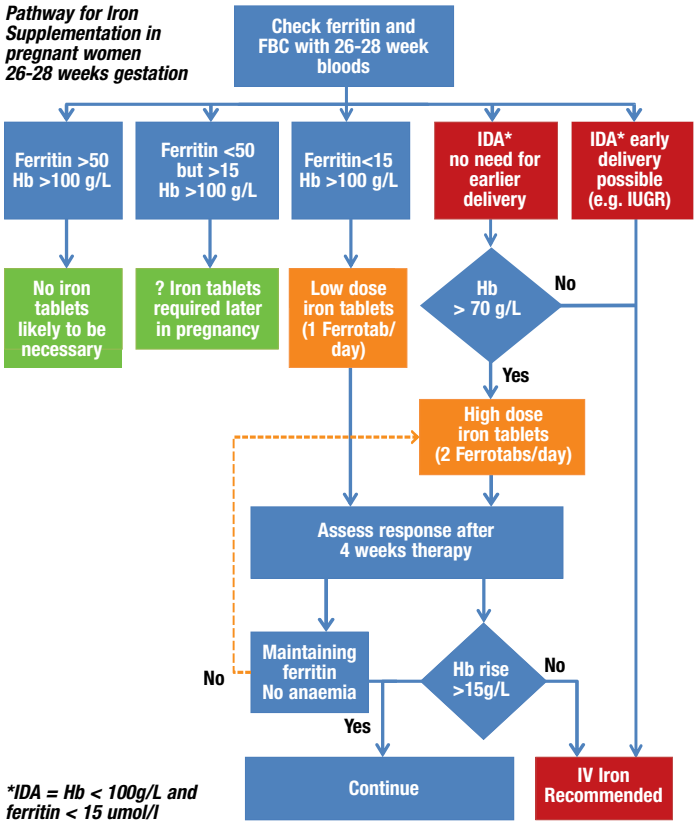
Figure 2: Iron supplementation pathway in pregnant women at 26-28 weeks gestation, adapted from ADHB (2015)

N.B. This algorithm and another for ≥ 30 weeks gestation is available from: https://nationalwomenshealth.adhb.govt.nz/assets/Womens-health/Documents/Referrals-and-info/Pathway-for-Iron-Supplementation-in-Pregnant-Women.pdf



TAKE-HOME MESSAGES

- IDA is end-stage iron deficiency; identify early and treat proactively.
- Iron deficiency during pregnancy cannot be treated by diet alone.
- Ferritin assessment is recommended at the first antenatal booking, especially if risk factors are present.
- Low-dose iron, given daily or on alternate days is the preferred regimen for oral supplementation.
- IV iron should be given to women who need it.

IRON DEFICIENCY AND RESTLESS LEGS

Syed Hussain, respiratory and sleep physician and clinical director of respiratory medicine at Auckland City hospital

Restless leg syndrome is characterised by:

- An urge to move the legs, usually but not always accompanied by or felt to be caused by uncomfortable and unpleasant sensations in the legs.
- Beginning or worsening during rest or inactivity, e.g. lying down or sitting.
- Being partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
- Occurring or being worse during the evening or night.
- The features above not solely accounted for by a medical or a behavioural condition (e.g. myalgia, venous stasis, leg oedema, arthritis, leg cramps, positional discomfort, habitual foot tapping).

RLS is not a fidgety or overall restlessness that occurs when waiting or sitting too long. The disorder can also involve the arms and other body parts, particularly when severe.

Prevalence and aetiology

RLS tends to be mostly patient expressed, rather than physician diagnosed. It is common but underdiagnosed and the prevalence (and severity) increases with age and ranges from 5-15%.[1]

RLS is often familial with an autosomal dominant pattern of inheritance, but there is no one causal gene. It is a neurological disorder where increased dopaminergic activity in the pre-synaptic terminal results in a down-regulated post-synaptic response to dopamine. The pathophysiology is compensated by movement but at night a lack of movement results in symptoms.

Types of restless leg syndrome

Primary RLS usually occurs before age 30 years with most people having an affected first degree relative. Secondary RLS occurs in 35% of patients with ID, 15-40% of patients receiving haemodialysis and 15-30% of pregnant women (peaking in the third

trimester). Secondary RLS may also be caused by medicines such as antidepressants or phenothiazine.

RLS is chronic-persistent when untreated symptoms occur at least twice-weekly. Intermittent RLS is defined as less than twice weekly symptoms when untreated, with at least five lifetime events.

Evaluating of restless leg syndrome

The assessment for RLS includes a neurological examination (usually normal), renal function and serum iron and serum ferritin. Ferritin levels are inversely related to RLS severity; > one-third have low levels and > two-thirds have levels ≤ 50 µg/L. Polysomnography is not routinely performed unless comorbid OSA is suspected. Approximately 80-90% of people with RLS also have PLMs.

Management of restless leg syndrome

Non-pharmacological management of RLS includes sleep hygiene, alcohol reduction and maintaining activity in the evening.

The pharmacological management of RLS may include:

- Dopaminergic long-acting agents, e.g. pramipexole, ropinirole, rotigotine
- Alpha-2-delta ligands, e.g. gabapentin, pregabalin
- Opioids for severe RLS that is not responding to other treatments
- Benzodiazepines to improve sleep continuity.

Medication may cause RLS augmentation which can be detected following initiation if:

- The symptoms start at least two hours earlier in the day
- Higher doses are needed or the medicine needs to be taken earlier
- The intensity of symptoms worsens
- Symptoms spread to other parts of the body (e.g. arms).

Augmentation is common with dopamine agonists, increases with increasing dosage and is minimal with alpha-2-delta ligands.

Managing augmentation

Augmentation is managed by eliminating or correcting exacerbating factors:

- Measure serum ferritin and replace if < 50-75 µg/L
- Address lifestyle changes, eg. sleep deprivation, alcohol use, decreased mobility.
- Medical factors, e.g. use of dopamine antagonists, antihistamines or antidepressants, recent opioid discontinuation, blood loss.

Differential diagnoses

Also consider nocturnal leg cramps, hypnic jerks, positional discomfort and enactment of dreams in patients with symptoms suggestive of RLS.

CASE STUDY

A 37-year-old woman complains of difficulty getting to sleep associated with an uncomfortable urge to move her legs. This occurs in the evening and is reduced with movement. A sleep study shows 47 leg movements per hour (normal ≤ 15/hr). Apnoea-hypopnea index is 3.7 hour/hr (normal < 5/hr). Which of the following is the most appropriate diagnosis?

- Periodic limb movement disorder
- Nocturnal leg cramps
- **Restless leg syndrome**
- Obstructive sleep apnoea

RLS is the most appropriate diagnosis because PLM occurs in 80-90% of patients with RLS.

Iron deficiency and restless legs

RLS is often associated with IDA. Iron is an important modulator of dopamine neurotransmission and is a co-enzyme for tyrosine hydroxylase which is essential for dopamine synthesis. Studies have shown the following in patients with RLS:

- Lower dopamine transporter binding potentials.[2]
- Reduced brain iron, particularly in the substantia nigra.[3]
- CSF ferritin is reduced and transferrin increased, despite normal peripheral iron.[4,5]
- ID in other brain areas, particularly the thalamus.

Evidence for iron supplementation for restless leg syndrome

A 12-week RCT found that oral iron resulted in a significant reduction in RLS symptoms.[6] In pregnant women with third trimester RLS, 500 or 700 mg of IV ferric carboxymaltose was associated with a reduction in RLS symptom rating from 23 to 13 after 7 days ($P < 0.01$) and a reduction in PLM from 35 to 25 over the same period ($P < 0.001$).[7]

A meta-analysis of ten studies (nine studies used IV iron) found that iron was significantly better than placebo at treating RLS.[8] There was low to moderate (non-significant evidence) that IV iron may be more effective than oral iron for RLS.[8] There was no difference in the risk of adverse events associated with IV iron, compared with placebo.[8]

CASE STUDY

A 37-year-old man complains of feeling uncomfortable in bed with an annoying tingling in his feet. His symptoms are improved by walking. He denies palpable leg cramps. His BMI is 25.7 kg/m^2 and the neurological examination is normal. What is the next useful approach to this patient?

- Neurologist review
- Sleep study (polysomnography)
- **Measure serum ferritin**
- Cognitive behavioural therapy

Measuring serum ferritin is a first-line investigation for patients with symptoms suggestive of RLS.

TAKE-HOME MESSAGES

- RLS is a neurological disease causing an urge to move the legs during periods of rest
- RLS occurs predominantly in the evening/night and is relieved by movement
- RLS is a common underdiagnosed disease
- RLS is associated with family history, iron deficiency, pregnancy, certain medicines
- Address non-pharmacological management in primary care, consider iron supplementation
- The optimal serum ferritin level is > 75 µg/L and this may improve response to medicines; patients generally report supplementation to be beneficial
- Refer if symptoms are causing distress (primarily Neurology; Sleep service if concomitant symptoms of OSA).

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IRON DEFICIENCY – THE GP EXPERIENCE

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Background

The Wellsford Clinic is the central practice for approximately 20,000 patients in the Waitematā DHB and the nearest hospital is a one-hour drive away.

A typical primary care case study

A 44-year-old female (*gravida* 2, *para* 2) with a history of menorrhagia and a BMI of 39, 12-weekly DMPA (amenorrhoeic 4 years) but no other regular medicines, no medical or surgical history and negative for Coeliac disease and IBD. Her Hb was 98 g/L, ferritin < 6 µg/L and TSAT 12%.

This patient was managed as unexplained IDA and oral iron tablets started with a review after three months. Following a lack of response, she was referred for OGD + colonoscopy where biopsy confirmed Coeliac disease. The initial Coeliac screen may have been a false negative or she may not have been exposed to insufficient gluten prior to testing.

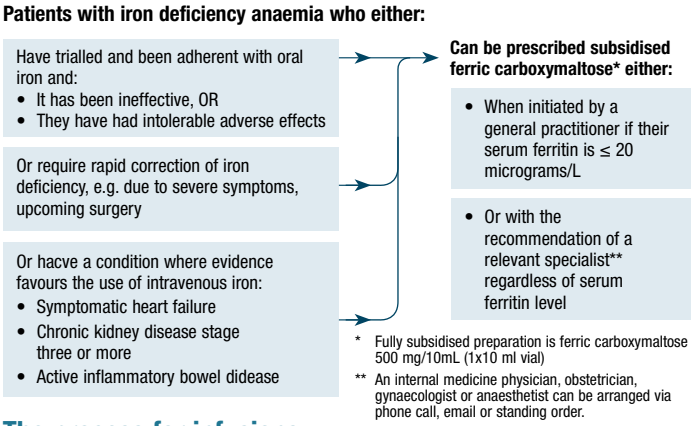
Iron tablets

In general, 100-200 mg/day of supplemental elemental iron is recommended and taking the tablets with fruit (vitamin C) may improve absorption and reduce adverse effects. Iron tablets purchased OTC may not have enough elemental iron. Oral iron polymaltose (Maltofer®) is not funded, however, experience suggests it is well tolerated in patients intolerant to other formulations and it can be taken with food. Alternate day iron may decrease adverse effects.

IV iron in the community

Since Q4 2017, Ferinject® (ferric carboxymaltose) has been funded in community based settings under Special Authority (**Figure 1**) and the Wellsford Clinic has been administering IV iron since June, 2018. There is variable funding for IV iron in the community which can be a barrier (funding in Auckland region is available here). Community administration of IV iron is beneficial for older patients who have difficulty travelling or for those with limited time or money to travel.

Figure 1: Pharmac funding criteria for Ferinject®, adapted from Anderson (2021)



The process for infusions

The Wellsford clinics have protocols for administering IV iron which are adapted from bpac^{nz} and a clinical checklist.[1]

Calculating the dose of Ferinject®

A simplified method for calculating the dose of ferric carboxymaltose uses the patient's ideal body weight (**Table 1**). Patients requiring ≥ 1500 mg of iron need two infusions, i.e. males taller than 175 cm or females taller than 180 cm. It is important to use the patient's ideal body weight, rather than actual weight when calculating doses. If a patient weighs <35 kg the Ganzoni formula for calculating the dose should be used.

Table 1: Bodyweight dosing of Ferinject® adapted from Anderson (2021)

Hb (g/L)	Ideal body weight 35-70 kgs	Ideal body weight >70kgs
< 100 g/L	1500 mg	2000 mg
>100 g/L	1000 mg	1500 mg

Adverse effects

The reported adverse effects of ferric carboxymaltose include: hypophosphataemia (2-27%), nausea (3-7%), hypertension (1-4%), injection site reactions (1-2%), headache (1%), dizziness (1%), increased liver enzymes (1%) and anaphylaxis (0.1-0.01%).

Patients are advised that they may experience adverse effects one to two days following administration.

Ferinject® audits

Two audits were conducted from June 2018-November 2020. Patients were followed-up post infusion to record adverse effects. During this period, 104 patients received Ferinject® with a total of 138 infusions.

The conditions that were treated were: ID (+/- anaemia) cause not specified (21), menorrhagia (15), malignancy (9), HHT (9), CKD (7), possible GI bleeding (6), previous gastric bypass (6), preoperative (5) and IBD (4).

A GP initiated 67 of the infusions, midwives 21 infusions and 16 cases were initiated by hospital specialists. For 62 patients the reason for treating was low Hb and low ferritin, for 19 patients there was low ferritin and normal Hb and 22 patients low Hb and ferritin.

No adverse effects at 12-month follow-up were reported by 70 patients and 16 patients reported muscle aches, fatigue and headache. Five patients reported no difference following treatment.

Case studies

Patient X is a 71-year-old male with HHT and recurrent epistaxis and GI bleeding, requiring blood transfusions every two to three years. Ferinject® began in July, 2018, resulting in a significant improvement in QoL. Adverse effects were myalgia and low phosphate that was eventually corrected by eating 3 bananas a day (phosphate tablets were not beneficial). In September 2020, he started two-weekly Avastin infusions and has not needed Ferinject® since.

Patient J is a 74-year-old female with recurrent IDA and end-stage COPD, hyperparathyroidism and heart failure. She had been admitted for blood transfusions. Oral iron was poorly absorbed and not tolerated. Ferinject® was initiated in mid-2019. She was lost to follow-up during the COVID pandemic and admitted for another infusion – adding this patient to a recall system may have prevented this.

Patient S is a 46-year-old with recurrent IDA. She has menorrhagia, no GI symptoms, no family history, no prescribed medicines and no significant alcohol intake. She is a vegetarian, poorly tolerant of oral iron. She declined Mirena, DMPA and gynaecological referral; Ferinject® was a reasonable treatment strategy.

Learnings from the Iron Matters Series

- More aware of tests to request, including the sTFR assay.
- More likely to actively screen patients with CKD, heart failure, active IBD and seek specialist approval.
- Interesting to note that no patients with heart failure received IV iron at the Wellsford Clinic; a future audit may be conducted.
- In the future antenatal infusions may not continue in the community.

In summary, offering Ferinject® in the community is massively beneficial for patients, although funding constraints may restrict access in some areas.

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