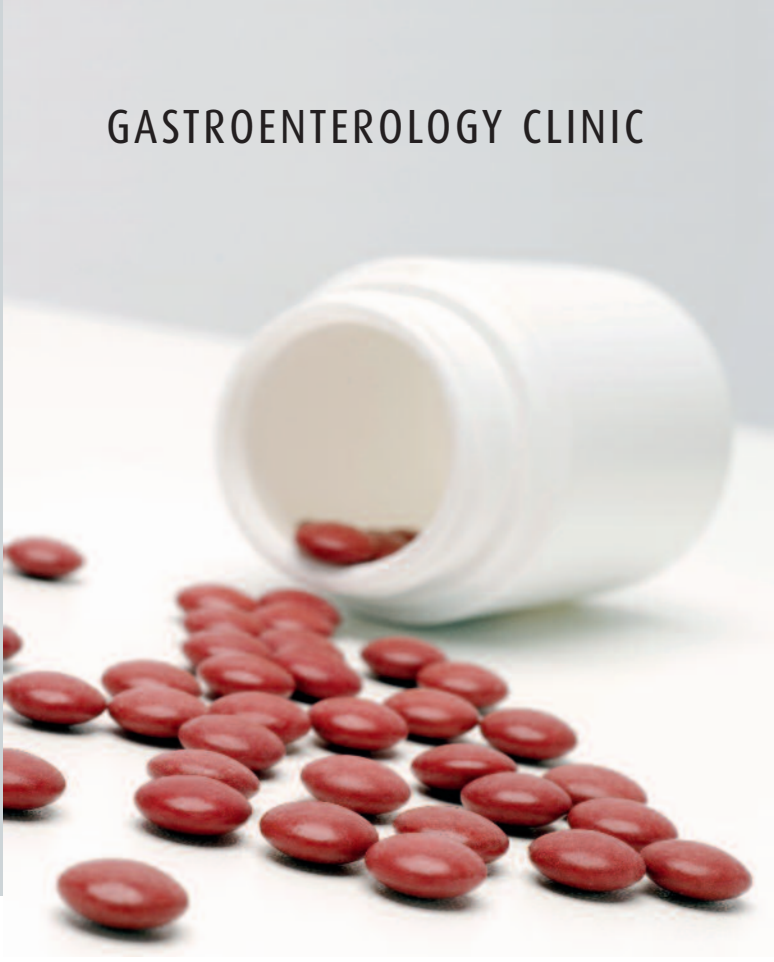
Correction of iron deficiency: a practical approach



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Diagnosing and preventing further iron loss is important in correcting iron deficiency, but so too is repleting iron stores with iron replacement therapy.

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REMEMBER

- Correcting the underlying cause and minimising further iron loss is essential when treating iron deficiency.
- Oral iron replacement is first-line therapy for repleting iron stores. It is generally effective and well tolerated.
- Intravenous (IV) iron replacement should be considered in patients who have not responded to, or who are genuinely intolerant of, oral iron therapy.
- IV iron replacement is generally safe, but about one in four patients will suffer side effects of infusion.
- Intramuscular (IM) iron replacement should be avoided unless no oral or IV alternative is available.
- Accidental overdoses of iron tablets can be lethal, particularly for children. Iron tablets should, therefore, be stored with care.

REPLACING IRON STORES

Iron deficiency anaemia is a common problem in medical practice. The interpretation of iron studies and the appropriate investigation of patients with iron deficiency are outside the scope of this article, but have been covered in recent articles in *Medicine Today*.[1,2]

This article aims to outline an evidence-based, practical approach to the correction of iron deficiency.

An important step in correcting iron deficiency is to diagnose and address any underlying pathology to prevent further iron loss. However, it is also important to replace iron for sufficient time to replete the patient's iron stores – generally about three months if bleeding has ceased. In the meantime, anaemia will be corrected and symptoms relieved.

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TABLE. ORAL AND PARENTERAL IRON PREPARATIONS

Trade name	Formulation	Elemental iron	Cost (MIMS)*
Oral iron preparations			
FGF (modified release tablet)	Ferrous sulfate 250 mg, folic acid 300 mcg	80 mg	$0.47 per tablet
Fefol (delayed release capsule)	Dried ferrous sulfate 270 mg, folic acid 300 mcg	87 mg	$0.43 per tablet
Ferro-F-tab (tablet)	Ferrous fumarate 310 mg , folic acid 350 mcg	100 mg	$0.13 per tablet
Ferrograd C (modified release tablet)	Ferrous sulfate 325 mg, sodium ascorbate 562.4 mg (equivalent to ascorbic acid 500 mg)	105 mg	$0.63 per tablet
Ferro-Liquid	Ferrous sulfate 150 mg per 5 mL	30 mg per 5 mL	$15 per 250 mL
Parenteral preparations			
Ferinject (intravenous)	Ferric carboxymaltose 100 mg per 2 mL and 500 mg per 10 mL	100 mg per 2 mL ampoule and 500 mg per 10 mL ampoule	About $40 per 2 mL ampoule†
Venofer (intravenous) ampoule	Iron sucrose 100 mg per 5 mL	100 mg per 5 mL ampoule	$139.48 per ampoule
Ferrosig Injection (intramuscular) Ferrum–H Injection (intramuscular) ampoule	Iron polymaltose 318 mg	100 mg per 2 mL ampoule	$49.57 per ampoule

* Costs at September 2011. Please note that the cost of intravenous iron replacement may be lower in hospitals where bulk discounts of medications, including intravenous iron, may apply.
† Cost not listed in MIMS.

Advice on adequate dietary intake of iron is also required, with its main role being prevention of recurrence of iron deficiency rather than acute treatment of the deficiency.

Options for replacing iron stores include oral, IV and IM preparations. These preparations and their associated cost are listed in the Table.[3]

Oral replacement

- Countless oral preparations contain - ing iron are available on the Australian market, but only a few contain sufficient iron to provide meaningful replacement therapy.
- Oral iron replacement is first-line therapy for most patients with iron deficiency. One exception is patients who have signs of end organ dys - function as a result of their anaemia. In this scenario, transfusion of red blood cells is generally indicated as first-line treatment.
- Oral iron replacement is generally well tolerated by patients and highly effective. Treatment should begin with a once-daily dose of 150 to 200 mg, which can be increased to up to three times daily as tolerated, depending on treatment effect and ongoing iron loss.
- The most common side effects are gastrointestinal, and these can lead to discontinuation of treatment in a minority of patients.
- Side effects can be reduced and compliance increased by changing the dosing schedule (e.g. second daily, third daily, weekly). This is a highly appropriate strategy when more gradual correction of haemoglobin levels and iron stores is acceptable.
- Compliance can be improved with the use of liquid iron supplement. The dose of this can be titrated as tolerated, and the formulation is especially useful in patients suffering constipation as a limiting side effect of the iron replacement. Patients with iron deficiency anaemia awaiting colonoscopy can take oral iron replacement provided it is withheld seven days prior to the procedure.
- A response to daily therapy as shown by a rise in haemoglobin levels of 10 to 20 g/L is generally expected within two to three weeks.
- Lack of response should lead to reconsideration of the diagnosis and consideration of reduced iron absorption – for example, secondary to coeliac disease – and an assessment of the patient's compliance.
- It is also important to consider factors that can interfere with iron absorption, including the use of proton pump inhibitors, fluoro-quinolones, antacids, oral calcium supplements, infection with *Helico-bacter pylori* and tea consumption.
- Absorption of oral iron can be optimised by co-administration with 250 mg of oral vitamin C and by taking the iron preparation on an empty stomach.
- Treatment failure ensues if the patient's ongoing iron losses exceed

the amount of iron that can be physiologically absorbed from the gut each day (about 10 to 20 mg).
- Oral iron treatment is generally not sufficient to correct iron deficiency in patients with end-stage kidney disease who are on dialysis and erythropoietin replacement, and parenteral iron replacement is generally required.

Parenteral replacement

- IV iron replacement is generally safe, but is more expensive and impractical compared with oral replacement.
- Available parenteral preparations in Australia include iron polymaltose and iron sucrose, both of which have a low incidence of anaphylaxis (between 0.6 and 0.7 %) compared with the superseded older iron dextran formulations.[4-6] However, milder side effects with the current preparations are common, and up to 25 to 35% of patients receiving IV iron report adverse events such as headaches, arthralgia, rash and bronchospasm.[4-6]
- The main benefit of IV iron is the ability to replace a large amount of iron quickly.
- Treatment with IV replacement should generally be reserved for patients who genuinely cannot tolerate oral iron or fail to adequately respond to treatment after seeking specialist advice. An attempt at adjusting dosing schedule and regimen to achieve tolerability should be made before abandoning oral iron therapy.
- Patients with end-stage renal failure on erythropoietin and those with ongoing high iron losses are also appropriate candidates for IV iron replacement.[7]
- IM iron replacement with iron polymaltase should only be considered when oral replacement has failed in a clinical setting where replacement with IV iron is unachievable.
- Side effects of IM iron replacement include permanent discolouration of the skin, inflammation and pain at the injection site and, possibly, the development of sarcomas.

CONCLUSION

- It is important to correct iron deficiency and replenish iron stores.
- Oral iron therapy is safe, effective and cheap.
- IV iron replacement has a limited role in selected patient groups, is more expensive than oral iron treatment and can usually be administered safely in an ambulatory environment.
- Monitoring treatment response and adjusting therapeutic regimens to achieve replenishment of iron stores is important. A rapid decline in ferritin after successful iron replacement should prompt further diagnostic investigation to identify the source of the ongoing iron loss. MT

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