Iron deficiency is common in pregnancy and has adverse effects for both the mother and child. It can and should be readily treated.

Iron deficiency leads to reduced iron stores and subsequently to anaemia. Iron deficiency and iron deficiency anaemia are frequently encountered in general practice: 41.8% of pregnant women experience anaemia with at least 50% of cases being due to iron deficiency.1

In pregnancy, there is an increased demand for iron to expand the maternal and fetal red cell mass and support placental growth, with a daily iron requirement of 4.4 mg.2 The impact can be exacerbated by insufficient pre-pregnancy iron stores.

Iron deficiency in pregnancy is associated with adverse feto-maternal outcomes (Box 1).3 The risk of adverse effects increases with increasing severity of anaemia. Every case of iron deficiency or iron deficiency anaemia in pregnant women should be identified and treated as early as possible to prevent unfavourable perinatal outcomes.

Assessment

Typical symptoms of iron deficiency, such as fatigue, exercise intolerance, weakness and irritability, are often present in normal pregnancies and this can hamper clinical assessment. Many pregnant women with iron deficiency appear asymptomatic and only recognise the symptoms after successful iron replacement treatment.

KEY POINTS

- Ideally, iron status should be checked and optimised before pregnancy.
- Iron deficiency should be treated before anaemia develops: aim for a target ferritin level of 60 µg/L.
- Not all microcytic anaemias are due to iron deficiency. Haemoglobinopathy, which has potential consequences for both mother and child, needs to be excluded as a cause of iron deficiency.
- Women should be educated about the side effects and interactions of oral iron replacement. This will increase the likelihood of them achieving adequate iron levels through oral replacement.
- Intravenous iron preparations are currently safer and more convenient for treating pregnant women with iron deficiency. Iron repletion before delivery is preferable, with a lower threshold to prescribe intravenous iron such as iron carboxymaltose.
A full blood count is recommended for all women in the first trimester (at the time of pregnancy confirmation or the hospital booking blood test) and at 28 weeks’ gestation. Patients with iron deficiency often, but not always, have red cells that are hypochromic (mean corpuscular haemoglobin <27 pg/cell) and microcytic (mean corpuscular volume <80 fL/cell), with or without anaemia (defined as haemoglobin <110 g/L in pregnancy). This can be indistinguishable from results for patients with haemoglobinopathy.

At present, neither the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) nor the UK guidelines recommend routine assessment of iron stores with the screening blood tests in pregnant women. These tests are rather only recommended in patients ‘at risk’ of iron deficiency or with confirmed anaemia (Box 2). In the authors’ opinion, ferritin levels should be part of routine antenatal blood tests for all pregnant women for the following reasons.

- It is valuable to treat iron deficiency before it progresses to anaemia and to ensure adequate placental and fetal iron supply during the crucial stages of fetal development.
- It is easier to treat patients with early iron deficiency, with lower oral iron doses and less side effects.
- High-risk patients may not otherwise be easily identified.
- Aboriginal and Torres Strait Islander women, who would not be identified under some guidelines, experience a higher prevalence of factors that contribute to iron deficiency.
- Ferritin can be assessed using an ethylenediaminetetra-acetic acid (EDTA) blood test with no additional blood sampling required.

Ferritin levels are the most useful indicator of iron stores. Results should be interpreted cautiously in the presence of infection or inflammation because ferritin is also an acute-phase reactant. Total serum iron level is not a reliable indicator of iron depletion because it is affected by recent iron intake, diurnal variation and an unclear reference range.

The authors would suggest that women should enter labour with a ferritin level of 60 µg/L to ensure there are adequate iron stores to cope with routine blood loss during delivery and the puerperium. The lower limit of the ‘reference range’ for ferritin varies between 15 and 30 µg/L. The average iron loss in 500 mL of blood (the average blood loss in a normal vaginal delivery) is 250 mg elemental iron – which approximates to a ferritin level of 30 µg/L. The losses are double in women undergoing a caesarean section.

### Management

**Routine supplementation in pregnancy**

Due to the high prevalence of iron deficiency in pregnant women, the World Health Organization and the US Centers for Disease Control and Prevention strongly recommend universal iron supplementation with 30 to 60 mg/day of...
elemental iron from the time of pregnancy confirmation, together with consumption of iron-rich foods and foods that enhance iron absorption. The UK guidelines do not recommend universal iron supplementation in pregnancy, citing the lack of demonstrated maternal and fetal benefit, noncompliance, cost and the theoretical risks of haemococentration and oxidant stress. Similarly, RANZCOG recommends iron supplements only for at-risk women (e.g. vegetarians, multiple pregnancy). Iron supplementation should be discussed on a case-by-case basis, aiming for a target ferritin level of 60 to 100 µg/L. Pregnancy multivitamins and minerals contain iron but patients should be aware that the amounts of elemental iron can vary greatly between products (Table 1).

**Oral iron replacement**

In pregnant patients with iron deficiency anaemia, first-line management is with oral iron therapy. A therapeutic dose of elemental iron (100 to 200 mg/day) should be prescribed; a lower dose of iron is insufficient to correct deficiency. Iron content in commercial products varies from 5 to 105 mg per dose. Therefore, ensure that patients choose a preparation with an adequate elemental iron content (Table 2). Available evidence suggests that different iron salts have similar efficacy and tolerability. Controlled-release and enteric-coated tablets may have reduced efficacy due to iron release being distal to the main site of absorption, and these preparations are not recommended. Patients will need to be educated on the best way to take iron supplements. Advice to give patients includes:

- consume food containing vitamin C (e.g. orange juice) when ingesting iron supplements, as ascorbic acid enhances iron absorption
- do not take inhibitors of iron absorption, such as calcium-rich food or dairy products, tea (tannins) and cereals (phytates), with iron supplements
- take iron supplements on an empty stomach or one hour before meals to improve absorption. There is potentially less nausea when taken with food, but absorption is reduced by up to 50%
- check with their GP about interactions with other medications, such as antacids, anticonvulsants and sulfonamides.

Pitfalls can be pre-empted by giving

### Table 2: Various Iron Preparations Showing Iron Content and Price, in Order of Decreasing Elemental Iron Content

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Iron type</th>
<th>Elemental iron content</th>
<th>Additional content</th>
<th>PBS listed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferro-Gradumet</td>
<td>Ferrous sulfate</td>
<td>105 mg per tablet</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Ferrograd C</td>
<td>Ferrous sulfate</td>
<td>105 mg per tablet</td>
<td>Vitamin C 500 mg</td>
<td>No</td>
</tr>
<tr>
<td>Ferro-F-Tab</td>
<td>Ferrous fumarate</td>
<td>100 mg per tablet</td>
<td>Folic acid 350 µg</td>
<td>Repatriation care item</td>
</tr>
<tr>
<td>Maltoper Tablets</td>
<td>Iron polymaltose</td>
<td>100 mg per tablet</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Maltoper Syrup</td>
<td>Iron polymaltose</td>
<td>100 mg per 10 mL</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Ferro-Liquid</td>
<td>Ferrous sulfate</td>
<td>90 mg per 15 mL</td>
<td>–</td>
<td>Yes</td>
</tr>
<tr>
<td>Fefol</td>
<td>Ferrous sulfate</td>
<td>87.4 mg per tablet</td>
<td>Folic acid 300 µg</td>
<td>No</td>
</tr>
<tr>
<td>FGF</td>
<td>Ferrous sulfate</td>
<td>80 mg per tablet</td>
<td>Folic acid 300 µg</td>
<td>No</td>
</tr>
<tr>
<td>Ferro-Tab</td>
<td>Ferrous fumarate</td>
<td>65.7 mg per tablet</td>
<td>–</td>
<td>Repatriation care item</td>
</tr>
<tr>
<td>Blackmores Pregnancy Iron</td>
<td>Iron glycinate</td>
<td>24 mg per tablet</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Fab Iron and Vitamin B Complex</td>
<td>Iron aminoate</td>
<td>10 mg per tablet</td>
<td>Various</td>
<td>No</td>
</tr>
<tr>
<td>SpaTone</td>
<td>Iron sulfate</td>
<td>5 mg per sachet</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Iron Melts</td>
<td>Ferrous fumarate</td>
<td>5 mg per tablet</td>
<td>Vitamin C 50 mg</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Folic acid 250 µg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vitamin B 10 µg</td>
<td></td>
</tr>
</tbody>
</table>

* This is not a comprehensive list of iron supplements. Information is correct at the time of going to press.
3. Indications for Intravenous Iron Supplementation

- Rapid restoration of haemoglobin and iron stores (e.g. in the third trimester)
- Oral iron replacement poorly tolerated or ineffective
- Impaired absorption of oral iron

Parenteral iron replacement

In pregnant patients with iron deficiency anaemia, intravenous iron is more effective at increasing haemoglobin and ferritin levels than oral iron plus folic acid. Box 3 lists the indications for intravenous iron supplementation. Parenteral iron replacement has become an attractive alternative in view of the tolerability issues of oral iron and ease of administration of iron carboxymaltose. Dosage should be calculated according to the patient’s iron deficit to ensure adequate long-term iron stores can be maintained (Table 4). Some women require a second dose.

Iron carboxymaltose is an attractive choice of iron supplement because of its short infusion time, availability on the PBS, low anaphylaxis risk and international experience. There are risks of skin staining with extravasation and resuscitation equipment should be available. Iron polymaltose requires a five-hour inpatient infusion for the equivalent dose that iron carboxymaltose delivers. Intravenous iron should not be given in the first trimester and the risks and benefits should be evaluated later in pregnancy. There is a growing body of evidence and experience supporting the use of iron carboxymaltose in pregnancy.

Intramuscular injections are no longer recommended because of skin staining in these young women.

Table 3. Troubleshooting Pitfalls in Oral Iron Replacement in Pregnancy

<table>
<thead>
<tr>
<th>Pitfall</th>
<th>Tip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inadequate dose</td>
<td>Ensure 100 to 200 mg/day elemental iron</td>
</tr>
<tr>
<td>Constipation</td>
<td>Manage constipation before commencing iron replacement</td>
</tr>
<tr>
<td>Inadequate absorption</td>
<td>Advise on directions: avoid simultaneous dairy intake, consume with food containing ascorbic acid (vitamin C)</td>
</tr>
<tr>
<td>Noncompliance</td>
<td>Educate</td>
</tr>
</tbody>
</table>

Table 4. Calculating the Dose of Intravenous Iron

<table>
<thead>
<tr>
<th>Haemoglobin level (g/L)</th>
<th>Dose of intravenous iron (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body weight 35 to &lt;70 kg</td>
</tr>
<tr>
<td>&lt;100</td>
<td>1500</td>
</tr>
<tr>
<td>≥100</td>
<td>1000</td>
</tr>
</tbody>
</table>

Dietary iron

Increased dietary iron intake is not adequate to treat iron deficiency; however, it is important to counsel women to maximise their consumption of foods rich in iron such as haem iron-rich meat (i.e. red meat, chicken, fish), lentils, beans, tofu and wholegrain cereals (especially fortified; see Figure).11

Follow up

Follow up is important to ensure compliance and to assess the patient’s response and side effects of the iron supplement. A full blood count and measurement of ferritin levels are recommended after six weeks of iron replacement, with shorter follow up in the third trimester or if there is associated anaemia. The target is a ferritin...
level more than 60 µg/L and a haemoglobin level more than 110 g/L.

After delivery, iron replacement can be ceased if the woman has adequate iron stores, especially if side effects include perineal pain and constipation. Breastfeeding women have low iron requirements – even less than menstruating females.

**When to refer**
Pregnant women should be referred to a haematologist if:

- there has been an inadequate response to oral iron
- the cause of anaemia is unclear or unknown
- there are unexplained abnormalities on the results of the full blood count or blood film
- there is co-existing haemoglobinopathy.

**Conclusion**
Iron deficiency is a common and important issue in pregnancy. Measures to minimise iron deficiency include screening, a recommendation for high dietary iron intake, careful selection of oral iron replacement if ferritin levels are less than 60 µg/L and follow up. If required, intravenous iron is an effective alternative to oral iron to manage iron deficiency in pregnant women.

**Further reading**


**References**
A list of references is included in the website version of this article (www.medicinetoday.com.au).

**COMPETING INTERESTS:** None.
Iron deficiency in pregnancy
What you need to know

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References