

Iron deficiency in pregnancy

What you need to know

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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 fetomaternal 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.

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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.

1. POTENTIAL CONSEQUENCES OF IRON DEFICIENCY ANAEMIA IN PREGNANCY

Maternal

- Fatigue
- Reduced physical and mental performance
- Haemorrhage
- Increased risk of need for transfusion
- Infection
- Risk of hospitalisation
- Inhibited lactation
- Postpartum depression
- Restless legs syndrome

Fetal

- Impaired placental growth/placental insufficiency
- Low birth weight
- Preterm birth
- Neurological impairment
- Increased mortality

2. UK GUIDELINES RECOMMENDATION FOR SERUM FERRITIN ASSESSMENT*

1. Anaemic women where estimation of iron stores is necessary
 - a. Known haemoglobinopathy
 - b. Prior to parenteral iron replacement
2. Nonanaemic women with high risk of iron depletion
 - a. Previous anaemia
 - b. Multiparity (3 or more)
 - c. Consecutive pregnancy <1 year following delivery
 - d. Vegetarians
 - e. Teenage pregnancies
 - f. Recent history of bleeding
3. Nonanaemic women where estimation of iron stores is necessary
 - a. High risk of bleeding
 - b. Jehovah's witnesses

- 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.³
- 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

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).⁴ 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.^{5,6} 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.

TABLE 1. COMPARISON OF IRON CONTENT IN SOME EXAMPLES OF PREGNANCY MULTIVITAMINS AVAILABLE IN AUSTRALIA

Brand	Recommended daily dose	Elemental iron content according to daily dose
Blackmores Pregnancy & Breast-feeding Gold	2 capsules	10 mg
Elevit	1 tablet	60 mg
FABFOL	1 tablet	12 mg
Swisse Pregnancy + Ultivite	1 capsule	5 mg

TABLE 2. VARIOUS IRON PREPARATIONS SHOWING IRON CONTENT AND PRICE, IN ORDER OF DECREASING ELEMENTAL IRON CONTENT

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

* This is not a comprehensive list of iron supplements. Information is correct at the time of going to press.

elemental iron from the time of pregnancy confirmation, together with consumption of iron-rich foods and foods that enhance iron absorption.^{7,8}

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 haemoconcentration and oxidant stress.⁶ Similarly, RANZCOG recommends iron supplements only for at-risk women (e.g. vegetarians, multiple pregnancy).⁹ 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.^{3,6} 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.¹⁰

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

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

the patient an information sheet and warning them about side effects such as abdominal discomfort, constipation, and stool discolouration and smell (Table 3).

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.³ 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

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

TABLE 4. CALCULATING THE DOSE OF INTRAVENOUS IRON

Haemoglobin level (g/L)	Dose of intravenous iron (mg)	
	Body weight 35 to <70 kg	Body weight ≥70 kg
<100	1500	2000
≥100	1000	1500

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

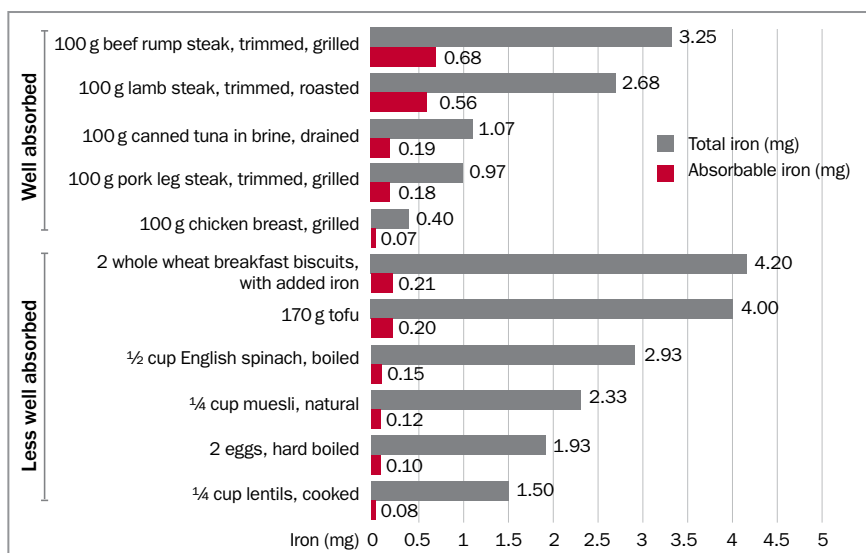


Figure. Iron content and absorption of various foods. Reproduced with permission from Meat & Livestock Australia.¹¹

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. Breast-feeding 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.⁶

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. **MI**

Further reading

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

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