Iron deficiency and anaemia in adults

RCN guidance for nursing staff

This publication is supported by industry. Full information inside.
Acknowledgements

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Iron deficiency anaemia (IDA) is a widespread problem affecting an estimated two billion people worldwide (Zimmermann and Hurrell, 2007) and is the most common cause of anaemia seen in primary care. It causes more than 57,000 emergency admissions to hospital each year, at a cost to the NHS of £55.48m (Goddard and Phillips, 2014).

Fatigue, weakness and impaired physical function are typical symptoms that can adversely affect an individual’s quality of life and wellbeing and results in a greater demand for health services.

Nursing staff in all clinical settings will encounter IDA but effective identification and management is often overlooked. Dealing with IDA improves the patient’s physical condition, prevents complications and blood transfusion use; an estimated cost saving of £8.43m per year (Goddard and Phillips, 2014).

This RCN guidance has been developed by expert nurses from several relevant specialties. It is aimed at all nurses, health care assistants (HCAs), midwives and health visitors from all specialities and backgrounds.

This publication:

- gives clear information on identifying IDA and escalating effective management
- makes it easier to understand when, why and how IDA occurs
- provides information on good dietary advice and the use of oral iron supplements
- encourages the use of intravenous iron and provides practical tips for its delivery
- provides good patient information website links
- offers specialist guidance to nursing staff working in the following specific therapeutic areas: chronic kidney disease (CKD), inflammatory bowel disease (IBD), heavy menstrual bleeding, pregnancy and postpartum, and patient blood management.

### Definition

Anaemia is defined as a reduced number of red blood cells (RBCs) or less than the normal amount of haemoglobin (Hb) in the blood. It can also be defined as a lowered ability of the blood to carry oxygen.

### World Health Organization (WHO) Haemoglobin thresholds used to define anaemia (Pavord et al, 2011)

<table>
<thead>
<tr>
<th>Age or gender group</th>
<th>Hb threshold (g/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0.5 to 5 years)</td>
<td>110</td>
</tr>
<tr>
<td>Children (5 to 12 years)</td>
<td>115</td>
</tr>
<tr>
<td>Teens (12 to 15 years)</td>
<td>120</td>
</tr>
<tr>
<td>Women, non-pregnant (over 15 years)</td>
<td>120</td>
</tr>
<tr>
<td>Women, pregnant</td>
<td>110 in first trimester 105 in second and third trimesters 100 post partum (up to six weeks post delivery)</td>
</tr>
<tr>
<td>Men (over 15 years)</td>
<td>130</td>
</tr>
</tbody>
</table>

The normal range for Hb also varies between different populations in the UK. There are several different types of anaemia and each one has a different cause, although IDA is the most common. IDA is a condition where a lack of iron in the body leads to a reduction in the number of red blood cells. Iron is normally stored in the liver and is essential to red blood cell production. If there is a shortage of stored iron then red cells become depleted.
Iron metabolism and pathophysiology

Iron

Iron metabolism involves a number of important processes, including the regulation of intestinal iron absorption, the transport of iron to the cells, the storage of iron, the incorporation of iron into proteins, and the recycling of iron after RBC degradation.

Under normal physiological conditions, as there is no active iron excretion mechanism, iron homeostasis is strictly controlled at the level of intestinal absorption.

Storage of iron

In healthy individuals, about 25 per cent of the total body iron (800 to 1,000mg) represents storage iron, mainly as ferritin in the liver, spleen, and skeletal muscle; consequently, serum ferritin is a useful marker for iron stores.

Hepcidin is a key regulator of the movement of iron out of cells. In states in which the hepcidin level is abnormally high (such as inflammation), serum iron falls due to iron trapping within macrophages and liver cells and decreased gut iron absorption. This typically leads to anaemia due to an inadequate amount of serum iron being available for developing red cells.

In patients with chronic inflammatory conditions, high hepcidin levels may affect the iron mobilisation rate, resulting in a failure to meet enhanced iron demands. This leads to functional iron deficiency (FID), which develops under conditions where the demand exceeds iron availability.

Measuring iron status

If Hb is reduced, further blood iron studies identify if the anaemia is caused by iron deficiency.

Ferritin

This is a measure of iron storage in the body. Reduced serum ferritin is always the first iron study to fall and show iron deficiency. However, it is not always accurate as it may increase if the patient has:

- inflammation/infection
- liver disease
- malignancy.

Transferrin

This is a measure of transferrin saturation (in per cent). Transferrin is the carrier protein transporting iron to bone marrow and transferrin saturation measures the degree of circulating transferrin loaded with iron. Levels will fall in iron deficiency.
Hypochromic small red blood cells
This is a measurement of the colour and size of red blood cells. MCV (mean cell volume) is reduced as there is less haemoglobin within them. The red cells are pale due to the reduced haemoglobin; this is called hypochromia. In iron deficiency the cells look smaller and paler. It gives a direct estimation of the iron available for red blood cell development in the bone marrow. This is produced when iron stores and/or mobilisation are insufficient.

Common symptoms of anaemia
The following are the common signs and symptoms of anaemia. It is important to remember that they can be overlooked or missed due to their vagueness and ability to be attributed to several causes. Patients rarely present with only one of the symptoms listed and often present them as a part of a list of other symptoms, sometimes obscuring information.

- Weakness.
- Shortness of breath.
- Dizziness.
- Fatigue.
- Fast or irregular heartbeat.
- Pounding or ‘whooshing’ in the ears.
- Headache.
- Cold hands or feet.
- Pale skin.
- Chest pain.
- Lack of concentration.
- Mouth ulcers or cracks at the corners of the mouth.
- Slow or poor wound healing.
- Tinnitus.

(Arnott et al, 2013)

Important questions to ask
To determine the underlying cause of anaemia, questions about the patient’s lifestyle and medical history should be asked. These questions should cover the following areas.

Diet
Certain types of food preferences or intolerances may lead to a diet that does not contain sufficient iron-rich foods.

Medicines
A comprehensive list of all medicines being taken is vital. Many patients will mention over the counter remedies, homeopathic and/or herbal remedies.
alongside any medications that are regularly prescribed by a physician. There can be contraindications and a comprehensive list will allow identification of any type of medicine that might cause gastrointestinal bleeding (bleeding from the stomach and intestines), such as ibuprofen or aspirin.

**Menstrual pattern**
Particularly heavy or prolonged periods can lead to anaemia, but this may go unreported if the patient has always had periods of this kind and has not seen a marked difference in what they are used to. Establishing an idea of volume of loss and length of bleeding in days, as well as what is a normal pattern for the individual patient, is important.

**Pregnancy and lactation**
Both pregnancy and lactation place heavier demands on the body for the use of iron and iron stores as the pregnancy and baby develops or the body responds to the demands to nurture the baby during feeding. In addition, there are greater physical demands on the body when caring for a new born and sleep and diety patterns of the mother change.

**Unexplained and heavy bruising**
It is valuable to ask if the patient has had any unexplained or unexpectedly heavy bruising from an otherwise light injury. This will allow a time frame to be established for the symptoms and concerns being investigated and may prompt the patient to recall episodes of weakness or dizziness they may have not otherwise mentioned.

**Family history**
Identification of immediate family members who have been diagnosed and treated for anaemia or who have a history of gastrointestinal bleeding or blood disorders can assist in identifying potential patterns or genetic commonalities that can lead to a more specific diagnostic pathway.

**Blood donation**
Regular donations of blood require a blood test to check that the donor’s haemoglobin level is sufficient for them to be able to safely donate. If the patient has recently been unable to meet that threshold after previously having no problems, it may give a time frame for the onset of the anaemia. If a donation has been made within 48 hours of a blood test then the patient will have a lower haemoglobin level as their body replaces the red cells that have been donated.

**Other medical conditions**
It is important to record any other illnesses or symptoms as listed previously.

**Travel**
Ask about any recent trips or contact with others who have been abroad. This can be instructive as certain destinations may increase the chances of the patient having a blood-borne infection or hookworm.

**Examination**
Investigations to determine IDA usually begins with blood tests.

**Full blood count (FBC)**
This checks the number and quality of red cells present in the blood sample taken including the Hb.

**Vitamin B₁₂ and folate levels**
This checks to see if the levels present are sufficient to make functioning red blood cells.

**Ferritin and iron saturation levels**
This checks the amount of iron stored (ferritin) and the amount available to use (iron saturation).

**Urinalysis for haematuria**
One per cent of patients with IDA will have renal tract malignancy. This may present with obvious or occult haematuria (Goddard et al, 2011).
Iron deficiency and anaemia in adults

Oral iron supplements

Oral iron supplements should be given to all patients with iron deficiency. These will help to correct anaemia and replenish iron stores. There are several iron compounds available as tablets (ferrous sulphate, ferrous fumerate, ferrous gluconate).

Oral iron preparations contain varying amounts of ferrous iron and the frequency of gastrointestinal side effects related to each different preparation tends to be directly related to the content of ferrous iron.

<table>
<thead>
<tr>
<th>Iron salt</th>
<th>Dose</th>
<th>Preparation</th>
<th>Content of ferrous iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous sulphate</td>
<td>200mg</td>
<td>tablets</td>
<td>65mg</td>
</tr>
<tr>
<td>Ferrous gluconate</td>
<td>300mg</td>
<td>tablets</td>
<td>35mg</td>
</tr>
<tr>
<td>Sodium feredate</td>
<td>380mg/10mls</td>
<td>elixir</td>
<td>55mg</td>
</tr>
</tbody>
</table>

Limitations to iron supplements

There are several limitations to taking iron supplements. Only a small amount is actually absorbed (particularly for patients with inflammation). Between 10 and 40 per cent of patients will experience gastrointestinal (GI) side effects and don’t fully adhere to the prescribed course.

Tips for successful supplementation

• Lower doses are better tolerated (start daily and build up dosing).
• Check FBC and iron levels monthly, once Hb is normal, continue oral iron for three months.
• Ascorbic acid (vitamin C) in combination may help absorption.
• Warn patients of GI side effects.

Where patients take iron supplements effectively, haemaglobin should rise by 2g/l every three weeks.

Dietary iron

In general a broad range of foods should be used to help with iron absorption. A normal balanced diet contains 12-18mg total iron per day. However, only a small amount of iron eaten is absorbed (3-5mg per day). It is advised that eating 70g of red meat per day is safe to meet iron requirements. Iron in the diet comes in two forms; haem iron and non-haem iron. Haem iron is found in animal derived foods and non-haem iron in plant derived foods. Non-haem iron (plant iron) is less easily absorbed through the gut. This means that vegetarians have a tendency to iron deficiency.

Foods that enhance or inhibit iron intake and absorption (Derbyshire, 2012)

<table>
<thead>
<tr>
<th>Foods that enhance iron intake</th>
<th>Foods that inhibit iron absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>lean red meat</td>
<td>calcium, particularly from milk and dairy products</td>
</tr>
<tr>
<td>oily fish</td>
<td>phytates, present in cereal brans, grains, nuts and seeds</td>
</tr>
<tr>
<td>vitamin C (fresh fruit and juices)</td>
<td>polyphenols and tannin (in tea, coffee herbal infusions, green leafy vegetables)</td>
</tr>
</tbody>
</table>

General tips

Don’t drink tea or coffee before or immediately after meals; wait at least one to two hours. Include vitamin C with meals where possible (such as a glass of fruit juice). Eat dairy products as snacks rather than with meals. Eat five portions of fruit and vegetables each day (Food Standard Agency, 2007).

For more patient information on iron in your diet visit: www.blood.co.uk/about-blood/information-for-patients
Intravenous iron: practical administration

Using iron intravenously (IV) used to be thought as a last resort. However, modern IV iron preparations are becoming standard practice now in the management of IDA (Arnott et al, 2013).

Randomised controlled trials show that:
• intravenous iron is at least as effective as oral iron
• intravenous iron delivers a faster response rate than oral iron.

IV iron is given when there is an oral iron intolerance/poor adherence, or if there is a poor response to oral iron. It needs to be given in a specialist environment. However, there are a number of contraindications. These include:
• known hypersensitivity to intravenous iron
• anaemias not caused by iron deficiency
• iron overload
• first trimester of pregnancy.

Precautions to take in account include:
• asthma, eczema or other atopic allergy
• liver dysfunction
• acute or chronic infection
• hypotension.

All health care practitioners should refer to the individual Summary of Product Characteristics before prescribing.

Use in pregnancy

Oral iron is generally the preferred method of supplementation for anaemia in pregnancy, although where anaemia is sufficiently severe intravenous preparations may be used.

Intravenous iron is contraindicated during the first trimester of pregnancy; whilst for the second and third trimesters it is suggested that pre-pregnancy weight should be used as the basis for iron requirement and dose calculation.

IV iron preparations

Currently four IV iron preparations are available for use.
1. Ferric carboxymaltose (Ferinject).
2. Iron sucrose (Venofer).
3. Low molecular weight iron (111) dextran (Cosmofer).
4. Iron isomaltoside 1000 (Monofer (100mg/ml)).

All preparations have been shown to be well tolerated, with few side effects. NICE (CKD) guidance (2011) does not differentiate between them.
Iron Deficiency and Anaemia in Adults

Dosing and infusion differences between IV iron preparations

<table>
<thead>
<tr>
<th>Ferinject (Ferric carboxymaltose)</th>
<th>Venofer (Iron sucrose)</th>
<th>Cosmofer (Low molecular weight iron dextran)</th>
<th>Monofer (Iron isomaltoside 1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td><strong>Total dosing</strong></td>
<td><strong>Repeated dosing</strong></td>
<td><strong>Total dosing and repeated dosing</strong></td>
</tr>
<tr>
<td>Total dose according to dosing schedule in product SPC</td>
<td>Total dose determined by Ganzoni calculation</td>
<td>Total dose determined by Ganzoni calculation</td>
<td>Total dose determined according to dosing schedule in SPC or by Ganzoni calculation</td>
</tr>
<tr>
<td>1000mg IV can be delivered in 250mls N/Saline over 15 mins</td>
<td>200mg IV in 200mls N/Saline minimum of 30 minutes three times/week</td>
<td>Maximum dose 20mg/kg in 500mls N/Saline over four hours</td>
<td>Maximum dose 20mg/kg. Larger doses will require separate infusions one week apart</td>
</tr>
<tr>
<td>Maximum single dose 20mg/kg up to 1g (maximum single dose of 200mg in haemodialysis patients)</td>
<td>Single, total dose (larger doses will require two infusions)</td>
<td>Doses up to and including 1000mg must be infused over 30 mins</td>
<td>Doses exceeding 1000mg must be infused over 60 mins</td>
</tr>
<tr>
<td>Larger doses will require separate infusions one week apart</td>
<td></td>
<td>Inpatient/haemodialysis 500mg three times a week. Undiluted or diluted in maximum 20ml sterile 0.9 per cent sodium chloride</td>
<td></td>
</tr>
</tbody>
</table>

1. **Ferinject**

Dose calculation for Ferinject

The cumulative dose of iron using Ferinject is determined based on the patient’s body weight and Hb level and must not be exceeded. The following table should be used to determine the cumulative dose.

<table>
<thead>
<tr>
<th>Hb (g/dL)</th>
<th>Patients with body weight 35kg to &lt;70 kg</th>
<th>Patients with body weight ≥70 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>1500mg</td>
<td>2000mg</td>
</tr>
<tr>
<td>≥10</td>
<td>1000mg</td>
<td>1500mg</td>
</tr>
</tbody>
</table>

Dosing should be based on ideal body weight. A single dose of Ferinject should not exceed 20mg/kg, up to 1000mg of iron. Do not administer 1000mg of iron more than once per week. Patients with a cumulative dose requirement of >1000mg will require a second infusion after seven days or more of the first.

Administration

No test dose required but a cumulative iron dose of 500mg should not be exceeded for patients with a body weight <35 kg. For overweight patients, a normal body weight/blood volume relationship should be assumed when determining the iron requirement. For patients with a Hb value ≥14 g/dL, an initial dose of 500mg iron should be given and iron parameters should be checked prior to repeat dosing. Post repletion, regular assessments should be completed to ensure that iron levels are corrected and maintained.
Maximum tolerated single dose
A single dose of Ferinject should not exceed 1,000mg of iron (20ml) per day. Do not administer 1,000mg of iron (20ml) more than once a week.

Intravenous injection
Ferinject may be administered by intravenous injection using undiluted solution up to 1,000mg iron (up to a maximum of 15mg/kg body weight). For doses up to 200mg iron, there is no prescribed administration time. For doses greater than 200 and up to 500mg iron, Ferinject should be administered at a rate of 100mg/min. For doses greater than 500 and up to 1,000mg iron, Ferinject should be administered over 15 minutes.

Intravenous infusion
Ferinject may be administered by intravenous infusion up to a maximum single dose of 1,000mg of iron (up to a maximum of 20mg/kg body weight). Ferinject must be administered only by the intravenous route: by bolus injection, or during a haemodialysis session undiluted directly into the venous limb of the dialyser, or by infusion. In case of infusion Ferinject must be diluted only in sterile 0.9 per cent m/V sodium chloride solution as shown in the table below.

<table>
<thead>
<tr>
<th>Ferinject</th>
<th>Iron</th>
<th>Maximum amount of sterile 0.9 per cent m/V sodium chloride solution</th>
<th>Minimum administration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 4ml</td>
<td>100  to 200mg</td>
<td>50ml</td>
<td>-</td>
</tr>
<tr>
<td>&gt;4 to 10ml</td>
<td>&gt;200 to 500mg</td>
<td>100ml</td>
<td>6 minutes</td>
</tr>
<tr>
<td>&gt;10 to 20ml</td>
<td>&gt;500 to 1,000mg</td>
<td>250ml</td>
<td>15 minutes</td>
</tr>
</tbody>
</table>

Note: For stability reasons, dilutions to concentrations less than 2mg iron/ml are not permissible. Ferinject must not be administered by the subcutaneous or intramuscular route.

Minimum observation is required (pulse and blood pressure should be checked before and after infusion). Facilities for cardiorespiratory resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

Haemodialysis patients
A single maximum daily injection dose of 200mg iron should not be exceeded in haemodialysis-dependent chronic kidney disease patients.
2. Venofer

**Dose calculation for Venofer**

Total iron deficit (mg) = body weight (kg) x (target Hb – actual Hb) x 0.24 + depot iron (mg).

- Below 35 kg body weight: target Hb = 130 g/l and depot iron = 15 mg/kg body weight.
- 35 kg body weight and above: target Hb = 150 g/l and depot iron = 500 mg.

*Factor 0.24 = 0.0034 x 0.07 x 1000

(Iron content of haemoglobin 0.34%; Blood volume 7% of body weight; Factor 1000 = conversion from g to mg). The total amount of Venofer required in mg is determined from the above calculation. The total single dose must not exceed 200mg of iron given and not more than three times a week.

**Administration**

No test dose required. Venofer may be administered by slow intravenous injection at a rate of 1ml undiluted solution per minute and not exceeding 10ml Venofer (200mg iron) per injection. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.

**Haemodialysis patients**

Venofer may be administered during a haemodialysis session. Administer directly into the venous limb of the dialyser.

3. Cosmofer

**Dose calculation for Cosmofer**

The normal recommended dosage schedule is 100-200mg iron corresponding to 2-4ml, two or three times a week, depending on the haemoglobin level. However, if clinical circumstances require rapid delivery of iron to the body iron stores, Cosmofer may be administered as a total dose infusion up to a total replacement dose corresponding to 20mg iron/kg body weight.

Total dose (mg Fe) = Hb in g/l: (Body weight (kg) x (target Hb - actual Hb) (g/l) x 0.24) + mg iron for iron stores.

**Total dose infusion**

Add the Cosmofer dose to 0.9 per cent sodium chloride solution or in five per cent glucose solution. Cosmofer in a dose of 100-200mg iron (2-4ml) may be diluted in 100ml. On each occasion the first 25mg of iron should be infused over a period of 15 minutes. If no adverse reactions occur during this time, the remaining portion of the infusion should be given at an infusion rate of not more than 100ml in 30 minutes.

**Administration**

On each occasion before administering a slow intravenous injection, 25mg of iron should be injected slowly over a period of one to two minutes. If no adverse reactions occur within 15 minutes, the remaining portion of the injection may be given.

**Low dose infusion**

Add the Cosmofer dose to 0.9 per cent sodium chloride solution or in five per cent glucose solution. Cosmofer in a dose of 100-200mg iron (2-4ml) may be diluted in 100ml. On each occasion the first 25mg of iron should be infused over a period of 15 minutes. If no adverse reactions occur during this time, the remaining portion of the infusion should be given at an infusion rate of not more than 100ml in 30 minutes.

**Total dose infusion**

Add total dose of Cosmofer to 500ml of sodium chloride 0.9 per cent or five per cent glucose solutions infuse the volume intravenously over four to six hours. The first 25mg of iron should be infused over a period of 15 minutes.

Minimum observation required (pulse and blood pressure before and after infusion). The patient must be kept under close medical observation during this period. If no adverse reactions occur during this time, then the remaining portion of the infusion should be given. The rate of infusion may be increased progressively to 45 to 60 drops per minute. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.

4. Iron isomaltoside 1000 (Monofer (100mg/ml); Diafer 50mg/ml)

**Dose calculation for Monofer**

The dose calculation for Monofer is as follows:

Total iron deficit (mg) = body weight (kg) x (target Hb – actual Hb) x 0.24 + depot iron (mg).

- Below 35 kg body weight: target Hb = 130 g/l and depot iron = 15 mg/kg body weight.
- 35 kg body weight and above: target Hb = 150 g/l and depot iron = 500 mg.

Minimum observation required (pulse and blood pressure before and after infusion). The patient must be kept under close medical observation during this period. If no adverse reactions occur during this time, then the remaining portion of the infusion should be given. The rate of infusion may be increased progressively to 45 to 60 drops per minute. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.

5. Iron isomaltoside 1000 (Monofer (100mg/ml); Diafer 50mg/ml)

**Dose calculation for Monofer**

The dose calculation for Monofer is as follows:

Total iron deficit (mg) = body weight (kg) x (target Hb – actual Hb) x 0.24 + depot iron (mg).

- Below 35 kg body weight: target Hb = 130 g/l and depot iron = 15 mg/kg body weight.
- 35 kg body weight and above: target Hb = 150 g/l and depot iron = 500 mg.

Minimum observation required (pulse and blood pressure before and after infusion). The patient must be kept under close medical observation during this period. If no adverse reactions occur during this time, then the remaining portion of the infusion should be given. The rate of infusion may be increased progressively to 45 to 60 drops per minute. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.

**Dosing table: Cumulative iron dose**

<table>
<thead>
<tr>
<th>Hb (g/dL)</th>
<th>Patients with bodyweight 50kg to &lt;70kg</th>
<th>Patients with bodyweight ≥70kg</th>
</tr>
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<tbody>
<tr>
<td>≥10</td>
<td>1000mg</td>
<td>1500mg</td>
</tr>
<tr>
<td>&lt;10</td>
<td>1500mg</td>
<td>2000mg</td>
</tr>
</tbody>
</table>
Administration
No test dose required. Monofer may be administered as an intravenous bolus injection up to 500mg three times a week at an administration rate of up to 50mg iron/minute. It may be administered undiluted or diluted in maximum 20ml sterile 0.9 per cent sodium chloride. For an intravenous drip infusion, the cumulative iron dose required may be administered in a single Monofer infusion up to 20mg iron/kg body weight or as weekly infusions until the cumulative iron dose has been administered. If the cumulative iron dose exceeds 20mg iron/kg body weight, the dose must be split in two administrations with an interval of at least one week. Doses up to 1,000mg must be infused over 30 minutes. Doses exceeding 1,000mg must be infused over 60 minutes. Monofer should be added to a maximum 500ml sterile 0.9 per cent sodium chloride.

Haemodialysis patients
Monofer can be administered either as an intravenous bolus injection, as an intravenous drip infusion or as a direct injection into the venous limb of the dialyser.

Patient monitoring
Monofer should only be administered if there are staff trained to evaluate and manage anaphylactic reactions immediately available. This should be in an environment where full resuscitation facilities can be assured. Each patient should be observed for adverse effects for at least 30 minutes following each Monofer injection. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately.
Blood transfusion

There are many reasons a blood transfusion may be considered as part of a patient’s care pathway. Whatever the cause or clinical decision that leads to a transfusion, it is important to provide evidence and information to support discussions with the patient about these treatment options. These discussions should take place as part of the process of obtaining informed consent.

Since the creation and implementation of the Department of Health’s Health Service Circular: Better Blood Transfusion: safe and appropriate use of blood in 1998, and the subsequent initiatives of 2002 and 2007 to improve the safe, effective and appropriate use of blood, there has been an emphasis to reduce inappropriate and over use of blood transfusions. There has also been a greater consideration of alternative treatments to ensure blood stocks are conserved and available to everyone at all times and an effort to reduce the risks of unnecessary and inappropriate use of a live human product where an alternative treatment could be used as effectively. In July 2014 Patient Blood Management – an evidence based approach to patient care was published. It provides clear recommendations on how patient blood management (PBM) should be implemented in hospitals.

PBM is a multidisciplinary concept with the patient at the centre of the decision-making process and has a clear focus on improving patient outcomes through appropriate use and employing alternatives to transfusion. It puts the patient at the heart of the decisions being made about blood transfusion to ensure they receive the best treatment and avoidable, inappropriate use of blood and blood components is reduced.

In March 2010, the Advisory Committee on the Safety of Blood, Tissues and Organs SaBTO (a Department of Health expert committee), initiated a public consultation on patient consent for blood transfusion, and as a result made a number of recommendations including:

- valid consent for blood transfusion should be obtained and documented in the patient’s clinical record by the health care professional.
- the provision of patient information is vital for valid consent.

There are a number of patient information leaflets available from NHS Blood and Transplant (NHSBT) such as Will I need a blood transfusion? These can help with discussions and decision making, ensuring patient-centric care and obtaining informed consent to treatment in a non-emergency setting.

Although blood transfusion is often used for iron deficiency anaemia blood, it can be an inappropriate choice. Evidence of inappropriate practice is shown in the box below.

**National Comparative Audit of Blood Transfusion (2013)**

The audit (which included 1,592 individual cases) revealed that 747 patients were identified as having possible reversible anaemia and that transfusion could have been avoided in 187 (25 per cent) of these. Of those patients who received avoidable transfusion, 18 per cent were not investigated to determine the cause of the anaemia and in 60 per cent the anaemia was not adequately treated. Of the 552 patients with possible iron deficiency, 372 were documented as having definite iron deficiency. Only 73 per cent of the 372 were prescribed iron therapy (252 oral and 20 parenteral). Of these, 37 (15 per cent) were intolerant of oral iron and only eight (22 per cent) were given parenteral iron.
Why were patients with potentially reversible anaemia being transfused?

The main reasons identified in the audit were:

• inadequate recognition, investigation and treatment of anaemia

• significant symptoms/signs of anaemia, according to the consultant reviewers. But is fatigue and shortness of breath on exertion sufficient to justify a transfusion in a patient with reversible anaemia?

Why were patients being transfused above the thresholds set in the audit?

The main reason identified in the audit was:

• significant symptoms/signs of anaemia, according to the consultant reviewers.

Why were patients being over transfused?

The main reason identified in the audit was:

• in many cases, the use of a standard prescription of two units which led to a higher increment than required (particularly in patients of lower body weight).

Although other reasons for transfusion were not specifically audited, the logistics of emergency patient care and the pressure on inpatient beds may mean that transfusion is selected as a matter of expediency.

Unnecessary and over transfusion may result in patient harm and a waste of precious resources.

Careful consideration should be given to the risks and benefits of using blood transfusion as a treatment option for the correction of iron deficiency anaemia only and the ease of use against the alternative treatments available.
Preoperative optimisation of patients

All patients should be suitably prepared for the surgery they require. The NHS Plan (DH, 2000) recommended the setting up of ‘preparing patients for surgery’ clinics. These should also explore those aspects of patient health relevant to their requirements for blood transfusion (both autologous and homologous). The National Institute for Health and Clinical Excellence (NICE, 2003) has published guidance on preoperative tests. Local haematologists and clinics need to work together to produce protocols. These protocols should take into account the surgical procedure and the medical history of the patient in order to determine the blood tests needed.

The Enhanced Recovery Programme is about improving patient outcomes and speeding up a patient’s recovery after surgery. It also aims to ensure that patients always receive evidenced based care at the right time. The preoperative assessment and optimisation of Hb plays an important role in this.

In the Handbook of Transfusion Medicine (5th edition) (United Kingdom Blood Services, 2013) recommendations are made regarding preoperative optimisation, ‘Anaemia (and other relevant health problems) should be identified and treated in a timely fashion before surgery.’

Assessment of patients

When considering blood conservation, nursing staff should:

• investigate, diagnose and treat anaemia, including correction of iron deficiency anaemia
• investigate, diagnose and treat any bleeding disorder or haemoglobin defect, for example, sickle or thalassaemia
• assess the patient’s current medication, its potential for increasing bleeding and whether it is safe to stop this prior to surgery to reduce the risk of bleeding
• identify problems which may require specialist intervention
• discuss a patient’s beliefs in relation to blood transfusion, for example, Jehovah’s Witnesses and other patients who may decline donated blood components.
References


Food Standards Agency (2007) FSA nutrient and food based guidelines for UK institutions. London: FSA.


Further reading


Useful websites and resources

The following list of websites provide information and/or resources to help with good practice in the treatment of anaemia and iron deficiency and will also help nursing staff signpost patients to useful further reading.

**Iron deficiency anaemia**
- www.patient.co.uk/health/iron-deficiency-anaemia-leaflet
- www.nhs.uk/Conditions/Aenaemia-iron-deficiency-/Pages/Diagnosis.aspx

**Patient blood management**
- hospital.blood.co.uk/patient-services/patient-blood-management/

**Blood transfusion practice**
- www.gov.uk/government/groups/advisory-committee-on-the-safety-of-blood-tissues-and-organs
- hospital.blood.co.uk/audits/national-comparative-audit
- www.nhs.uk/Conditions/Blood-transfusion/Pages/Introduction.aspx
- www.transfusionguidelines.org.uk/index.aspx

**Preoperative assessment**
- www.pre-op.org

**Perioperative care**
- www.afpp.org.uk
- www.institute.nhs.uk/quality_and_service_improvement_tools/quality_and_service_improvement_tools/enhanced_recovery_programme.html
Appendices

Patients should be aware that the increase in Hb is a slower process with oral iron and iron infusions than with a blood transfusion and that this may be a contributing factor to the clinical recommendations made. Following treatment, all patients with IDA should be encouraged to see their GP or usual medical practitioner to find the underlying cause of the iron deficiency anaemia (if not identified) and to check that the treatment has been effective. They should have regular Hb monitoring blood tests to ensure that treatment is given in a timely manner and its effectiveness monitored.

Gastroenterology

Introduction

Gastroenterological conditions account for the most common causes of IDA. These may present both with and without GI symptoms. Nurses working within GI practice will encounter patients with IDA in all areas of care, whether in the outpatient clinics or endoscopy during investigation, in acute inpatient care following episodes of acute bleeding, in specialist roles with patients preoperatively or with inflammatory bowel disease (IBD) or coeliac disease.

Whilst the principles of the nursing management of patients with IDA are discussed in the main body of this guidance, this appendix aims to inform the care of GI patients in more detail.

GI causes of IDA

The most common cause of IDA in adult men and post menopausal women is blood loss from the GI tract. The following may also be causes:

- helicobacter pylori decreases iron uptake
- Giardia lamblia.

GI history

When taking a GI history of someone with IDA consider the following checks.

1. Use of aspirin and NSAIDS.
2. Family history, to include:
   - haematological disorders
   - colorectal cancer
   - coeliac disease
   - iron deficiency.
3. History of blood donation.
4. Epistaxis.
5. Dietary and lifestyle, for example, heavy alcohol intake, vegetarianism.

Investigation

Investigation should include:

- screening for coeliac disease (blood tests for coeliac antibodies)
- upper and lower GI evaluation (oesophago-gastro-duodenoscopy, colonoscopy, CT colonoscopy)
- small bowel investigation if poor response to oral/parenteral iron therapy (small bowel video capsule endoscopy, MRI enteroclysis, CT enterography)
- stool culture if the patient reports diarrhoea.

Coeliac disease

Coeliac disease (CD) is a chronic, auto immune enteropathy that affects the small intestine. It is caused by exposure to gluten (a protein in wheat, rye and barley) in the diet. Eating gluten causes small bowel inflammation, and blunting of the intestinal villi. This, in turn, leads to a range of nutritional deficiencies, particularly IDA.

CD affects up to 1:100 of the population, although only about 10 to 15 per cent of people living with it are diagnosed (NICE, 2009). In children and adults, coeliac
Inflammatory bowel disease (IBD)

In the UK, IBD is thought to affect approximately 400 people per 100,000. IDA occurs in 60 to 80 per cent of patients with IBD. There are several reasons for this:

- the increase in hepcidin, a protein produced in response to inflammation.
- intestinal bleeding
- poor iron absorption
- dietary restrictions.

Diagnosing IDA in IBD

The implications of not diagnosing IDA in IBD are significant to patients. Symptoms can significantly reduce quality of life and complications lead to increased admission and post-operative problems. There are two common types of anaemia in IBD; iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD). Distinguishing between the two is most important.

As more nurses are carrying out specialist roles in IBD they have increasing responsibility for interpreting and acting on blood tests. The minimum monitoring blood tests should include haemoglobin, serum ferritin, transferrin saturation and C-reactive protein (CRP).

Iron deficiency can be identified using the ferritin and saturation levels, but interpreting these depends on the level of inflammation (CRP). Serum ferritin levels increase in acute inflammation, so where CRP is raised, patients may appear to have a normal ferritin level. Therefore, when CRP is raised, the cut of ferritin level indicating iron deficiency increases to <100 µg/l. In quiescent disease (where CRP is normal) the standard value (<30 µg/l) applies.

The IBD nursing role

Identifying and appropriately managing IDA is an essential part of the IBD nursing role. This should include:

- ensure monitoring blood tests cover iron studies and CRP. Remember that a normal ferritin level does not always exclude iron deficiency.

Case history

Miss R is a 25-year-old fashion student who went to her GP feeling tired and run down and with a long history of unpredictable bowel habit which she had always assumed was an irritable bowel. The GP found her to be anaemic and iron deficient (Hb 92 g/l, ferritin 10 µg/l). She was given some oral iron supplements, and sent for coeliac serological blood testing. tTTGA (coeliac antibodies) was found to be positive (73 units). She was immediately referred to the nurse-run coeliac clinic in secondary care for gastroscopy and duodenal biopsy. The biopsy confirmed coeliac, and with support from the nurse specialist and the GI dietitian, she started a gluten-free diet. During this time, she struggled to take oral iron (it caused constipation), so as part of her management she had one dose of intravenous iron, which corrected her iron deficiency.
Heavy menstrual bleeding and irregular bleeding

Definition of heavy menstrual bleeding (HMB)

A NICE guideline in 2007 changed the definition of HMB to a more subjective one (away from the traditional blood loss of 80mls or more) to:

‘HMB should be defined as excessive menstrual blood loss which interferes with the woman’s physical, emotional, social and material quality of life, and which can occur alone or in combination with other symptoms. Any interventions should aim to improve QoL measures.’

HMB or heavy periods can be as a result of pathology and disease such as fibroids, which impact on the endometrium and increase the surface area, and irregular heavy bleeding from polycystic ovary syndrome (where there is anovulation leading to a disturbance of the feedback system, causing the endometrium to be thicker under the influence of oestrogen and not to shed regularly due to no ovulation and lack of progesterone). However, in up to 50 per cent of women there may not be a cause found.

HMB is the most common cause of IDA in the developed world, and has an impact on quality of life in excess of the periods by causing weakness, fatigue and impaired cognitive function.

The recent quality guidelines (NICE, 2013) also highlight the need for women with HMB to have a FBC and look at the possibility of IDA. However, an audit by the Royal College of Obstetricians and Gynaecologists (2014) has found that a third of women who presented to a GP in primary care had not had any treatment in primary care.

Case study

Mr P is a 46-year-old taxi driver with long standing Crohn’s disease. His bowel symptoms fluctuate, but have been reasonably controlled with azathioprine and pentasa. He has been feeling tired for many months and finds it significantly affects his home and work life. He calls the IBD nurse advice line with a recent increase in diarrhoea and some rectal pain. The nurse looks back over his blood tests whilst she is talking to him on the phone and sees that he has been anaemic for some time. However, his iron levels have not been measured.

She organises to see him in the outpatient clinic and checks his blood tests which show Hb 94 g/l, CRP 27, Ferritin 46µg/l and reduced iron sat's. Carrying out a full range of screening blood tests (including iron studies) allows her to identify active inflammation and iron deficiency and escalate his care to include suitable iron supplementation.

References


Prevalence
HMB is one of the most common and economically significant gynaecologic complaints and referrals to secondary care. It is estimated that it affects approximately 10 per cent of women of childbearing age, this may be an underestimate as women may not seek help or recognise that they have heavy periods, and it may change throughout a woman’s lifespan.

Investigations
All women with heavy periods or bleeding should have a full history taken. This should concentrate on the periods.

Questions need to include:
- is the cycle regular – minimum and maximum length of time from the first day of one cycle to the first day of the next
- total days bleeding, if over seven consider heavy or excessive
- total number of days of bleeding that are heavy, this can be established by asking about the use of protection (tampons or pads and the absorbency of these) and what types. Also ask about length of time between changes. For example, using double protection and changing one-hourly would be considered heavy
- any flooding
- any clots
- the use of any medication and if this helped
- any pain with, or around, periods
- any bleeding with sex or in between periods.

A full pelvic and speculum examination should also be undertaken and referral for an ultrasound if there is pathology suspected.

Treatment options
NICE guidelines discuss a number of treatment options for HMB, including pharmacological and surgical options, which will depend on the cause of the HMB.

Any treatment of the IDA, in any form will not treat the underlying problem so will need to be in combination with a strategy to reduce the periods. This can be in the form of medication, contraceptive pills, Mirena Intrauterine system (IUS), an operation (such as removal of fibroids or removal of the womb lining) and ultimately hysterectomy if all other interventions fail. These all need to be balanced with the need for contraception and fertility wishes in the future. Many of the treatments used to treat heavy periods will also provide contraception such as the IUS, so if a woman wishes to conceive and there is no cause then there are limited options. One of the issues for women who need surgery is achieving Hb and iron stores to an optimum level preoperatively, especially if they continue to bleed in that period.

The nursing role in managing women with heavy periods can be varied and it is important that nursing staff in primary care ensure that women are monitored for their Hb if they are presenting with HMB. Nursing staff in secondary care who are working in a specialist role need to ensure that Hb has been checked and acted upon, and that the cause if known or the treatment for the periods is working. Their role involves trying to stop the cause of the blood loss. Nursing staff in pre-assessment clinics may need to refer women to have iron infusions if operations are needed and the above steps have not rectified the IDA.

All nursing staff working with women need to be aware that HMB is a very common cause for IDA and should ensure that women are aware of this and are taking good dietary iron to help to try and prevent IDA in the future.
Patient blood management

Patient blood management (PBM) is a multidisciplinary, evidence-based approach to optimising the care of patients who might need a blood or blood component transfusion as part of their planned or emergency stay in hospital.

In July 2014, national guidance on PBM was published, Patient Blood Management – an evidence-based approach to patient care. The guidance provides recommendations on how PBM should be implemented in hospitals. PBM is being rolled out across England and North Wales. Local, national and international experts are supporting doctors, nurses, scientists and other health professionals to work together with patients on a case-by-case basis to deliver PBM.

PBM should be considered in every case where a transfusion may be an appropriate treatment consideration regardless of the specialty and in both elective, long term and emergency arenas. It puts the patient at the heart of decision making to ensure they receive the best treatment and to also avoid the inappropriate use of blood components. This means that PBM focuses on measures for blood avoidance as well as the correct use of blood when it is needed, with improved patient outcomes as the key driver.

Recent studies suggest that if the three basic principles of PBM are followed and transfusion is reduced or avoided, patients have:

- fewer complications
- faster recoveries
- shorter stays in hospital.

The three basic principles

1. **Optimising blood volume and red cells before treatment**

   This means making sure patients are as healthy as possible before surgery or treatment to help them recover afterwards. It includes identifying and treating anaemia well in advance of any planned surgery or medical treatment.

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**Case study**

Mrs B referred to clinic with heavy periods and some irregular bleeding. She was 45 years old, had two children and was using condoms for contraception. Her GP had examined her and found that her uterus was enlarged. Simple medication, such as tranexamic acid, had not helped and she was having her periods every 21 days, she was bleeding for up to ten each cycle and for five of these she was using tampons and pads and changing up to 45 to 60 minutes. She was also flooding and had clots, the flooding was worse at night and she was finding it difficult to go out during her periods.

Her scan showed that she had fibroids, one was submucosal and impacting on the endometrial cavity. Her Hb on referral was 64 g/l. She was placed on oral iron by her GP but was not taking it regularly as she did not like the GI side effects. After being seen in a gynaecology clinic, she was booked for a resection of fibroid. In order to optimise her preoperatively, she was assessed and given iron infusions by the anaemia clinic and from gynaecology was started on a preoperative medication Zoladex, which put her into a temporary medical-induced menopause.

Post-operatively, after the removal of the fibroids, the bleeding in between periods had stopped and her periods were now five days and she was not needing to use double protection and able to change every few hours. Her Hb was checked at four months, post-operation, after she had been on the oral iron and was 124 g/l.

**References**


2. Minimising blood loss throughout the treatment process

This is done by using modern techniques and medicines to prevent patients from losing blood in the first place. This includes using modern surgical tools and medicines, and intraoperative cell salvage to reduce bleeding in the operating theatre.

3. Maximising the body’s own abilities to cope during recovery

The body has a natural ability to adapt to lower haemoglobin or blood counts without resorting to a blood transfusion. However, to increase an individual’s own capabilities, improving their iron intake through diet might help in their recovery.

The use of iron tablets or an intravenous iron infusion might also need to be considered as a method to help increase their haemoglobin.

In order to assist patient’s to make an informed decision about the treatments they are being offered, NHSBT has prepared a suite of patient information leaflets that cover all key aspects of blood and blood component transfusion. These are available for all age groups and for specific types of transfusion.

Some NHSBT patient information leaflets available include:
- Will I need a blood transfusion?
- Will I need a platelet transfusion?
- Information for patients needing irradiated blood
- Iron in your diet
- Will your baby need a blood transfusion?
- Will your child need a plasma transfusion?
- Will your child need a blood transfusion?
- Unexpected blood transfusion
- Patient blood management
- Anaemia patient information leaflet
- Fresh frozen plasma (FFP) and cryoprecipitate.

These can all be ordered through your hospital transfusion practitioner or downloaded at www.blood.co.uk

Case study

A 19-year-old female presented in the emergency department following a road traffic accident. Routine blood tests on admission revealed her Hb was 88g/l. She was distressed and feeling very unwell, showing signs and symptoms of anaemia as she was feeling short of breath and dizzy with palpitations and a headache. Her attending doctor discussed how she felt and, during the conversation, learned that she had started to suffer from very heavy and prolonged periods recently but had not had treatment for this, taking this and her low Hb into account, as well as her symptoms, he decided that a blood transfusion would be beneficial and explained this to her. He left her with patient information leaflets on having a blood transfusion and took further samples to send to the laboratory for cross matching so that the unit for transfusion could be authorised and prepared.

As part of the preparation for the transfusion a nurse attended the patient to take a set of baseline observations and found her to be very distressed and upset. She sat with the patient who explained she was very squeamish and afraid of the sight of blood and the thought of a transfusion was making her feel sick.

Further conversation revealed that she was a first-year student away from home for the first time and that her diet and lifestyle had undergone significant changes. She had decided to become vegetarian for the first time as well. Although she had understood the information given to her she was becoming increasingly distressed by the idea of having a blood transfusion and asked the nurse if there was anything else she could have instead.

In her role as patient advocate, the nurse went to the authorising physician and discussed this and the balance between the risks and benefits of a transfusion against the use of alternatives were considered.

It was agreed that as the patient was otherwise fit and healthy and, although the need for a transfusion could be said to be clinically indicated, it could be managed appropriately by use of an alternative to an allogeneic blood transfusion. This would prevent a possibly inappropriate transfusion and exposure to a live human product and would decrease the patient’s anxiety and allow her to remain a blood donor if and when her Hb was high enough.
This was explained to the patient who was relieved and happy and felt that she had been able to be involved in this part of her treatment plan and able to understand the options given to her. The dietician was contacted and oral iron was prescribed and clear instructions on how and when to take it were given along with advice on diet and lifestyle, including the NHSBT patient information leaflet *Iron in your diet to support sensible choices in a vegetarian diet*.

At discharge, a letter was sent to her current GP and a copy was given to the patient. She agreed that she would take this copy and register with the GP on campus and make appointments for regular Hb checks to ensure she was getting the corrective treatment needed and it was effective.

**Reference**


**Useful websites and resources**

**Online transfusion training**

[www.learnbloodtransfusion.org.uk](http://www.learnbloodtransfusion.org.uk)

**Serious Hazards Of Transfusion (SHOT) – the United Kingdom's independent professionally lead haemovigilance scheme**

[www.shotuk.org](http://www.shotuk.org)

**The British Committee for Standards in Haematology (BCSH)**

[www.bcsghguidelines.com](http://www.bcsghguidelines.com)
Renal

Chronic kidney disease

Chronic kidney disease (CKD) is defined as abnormalities of kidney function or structure which are present for more than three months, with implications for health. CKD is an irreversible condition, strongly associated with high blood pressure and diabetes. This includes all people with markers of kidney damage and those with a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m² on at least two occasions, separated by a period of at least 90 days (with or without markers of kidney damage).

CKD has been categorised from stage 1, indicating slight kidney damage, to stage 5 CKD, indicating severe kidney damage. It is estimated that nine per cent of the English adult population have CKD stages 3 to 5. Within this group there is a four per cent risk of these patients reaching stage 5 CKD, with disproportionate numbers of older patients contributing to this number (Johnston et al, 2013).

Renal anaemia

Moderate to severe CKD may affect the ability of the kidneys to help stimulate production of red blood cells, which carry oxygen around the body. Anaemia occurs when the quality or quantity of red blood cells are below normal. If untreated, anaemia can increase the risk of cardiovascular complications (for example, left ventricular hypertrophy) and exacerbate symptoms (for example, tiredness, lethargy, sleep disturbance and shortness of breath) (NICE, 2014).

Patients with CKD are at an increased risk of negative iron balance compared with non-uraemic individuals (Taol and Tomson, 2007). We know that the human body normally absorbs up to 1mg per day of iron from the diet, adequately balancing daily iron losses from the gut. Oral iron supplementation is not recommended for patients with CKD as the ferric salt which binds the oral iron preparation can cause gastrointestinal problems, such as constipation. It is also thought that iron is not absorbed well from the gut in a uraemic state. Intravenous iron has been proved to be more effective for this group of patients.

The use of IV iron in CKD

Patients with CKD should receive iron supplementation to maintain:

- serum ferritin levels between 200 and 500 µg/L. Ferritin is the iron stored in the liver. Serum ferritin levels can become elevated in iron overload, but also in the presence of infection or inflammation
- transferrin saturation level above 20 per cent (unless ferritin is greater than 800 µg/L). Transferrin saturation is the amount of circulating free iron in the blood
- percentage of hypochromic red cells (% HRC) less than 6 per cent (unless ferritin is greater than 800 µg/L, HRC are ‘pale’ red blood cells and indicate iron deficiency) (NICE, 2006).

IV iron therapy (at doses more than 100mg) should be stopped for at least one week before performing these measurements to avoid the IV iron abnormally influencing the test results.

### Stages of chronic kidney disease (NICE, 2008)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>eGFR ml/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Slight kidney damage with normal or increased filtration</td>
<td>More than 90</td>
</tr>
<tr>
<td>2</td>
<td>Mild decrease in kidney function</td>
<td>60–89</td>
</tr>
<tr>
<td>3A</td>
<td>Moderate decrease in kidney function with or without other evidence of kidney damage</td>
<td>45–59</td>
</tr>
<tr>
<td>3B</td>
<td>Moderate decrease in kidney function with or without other evidence of kidney damage</td>
<td>30–44</td>
</tr>
<tr>
<td>4</td>
<td>Severe decrease in kidney function</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure requiring dialysis or transplantation</td>
<td>Less than 15</td>
</tr>
</tbody>
</table>

Renal

Chronic kidney disease

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CKD has been categorised from stage 1, indicating slight kidney damage, to stage 5 CKD, indicating severe kidney damage. It is estimated that nine per cent of the English adult population have CKD stages 3 to 5. Within this group there is a four per cent risk of these patients reaching stage 5 CKD, with disproportionate numbers of older patients contributing to this number (Johnston et al, 2013).
Anaemia is a common symptom of CKD and is primarily caused by a reduction in endogenous erythropoietin (EPO) production. EPO is predominantly produced by peritubular cells in the kidney and is the hormone responsible for the production of red blood cells. CKD leads to a loss of peritubular cells, resulting in a low level of circulating EPO (NICE, 2006).

The introduction of erythropoietin simulating agents (ESA) were an important therapeutic innovation in the treatment of anaemia in CKD and has largely replaced the need for blood transfusions in this group of patients. ESAs are usually administered by a subcutaneous injection which may be done by the patient, a family member or a community nurse. Iron levels and other haematinics are usually monitored by the specialist team, but can be measured in the community if more convenient. Treatment with an ESA should continue for as long as the patient can benefit from it. ESAs are not interchangeable and the patient should continue on the preparation prescribed by the specialist team.

**Target haemoglobin range in CKD**

NICE (2011) advises health care professionals treating anaemia of CKD with erythropoiesis stimulating agents to maintain the haemoglobin range between 100 and 120g/l for adults. NICE is also urging clinicians to not wait until a patient’s haemoglobin levels are outside of these ranges before adjusting their treatment (for example, they should act when the patient’s haemoglobin levels are within 5 g/l of the range’s limit).

**Patient monitoring**

- Take blood samples to check iron status no earlier than one week after receiving IV iron and at intervals of four weeks to three months routinely.
- Hb every two to four weeks (induction phase) or one to three months (maintenance phase) during ESA therapy.
- Hb more actively after adjusting ESA dose.
- Monitor in a clinical setting agreed with patient.
- Maintain iron levels (NICE’s *Anaemia of chronic disease overview* – see below in Useful websites).

- Serum ferritin 200–500 μg/l in both haemodialysis and non-haemodialysis patients and either TSAT greater than 20 per cent (unless ferritin greater than 800 µg/l), or per cent HRC less than six per cent (unless ferritin greater than 800 µg/l).

Blood pressure (BP) should be monitored closely in all patients with CKD, particularly during the initiation of ESA therapy. A rapid increase in Hb may be associated with a rise in BP. Antihypertensive therapy may need to be initiated or current antihypertensive medication increased. The ESA dose may need to be reduced, especially if there is a rapid increase in Hb (more than 10-20 g/l (1–2 g/dL) per month) (NICE, 2006).
Examples of erythropoietin stimulating agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cautions</th>
<th>Side effects</th>
<th>Route/dose</th>
</tr>
</thead>
</table>
| Epoetin beta (for example, NeoRecormon) | Inadequately treated or poorly controlled blood pressure, sickle-cell disease; exclude other causes of anaemia; ischaemic vascular disease, thrombocytosis, epilepsy, malignant disease | Dose-dependent increase in blood pressure or aggravation of hypertension in isolated patients with normal or low blood pressure; dose-dependent increase in platelets, influenza-like symptoms, thromboembolic events, sudden loss of response as a result of pure red cell aplasia | By subcutaneous injection  
 **Correction phase**  
 Until Hb 105-115 g/dL use 20 units/kg three times per week  
 **Maintenance phase**  
 Reduce dose by half then adjust accordingly to Hb level at intervals of two weeks. Reduce frequency to once weekly injection |
| Darbepoetin alfa (for example, Aranesp) | Inadequately treated or poorly controlled blood pressure, sickle-cell disease; exclude other causes of anaemia; ischaemic vascular disease, thrombocytosis, epilepsy, malignant disease, hepatic disease | Peripheral oedema; dose-dependent increase in blood pressure or aggravation of hypertension in isolated patients with normal or low blood pressure; dose-dependent increase in platelets, influenza-like symptoms, thromboembolic events, sudden loss of response as a result of pure red cell aplasia. Contraindicated if breastfeeding | By subcutaneous injection  
 **Correction phase**  
 450 nanograms/kg for one week 750 nanograms/kg once every two weeks, adjusted according to response by 25 per cent of initial dose at four weekly intervals  
 **Maintenance phase**  
 Dose required in correction phase to achieve target Hb can now be changed to once monthly |

Treatment with ESAs is highly effective, correcting the anaemia of CKD in approximately 90 to 95 per cent of treated patients. Side effects are very rare owing to the similar genetic make-up as endogenous (derived internally) EPO.

Between 1988 and 1998, antibody-associated pure red-cell aplasia (PRCA) was reported in renal patients treated with ESAs (Bennett et al, 2004). The condition has a number of causes, including pharmacological treatment. PRCA can be determined by the presence of anti–EPO antibodies, which neutralise the action of the ESA, a low reticulocyte count (immature red blood cells), and anaemia (NICE, 2006). The Hb concentration declines at a rate of 1 g/dL per day and it may be necessary to transfuse one unit of red blood cells per week to avoid severe anaemia (Macdougall, 2004).

Regular monitoring of anaemia in patients with CKD is vital to early intervention with IV iron and ESA.
**Case study**

Mrs Brown is an 84-year-old lady with stable stage 4 CKD due to diabetic nephropathy. She comes to the clinic complaining of feeling increasingly tired, a little short of breath and feels cold most of the time. She is taking Aranesp 40mcgs once a fortnight.

**What is your differential diagnosis for her symptoms?**

Her renal function could have declined. She could have an under-active thyroid. She could be anaemic despite being on an ESA. A full history and physical assessment is needed to rule out other causes for her symptoms. For example, does she report any dysuria which could indicate a urinary tract infection? Does she report any chesty coughs, temperature or flu like symptoms? Infection and inflammation affect both iron absorption and the efficacy of ESA. She did not complain of any recent infections.

Bloods were checked for U and Es, FBC, CRP and iron studies. Hb was 90g/L. Iron levels were low, serum ferritin was 74 µg/l. TSATS 20 per cent. CRP was within normal range.

**What is your diagnosis? What is your clinical management plan?**

Mrs Brown was diagnosed with absolute iron deficiency. The ESA was less effective due to iron deficiency therefore her Hb had dropped to below the target range. Mrs Brown was booked into the nurse-led anaemia clinic for a total dose of Ferinject which she had infused without any adverse reactions.

**What would your follow-up plan and advice be to Mrs Brown?**

Mrs Brown was booked back into the clinic in two weeks to recheck her symptoms and check bloods for FBC to measure the response to iron. She was advised to call should she experience any side effects from the iron infusion. A follow-up appointment letter for two weeks’ time was given to Mrs Brown with the contact details of the nursing team.

**References**


**Useful websites**


**IDA in pregnancy, primary postpartum haemorrhage and post delivery**

Anaemia is the most common medical disorder in pregnancy. Pregnancy causes a two to three fold increase in requirement of iron and 10 to 20 fold increase in folate requirement. In pregnant women who are anaemic in the UK, 90 per cent of them are iron deficient. Iron deficiency causes maternal morbidity due to increased susceptibility to infections, physical weakness, pre-term labour, increased risk of primary postpartum haemorrhage (PPH), low birth weight babies and postnatal depression. The chronic tiredness that it can cause is also often blamed for new mothers abandoning breastfeeding, which has major health benefits for both mother and baby. Maternal iron depletion also increases the risk of iron deficiency in the neonate. Managing anaemia in pregnancy will therefore help to prevent adverse fetal and maternal outcomes as well as reduce the need for allogeneic red blood cell transfusion.

**Definition**
The definition of anaemia in pregnancy is Hb levels of:
- <110g/l in the first trimester
- <105g/l in the second and third trimesters
- <100g/l in the postpartum period (defined by WHO as up to six weeks post delivery).

(British Committee for Standards in Haematology, 2011)

**Clinical signs and symptoms**
Pregnancy anaemia can be asymptomatic and may be diagnosed following routine screening. The signs and symptoms are often non-specific with tiredness being the most common. Women may also complain of weakness, headaches, palpitations, dizziness, dyspnoea and hair loss.

Signs of anaemia can occur in the absence of a low Hb. In this instance it would be diagnosed by a full blood count with a reduced MCV (mean cell volume) and MCHC (mean corpuscular haemoglobin concentration).

In these patients, a ferritin needs to be checked and if it is <30µg/l iron therapy should be commenced.

**Diagnosis**
A trial of oral iron therapy can be both diagnostic and therapeutic. If haemoglobinopathy status is unknown, then it is reasonable to start oral iron therapy whilst screening is carried out. A trial of oral iron should demonstrate a rise in Hb within two to three weeks. If there is a rise then this confirms the diagnosis of iron deficiency. If there is no rise, further tests must be carried out. In patients with a known haemoglobinopathy, serum ferritin should be checked first. Ferritin levels below 30µg/l should prompt treatment and levels below 15µ/l are diagnostic of established iron deficiency.

**Management**
NICE guidelines recommend that women are screened for anaemia at booking and again at 28 weeks gestation. All women should be given advice regarding diet in pregnancy with details of foods rich in iron along with factors that may promote or inhibit the absorption of iron. This should be backed up with written information. Dietary changes alone are not sufficient to correct an existing iron deficiency in pregnancy and iron supplements are necessary.

**Antenatal**
If at booking Hb <110g/l: start on a trial of oral iron. The necessary dose is 100-200mg of elemental iron daily.

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<table>
<thead>
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<th>Dose and elemental iron content per tablet</th>
<th>Preparation</th>
<th>Dose per tablet</th>
<th>Elemental iron</th>
<th>Number of tablets per day</th>
</tr>
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<td></td>
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<td>65mg</td>
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<tr>
<td>Ferrous gluconate</td>
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<td>6</td>
<td></td>
</tr>
<tr>
<td>Ferrous fumarate</td>
<td>210mg</td>
<td>68mg</td>
<td>3</td>
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</tr>
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</table>
Women should be counselled as to how to take oral iron supplementation correctly. This should be on an empty stomach, one hour before meals, with a source of vitamin C to maximise absorption. Other medications or antacids, tea or coffee should not be taken at the same time. Women with a normal Hb but a low MCV should have their ferritin checked and if ferritin is <30µg/l, oral iron should be commenced.

Repeat Hb levels three weeks after commencement of iron therapy (this should fit in with the 15 to 16 week antenatal appointment) and a rise in Hb should be demonstrated. If there is no rise in Hb, despite compliance with therapy, serum ferritin should be checked and concomitant causes of the anaemia need to be excluded. Referral to consultant obstetrician is required.

If at booking Hb <90 g/l: oral iron - 200mg elemental iron in divided doses each day should be commenced and follow up as above. Referral to consultant obstetrician if symptomatic.

If at booking Hb <70g/l: send an urgent referral to joint obstetric/haematology clinic to investigate further and make management plan. Do not offer blood transfusion unless symptomatic or currently actively bleeding. Consider total dose IV iron infusion. 200mg of elemental iron each day. (If 200mg ferrous sulphate is used, need three to four tablets each day) if taken correctly this will give a rise in Hb of 20g/l every three weeks.

Once Hb is within the normal range, treatment should be continued for a further three months.

At 28 weeks: all women should have their Hb re-checked (NICE, 2008).

If at 28 weeks Hb < 105g/l: trial of oral iron as above. Re-check Hb in three weeks. If no response, check serum ferritin and refer to consultant obstetrician to consider total dose iron infusion.

If at 28 weeks Hb <90g/l: start oral iron - 200mg elemental iron in divided doses each day, as above. Consultant obstetrician referral if symptomatic.

If at 28 weeks Hb <70g/l: urgent referral to joint obstetric/haematology clinic to investigate and make management plan. Do not offer blood transfusion unless symptomatic or currently actively bleeding. Consider total dose IV iron infusion. (Gastrointestinal toxicity affects 35 to 59 per cent of patients and can result in non-adherence to treatment with oral preparations (Auerbach and Ballard, 2010). These effects can be reduced by taking oral iron with food or taking a reduced dose.

Parenteral iron should be considered from the second trimester onwards and during the third trimester for women with confirmed iron deficiency that fail to respond to, or are intolerant of, oral iron. Intravenous iron is the appropriate treatment for those patients where oral preparations are not tolerated or contraindicated.

Management of labour and delivery
With effective management of anaemia antenatally, anaemia at delivery is usually avoided. If this occurs, all measures must be taken to avoid blood loss at delivery.

- Deliver in consultant unit.
- Ensure IV access and group, and screen on admission.
- Active management of third stage of labour.
- In the event of a PPH, prompt active management is required to stop bleeding.
- Consider the use of prophylactic syntocinon infusion.
- Postnatal FBC and serum ferritin on day one and iron replacement (as outlined below).

Postnatal

Hb <100g/l in postnatal period: Haemoglobin measurement is not required following an uncomplicated, normal birth. Check FBC and serum ferritin on day one post delivery in the following cases:

- PPH of >500mls
- uncorrected antenatal anaemia
- known iron deficiency anaemia
- any woman with signs or symptoms of anaemia.
Clinical assessment alongside Hb concentration is necessary postpartum to make a decision on the best method of iron replacement. In fit, healthy asymptomatic women there is little evidence to support blood transfusion.

**Hb 80-100g/l:** If asymptomatic and haemodynamically stable, offer 200mg elemental iron per day for three months. FBC and ferritin should be checked after a month to ensure that Hb and iron stores are replete.

**Hb<80g/l:** Consider total dose intravenous iron. Repeat FBC and ferritin at ten days to ensure response and at three months in community to ensure Hb and iron stores are replete.

**Hb<70g/l:** Consider and discuss alternatives with the woman. Consider transfusion and/or total dose IV iron.

IV iron has been shown to increase Hb faster and also to replenish iron stores faster when compared with oral iron therapy (Bhandal, 2007; Van Wyk and Martins, 2007; Breymann et al, 2008). Minimum transfusion volumes should be considered and review after one unit.

Women who are symptomatic of anaemia, haemodynamically unstable or continuing to bleed heavily will need a full senior obstetric review to investigate the origin of the blood loss and decide further treatment.

**Contraindications and precautions for IV iron therapy**
- First trimester of pregnancy.
- Previous hypersensitivity to IV iron.
- Anaemia not attributable to iron deficiency.
- Iron overload.
- Acute infection/inflammation.
- Clinical or biomedical evidence of liver damage.
- Asthma.

**Case study**
Mrs H had an uncomplicated pregnancy other than nausea and had Hb of 107g/l at 28 weeks gestation. She went into spontaneous labour at 39 weeks + four days. She then went on to have a long labour with a normal delivery. She subsequently had a postpartum haemorrhage with an estimated blood loss of 750mls. Her Hb was checked following delivery and found to be 75g/l. She was given total dose intravenous iron as she was very keen to avoid oral iron due to her nausea. Five days postnatally her Hb was checked and found to be 99 g/l and at 14 days it was 111 g/l. She felt well, bonded well with her baby and successfully breastfed as she had wanted to do.

**References**


**Useful website**
http://hospital.blood.co.uk/patient-services/patient-blood-management/patient-information-leaflets/
Acronyms and abbreviations

ACD  anaemia of chronic disease
AID  absolute iron deficiency
BP   blood pressure
CD   coeliac disease
CKD  chronic kidney disease
CRP  C-reactive protein
EPO  endogenous erythropoietin
ESA  erythropoietin simulating agents
FBC  full blood count
FID  functional iron deficiency
GFR  glomerular filtration rate
GI   gastrointestinal
Hb   haemoglobin
HMB  heavy menstrual bleeding
IBD  inflammatory bowel disease
IDA  iron deficiency
MCV  mean cell volume
PBM  patient blood management
PPH  primary postpartum haemorrhage
PRCA pure red-cell aplasia
RBC  red blood cells
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