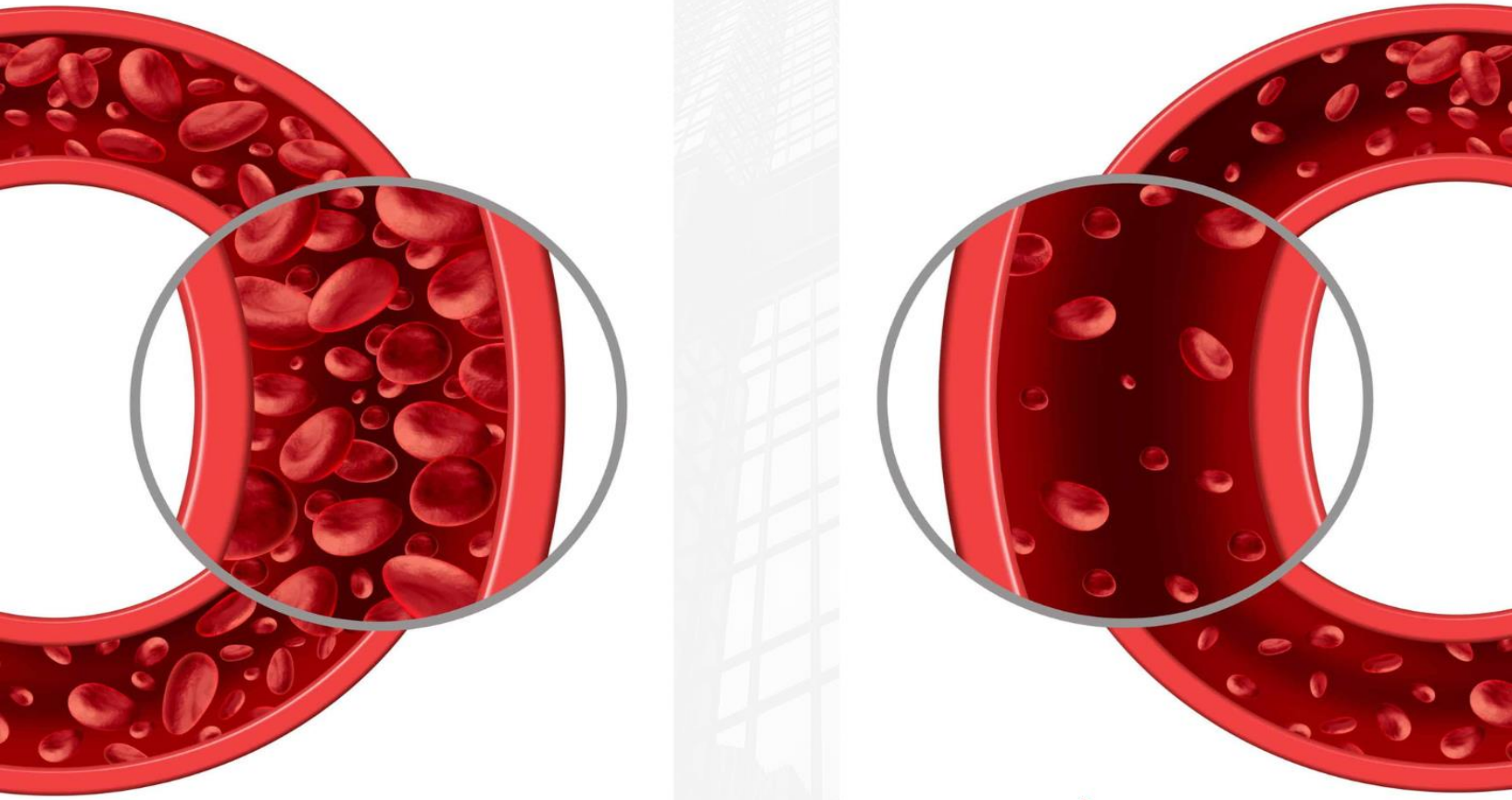
GUIDELINE FOR THE MANAGEMENT OF IRON DEFICIENCY ANEMIA IN ADULTS



World Health Organization
Maldives

Ministry of Health

RELEASE RECORD

Version Number	Version Date	Description of change
1	2025	Initial release

DOCUMENT NUMBER: MOH/QA/G/25/198-0

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Published by:	Ministry of Health in collaboration with WHO Maldives

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Management of Iron Deficiency Anemia in Adults

1.0 Introduction

Iron deficiency anemia is diminished red blood cell production due to low iron stores in the body. The World Health Organization states iron deficiency anemia as the most common nutritional deficiency worldwide accounting for approximately one-half of the cases of anemia. In 2013, iron deficiency was identified as the leading cause of anemia among the 1.93 billion anemic people (27% of the world's population), making iron deficiency anemia, a major global health issue. Those most at risk for iron deficiency anemia are women and children, regardless of socioeconomic status or geography. [1]

Iron is an essential element and is required for various cellular functions including oxygen transport, enzymatic processes, production of hemoglobin and DNA synthesis. There are many causes of Iron deficiency that result from inadequate iron intake in diet, decreased iron absorption, increased demand, and increased iron loss. Chronic blood loss in the form of menstrual blood loss, especially those with menorrhagia is the commonest cause of iron deficiency anemia in premenopausal women whereas blood loss from the gastrointestinal tract is the commonest cause in post-menopausal women and adult men. Colonic and gastric cancers may also present with Iron deficiency anemia and exclusion of these conditions should also be done in the evaluation of causes for iron deficiency anemia. [1,4]

There are many other causes of Iron deficiency anemia which include previous gastrectomy, use of non-steroidal anti- inflammatory drugs and frequent blood donation. Iron deficiency also occurs in many chronic inflammatory conditions including chronic kidney disease, congestive cardiac failure, and inflammatory bowel disease.

Management of iron deficiency anemia includes establishing the diagnosis, identifying the underlying etiology and administering the appropriate therapy for management of this condition and iron repletion.

2.0 Scope of the Guideline

Patients with Iron deficiency anemia present to all the tiers of health care provision, from primary care to specialties in secondary and tertiary care depending on the symptoms.

In addition, due to its insidious nature, it is seen that quite often, the condition is not optimally managed despite the considerable burden of disease. Investigations are sometimes incomplete, the etiology for iron deficiency is not evaluated and patients are not properly followed up. It is therefore important that a guideline for the diagnosis and management of iron deficiency anemia is available to all clinicians and health care professionals for guidance.

The guideline is based on the current updated available evidence and is intended to provide health care professionals with recommendations for the diagnosis, investigations and treatment of iron deficiency anemia in adults. It is also intended to be used as a reference document by healthcare policy makers as a guidance to consider when formulating health care policy decisions related to management of iron deficiency anemia.

3.0 Causes of iron deficiency

Table1: Causes of iron deficiency

INCREASED REQUIREMENT • Rapid growth (infants and adolescents), Menstruation • Pregnancy (second and third trimesters), Lactation • Chronic kidney disease	**DECREASED INTAKE** • Malnutrition Diet (e.g.vegetarian, iron poor) • Elderly • Alcoholism
INCREASED LOSS • Gastrointestinal: Esophagitis, Erosive gastritis, Peptic ulcer, variceal bleeding, Inflammatory bowel disease e.g., ulcerative colitis, Crohn's disease • Benign tumors, Intestinal and gastric cancer, Angiodysplasia, diverticulosis, hemorrhoids, anal fissures • Hookworm infestation • Occult blood loss is secondary to cow's milk protein-induced colitis. • Chronic or high dose use of salicylates or NSAIDs • Genitourinary: Menorrhagia, Chronic hematuria, uterine cancer • Hemolysis: Intravascular hemolysis • Other: Regular blood donors, Frequent epistaxis, hemoptysis, Hemorrhagic telangiectasia (rare)	**DECREASED ABSORPTION** • Dietary factors (carbonated drinks, coffee, etc.) • Gastrointestinal: Gastrectomy, Duodenal bypass, Bariatric surgery, Celiac disease, Atrophic gastritis, Inflammatory bowel disease e.g., ulcerative colitis, Crohn's disease • Helicobacter pylori gastritis

4.0 Evaluation of the patient

The evaluation of the patient should begin with a thorough history and physical examination to identify the possibility of iron deficiency anemia and a potential cause for iron deficiency. Most patients with iron deficiency anemia are often asymptomatic and may have limited findings on examination.

4.1 History taking

4.1.1. It is recommended to take a detailed history of the patient, as it may provide important information as to the cause of iron deficiency anemia, in the patient.

4.1.2. History taking should focus on risks and likely causes for iron deficiency anemia and should include questions about:

- Diet
- History of Pica (craving/consumption of non-food substances such as dirt, clay, chalk) and pagophagia (ice craving)
- Gastrointestinal symptoms
- History of blood loss (e.g., epistaxis, menorrhagia, melena, hematuria, hematemesis)
- Surgical history (e.g., gastric bypass) and family history of GI malignancy.
- History of blood donation as blood donors are at risk of iron deficiency, particularly females donating more than twice a year and males donating more than three or four times a year.
- Medication history, especially use of aspirin, NSAIDS and anticoagulants
- Family history of hematological disorders like thalassemia, sideroblastic anemia and bleeding disorders

4.2 Clinical Examination

4.2.1. A thorough clinical examination should be done as it may provide clues to the identification of iron deficiency anemia and signs secondary to iron deficiency such as:

- Pallor (facial, conjunctival, or palmar)
- Glossitis or loss of tongue papillae, angular cheilitis
- Koilonychia (spoon nails)
- Alopecia
- Decreased cognitive abilities, attention, and concentration.
- Systolic murmur
- Tachycardia, cardiac failure

5.0 Diagnosis

The diagnosis of iron deficiency anemia is confirmed by the findings of low iron stores and a hemoglobin level two standard deviations below normal for age and sex.
Iron deficiency can also occur in the presence or absence of anemia.

The World Health Organization defines anemia as a hemoglobin level:

- less than13 g/dL in adult males
- less than 12 g/dL in adult females who are not pregnant and
- <11g/dL in pregnant women in 2nd and 3rd trimester.

5.1 Investigations for diagnosis of iron deficiency anemia

5.1.1. Perform a complete blood count and red cell Indices for the hemoglobin level and presence of changes in red cells that occur in iron deficiency including reduced mean cell volume (MCV) and reduced mean cell Hb.

5.1.2. Perform a blood smear for the presence of hypochromia and microcytosis which is suggestive of iron deficiency and confirmed by doing iron studies[6]

5.1.3. Reduced MCV (microcytosis) and MCH (hypochromia) may also occur in hemoglobinopathies like thalassemia, sideroblastic anemia and in anemia of chronic disease, Hb electrophoresis is recommended in those with microcytosis and normal iron studies to evaluate for hemoglobinopathies.[4,6]

5.1.4. Serum Ferritin is the test of choice for the diagnosis of iron deficiency. A ferritin level less than 30 µg/L is generally indicative of low body iron stores.[1,4]

5.1.5. In inflammatory conditions and elderly, additional tests including serum iron, low transferrin saturation (<20%), increased total iron binding capacity and low reticulocyte-Hb (<29pg) can help to diagnose iron deficiency.[4]

5.1.6. Higher ferritin thresholds are recommended in inflammatory conditions in combination with transferrin saturation levels. (<100 µg /L with TSAT<20%)[4,6]

5.1.7. A therapeutic trial of oral iron replacement therapy for 2-4 weeks may also help in the diagnosis in some cases, but the response would be dependent on the patient's compliance with medication. A rise ≥ 10g/L rise in Hemoglobin over 2 weeks of iron therapy is quite sensitive for iron deficiency.[1,4]

6.0 Evaluating the cause of iron deficiency

The cause of iron deficiency should be identified and treated for effective management of iron deficiency anemia. Iron deficiency is indicative of an underlying etiology that is decreasing iron availability and /or increasing iron needs.

Excessive menstruation is a common cause of iron deficiency anemia in pre-menopausal women which may be due to underlying causes such as thyroid disease, polycystic ovary syndrome, coagulopathies, uterine fibroids, or endometrial hyperplasia.

Gastrointestinal conditions are a primary cause of iron deficiency anemia in post-menopausal women and adult and must be investigated.

6.1. Determine the cause of iron deficiency. Consider age and clinical presentation when investigating for cause.

6.2. Patients with overt bleeding specific to a system e.g., bleeding from gastroenterological tract or urological source of bleeding, should be referred to appropriate specialty for evaluation. Upper GI endoscopy and colonoscopy as indicated should be done as part of gastrointestinal evaluation. Urine analysis for hematuria, USG abdomen, intravenous urography and CT abdomen and pelvis should be done if indicated, to establish the cause of urological source of bleeding.

6.3. Premenopausal women should be evaluated for menorrhagia, which is the most common cause of iron deficiency anemia in them. Perform investigations including thyroid profile, coagulation profile and ultrasound of abdomen and pelvis, to identify the cause of menorrhagia.[4]

6.4. Premenopausal women with menorrhagia should be referred to the gynecologist for evaluation.

6.5. If the cause of menorrhagia is suspected to be a coagulation disorder, the patient should be referred to the physician/hematologist.

6.6. In certain situations, endoscopic investigation in premenopausal women may be indicated at outset. These include those age >50 years, women with hysterectomy <50 years with gastrointestinal symptoms and those having strong genetic risk for gastrointestinal pathology such as history of colorectal cancer in a first degree relative.[1]

6.7. in all post-menopausal females and all male patients in whom iron deficiency been confirmed with uncertain etiology, unless there is a history of significant non-gastrointestinal blood loss, gastrointestinal evaluation with upper GI endoscopy and colonoscopy should be considered [4]

6.8. In frequent blood donors, additional investigations are not required unless there is history of any other underlying cause. If iron deficiency is not corrected by iron repletion, further investigations to rule out other causes should be done. [4]

6.9. For helicobacter pylori infection associated iron deficiency, noninvasive testing for Helicobacter pylori can be done (serology or urea breath test) and if positive, endoscopy with a biopsy to confirm the diagnosis can be done. [4]

6.10. Testing for malabsorption is recommended if small bowel disease is clinically suspected, or if oral iron supplementation results in inadequate response despite compliance.
Celiac serology should also be considered for all adults presenting with iron deficiency anemia, especially those with a family history of the disease, a personal history of autoimmune diseases, or gastrointestinal symptoms. [1]
Upper endoscopy with duodenal biopsies should be performed to confirm the diagnosis only if there is positive serologic testing.[1]

6.11. Stool occult blood testing may be useful in identifying those who may have gastrointestinal lesions. A positive test calls for invasive gastrointestinal evaluation, but a negative test does not exclude gastrointestinal bleeding and all those with a high risk should undergo gastrointestinal evaluation.

6.12. In patients in whom endoscopy may be contraindicated because of procedural risk, radiographic imaging may offer sufficient screening.
CT colonography is a reasonable alternative in those not suitable for colonoscopy. The use of barium enema is less reliable but may be of use if colonoscopy or CT colonography is not available.[4]

6.13. In patients who do not respond to iron therapy and initial endoscopy findings are negative, repeating upper and lower endoscopy may be justified as in some instances, lesions may not have been detected on initial examination (e.g., missed mucosal erosions in a large hiatal hernia, suboptimal preparation for colonoscopy, inadequate biopsy of a suspected lesion).[4]

6.14. Additional further evaluation of the small intestine by capsule endoscopy is indicated if only there is inadequate response to iron therapy, the patient is transfusion dependent, or fecal occult blood testing suggests that the patient has obscure GI bleeding with the source undiscovered on initial or repeat endoscopy of acceptable quality [1,4]

If capsule endoscopy is unavailable or unsuitable, then CT/MRI enterography, if available may be considered.[4]

6.15. In frail patients with severe comorbidities, the appropriateness of investigating should be considered on a case-to-case basis considering the severity of anemia, risk of bowel preparation and the potential of tolerating treatment if colorectal cancer is detected.
The least invasive test should be used where appropriate in such patients. CT imaging may benefit such patients prior to doing invasive tests. [4]

7.0 Differential Diagnosis

- Anemia of chronic disease
- Beta thalassemia
- Alpha Thalassemia
- Hereditary spherocytosis
- Sideroblastic Anemia

8.0 Management of Iron Deficiency Anemia

The goals of management in iron deficiency anemia include:

- identification and treatment of underlying cause
- normalization of hemoglobin concentration
- replenishment of iron stores and
- improvement of symptoms and quality of life.

Treatment involves dietary advice, oral iron therapy, parenteral iron therapy and, less commonly, the use of blood transfusions.

Blood transfusion should be avoided in iron deficiency anemia and should be restricted only for patients with cardiovascular compromise and/or debilitating symptoms.

Prompt treatment of iron deficiency anemia with iron supplementation in all the patients who are hemodynamically stable, alleviates the symptoms of fatigue and cognitive difficulties, improves the quality of life, and reduces the need for blood transfusions. With consistent oral iron supplementation, reticulocytosis starts in 4 to 5 days, and Hemoglobin begins to improve by the second week of treatment. It may take up to 6 months to replenish iron stores.

8.1 Treatment considerations

8.1.1. Patients should be provided with information regarding an iron-rich diet and referred to a dietician, if available.

8.1.2. The treatment of those patients with an underlying condition that causes iron deficiency anemia should be referred to or managed in conjunction with the appropriate specialist.

8.1.3. Prescribe oral iron supplements as first line therapy for iron deficiency anemia. One preparation is not preferred over another; patient tolerance should be the guide.

8.1.4. Iron therapy without further diagnostic testing may be initiated in those patients that are predisposed to iron deficiency anemia without concurrent risk

conditions, including frequent blood donors, pregnant women, premenopausal women with menorrhagia and endurance athletes.
If anemia is severe or if there is no adequate response to therapy, further gastrointestinal evaluation should be considered.

8.1.5. In frequent blood donors, additional investigations are not required unless there is history of any other underlying cause. Iron repletion, donation at reduced frequency and monitoring to ensure that iron deficiency is corrected is sufficient.

8.1.6. Consider prescribing intravenous iron therapy when there is inadequate response to oral iron, intolerance to oral iron therapy, or ongoing blood loss.[4,6]

8.1.7. Indications for the use of intravenous iron as initial treatment include iron-deficient patients with active inflammatory bowel disease, malabsorption, chronic kidney disease undergoing dialysis and receiving erythropoietin, heart failure, genetic iron refractory iron deficiency anemia and the need for quick increase in iron levels, such as after chronic blood loss or peri operatively in urgent surgery[4]

8.1.8. Blood transfusion should be avoided in iron deficiency anemia and should be restricted only to patients with cardiovascular compromise and/or debilitating symptoms[4]

8.2 Oral Iron therapy

Oral iron represents first line and mainstay of treatment for most patients with Iron deficiency anemia. Oral preparations are readily available, inexpensive, and convenient to take and are effective when intestinal uptake is intact.

Several iron formulations are available, but ferrous iron salts like ferrous gluconate, ferrous sulphate, and ferrous fumarate remain the standard first line preparations.[7] Ferrous sulphate is the least expensive formulation.

Common adverse effects of oral iron include gastrointestinal side effects such as abdominal pain, nausea, vomiting, constipation, diarrhea and metallic taste. Black discoloration of faeces is an expected occurrence when taking iron replacement therapy.

Failure to respond to oral iron therapy should be evaluated for the cause, the commonest being noncompliance with oral iron therapy which may also occur due to gastrointestinal adverse effects to oral iron. Other causes include malabsorption, ongoing bleeding or hemolysis, underlying systemic diseases, and coexistent folic acid or B12 deficiency.

8.2.1. Oral iron is a first line treatment for most patients with Iron deficiency anemia and a once daily dose of oral ferrous salt should be initiated. If not, tolerating the dose could be changed to once every other day.[4,6]

8.2.2. Oral iron therapy is often required for at least 3 to 6 months to replete iron stores and normalize ferritin levels, although more time may be required depending upon the severity of Iron deficiency anemia and ongoing losses.

8.2.3. The dosage of elemental iron required to treat iron deficiency anemia in adults is 40-80 mg[14] of elemental iron per day and should be continued for 3 months after the anemia is corrected to allow iron stores to be replenished[4,6]

8.2.4. Iron should be taken either in a fasting state or between meals as the absorption of iron salts is significantly impaired when taken with food

8.2.5. Inhibitors of iron absorption (calcium-containing foods such as dairy products, tea, and coffee) should be avoided within the hour when the iron supplement is taken. Medications that reduce gastric acidity such as antacids may also impair oral iron absorption and should be avoided.

8.2.6. Oral iron taken with vitamin C (orange juice or ascorbic acid) may enhance iron absorption[1,7]

8.2.7. The frequency of subsequent monitoring depends upon the severity of the anemia, the underlying cause of the iron deficiency, and the clinical impact on the patient.

8.2.8. Patients should be reevaluated for hemoglobin response after at least 4 weeks of treatment.[4,6]

8.2.9. A ≥ 10g/L rise in Hemoglobin over 2 weeks of iron therapy shows an adequate response to treatment and the absence of a Hb rise after 2 weeks of daily iron is predictive of subsequent failure to achieve a hematological response.[4]

8.2.10. Hemoglobin will usually be corrected within 2 to 4 months, if appropriate iron dosages are taken as prescribed and the underlying cause of iron deficiency is corrected.

8.2.11. If the hemoglobin is not responding to oral iron repletion as anticipated, consider adherence to medicine, ongoing bleeding, malabsorption, or alternate diagnosis.

8.2.12. If there are adverse effects of oral iron, strategies should be taken to minimize them and increase compliance with the medicine.[4]
Strategies to minimize adverse effects include:

- Advising to take medicine with or shortly after food or at night
- Starting oral iron at a low dose and gradually increasing the dose
- Prescribing the lowest effective dose
- Trying alternative dosing schedules such as every other day dosing

8.2.13. A switch to intravenous iron and further gastrointestinal evaluation should be considered if there is no adequate response to therapy.

8.2.14. Ferritin should be re-checked 3 to 6 months after normalization of hemoglobin in anemic patients

8.2.15. After restoration of Hb and iron stores, blood counts should be monitored periodically, every 6 months initially to detect recurrent iron deficiency anemia[4]

8.2.16. Long term iron replacement therapy may be considered when the cause of recurrent iron deficiency anemia is unknown or irreversible. [4]

8.3 Parenteral Iron therapy

Parenteral iron therapy may be used in patients who cannot tolerate or absorb oral preparations, such as those who have undergone gastrectomy or other small bowel surgeries, malabsorption, and non-response.

Indications for intravenous therapy include:

- Inadequate response oral iron therapy (in compliant patients)
- Intolerance to iron therapy (including daily and alternate day dosing)
- Worsening symptoms of inflammatory bowel disease
- Unresolved or on-going bleeding
- Chronic kidney disease on dialysis and treated with erythropoietin
- Insufficient absorption in patients with celiac disease
- After bariatric surgery
- When rapid iron replacement is required (preoperative anemic patient when surgery is urgent or cannot be delayed)

Intravenous iron preparations are more expensive than oral iron preparations, and there are additional associated costs relating to the facilities, staffing and equipment required for administering infusions requiring any intervention.

Dosing parenteral iron depends on the total iron deficit of the patient, which is calculated based on body weight, target hemoglobin level and current Hb level using Ganzoni formula.

Total iron deficit(mg) =weight(kg) x (target Hb -actual Hb(g/dL) x 2.4 + 500 mg iron for iron stores (mg).

Intravenous iron is generally well tolerated by most patients and infusion related hypersensitivity reactions are not that common with modern, safer intravenous iron preparations.

Hypophosphatemia has been reported with parenteral iron preparations. The incidence is highest following administration of ferric carboxy maltose and has been associated with severe and prolonged hypophosphatemia[4,6,14]

Table 2: Risk factors for the development of hypophosphatemia

Malabsorptive disorders: inflammatory bowel disease, celiac disease, bariatric surgery
Recurrent or ongoing blood loss: abnormal uterine bleeding, hereditary hemorrhagic telangiectasia, other gastrointestinal bleeding
Severe Iron deficiency
Lower body weight
Low baseline serum phosphate
Higher serum PTH
Treatment with ferric carboxy maltose

Table 3: Factors increasing risk and /or severity of hypersensitivity reactions with Intravenous iron infusions[10]

Previous reaction to intravenous iron
Fast iron infusion rate
History of other drug and other allergies
Underlying severe asthma or eczema
Mastocytosis
Old age
Severe respiratory or cardiac disease
Systemic inflammatory disease (Systemic lupus erythematosus)

Parenteral Iron formulations

Some preparations such as ferric carboxymaltose, iron derisomaltose can effectively replenish total body iron stores in one or two infusions. Iron dextran is rarely used, as the much longer time required for infusion (4–6 hours) making it less convenient than the other total dose preparations, which can be given over 15–40 min.

Compound	Recommended dose per session	Special considerations
Low molecular weight iron dextran	1000 mg IV at < 50mg/min after uneventful 25-mg test dose over 2-6 hours	
Ferric gluconate	62.5 -125 mg intravenously at 12.5 mg/min or infusion over 1 hour, up to 1000 mg over 8 sessions (given no closer than every other day)[14]	
Iron sucrose	100 -200mg mg infusion over 15 to 30 min, 2-3 times a week given as a cumulative dose of 1000mg over 14 days	
Ferumoxytol	510 mg x 2, given intravenous infusion over 15 min or 1020mg x 1[1]	Also used as a magnetic resonance contrast agent. Consult Radiologist if MRI requested within 3 months of infusion.
ferric carboxymaltose	50mg x2 one week apart or 1000mg over 15 min as single dose [1]	High risk of hypophosphatemia, particularly with repeated dosing
iron isomaltoside	1000mg (max 20mg/kg) administered >15 min [1]	

Diagnosis of iron deficiency should be confirmed before starting parenteral therapy and should be decided in consultation with a specialist physician.

8.3.1. Intravenous iron is indicated if a patient does not tolerate oral iron, or there is no response to oral iron, or the patient has a condition in which oral iron is not likely to be absorbed [1]

8.3.2. Intravenous iron therapy is indicated in individuals who have undergone bariatric procedures, particularly those that are likely to disrupt normal duodenal iron absorption, and have iron-deficiency anemia with no identifiable source of chronic gastrointestinal blood loss[1]

8.3.3. Intravenous iron therapy is indicated in individuals with inflammatory bowel disease with active inflammation and compromised absorption. Treatment in these patients should focus on addressing and effective treatment of underlying inflammation. which may cause ulceration and chronic blood loss, as well as reduced iron absorption. [1,6]

Oral iron may be appropriate in carefully selected patients, who have mild anemia, clinically inactive disease and who are able to tolerate oral iron. [1]

8.3.4. Intravenous iron should not be given to a pregnant woman during the first trimester.[10]

8.3.5. Intravenous iron should be administered in a health facility with adequate supervision and availability for the management of anaphylaxis

8.3.6. Patients at high risk of treatment emergent hypophosphatemia should be identified (Table 2) and FCM avoided in these patients as repeat infusions may cause osteomalacia and fractures [15]

8.3.7. History of anaphylactic reaction to any parenteral iron product is a contraindication for administering intravenous iron [4]

8.3.8. Patients should be closely monitored for signs of hypersensitivity during and at least 30 minutes after intravenous iron administration [10]

8.3.9. Patients at increased risk for hypersensitivity reactions should be monitored with caution, with infusion given at a reduced rate (10% of the required rate) for the first 15 minutes and monitored for 1 hour after the infusion[10]

8.3.10. For mild hypersensitivity reactions (itching, flushing, sensation of heat, slight chest tightness, arthralgia) during iron infusion, infusion should be stopped and the patient monitored for 15 minutes. If the patient improves, then the infusion can be re-started at a reduced rate (50%) and patient observed for 1 hour after infusion.[10]

8.3.11. For moderate hypersensitivity reactions (flushing, chest tightness, nausea, dyspnea, urticaria, tachycardia, hypotension), iron infusion should be stopped. Consider volume load (0.9%saline 500ml) and IV hydrocortisone 200mg and monitor the patient for resolution or deterioration of symptoms. [10]

8.3.12. In severe hypersensitivity reactions or anaphylaxis, the infusion should be stopped immediately and promptly administer adrenaline, oxygen, nebulization with beta agonist, ACLS if indicated and transfer to intensive care if not better [10]

8.3.13. Once iron deficiency anemia is corrected, periodic monitoring is advised, given the possibility of recurrence. Complete blood counts should be checked every three months for one year. If hemoglobin and red blood cell indices remain normal, the patient can recheck periodically every 6 months for 2 to 3 years. Further follow-up may not be necessary if the patient is asymptomatic, and the hematocrit level remains normal.[4]

8.3.14. Evaluation of the ferritin level should be considered 8 to 12 weeks after the end of treatment. Within the first 8 weeks after infusion, the serum ferritin level is highly elevated and does not correlate well with body iron stores.

8.4 Iron deficiency anemia and comorbidities

8.4.1 Iron Deficiency anemia in surgical patients

Anemia and RBC transfusions remain independent risk factors in predicting poor clinical outcomes in surgical patients.[9]
Early detection and management of preoperative anemia should be done in surgical patients, given its recognized associations with poor outcomes, including mortality. The etiology of preoperative anemia can be multifactorial, but almost two thirds of anemic elective surgical patients have iron-deficiency anemia.[9] The aim of treating anemia includes improving the concentration of hemoglobin and decreasing the need for blood transfusions.

8.4.1.1. All patients should be screened for anemia preoperatively (except those undergoing minor procedures)[9]

8.4.1.2. Appropriate therapy for anemia should be guided by identifying the cause of anemia.

8.4.1.3. Iron repletion should be done in preoperative patients with ferritin <30 mg/L and/or TSAT <20%, or ferritin <100 mg/L in the setting of inflammation with C-reactive protein >5 mg/L, targeting an Hb of .13.0 g/dL[9]

8.4.1.4. For surgeries with 6 weeks or more lead time, oral iron once per day or once every other day is recommended and for those with less lead time, intravenous iron is recommended.

8.4.1.5. Intravenous iron is also recommended in patients with iron deficiency anemia who cannot tolerate or absorb iron or are unable to adhere to oral iron.

8.4.1.6. Consider erythropoiesis stimulating agents

8.4.1.7. Use a restrictive blood threshold and consider preoperative transfusion if there is active bleeding and symptomatic severe anemia (Hb <7g/dL)

8.4.1.8. Post operative anemia should be identified promptly and treatment started before discharge.

8.4.1.9. Blood transfusion should be considered for severe, symptomatic postoperative anemia where clinical need cannot be met by volume replacement or hematinic medication alone.[9]

8.4.2 chronic kidney disease

Ferritin levels in patients with chronic kidney disease (CKD) may be elevated due to inflammation and may not accurately reflect iron status and the need for supplementation. TSAT <30% and ferritin <500ng/ml has been used as the values for treating iron deficiency in adults in the Kidney Disease Improving Global Outcomes guideline.

8.4.2.1. There are multiple causes of anemia in patients with CKD including iron deficiency, so evaluation of anemia should focus on all potential causes and investigations including a complete blood count, red cell indices, platelet count, absolute reticulocyte count, serum ferritin and TSAT as well as serum vitamin B12 and folate levels should be done in the initial evaluation

8.4.2.2. For Chronic kidney disease patients not on dialysis, who require iron supplementation, the route of iron administration should be based on the severity of iron deficiency, availability of venous access, response to prior oral iron therapy, side effects with prior oral or IV iron therapy and patient compliance.

8.4.2.3. For CKD, non-dialysis patients with Hb < 10g/dl, the decision whether to initiate erythropoiesis stimulating agents should be individualized based on the hemoglobin concentration, presence of symptoms of anemia, prior response to iron therapy, the risk of needing a transfusion and the risks related to erythropoiesis stimulating agent therapy.

8.4.2.4. For Chronic kidney disease, stage 5 dialysis patients, erythropoiesis stimulating agent therapy be used to avoid having the hemoglobin concentration fall below 9.0g/dl.

8.4.2.5. For patients on an erythropoiesis stimulating agent and not on iron supplementation, a trial of Intravenous iron or in CKD non dialysis patients alternatively oral iron therapy to be prescribed.

8.4.2.6. Treatment in chronic kidney disease is usually initiated and monitored by the nephrology team and patients should be referred to the nephrologist for evaluation and management.

8.4.3 Pregnancy

Anemia is common during pregnancy, and while most anemia is physiological, the most common pathologic cause is iron deficiency.

Maternal iron deficiency anemia has been associated with increased risk of postpartum anemia and blood transfusion. Maternal consequences of iron deficiency anemia include abnormal thyroid function, placental abruption, pre-eclampsia, eclampsia and is a risk factor for postpartum hemorrhage.[6]

Iron deficiency anemia in pregnancy may also adversely impact the fetus, resulting in an increased risk of prematurity, low birth weight, physical developmental delay, and morbidity

8.4.3.1. All pregnant women should be screened for iron deficiency anemia

8.4.3.2. Hemoglobin levels used to define anemia are based on the trimester of pregnancy (<11 g/dL in first and third trimesters, <10.5 g/dL in second trimester and <10 g/dL post-partum).[6]

8.4.3.3. To define ID in pregnancy, there are no standardized serum ferritin thresholds. Ferritin is an acute phase reactant and may be elevated because of pregnancy itself. While a low ferritin invariably indicates iron deficiency in this population, a normal ferritin cannot reliably exclude it.[6]

8.4.3.4. Pre-conceptual normalization of iron status and prompt, effective treatment of iron deficiency anemia identified during pregnancy and postpartum should be done

8.4.3.5. Oral iron should be the preferred treatment option. Intravenous iron is indicated when oral iron is not tolerated or if the patient is near term and there is not enough time for oral iron supplementation to be effective.

8.5 Blood transfusion

Blood transfusion is rarely required to treat iron deficiency anemia and should only be based on clinical condition and can be restricted to those with cardiovascular compromise and/or debilitating symptoms. Although severe anemia is defined as Hb <7g/dL, many of these patients may be hemodynamically stable and rather have chronic anemia, remaining asymptomatic.

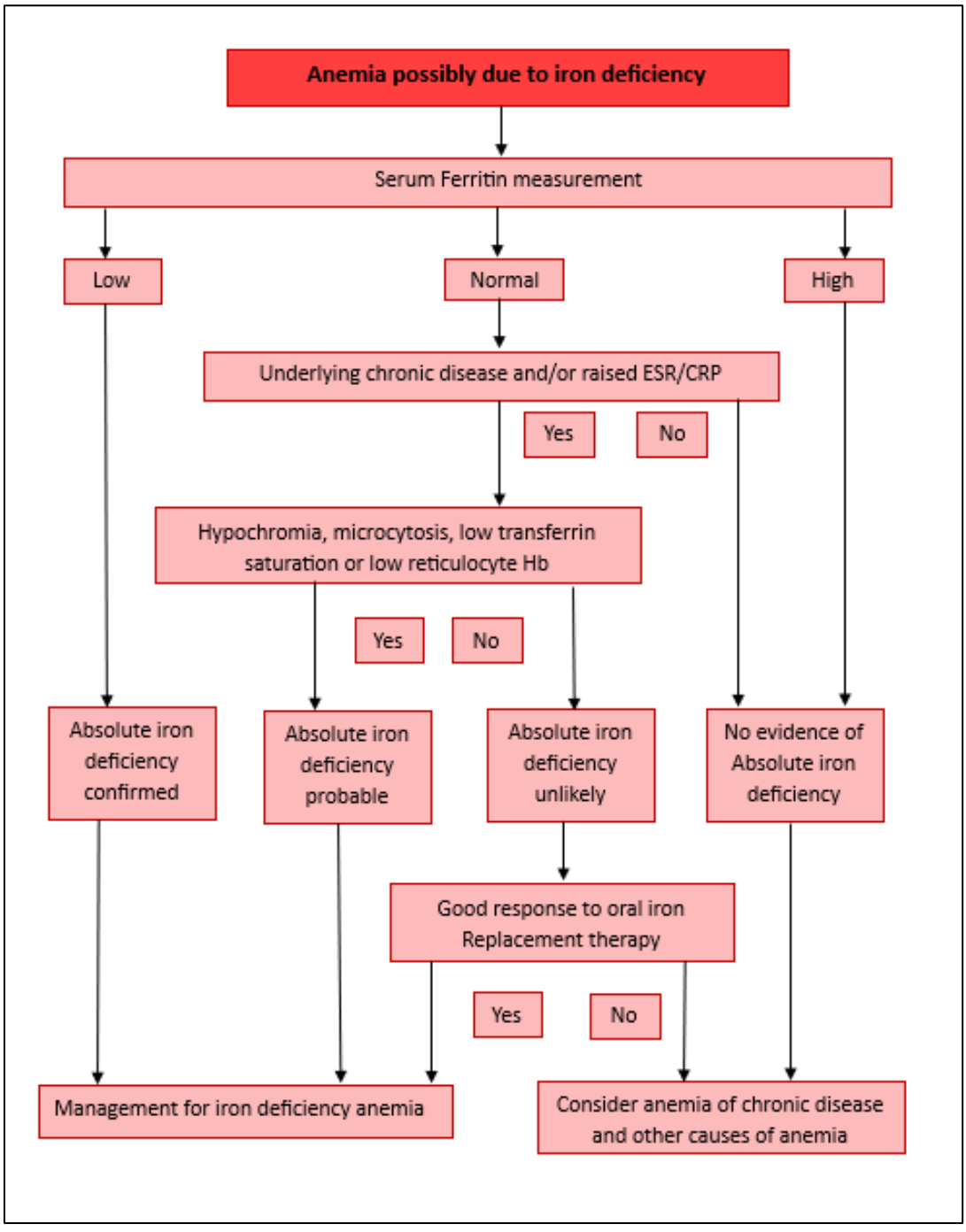
If the transfusion is performed, packed red cells should be transfused with a target Hb of 7-9mg/dL and transfusion should be followed by iron replacement to adequately replenish the iron stores.

Transfusion is recommended in pregnant women with severe anemia hemoglobin levels of less than 6 g per dL because of potentially abnormal fetal oxygenation resulting in non-reassuring fetal heart tracings, low amniotic fluid volumes, fetal cerebral vasodilation, and fetal death.

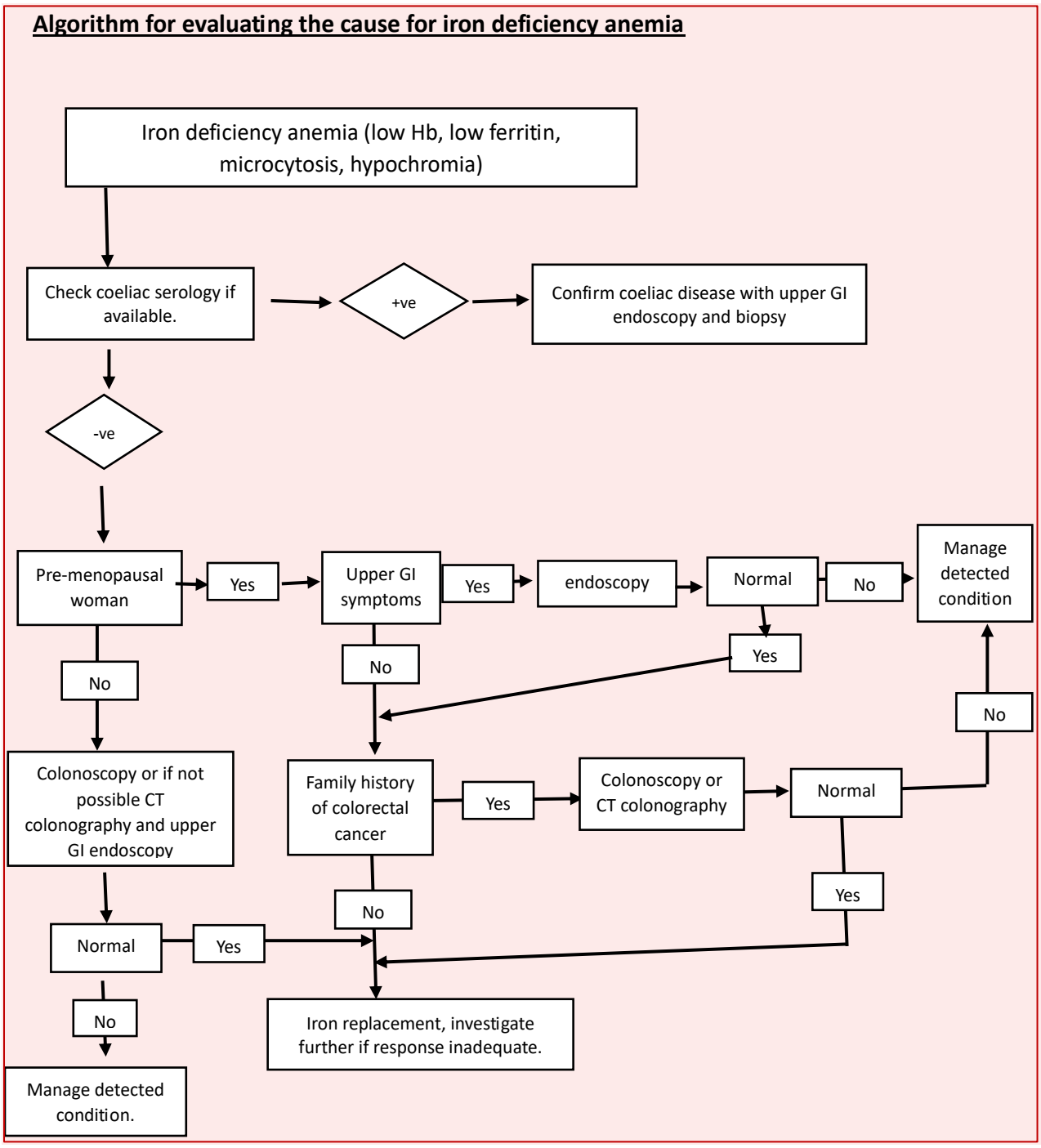
Consider single unit RBC transfusions in those patients who do not have active bleeding. Reassess the patient and check the hemoglobin level after the unit of transfusion. Further transfusions should be done, if indicated.

9.0 Algorithms

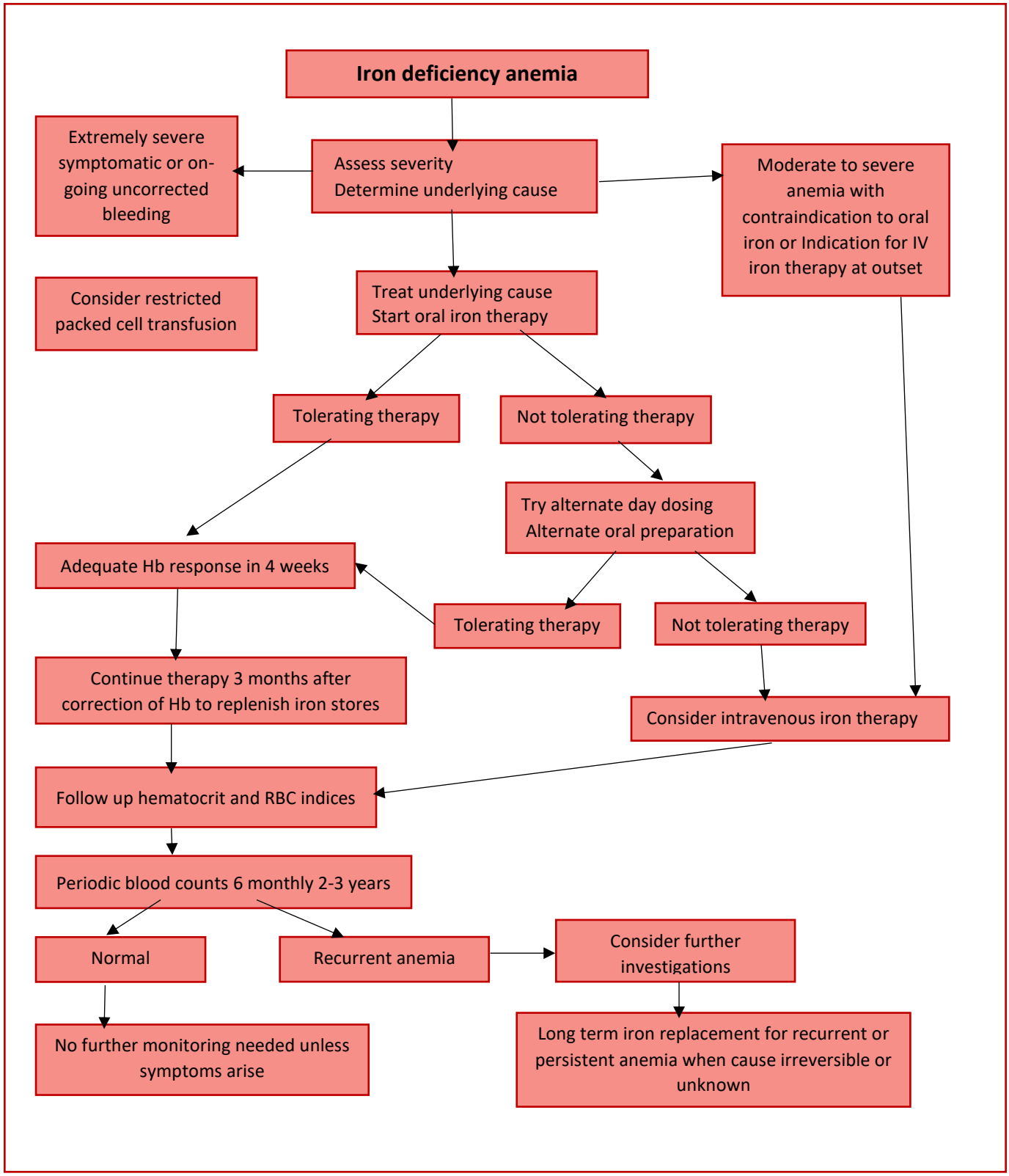
9.1 Algorithm for diagnosis of iron deficiency anemia



9.2 Algorithm for evaluating cause of iron deficiency anemia



9.3 Algorithm for Management of Iron deficiency Anemia



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