Administration of Intravenous Iron

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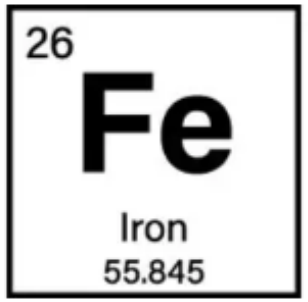


Disclosure

Ontario Transfusion Coordinators

Unity Health

Guelph General Hospital

Hamilton Health Sciences Center

Health Sciences North

Hospital for Sick Children

Humber River Hospital

Kingston Health Sciences Centre

Lakeridge Health

London Health Sciences Centre

Michael Garron Hospital

Mt. Sinai Hospital

Niagara Health System

North Bay Regional Health Centre

The Ottawa Hospital

Peterborough Regional Health Centre

Sault Area Hospital

Scarborough Health Network

Southlake Regional Health Centre

St. Mary's General Hospital

Sunnybrook health Sciences Centre

Trillium Health Partners

University Health Network

Windor Regional Hospital

Objectives

Appreciate the role of IV Iron as a strategy for blood conservation

Understand the causes of iron deficiency and need for investigation

Learn how to administer IV Iron (Venofer and Monoferric)

Immediate management of an infusion reaction

Iron Deficiency Anemia: a Health Care Burden

- **Iron deficiency** - not having sufficient iron to meet the body's needs (around 3-4 grams)
- **Anemia** – low hemoglobin level
  - Affects 2.4 billion individuals globally = 1 out of 4 people
  - Leading cause of anemia is iron deficiency = 1.2 billion people

❖ Most at risk: infants, children, women of childbearing age/pregnancy, elderly

Iron Deficiency Anemia: a Health Care Burden

Patients having surgery with anemia

- 4x more likely to suffer kidney damage
- 2-fold increased risk of infection
- 1.3-fold increased risk of stroke
- 5-fold increased risk of red cell transfusion

Iron deficiency without anemia must also be recognized for appropriate investigations and treatment to prevent the development of anemia

Patient Blood Management

Patient Blood Management is a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment

~ 2021 Global Definition

Patient Blood Management

- Blood transfusion has been identified as one of the most overused treatments that can harm patient safety and quality
- PBM is an international standard of care
- The best blood in your veins is your own blood
- 5 rights of patient safety – right treatment?
  - Should we use blood when iron alone will help?
  - Remember blood is a liquid transplant with lasting side effects

Pre-Knowledge Question- Case Study

42F visits the Emergency Department for heavy menstrual bleeding

Hemoglobin 71 g/L, ferritin 22 – sent by her GP

Vital signs within normal limits, patient reports SOBOE, fatigue, craving ice

Seen by ED doctor - abdominal ultrasound, Tranexamic acid IV and 1 unit of packed red blood cells.

Sent home to follow-up with GP/OBGYN

Pre-Knowledge Question

This patient received a blood transfusion, therefore IV Iron is not needed.

True

False

Pre-Knowledge Question

The risk of severe allergic/anaphylaxis reaction with an iron infusion is

a) 1 in 100 doses

b) 1 in 200,000 doses

c) 1 in a million doses

d) No risk

Pre-Knowledge Question

The risk of anaphylaxis to IV iron is less if you have tolerated IV iron in the past

True

False

Iron Hemostasis

- Too much iron is bad!
- Iron is kept in tight hemostasis because the body cannot rid the excess – only 1-2 mg per day are lost during physiological processes - sweating, epithelial shedding
- Most iron is stored in hemoglobin and when red blood cycles die, iron is recycled to regenerate new red cells
- During time of blood loss, iron is lost and iron deficiency can result
- Most iron is absorbed in the duodenum – gut/bowel issues, can impair absorption

Causes of Iron Deficiency?

Blood loss – chronic (upper or lower gastrointestinal, genitourinary, gynecological, blood donation)

Malabsorption of nutrients (celiac, crohns, H. pylori, PPI/antacids, infection, gastric bypass, gastrectomy)

Decreased intake of iron (vegan not supplementing iron-rich foods, low meat consumption, Total Parenteral Nutrition)

High iron demand states (pregnancy, childhood, exercise, surgery)

Diagnosing Iron Deficiency

- It is important to identify ID/IDA and treat that deficiency with iron supplements
- The underlying cause needs to be sought (FIT test, endoscopy)
- Referral to primary care practitioner for further investigation

Laboratory findings

Evaluating iron deficiency using ferritin and iron studies:

- Ferritin less than **30** = absolute iron deficiency
- When ferritin is elevated, it is not useful in determining iron deficiency as it is an acute phase reactant (increases with inflammation – infection, cancer, renal)

www.hemequity.com/raise-the-bar-home

Laboratory findings

‘Iron studies’ are used when ferritin is above 30 to determine iron deficiency

Iron studies

- Transferrin saturation – less than 0.20 or 20% iron stores are low
- Serum Iron – usually low but can be influenced by oral intake
- Total Iron binding capacity – usually very high in absolute iron deficiency

Iron saturation is used a lot with nephrologists to monitor iron stores

Ferritin’s over 400 – usually IV Iron is cautioned – not indicated, other treatment might be needed for inflammation (RA, infection)

What is IV Iron?

IV Iron is the intravenous form of iron supplementation

IV Iron is used in the follow situations:

- Unable to tolerate oral iron due to side effects (constipation*, diarrhea, nausea)
- No response proven by labs to oral iron (approx. 1/3 of patient will not absorb oral iron)
- Urgency/timeliness to replete iron stores and/or optimize hemoglobin (surgery, pregnancy, ongoing chronic blood loss)

Types of IV Iron

Iron Sucrose (Venofer)

- Low dose
- Need multiple infusions to replace iron
- Used in pregnancy from second trimester onward

Ferric dersiomaltose (Monoferric)

- High dose iron infusion
- Can replace iron needs in 1-2 infusions
- Currently not indicated for use in pregnancy*

Risks and Considerations

Informing patients as to the risk of reactions

- Anaphylaxis less than 1:200,000 doses – same risk for both formulations
  - The risk is the same for each and every infusion

- Mild reaction (flushing, chest, back pain or tightening) ‘Fishbane’ - 1:100-200
  - More common for Monoferric

❖ Iron infusions must be administered where there are trained personnel to provide emergency treatment for anaphylaxis

Risks and Considerations

Contraindication to administration of IV Iron

- Allergy to intravenous iron
- Iron overload/hemochromatosis
- Decompensated cirrhosis/active hepatitis
- Hemolytic Anemia
- First trimester of pregnancy
- Active infection (Sepsis)

Monoferric has further *precautions* for hypersensitivity in patients with:

- Severe asthma, eczema, RA, Lupus, multiple allergies

Pre-Administration

- Establish a comfortable IV catheter - catheter size – 22 or 24 gauge, most CVAD's
- Ensure patency – permanent dark staining can occur if interstitial
- Baseline vital signs – blood pressure, heart rate, respiratory rate, pulse oximetry, temperature
- Inspect vial/solution for sediment and do not use if this is present – stop and call pharmacy for new vials

Administration

- Run IV Iron as a piggyback or secondary medication line
- Mainline should be primed with NS – usually 250 mL bag NS
- Measure vitals 15 minutes after starting infusion, hourly and prior to discharge (or as hospital policy)
- If a reaction occurs, stop infusion and assess patient – see algorithm

Administration – Iron Sucrose

Iron Sucrose (Venofer*) 100 mg/5 mL

Common doses 200 mg or 300 mg (repeated at least 24 hours apart, usually weekly)

Only diluted into 0.9% normal saline (NS)

- Iron sucrose 200 mg in 100 mL NS, administered over 60 minutes
  - *INFUSION PUMP RATE = 110 mL per hour*

- Iron sucrose 300 mg in 250 mL NS, administered over 90-120 minutes
  - *INFUSION PUMP RATE = 176 mL per hour for 90 minute infusion or,*
    = 135 mL per hour for 120 minute infusion

Administration – Iron Sucrose

- ✓No test dose
- ✓Vitals signs periodically throughout and 30 minutes post-infusion
- ✓Observe patient for 30 minutes post-infusion for signs of reaction

If iron site is interstitial – iron sucrose monograph instructs to apply ice. Of course re-site IV and finish infusion

Administration - Monoferric

Monoferric 100 mg/1 mL – typically 5 or 10 mL dose

- Common doses 500 mg or 1000 mg, no more than 1500 mg in one infusion
- Only dilute into 0.9% normal saline (NS)
- Initial rate for first 10 minutes (*set pump at 25 mL/h for the first 5 mL*)

Administration - Monoferric

- Monoferric 500 mg in 50 or 100 mL NS, administered over 30-60 minutes
  - *INFUSION PUMP RATE = 110 mL for 500 mg dose in 50 mL bag*

    = 220 mL for 500 mg dose in 100 mL bag
- Monoferric 1000 mg in 100 mL NS, administered over 30-60 minutes
  - *INFUSION PUMP RATE = 110 mL for 1000 mg dose to infuse over 60 minutes*

    = 220 mL for 1000 mg dose to infuse over 30 minutes

✓Vitals signs periodically throughout and 30 minutes post-infusion

✓Observe patient for 30 minutes post-infusion for the signs of reaction

✓Dose can be repeated 7 days from the first infusion

Reaction Management

- **Most common** - symptoms such as flushing, chest pain, back pain, tightness (Fishbane)
- **Less but somewhat common** - isolated symptoms: urticaria, hypotension, diarrhea, nausea
- **Rare** - anaphylaxis

Reactions – Fishbane Type

Slight chest tightness, arthralgia, transient facial flushing, without other symptoms of anaphylaxis

1. Stop infusion
2. Obtain Vital signs (BP, pulse, respiratory rate, O2 saturation)
3. Call prescriber/MD/NP for direction on resuming if symptoms resolve
4. Do not administer diphenhydramine
5. If unstable or worsening, treat symptoms or call code blue/anaphylaxis
6. If the patient is stable after 15 minutes and symptoms resolve, consider re-challenging iron infusion at 50% of the previous rate (if prescriber approves or standing order)
7. Observe and discharge as directed by prescriber

Reactions – Moderate Hypersensitivity

Transient cough, low blood pressure, vomiting or diarrhea, shortness of breath, rash, hives, itching, tachycardia

1. Stop infusion
2. Obtain Vital signs (BP, pulse, respiratory rate, O2 saturation)
3. Call prescriber/MD/NP
4. Treat symptoms i.e. Oxygen for hypoxia, fluid bolus for low BP, diphenhydramine/steroids for rash, Ventolin for wheezing
5. If unstable or worsening, call code blue/anaphylaxis
6. Do not re-challenge or resume.
7. Observe and discharge as directed by prescriber

*Follow-up with prescriber for pre-medication if future infusions or allergist

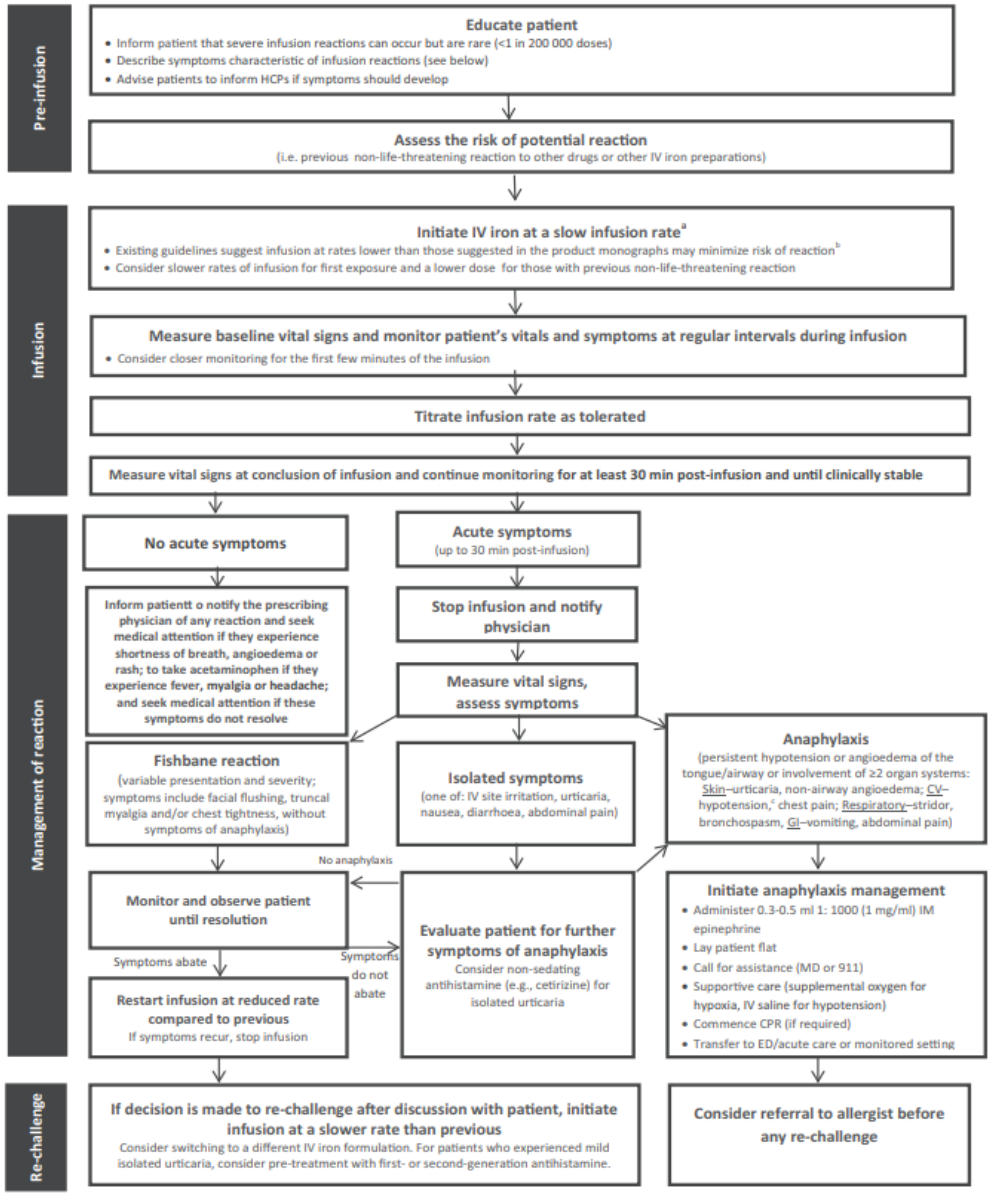
Reactions – Severe/Anaphylaxis

Symptoms progressing – hypotension, wheezing, stridor, periorbital edema, unconscious

1. Stop infusion
2. Obtain Vital signs (BP, pulse, respiratory rate, O2 saturation)
3. Call prescriber/MD/NP for direction on resuming if symptoms resolve
4. Treat for anaphylaxis/Call code blue
5. Epinephrine, ACLS
6. Supportive care for symptom management
7. Do not re-challenge or resume

*Refer to allergist

Management of hypersensitivity reactions – Flowchart



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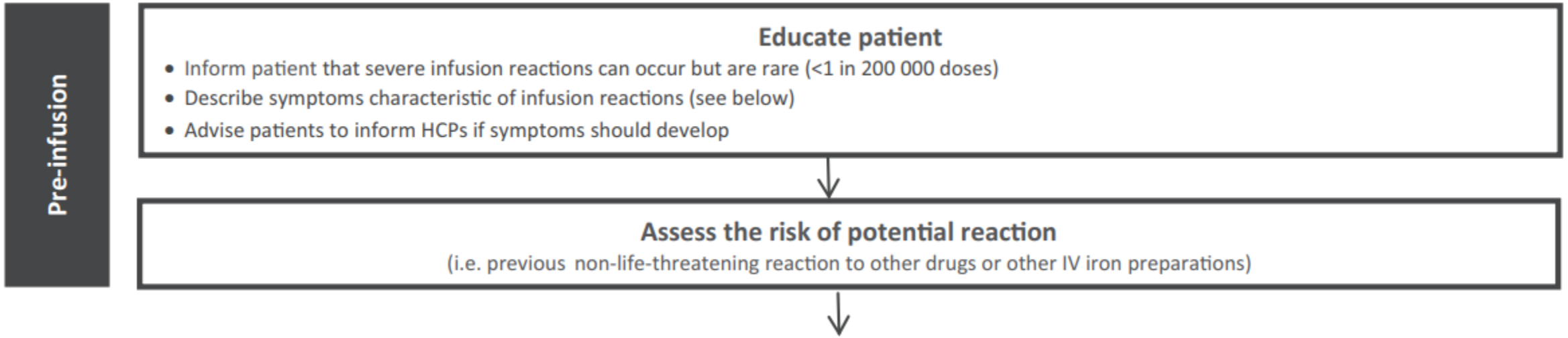
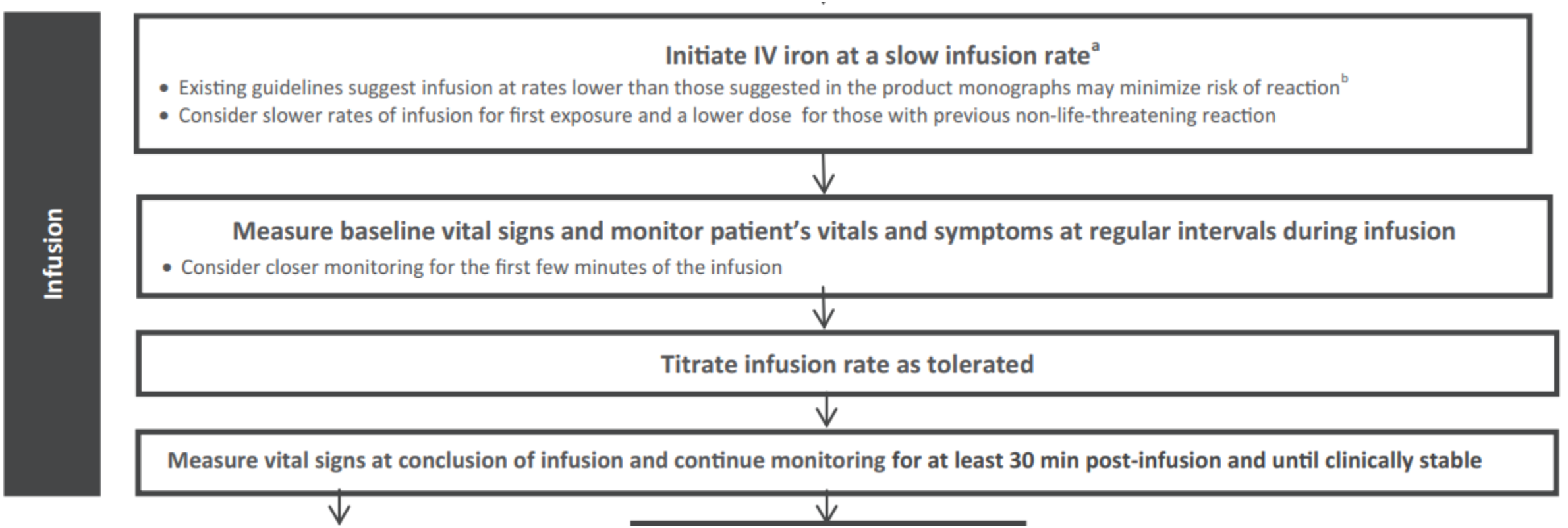
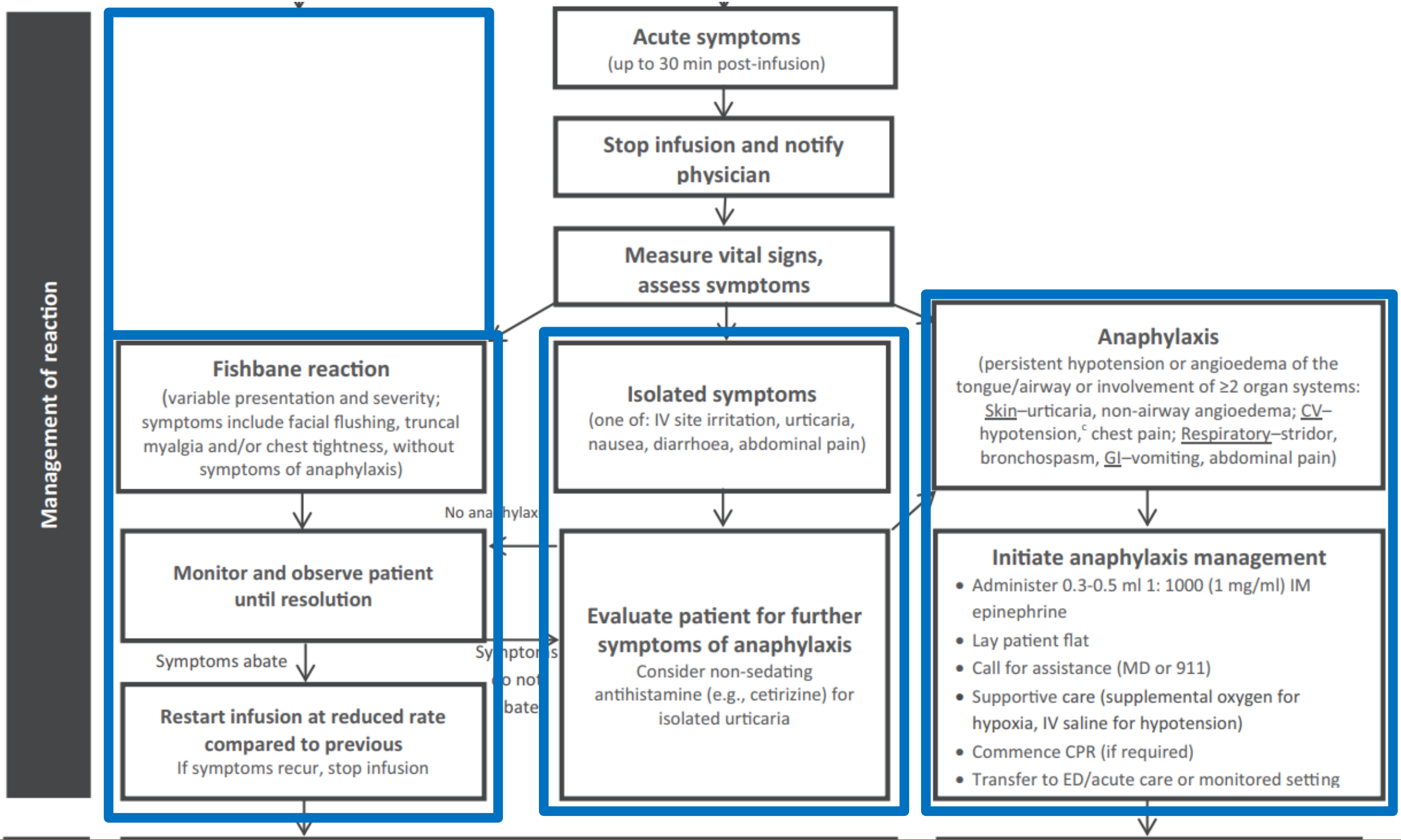

Pre-infusion
Educate patient
• Inform patient that severe infusion reactions can occur but are rare (<1 in 200 000 doses)
• Describe symptoms characteristic of infusion reactions (see below)
• Advise patients to inform HCPs if symptoms should develop
Assess the risk of potential reaction
(i.e. previous non-life-threatening reaction to other drugs or other IV iron preparations)


Infusion
Initiate IV iron at a slow infusion rate[a]
• Existing guidelines suggest infusion at rates lower than those suggested in the product monographs may minimize risk of reaction[b]
• Consider slower rates of infusion for first exposure and a lower dose for those with previous non-life-threatening reaction
Measure baseline vital signs and monitor patient's vitals and symptoms at regular intervals during infusion
• Consider closer monitoring for the first few minutes of the infusion
Titrate infusion rate as tolerated
Measure vital signs at conclusion of infusion and continue monitoring for at least 30 min post-infusion and until clinically stable


Management of reaction
Acute symptoms
(up to 30 min post-infusion)
Stop infusion and notify physician
Measure vital signs, assess symptoms
Fishbane reaction
(variable presentation and severity; symptoms include facial flushing, truncal myalgia and/or chest tightness, without symptoms of anaphylaxis)
Isolated symptoms
(one of: IV site irritation, urticaria, nausea, diarrhoea, abdominal pain)
Anaphylaxis
(persistent hypotension or angioedema of the tongue/airway or involvement of ≥2 organ systems: Skin–urticaria, non-airway angioedema; CV–hypotension,[c] chest pain; Respiratory–stridor, bronchospasm, GI–vomiting, abdominal pain)
No ana hylax
Monitor and observe patient until resolution
Symptoms abate
Restart infusion at reduced rate compared to previous
If symptoms recur, stop infusion
Sy nptom s
o not
bate
Evaluate patient for further symptoms of anaphylaxis
Consider non-sedating antihistamine (e.g., cetirizine) for isolated urticaria
Initiate anaphylaxis management
Administer 0.3-0.5 ml 1: 1000 (1 mg/ml) IM epinephrine
Lay patient flat
Call for assistance (MD or 911)
Supportive care (supplemental oxygen for hypoxia, IV saline for hypotension)
Commence CPR (if required)
Transfer to ED/acute care or monitored setting


Re-challenge
Isolated symptoms
If decision is made to re-challenge after discussion with patient, initiate infusion at a slower rate than previous
Consider switching to a different IV iron formulation. For patients who experienced mild isolated urticaria, consider pre-treatment with first- or second-generation antihistamine.
Severe Hypersensitivity/Anaphylaxis
Consider referral to allergist before any re-challenge

Delayed Reactions

- There is a chance of delayed reaction that can occur from several hours up to days after administration e.g. flu-like symptoms, arthralgia, myalgia and sometimes fever

- These usually settle but if prolonged fatigue, muscle weakness and bone pain it is recommended to measure phosphate – see GP/NP

Case Study

42F recent visit to the ED for heavy menstrual bleeding.

Hemoglobin 71 g/L, ferritin 22.

Vital signs within normal limits, patient reports SOBOE, fatigue, craving ice

Seen by ED doctor - abdominal ultrasound, Tranexamic acid IV and 1 unit of packed red blood cells.

Sent home to follow-up with GP/OBGYN

Post-Knowledge Question

This patient received a blood transfusion, therefore IV Iron is not needed.

True

False

Post-Knowledge Question

The risk of severe allergic/anaphylaxis reaction with an iron infusion is

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d) No risk

Pre-Knowledge Question

The risk of anaphylaxis to IV iron is less if you have tolerated IV iron in the past

True

False

Case Study

Patient listed for surgery now in 2 weeks. Plan open hysterectomy. Has been taking oral iron sporadically and using Tranexamic acid prn but still has prolonged menstrual bleeding

Hemoglobin 87 g/L, ferritin 12

IV Iron is indicated both due to the ongoing bleeding and timeline to surgery

Patient has no contraindications – NKDA, PmHx of high blood pressure, depression, GERD (on PPI), weight 75 kg

Case Study

Contraindication to IV Iron:

- Allergy to intravenous iron
- Iron overload or hemochromatosis
- Decompensated cirrhosis/active hepatitis
- Hemolytic Anemia
- First trimester of pregnancy
- Active infection (Sepsis)

Case Study – Monoferric Dose

. Simplified Table:

Hb (g/dL)	Patients with bodyweight <50 kg	Patients with bodyweight 50 kg to <70 kg	Patients with bodyweight ≥70 kg
≥10	500 mg	1000 mg	1500 mg
<10	500 mg	1500 mg	2000 mg

A single Monoferric infusion should not exceed 20 mg iron/kg body weight

Single doses above 1500 mg are not recommended

Reassessment

- IV iron monographs instruct to recheck hemoglobin levels 4 weeks after treatment and not before (4-6 weeks for maximal effect)
- If you check ferritin and iron studies within 48h of infusion, results will be high
- If someone is bleeding, they may require more frequent blood work and more iron than the initial course set out
- How long iron lasts is different for everyone, depending on their clinic situation

Thank you!

Questions and Comments?

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References

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