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Blood Disorders Day 2020

FOR Health Professionals

Iron Chef: Serving up high quality care in the setting of iron deficiency and iron overload

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May 1, 2020

University of Manitoba

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Iron deficiency anemia (IDA): It's easy as 1,2,3 ♪♫

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May 1, 2020

University of Manitoba

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Presenter Disclosure

- **Faculty / Speaker's name:** Emily Rimmer

- **Relationships with commercial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** none
  - **Consulting Fees:** none
  - **Other:** none

Mitigating Potential Bias

- Not Applicable

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Learning Objectives

1. Recognize the burden of iron deficiency
2. Understand investigations to diagnose iron deficiency
3. List the investigations required to identify cause of iron deficiency
4. Apply strategies to manage iron deficiency

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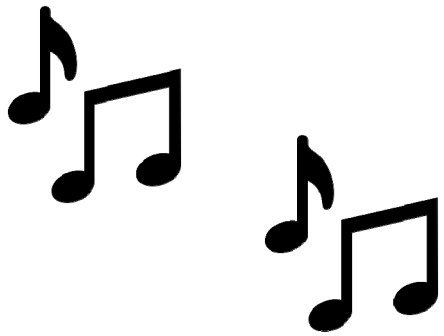
Come on, come on, come on, let me tell you what it's all about….

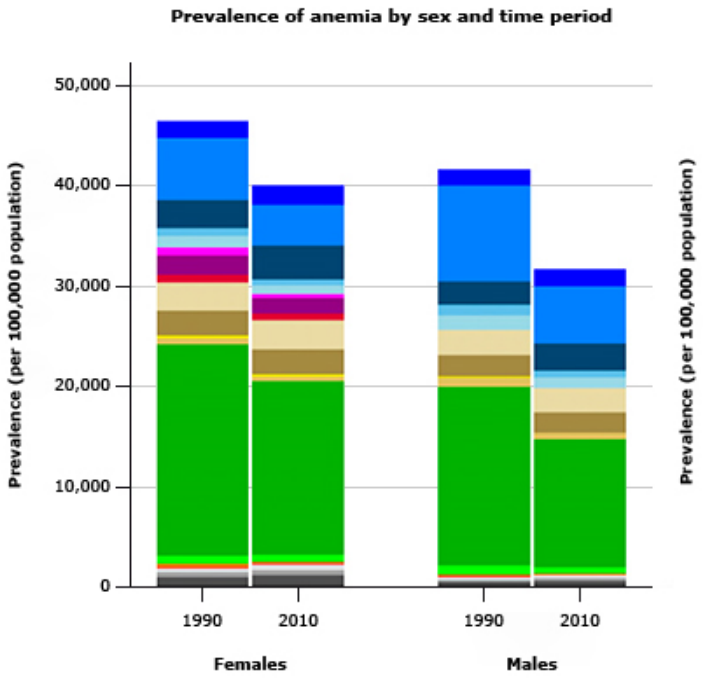


- I-D-A, its easy as 1-2-3…

- Step 1 – Identify iron deficiency
- Step 2 – Investigate cause of iron deficiency
- Step 3 – Iron repletion

Epidemiology of iron deficiency

- ~30% of the global population have anemia[1]
- Iron deficiency is the predominant cause of anemia[2]
  - Women and children are most at risk
  - Regardless of geography or SES
- Green represents iron deficiency anemia (IDA)



1. Ning and Zeller. Management of iron deficiency. Hematology 2019.
2. Kassebaum et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood 2014

Iron deficiency (ID)

- Iron deficiency is highly prevalent: ~2 billion individuals
- Symptoms:
  - Fatigue, pica, depression, headache, restless legs syndrome
  - Anemia: dyspnea with exertion, lightheadedness, palpitations
- Many patients with ID are not anemic. Do they require treatment?
  - Will treatment improve their fatigue or quality of life?
  - Will it enhance physical performance?

The iron deficient but non-anemic patient…

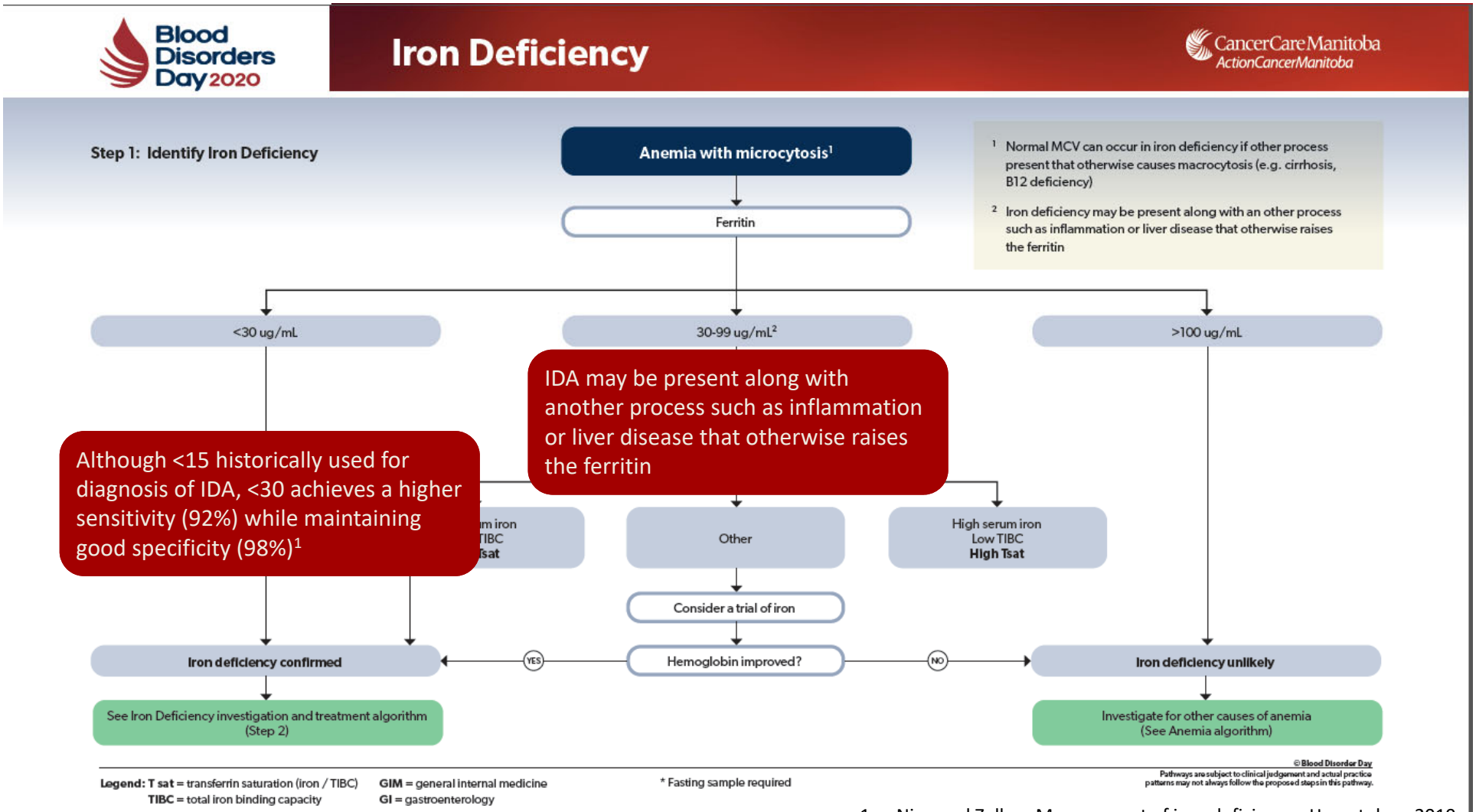
- Meta-analysis of 18 randomized controlled trials
- Total n = 1162 individuals; mostly young healthy females
- Follow up duration: 90 days to 4 months
- Oral iron preparations studied in 14 trials
- Mean daily dose was 87 mg (elemental)

Bottom line: Iron supplementation reduced self reported fatigue, but didn't really change measures of work capacity

1. Efficacy of iron replacement therapy on fatigue and work capacity in non-anemic adults with iron depletion: a systematic review of randomized trials. Houston et al *BMJ Open. 2018*

Step 1: Identify iron deficiency (ID)

- ID can occur in presence or absence of anemia (A)
- IDA is typically associated with microcytosis
  - All microcytic anemia are due to impairment of hemoglobin synthesis
- Serum **ferritin** is the single best test to identify ID/IDA
  - Drawback is ferritin is acute phase reactant



1. Ning and Zeller. Management of iron deficiency. Hematology 2019.

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Tests consistent with ID/IDA

	Iron overload	Iron deficiency	Inflammation	Iron deficiency + inflammation
Hemoglobin	↔	↓	↓	↓
MCV, MCHC	↔	↓	↓ or ↔	↓
Serum iron	↑	↓	↓	↓
TIBC	↓	↑	↓	↔
Tsat	↑**	↓↓	↓ or ↔	↓
Ferritin	↑	↓**	↑	↔

Step 2: Investigate cause of IDA

- NB: IDA is a symptom NOT a diagnosis
- To effectively manage IDA, the etiology MUST be identified and, if possible, corrected

Conditions associated with ID

Decreased iron availability

- Malabsorption
  - Gastric bypass, celiac, etc
- Inflammatory diseases
- CHF
- CKD
- (Diet)

Increased iron need

- Pregnancy, and breastfeeding
- Childhood

Iron loss in pregnancy/breastfeeding ~1000mg
Menstrual blood loss ~1mg/day
Iron loss in hemodialysis ~2000mg / year

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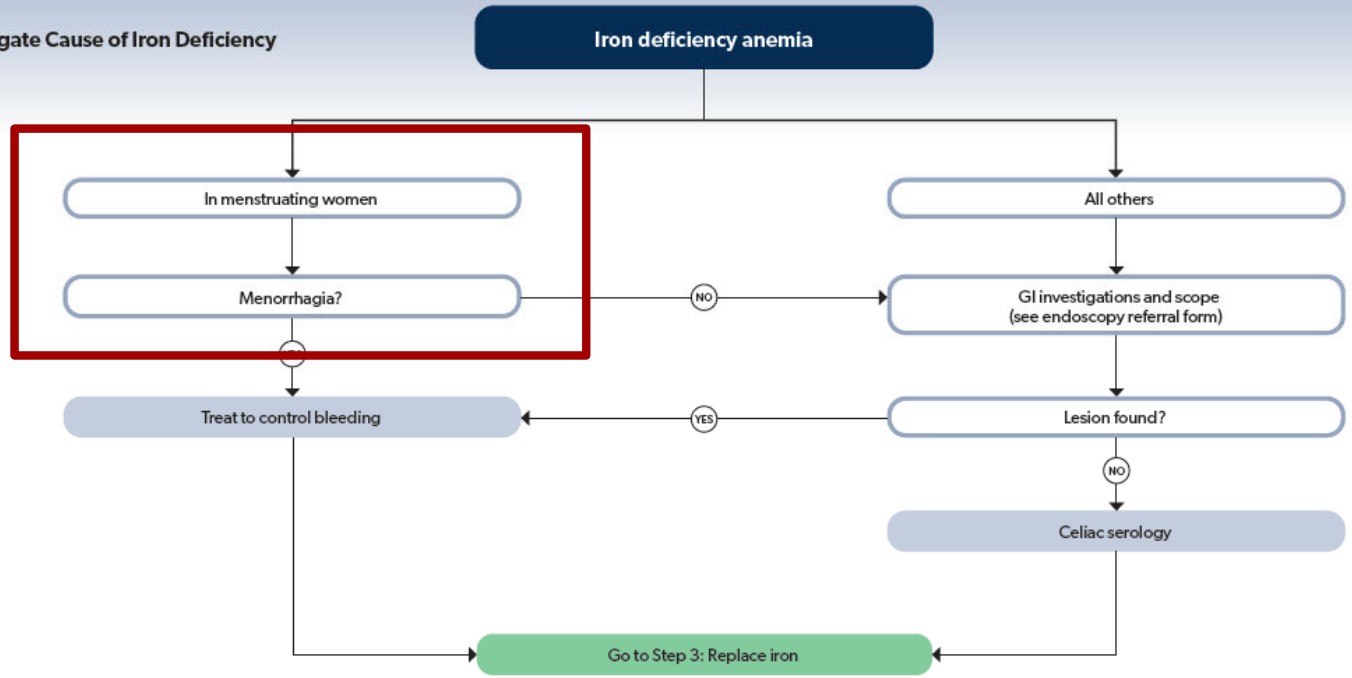
Step 2: Investigate Cause of Iron Deficiency



Legend: **T sat** = transferrin saturation (iron / TIBC)
TIBC = total iron binding capacity
GIM = general internal medicine
GI = gastroenterology

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Menstrual blood loss

- Most common cause in women of reproductive age
  - Detailed bleeding history is recommended
  - Use of a validated bleeding score recommended[1]
- Strategies to reduce menstrual blood loss
  - Hormonal contraception (OCP, progesterone secreting IUD)
  - Anti-fibrinolytic agents (tranexamic acid)

1. www.letstalkperiod.ca

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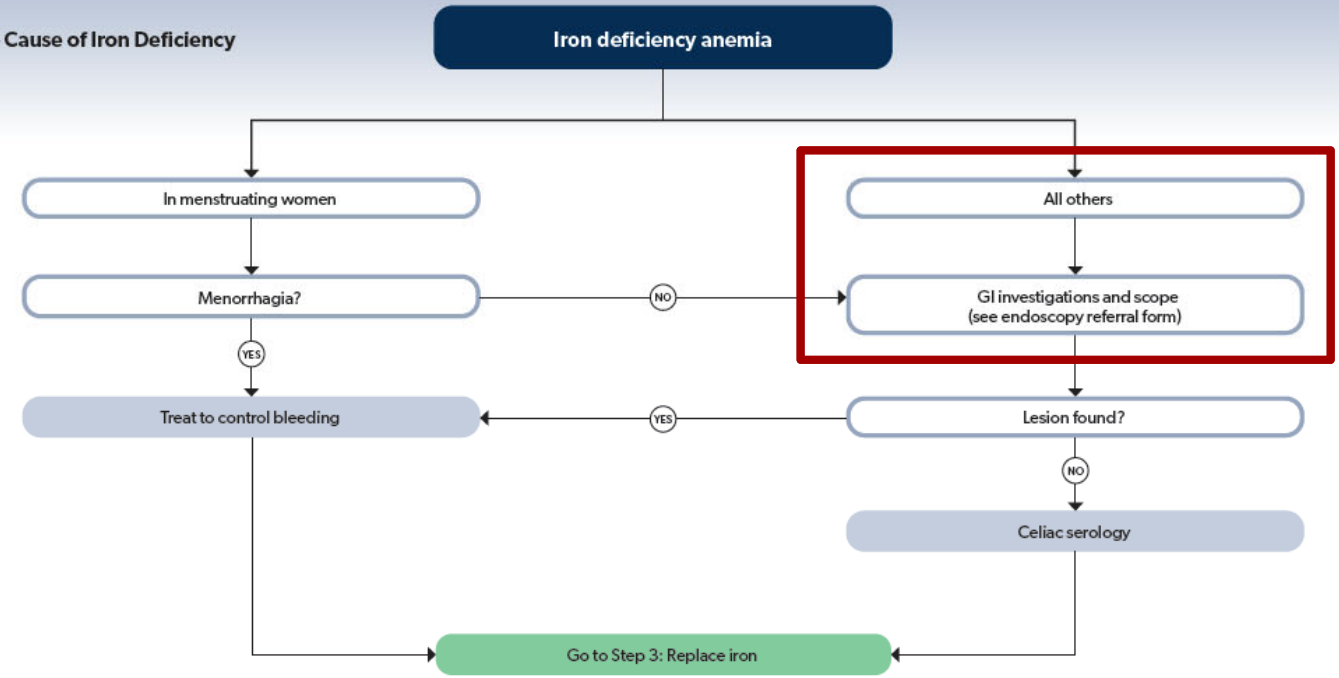
Step 2: Investigate Cause of Iron Deficiency



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GI investigations

- Endoscopy referral for upper/lower scope
  - FOBT is NOT recommended when ID/IDA present

SEMI-URGENT *(4 WEEKS)*

- ☐ Concerning/High risk rectal bleeding
  NOTE: ONLY if symptoms have not been investigated recently AND one or more of: weight loss, new change in bowel habits, new anemia, or family history of colorectal cancer (Include: CBC)
- ☐ Unexplained iron deficiency anemia (Include: CBC and ferritin, iron/TIBC and creatinine)
- ☐ Bloody diarrhea/features suggestive of Inflammatory bowel disease (IBD) (Include: CBC, ferritin, albumin)
- ☐ Severe/Progressive odynophagia/dysphagia (Include: CBC)
- ☐ FOBT positive – (Include FOBT result) (NOTE: FOBT only in ages 40 - 75 years of age and not a single office-based FOBT from DRE)
- ☐ Suspected stable upper GI bleed (Include CBC) Details: _____

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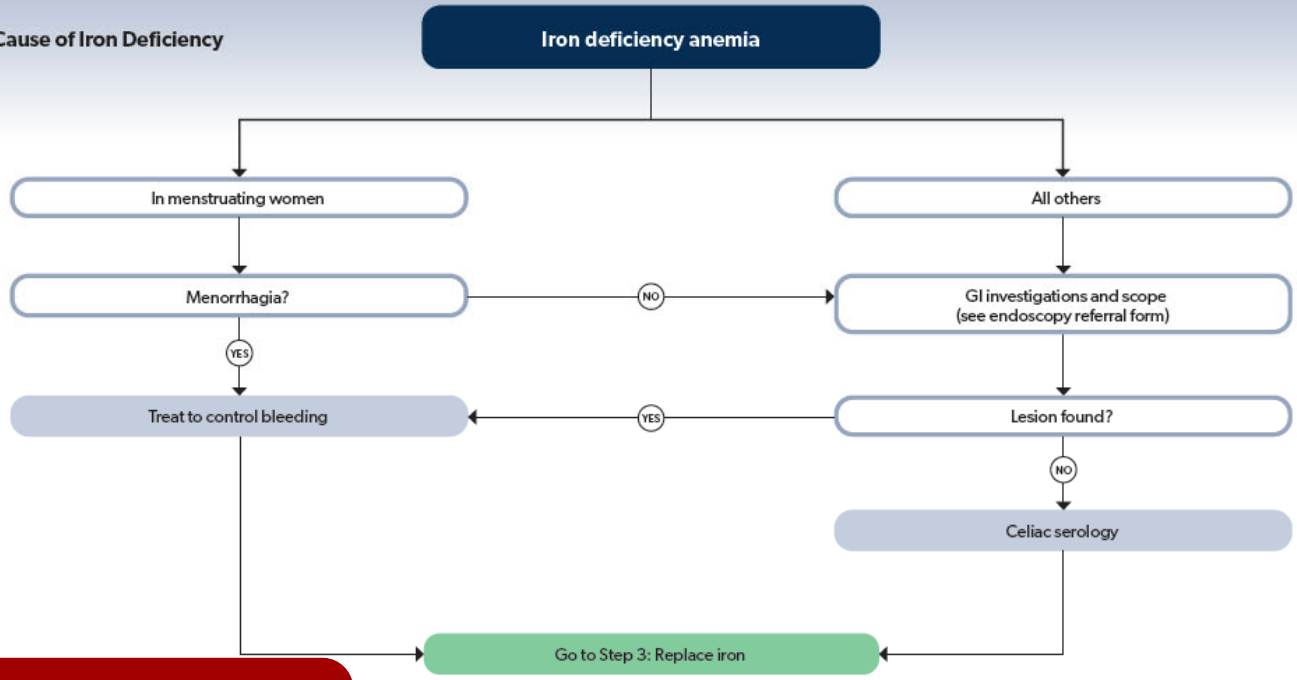
Step 2: Investigate Cause of Iron Deficiency



Additional tests to consider:
Urinalysis
Hemolysis screen: LDH, haptoglobin

Legend: **T sat** = transferrin saturation (iron / TIBC)
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Step 3: Iron replacement

- When to treat:
  - When ID confirmed AND causes considered
  - With anemia, but likely without anemia
- Oral iron supplementation
  - Preferred
- Intravenous iron
- Avoid RBC transfusion in IDA unless hemodynamic instability

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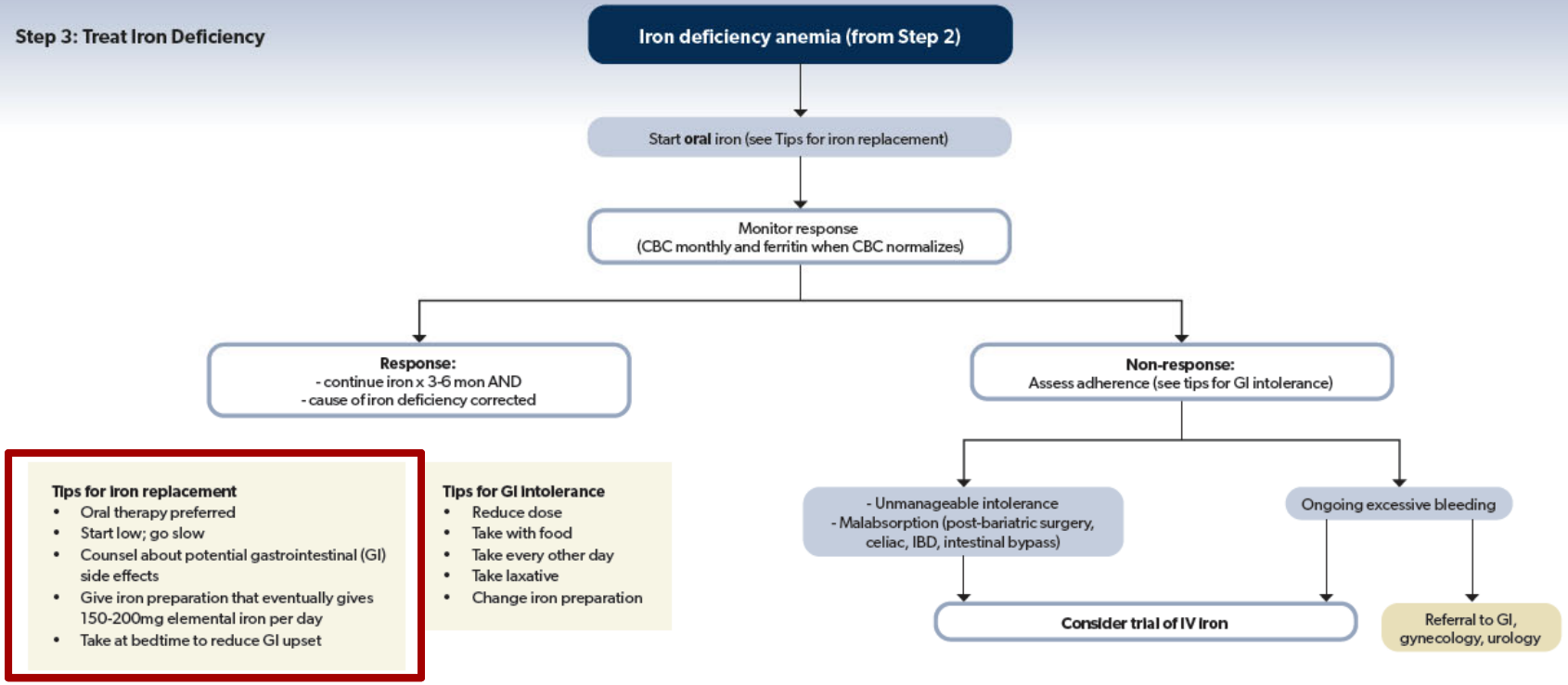
Step 3: Treat Iron Deficiency



Tips for iron replacement

- Oral therapy preferred
- Start low; go slow
- Counsel about potential gastrointestinal (GI) side effects
- Give iron preparation that eventually gives 150-200mg elemental iron per day
- Take at bedtime to reduce GI upset

Tips for GI intolerance

- Reduce dose
- Take with food
- Take every other day
- Take laxative
- Change iron preparation

Legend: **T sat** = transferrin saturation (iron / TIBC)
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Oral iron preparations (Full Replacement doses)

Recommended first line

Unproven claims of increased GI tolerability

Ferrous gluconate	~35 mg elemental iron /300 mg tab (target dose: 4-6 tabs per day)
Ferrous sulphate $10 /mo	~60 mg elemental iron /300 mg tab (target dose: 2-3 tabs per day)
Iron fumarate	~108 mg elemental iron /300 mg tab (target dose: 1-2 tabs per day)
Ferrous sulphate elixir	44 mg elemental iron / 5 mL (target dose: 15-20 mL)
Polysaccharide iron complex (FeraMAX) $22 /mo	150 mg elemental iron per capsule (dose is 1 capsule OD)
heme-iron polypeptide (Proferrin)	11 mg of elemental iron per tab

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Which oral supplement is preferred?

Which one is most efficacious?

- The one with the most iron

Which one is best tolerated?

- The one with the least iron

- There is no evidence that one preparation is more effective than another or has fewer side effects than another[1]

1. Cancelo-Hildalgo MJ et al. 2013. Tolerability of different oral iron supplements: a systematic review. *Curr Med Res Opin*. 2013;29(4):291.

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Oral vs. Parenteral Iron

	Oral	IV
Pro	Inexpensive ($5 – 25 /mo)	Fewest GI side effects
	No risk of anaphylaxis	Certain compliance
	Does not require clinic visit	Rapid correction of anemia
	Lengthy Tx duration	Malabsorption? Still works
Con	Highest incidence of GI side effects	Iron dextran associated with anaphylaxis
	May be insufficient in the face of substantial bleeding	Requires 3-4 hour infusion/trip to centre*
	Requires consistent adherence of the patient	Patients can feel ill after large doses

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When to consider IV iron?

- Intolerance to more than 1 oral regimen, even when ramping up slowly and taking with food and management of constipation
  - Try iron sulphate elixer EOD
- Malabsorption syndromes
- Inflammatory bowel disease
- Post gastric bypass surgery
- Chronic kidney disease – on dialysis (standard of care)

**In almost all instances, try oral replacement first

Barriers to Practice Change

- Access to IV iron is challenging in Winnipeg
  - Community hematology (Dr. Harris) can provide some of this service to patients in Winnipeg
  - If patient followed by gastroenterologist, they should be able to provide this as well
  - Rural MD are encouraged to provide in local hospital

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Take home message(s)

- Iron deficiency anemia is common
- Oral iron supplementation is preferred
- Forewarn patients about GI side effects
- Start low, go slow

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Thank you

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