Women's Health Care
Iron Deficiency

May 16, 2025 | Kylee Martens, MD and Johanna Nesse, FNP

Objectives

- Understand the approach to iron deficiency
- Identify causes of iron deficiency and defining features of heavy menstrual bleeding
- Compare and contrast treatment options for iron deficiency

Case

- 25 yo female here for annual follow up
- Up to date on maintenance screening
- No chronic medical problems or meds
- ROS:
  - +fatigue
  - +poor concentration
  - +decreased exercise capacity

Ferritin 15 ug/L (ref 20-200)
Hgb 12.1 g/dL (ref 12-16)

Approach to Iron Deficiency

Approach to Management

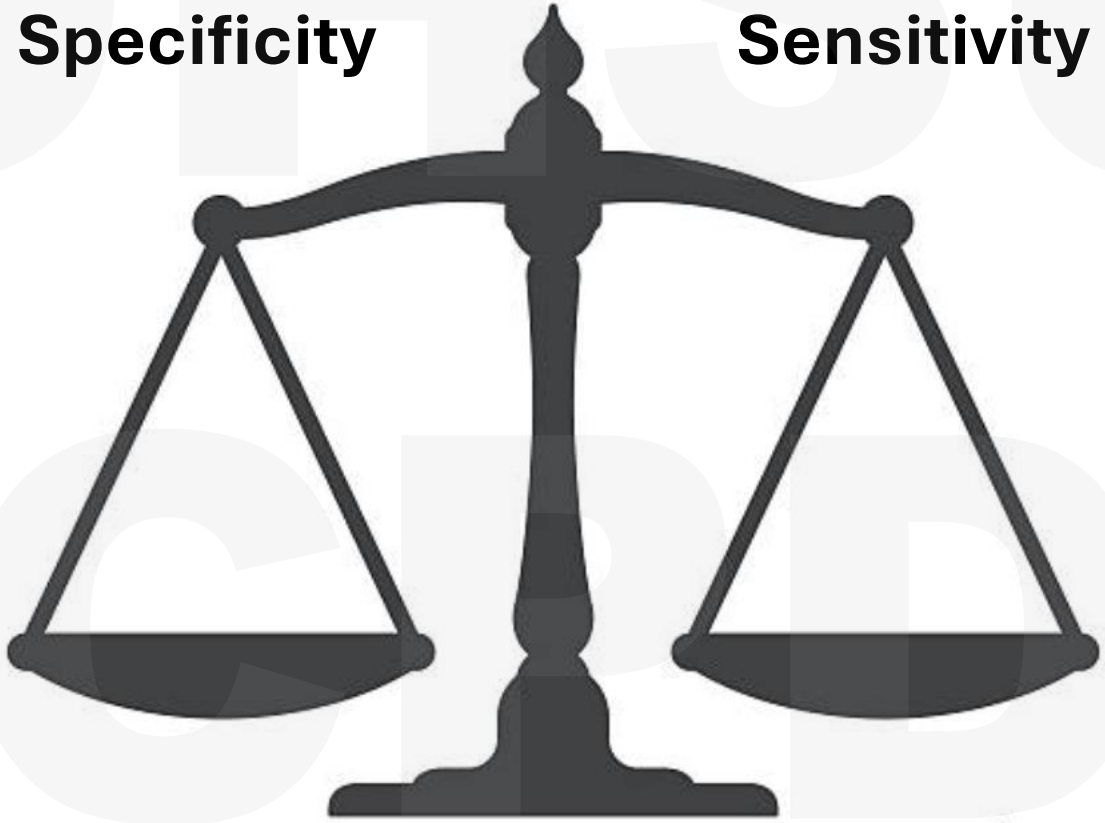
1. Confirm the diagnosis
2. Identify the cause
3. Correct or manage the cause
4. Provide iron therapy, IV or PO
5. Confirm repletion and monitor

Optimal threshold to define iron deficiency?

Specificity **Sensitivity**

WHO 2022
Ferritin < 15 ug/L

98% specific 75% sensitive



AGA Guidelines
Ferritin < 45 ug/L

92% specific 85% sensitive

Movement toward a higher (and standardized) threshold…

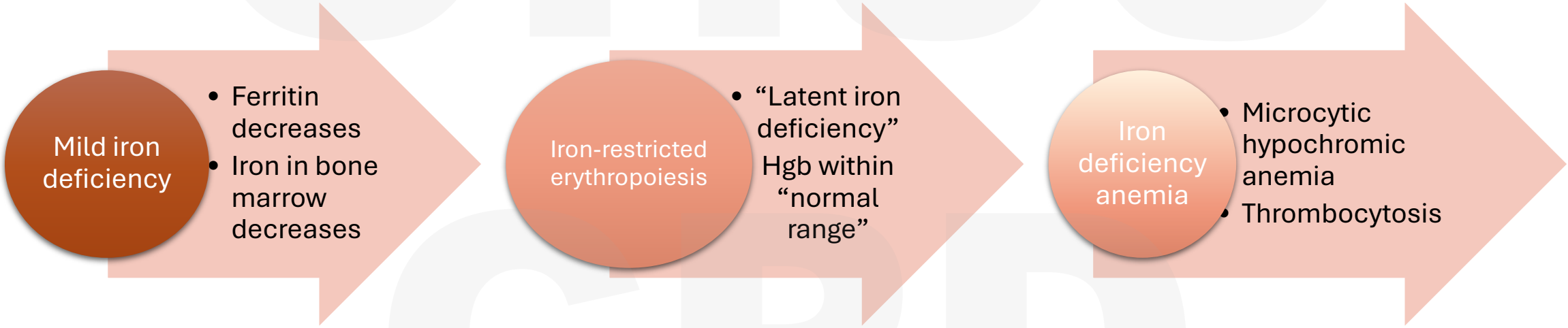
- Physiologic studies using stable iron isotope[1]
  - Increased iron absorption in GI tract in iron deficiency
  - Physiologic compensation does not return to baseline until ferritin >50

- Multiple studies demonstrating improvement in fatigue when ferritin repleted > 50 ug/L in adults[2,3]

[1]Galetti et al. E Clin Med 2021
[2]Beutler et al. Ann Intern Med 1960
[3]Vaucher et al. CMAJ 2012

Iron deficiency exists on a spectrum

Iron deficiency even in the absence of anemia can be symptomatic!



- Fatigue
- Lethargy
- Cold intolerance

- Decreased exercise capacity
- Reduced concentration
- Pica/ restless leg syndrome

- Palpitations
- Dizziness
- Shortness of breath

Case continued

- You astutely diagnose your patient with iron deficiency
- Now what??

Approach to Management

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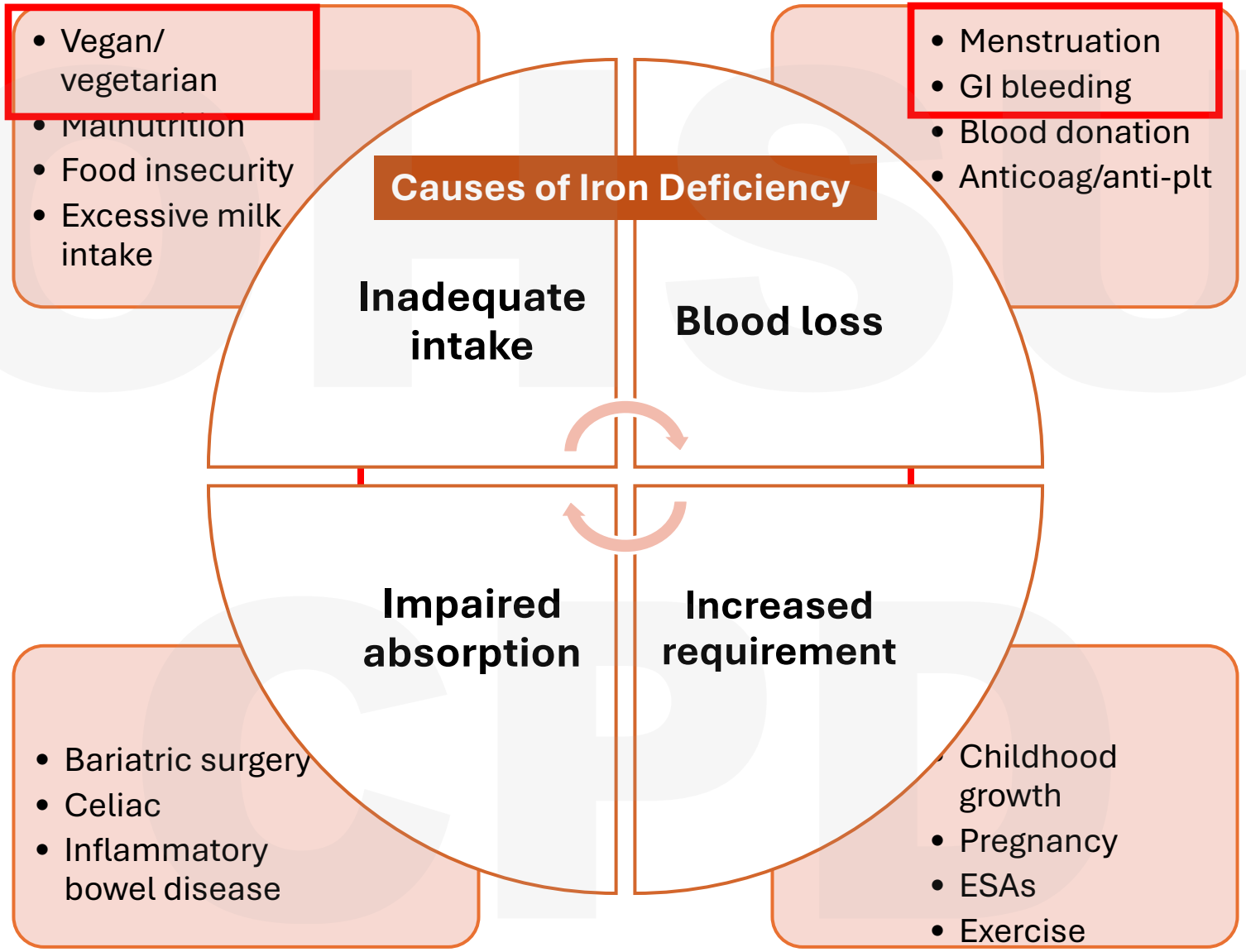
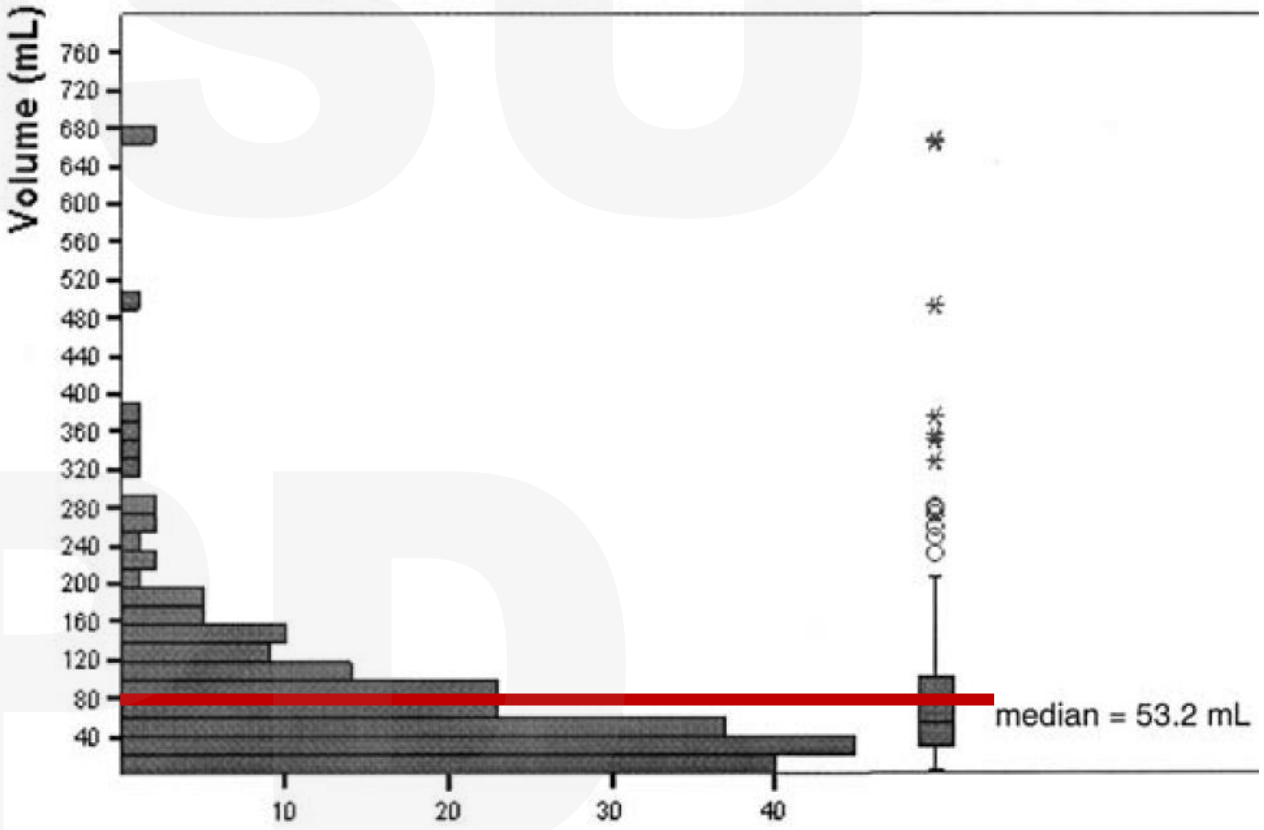

Causes of Iron Deficiency
Inadequate intake
Blood loss
Impaired absorption
Increased requirement
• Vegan/ vegetarian
• Malnutrition
• Food insecurity
• Excessive milk intake
• Menstruation
• GI bleeding
• Blood donation
• Anticoag/anti-plt
• Bariatric surgery
• Celiac
• Inflammatory bowel disease
• Childhood growth
• Pregnancy
• ESAs
• Exercise

Menstrual bleeding: normal vs abnormal?

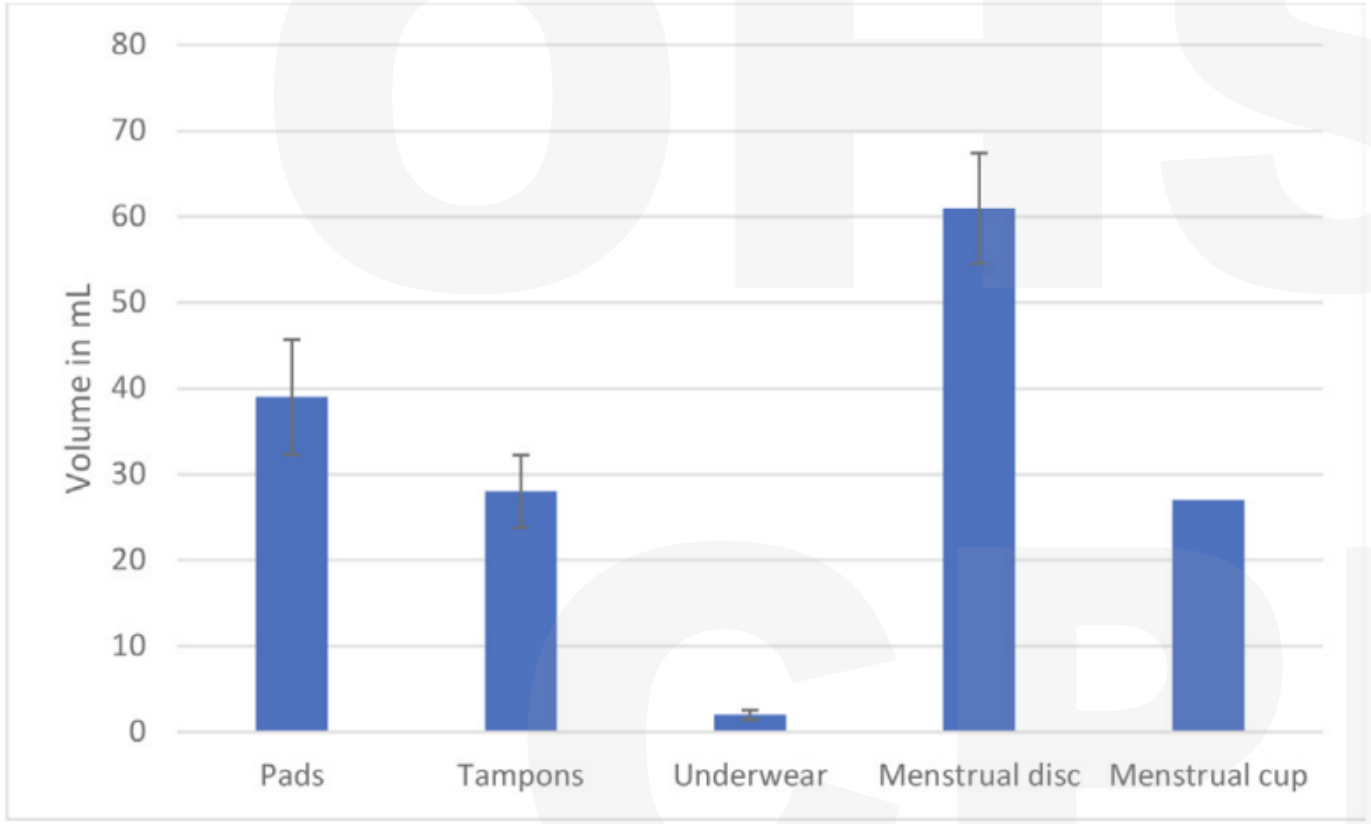
- Menorrhagia I Study
  - 226 individuals completed menstrual blood collection
  - 34% had losses **>80 mL/cycle**

- Clinical predictors
  - Low ferritin
  - Clots > 1 inch in diameter
  - Changing protection > hourly



Warner et al. Am J Obstet Gynecol 2004

Three questions



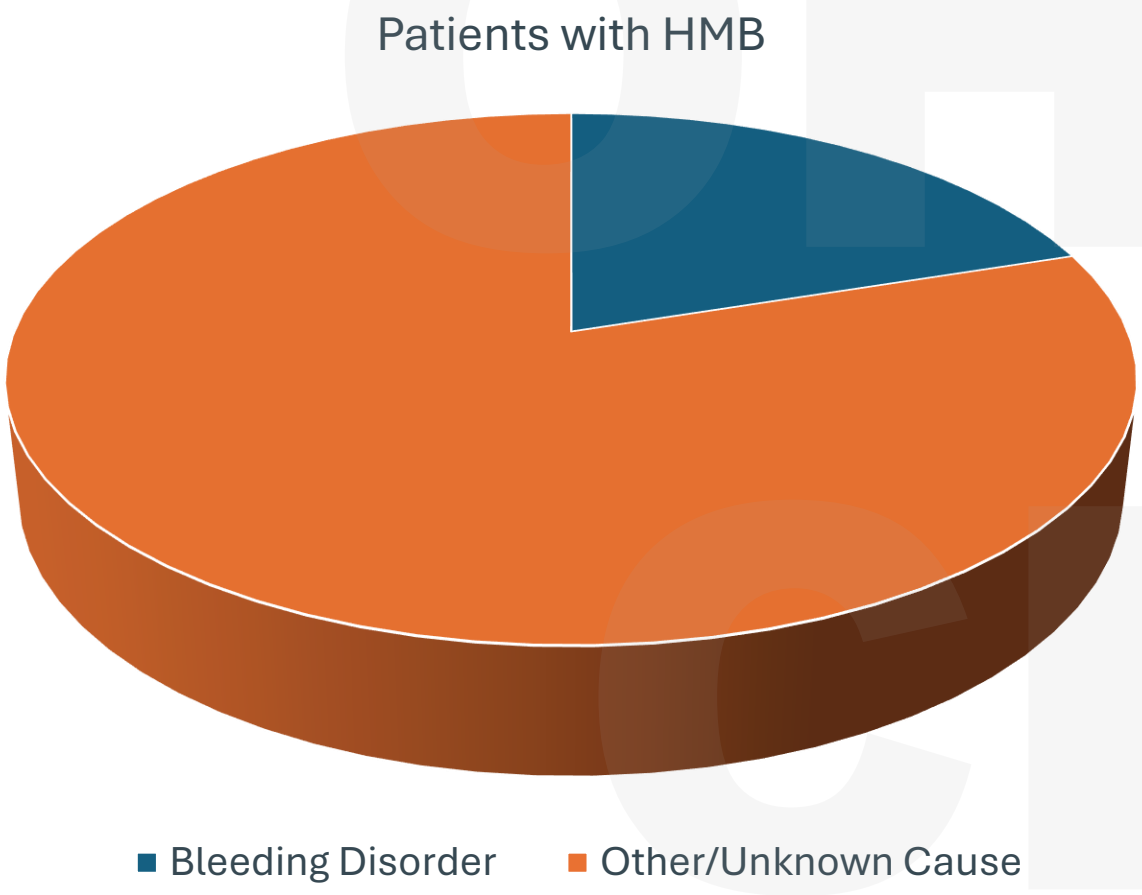
Deloughery et al. BMJ Sex Reprod Health 2024

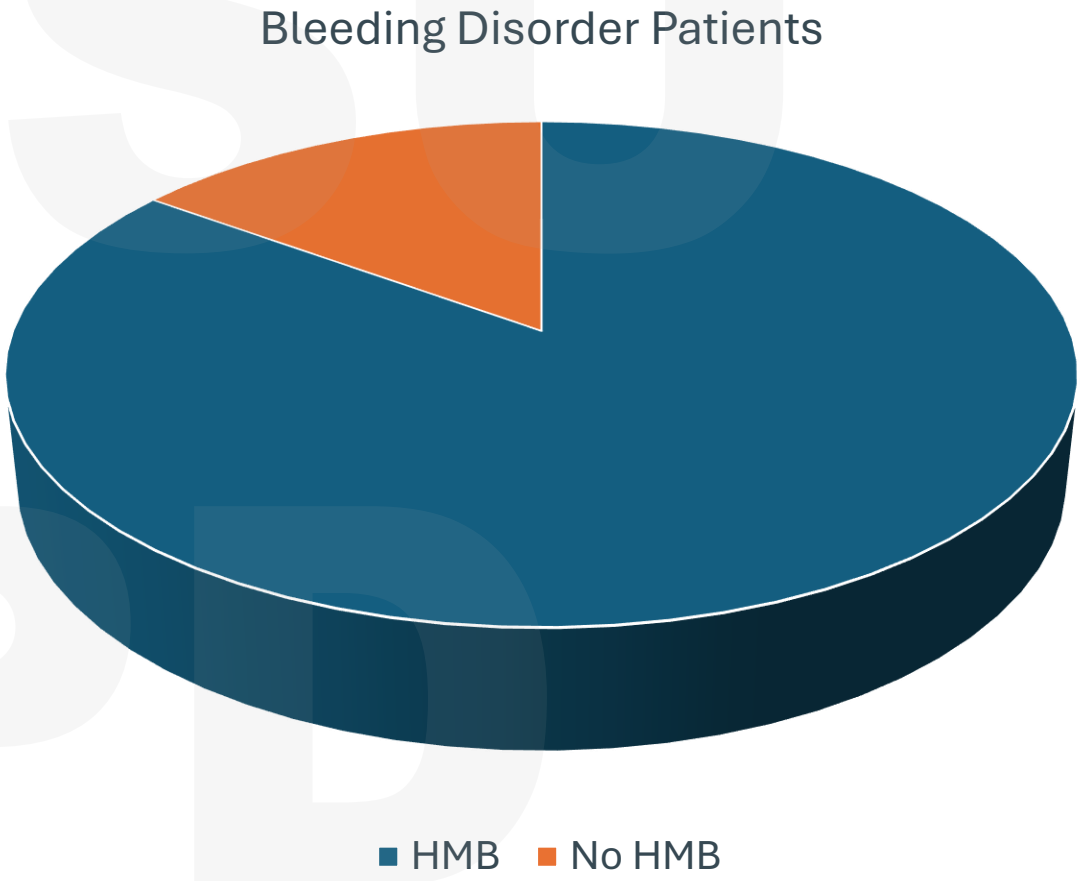
- How often do you change protection?
  - Including "doubling up" on protection
  - And the *type* of protection
- Do you pass clots > 1 inch?
- Have you ever been diagnosed with iron deficiency?
  - Check a ferritin!

7-2-1 Rule

- Cycles lasting longer than 7 days
- Changing menstrual protection more often than every 2 hours
- Passing clots > 1 inch (or a quarter in size

HMB and bleeding disorders





Patients presenting with HMB

- Bleeding history
- Family history
- Gynecology referral
- Labs:
  - Ferritin + CBC
  - Coags/fibrinogen, vWD panel

LET'S TALK PERIOD

HOME ABOUT OUR THINKING SELF-BAT RESOURCES

www.letstalkperiod.ca

Case continued

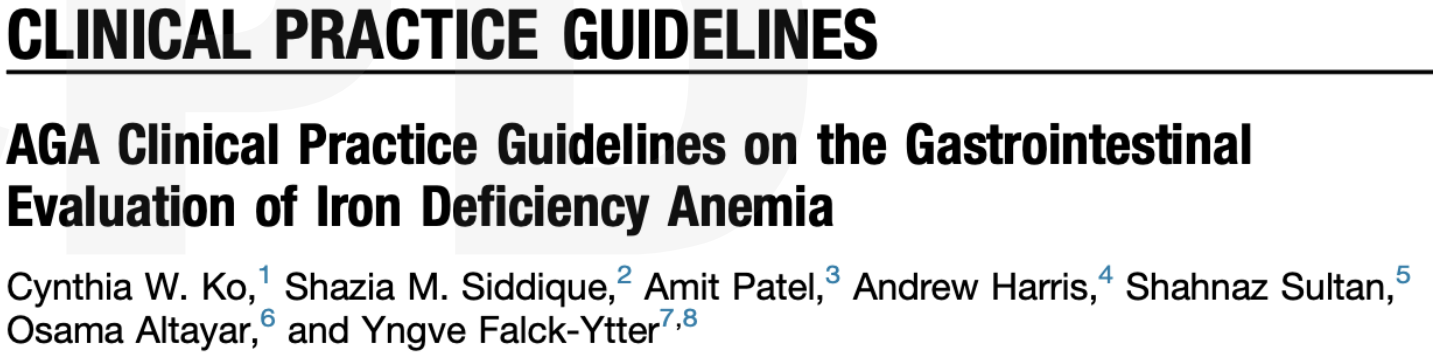
- Confirms she is amenorrheic
- Mirena IUD placed 2 years ago
- No dietary restrictions

- What next?

When to consider GI workup?

- In postmenopausal women and men with iron-deficiency anemia, the AGA recommends bidirectional endoscopy over no endoscopy

- In premenopausal women with iron deficiency anemia, the AGA suggests bidirectional endoscopy over iron replacement therapy only



CLINICAL PRACTICE GUIDELINES

AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia

Cynthia W. Ko,[1] Shazia M. Siddique,[2] Amit Patel,[3] Andrew Harris,[4] Shahnaz Sultan,[5] Osama Altayar,[6] and Yngve Falck-Ytter[7,8]

Key Takeaways

- Yield of endoscopy in asymptomatic premenopausal individuals is likely to be low

- Consider historical blood loss and/or inadequate repletion

- Trial iron therapy:
  - If ferritin is stable, continue monitoring
  - If recurrent, especially if requiring >1 iron infusion/yr -- recommend additional workup

Case continued

- History of heavy menstrual bleeding now resolved with mirena IUD
- Asks about next steps…

Approach to Management

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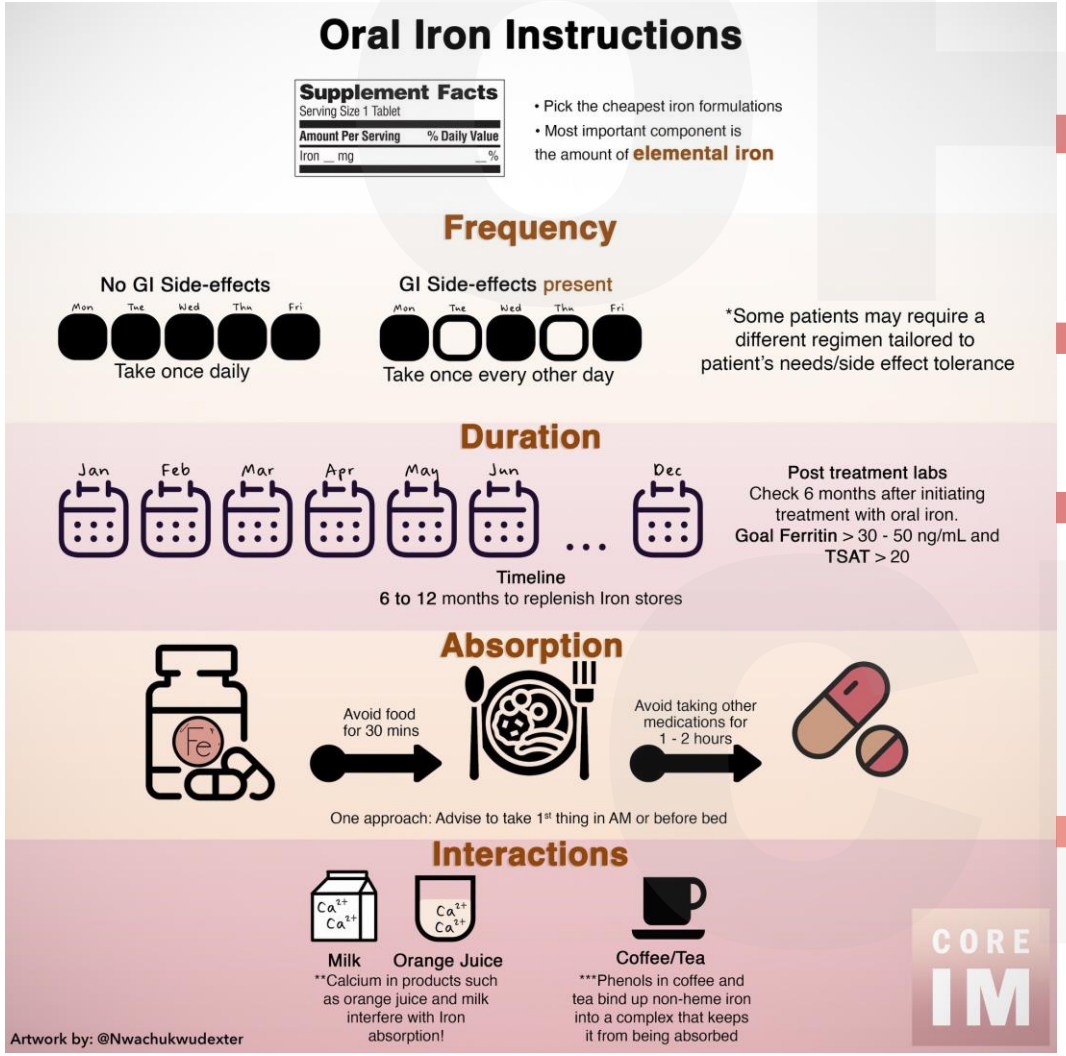
Best practices for oral iron administration



Formulation: iron salt (i.e., ferrous sulfate, gluconate)
Dosing: 60-110mg **elemental** iron daily

Frequency: daily dosing = faster time to correction
Consider QOD if GI side effects (nausea, constipation)

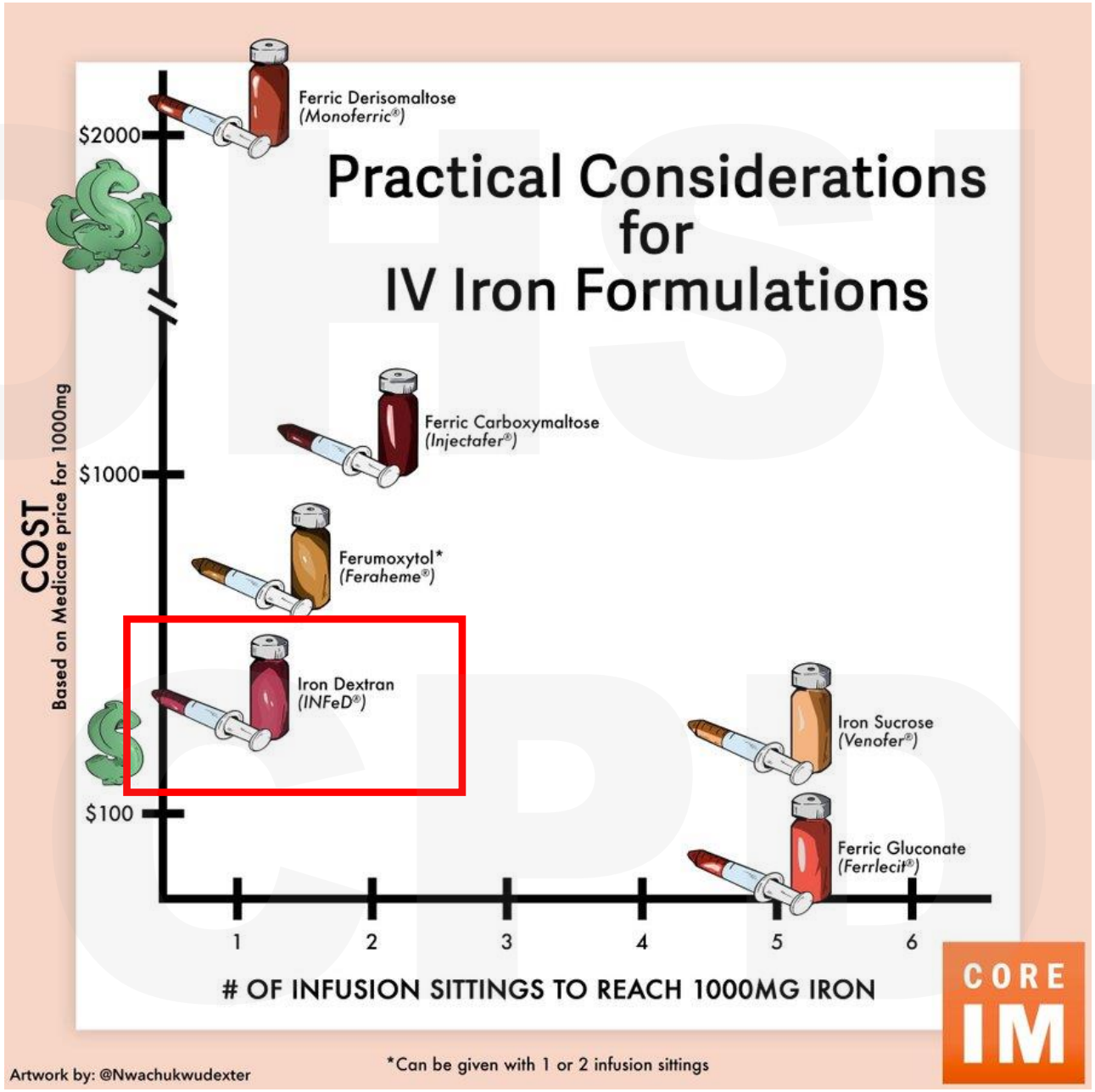
Labs: check ferritin and CBC in 4 weeks
Expect Hgb rise ~1g/dL

Absorption inhibited by:
- divalent cations (Ca and Mg)
- phytates (seeds and grains)
- tannins (tea and coffee)
- medications (PPIs, H2 blockers)

https://www.coreimpodcast.com/2024/03/27/fe-deficiency-treatment-5-pearls-segment/

Indications for IV iron

- Inadequate response or intolerance to oral iron
  - 3 month trial of oral iron
- Rapid repletion indicated
  - Pregnancy (2nd and 3rd trimesters)
  - Preoperative
- Chronic and/or rapid blood loss
- Impaired GI absorption
  - Inflammatory bowel disease
  - Bariatric surgery
- Chronic inflammatory conditions
  - HFrEF
  - CKD


Practical Considerations for IV Iron Formulations
COST
Based on Medicare price for 1000mg
$2000
$1000
$100
Ferric Derisomaltose (Monoferric®)
Ferric Carboxymaltose (Injectafer®)
Ferumoxytol* (Feraheme®)
Iron Dextran (INFeD®)
Iron Sucrose (Venofer®)
Ferric Gluconate (Ferrlecit®)
1
2
3
4
5
6
OF INFUSION SITTINGS TO REACH 1000MG IRON
Artwork by: @Nwachukwudexter
*Can be given with 1 or 2 infusion sittings
CORE IM

IV iron infusion reactions

JAMA Network Open

Original Investigation | Hematology

Analysis of Adverse Events and Intravenous Iron Infusion Formulations in Adults With and Without Prior Infusion Reactions

Asad H. Arastu, MD; Benjamin K. Elstrott, BA; Kylee L. Martens, MD; Jonathan L. Cohen, PharmD; Michael H. Oakes, MD; Zhoe T. Rub, MS; Joseph E. Aslan, PhD; Thomas G. DeLoughery, MD; Joseph Shatzel, MD

- No difference in rate of reactions between formulations
  - Avoid ferric carboxymaltose if able (hypophosphatemia)

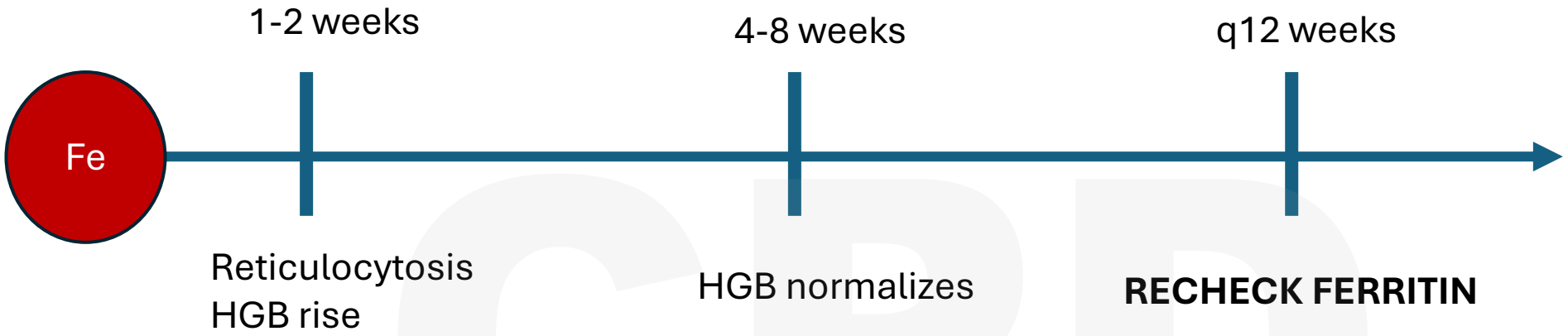
- Two types of reactions:
  - Anaphylaxis (incidence <1:200,000)
  - Fishbane reaction (incidence 1-3%)
    - NOT life threatening
    - Symptoms: back pain, arthralgias / myalgias, flushing, chest tightness
    - Treatment: pause infusion and start at slower rate

- Routine pre-meds are <u>not indicated</u> unless history of anaphylaxis or inflammatory arthritis

- Flu-like symptoms (headache, mild fever, myalgias)
  - Onset: 2-5 days post-infusion
  - Self-resolve in 24-48 hours

Monitoring

- Confirm repletion and monitor for recurrence



Key Takeaways

- Iron deficiency in the absence of anemia can be symptomatic and should be treated
- Taking a detailed menstrual history is essential… and consider GI evaluation in unexplained iron deficiency
- Frequently reassess response and tolerance of oral iron
- IV iron should be considered first-line in certain populations (i.e., pregnancy, CKD, HFrEF, IBD, bariatric surgery, chronic bleeding)