Evaluating Anemia:
When to Refer, When to Follow

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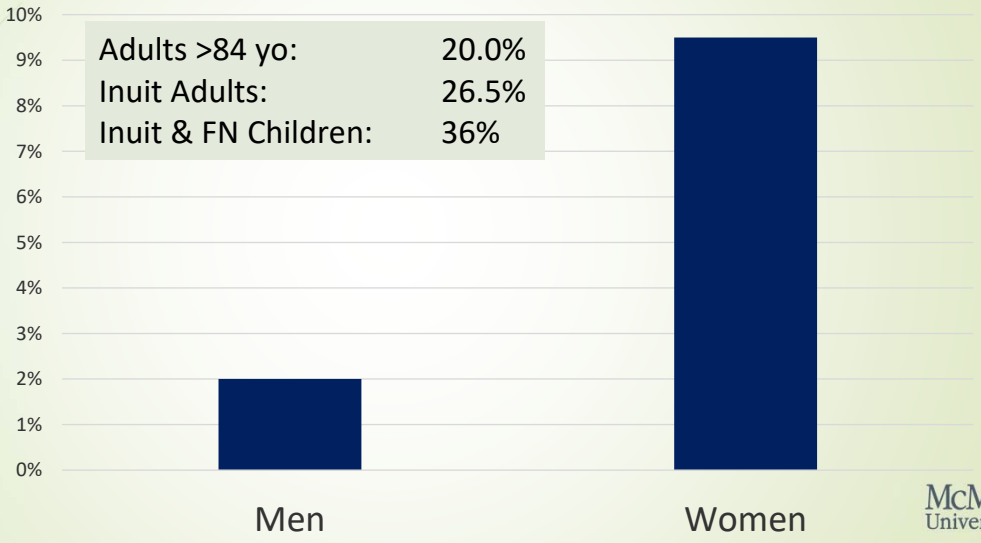
The Scope of the Problem



Adults >84 yo:	20.0%
Inuit Adults:	26.5%
Inuit & FN Children:	36%

Kenny TA et al. BMC Nutrition. 2019 Dec 1;5(1):30.
World Health Organization, Global Health Observatory Data Repository/World Health Statistics (http://apps.who.int/gho/data/node.main.1?lang=en)
Patel KV. Epidemiology of anemia in older adults. Semin Hematol. 2008;45:210–217.

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What are going to discuss?

- A simplified approach to anemia that will help you…
  - rapidly sort through causes of anemia
  - identify “red flags” in anemia presentation
  - treat and monitor common causes of anemia
- We’ll end with a case-based discussion of iron deficiency – a common foe!

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Treat the patient, not the numbers

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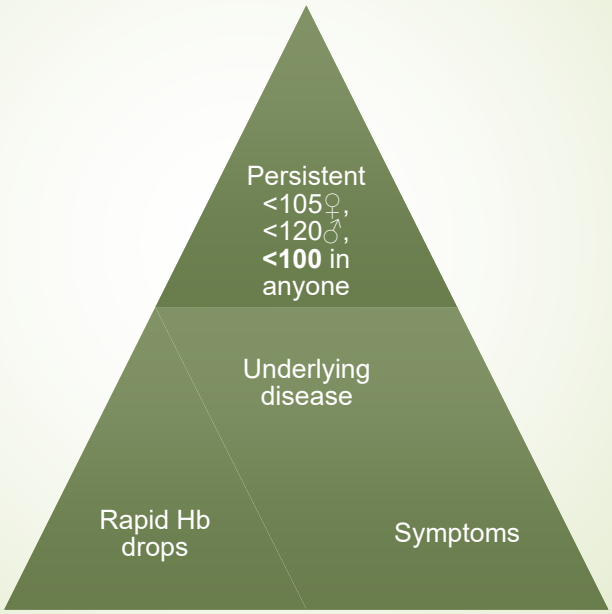
When should you care about anemia?



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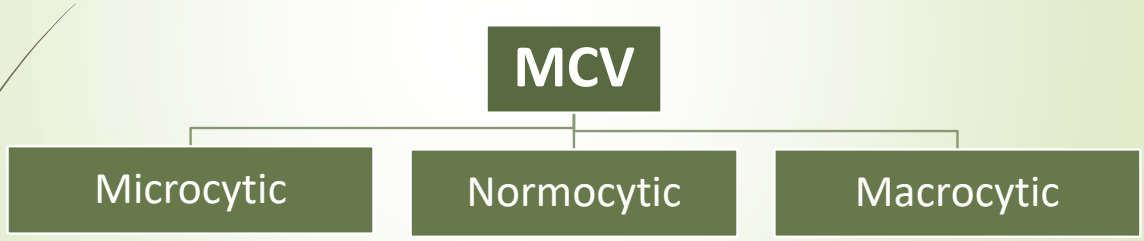
We commonly categorize anemia based on red cell size (MCV)



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The MCV approach can be problematic

- Mixed conditions not captured (anemia of chronic inflammation, B12 + Fe deficie
- Ignores other valuable clues in t BC
- Laundry lists don't help u age patients

A More Action Oriented Approach?

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Make your lab results do the work!

- Is the lab trying to tell me something?
- Is the rest of the CBC normal?
- Think about microcytic anemias
- Think about macrocytic anemias
- Think about normocytic anemias

BONUS QUESTIONS:
Kidney responsible?
Patient elderly?

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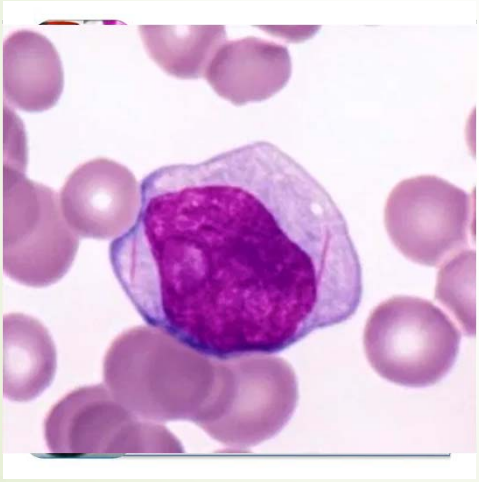
Question 1. Is the lab trying to tell me something?



- Always read the comments on the CBC!
  - Fragments, nucleated RBCs, spherocytes, hemolysis, blasts

Wikipedia

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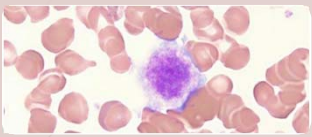
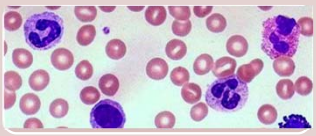
Question 2. Is the rest of the CBC normal?



PLATELETS

- High plts seen in iron deficiency
- Low plts seen in autoimmune disease



WBC

- High WBC seen in cancer or infection
- Low WBC seen in autoimmune disease

- Bone marrow may be the culprit
  - I worry about plts <75 - 100 x 10^9/L
  - I REALLY WORRY about plts <20 x 10^9/L
  - I want to know *which* WBC subtypes are low or high, not total WBCs

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Question 3. Microcytic: Is the patient iron deficient? (Are you sure?)

- Iron deficiency is a “bathtub problem”
  - Ask about GI blood loss, consider endoscopy referral, test for celiac
  - Ask about menses and pregnancy, manage menstrual bleeding, consider gyne referral
  - Hematology referral is almost never useful!

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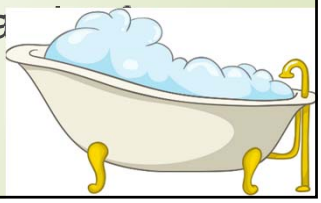
Question 3. Microcytic: Is the patient iron deficient? (Are you sure?)

- Order a ferritin… then a transferrin saturation
  - Ferritin ONLY useful when it’s <40 in an anemic patient
  - Transferrin saturation <20% tells us iron delivery impaired
  - Explore “inflammatory disease” a accordingly



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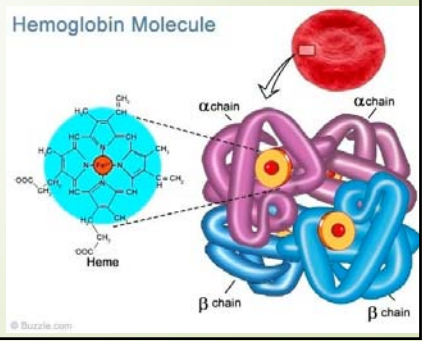
Microcytic: Other blood cell shrinkers

- Microcytosis can be further explored by…
  - Hemoglobinopathy testing
  - Lead levels
  - Bone marrow exam



Buzzle.com

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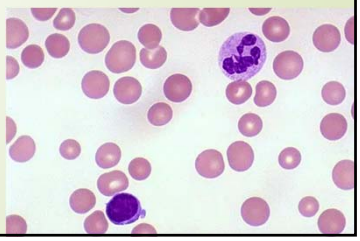
Question 4. Macrocytic: Is the patient B12 deficient? (Are you sure?)

- Most hematologists believe “normal” B12 is >200 pmol/L
  - Watch out for megaloblastic changes, neurocognitive effects
  - Should you run other tests?
  - Parenteral vs oral B12?
  - Is all B12 deficiency “pernicious anemia?”



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Macrocytic: Other blood cell expanders

- Betting that it's not folate deficiency is a good bet
- Macrocytosis can be further explored by…
  - A thorough history, physical, social history, and med list
  - A look at the other cells

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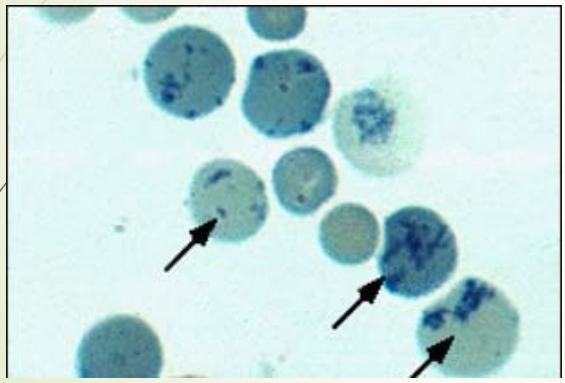
Question 5. Normocytic anemia: Retics, LDH, bili



- Scary causes involve hemolysis, bleeding, and malignancy
- **Retic count** should go UP with worsening anemia IF the marrow and erythropoeitin response is normal
- **LDH and bili** are quick ways to rule out hemolysis
- Look for other lab clues!

eClinPath

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Bonus question: Is the kidney responsible?

- Look for low eGFR (<60), low reticulocytes, and maybe a low erythropoeitin level
- Consider ordering SPEP, IFE, and qIg to rule out multiple myeloma! (And check a calcium and a skeletal survey to confirm your suspicions)
- Anemia of renal failure is tough to manage
- It is not always necessary to "fix" it

https://www.ontariorenalnetwork.ca/

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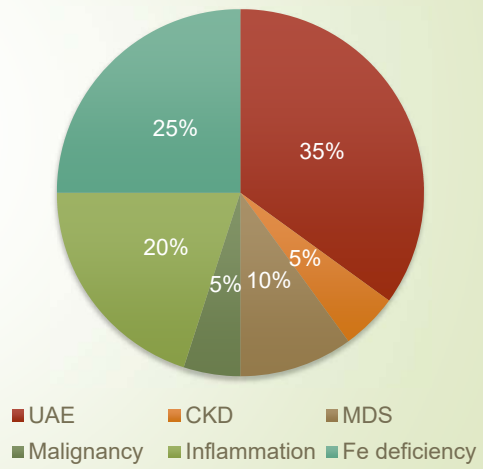
Bonus question: Is the patient elderly?

- 10% to 25% of community dwelling elderly are anemic
- It is associated with adverse outcomes



Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. American journal of hematology. 2014 Jan;89(1):88-96.

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What is UAE (unexplained anemia of the elderly)?

- A hypoproliferative normocytic anemia ("sluggish marrow")
  - Blunted Epo production?
  - Sluggish response to Epo and reticulocyte production?
  - Reduced testosterone?
  - Increased IL-6?
- Guiding principles:
  - Don't miss underlying treatable disorder
  - Pay attention to symptoms
  - Don't treat unexplained, n ymptomatic anemia

Treat the patient, not the numbers

Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. American journal of hematolog 00

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Three patients with iron deficiency – and some evidence around treatment

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Patient 1

- A 29 year old nurse (born in Hamilton, parents from Laos) has just joined your practice. She is diligent about taking her daily ferrous sulfate, but it doesn't seem to work! She feels run down.

WBC 5.5	Ferritin 4
Hb 90	TSAT 0.11
MCV 70	Creat 70
Plt 390	Retic 90

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POLLING Q 1

- What's the best next step?
  - a) Repeat CBC
  - b) Hemoglobinopathy screen
  - c) Repeat ferritin
  - d) Take more history

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Patient 1

On further questioning, she tells you her period is 7 days long, with 3 heavy days. She changes her tampon hourly on heavy days, has frequent accidents, and her menses interfere with her QOL.

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Iron deficiency caused by heavy menstrual bleeding is a bathtub problem

- **In my lane**
  - Tranexamic acid 500 mg tablets, 1-2 q 8 hours on the 2-3 heaviest days of your period
  - NSAIDs
- **Not in my lane**
  - Progestin only IUD
  - Cyclic oral progestins
  - Surgery
  - Other strategies for managing structural causes of heavy menstrual bleeding

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PATIENT EDUCATION

HHS ONTraC Patient Blood Management

Choosing an Iron Pill

ONTraC

Always start with taking 1 pill a day. If you tolerate it well, increase the amount after 3 to 4 days to the recommended amount. The most common side effects are constipation or diarrhea, stomach discomfort and dark or black stool. This is more common with the last 3 pills (iron salts) listed below. Do not take iron at same time as antibiotics, Parkinson or thyroid medications.

Iron pills	Amount	Approximate cost per day	Information
Heme-Iron Polypeptide examples — **Optifer®α**, **Proferrin®**	One tablet (11 mg) 1 to 3 times a day or per doctor's advice	**59¢ to $1.77 a day** $58.89 for 100 tablets (Optifer®α)	Very easy to absorb. Take with or without food. Excellent choice if you are prone to constipation or upset stomach or take medicines that reduce stomach acid.* These pills are made from animal proteins (bovine source). Do not take if you have an allergy to cow products.
Polysaccharide-Iron Complex examples — **EZfer®**, **FeraMAX®**, **Polyride Fe**, **Triferexx®**	One capsule (150 mg) once daily or per doctor's advice	**45¢ a day** $45.49 for 100 capsules (Triferexx®)	Take with vitamin C (ascorbic acid) 250 - 500 mg or with a glass of orange juice. Take with or without food. Good choice if you are prone to constipation or upset stomach. Available in vegan certified capsules. Almost tasteless.
Ferrous fumarate 300 mg tablets examples — **Eurofer**, **Palafer®**	One tablet once daily or per doctor's advice	**25¢ a day** $7.49 for 30 tablets (Palafer)	These pills may also be called 'iron salts'. Take with vitamin C (ascorbic acid) 250 - 500 mg or with a glass of orange juice. Take on an empty stomach — at least 1 hour before or 2 hours after meals or drinking coffee, tea or red wine. Do not take antacids or calcium supplements within 2 hours of taking iron salts. Iron absorption may be decreased if pills are taken with medicines that reduce stomach acid.* Iron salts are more likely to cause … or constipation when compared … formulations. If unable to tolerate stom… taking iron every other day and not … or orange juice.
Ferrous sulphate 300 mg tablets examples — **Feosol**, **Fer-In-Sol**	One to two tablets once daily or per doctor's advice	**3¢ to 7¢ a day** $3.47 for 100 tablets	
Ferrous gluconate 300 mg tablets	One to three tablets once daily or per doctor's advice	**5¢ to 15¢ a day** $5.20 for 100 tablets	

Prices are approximate and subject …ge.

*Examples of brand name medicines that reduce stomach acid are:
Prevacid, Nexium, Tecta, Pantoloc, Losec, Prilosec, Zantac

Hamilton Health Sciences 2020
Original date of completion: 01/2016
Date of last updated: 01/2020
PD 9174

https://www.hamiltonhealthsciences.ca/wp-content/uploads/2019/08/Ch…Pill.pdf

Dosing? Administration? Side effects?

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Best pill taking practices

- Iron salts absorb best on an empty stomach, spaced out from food and calcium carbonate, and with orange juice or vitamin C
- Daily dosing boosts iron stores more effectively, but causes more GI side effects

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Patient 2

- A 66 year old Sunday School teacher has felt fantastic since her bariatric surgery. But she's been "running out of gas" lately. She'd like you to renew her metformin and draw some labs.

WBC 5.5	Ferritin 4
Hb 103	TSH 3.6
MCV 98	Creat 65
Plt 190	HbA1C 5%
Random glucose 7	Retic 30
B12 80	

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POLLING Q 2

- What's the best next step?
  - a) Repeat CBC
  - b) Check folate
  - c) Prescribe oral iron and B12
  - d) Prescribe IV iron and SC B12

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What is the role of IV iron?

- Give IV iron in patients…
  - who can't absorb via the oral route
  - who have been "failed" by oral iron after 3 to 6 months of good adherence
  - with rapid iron loss
  - with elevated hepcidin (anemia of chronic inflammation)
- IV iron is SAFE (0.0005% to 0.1% anaphylaxis)

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Patient 3

- A 59 year old farmer tried to give blood at the Legion, but is declined due to "low blood." He arrives at your office to discuss his lab results. He insists that he feels fine.

WBC 5.5	Ferritin 6
Hb 95	Lytes normal
MCV 68	Creat 80
RDW 25%	Glucose N
Plt 500	

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POLLING Q 3

- What's the best next step?
  - a) FIT testing
  - b) Transferrin saturation
  - c) Hematology referral
  - d) Endoscopy referral

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Iron deficiency is a symptom, not a disease.

(And it's not a hematologic disease!)

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Take Home Messages

- Iron deficiency is a bathtub problem
- Treat the patient, not the numbers
- You can often identify the cause of anemia with clinical assessment and simple lab tests

- Thank you to…
  - Dr. Kate J. Miller
  - Dr. Mickey Zeller
  - My colleagues in laboratory medicine - who work tirelessly to provide safe, timely, high quality care

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