

APPROACH TO AND MANAGEMENT OF ANEMIA

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Freeport Physicians' Education Days Declaration of Conflict of Interest

- Relationships with commercial interests:
 - **Grants/Research Support: None**
 - **Speakers Bureau/Honoraria: Pfizer**
 - **Consulting Fees: None**
 - **Other: None**
- I ***do not intend*** to make therapeutic recommendations for medications that have not received regulatory approval (e.g. off label use)

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Potential for conflict(s) of interest:

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Mitigating Potential Conflict of Interest:

- **Recommendations for drug therapy will be based on peer reviewed journal articles and published guidelines**

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Goal: To review the current approach to anemia in the elderly

Objectives:

- 1. Participants will understand how to approach the diagnosis of anemia in the elderly**
- 2. Participants will be able to appropriately investigate anemia in the elderly**
- 3. Participants will be able to select appropriate treatments for anemia in the elderly**

Definition of Anemia

- World Health Organization Criteria:
 - < 130 g/L males
 - < 120 g/L females

Anemia in the Elderly...

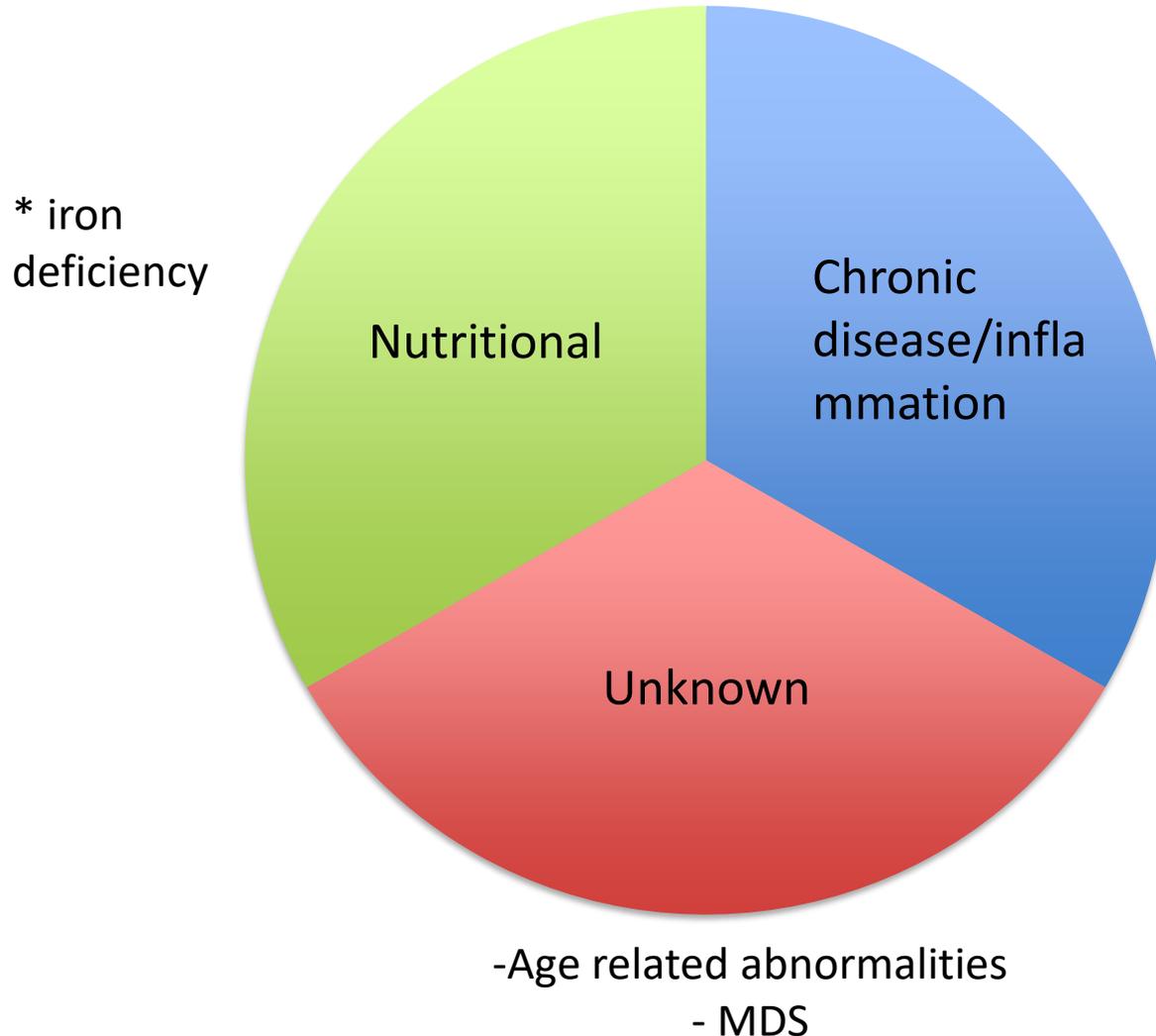
A common issue

- Incidence of anemia in men and women > 65 years old: 11% and 10% respectively
- Increases with age: 20% in individuals >85 years old
- Anemia is usually mild in degree (>100 g/L)

Anemia in the Elderly...

- Despite this, elderly anemia is associated with increased morbidity and mortality and is a risk factor for adverse outcomes
 - Decreased physical performance, increased falls, frailty, decreased cognition, increased dementia, decreased quality of life
- The basis for this negative association is not clear

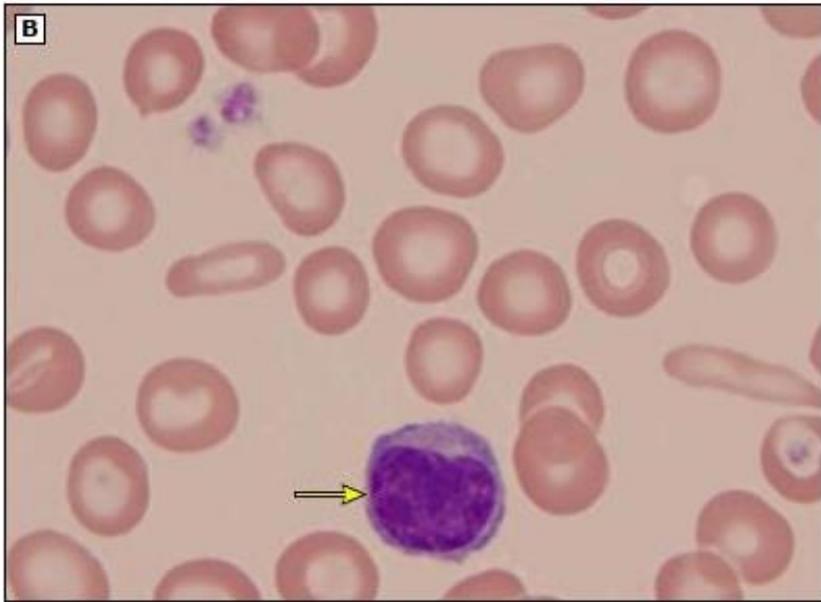
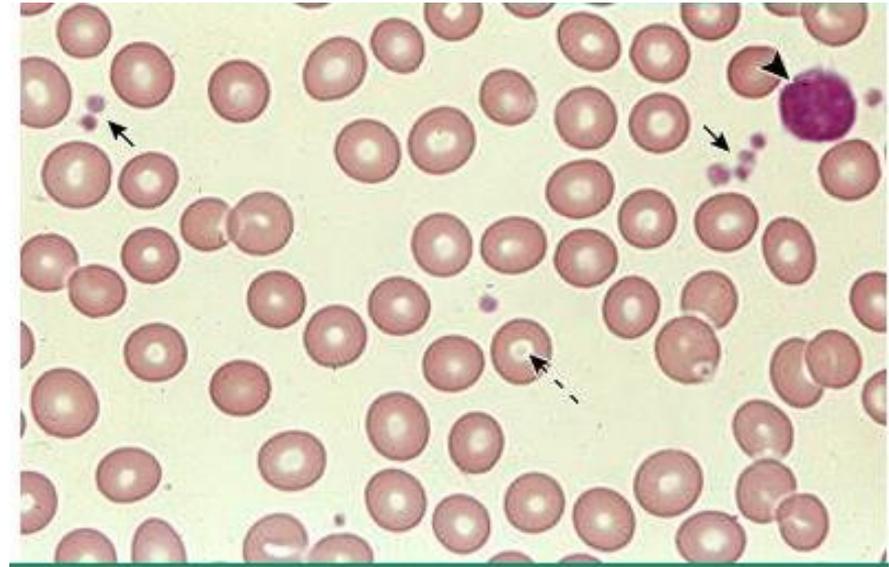
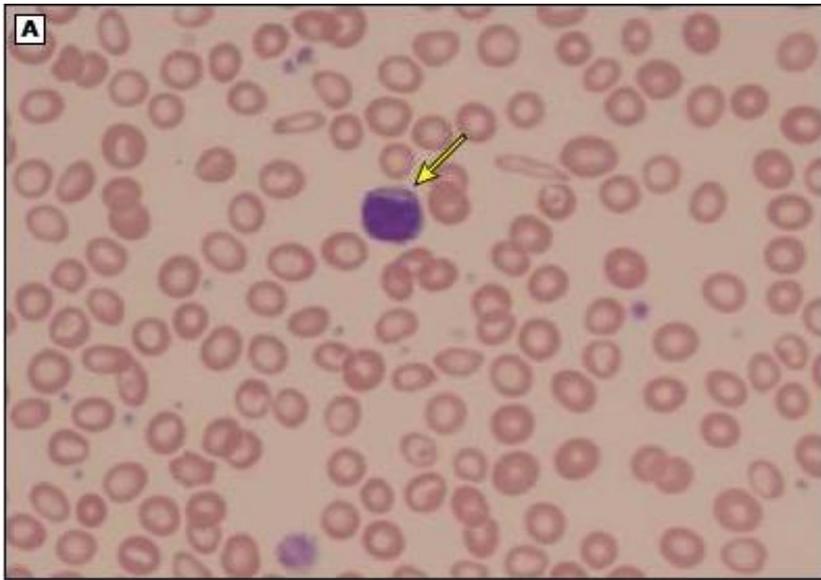
Causes of Anemia in the Elderly





Nutritional – Iron deficiency

- Diagnosis: low MCV, low ferritin (<30mcg/L), low transferrin saturation, low serum iron, high TIBC
- Diagnostic pitfalls in the elderly:
 - Study showed that 22% of elderly patients identified as having iron deficiency anemia (hemoglobin response to a course of oral iron), did not have typical laboratory findings of transferrin saturation < 16% and ferritin < 30 ng/mL
 - MCV does not appear to correlate well with etiology in the elderly:
 - Microcytosis/low MCV present in only 27.5% of elderly patients with iron deficiency
 - Ferritin – acute phase reactant/increases with age
 - Iron studies difficult to interpret in the setting of inflammation





Iron deficiency - Treatment

- Trial of oral Iron:
 - Iron best absorbed on an empty stomach
 - Do not take with dairy or calcium
 - Avoid taking with coffee or tea
 - Can take with Vitamin C containing products to increase absorption
 - Warn patient about side effects (GI upset and constipation) – can take stool softeners if needed
- If cannot tolerate/increment with oral iron can try IV iron



Iron deficiency - Treatment

- Choice of oral iron dependent on patient:

- Ferrous Fumarate:

- 33% elemental iron
- ~\$10/100 tabs
- ODB covered with prescription



- Ferrous Gluconate:

- 10-14% elemental iron
- ~\$10/100 tabs

- Polysaccharide-iron complex:

- Various amounts of elemental iron
- Feramax150: 150 mg elemental iron
- ~100/100tabs





Iron deficiency – follow-up

- Determine the cause:
 - Bleeding (GI investigations)
 - Lack of absorption (Celiac, gastric bypass)
 - Poor intake
- Ensure normalization of hemoglobin with iron supplementation
 - study suggested that only 50% of elderly patients with iron deficiency anemia had full correction of their anemia with repletion of their iron stores – suggesting a multifactorial cause may exist in many patients



Vitamin B12 and Folate deficiency

- Relatively rare causes of anemia in the elderly population
- Study showed ~10-20% anemic elderly individuals have Vitamin B12 deficiency (ie. low B12 levels) but only 10% of those (1-2% in total) had anemia because of that deficiency (ie. most did not have a clear response to B12 supplementation)
- Folate deficiency exceedingly rare – supplementation of flour with folate
- Elderly diagnostic pitfalls:
 - Macrocytosis present in just 7.4% of patients with folic acid/VB12 deficiency



Anemia of Chronic disease/ inflammation

- Difficult to diagnose, and different definitions used in various studies
- Often normocytic, low serum iron, low transferrin saturation, **low TIBC, normal/elevated ferritin**
- 6-24% of anemia in elderly
 - Incidence varies depending on criteria – active inflammatory disease: infection, autoimmune, malignancy
- Diagnostic issues in elderly:
 - Normal aging – increased markers of inflammation



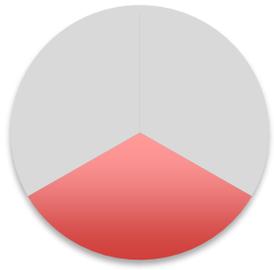
ACD/ inflammation – pathophysiology

- Inflammatory cytokines (TNF-alpha, IL-6 etc)
 - Increased hepcidin → decreased intestinal iron absorption and decreased delivery of iron from macrophages to developing erythrocytes
 - functional iron deficiency
 - Progressive EPO resistance of erythroid progenitors



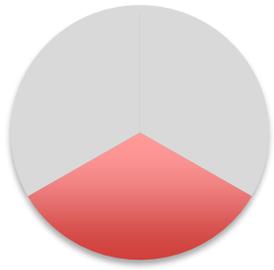
Anemia related to renal impairment

- Decreasing renal function associated with lower EPO levels
- Degree of renal impairment required to result in anemia in elderly individuals is controversial
- Estimated that anemia secondary to renal impairment in 3-12.5% elderly patients – depending on criteria used



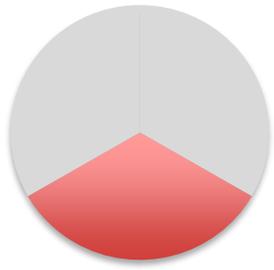
Unknown causes

- Undiagnosed/early MDS
- Relative EPO deficiency
- Testosterone deficiency in males
- Stem cell deficiency decreased quantity and quantity
- ?Pro-inflammatory state (possibly without typical abnormalities in iron studies)



EPO

- Aging associated with decreased sensitivity of RBC progenitors to EPO
- Studies suggest that EPO levels increase with age in healthy non-anemic individuals
- There appears to be a greater slope of EPO increase in those without chronic disease (diabetes, hypertension, renal disease), and decreased slope in those with anemia
- ? Anemia as a failure of normal compensatory increase in EPO levels required to maintain a normal hemoglobin in elderly subjects



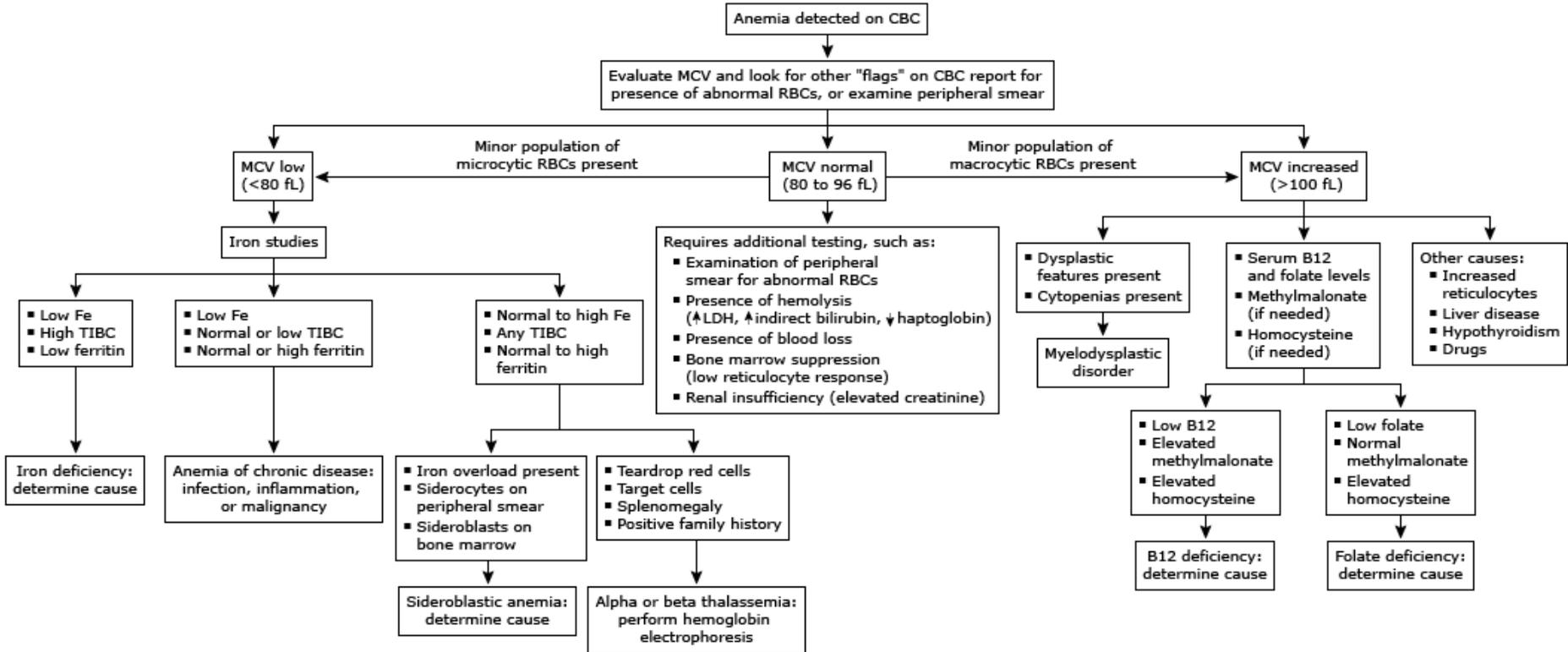
EPO

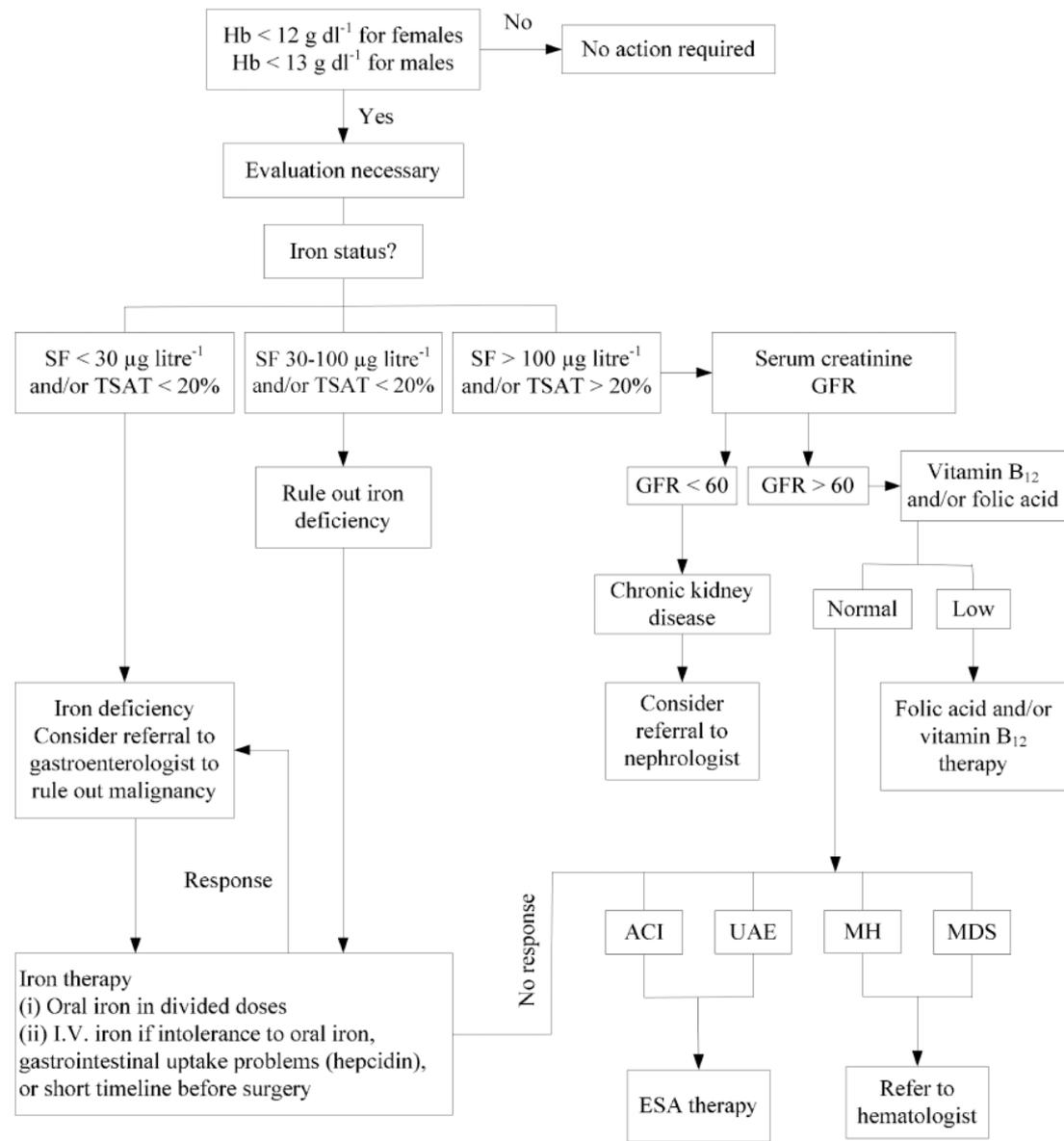
- Erythropoiesis stimulating agent approved for:
 - Anemia in end stage renal disease
 - Anemia in patients with inflammation/chronic disease scheduled for elective surgery
 - Anemia due to MDS in patients who have moderate to severe anemia
 - Cancer-associated anemia

Who to investigate... who to refer

- Given the potentially large number of elderly individuals with mild anemia there are significant cost-benefit issues involving the investigation and specialist referral
- Currently no accepted guideline for investigation of anemia in the elderly

Evaluation of anemia in the adult according to the mean corpuscular volume





Hb Hemoglobin
 SF Serum Ferritin
 GFR Glomerular Filtration Rate
 ACI Anemia of Inflammation

UAE Undifferentiated Anemia of the Elderly
 MDS Myelodysplastic Syndrome
 ESA Erythropoiesis Stimulating Agent
 MH Malignant Hematology (e.g. chronic lymphocytic leukemia)

Important lab considerations

- Review previous CBCs – rate of fall in hemoglobin; acute vs chronic
- Is there associated thrombocytopenia and neutropenia?
- Is this a hypo- or hyperproliferative anemia? Is the reticulocyte count appropriately elevated?
- Are there abnormalities on the peripheral blood film? Dysplasia, rouleaux, immature white blood cell forms?
- Is there a paraprotein?

Case

- **ID:** 92yoM referred to hematology for macrocytic anemia
- **PMH:** CAD with previous CABG; HTN; DM2; atrial fibrillation; BPH; hypothyroidism; excised BCC; remote cholecystectomy
- **MEDS:** warfarin; candesartan/HCTZ; atorvastatin; diltiazem; eltroxin; metformin
- **SOCIAL:** Lives with wife. Highly functioning, active. Lifelong non-smoker. Infrequent alcohol intake (1/6mo)

Case

HPI:

- CBC normal ~6mo ago. Since then -slowly progressive anemia with mild macrocytosis.
- Asymptomatic
- No constitutional symptoms, no signs of GI bleeding, no change in bowel habits – long standing history of mild constipation. Unsure of previous CRC screening.
- Endorsed a well balanced diet

Patient Case

P/E:

- Unremarkable. No scleral icterus, no lymphadenopathy, no hepatosplenomegaly. No signs of malnourishment

LABS:

- Hemoglobin 140 → 125 → 119 → 113 (over ~6mo)
- MCV 101-102
- Normal platelet and WBC count

Case

LABS:

- Vitamin B12: 222 (N)
- RBC folate: 1493 (N)
- Ferritin: 112 (N); Fe 17 TIBC 52 Tsat 25% (N)
- LDH 680 (mildly increased); bilirubin 14; DAT negative
- Reticulocyte count 65
- Creatinine: 144 (stable); eGFR: 36
- Calcium: 2.3 Albumin: 38
- TSH 3.80 (N)
- SPEP: IgG lambda paraprotein 2g/L, IgG normal, IgA normal, mildly low IgM. Serum free light chain ratio mildly abnormal 2.25
- Blood film: RBCs normocytic normochromic, mild rouleaux, mild anisocytosis

Case

IMAGING:

- Skeletal survey: no lytic lesions

Main DDx:

- MDS
- Anemia related to CKD?
- Plasma cell dyscrasia/myeloma

F/U labs:

- Fluctuating hemoglobin, trending down → 110

Case

Bone marrow aspiration and biopsy:

- No dysplasia
- No increased plasma cells (paraprotein unrelated to anemia → MGUS)
- Normal cellularity
- Trace iron stores (bone marrow gold standard to assess iron stores)

Case

Diagnosis: iron deficiency

Management: Ferrous gluconate 300mg OD – BID.
Patient advised to take on empty stomach, avoid taking with dairy/Calcium/coffee/tea. Warned about constipation.

Follow-up after 3month oral iron therapy:

- Hemoglobin normalized to 142
- GI work-up recommended
- Patient D/C'd

Summary

- Anemia is common in the elderly population and associated with significant morbidity and mortality
- Most common identifiable causes include iron deficiency, anemia of chronic disease/inflammation
- MCV/ferritin/iron studies in elderly population can be misleading → Algorithms to guide investigations may not be as useful in this patient population