

# Hematology for Family Practice

## When to treat and when to refer

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# How long do cells live?

- Red blood cells live approximately 120 days.
- Platelets live 8 -11 days.
- White blood cells live about 4 days.

There are millions of RBCs in just one drop of blood. People who live at higher altitudes have more (like in the mountains of Peru). They are produced in the bone marrow of large bones at a rate of 2 million per second. In the minute it took you to read this, you made 120 million of them!

First thing to do with an abnormal CBC is to repeat it and get a smear to pathology, manual diff, and reticulocyte count.

### MICROCYTOSIS:

Low MCV (mean corpuscular volume) under 80.

Low MCH (mean corpuscular hemoglobin) under 27.

Low MCHC (mean corpuscular hemoglobin concentration) under 30.

### MACROCYTOSIS:

High MCV over 93

High MCH over 33

High MCHC over 37

### NORMOCYTIC ANEMIA:

NORMAL INDICES

## DEFINITIONS

**Reticulocyte:** The youngest of the circulating red cells, normally they comprise about 1% of the red cell population. They are **increased** in response to bleeding, or hemolysis, or in response to treatment with B 12, iron, or folic acid. **Decreased** in the presence of a suppressed or otherwise abnormal bone marrow, aplastic anemia, pure red cell aplasia or following chemotherapy.

**Nucleated red blood cells:** Are NORMOBLASTS. Are not normally seen in peripheral blood. They usually indicate the presence of severe degrees of hemolysis, profound stress, hypoxemia, or myelofibrosis.

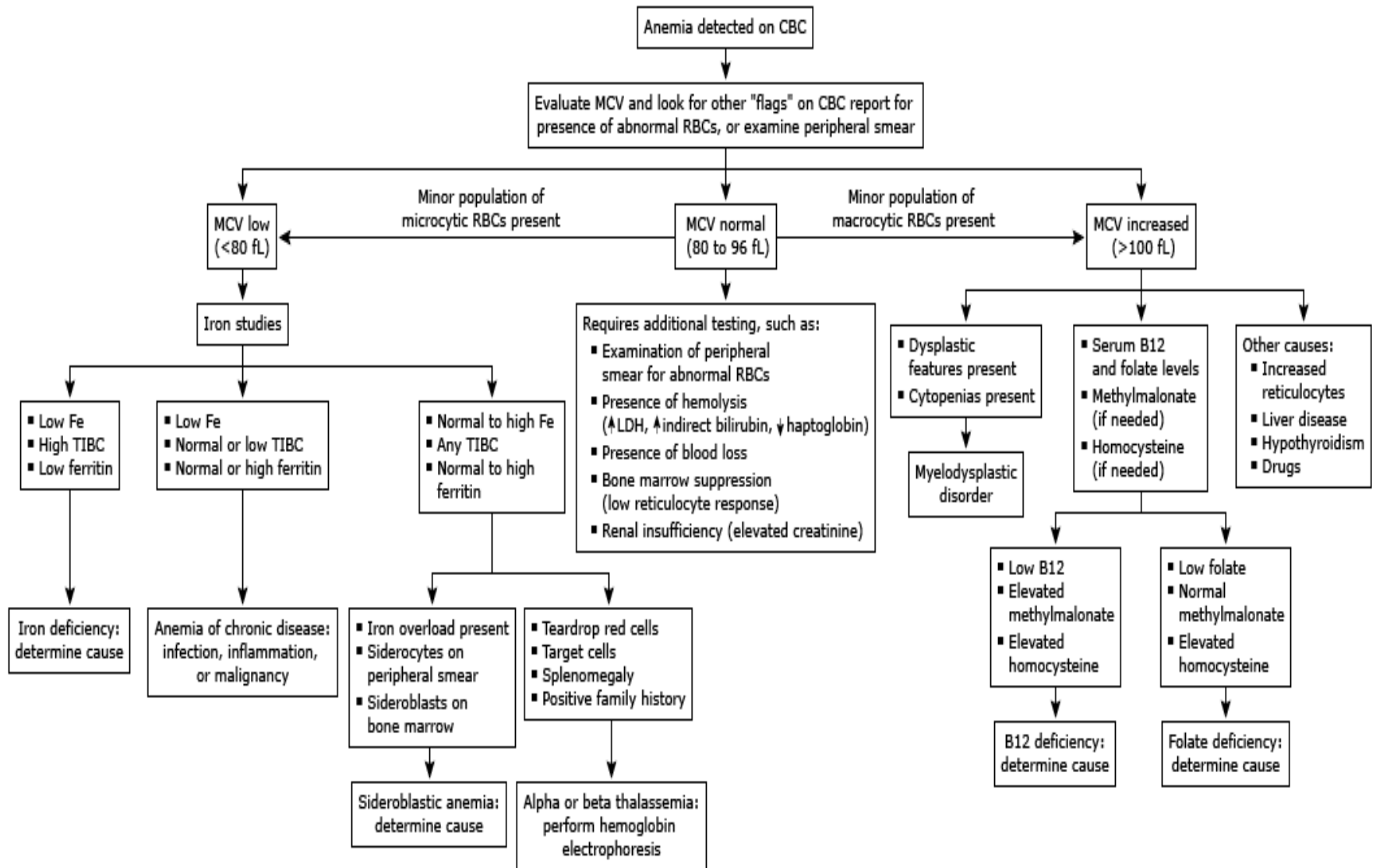
**Erythrocyte:** A mature red blood cell that contains hemoglobin, confined within a lipid membrane, its main purpose is to transport oxygen.

**Leukocyte:** Is a white blood cell. 5 types of leukocytes are classified by the presence or absence of granules in the cytoplasm of the cell. The agranulocytes are lymphocytes and monocytes. The granulocytes are neutrophils, basophils, and eosinophils.

Leukocytes function as phagocytes of bacteria, fungi, and viruses, detoxifiers of toxic proteins that may result from allergic reactions and cellular injury, and immune system cells.

**Platelet:** The smallest cells in the body, they are formed in the bone marrow and some are stored in the spleen, they do not contain hemoglobin and are essential for the coagulation of blood and in maintenance of hemostasis.

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



CBC: complete blood count; MCV: mean corpuscular volume; RBCs: red blood cells; Fe: iron; TIBC: total iron-binding capacity (transferrin); LDH: lactate dehydrogenase.

# Anemia Testing

[Click here for topics associated with this algorithm](#)

**INDICATIONS FOR TESTING**  
Fatigue, weakness, pallor, dizziness, fainting

**ORDER**

- CBC with Platelet Count and Automated Differential (including RBC indices and morphology on manual differential)
- Reticulocytes, Percent & Number

Anemia present on CBC (males Hgb <13g/dL, females Hgb <12g/dL)  
**AND**  
Corrected reticulocyte index ≥2.5

No Yes

Classify by RBC indices

Fragmented cells on peripheral smear

Normocytic, normochromic (normal MCV, MCHC) (suggests hypoproliferation)

Microcytic, hypochromic (low MCV, MCHC) (suggests maturation defects)

Macrocytic (high MCV) (suggests maturation defects)

No

Yes (suggests hemolysis)

- Bone marrow disorder (infiltration, aplasia)
- Inflammation
- Autoimmune disease
- Chronic renal disease
- Critical illness
- Chronic endocrine disorders
- Aplastic anemia, pure red cell aplasia

- Iron deficiency
- Chronic disease
- Thalassemia – see Hemoglobinopathies topic
- Sideroblastic anemia
- Lead toxicity

- B<sub>12</sub> deficiency, (less commonly folate deficiency) – see Megaloblastic Anemia Testing Algorithm
- Drug effect
- Excessive alcohol use
- Hypothyroidism
- Myelodysplasia – see Myelodysplastic Syndromes Consult topic

Suggests acute blood loss (eg, hemorrhage)

- Metabolic defect (see PNH Consult topic)
- Hemoglobinopathies (eg, sickle cell) – see Hemolytic Anemias Testing Algorithm
- Autoimmune destruction
- Splenic sequestration
- RBC membrane defect – see Hemolytic Anemias Consult topic
- Intravascular hemolysis – see Hemolytic Anemias Consult topic

Abnormal peripheral smear

No  
Vitamin B<sub>12</sub> & Folate

**ORDER**

- Iron and Iron Binding Capacity
- Ferritin

No

Yes

High TIBC  
Low iron  
Low ferritin

Low/normal TIBC  
Normal/high ferritin  
Low/normal iron

Workup based on smear characteristics

Iron deficiency anemia

- Suggests
- Inflammation
  - Chronic disease
  - Thalassemia

Bone marrow biopsy may be necessary

If no obvious chronic disease present, consider bone marrow biopsy; for Thalassemia suspicion, consider hemoglobin electrophoresis

**Abbreviations and Formula**

MCV = mean cell volume  
MCHC = mean cell hemoglobin concentration  
TIBC = total iron binding capacity

Reticulocyte correction for anemia:

$$\text{ReticCount\%} \times \frac{\text{Hgb}}{\text{Htc}} \times \frac{1}{\text{Maturation time correction (use 2\% for most patients)}}$$



# Red Cell Morphology and associated Conditions

**Auer Rods:** observed in Blasts associated with AML

## Red Cell Morphology and associated Conditions

**Anisocytosis:** Various types of anemia

**Acanthocytosis (spur cells):** Alcoholic cirrhosis, post splenectomy, hemolytic anemia

**Anisocytosis:** Various types of anemia

**Basophilic Stippling: Fine:** various anemias **Course:** lead toxicity and thalassemias

**Bite Cells:** Chemical poisoning, G-6PD deficiency, hemolytic anemia

**Burr Cells:** Myeloproliferative states, heparin therapy, uremia, Chronic renal disease, bleeding, peptic ulcers

**Howell-Jolly bodies:** Post Splenectomy, megaloblastic and hemolytic anemias

**Hypersegmented neutrophils:** megaloblastic anemias, pernicious, B12, and folate deficiencies

**Dohle bodies:** (toxic granulation are usually seen together) Acute infection, pneumonia, scarlet fever, measles,

**Dohle bodies:** (toxic granulation are usually seen together) Acute infection, pneumonia, scarlet fever, measles,

septicemia, pregnancy, burns

**Reactive lymphocytes:** (Downey cells) mono, CMV, viral hepatitis, chronic inflammatory disease

**Smudge Cells:** atypical lymphocytosis, CML

**Schistocytosis:** cardiac valve disease, DIC, severe burns, uremia

**Spherocytes: (helmet cells)** hereditary spherocytosis, thermal injuries, immune and hemolytic diseases, TTP, DIC

**Rouleaux:** multiple myeloma, elevated protein

**Target cells:** chronic liver disease, iron deficiency, post splenectomy

**Tear drop cells:** Thalassemias, pernicious anemia, Myeloproliferative disorders.

**Band Neutrophils:** normal 5-11% increased # = LEFT SHIFT (stress, infection, Myeloproliferative disease)

**Basophils:** <2% are normal. Allergic reaction, hypothyroid, chronic hemolytic anemia, post splenectomy

**Eosinophils:** increased in asthma, hay fever, extensive skin lesions,

**Metamyelocyte:** Myelocytic hyperplasia

**Myelocyte:** CML, AML

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**Myelocyte:** CML, AML

**Plasma cells:** Not usually seen in peripheral blood. Chronic infections, autoimmune disorders, alcoholic liver disease.

**Monocytes:** increased in chronic neutropenia, IBD, chronic infection, CMV, TB and can be elevated in AMML.

## Evaluating Anemia

Number one reason for microcytic anemia is bleeding, either GU or GI. Ask the right questions. A good physical exam and a good history is essential to your investigation. Don't forget family history.

## Laboratory findings in iron deficiency anemia, thalassemia, and anemia of chronic disease/inflammation

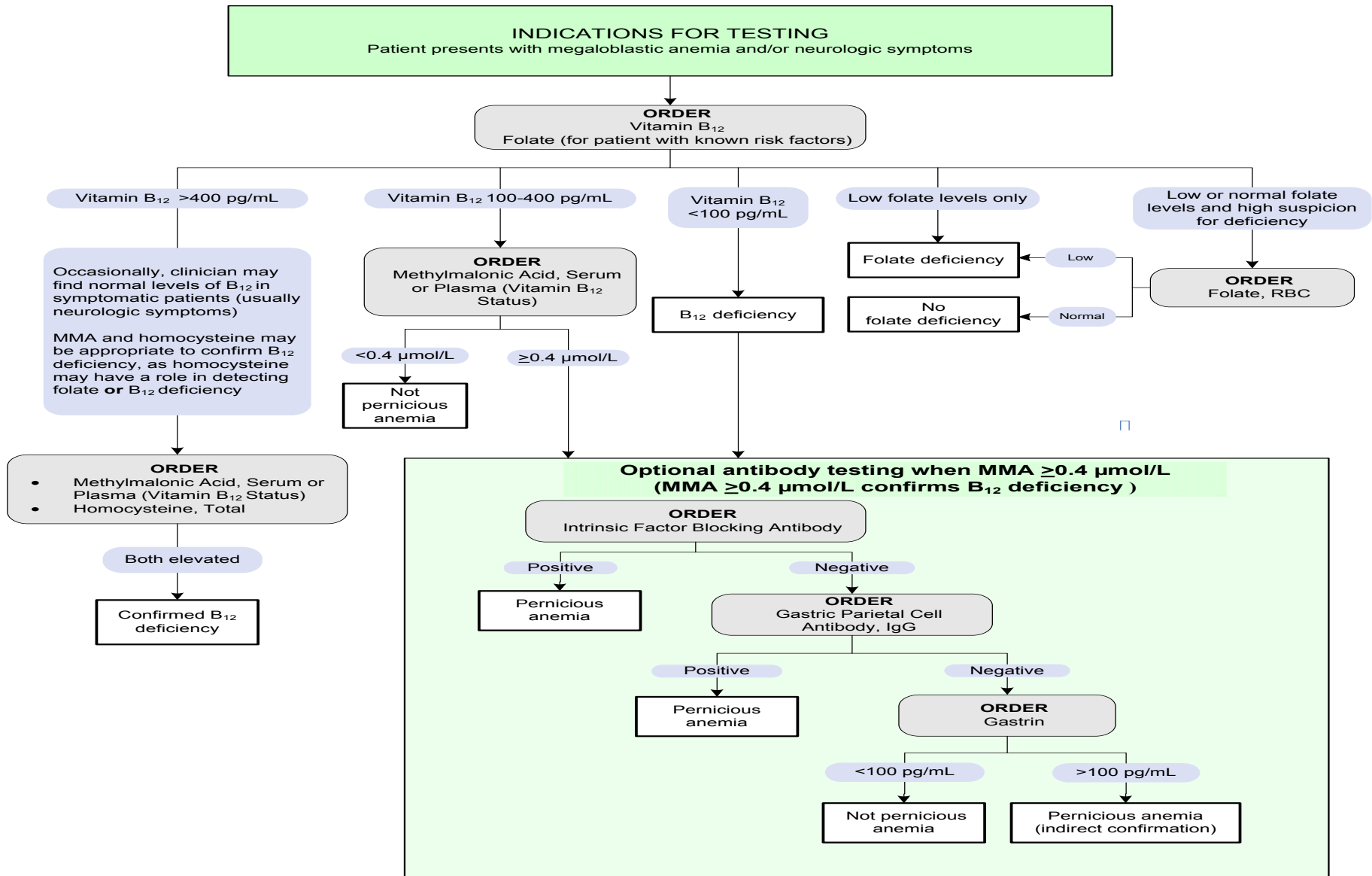
Test	Iron deficiency anemia	Alpha or beta thalassemia	Anemia of chronic disease/inflammation
Complete blood count			
Hemoglobin	Decreased	Decreased	Decreased
Mean corpuscular volume (MCV)	Decreased or normal	Decreased	Normal to decreased
Red cell distribution width (RDW)	Increased	Increased	Normal to increased
Red blood cell count	Decreased	Increased or normal	Decreased
Iron studies			
Serum iron	Decreased	Normal or increased	Decreased
Total iron-binding capacity (TIBC); transferrin	Increased	Normal	Decreased
Transferrin saturation	Decreased	Normal	Decreased
Serum ferritin	Decreased	Normal	Increased
Erythrocyte protoporphyrin*	Increased	Normal or increased	Increased
Soluble transferrin receptor*	Increased	Increased	Normal

Refer to UpToDate topics on anemia for further details of the evaluation and interpretation.

\* Not used in the routine evaluation of anemia.

# Megaloblastic Anemia Testing

[Click here for topics associated with this algorithm](#)



## Differential diagnosis of anemia in the adult

<b>Low mean corpuscular volume (microcytic anemia: MCV &lt;80 fL)</b>
Iron deficiency anemia
Thalassemic disorders
Anemia of inflammation/anemia of chronic disease (late; uncommon)
Sideroblastic anemia (eg, congenital, lead, alcohol, drugs; uncommon)
Copper deficiency, zinc poisoning (rare)
<b>Normal mean corpuscular volume (normocytic anemia: MCV 80 to 100 fL)</b>
Acute blood loss
Iron deficiency anemia (early)
Anemia of inflammation/anemia of chronic disease (eg, infection, inflammation, malignancy)
Bone marrow suppression (may also be macrocytic)
Bone marrow invasion (eg, leukoerythroblastic blood picture)
Acquired pure red blood cell aplasia
Aplastic anemia
Chronic renal insufficiency
Endocrine dysfunction
Hypothyroidism (most commonly normocytic)
Hypopituitarism
<b>Increased mean corpuscular volume (macrocytic anemia: MCV &gt;100 fL)</b>
Ethanol abuse
Folate deficiency
Vitamin B12 deficiency
Myelodysplastic syndromes
Acute myeloid leukemias (eg, erythroleukemia)
Reticulocytosis
Hemolytic anemia
Response to blood loss
Response to appropriate hematinic (eg, iron, B12, folic acid)
Drug-induced anemia (eg, Hydroxyurea, AZT, chemotherapeutic agents)
Liver disease
Hypothyroidism (less commonly macrocytic)

This list is not meant to be exhaustive; only the most common causes are mentioned. In addition, two or more of these conditions may be present (eg, combined iron and folate deficiencies), resulting in a misleadingly normal mean corpuscular volume.

## Causes for failure to respond to oral iron therapy

<b>Coexisting disease interfering with marrow response</b>
Infection
Inflammatory disorder (eg, rheumatoid arthritis)
Concomitant malignancy
Coexisting folate and/or vitamin B12 deficiency
Bone marrow suppression from another cause
<b>Patient is not iron deficient, possible correct diagnoses include</b>
Thalassemia
Lead poisoning
Anemia of (chronic) inflammation
Copper deficiency (zinc toxicity)
Myelodysplastic syndrome/refractory sideroblastic anemia
<b>Patient is not taking the medication</b>
Prescription has not been filled
Prescription has been filled but patient is no longer taking the medication
<b>Medication is being taken but is not being absorbed</b>
Rapid intestinal transport bypasses area of maximum absorption
Enteric coated product: coating is not dissolving
Patient has acquired malabsorption for iron (eg, sprue, atrophic or autoimmune gastritis, H. pylori infection)
Medication taken in association with an agent interfering with absorption (eg, antacids, tetracycline, tea)
Congenital cause for iron malabsorption (eg, iron-resistant iron deficiency anemia, IRIDA)
<b>Continued blood loss or need in excess of iron dose ingested</b>
Cause of blood loss treatable (eg, bleeding peptic ulcer)
Initiate appropriate treatment
Cause of blood loss not treatable (eg, hereditary hemorrhagic telangiectasia [Osler-Weber-Rendu syndrome]) or need cannot be met by oral iron preparation (eg, renal failure or malignancy being treated with erythropoietin)
Switch patient to intravenous iron product

Assumes that original diagnosis was iron deficiency anemia with hypochromic microcytic red blood cells, low ferritin, and low transferrin saturation.

## Iron preparations:

Ferrous gluconate orally is less likely to cause GI upset and is more tolerated than ferrous sulfate. It is equally absorbable with less side effects. Comes in many strengths and is generally OTC. Severe iron deficiency may require 325 mg TID. Most patients don't take it as directed for a variety of reasons. Nausea and constipation are the biggest reasons.

I never order ferrous sulfate, for those reasons.

There are many conditions that can interfere with oral iron absorption and or cause iron deficiency:

Being older, poor tolerance of oral iron preparations

Inflammatory bowel disease, ulcerative colitis

Gastric surgery and gastric bypass

H. Pylori, autoimmune gastritis and celiac disease.

Chronic kidney disease and dialysis

Cancer patients



**IV iron preparations:** (use them when patients cannot tolerate oral)

**AVOID IM:** It's painful, stains the buttocks, and has variable absorption. Case reports have also described development of sarcomas.

**Iron Dextran (Infed):** Black Box warnings for anaphylaxis, requires pre medications and takes long to give. Usually including premeds and test dose, 4-6 hours. Dosing is by weight and Hgb. (Chart) can be up to 1.5 Gms. More than a Gram doesn't work any better.

**Ferumoxytol (Feraheme):** Given in 2 doses, one week apart. 510 mg Often given with premeds and has an increase in second dose reactions.

**Iron sucrose (Venofer):** Should have a test dose. Given in multiple doses, not over 300 mg. Used in CKD, and in the setting of dialysis.

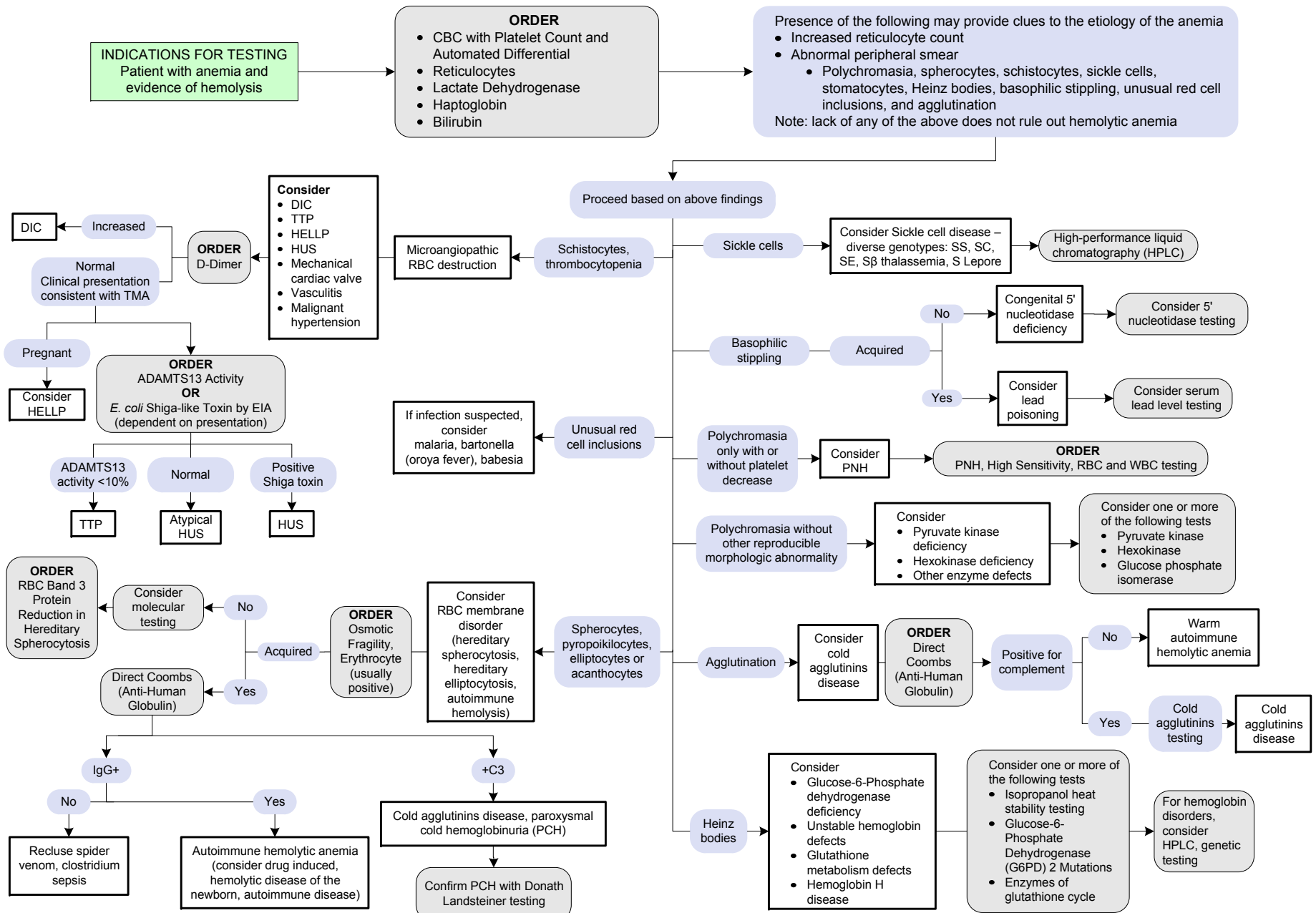
**Ferric carboxymaltose (Injectafer):** is a colloidal iron hydroxide complex with a tighter binding of elemental iron. It's a 15 minute infusion and doesn't require premeds and is given in NSS 750 mg in 2 doses, one week apart.

## **Monitoring:**

For chronic iron deficiency anemia patients that require ongoing IV iron treatments, monthly CBC's and iron studies including ferritin. Treat again when ferritin goes below 50.

Oral iron treatment F/U should be checked monthly during replacement until repleted. Continue oral iron up to 3-6 months after normalization of iron levels to replete iron stores. When ferritin is normalized, a trial off iron for 3 months and recheck CBC, iron, TIBC and ferritin.

If the cause of the iron deficiency has been treated, no further iron should be necessary. (normalization of periods, post uterine ablation, GI bleed is successfully treated, etc.)



## **Hemolytic Anemia:**

Tests: CBC, with manual diff, reticulocyte count, LDH, Haptoglobin, Bilirubin.

### **Findings:**

Elevated reticulocyte count

Elevate LDH

Decreased Haptoglobin < 25 (if LDH and Haptoglobin are normal, 90% probability it's not hemolytic anemia)

Positive Direct Coombs test

Increased indirect Bilirubin

### **Peripheral smear:**

Fragmented RBC (schistocytes or helmet cells

Spherocytes seen in hereditary spherocytosis

Spur cells seen in liver disease

Tear drop RBC's with circulating nucleated RBC indicating the presence of marrow involvement.

## **Treatment for Hemolytic Anemia (Autoimmune):**

**Diagnosis** – Accurate diagnosis of warm agglutinin autoimmune hemolytic anemia

## **Treatment for Hemolytic Anemia (Autoimmune):**

**Diagnosis** – Accurate diagnosis of warm agglutinin autoimmune hemolytic anemia (AIHA) requires accurate diagnosis of the presence of red cell destruction (hemolysis) along with demonstration of the presence of an autoantibody or complement on the surface of the patient's red cells.

patients with underlying cardiac disease, AIHA can present as a medical emergency, requiring immediate institution of treatment with glucocorticoids

confirmed, we recommend immediate institution of treatment with glucocorticoids over splenectomy,

**Poorly responsive, severe, or resistant disease**

For adults, it is preferred splenectomy over Rituximab, as it is the only modality with potential for long-term cure, while rituximab is the treatment of choice for adults who either are not surgical candidates or refuse surgery.

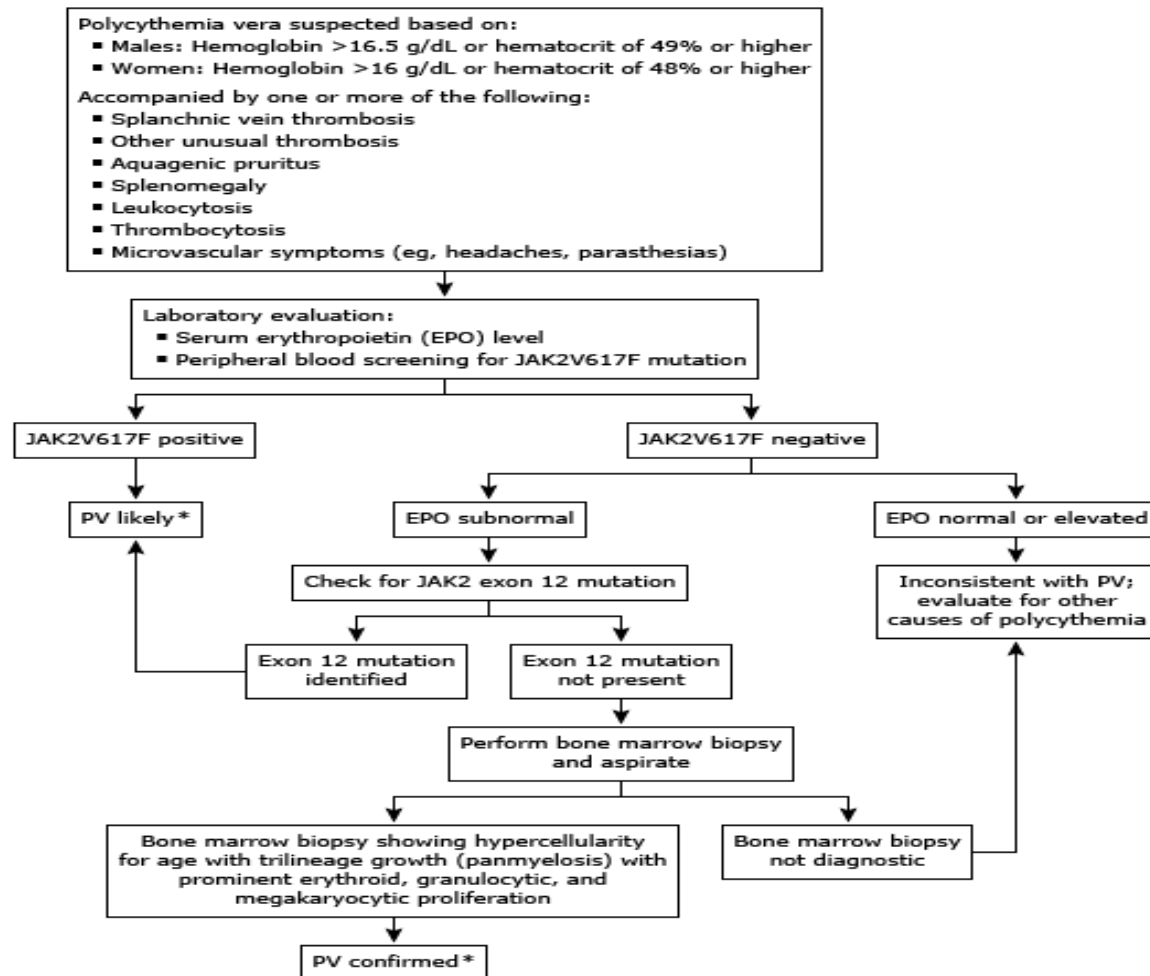
**Third-line treatment** – For those who have failed treatment with both splenectomy and rituximab, should institute immunosuppressive or cytotoxic agents such as azathioprine (Imuran), cyclophosphamide, or cyclosporine.

**Obviously you have already referred to Hematology!**

## Major causes of erythrocytosis (polycythemia)

<b>Autonomous (inappropriate) increase of Epo - inappropriately high serum Epo</b>
<b>Erythropoietin-producing neoplasms (most common)</b>
Renal cell carcinoma
Hepatocellular carcinoma
Cerebellar hemangioblastoma
Pheochromocytoma
Uterine fibroids
<b>Erythropoietin-producing renal lesions (eg, cysts, hydronephrosis, renal artery stenosis, distal renal tubular acidosis [rare])</b>
Following renal transplantation (some cases are independent of erythropoietin)
<b>Appropriate increases in erythropoietin - appropriately high serum erythropoietin</b>
<b>Hypoxemia secondary to:</b>
Chronic pulmonary disease
Right-to-left cardiac shunts
Sleep apnea
Massive obesity (Pickwickian syndrome)
High altitude
Red cell defects
Some cases of congenital methemoglobinemia
Chronic carbon monoxide poisoning (including heavy smoking)
Cobalt
<b>Germline and somatic mutational causes of polycythemia</b>
Polycythemia vera (JAK2 mutation)
Activating mutations of the erythropoietin receptor (EPOR gene)
Chuvash polycythemia (VHL gene mutation)
Congenital methemoglobinemia
Idiopathic familial polycythemia
High oxygen affinity hemoglobins
2,3 bisphosphoglycerate (BPG) mutase deficiency
Other rare gene mutations (eg, PHD2, HIF2-alpha)
<b>Miscellaneous causes</b>
Use of androgens or anabolic steroids
Diuretics (reduced plasma volume rather than erythrocytosis)
Blood doping in athletes (ie, autologous blood transfusion)
Self-injection of erythropoietin
POEMS syndrome

## Evaluation of suspected polycythemia vera

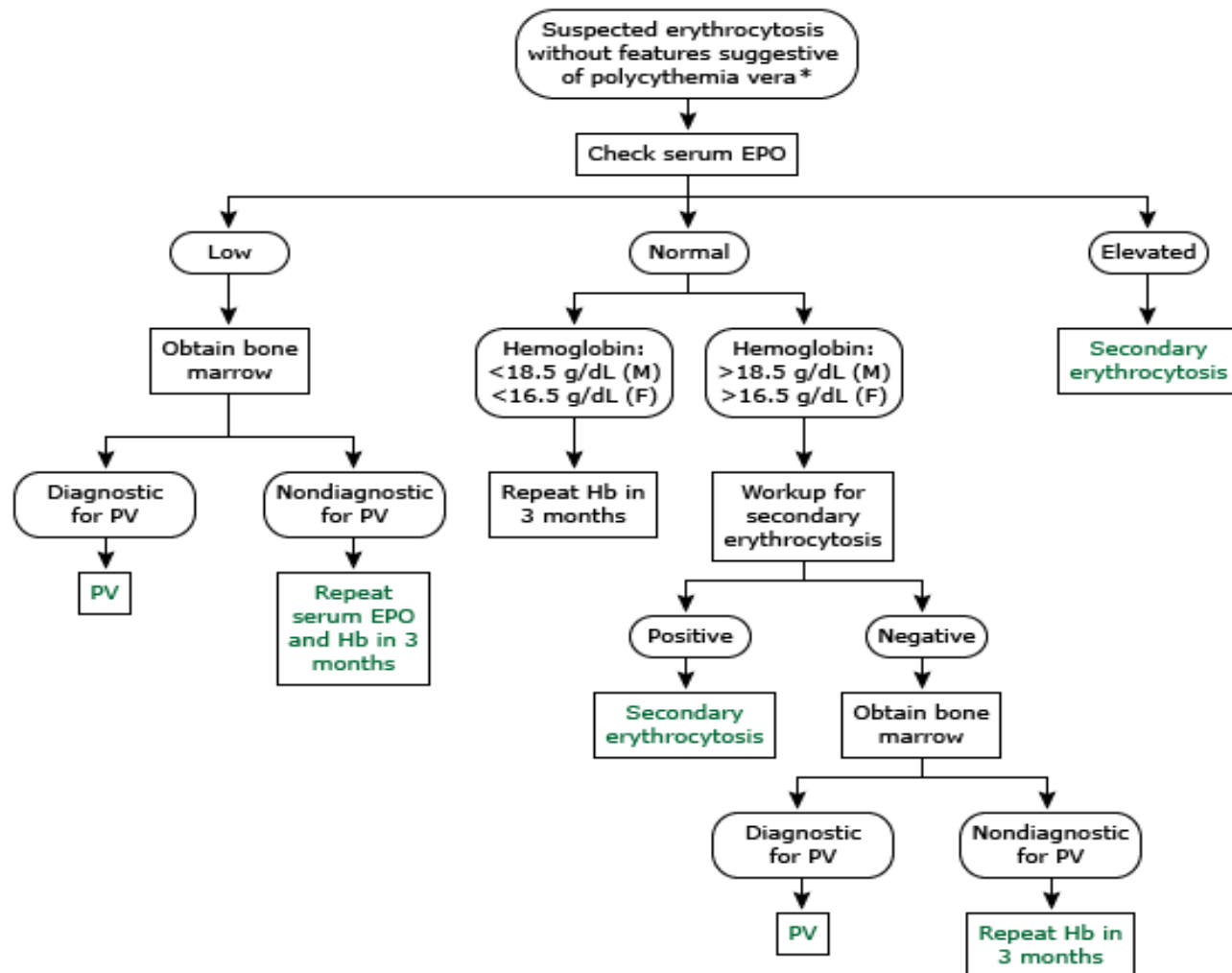


PV: polycythemia vera; EPO: erythropoietin.

\* WHO diagnostic criteria met for patients with both major criteria (hemoglobin >18.5 g/dL in men, 16.5 g/dL in women or other evidence of increased red cell volume AND presence of JAK2V617F or functionally similar mutation such as JAK2 exon 12 mutation) or the first major criterion plus two minor criteria (consistent bone marrow biopsy findings, subnormal serum EPO, or endogenous erythroid colony formation in vitro). Bone marrow biopsy might not be necessary if hemoglobin is >18.5 g/dL in men or 16.5 g/dL in women. Bone marrow biopsy is recommended for lower hemoglobin levels in order to avoid confusing PV with JAK2-mutated essential thrombocythosis. For practical purposes, PV likely and PV confirmed cases are treated similarly.



## Diagnostic approach to suspected erythrocytosis in the absence of polycythemia vera-related features



PV: polycythemia vera; EPO: erythropoetin; Hb: hemoglobin; M: male; F: female.

\* Features suggestive of PV include splanchnic vein thrombosis or other unusual thrombosis, aquagenic pruritus, splenomegaly, leukocytosis, thrombocytosis, and microvascular symptoms (eg, headaches, paresthesias).

## Classification of neutrophilia

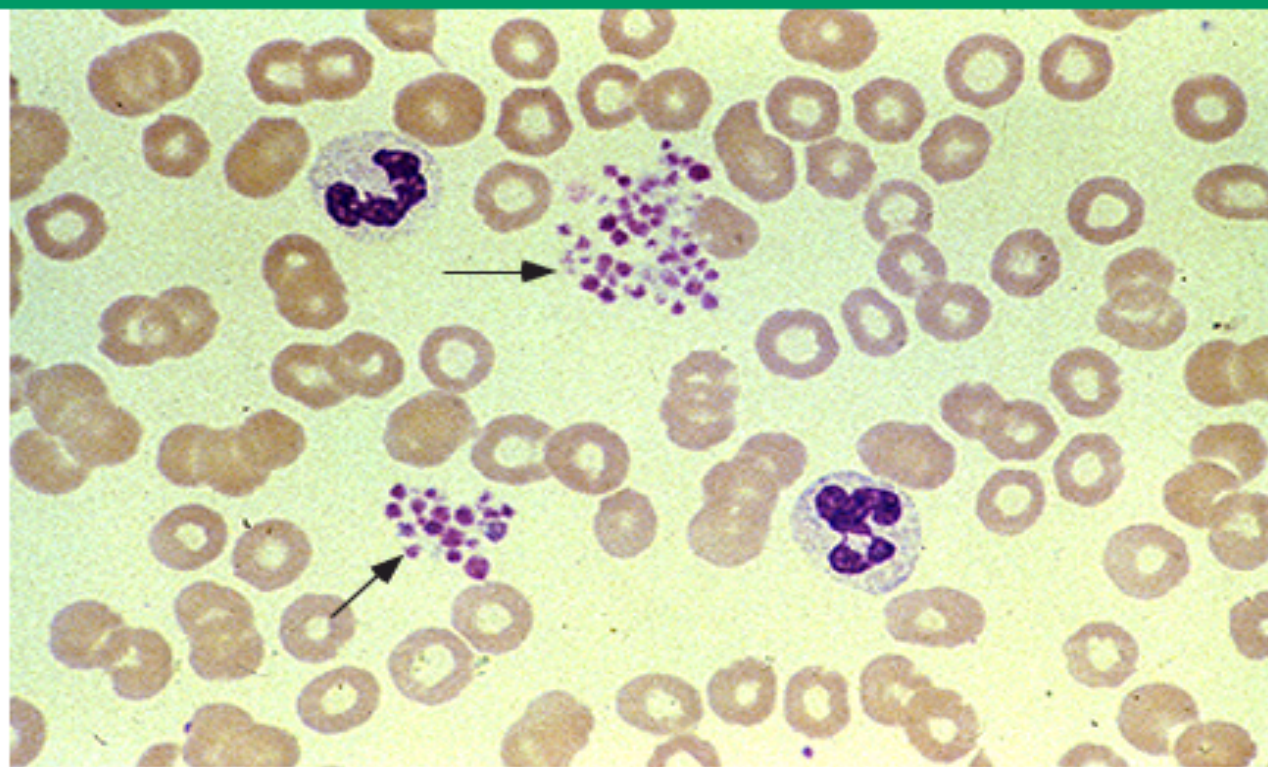
<b>Spurious</b>
Platelet clumping
Mixed cryoglobulinemia
<b>Primary (no other evident associated disease)</b>
<b>Myeloproliferative disorders (eg, CML, PV, ET)</b>
Hereditary neutrophilia
Chronic idiopathic neutrophilia
Familial myeloproliferative disease
Congenital anomalies and leukemoid reaction
Down syndrome
Leukocyte adhesion factor deficiency
Familial cold urticaria and leukocytosis
<b>Secondary</b>
<b>Infection</b>
<b>Stress (physical or emotional stress, vigorous exercise)</b>
<b>Cigarette smoking</b>
Drugs
<b>Glucocorticoids</b>
<b>Recombinant G-CSF or GM-CSF*</b>
Catecholamines (epinephrine)
Lithium
All-trans retinoic acid
Isolated case reports for occasional other drugs
Nonhematologic malignancy
Heatstroke
Generalized bone marrow stimulation (as in hemolysis)
Asplenia and hyposplenism

Most commonly encountered causes of neutrophilia are shown in **bold**.

CML: chronic myelogenous leukemia; PV: polycythemia vera; ET: essential thrombocythemia; G-CSF: granulocyte colony-stimulating factor; GM-CSF: granulocyte-macrophage colony-stimulating factor.

\* These agents are used therapeutically to raise the neutrophil count.

## Pseudothrombocytopenia due to platelet clumping in EDTA



This peripheral blood smear shows platelet clumping (arrows) in an EDTA-anticoagulated blood sample. This patient had an EDTA-dependent platelet agglutinin which caused in vitro platelet clumping, resulting in an artifactually low platelet count (ie, "pseudothrombocytopenia"). No platelet clumping was seen, and the platelet count was normal, in a blood sample from this patient anticoagulated with sodium citrate. *Reproduced with permission from Beutler, E, Lichtman, MA, Coller, BS, et al, Hematology, 5th ed, McGraw-Hill, New York, 1995.*

## Major medications with a definite association with agranulocytosis

<b>Antithyroid drugs (thionamides)</b>
Methimazole
Carbimazole
Propylthiouracil
<b>Antiinflammatory drugs</b>
Sulfasalazine
Nonsteroidal antiinflammatory drugs
Gold salts
Penicillamine
Phenylbutazone
Antipyrine
Dipyrone
Phenacetin
<b>Psychotropic drugs</b>
Clozapine
Phenothiazines
Tricyclic and tetracyclic antidepressants
Meprobamate
Cocaine/heroin (adulterated with levamisole)
<b>Gastrointestinal drugs</b>
Sulfasalazine
Histamine H2- receptor antagonists
<b>Cardiovascular drugs</b>
Antiarrhythmic agents (tocainide, procainamide, flecainide)
Ticlopidine
ACE inhibitors (enalapril, captopril)
Propranolol
Dipyridamole
Digoxin
<b>Dermatologic drugs</b>
Dapsone
Isotretinoin

<b>Antibiotics</b>
Macrolides
Trimethoprim-sulfamethoxazole
Chloramphenicol
Sulfonamides
Semisynthetic penicillins
Vancomycin
Cephalosporins
Dapsone
<b>Antimalarial drugs</b>
Amodiaquine
Chloroquine
Quinine
<b>Antifungal agents</b>
Amphotericin B
Flucytosine
<b>Anticonvulsants</b>
Carbamazepine
Phenytoin
Ethosuximide
Valproate
<b>Diuretics</b>
Thiazides
Acetazolamide
Furosemide
Spirolactone
<b>Sulfonylureas</b>
Chlorpropamide
Tolbutamide
<b>Iron chelating agents</b>
Deferiprone

# CAUSES OF REACTIVE THROMBOCYTOSIS

## NON MALIGNANT HEMATOLOGIC CONDITIONS:

ACUTE BLOOD LOSS

ACUTE HEMOLYTIC ANEMIA

ACUTE IRON DEFICIENCY ANEMIA

TREATMENT OF VITAMIN B DEFICIENCY

REBOUND EFFECT AFTER TREATMENT OF IMMUNE THROMBOCYTOPENIA

REBOUND EFFECT AFTER ETHANOL-INDUCED THROMBOCYTOPENIA

## MALIGNANT CONDITIONS:

METASTATIC CANCER

LYMPHOMA

REBOUND EFFECT FOLLOWING USE OF MYELOSUPPRESSIVE AGENTS

## ACUTE AND CHRONIC INFLAMMATORY CONDITIONS:

RHEUMATOLOGIC CONDITIONS, VASCULITIS, IBS, CELIAC DISEASE

## **TISSUE DAMAGE:**

THERMAL BURNS

MYOCARDIAL INFARCTION

SEVERE TRAUMA

ACUTE PANCREATITIS

POST-SURGICAL PERIOD, ESPECIALLY POST-SPENECTOMY

CORONARY ARTERY BYPASS PROCEDURES

## **INFECTIONS:**

CHRONIC INFECTIONS AND TUBERCULOSIS

## **EXERCISE**

## **ALLERGIC REACTIONS**

## **FUNCTIONAL AND SURGICAL ASPLENIA**

## **REACTION TO MEDICATIONS:**

VINCRIStINE

EPINEPHERINE, GLUCOCORTICOIDs

INTERLEUKIN-1B

ALL-TRANS RETINOIC ACID

THROMBOPOIETIN, THROMBOPOITIN MIMETICS

LOW MOLECULAR WEIGHT HEPARINS (ENOxAPARIN)

## Hydroxyurea:

Used mostly these days for **Essential Thrombocythemia**. It can be used in CML. Dosing is 500 mg tablets titrated to keep the platelet count below 400K. Monitoring CBC's should be weekly at first and then changed to every 2 weeks until stabilization occurs.

It can drop Hgb and WBC's so titration can be tricky.

Usually changes in dosing shouldn't be sooner than every 2 weeks as it takes that long to stabilize on a new dose.

It is an antineoplastic agent and is carcinogenic. Advise sun protection and monitor for malignancies.

Adjustments for lower Creatinine clearance.

Most people tolerate it without side effects.

**Causes macrocytosis**



## **Eltrombopag (Promacta):**

Colony stimulating Factor; Hematopoietic Agent; Thrombopoietic Agent.

Used for Chronic immune idiopathic Thrombocytopenia (ITP)

Max dose is 150 mg daily.

Titrate to maintain platelets with lowest dose.

Weekly CBC monitoring until Platelets get up to 30K and you are seeing an upward trend, the CBC's every 2 weeks.

Pricing:

12.5 mg tabs # 30 = \$4124.09

75 mg tabs # 30 = \$11,509.09

Monitor liver functions

Should be taken on an empty stomach

Can be used in Hepatitis C for thrombocytopenia with caution.

Dosing is usually tolerated well.

SE: fatigue, nausea, diarrhea, elevated LFT's are the most common.

## **Anagrelide (Agrylin):**

Antiplatelet Agent, used for **Essential Thrombocythemia (ET)**

Well tolerated, and can be used with Hydroxyurea on tough cases.

Caution in Hepatic impairment.

Initial dosing is 0.5 mg 1 to 4 times daily Max daily dose of 10 mg

Titrate up slowly, must not be increase by more than 0.5 mg a day in any one week. Most patients will stabilize between 1.5 and 3 mg daily.

Generic form available

Pricing:

0.5 mg (100) = \$585.70 (generic)

1 mg (100) = \$1171.35 (generic)

Monitoring parameters CBC Q 2 days during the first week with pretreatment

EKG and CMP frequently during treatment.

Monitor for interstitial lung disease.

**SE:** palpitations, chest pain, CHF, fatigue, edema, rash, diarrhea, nausea, elevated LFT's

## **Hematopoietic Growth Factors:**

**Erythropoietin, Granulocyte and granulocyte-macrophage colony stimulating factors (G-CSF and GM-CSF), Thrombopoietin**

The family of glycoproteins known as the hematopoietic growth factors (HGFs) plays a major role in the proliferation, differentiation, and survival of primitive hematopoietic stem and progenitor cells, as well as in functional activation of some mature cells. These effects are mediated by high affinity binding of the HGFs to specific receptors expressed on the surface of the target cells.

## **Recombinant HGFs are administered in the following clinical settings:**

Transient bone marrow failure following chemotherapy

Hematopoietic stem cell and progenitor cell mobilization

Recovery from hematopoietic cell transplantation

Myelodysplastic syndrome

Aplastic anemia

Some forms of neutropenia

Inherited bone marrow failure syndromes

Human immunodeficiency virus (HIV) infection-associated neutropenia

Chronic anemias (eg, renal failure, prematurity, chronic disease/inflammation, HIV infection)

Reducing the need for perioperative blood transfusion

**Potential toxicities of the recombinant HGFs include the following (see 'Toxicity of colony-stimulating factors' above and 'Toxicity of erythropoietin' above):**

Transient leukopenia

Systemic reactions (eg, flu-like symptoms, capillary leak, hypertension, thrombosis)

Production of deleterious neutralizing antibodies

Possible stimulation of malignancy

Possible enhancement of HIV replication

Multiorgan failure when used in sickle cell syndromes

## **PEARLS:**

1. ANC (absolute neutrophil count) is the neutrophil # on the differential of a CBC. Always order CBC with diff so you can find this number. If it is  $< 1.5$  or below 1500 you have neutropenia.
2. Thrombocytopenia alone, may be due to platelet clumping. Have the lab do a manual diff to verify if there is clumping. If so have the next CBC, have drawn in a sodium citrate tube. Clumping can be seen with EDTA tube.

## **Monocytosis:**

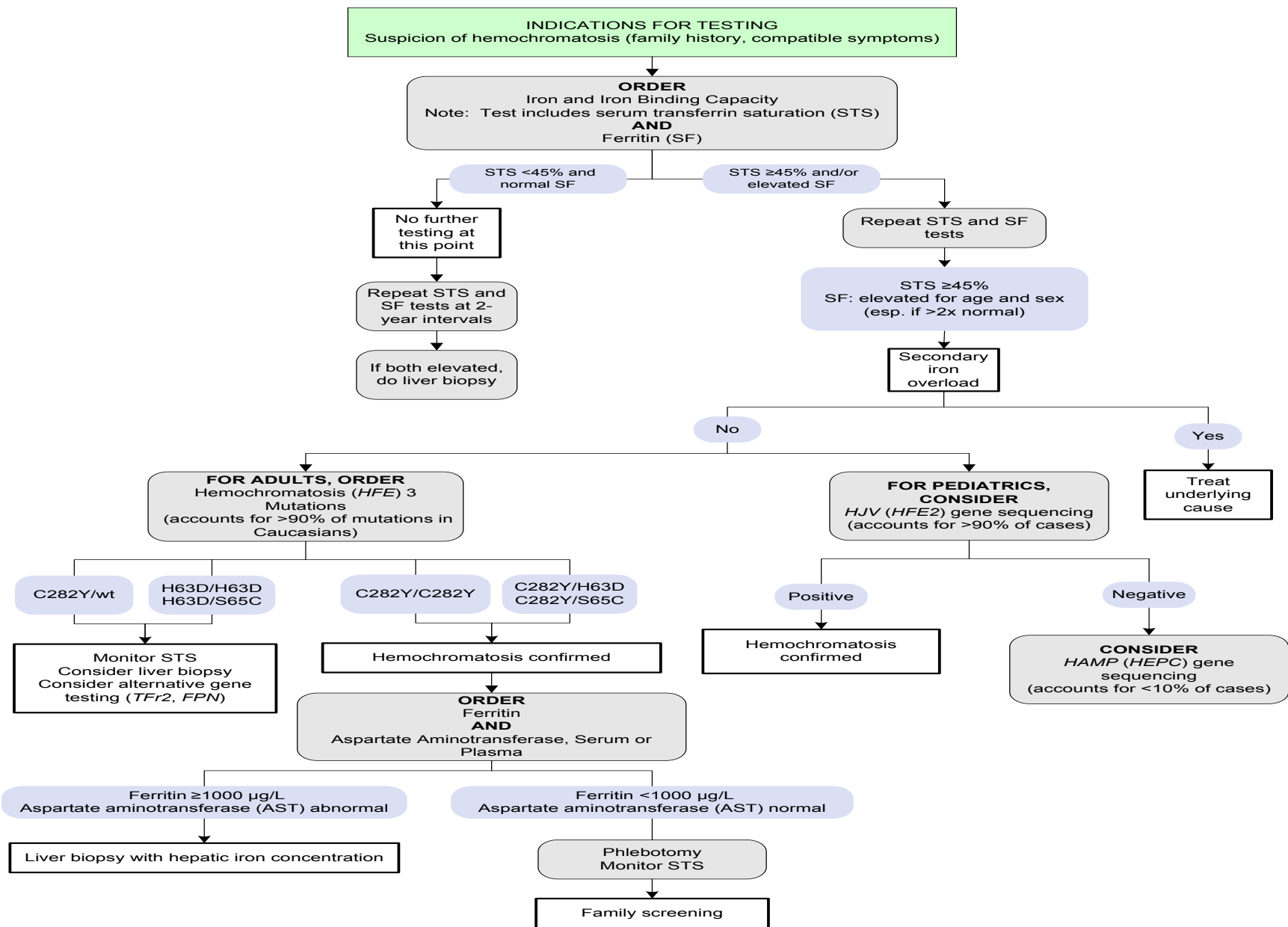
A number of conditions which cause neutrophilia can also cause monocytosis, making this combination a relatively nonspecific finding. These include pregnancy, the asplenic state, inflammatory (eg, sarcoidosis, inflammatory bowel disease) and autoimmune conditions, depression, and treatment with corticosteroids or colony stimulating factors. Monocytosis may also accompany conditions associated with neutropenia, presumably as a compensatory mechanism.

A large number of infections have been associated with monocytosis including brucellosis, varicella-zoster, bacterial endocarditis, tuberculosis, malaria, typhoid fever, syphilis, and trypanosomiasis.

Monocytosis may also be seen in certain malignancies, such as Hodgkin lymphoma. Neutrophilia with monocytosis may also suggest chronic myelomonocytic leukemia, one of the myelodysplastic disorders. Additional associated findings in this condition are anemia, thrombocytopenia and abnormal cellular maturation (eg, macrocytic red cells, defective lobulation in neutrophils, and abnormal size and granulation in platelets).

# Hemochromatosis Testing

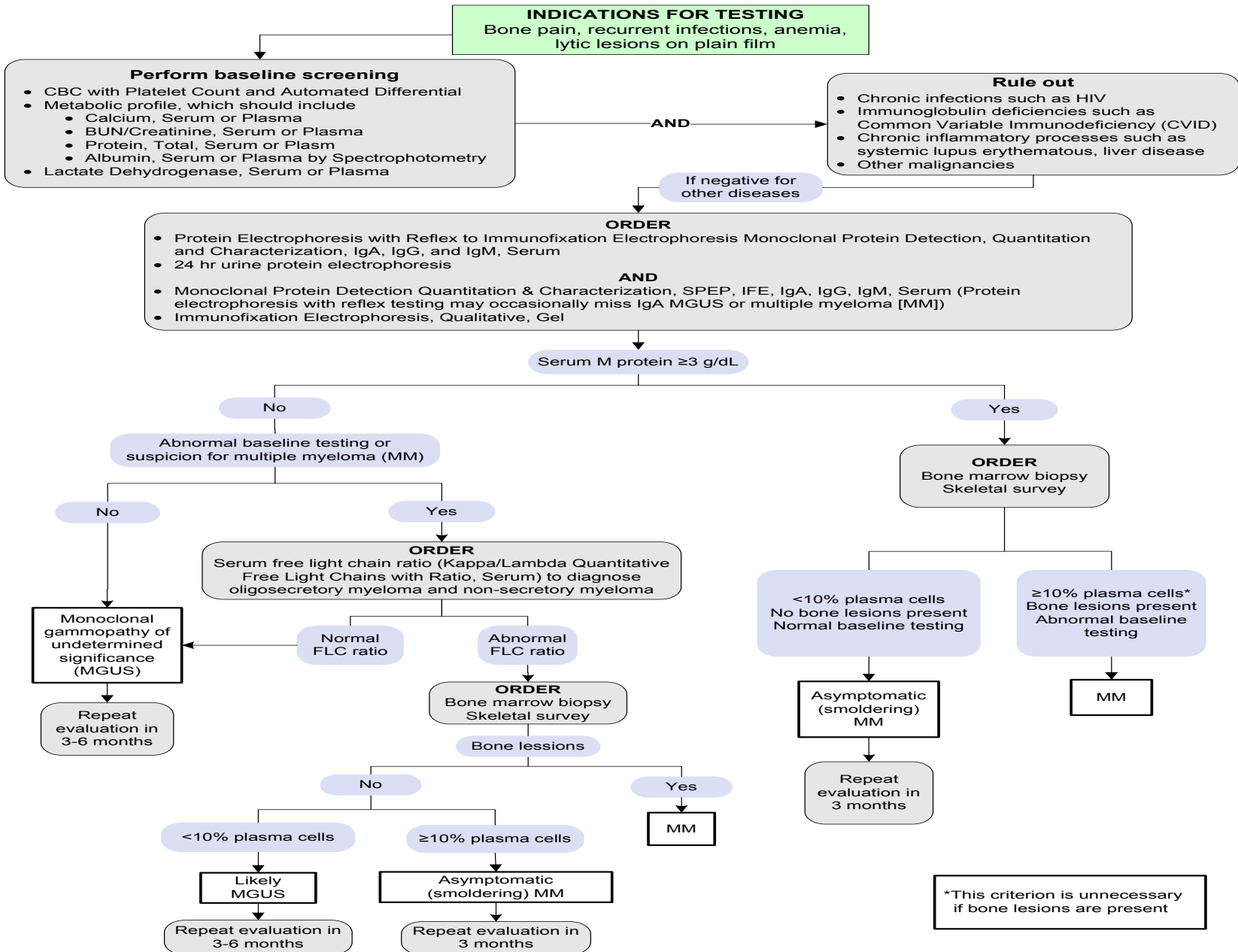
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# Plasma Cell Dyscrasias

[Click here for topics associated with this algorithm](#)



## RESCOURCES :

UP TO DATE has apps for cell phone, expensive but great!

ARUP Consult apps for cell phone, great reference for algorithms.

iHematology apps for cell phone, quick reference to describe smear morphology.

Medical Lab Tests for cell phones

[labtestsonline.org](http://labtestsonline.org)

# WHEN TO REFER

1. PANCYTOPENIA
2. PLATELETS TREND DOWN OVER TIME AND ARE STAYING UNDER 100 K
3. YOU CAN'T FIND A REASON FOR IRON DEFICIENCY
4. UNEXPLAINED LEUKOCYTOSIS
5. UNEXPLAINED ADENOPATHY.... GET IT BIOPSIED!
6. INTOLERANCE TO ORAL IRON AND PERSISTANCE OF IRON DEFICIENCY WITH NEGATIVE WORKUP
7. YOU HAVE A BAD FEELING AND TOO MAY ABNORMALS ON THE SMEAR...

## **MY ADVICE:**

GET TO KNOW YOUR LOCAL HEMATOLOGIST AND ASK FOR ADVICE. THEY MAY HAVE A FRIENDLY NP TO TALK TO. SHE OR HE MAY HAVE GOOD ADVICE!!!