1. Identify common causes of anemia.
2. Describe common signs and symptoms of anemia.
3. Describe diagnostic evaluation required to determine the etiology of anemia.
4. Recommend a treatment regimen considering the underlying cause and patient-specific variables.
5. Compare and contrast oral and parenteral iron preparations.
6. Explain the optimal use of folic acid and vitamin B_{12} in patients with macrocytic anemia.
7. Evaluate the proper use of epoetin and darbepoetin in patients with anemia caused by cancer chemotherapy or chronic kidney disease.
8. Develop a plan to monitor the outcomes of pharmacotherapy for the treatment of anemia.

Prevalence of Anemia[1,2]

Children (1–16 years)	6%–9%
Males (16–69 years)	2%
Males (85+ years)	26%
Females (16–19 years)	16%
Females (20–49 years, nonpregnant)	12%
White, non-Hispanic	10%
Black, non-Hispanic	19%
Mexican American	22%
Females (85+ years)	20.1%

IRON DEFICIENT ANAEMIA

Iron Deficient Anaemia (IDA) is the only nutrient deficiency which is **also significantly prevalent in high-income countries**

Those most seriously affected by IDA are **young children** and **women** in low and middle income countries

IDA is associated with **heart problems** and may lead to rapid or irregular heartbeat, an enlarged heart and ultimately **heart failure**

IDA can cause **extreme fatigue** and **depression**

IDA can lead to **maternal haemorrhage** and is associated with

20%

of all maternal death

IDA impacts **cognitive development** and **productivity**, however timely treatment can restore personal health and raise **national productivity levels by as much as**

20%

In many low and middle income countries, IDA is aggravated by **worm infections**, **malaria** and other infectious diseases such as **HIV** and **tuberculosis**

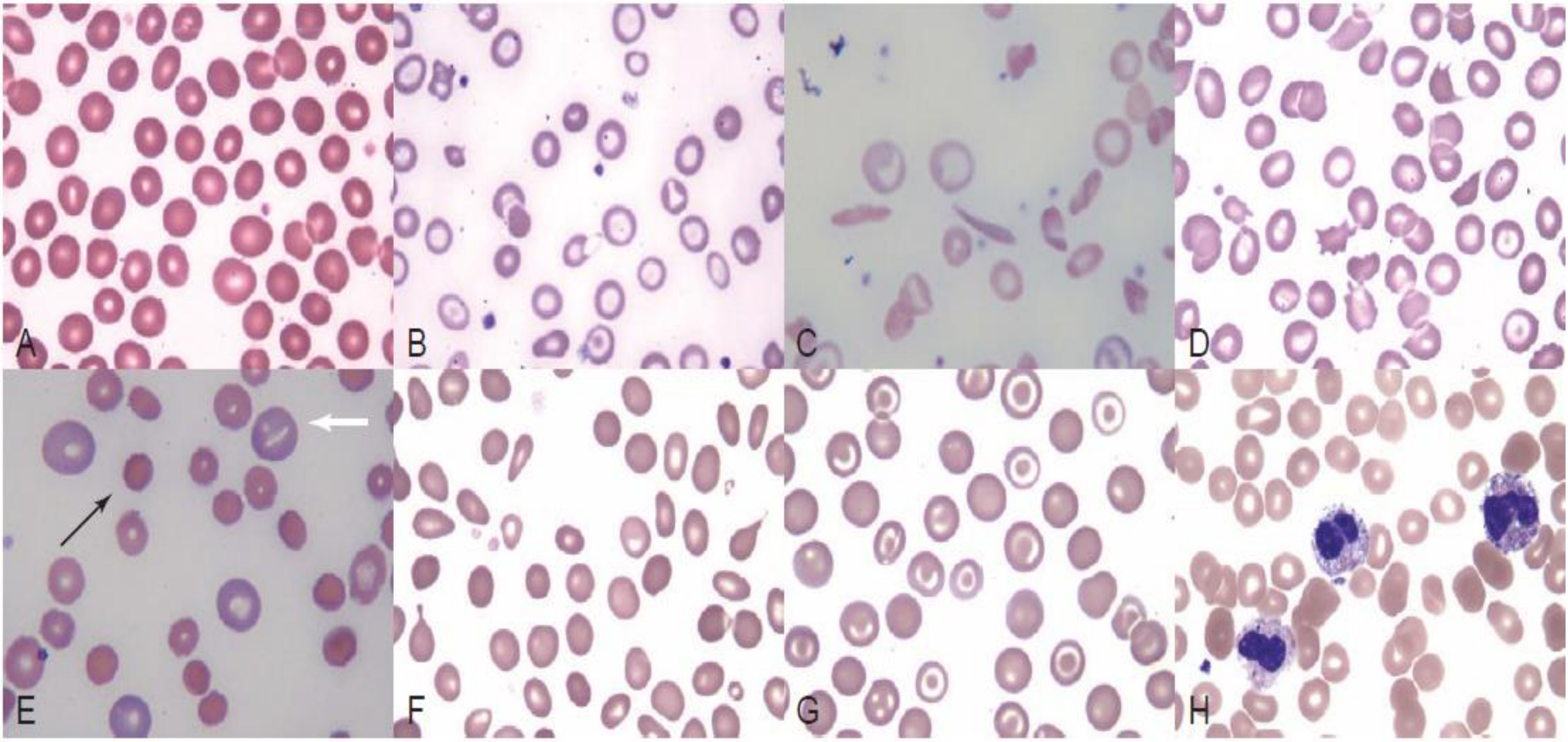
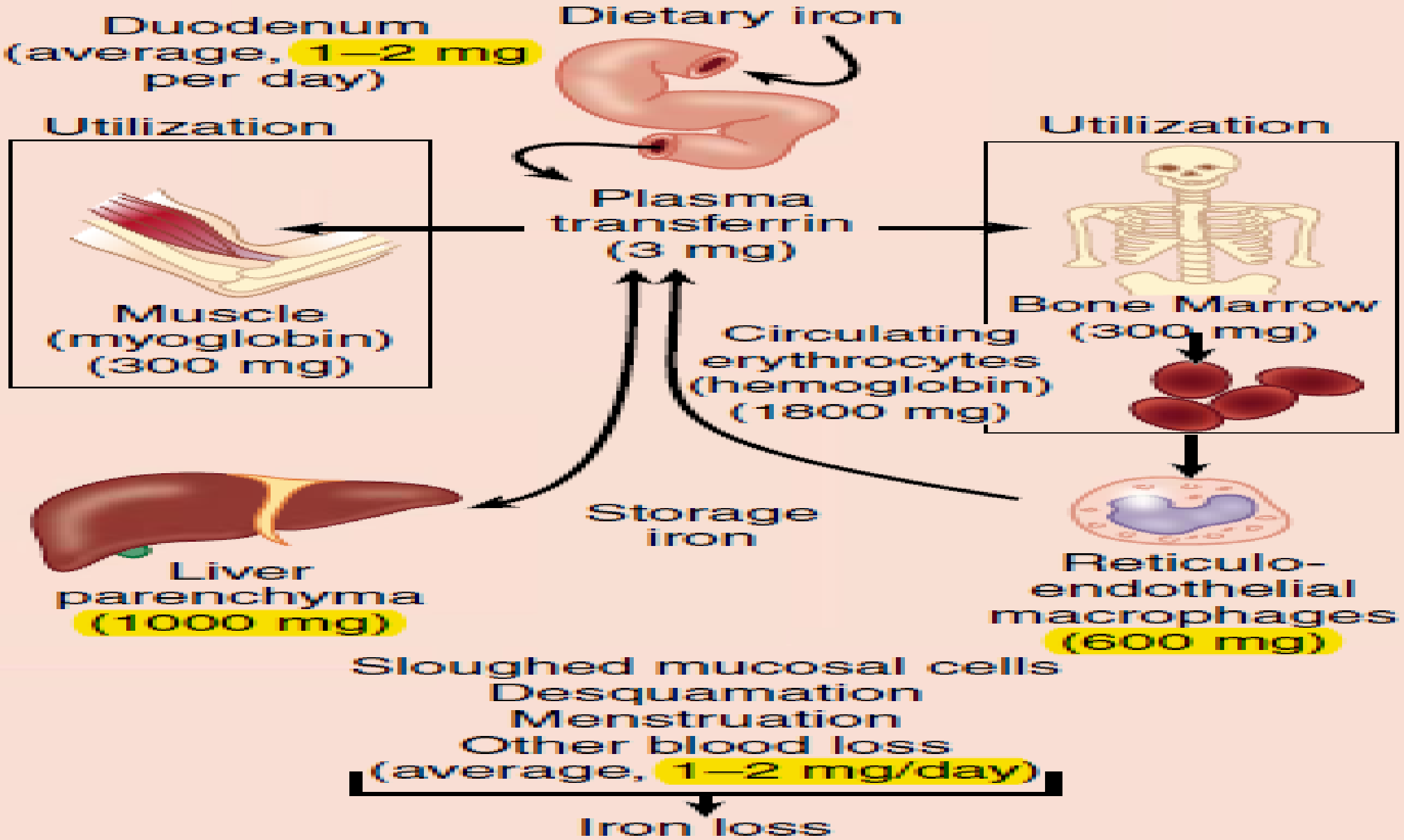


FIGURE 47-2 Peripheral blood smears in patients with anemia. **A,** Normal red blood cells. **B,** Iron deficiency anemia. **C,** Sickle cell anemia. **D,** Microangiopathic hemolytic anemia. **E,** Spherocytosis *(black arrow)* and reticulocytosis *(white arrow)* in autoimmune hemolytic anemia. **F,** Teardrops in myelofibrosis. **G,** Target cells. **H,** Pseudo-Pelger-Huet anomaly in myelodysplasia.


Duodenum
(average, 1—2 mg
per day)
Dietary iron
Utilization
Plasma
transferrin
(3 mg)
Utilization
Muscle
(myoglobin)
(300 mg)
Bone Marrow
(300 mg)
Circulating
erythrocytes
(hemoglobin)
(1800 mg)
Storage
iron
Liver
parenchyma
(1000 mg)
Reticulo-
endothelial
macrophages
(600 mg)
Sloughed mucosal cells
Desquamation
Menstruation
Other blood loss
(average, 1—2 mg/day)
Iron loss

Clinical Presentation and Diagnosis of Anemia

Signs and Symptoms

Generally, the signs and symptoms of anemia are nonspecific and may include the following:

- Fatigue, lethargy, dizziness
- Shortness of breath
- Headache
- Edema
- Tachycardia

Other findings that may be present in some patients include:

- Dry skin, chapped lips
- Nail brittleness
- Hunger for ice, starch, or clay (termed pica)

Past Medical History

Inquire about the following conditions:

- History of blood loss, such as hemorrhoids, melena, or menorrhagia (IDA)
- Malnourished or recent weight loss (vitamin B_{12} or folate deficiency)
- Alcoholism (folate deficiency)
- Cancer or chronic kidney disease (CKD)
- Chronic autoimmune disorders or infections, such as HIV infection or rheumatoid arthritis (anemia of chronic disease)

Physical Examination

These findings aid the clinician in determining the severity of the anemia:

- Orthostatic hypotension and tachycardia secondary to volume depletion
- Cutaneous changes such as pallor, jaundice, and nail brittleness

Laboratory Evaluation

Table 66–2 describes common tests used to determine the etiology of anemia. A diagnostic and treatment algorithm for anemia is outlined in Figure 66–3.

1. A CBC is a necessary first step in evaluating a patient with anemia. If the Hgb and Hct are less than the normal range, the patient is anemic. Subsequent evaluations of RBC indices and the peripheral smear often are necessary to determine the etiology (and ultimately, the treatment) of the anemia.
2. Evaluating the mean corpuscular volume (MCV) is the next step in an anemia workup. It is classified as microcytic, normocytic, or macrocytic if the MCV is below, within, or above the normal range of 80 to 96 fL/cell, respectively.

Microcytic Anemia and Iron Evaluation

Iron studies (see Table 66–2) should be evaluated in the setting of a low MCV. These include:

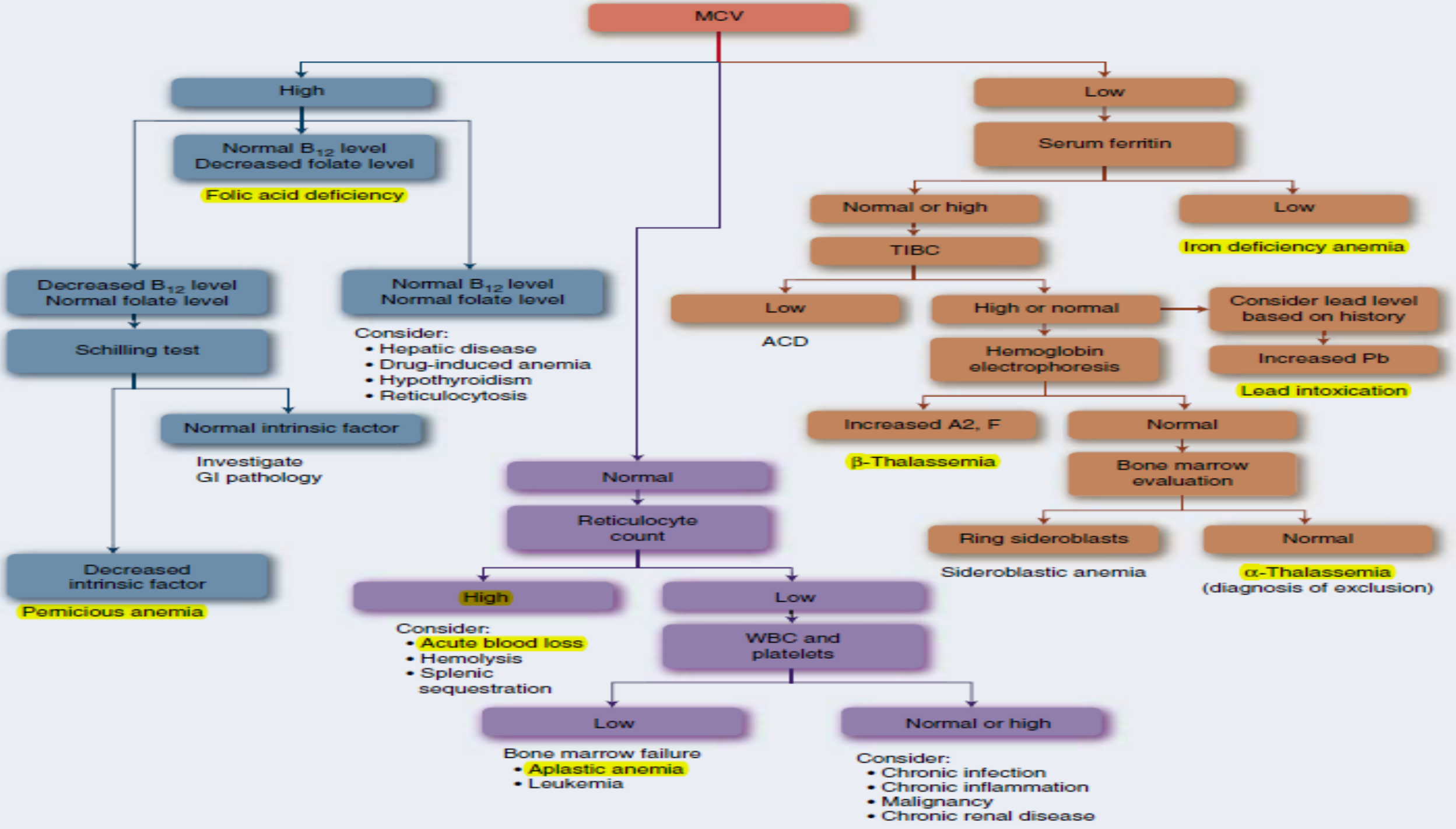
- Serum iron
- Serum ferritin—the best indirect determinant of body iron stores. It is commonly decreased in patients with IDA
- Total iron-binding capacity (TIBC)—quantifies the iron-binding capacity of transferrin and is increased in IDA
- Transferrin saturation (serum iron/TIBC)—indicates the amount of transferrin that is bound with iron; it is lower in IDA

Macrocytic Anemia

- Evaluate folic acid and vitamin B_{12} levels in the setting of an elevated MCV
- Further investigation by administering radiolabeled B_{12} (ie, Schilling test) to determine if lack of intrinsic factor

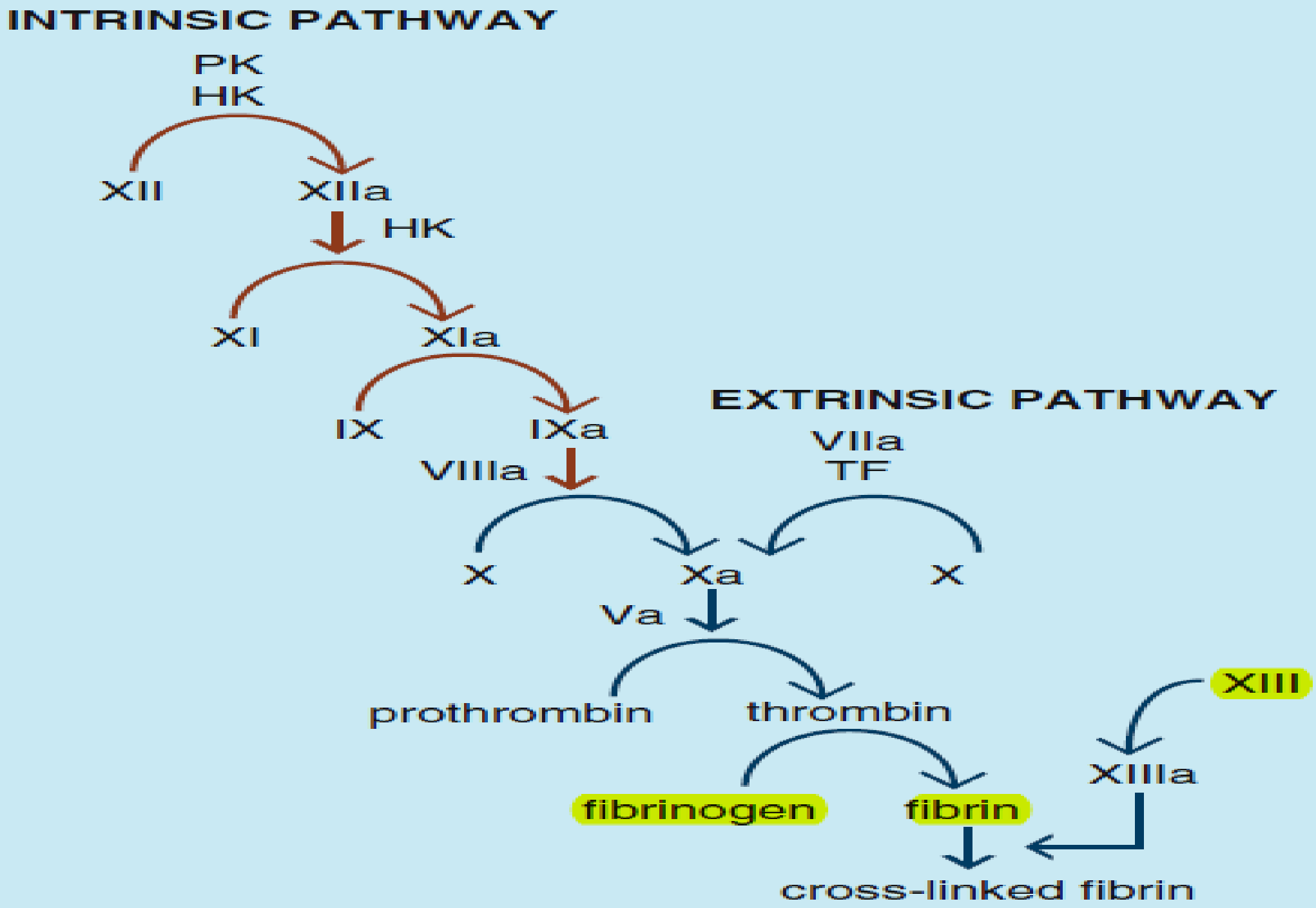
Normocytic Anemia

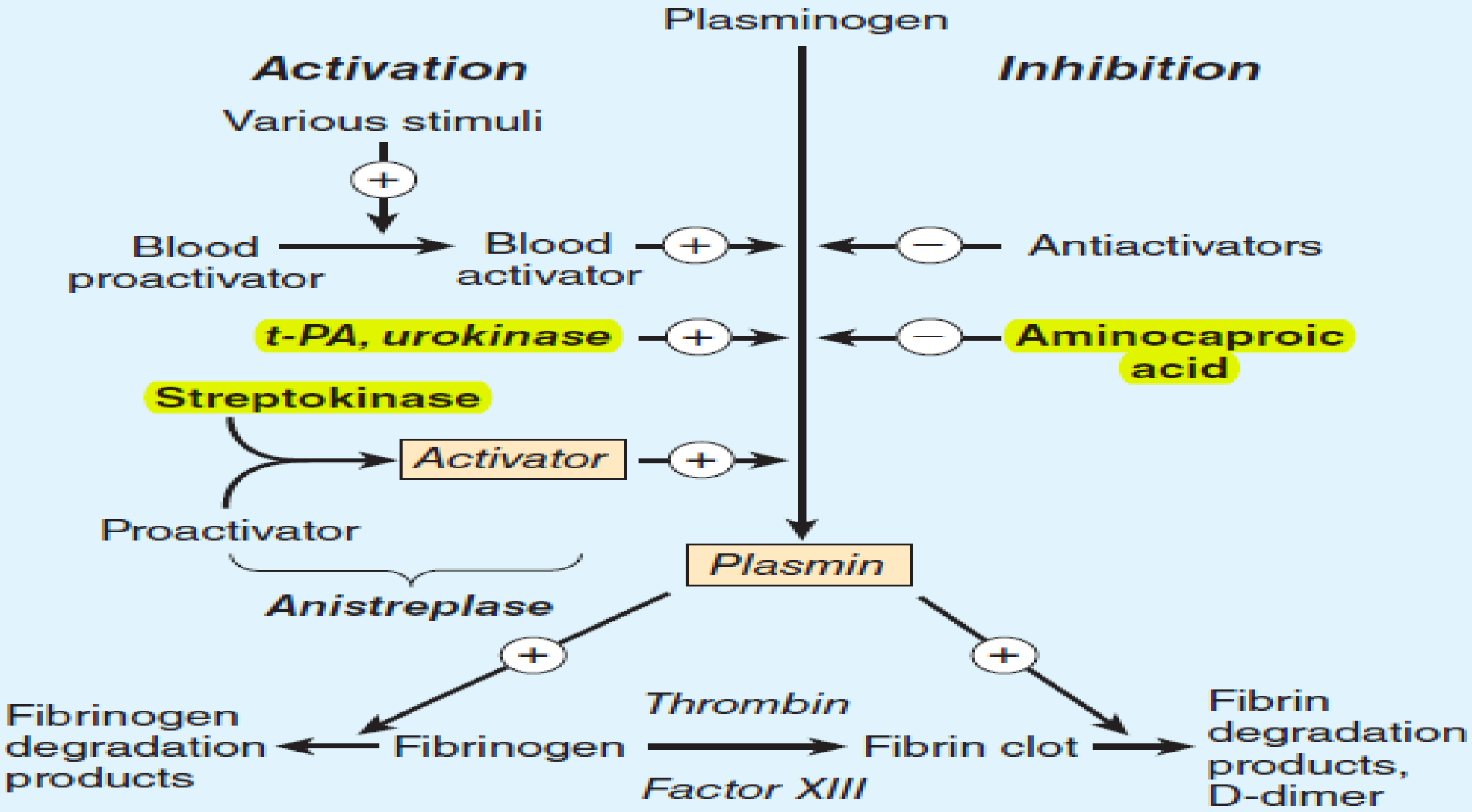
- Evaluate reticulocytes and CBC
- High reticulocyte counts may indicate RBCs loss via acute blood loss, hemolysis, or splenic sequestration
- Low serum iron with normal to increased ferritin consistent with ACD


MCV
High
Normal B_{12} level
Decreased folate level
Folic acid deficiency
Decreased B_{12} level
Normal folate level
Schilling test
Normal intrinsic factor
Investigate
GI pathology
Decreased
intrinsic factor
Pernicious anemia
Normal B_{12} level
Normal folate level
Consider:
• Hepatic disease
• Drug-induced anemia
• Hypothyroidism
• Reticulocytosis
Normal
Reticulocyte
count
High
Consider:
• Acute blood loss
• Hemolysis
• Splenic
sequestration
Low
WBC and
platelets
Low
Bone marrow failure
• Aplastic anemia
• Leukemia
Normal or high
Consider:
• Chronic infection
• Chronic inflammation
• Malignancy
• Chronic renal disease
Low
Serum ferritin
Normal or high
TIBC
Low
ACD
High or normal
Hemoglobin
electrophoresis
Increased A2, F
β-Thalassemia
Normal
Bone marrow
evaluation
Ring sideroblasts
Sideroblastic anemia
Normal
α-Thalassemia
(diagnosis of exclusion)
Low
Iron deficiency anemia
Consider lead level
based on history
Increased Pb
Lead intoxication

Oral Iron Products and Elemental Iron Content

Salt Form	Brand Name(s)	Elemental Iron Content per Dose Form
Ferrous sulfate	Feosol	65-mg/325-mg tablet
		60-mg/300-mg tablet
Ferrous sulfate, anhydrous	N/A	65-mg/200-mg tablet
Ferrous gluconate	Fergon	39-mg/325-mg tablet
		37-mg/300-mg tablet
Ferrous fumarate	Feostat	33-mg/100-mg tablet
Polysaccharide–iron complex	Niferex, Ferrex	150-mg/150-mg capsule 50-mg/50-mg tablet


INTRINSIC PATHWAY
PK
HK
XII
XIIa
HK
XI
XIa
IX
IXa
VIIIa
EXTRINSIC PATHWAY
VIIa
TF
X
Xa
X
Va
prothrombin
thrombin
XIII
XIIIa
fibrinogen
fibrin
cross-linked fibrin


Plasminogen
Activation
Inhibition
Various stimuli
Blood proactivator
Blood activator
Antiactivators
t-PA, urokinase
Aminocaproic acid
Streptokinase
Activator
Proactivator
Anistreplase
Plasmin
Fibrinogen degradation products
Fibrinogen
Thrombin
Factor XIII
Fibrin clot
Fibrin degradation products, D-dimer