

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Arabic calligraphy in a highly stylized, bold script. The text is written in black ink on a white background. The calligraphy features thick, expressive strokes and includes various diacritical marks (vowels and consonants) written above and below the main text. The overall style is characteristic of modern Arabic calligraphy, emphasizing geometric forms and dynamic movement.

Evaluation of Anemia

M.R.Ravanbod

Hematologist/medical oncologist

SUMS

Anemia

- Low red blood cell mass, manifested by a low hemoglobin or hematocrit for that person's age, sex and physiologic state

Normal values

	<u>Men</u>	<u>Women</u>
• Hemoglobin (gm/dL)	13.5-15.5	12-14
• Hematocrit (packed cell volume)	41-47%	36-41

Physiologic states of low hematocrit but not functional anemia

- Plasma volume expansion (pregnancy)
- Hypothyroidism
- Low oxygen affinity hemoglobinopathies

Anemia: Clinical manifestations

Symptoms:

- Reflective of tissue hypoxia
- Fatigue, dyspnea on exertion, chest pain, palpitations, headaches, confusion
- More likely to be symptomatic if acute than chronic, gradual decrease in hct

Anemia: Clinical manifestations

Signs:

- Non-specific
- Often not apparent until severely anemic
 - Pallor
(skin, mucosa, nail beds, conjunctiva)

Anemia: Diagnostic clues from the physical exam

- Orthostatic hypotension
 - Fever
- Jaundice, scleral icterus
 - Vitiligo
 - Leg ulcers
 - Splenomegaly
 - Lymphadenopathy
 - Neurologic deficits
- Hemoccult positive stool

Anemia work-up: Clues from the history

- Acuity of the anemia
- Concomitant illness
- GI bleeding, any change in bowel habits
 - Neurologic complaints
 - Family history
- Social habits (IVDA, EtOH)
 - Medications
- Occupational exposures
 - Travel history
 - Diet

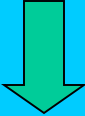
Laboratory evaluation of anemia

- **Reticulocyte count**
- **Bilirubin and LDH**
- **Peripheral blood smear**
- **Red blood cell indices**

Reticulocyte count

- Reticulocyte: Young RBC with residual RNA
- Normally circulate 1 day before becoming mature RBC
- Normal = 1% (1 retic/100 RBC's)

Retic count

- Reflects marrow red cell production:
 - Anemia

 - Increased erythropoietin

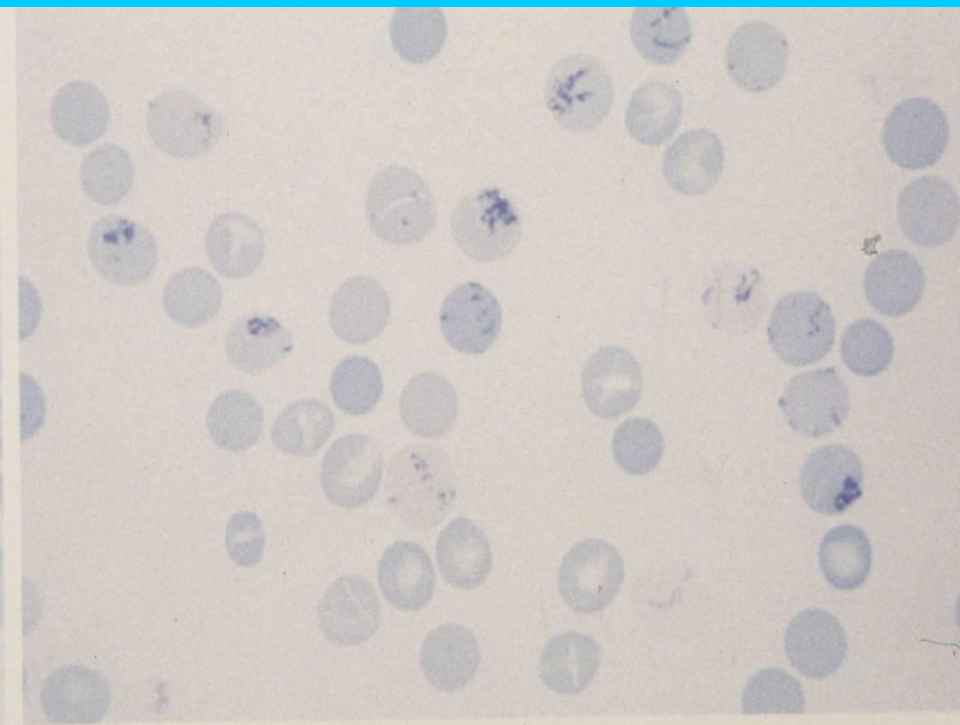
 - Increased marrow production

 - Reticulocytosis

Retic count

- **High retic**: Productive bone marrow
(Blood loss or hemolysis)

Low retic: Underproductive marrow
(Hypoproliferative processes or
ineffective erythropoiesis)

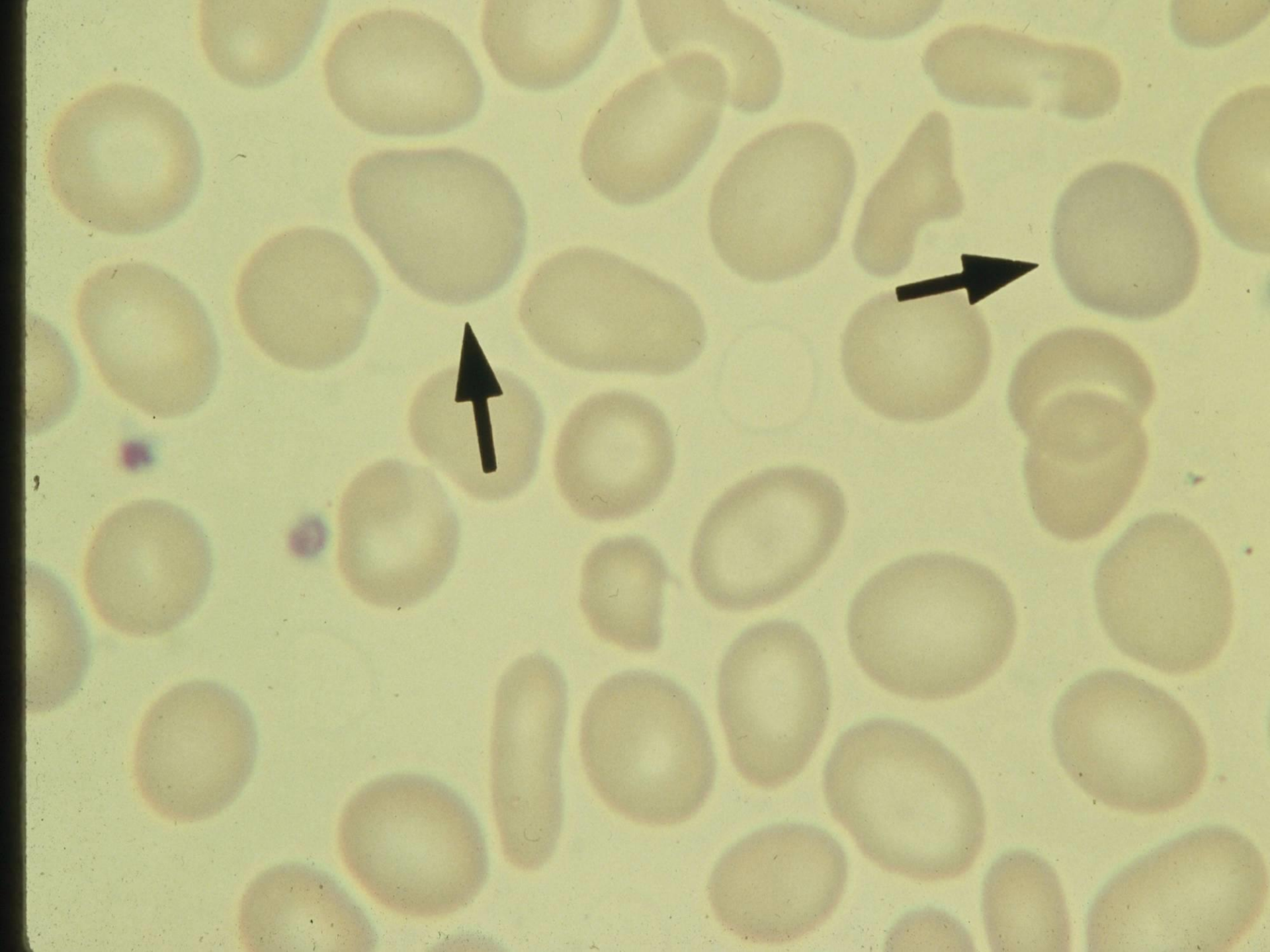


Corrected retic count

- Need to correct for *early release* and the *degree of anemia*
- With severe anemia young retic's are released from marrow, lasting in circulation 2-3 days (instead of 1 day)
- Young retics on peripheral smear:
Polychromasia

Correcting the retic for early release

- Early release of young retics leads to spuriously elevated retic count
- For a Hct <20 (if polychromasia is seen) need to correct retic by dividing by 3; for Hct in mid-20's divide by 2



Correcting the retic for anemia

- Retic count is a % of RBC's, so it will be falsely elevated when RBC's are low
(ie ANEMIA)
- Example: Retic=2%, Hct=20%. Corrected retic= $20/40 \times 2 = 1\%$
- If polychromasia present=> Divide by 2,
For a *Corrected Retic Index* of 0.5%

Corrected Retic Index

- If $< 2 \rightarrow$ Marrow underproduction
- If $> 3 \rightarrow$ Bleed or hemolysis

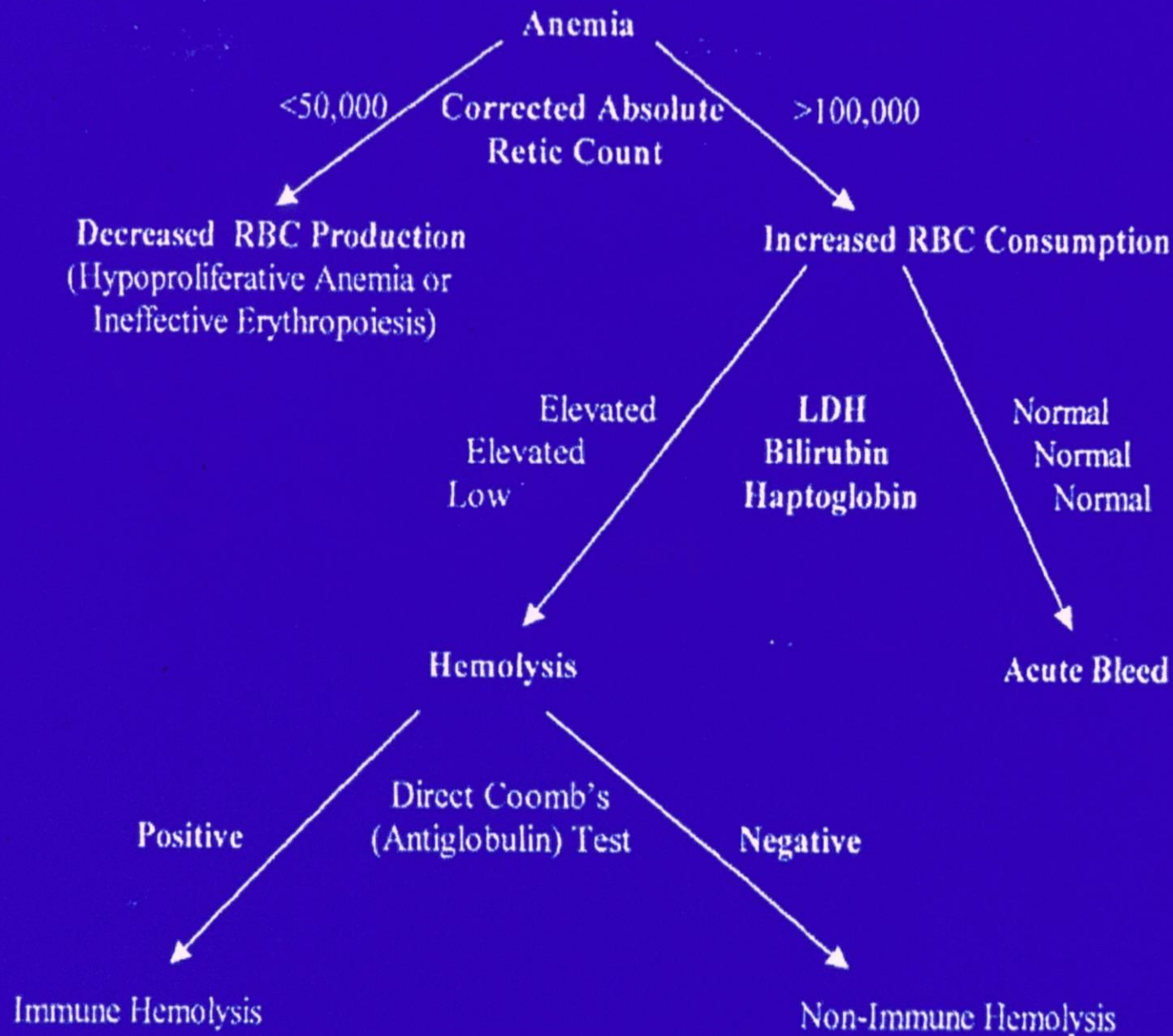
Bilirubin and Lactate dehydrogenase (LDH)

- Most bilirubin comes from degradation of hemoglobin from dying RBC's
- In absence of liver disease an elevated bilirubin (unconjugated) is a good indicator of RBC destruction
- LDH levels rise w/red cell destruction but also w/many other processes

Major causes of anemia

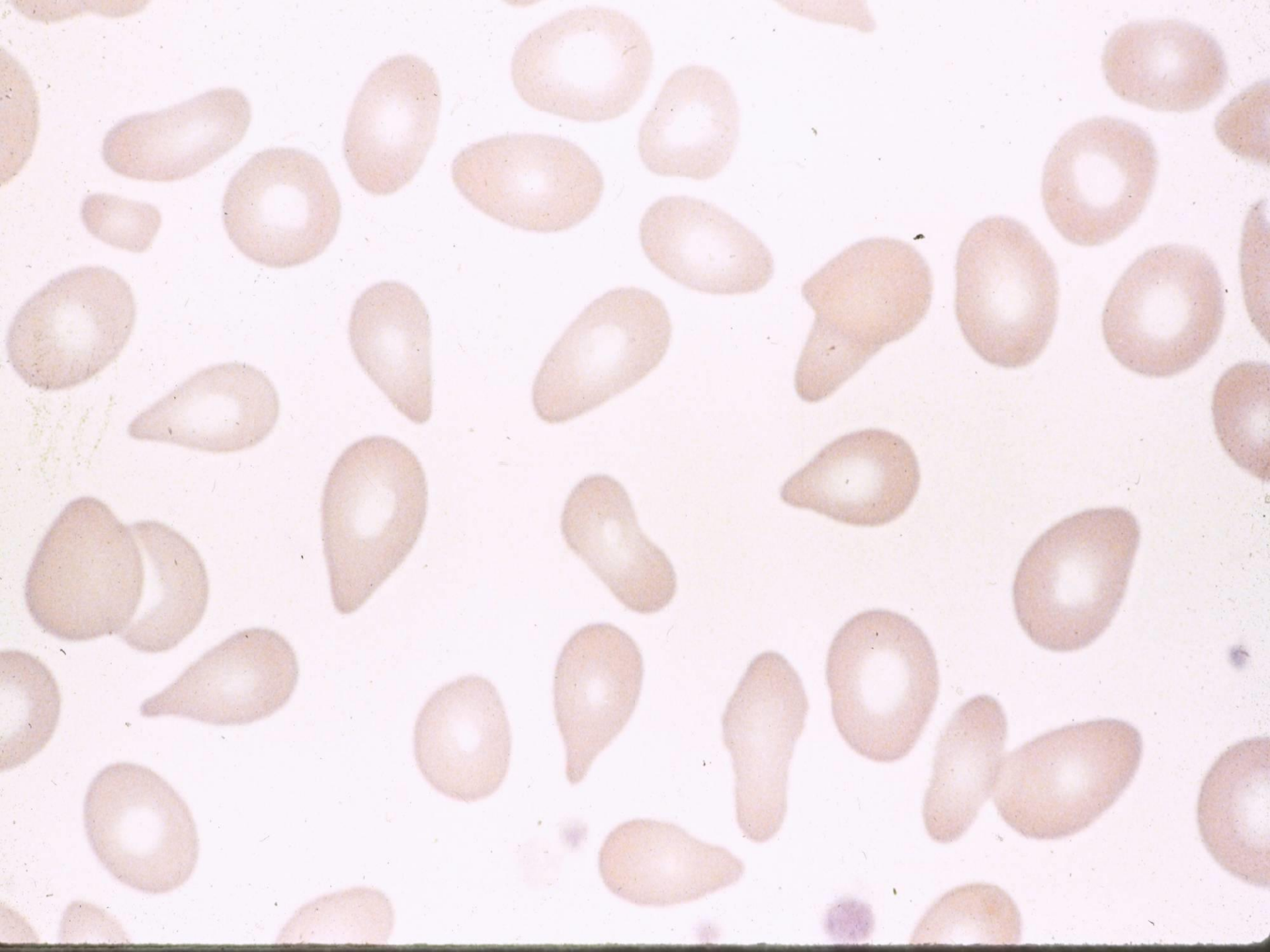
- Low retic, normal bili & LDH →
Hypoproliferative Anemia
(Fe studies; bone marrow biopsy)
- Low retic, high LDH & bili →
Ineffective erythropoiesis
- High retic, LDH & bili → **Hemolysis**
- High retic, normal LDH & bili → **Bleed**

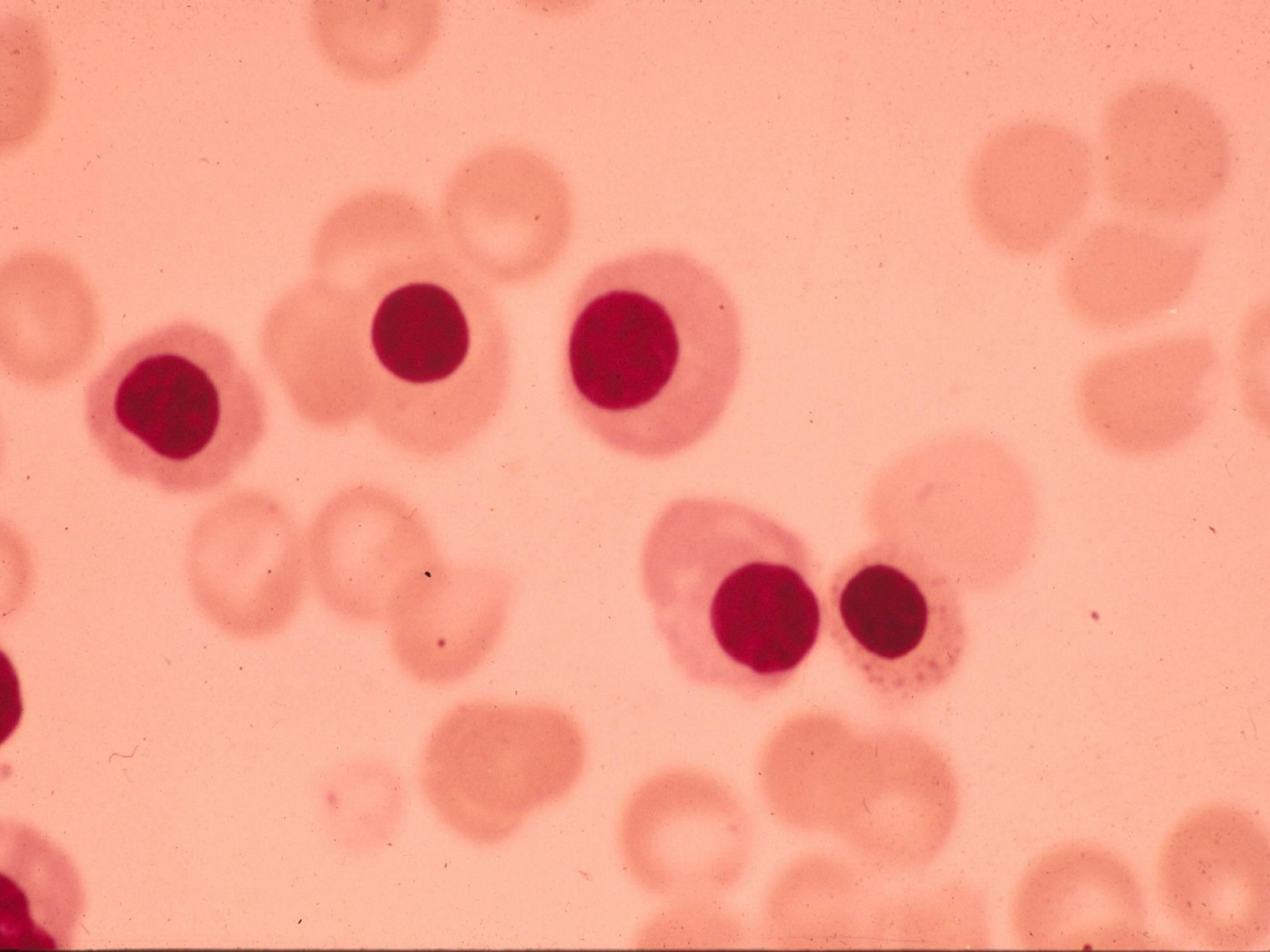
Diagnostic Algorithm

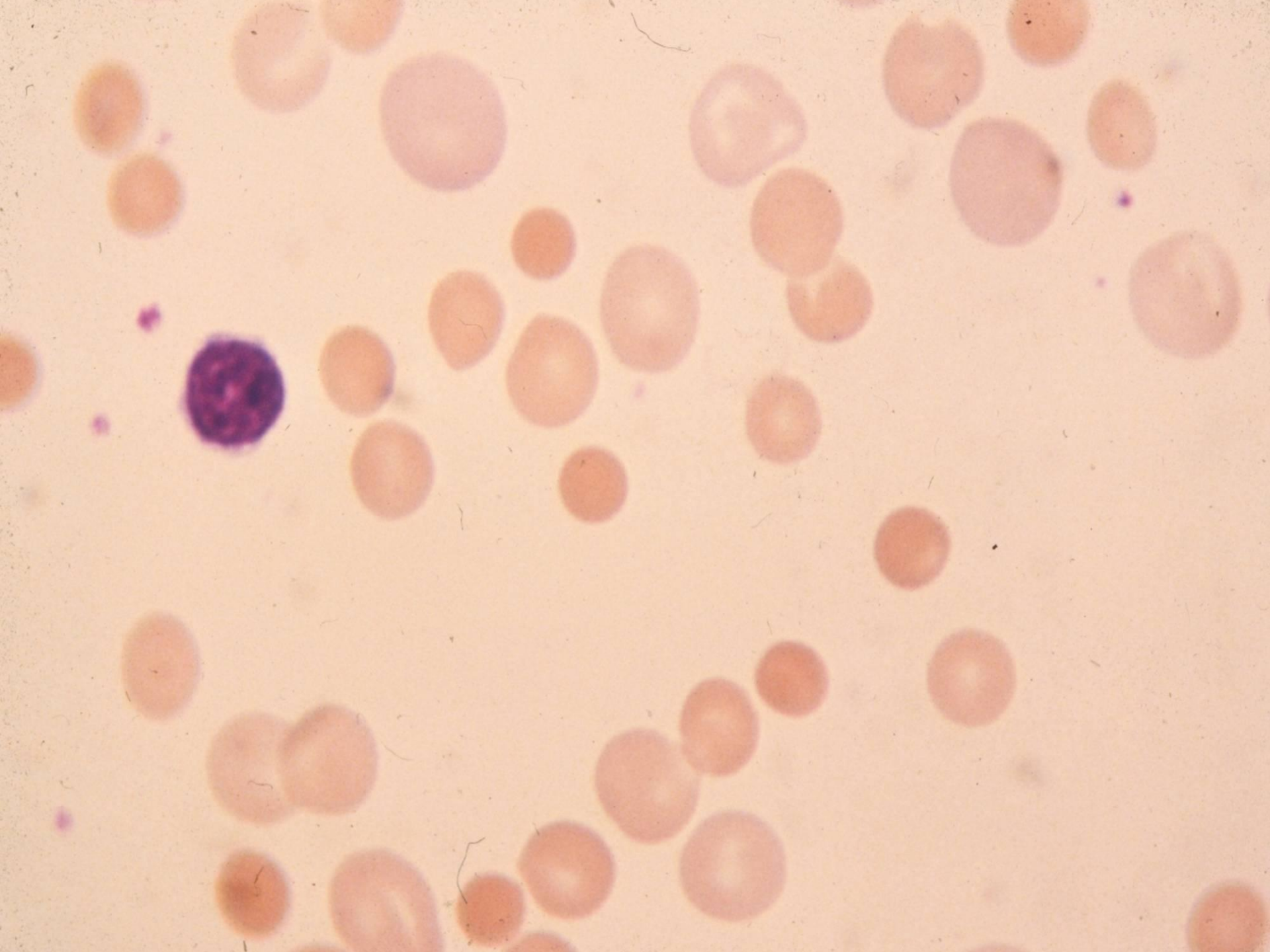


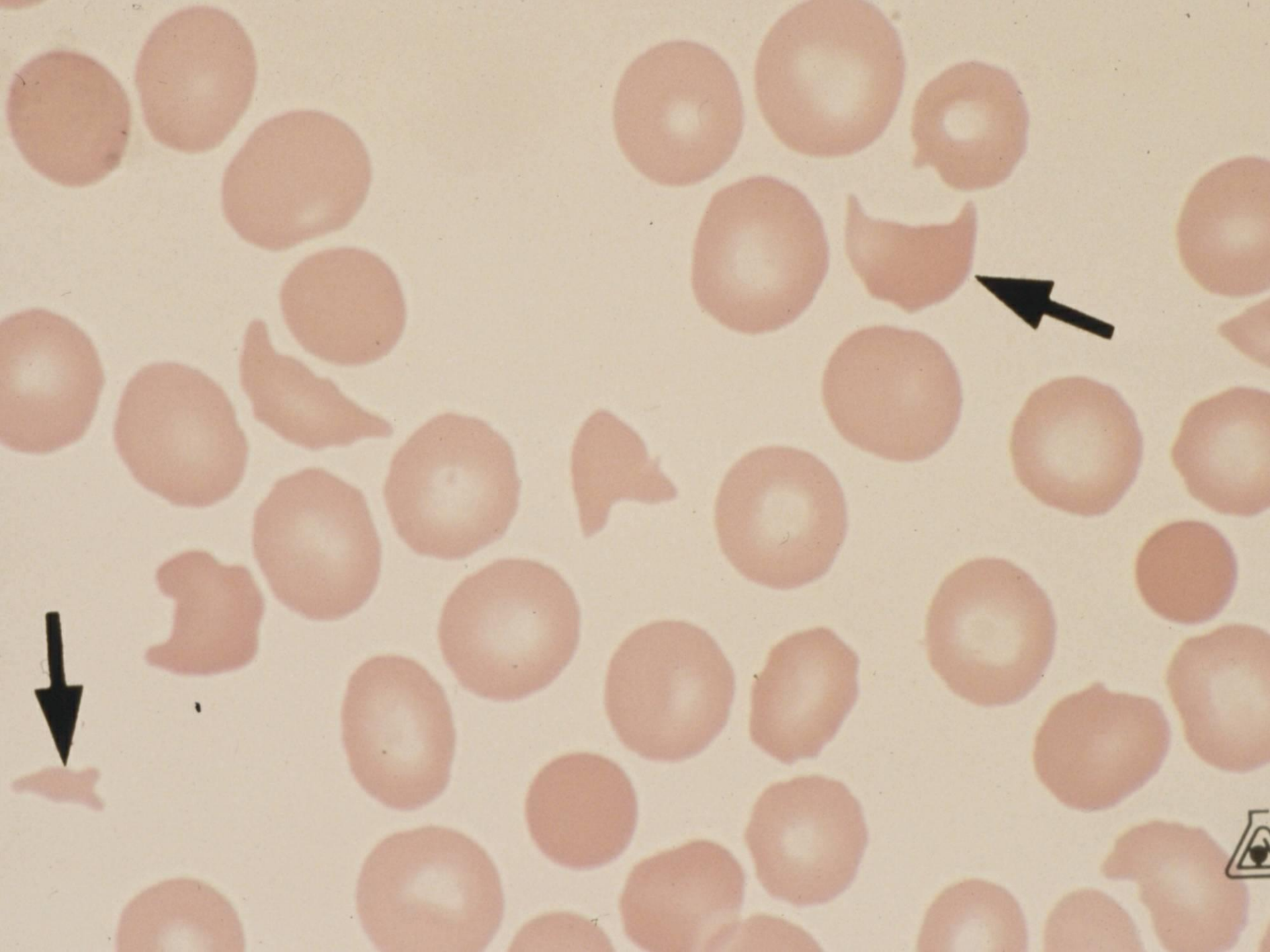
Anemia work-up: Use of the peripheral blood smear

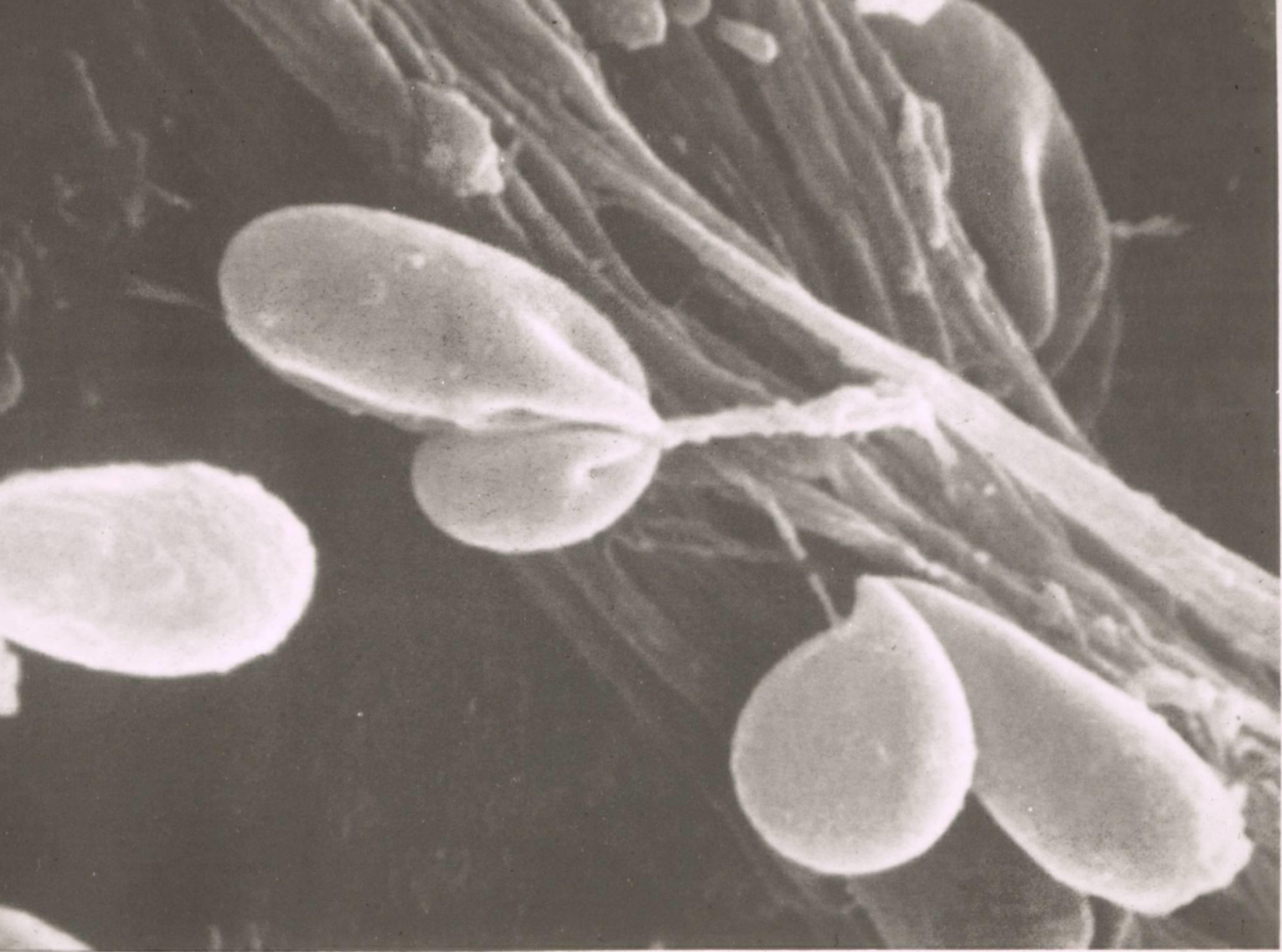
- Polychromasia
- RBC morphology helpful in narrowing diagnosis of hemolysis (spherocytes, bite cells, etc) or hypoproliferative disorders (tear drops, nucleated RBC's, rouleaux)
- White blood cell morphology (hypersegmented neutrophils, toxic PMN's)
- Smear can confirm red cell indices

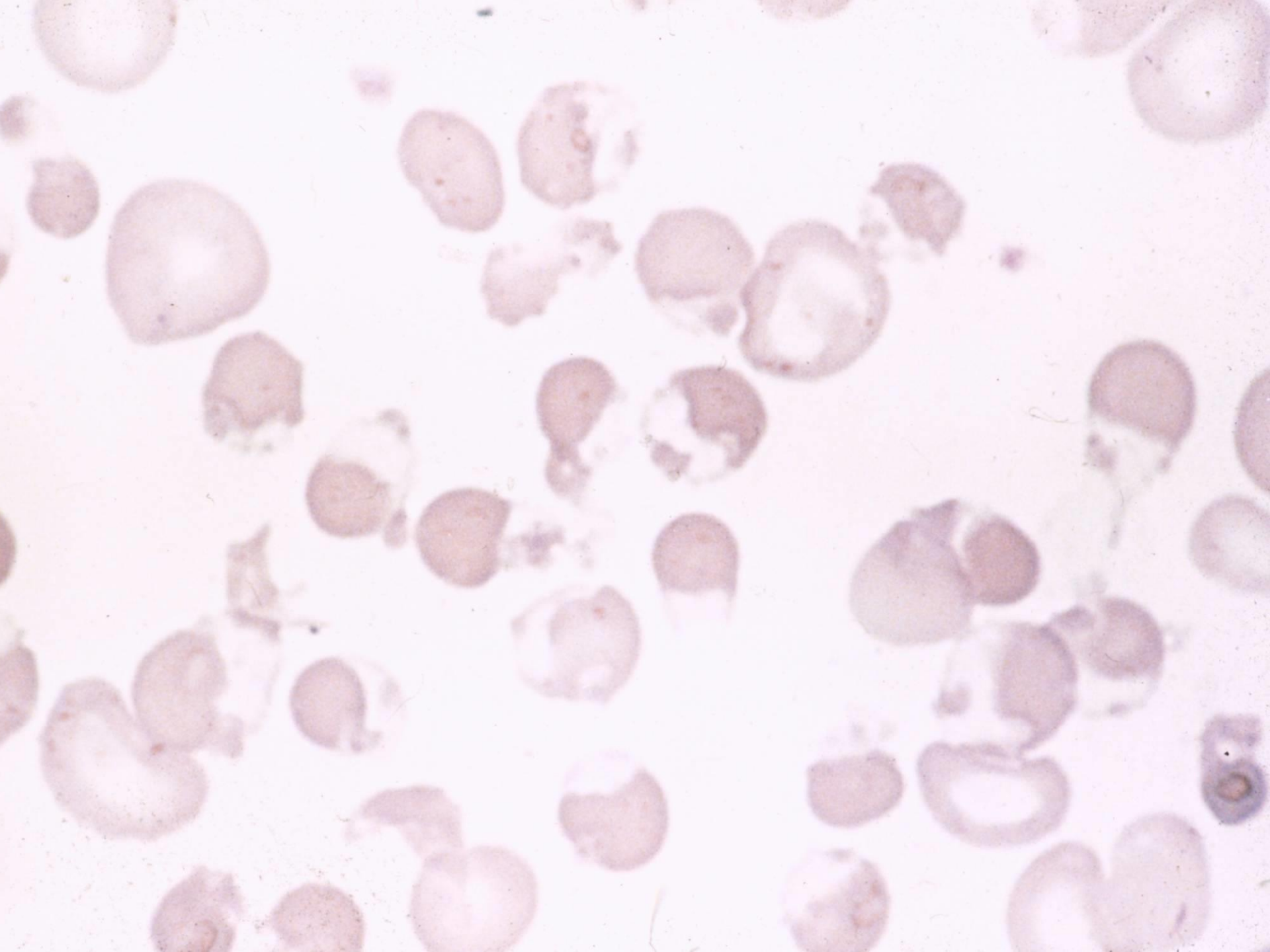




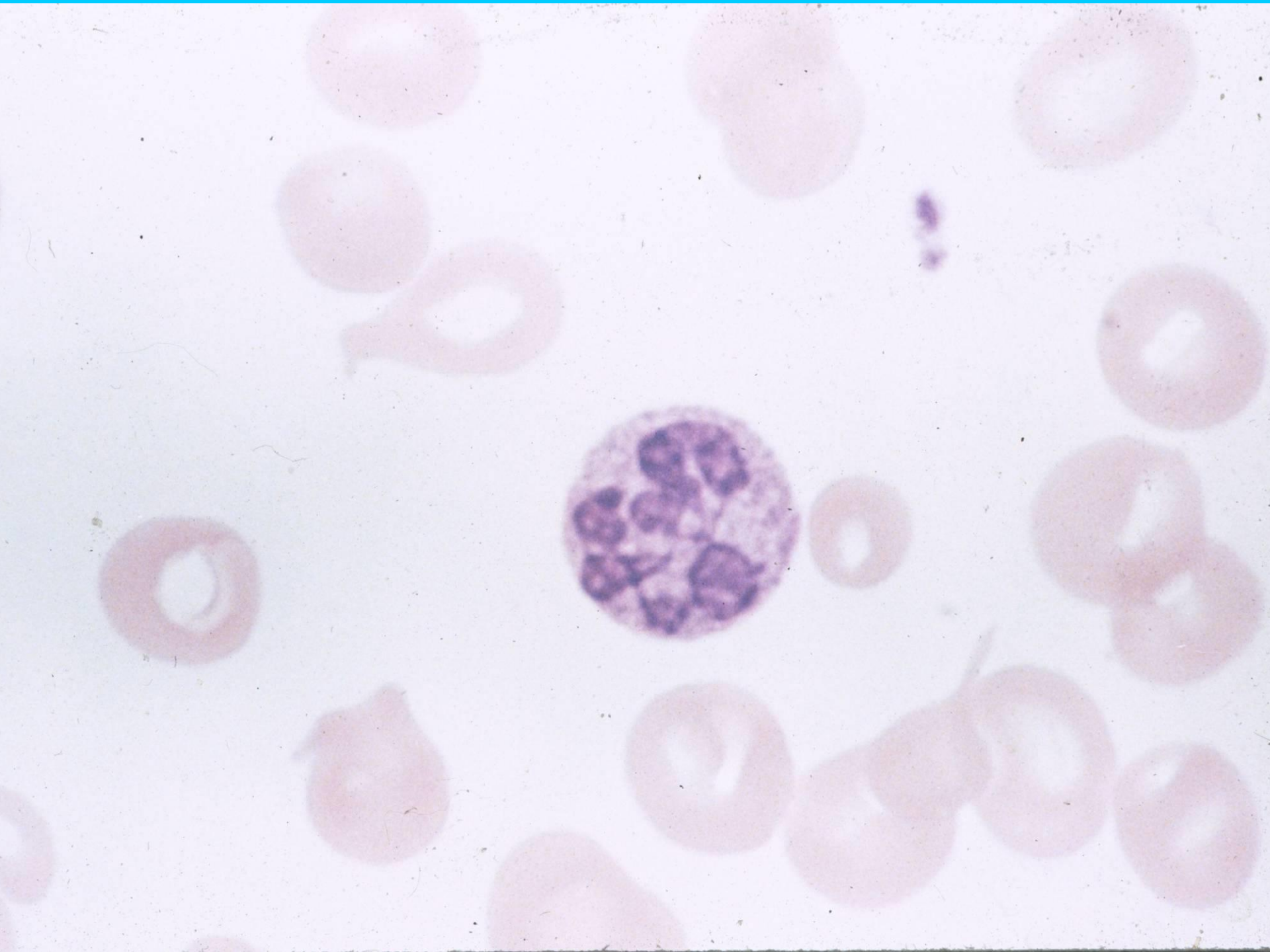












Red cell indices

	<u>Normal values</u>
• Mean corpuscular volume (MCV)	80- 100 fL
• Mean corpuscular hemoglobin (MCH)	27.5- 33pg
• Mean corpuscular hb concentration (MCHC)	33.4-35.5g/dL
• Red cell distribution width (RDW)	11.5-13.5
• Red cell count	4-6 x 10 ⁶ /μL

Use of the RDW

- 1st index to become abnormal (elevated) in Fe deficiency
- Elevated in cases of dimorphic RBC population (Fe & B12 deficiency), in which MCV may be normal

Microcytic (low MCV) Anemias

Impaired hemoglobin synthesis from:

1) Inadequate **Fe** incorporation into heme

- *Fe deficiency, Anemia of chronic disease*

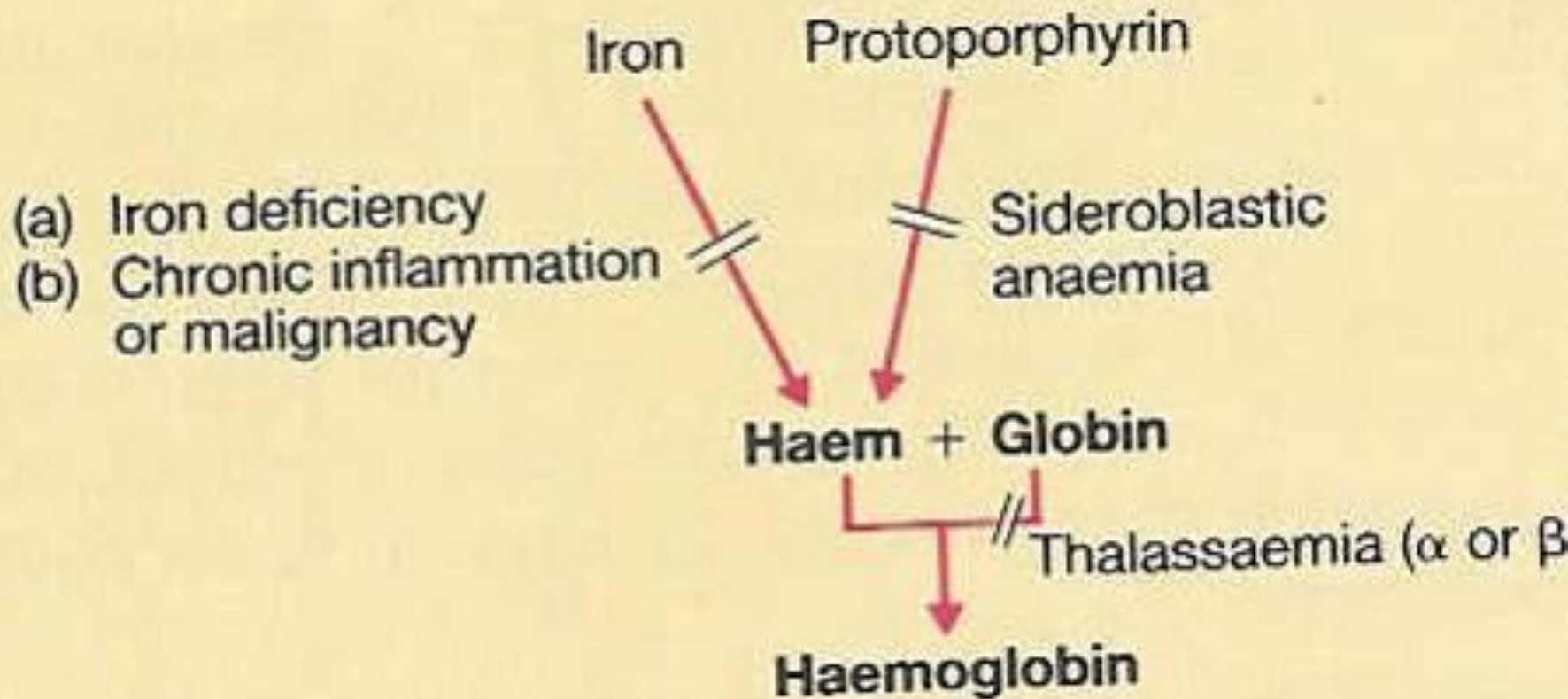
2) Defective **globin** synthesis

- *Thalassemia*

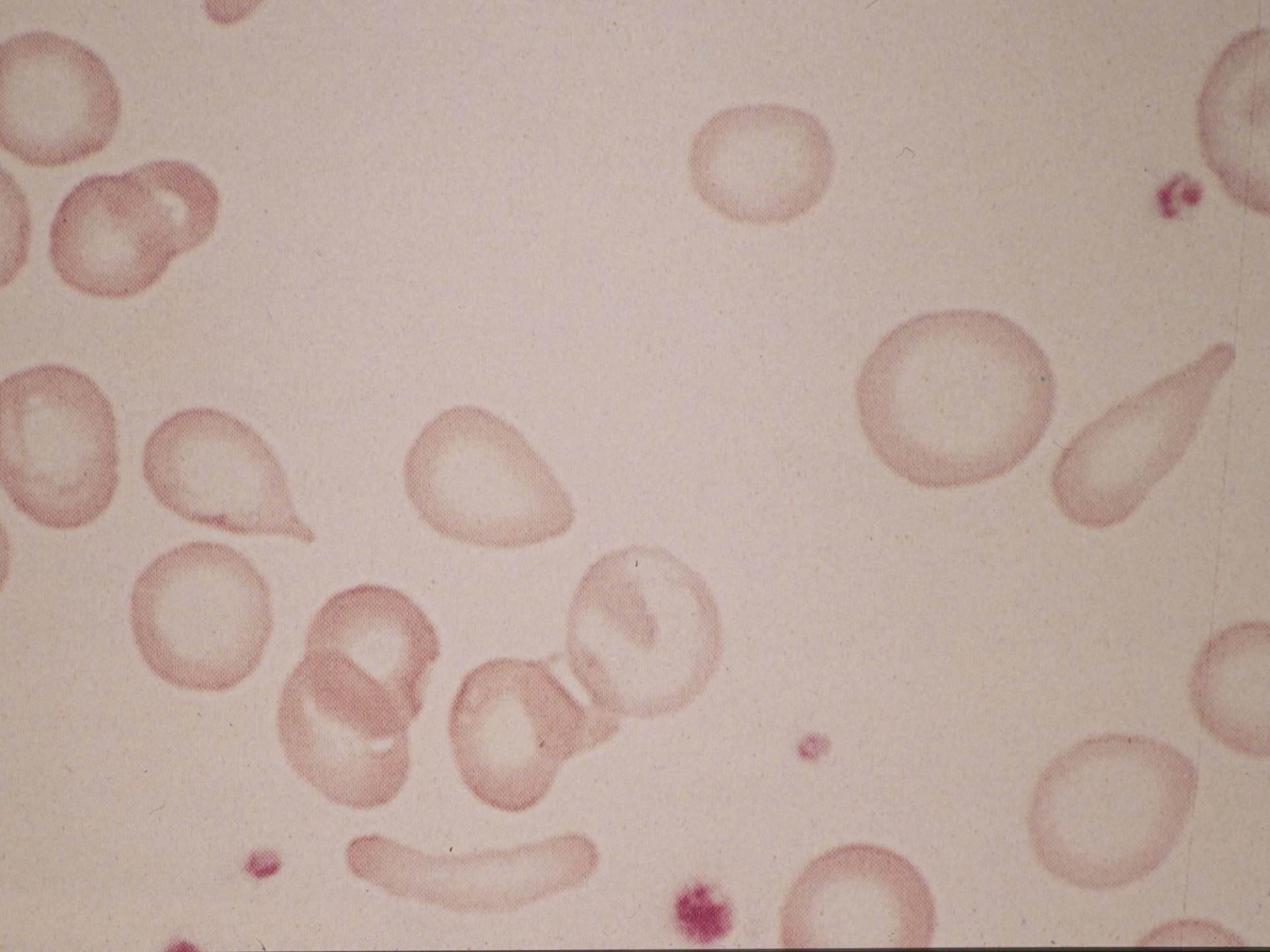
3) Defective **heme** synthesis

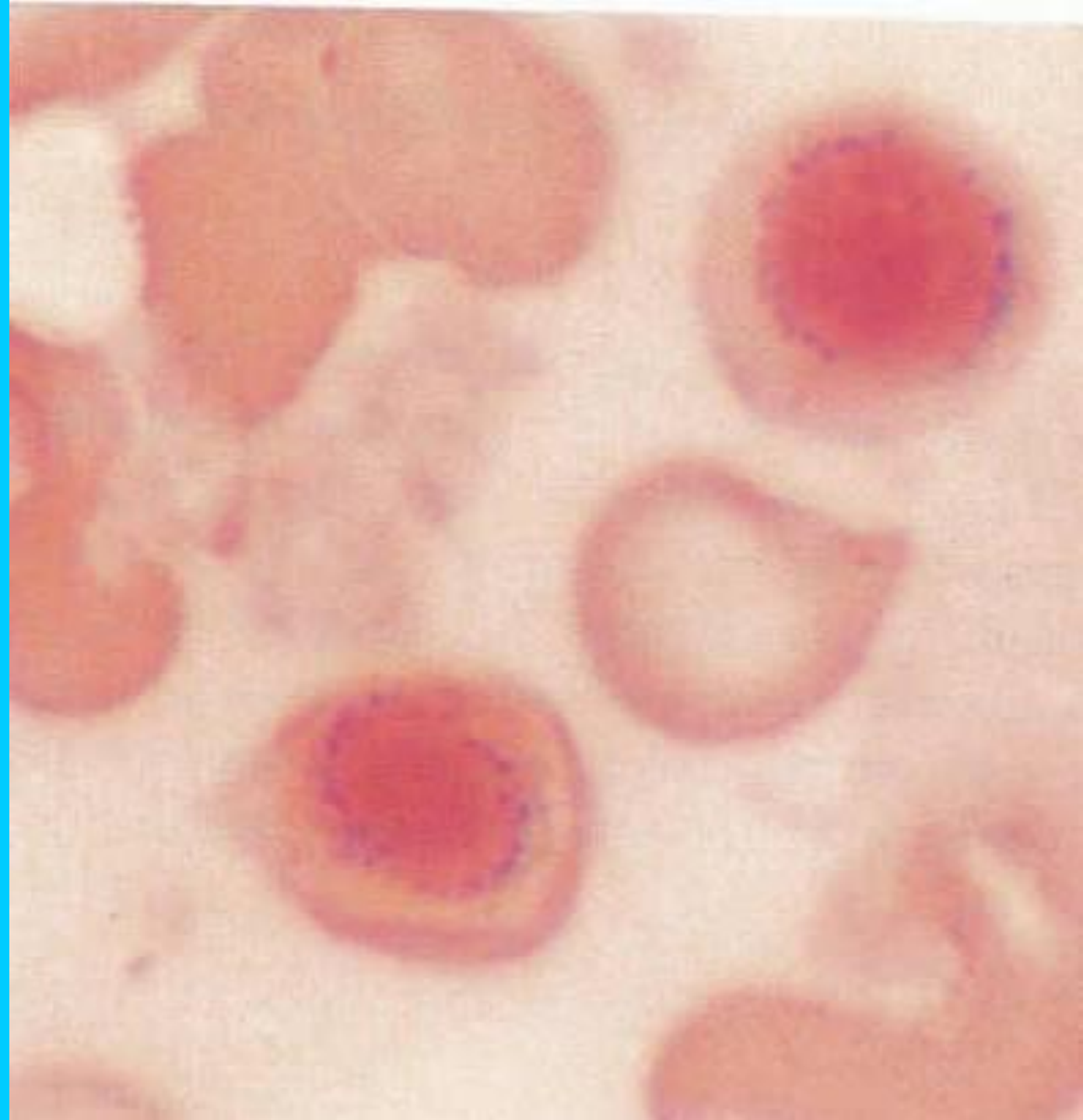
- *Sideroblastic anemias, lead toxicity*

Microcytic Anemias









Macrocytic Anemias

- Due to either:
 - 1) Ineffective erythropoiesis
 - 2) RBC membrane cholesterol defects
(Liver disease, hypothyroidism)

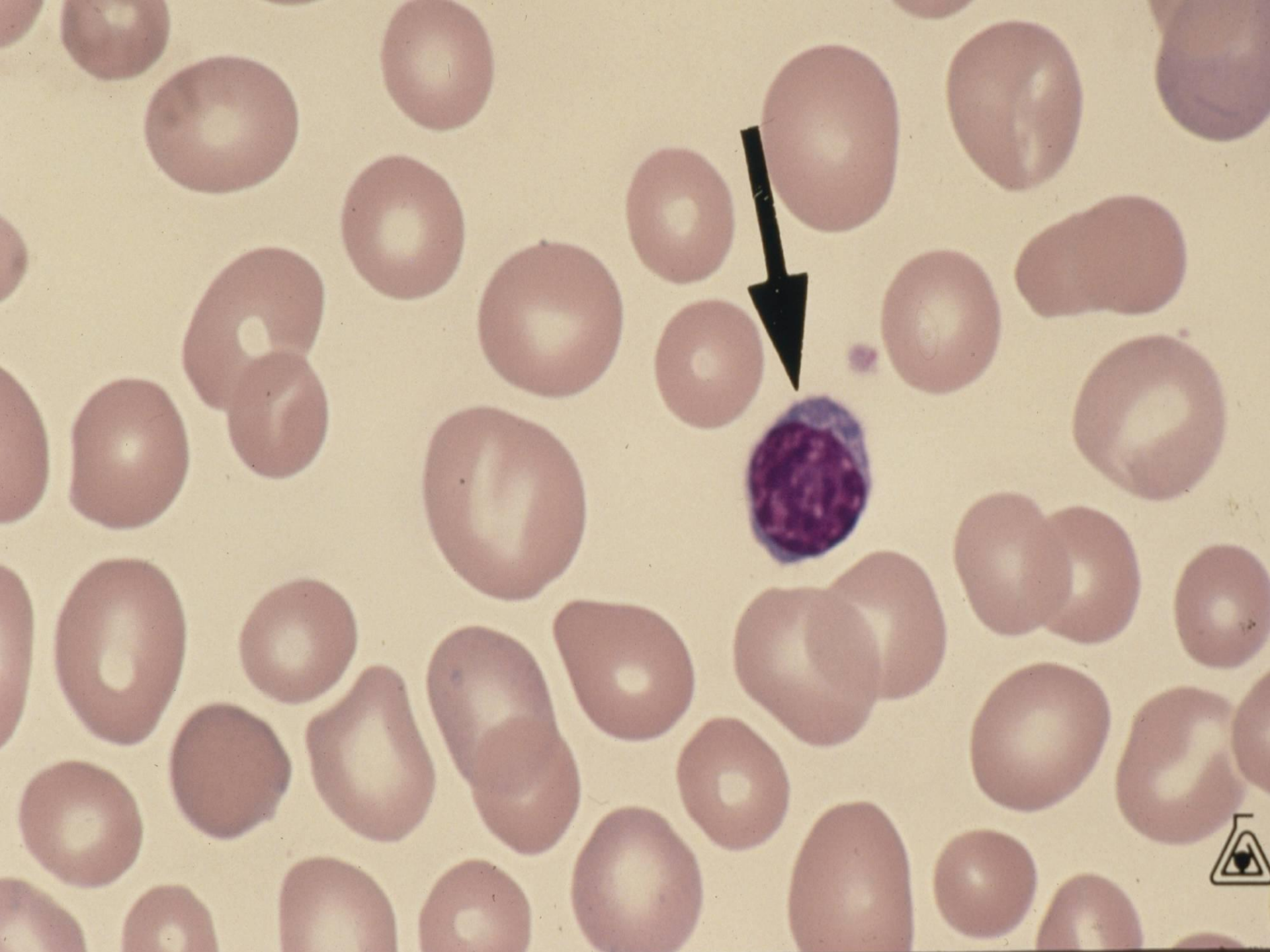
Ineffective erythropoiesis

- Intramedullary (marrow) destruction of RBC precursors
- Low retic, High LDH & bili-, high MCV
- Causes: **Vit B12 or folate deficiency**

Alcohol

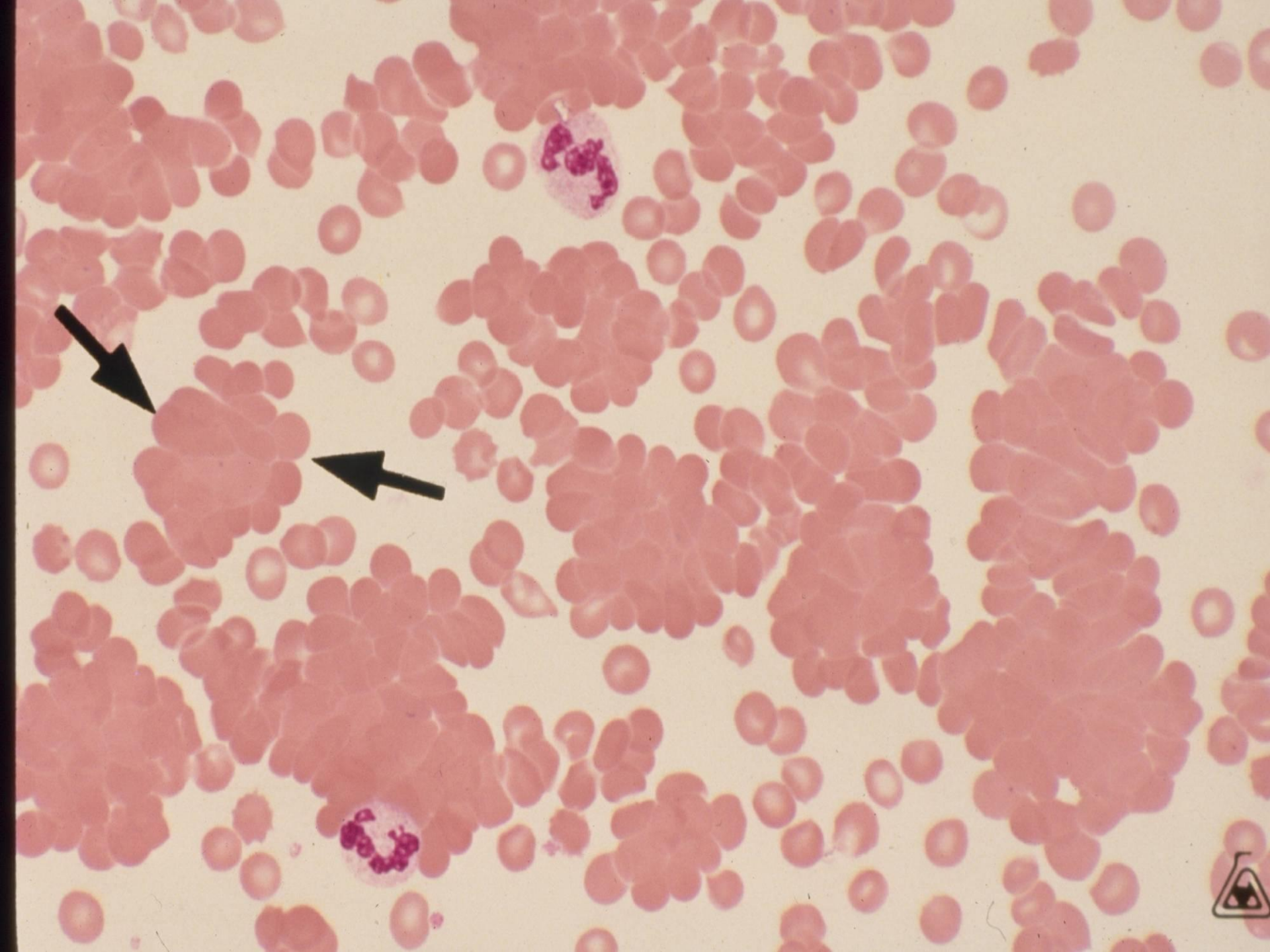
Myelodysplasia

**Medications (antiepileptics,
antimetabolites, ziduvodine)**



Pseudomacrocytosis

- Marked reticulocytosis
 - Cold agglutinins
 - Hyperglycemia



Normocytic Anemias

- Anemia of chronic disease
 - Early Fe deficiency
 - Blood loss
 - Renal disease
 - Hemolysis
 - Bone marrow failure

(tumor involvement, leukemia, lymphoma)

- Multiple myeloma

Major causes of anemia

- Low retic, normal bili & LDH → **Hypoproliferative Anemia**
- Low retic, high LDH & bili → **Ineffective erythropoiesis**
- High retic, LDH & bili → **Hemolysis**
- High retic, normal LDH & bili → **Bleed**

Hypoproliferative Anemias

- Fe deficiency
- Anemia of chronic disease
 - Renal disease
- Myelophthistic processes
 - Multiple myeloma
 - Lead poisoning
 - Aplastic anemia

Ineffective erythropoiesis

- B12 or Folate deficiency
 - Myelodysplasia
 - Thalassemias
 - Medications

Hemolysis

- Thalassemias
- Hemoglobinopathies
- Autoimmune hemolysis
 - Microangiopathic
- Inherited RBC membrane disorders
- RBC enzyme deficiency disorders

Blood loss

- Consider work-up for an underlying hemostatic defect

Most common causes of anemia

- 1) Fe deficiency**
- 2) Anemia of chronic disease***
- 3) Hemolysis**
- 4) B12 or folate deficiency**
- 5) Renal disease**

You are asked to see a 75 year old man in the ER who is severely anemic. He normally plays racquetball for 3 hrs 3x/wk but lately has only been able to play 2hrs at a time. His exam is notable only for white patches over his skin and that he appears minimally symptomatic. Hct=15, MCV=122, RDW=25, Retic=2.5%, abs retic= 20,000, LDH=2600, bili=2.3 (indirect =1.9).

- What is the most likely diagnosis?

- 1) Vitamin B12 deficiency
- 2) Hemolytic anemia
- 3) Fe deficiency
- 4) Thalassemia
- 5) Acute blood loss

A 24 year old medical student is shot in the abdomen by an irate professor for not showing up to his lecture. Several hrs later he is brought to the ER and found to be anemic, Hct=20, MCV=87, RDW, bili, LDH and smear are all normal. Retic=1%, abs retic=20,000.

- Why is he anemic?

- 1) Alcohol

- 2) Lead toxicity

- 3) Formaldehyde exposure

- 4) Hypoproliferative process

- 5) Acute blood loss

A 28 y.o. woman comes to your office c/o severe fatigue, worsening over several months. She has been having heavy menses for the past several yrs. Hgb=5, Hct=15, MCV=74, RDW=26, Retic=2%, Abs retic=27,000, normal bili & LDH.

- What is the most likely diagnosis?

- 1) B12 def

- 2) Hemolysis

- 3) Fe def

- 4) Thalassemia

- 5) Acute blood loss

A 41y.o. man is emergently admitted to the hospital w/severe SOB, near syncope and palpitations. He appears acutely ill; is febrile (T=39), tachycardic and has scleral icterus. Hct=15, MCV=126, Retic=37%, LDH=839, bili=3.9; spherocytes are noted on his peripheral smear.

- What is the most likely diagnosis?
 - 1) Folate deficiency
 - 2) Anemia of chronic disease (infection)
 - 3) B12 deficiency
 - 4) Acute blood loss
 - 5) Autoimmune hemolytic anemia

