Etiology-Specific Investigations

Child with pallor

Once first-line tests (CBC, indices, reticulocyte count, and peripheral smear) suggest a specific category of anemia, targeted investigations are ordered to confirm the exact etiology. These include:

- Iron studies
- Hemolysis workup
- Hemoglobin electrophoresis
- Bone marrow examination
- Renal investigations

Iron Studies

Indication:

Ordered in microcytic, hypochromic anemia with low RPI.
Helps differentiate Iron Deficiency Anemia (IDA) from Anemia of Chronic Disease (ACD) and thalassemia trait.

- **Typical findings in IDA:**

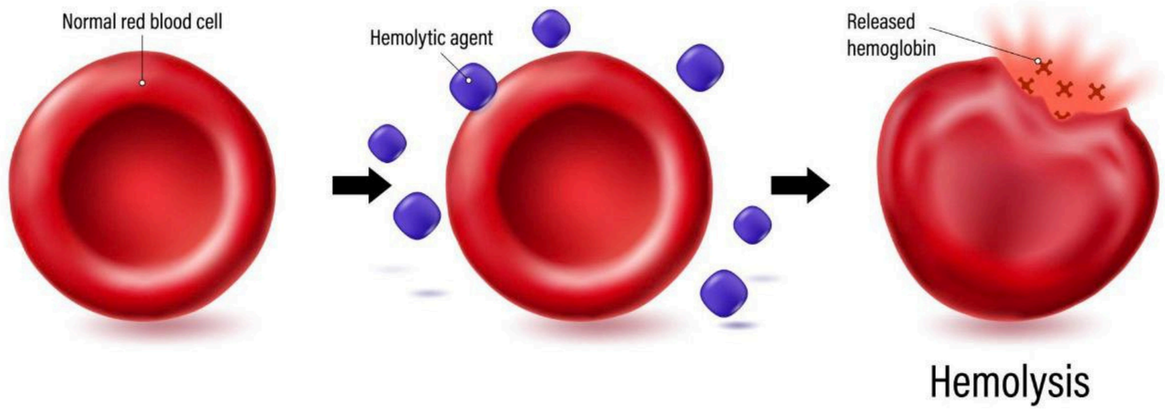
↓ Serum ferritin: Reflects decreased iron stores.
↓ Serum iron: Indicates reduced circulating iron.
↑ TIBC: Increased iron-binding capacity.
↓ Transferrin saturation: Reduced iron available for hemoglobin synthesis.

Note: Ferritin may be falsely elevated in inflammation (acute-phase reactant).

Hemolysis Workup

Indication:

Ordered in normocytic or macrocytic anemia with high reticulocyte count, or when hemolysis is suspected (jaundice, dark urine, splenomegaly).



1. General screening for hemolysis

↑ Serum LDH: Due to RBC destruction.
↑ Indirect bilirubin: Due to hemoglobin breakdown.
↓ Haptoglobin: Due to binding with free hemoglobin.

2. Tests to identify the cause of hemolysis

- Direct Coombs test: Detects RBC antibodies/complement → Immune hemolytic anemia.
- Red cell enzyme assay: Detects enzyme deficiencies (e.g., G6PD, pyruvate kinase).
- Hereditary spherocytosis screening: EMA binding or osmotic fragility test detects RBC membrane defects.

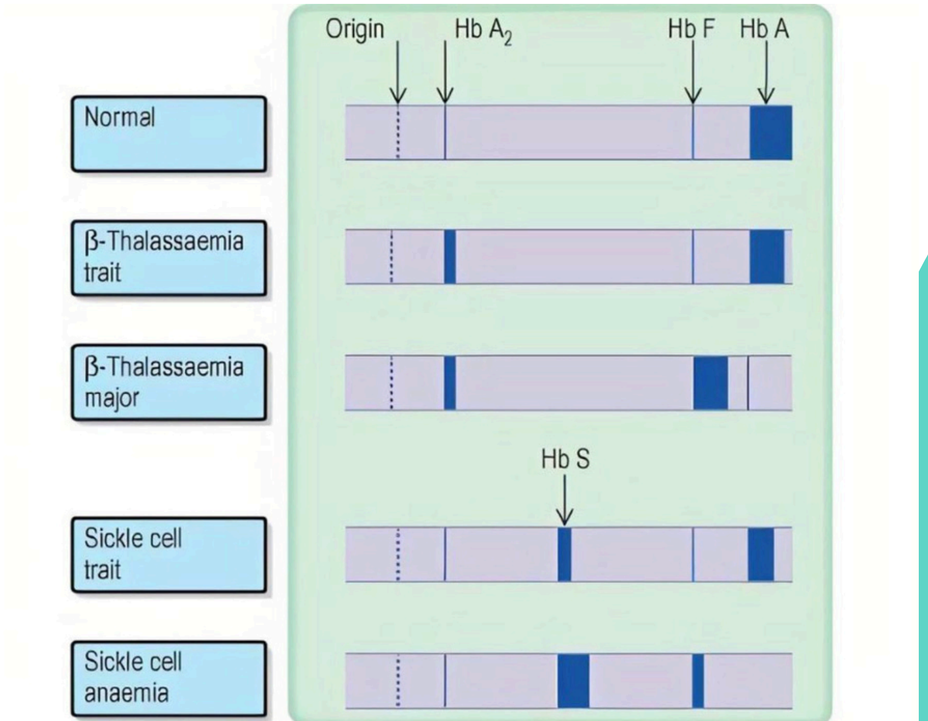
Hemoglobin Electrophoresis

Normal (after 1 year):

HbA: >95%
HbA_2: 1.5–3.5%
HbF: <1–2%

Indication:

Ordered when hemoglobinopathy is suspected (e.g., SCD or thalassemia) based on family history, ethnicity, microcytic anemia unresponsive to iron, or positive newborn screening.

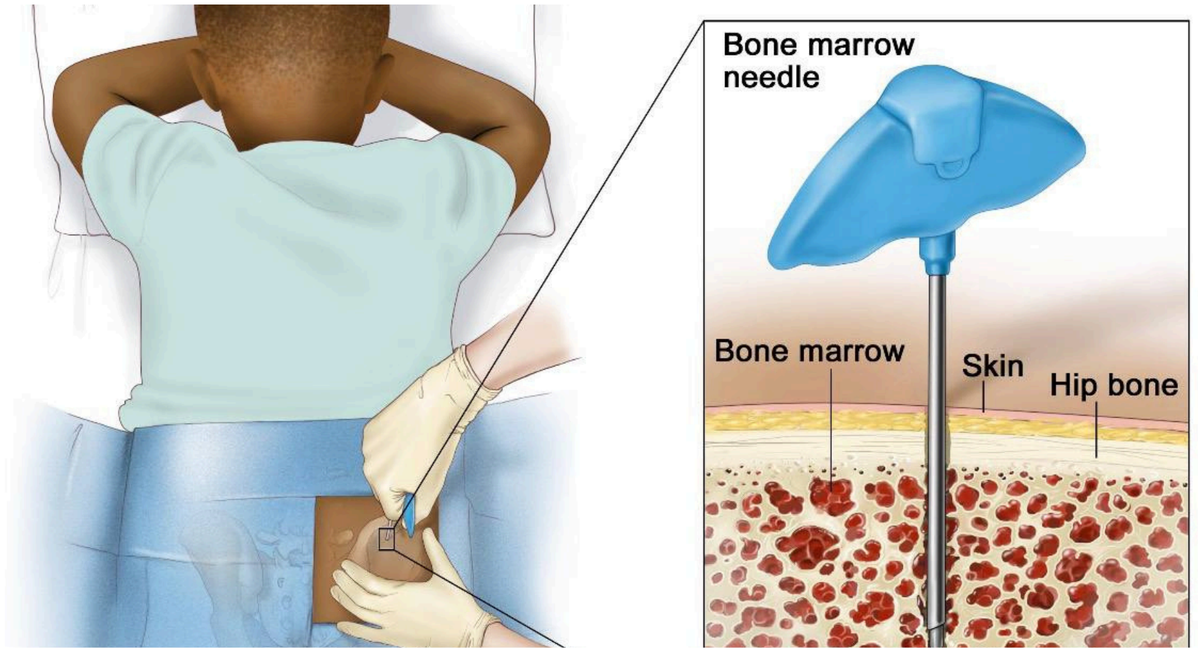


Typical findings:

β-Thalassemia Trait: ↑ HbA_2 (>3.5%), ± slight ↑ HbF.
β-Thalassemia Major: ↓ or absent HbA, HbF predominates (>90%).
Sickle Cell Disease (HbSS): Predominantly HbS (80–90%), ↑ HbF, absent HbA.

Note:
α-thalassemia trait is not reliably diagnosed by electrophoresis; genetic testing is required.

Bone Marrow Examination



Indication

An invasive procedure reserved for red flags in children with anemia.

Main indications:

- Pancytopenia / bicytopenia: Anemia with low WBCs and/or platelets → suspect aplastic anemia or leukemia.
- Abnormal peripheral smear: Unexplained blasts or atypical cells.
- Refractory anemia: No response to appropriate therapy.
- Suspected marrow infiltration or storage disease (e.g., Gaucher disease).

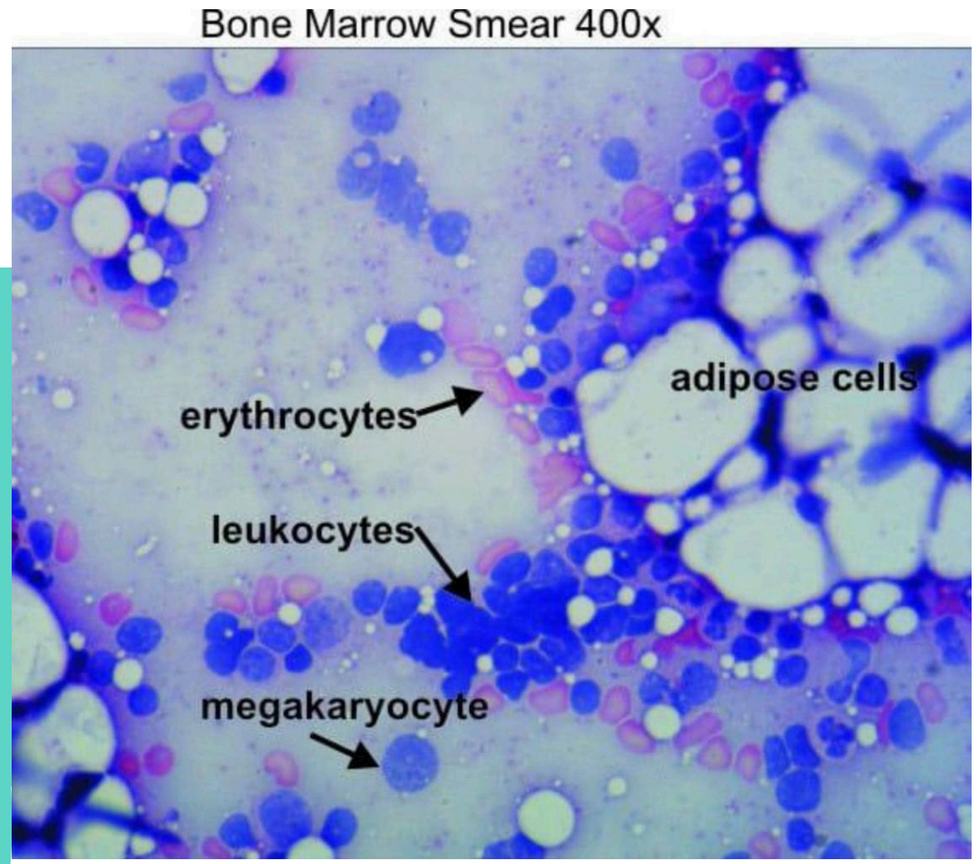
Bone Marrow Examination

What it evaluates:

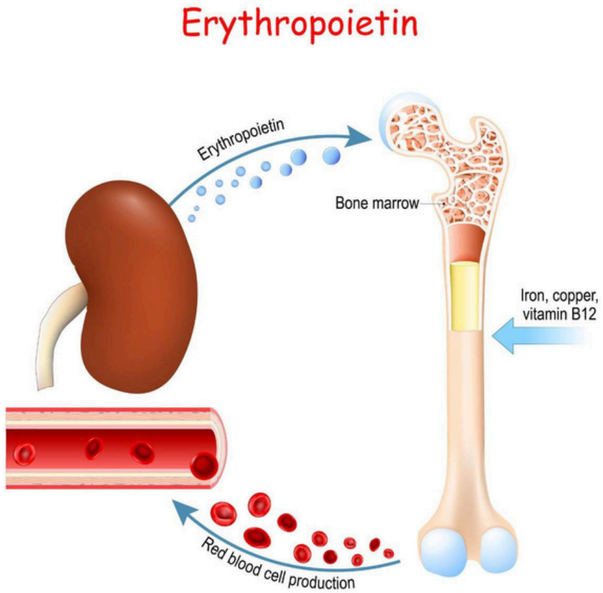
- Cellularity.
- Erythroid and myeloid maturation.
- Megakaryocytes.
- Abnormal infiltrates (e.g., blasts).

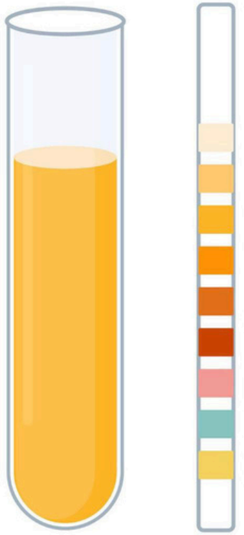
Findings:

- ↑ Erythroid precursors: Increased RBC production response (seen in some hemolytic anemias).
- ↓ Erythroid activity: Reduced RBC production (e.g., aplastic anemia, marrow suppression).
- Abnormal cells or infiltration: Suggests leukemia or malignancy.



Renal Investigations





Indication

Considered in normocytic, normochromic anemia with low reticulocyte count, hypertension, edema, altered urine output, or suspected kidney disease.

Main investigations

1. Serum Creatinine & Blood Urea Nitrogen (BUN)

Assess renal function.
↑ Creatinine / ↑ BUN → Impaired kidney function.

2. Estimated GFR (eGFR)

Measures kidney filtration capacity.
↓ eGFR → Reduced renal function.

3. Urinalysis

Proteinuria → Renal disease.
Hematuria → Possible renal pathology.

4. Erythropoietin (EPO) level (when indicated)

Produced by kidneys and stimulates RBC production.
CKD: ↓ EPO → ↓ RBC production → anemia.

Thank You ...