Aplastic Anemia 🩸

Definition:

Aplastic anemia is a disorder in which multipotent myeloid stem cells are suppressed, leading to bone marrow failure and pancytopenia.

> Note: Must be distinguished from pure red cell aplasia, where only erythroid progenitors are affected → anemia only, no pancytopenia.

Pathogenesis 🔬

The exact cause of aplastic anemia is not fully understood, but two major mechanisms are recognized:

1. Extrinsic: Immune-Mediated Suppression

- Mechanism: Activated T cells (Th1) suppress hematopoietic stem cells.

- Trigger: Stem cells altered antigenically by drugs, infections, or environmental factors → provoke T-cell response.
- Evidence: Immunosuppressive therapy targeting T cells restores hematopoiesis in 60–70% of patients.

Flowchart:

Environmental insult (drug/infection/unknown) → Stem cells altered antigenically → Activation of Th1 T cells → Cytokine release → Suppression of hematopoietic progenitors → Pancytopenia / Bone marrow failure

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2. Intrinsic: Stem Cell Abnormality

- Telomerase defects: 5–10% of patients have inherited telomerase mutations → premature senescence of stem cells.
- Short telomeres: Seen in ~50% of patients, possibly due to:

    - Unknown telomerase defects
    - Excessive replication of stem cells
- Combined effect: Genetically abnormal stem cells may express neoantigens, making them targets for T-cell attack.

Key Point: Both extrinsic and intrinsic mechanisms may coexist.

Clinical Features 🩺

- Age/Sex: Can affect all ages and both sexes.
- Anemia: Slowly progressive → weakness, pallor, dyspnea.
- Thrombocytopenia: → petechiae, ecchymoses.
- Neutropenia: → Predisposes to serious infections.

Important Differential Diagnoses:

Condition	Distinguishing Feature

Myelophthisic anemia	Marrow infiltration (e.g., metastasis)
Aleukemic leukemia	Blasts in marrow without circulating leukemia cells
Granulomatous diseases	Granulomas visible in marrow
Aplastic anemia	No splenomegaly

⚠️ Presence of splenomegaly suggests another diagnosis.

Prognosis & Management ⚕️

Prognosis

- Unpredictable; withdrawal of causative drug rarely leads to recovery.
- Hematopoietic stem cell transplantation is curative, especially <40 years.

- Blood transfusions should be minimized before transplantation to avoid alloimmunization.

Treatment Overview

Flowchart:

Patient diagnosed with aplastic anemia

- <40 yrs & suitable donor

Hematopoietic stem cell transplantation → Conditioning with immunosuppressive therapy/radiation → High chance of cure

- Not transplant candidate / older patients → Immunosuppressive therapy (anti-T cell) → 60–70% response rate

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💡 Exam Tip:

- Always remember: pancytopenia + empty marrow + no splenomegaly = aplastic anemia.
- Telomerase defects are key intrinsic cause; Th1-mediated immune attack is key extrinsic cause.
- Distinguish from pure red cell aplasia → anemia only.

-> The End <-