Pathology - Topic 17 - Aplastic anemia

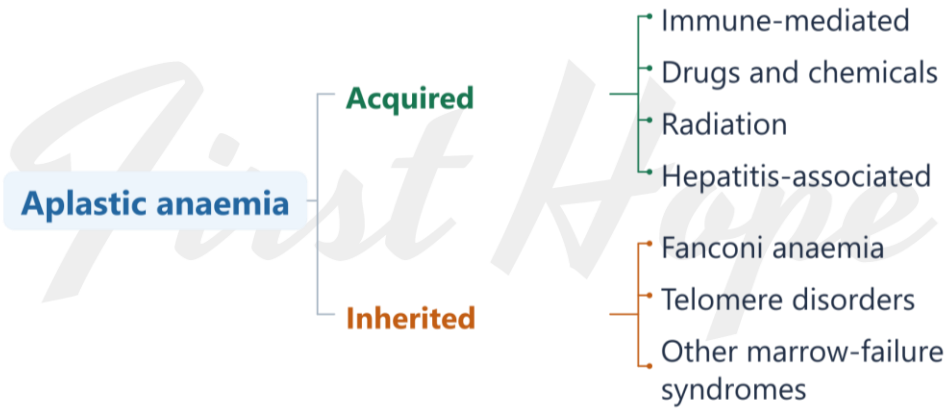
Aplastic Anaemia

- **Aplastic anaemia** is a marrow-failure disorder in which blood-forming cells are markedly reduced and replaced by fat.

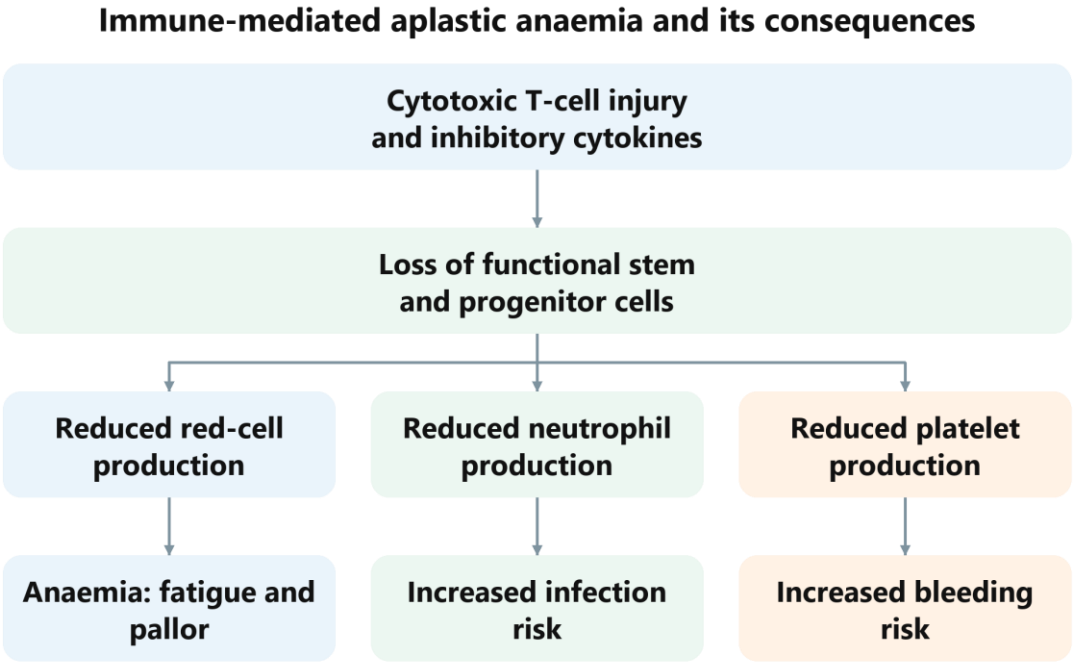
Pancytopenia and Marrow Failure

- The patient commonly develops anaemia, neutropenia and thrombocytopenia together, a pattern called pancytopenia.
- Aplastic anaemia is a failure of blood-cell production rather than excessive peripheral destruction.
    - The reticulocyte count is therefore low, even when the anaemia is severe.
- Pancytopenia alone does not establish the diagnosis because many other diseases can reduce all three blood-cell lines.

Causes and Mechanisms



1. Acquired Immune-Mediated Disease



Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Immune Injury to Stem Cells

- Many acquired cases involve cytotoxic T cells that damage haematopoietic stem and progenitor cells.
- T-cell cytokines, including interferon-gamma and tumour necrosis factor, inhibit progenitor growth and promote apoptosis, leaving too few functioning stem cells.

Causation and Consequences

- A definite initiating event is not identified in many patients.
- An unexplained case should not automatically be attributed to a recent minor illness without supporting evidence.
- Depletion of the multipotent stem-cell pool explains why red cells, granulocytes and platelets can fall together.
- Relatively preserved lymphocytes in a hypocellular sample do not imply preservation of normal trilineage blood production.

2. Drugs, Chemicals and Radiation

Exposures and Marrow Injury

- Some medicines can produce dose-related marrow suppression, while others rarely trigger an idiosyncratic aplastic process.
- Benzene exposure and substantial ionising radiation can damage stem cells.

Exposure Assessment and Causal Interpretation

- The exposure history should include occupation, traditional remedies, prescribed medicines and non-prescription products.
- A temporal association supports investigation but does not by itself prove causation.
- Cytotoxic chemotherapy predictably suppresses dividing marrow cells, while rare idiosyncratic reactions have been associated with medicines such as chloramphenicol and selected antithyroid or anticonvulsant drugs.
- Deliberate rechallenge should not be used to establish causality when aplasia is suspected.

3. Associated Illnesses

- Aplastic anaemia can follow an episode of hepatitis, including cases in which a routine hepatotropic virus is not identified.
- Other immune disorders and selected infections may be associated with marrow suppression.
  - Parvovirus B19 more typically causes a selective red-cell production failure rather than classic trilineage aplasia.

4. Inherited Marrow-Failure Syndromes

- Fanconi anaemia involves impaired DNA repair and can present with marrow failure and congenital abnormalities.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- Short stature, abnormal thumbs or radii and pigmentation changes are clues, but their absence does not exclude an inherited disorder.

➢ Telomere biology disorders and other inherited syndromes can also cause marrow failure.

- A young age, family history or characteristic extra-marrow features should prompt specialist testing because management and donor selection can be affected.

Clues from Extra-Marrow Disease

- Dyskeratosis congenita and related telomere disorders may include nail dystrophy, reticular pigmentation, oral leukoplakia, pulmonary fibrosis or liver disease.
- Shwachman–Diamond syndrome can combine pancreatic exocrine insufficiency, skeletal abnormalities and neutropenia or broader marrow failure.
- Inherited disease can present in adulthood without the full childhood phenotype, so age alone cannot exclude it.

Clinical Presentation

1. Anaemia

➢ Reduced red-cell production causes fatigue, pallor, exertional breathlessness and palpitations.

- The symptoms depend on the severity and speed of the fall in haemoglobin.

2. Neutropenia

➢ Reduced neutrophils increase the risk of bacterial and fungal infection.

- Fever with severe neutropenia is a time-sensitive clinical problem even when local signs are subtle.

3. Thrombocytopenia

➢ Reduced platelets cause petechiae, bruising, gum bleeding, nosebleeds or heavy menstrual bleeding.

- Severe thrombocytopenia can lead to serious internal bleeding.

Features That Suggest an Alternative

- Prominent lymphadenopathy, marked splenomegaly, bone pain or circulating blasts suggest another or an additional diagnosis.
  - Their presence should prompt careful evaluation for leukaemia, lymphoma, infiltration, infection or hypersplenism.

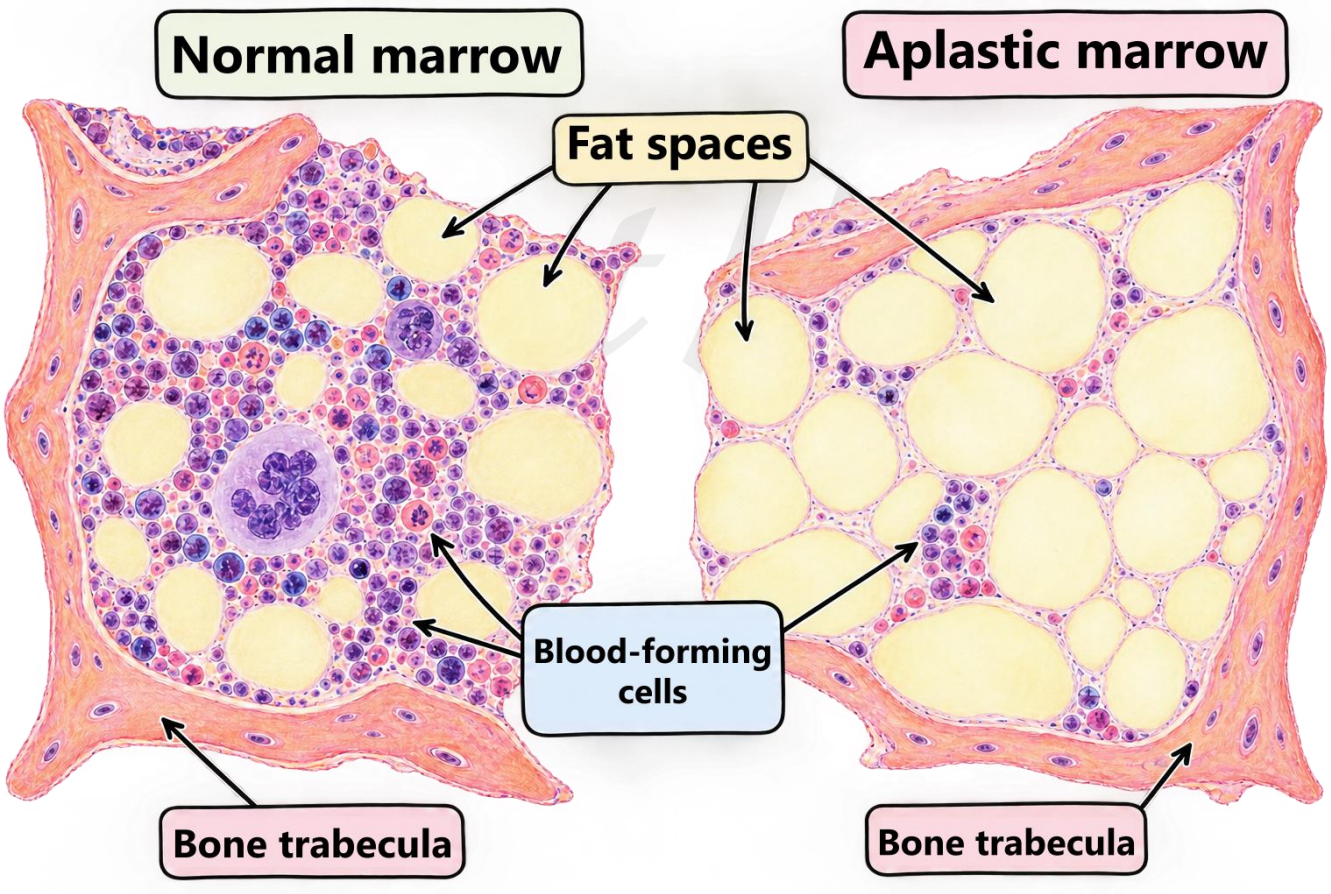
Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Peripheral Blood and Marrow Findings in Aplastic Anaemia

- Aplastic anaemia produces reduced blood-cell formation, so its diagnosis requires correlation of peripheral counts with marrow cellularity.

Peripheral Blood

- The CBC usually shows pancytopenia with a markedly reduced absolute reticulocyte count.
- Red cells are often normocytic or mildly macrocytic, and the blood film has no single diagnostic red-cell shape.
    - Unexpected blasts, marked dysplasia or a leukoerythroblastic picture require further investigation.
- The absolute neutrophil count and platelet count help assess the immediate infection and bleeding risks.
    - A differential percentage alone is not enough to judge neutropenia.



Aplastic marrow contains abundant fat and very few blood-forming cells

Aplastic Marrow Appearance

Cellularity and Residual Haematopoiesis

- The trephine biopsy shows very low cellularity with extensive fat spaces and sparse residual blood-forming cells.
- Megakaryocytes are markedly reduced, and normal trilineage haematopoiesis is depleted.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Sampling and Diagnostic Interpretation

Specimen Adequacy and Age-related Cellularity

- Cellularity must be interpreted for age and from an adequate biopsy because normal marrow becomes fattier with age.
- The aspirate may be scanty or yield few particles and cannot always show the overall extent of hypocellularity.
- A good trephine biopsy is therefore important when aplasia is suspected.

Residual Cells and Exclusion of Other Causes

- Small islands of residual erythropoiesis may make the marrow appear patchy rather than uniformly empty.
- Lymphocytes, plasma cells, macrophages and mast cells may appear relatively prominent because normal precursors are depleted.
- There should be no infiltrating malignant population or substantial fibrosis to explain the hypocellularity.

Sampling Pitfalls

- A subcortical or too-small biopsy can appear misleadingly fatty, so specimen adequacy is part of interpretation.

Bone Marrow Aspiration and Biopsy

- An aspirate provides individual-cell detail, differential counts and material for flow cytometry, cytogenetics and molecular tests.

Bone marrow aspirate and trephine provide complementary information

Aspirate	Trephine biopsy
Individual cells and maturation	Architecture and overall cellularity
Differential counts, flow cytometry, cytogenetics and molecular tests	Fibrosis, focal infiltrates and cell distribution

A dry tap is a sampling outcome, not a diagnosis of aplastic anaemia

Bone marrow aspirate and trephine provide complementary information

What Aspiration Shows Best

- Iron staining and selected organism studies can also be performed on appropriate samples.
- Aspirate material is useful when the main question concerns cell morphology or the proportion of particular precursor populations.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

FREE PREVIEW

Click here to visit our website

MBBS PREMIUM NOTES

Complete MBBS notes for every subject and year are available only in the FirstHope app.

Scan or click here

Click here to get the app >

Available on Google Play

Browse MBBS notes by year

firsthope.co.in/mbbs

Click here to explore MBBS >

Scan or click here

FirstHope Medical on Instagram

@firsthope.medical

Click here to follow

App and notes help

Find answers about access and downloads

Click here for help

YEAR 1 / YEAR 2 / YEAR 3 / YEAR 4