

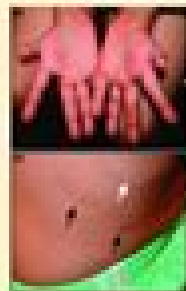
Aplastic Anemia and Bone Marrow Failure Syndromes with Pancytopenia

Common causes of pancytopenia

Impaired production	Peripheral destruction	Impaired production and peripheral destruction
Aplastic anemia - acquired and congenital	Autoimmune hemolytic pancytopenia	Paroxysmal nocturnal hemoglobinuria
Bone marrow infiltrating disorders	Spleen sequestration	Spl
- Malignancy		Drugs
- Primary and secondary myelodysplasia		Leukemia
- Granulomatous disorders		Hemophagocytosis
- Metabolic disorders		Lymphohistiocytosis (HLH)
Nutritional deficiencies		Transfusion-associated Graft-versus-host disease
- Vitamin B12		Infections
- Folate acid		
- Copper		
Myelodysplastic syndromes		

Fanconi Anemia

- DNA DSB repair defect, usually AR mutation in **FANCA** gene
- Bone, skin, and renal abnormalities, developmental delay
- Blood: **thrombocytopenia** progressing to **pancytopenia** by mid-childhood. Decreased retics and macrocytosis. Elevated HbF.
- BM: Initially normo- to hypocellular with megaloblastic changes ± erythroid dysplasia, progressing to **aplasia**. Late development of **MDS or AML** (~10%). +1q, +3q are characteristic
- Initial testing: mitomycin-induced chromosomal breaks



REDS: Blood Reviews 33 (2018) 365-367; Hematopathology 2nd Ed, Jaffe, Am J Clin Pathol 2013;138:9-20; Genet Med. 2010 Dec; 12(12)

Acquired Aplastic Anemia

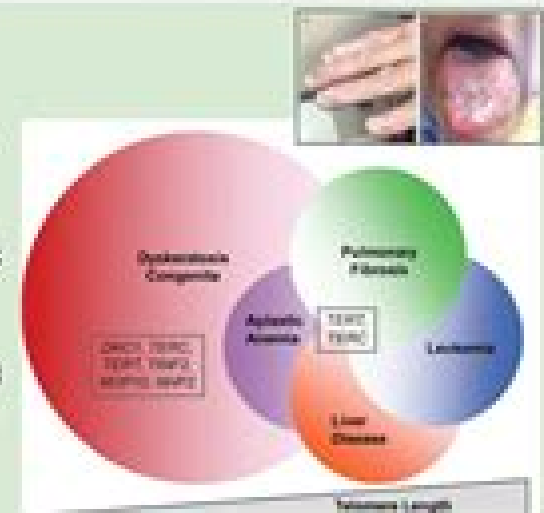
- Immune-mediated; triggered by environmental or genetic factors
- Severe AA: markedly hypocellular BM (usually <25% of normal for age) + 2 of the following: grans <0.5; platelets <20; or corrected retics <1%. Very serious disease has grans <0.2. Markedly decr. megs is a clue.
- Infection is the major cause of mortality, may also progress to MDS/AML (erythroid changes in AA are okay, megs/gran dysplasia is suspicious).
- Up to 1/3 of patients have short telomeres
- 50-60% have PNH clones, rarely progress to clinical PNH; a/w better response to rx.
- Rx is immunosuppression and/or SCT

81aureabrown



Dyskeratosis Congenita & Telomere Biology Disorders

- Most commonly X-linked recessive defect in telomere maintenance (**DKC1** gene), or very short germline telomere length (<1st percentile).
- Spectrum of presentations: skin and nail abnormalities, oral leukoplakia, increased risk of malignancies
- Blood: Gradual development of **pancytopenia** with decreased retics and macrocytosis. Elevated HbF. Normal platelet morph.
- BM: eventual **aplasia** with substantial risk of **MDS/AML**.
- Initial test: lymphocyte telomere length



Shwachman-Diamond Syndrome

- AR defect in ribosome biogenesis due to mutation in **SBDS** gene
- Exocrine pancreatic insufficiency, bone abnormalities
- In SDS (DBA also), ribosomal stress → p53 stabilization and cell-cycle arrest/apoptosis. TP53 mutations → escape from apoptosis → improved function, but increased risk of **leukemia**
- Blood: **neutropenia with macrocytosis** is the dominant initial feature, 1/3 of cases then progress to **pancytopenia** with decreased retics. Elevated HbF.
- BM: Granulocyte hypoplasia/dysplasia, progressing to pancytopenia. Some develop late AML.



Bone Marrow Failure Syndromes

K Payea

A decorative red circular graphic with a gradient, appearing as a partial circle or a stylized arrow pointing to the right, located on the right side of the light blue horizontal bar.

Bone Marrow Failure Syndromes:

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