Pancytopenia in children

Objectives:
Describe the organ / system of origin, the typical signs and symptoms and common clinical associations with aplastic anemia whether congenital or acquired.

The Pancytopenia
It refers to a reduction below normal values of all 3 peripheral blood lineages: leukocytes, platelets, and erythrocytes.
Hypocellular marrow on biopsy is seen with constitutional (inherited) marrow failure syndromes, acquired aplastic anemia of varied etiologies

Fanconi (Aplastic) Anemia
This syndrome is inherited in an autosomal recessive manner; at presentation, patients may have:
(1) Typical physical anomalies, but normal hematologic findings;
(2) Normal physical features, but abnormal hematologic findings; or
(3) Physical anomalies and abnormal hematologic findings,
Approximately 75% of patients are 3–14 yr of age at the time of diagnosis

Clinical Manifestations
- The most common anomaly is hyperpigmentation of the trunk, neck, as well as café-au-lait spots and vitiligo.
- Short stature & growth failure may be associated with abnormal growth hormone secretion, or with hypothyroidism.
- Absent radii and hypoplastic, bifid, or absent thumbs are common.
- Many patients have a Fanconi “facies,” including microcephaly, small eyes, and epicanthic folds. Approximately 10% of patients are mentally retarded.
- Ectopic, pelvic, or horseshoe kidneys are detected by imaging,

Laboratory Findings
- Marrow failure usually ensues in the 1st decade of life
- The marrow becomes progressively hypocellular and fatty, similar to severe acquired aplastic anemia.
- Chromosome fragility is indicated by spontaneously occurring chromatid breaks

Treatment
- If the hematologic findings are stable and there are no transfusion requirements, observation is indicated
- Hematopoietic stem cell transplantation is the only curative therapy for the hematologic abnormalities.
The Acquired Pancytopenias
- The majority of cases in childhood are “idiopathic” in that no causative agent is identified
- Drugs, chemicals, toxins, infectious agents, radiation, and immune disorders can result in pancytopenia.

Pathology & Pathogenesis
- The hallmark of aplastic anemia is peripheral pancytopenia, coupled with hypoplastic or aplastic bone marrow
- Severe aplastic anemia a condition in which 2 or more cell components have become seriously compromised (absolute neutrophil count [ANC] of <500/mm$^3$, platelet count of <20,000/mm$^3$)
- Moderate form of aplastic anemia (ANC of 500–1,000/mm$^3$, platelet count of 20,000–50,000/mm$^3$)

Clinical manifestation & Lab. findings
- Acquired pancytopenia is typically characterized by anemia, leukopenia, and thrombocytopenia in the setting of elevated serum cytokine levels, results in increased risks of cardiac failure, infection, bleeding, and fatigue.
- Bone marrow examination should include both aspiration and a biopsy, and the marrow should be carefully evaluated for morphologic features, cellularity, and cytogenetic findings

Complications
The major complications of severe pancytopenia are predominantly related to the risk of life-threatening bleeding from prolonged thrombocytopenia or to infection secondary to protracted neutropenia.
Patients with protracted neutropenia due to bone marrow failure are at risk, not only for serious bacterial infections but also for invasive mycoses

Treatment
- Comprehensive supportive care coupled with an attempt to treat the underlying marrow failure
- For patients with HLA–identical sibling marrow donor, allogeneic bone marrow transplantation (BMT) offers a 90% chance of long-term survival
- For patients without a sibling donor, the major form of therapy is immunosuppression with ATG combined with cyclosporine, with a response rate of 60–80%
- For those who do not respond to first-line therapy, the prognosis remains poor.