

Epidemiology and Disease Pathophysiology: Other Anaemias

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The presence of rare anaemias, such as Diamond Blackfan anaemia, Fanconi's anaemia, congenital dyserythropoietic anaemia and sideroblastic anaemia, may lead to the need for transfusions. This can result in iron overload. *Epidemiology and Disease*

Pathophysiology: Other Anaemias reviews pathophysiology, clinical features, diagnosis, and treatment of these anaemias.

Diamond-Blackfan Anaemia

Named for Louis Diamond and Kenneth Blackfan, physicians who documented the first cases of this anaemia in the 1930s, Diamond Blackfan anaemia (DBA) results from a failure within the bone marrow, which causes the inability to produce red blood cells. Affecting 600 to 700 individuals worldwide, this condition is typically diagnosed between 4 months and 2 years of age. Twenty-five percent of cases have an associated defect in small ribosomal protein 19 (RPS 19); however, pathogenic mechanisms in DBA have not been fully elucidated. Thirty to 50 percent of patients present with congenital abnormalities, including craniofacial abnormalities, short stature, neck and thumb anomalies, and genitourinary malformation; these are more common in males. Corticosteroids and blood transfusions are considered the mainstays of therapy in DBA; bone marrow transplantation represents an option for steroid-refractory patients. Prognosis is related to need for transfusions and the development of iron overload complications.

Fanconi's Anaemia

Fanconi's anaemia is an aplastic anaemia that results in bone marrow failure. It is a recessive disorder that has been linked to 13 FA genes. Worldwide prevalence of this anaemia is unknown, but carrier frequency ranges between 1 per 600 and 1 per 100. Children with FA are typically diagnosed between 6 and 9 years of age; however, some patients are recognized in infancy, others in adulthood. Patients present with typical

physical abnormalities, including hypo- or hyperpigmentation, short stature, developmental delay, and anomalies in upper limbs, gonads, head, eyes, kidney, or ears. The chromosome breakage test is considered definitive for FA, and should be performed prior to performing bone marrow transplant for aplastic anaemia. Treatment for FA includes androgens, growth factor, and bone marrow transplantation. Twenty-five percent of patients with FA will subsequently develop a malignancy.

Congenital Dyserythropoietic Anaemias

The congenital dyserythropoietic anaemias (CDA, types I, II, III, and IV) form a rare group of disorders that result in anaemia caused by ineffective erythropoiesis and may present in childhood. These disorders have pathognomonic cytopathologic findings consisting of nuclear abnormalities in bone marrow erythroid precursors. Loci of the genes for types I, II, and III have been identified, but only one gene, associated with type I CDA, has thus far been identified. This gene has been termed codanin-1, and may be involved in nuclear envelope integrity. The type II variant is typically associated with anaemia, jaundice, and splenomegaly. Therapy depends upon the type, and may include: splenectomy (effective in type II CDA but not in type I), interferon α (effective in most patients with type I), and transfusion in symptomatic patients. Transfused patients are vulnerable to iron overload and subsequent organ damage and should receive iron chelation therapy.

Sideroblastic Anaemia

Sideroblastic anaemia shares clinical features of an indolent or progressive anaemia; some cases can be linked to a particular molecular defect. There are three forms of variants of sideroblastic anaemia: hereditary, acquired idiopathic, and reversible. While this condition typically remains stable over many years, in some individuals the condition progresses, typically caused by pyridoxine intake, ionization, or iron overload toxicity. Diagnosis is accomplished through laboratory testing, including complete blood count, iron studies, bone marrow examination, molecular studies, and free erythrocyte protoporphyrin levels. Treatment varies by cause: in reversible forms, removal of the offending agent or treatment of the inflammatory condition may allow anaemia to

resolve. Administration of pyridoxine (vitamin B6) 50 to 200 mg/day can effectively treat this condition. Transfusion may be needed to treat extreme cases; patients typically require iron chelation therapy.

Iron Overload in Rare Anaemias

Iron overload, caused by multiple red blood cell transfusions and increased absorption of intestinal iron, is a problem for patients with all types of transfusion-dependent anaemia. Iron chelation may be used in the prevention and treatment of the iron overload state. Iron therapy is almost always contraindicated in these patients because of their predisposition to develop iron overload.

Suggested Reading

Bottomley, SS. Sideroblastic anemias. In: Greer JP, Foerster J, Lukens J, et al, eds. *Wintrobe's Clinical Hematology*, 11th Ed., Philadelphia, PA: Lippincott, Williams and Wilkins, 2004:1011.

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