

The megaloblastic anemias are a group of disorders characterized by the presence of distinctive morphologic appearances of the developing red cells in the bone marrow. The marrow is usually hypercellular, and the anemia is based on ineffective erythropoiesis. The cause is usually a deficiency of either cobalamin (vitamin B₁₂) or folate, but megaloblastic anemia may occur because of genetic or acquired abnormalities that affect the metabolism of these vitamins or because of defects in DNA synthesis not related to cobalamin or folate (**Table 99-1**).

TABLE 99-1 Causes of Megaloblastic Anemia

Cobalamin deficiency or abnormalities of cobalamin metabolism

(**see Tables 99-3, 99-4**)

Folate deficiency or abnormalities of folate metabolism (**see Table 99-5**)

Therapy with antifolate drugs (e.g., methotrexate)

Independent of either cobalamin or folate deficiency and refractory to cobalamin and folate therapy:

Some cases of acute myeloid leukemia, myelodysplasia

Therapy with drugs interfering with synthesis of DNA (e.g., cytosine arabinoside, hydroxyurea, 6-mercaptopurine, azidothymidine [AZT])

Orotic aciduria (responds to uridine)

Thiamine-responsive

COBALAMIN

Cobalamin (vitamin B₁₂) exists in a number of different chemical forms. All have a cobalt atom at the center of a corrin ring. In nature, the vitamin is mainly in the 2-deoxyadenosyl (ado) form, which is