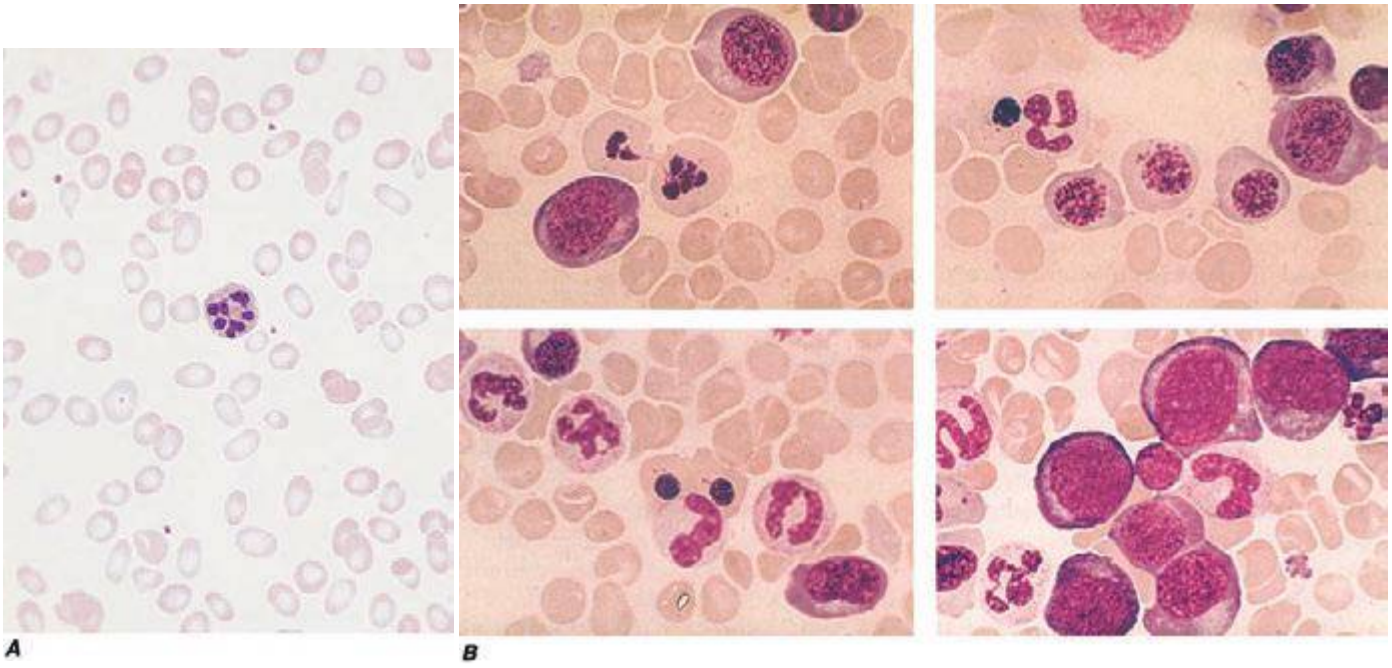

FIGURE 128-2 ***A.*** The peripheral blood in severe megaloblastic anemia. ***B.*** The bone marrow in severe megaloblastic anemia. *(Reprinted from AV Hoffbrand et al [eds]: Postgraduate Haematology, 5th ed. Oxford, UK, Blackwell Publishing, 2005; with permission.)*

serum lactate dehydrogenase. A weakly positive direct antiglobulin test due to complement can lead to a false diagnosis of autoimmune hemolytic anemia.

CAUSES OF COBALAMIN DEFICIENCY

Cobalamin deficiency is usually due to malabsorption. The only other cause is inadequate dietary intake.

INADEQUATE DIETARY INTAKE

Adults Dietary cobalamin deficiency arises in vegans who omit meat, fish, eggs, cheese, and other animal products from their diet. The largest group in the world consists of Hindus, and it is likely that many millions of Indians are at risk of deficiency of cobalamin on a nutritional basis. Subnormal serum cobalamin levels are found in up to 50% of randomly selected, young, adult Indian vegans, but the deficiency usually does not progress to megaloblastic anemia since the diet of most vegans is not totally lacking in cobalamin and the enterohepatic circulation of cobalamin is intact. Dietary cobalamin deficiency may also arise rarely in nonvegetarian individuals who exist on grossly inadequate diets because of poverty or psychiatric disturbance.

Infants Cobalamin deficiency has been described in infants born to severely cobalamin-deficient mothers. These infants develop megaloblastic anemia at about 3–6 months of age, presumably because they are born with low stores of cobalamin and because they are fed breast milk with low cobalamin content. The babies have also shown growth retardation, impaired psychomotor development, and other neurologic sequelae.

GASTRIC CAUSES OF COBALAMIN MALABSORPTION

See Tables 128-3 and 128-4.

Pernicious Anemia Pernicious anemia (PA) may be defined as a severe lack of IF due to gastric atrophy. It is a common disease in north Europeans but occurs in all countries and ethnic groups. The overall incidence is about 120 per 100,000 population in the United Kingdom (UK). The ratio of incidence in men and women among whites is ~1:1.6, and the peak age of onset is 60 years, with only 10% of patients being <40 years of age. However, in some ethnic groups, notably black individuals and Latin Americans, the age at onset of PA is generally lower. The disease occurs more commonly than by chance

TABLE 128-3 CAUSES OF COBALAMIN DEFICIENCY SUFFICIENTLY SEVERE TO CAUSE MEGALOBLASTIC ANEMIA

Nutritional	Vegans
Malabsorption	Pernicious anemia
Gastric causes	Congenital absence of intrinsic factor or functional abnormality
	Total or partial gastrectomy
Intestinal causes	Intestinal stagnant loop syndrome: jejunal diverticulosis, ileocolic fistula, anatomic blind loop, intestinal stricture, etc.
	Ileal resection and Crohn's disease
	Selective malabsorption with proteinuria
	Tropical sprue
	Transcobalamin II deficiency
	Fish tapeworm

TABLE 128-4 MALABSORPTION OF COBALAMIN MAY OCCUR IN THE FOLLOWING CONDITIONS BUT IS NOT USUALLY SUFFICIENTLY SEVERE AND PROLONGED TO CAUSE MEGALOBLASTIC ANEMIA

Gastric causes
Simple atrophic gastritis (food cobalamin malabsorption)
Zollinger-Ellison syndrome
Gastric bypass surgery
Use of proton pump inhibitors
Intestinal causes
Gluten-induced enteropathy
Severe pancreatitis
HIV infection
Radiotherapy
Graft-versus-host disease
Deficiencies of cobalamin, folate, protein, ?riboflavin, ?nicotinic acid
Therapy with colchicine, para-aminosalicylate, neomycin, slow-release potassium chloride, anticonvulsant drugs, metformin, phenformin, cytotoxic drugs
Alcohol