TABLE 248-3 FEATURES INDICATING A POOR PROGNOSIS IN SEVERE FALCIPARUM MALARIA

Clinical
Marked agitation
Hyperventilation (respiratory distress)
Hypothermia (<36.5°C; <97.7°F)
Bleeding
Deep coma
Repeated convulsions
Anuria
Shock
Laboratory
Biochemistry
Hypoglycemia (<2.2 mmol/L)
Hyperlactatemia (>5 mmol/L)
Acidosis (arterial pH <7.3, serum HCO_3 <15 mmol/L)
Elevated serum creatinine (>265 μmol/L)
Elevated total bilirubin (>50 μmol/L)
Elevated liver enzymes (AST/ALT 3 times upper limit of normal)
Elevated muscle enzymes (CPK ↑, myoglobin ↑)
Elevated urate (>600 μmol/L)
Hematology
Leukocytosis (>12,000/μL)
Severe anemia (PCV <15%)
Coagulopathy
Decreased platelet count (<50,000/μL)
Prolonged prothrombin time (>3 s)
Prolonged partial thromboplastin time
Decreased fibrinogen (<200 mg/dL)
Parasitology
Hyperparasitemia
Increased mortality at >100,000/μL
High mortality at >500,000/μL
>20% of parasites identified as pigment-containing trophozoites and schizonts
>5% of neutrophils with visible pigment

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; PCV, packed cell volume.

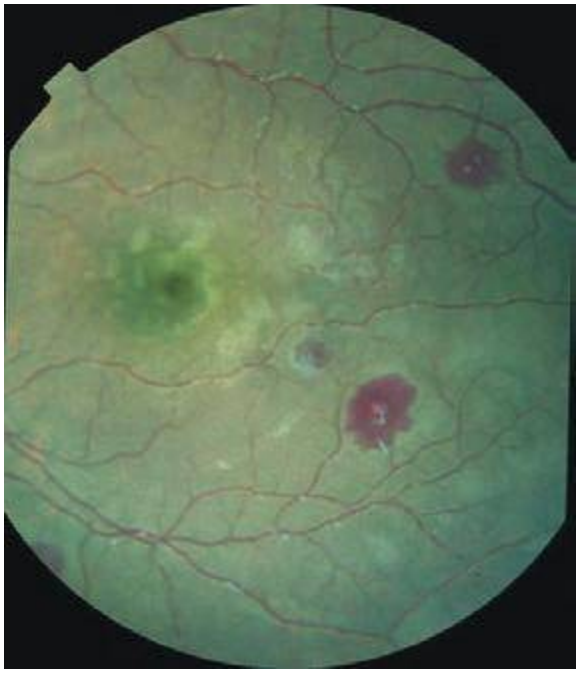

FIGURE 248-3 The eye in cerebral malaria: perimacular whitening and pale-centered retinal hemorrhages. *(Courtesy of N. Beare, T. Taylor, S. Harding, S. Lewallen, and M. Molyneux; with permission.)*

Cerebral Malaria Coma is a characteristic and ominous feature of falciparum malaria and, despite treatment, is associated with death rates of ~20% among adults and 15% among children. Any obtundation, delirium, or abnormal behavior should be taken very seriously. The onset may be gradual or sudden following a convulsion.

Cerebral malaria manifests as diffuse symmetric encephalopathy; focal neurologic signs are unusual. Although some passive resistance to head flexion may be detected, signs of meningeal irritation are absent. The eyes may be divergent and a pout reflex is common, but other primitive reflexes are usually absent. The corneal reflexes are preserved, except in deep coma. Muscle tone may be either increased or decreased. The tendon reflexes are variable, and the plantar reflexes may be flexor or extensor; the abdominal and cremasteric reflexes are absent. Flexor or extensor posturing may be seen. On routine funduscopy, ~15% of patients have retinal hemorrhages; with pupillary dilation and indirect ophthalmoscopy, this figure increases to 30–40%. Other funduscopic abnormalities (Fig. 248-3) include discrete spots of retinal opacification (30–60%), papilledema (8% among children, rare among adults), cotton wool spots (<5%), and decolorization of a retinal vessel or segment of vessel (occasional cases). Convulsions, usually generalized and often repeated, occur in ~10% of adults and up to 50% of children with cerebral malaria. More covert seizure activity also is common, particularly among children, and may manifest as repetitive tonic-clonic eye movements or even hypersalivation. Whereas adults rarely (i.e., in <3% of cases) suffer neurologic sequelae, ~10% of children surviving cerebral malaria—especially those with hypoglycemia, severe anemia, repeated seizures, and deep coma—have residual neurologic deficits when they regain consciousness; hemiplegia, cerebral palsy, cortical blindness, deafness, and impaired cognition have been reported. The majority of these deficits improve markedly or resolve completely within 6 months. However, the prevalence of some other deficits increases over time; ~10% of children surviving cerebral malaria have a persistent language deficit. There may also be deficits in learning, planning and executive functions, attention, memory, and nonverbal functioning. The incidence of epilepsy is increased and life expectancy decreased among these children.

Hypoglycemia Hypoglycemia, an important and common complication of severe malaria, is associated with a poor prognosis and is particularly problematic in children and pregnant women. Hypoglycemia in malaria results from a failure of hepatic gluconeogenesis and an increase in the consumption of glucose by both the host and, to a much lesser extent, the malaria parasites. To compound the situation, quinine, which is still widely used for the treatment of both severe and uncomplicated falciparum malaria, is a powerful stimulant of pancreatic insulin secretion. Hyperinsulinemic hypoglycemia is especially troublesome in pregnant women receiving quinine treatment. In severe disease, the clinical diagnosis of hypoglycemia is difficult: the usual physical signs (sweating, gooseflesh, tachycardia) are absent, and the neurologic impairment caused by hypoglycemia cannot be distinguished from that caused by malaria.

Acidosis Acidosis, an important cause of death from severe malaria, results from accumulation of organic acids. Hyperlactatemia commonly coexists with hypoglycemia. In adults, coexisting renal impairment often compounds the acidosis; in children, ketoacidosis also may contribute. Other, still-unidentified organic acids are major contributors to acidosis. Acidotic breathing, sometimes called "respiratory distress," is a sign of poor prognosis. It is followed often by circulatory failure refractory to volume expansion or inotropic drug treatment and ultimately by respiratory arrest. The plasma concentrations of bicarbonate or lactate are the best biochemical prognosticators in severe malaria. Hypovolemia is not a major contributor to acidosis. Lactic acidosis is caused by the combination of anaerobic glycolysis in tissues where sequestered parasites interfere with microcirculatory flow,