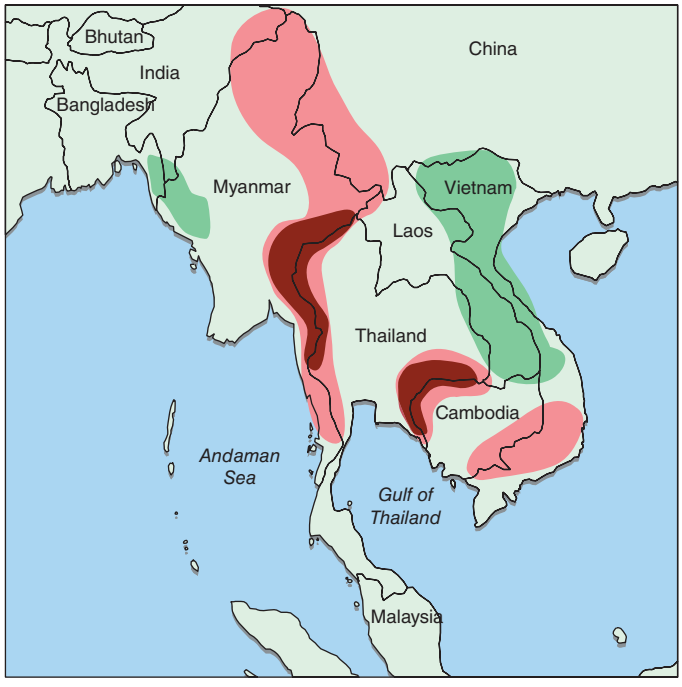

FIGURE 248-10 Mefloquine and artemisinin resistance in *Plasmodium falciparum* in Southeast Asia: high-level mefloquine resistance (*dark red*), low-level mefloquine resistance (*pink*), and mefloquine sensitivity (failure rate, <20%; *green*). There is insufficient information for other areas. Artemisinin resistance is now prevalent in areas where mefloquine resistance has been reported (*pink areas*).

used. Pyronaridine-artesunate is still under evaluation. Atovaquone-proguanil is highly effective everywhere, although it is seldom used in endemic areas because of its high cost and the propensity for rapid emergence of resistance. Of great concern is the emergence of artemisinin-resistant *P. falciparum* in western Cambodia and eastern Myanmar. Infections with these parasites are cleared slowly from the blood, with clearance times typically exceeding 3 days, and cure rates with ACTs are reduced.

The 3-day ACT regimens are all well tolerated, although mefloquine is associated with increased rates of vomiting and dizziness. As second-line treatments for recrudescence following first-line therapy, a different ACT regimen may be given; another alternative is a 7-day course of either artesunate or quinine plus tetracycline, doxycycline, or clindamycin. Tetracycline and doxycycline cannot be given to pregnant women or to children <8 years of age. Oral quinine is extremely bitter and regularly produces cinchonism comprising tinnitus, high-tone deafness, nausea, vomiting, and dysphoria. Adherence is poor with the required 7-day regimens of quinine.

Patients should be monitored for vomiting for 1 h after the administration of any oral antimalarial drug. If there is vomiting, the dose should be repeated. Symptom-based treatment, with tepid sponging and acetaminophen administration, lowers fever and thereby reduces the patient's propensity to vomit these drugs. Minor central nervous system reactions (nausea, dizziness, sleep disturbances) are common. The incidence of serious adverse neuropsychiatric reactions to mefloquine treatment is ~1 in 1000 in Asia but may be as high as 1 in 200 among Africans and Caucasians. All the antimalarial quinolines (chloroquine, mefloquine, and quinine) exacerbate the orthostatic hypotension associated with malaria, and all are tolerated better by children than by adults. Pregnant women, young children, patients unable to tolerate oral therapy, and nonimmune individuals (e.g., travelers) with suspected malaria should be evaluated carefully and hospitalization considered. If there is any doubt as to the identity of the infecting malarial species, treatment for falciparum malaria should be given. A negative blood smear makes malaria unlikely but does not rule it out completely; thick blood films should be checked again 1 and 2 days later to exclude the diagnosis. Nonimmune patients receiving treatment for malaria should have daily parasite counts performed until the thick films are negative. If the level of parasitemia does not fall below 25% of the admission value in 48 h or if parasitemia has not cleared by 7 days (and adherence is assured), drug resistance is likely and the regimen should be changed.

To eradicate persistent liver stages and prevent relapse (radical treatment), primaquine (0.5 mg of base/kg or, in infections acquired in temperate areas, 0.25 mg/kg) should be given daily for 14 days to patients with *P. vivax* or *P. ovale* infections after laboratory tests for G6PD deficiency have proved negative. If the patient has a mild variant of G6PD deficiency, primaquine can be given in a dose of 0.75 mg of base/kg (45 mg maximum) once weekly for 8 weeks. Pregnant women with vivax or ovale malaria should not be given primaquine but should receive suppressive prophylaxis with chloroquine (5 mg of base/kg per week) until delivery, after which radical treatment can be given.

COMPLICATIONS

Acute Renal Failure If the plasma level of BUN or creatinine rises despite adequate rehydration, fluid administration should be restricted to prevent volume overload. As in other forms of hypercatabolic acute renal failure, renal replacement therapy is best performed early (Chap. 334). Hemofiltration and hemodialysis are more effective than peritoneal dialysis and are associated with lower mortality risk. Some patients with renal impairment pass small volumes of urine sufficient to allow control of fluid balance; these cases can be managed conservatively if other indications for dialysis do not arise. Renal function usually improves within days, but full recovery may take weeks.

Acute Pulmonary Edema (Acute Respiratory Distress Syndrome) Patients should be positioned with the head of the bed at a 45° elevation and given oxygen and IV diuretics. Pulmonary artery occlusion pressures may be normal, indicating increased pulmonary capillary permeability. Positive-pressure ventilation should be started early if the immediate measures fail (Chap. 326).

Hypoglycemia An initial slow injection of 50% dextrose (0.5 g/kg) should be followed by an infusion of 10% dextrose (0.10 g/kg per hour). The blood glucose level should be checked regularly thereafter as recurrent hypoglycemia is common, particularly among patients receiving quinine or quinidine. In severely ill patients, hypoglycemia commonly occurs together with metabolic (lactic) acidosis and carries a poor prognosis.

Other Complications Patients who develop spontaneous bleeding should be given fresh blood and IV vitamin K. Convulsions should be treated with IV or rectal benzodiazepines and, if necessary, respiratory support. Aspiration pneumonia should be suspected in any unconscious patient with convulsions, particularly with persistent hyperventilation; IV antimicrobial agents and oxygen should be administered, and pulmonary toilet should be undertaken. Hypoglycemia or gram-negative septicemia should be suspected when the condition of any patient suddenly deteriorates for no obvious reason during antimalarial treatment. In malaria-endemic areas where a high proportion of children are parasitemic, it is usually impossible to distinguish severe malaria from bacterial sepsis with confidence. These children should be treated with both antimalarials and broad-spectrum antibiotics from the outset. Because nontyphoidal *Salmonella* infections are particularly common, empirical antibiotics should be selected to cover these organisms. Antibiotics should be considered for severely ill patients of any age who are not responding to antimalarial treatment.

PREVENTION

In recent years, considerable progress has been made in malaria prevention, control, and research. Distribution of insecticide-treated