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for patients whose acute attacks do not respond rapidly to other measures (see above) is the most important component of therapy. (ref 15, 16, 17) Because heme and hematin are powerful repressors of hepatic ALA synthetase and because ALA synthetase has a relatively short half-life, plasma and urine levels of ALA and PBG can be markedly reduced within one to two days. A prompt reduction in pain and discomfort accompanies this biochemical response. Established peripheral neuropathies are not reversed immediately, but their progression is stopped. The dosage of hematin is 1 to 4 mg/kg dissolved in normal saline and given intravenously, preferably through a large peripheral vein or central line, over 20 minutes every 12 or 24 hours. (ref 18) Improvement is usually seen within two to seven days. Occasional instances of coagulopathy associated with prolonged partial thromboplastin time, increased prothrombin time, and fibrinolysis have been reported with hematin infusion. (ref 19)

• Evidence of activation of factor XII-dependent pathways by hematin and of activation of other procoagulants by hematin degradation products has been reported. In the latter case, ineffectiveness of therapy for AIP is compounded by increased prothrombin and bleeding times. Heme arginate, which has been introduced in Europe and is now being investigated in the United States, is a much more stable preparation of heme that has excellent efficacy and causes few or no thrombotic effects. (ref 19, 20)

• Hematin is also useful in women with menstrual exacerbation of AIP. When this drug was given prophylactically at weekly intervals to a woman with recurrent severe attacks precipitated by her menses, porphyrin precursor excretion was reduced to near-normal levels and symptoms ceased. (ref 16) Other approaches for women with menstrual exacerbation of AIP have included oral combinations of estrogen and progestin or injection of a luteinizing hormone-releasing hormone analogue at weekly intervals to inhibit ovulation. (ref 21) Although oral contraceptives and estrogens increase ALA and PBG excretion and have precipitated attacks, they paradoxically have also been useful in some patients by inhibiting the menstrual cycle and, as a result, the acute attacks that can occur during the premenstrual and menstrual periods. Although pregnancy may be complicated by AIP, symptomatic attacks are rare. (ref 2) Prophylaxis and treatment are the same as those outlined above.

• The prognosis for patients with AIP is probably better than the medical literature commonly suggests. With the advent of the erythrocyte PBG deaminase assay, it is clear that there are many more patients with AIP than had been assumed from assessment of individuals who were symptomatic and had

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