porphyrias that involved cutaneous and neurovisceral manifestations compatible with coexisting AIP and PCT (ref 24) and coexisting VP and PCT. (ref 11) It is likely that dual porphyrias are more common than has been thought.

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Summary

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All of the acute porphyrias--AIP, VP, HCP, and ALA dehydratase deficiency--are associated with hepatic overproduction of ALA as well as of other heme precursors. Unlike other porphyrias, the acute porphyrias are characterized by acute, painful, life-threatening neurovisceral attacks, the mechanisms of which are unclear. It has been proposed that ALA may be responsible for the observed neurotoxicity. Infusion of ALA into human volunteers, however, has not reproduced the symptoms of the acute porphyrias. (ref 25) In addition, a pregnant patient with AIP who had elevated levels of circulating ALA in cord blood and maternal plasma gave birth to an infant who had no neurologic lesions. (ref 26) However, ALA does not cross the blood-brain barrier into the cerebrospinal fluid.

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Urinalysis during acute episodes facilitates the diagnosis of an acute porphyria. During latent periods, urinary excretion of porphyrin precursors may not be elevated. In such cases, an analysis of stool porphyrins and an assay of erythrocyte or tissue enzymes (available at specialized laboratories), which remain persistently abnormal, are diagnostic. In the future, the use of the polymerase chain reaction (PCR) to analyze a patient's DNA may provide direct genetic diagnosis.

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Successful therapy for the acute porphyrias consists of the use of the end product of the synthetic pathway, heme, to repress ALA synthetase, thereby reversing the biochemical and clinical manifestations of disease.

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Porphyria Cutanea Tarda

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PCT is the most common porphyria. In contrast to the other hepatic porphyrias, PCT is more common among men than women. At least 20 percent of cases appear to be familial.

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PCT is caused by partial loss of activity of hepatic uroporphyrinogen decarboxylase, and lesions are caused by overproduction and excretion of uroporphyrin. PCT has developed in patients after exposure to estrogens or exogenous chemicals; one large outbreak was traced to consumption of grain contaminated with hexachlorobenzene, a fungicide. PCT is sometimes associated with chronic hepatitis, alcoholic liver disease, and iron overload. Hepatoma has been reported in a small number of cases.