(erythrocytes) and liver, the porphyrias are conveniently grouped as erythropoietic, hepatic, or both, depending on the primary site affected. Because of their striking clinical manifestations, their readily visible urinary chemical markers, and their familial mode of inheritance, the porphyrias were among the earliest diseases to be defined as inborn errors of metabolism.

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With the exception of congenital erythropoietic porphyria (CEP) and ALA dehydratase deficiency (plumboporphyria), the porphyrias are usually inherited in an autosomal dominant pattern. An afflicted parent with a defect in one of two alleles has an even chance of transmitting the disease to an offspring of either sex. Furthermore, two parents who are heterozygous for the same enzymatic deficiency can produce offspring with a much more severe form of the disease, whereas those who are heterozygous for different enzymatic deficiencies may have offspring with a mixed or so-called dual porphyria.

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Although specific genetic and enzymatic defects are present throughout life, most persons with these defects never experience symptoms of disease. (ref 2) When symptoms develop, they usually do so after puberty. The course of the acute forms of disease is characterized by long latent periods interrupted by acute attacks. During latency, urinary porphyrin and porphyrin precursor excretion ranges from minimal to marked. When symptoms are manifest, biochemical tests for these products are typically positive.

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Genetic Pathology

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In the past decade, advances in molecular biology have elucidated much of the nature and variety of the genetic and biochemical abnormalities that characterize the porphyrias. These techniques have permitted more accurate classification and eliminated much of the confusion that was engendered by using the porphyrin excretion profile as the only diagnostic criterion. The occurrence of latency (when urinary porphyrin and porphyrin precursor excretion may be normal), overlap syndromes (when excretion patterns fail to differentiate diagnostic categories clearly), or selective organ-specific enzymatic deficiencies no longer limits clinical evaluation and diagnosis.

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Among the advances in molecular biology that have been made are the mapping of the chromosomal locations of the genes coding for the enzymes involved in porphyrin biosynthesis (ref 1) [see Table 1] and, in many instances, the identification of the specific genetic aberrations. It is now clear that abnormal enzymatic activity may be caused by a point mutation in which a single base substitution changes