



PIC Question of the Week: 11/14/05

Q: Is there a reason to avoid administration of rifampin in a patient with acute porphyria?

A: The term *porphyria* refers to a group of disorders, each characterized by a deficiency in one of the eight enzymes responsible for *heme* biosynthesis. The heme molecule is subsequently incorporated into hemoglobin and also contributes to the synthesis of the cytochrome P450 enzymes. There are seven types of porphyria, each associated with the deficiency of a specific enzyme in the synthetic pathway of heme. These are grouped into two classes: porphyrias having only cutaneous photosensitivity (congenital erythropoietic, porphyria cutanea tarda, erythropoietic protoporphyria) and acute or inducible porphyrias (acute intermittent, 5-aminolevulinic acid dehydratase, variegate, hereditary coproporphyria). Most forms of porphyria are hereditary; however, porphyria cutanea tarda (the most common type) develops during life. *Acute porphyrias* typically present with gastrointestinal (abdominal pain, vomiting, etc.), neurological (pain, paresis, etc.) and cardiovascular (tachycardia, hypertension) signs and symptoms. Two types of acute porphyria, variegate and hereditary coproporphyria, occasionally exhibit cutaneous photosensitivity. Presence of an overproduction of the porphyrin precursors ALA and porphobilinogen distinguish acute porphyrias from other types. This is an important feature for laboratory diagnosis. Acute attacks may be induced by endogenous changes in sex hormones, dietary restriction, alcohol, cigarette smoking, severe infections, and stress. However, the most common cause of exacerbation of *acute* porphyrias is the administration of drugs. Notably, these *acute* types are the only forms of porphyria affected by drugs. Pharmacists may be asked to provide lists of drugs that are safe or unsafe for patients with porphyria. Unfortunately, most drugs cannot be definitely classified as harmful or safe due to insufficient information. The proposed mechanism by which drugs exacerbate porphyria is by increasing the hepatic synthesis of heme and its precursors. Inhibition of the heme biosynthetic pathway in porphyria becomes exaggerated when negative feedback stimulates the liver to produce even more heme, leading to an accumulation of heme precursors. In most cases, these drugs are inducers of cytochrome P450 (CYP450) enzymes. Porphyria has been exacerbated by drugs which do not induce cytochrome P450 enzymes as well; however, these mechanisms are not well understood. An updated list of drugs shown to be safe and unsafe in patients with porphyria can be found at the American Porphyria Foundation website below. *Rifampin*, the drug in question, is included in the list of *unsafe* medications because it is a potent inducer of CYP450.

References:

- American Porphyria Foundation. Porphyria overview. <http://www.porphyrifoundation.com> (accessed 2005 Nov 8).
- Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. *Ann Intern Med* 2005;142:439-50.

Barbara J. Schmitz, Pharmacy Clerkship Student
Jennifer E. Huber, Pharmacy Clerkship Student