



Figure 1. The Heme Pathway

The highly regulated heme pathway consists of eight enzyme-driven reactions. Reactions begin and end inside the mitochondria, with intervening steps carried out in the cytosol. When porphyrinogens build up, they are easily oxidized to porphyrins that appear in urine. Toxicants like heavy metals and organic xenobiotics bind to one or more enzymes to produce specific patterns of urinary porphyrin elevation. Oxidized porphyrins that accumulate in the body become additional toxicants that cause further tissue degradation. The blockages also slow down the production of the heme-requiring proteins listed at the upper left.

Uroporphyrinogen I is produced in a non-enzymatic reaction that leads to the inactive by-product coproporphyrin I. Some toxicants (especially arsenic) slow the metabolism of uroporphyrinogen III, causing diversion to coproporphyrinogen I, so the copro I/III ratio becomes elevated.