

**CONTRASTING RESPONSE OF LIVER AND KIDNEY TO
EXPERIMENTALLY INDUCED HEPATIC DAMAGE**

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The effects of induction of liver injury on the response to chemicals affecting both liver and kidney were examined using ICR male mice. A hepatotoxic dose of carbon tetrachloride (CCl₄; 0.05 ml/kg, ip) administered 24 hr before decreased the hepatotoxicity, but potentiated the nephrotoxicity of a following dose of either CCl₄ (0.02 ml/kg, ip), chloroform (CHCl₃; 0.025 or 1.0 ml/kg, ip) or acetaminophen (APAP; 350 mg/kg, ip) as shown by increases in activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), sorbitol dehydrogenase (SDH), blood urea nitrogen (BUN) and creatinine (Cr) levels. The hepatic microsomal drug metabolizing enzyme activity was decreased by a 24 hr prior dose of CCl₄, however, the renal metabolizing activity was significantly elevated as indicated by increases in *p*-nitrophenol hydroxylase, *p*-nitroanisole demethylase, and aminopyrine demethylase activities. In two-thirds hepatectomized mice the hepatotoxicity of CCl₄ (0.02 ml/kg, ip) was reduced, but the surgery resulted in significant elevation of nephrotoxicity by either CCl₄ or CHCl₃ (0.025 ml/kg, ip). Also corresponding increases in the renal metabolizing activity accompanied by decreases in the hepatic metabolizing activity were observed in animals 24 hr following the partial hepatectomy. Induction of renal drug metabolizing activity by CCl₄ was much greater in male mice compared to female or castrated male mice. Pretreatment of female mice with testosterone (30 mg/kg/day, sc, on alternate day for 3 weeks) increased the inducing effect of CCl₄ on the renal activity reaching the levels comparable to those of normal male. The results indicate that the paradoxical effects on the renal drug metabolizing enzyme activity induced by hepatic damage may be associated with reduction of hepatic metabolizing activity. It is suggested that testosterone plays an important role in the compensatory induction of renal drug metabolizing activity observed in this study.