

HEPATOTOXIC ACTION OF NEPTUNIUM-237 IN THE RAT

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Female rats have been shown to possess a greater susceptibility to  $\text{Np}^{237}$  toxicity as judged by mortality and histopathologic and chemical examinations. Female rats showed 100 percent mortality within 72 hours after receiving 12 or 24 mg/kg of  $\text{Np}^{237}$  intravenously. Males tolerated this dose level and were apparently healthy six months afterwards.

Livers from female rats treated with  $\text{Np}^{237}$  were a tan or yellowish color suggesting fatty infiltration. Microscopic examination showed damage ranging from cloudy swelling six hours post injection to necrosis with severe fatty change by 48-72 hours. Cloudy swelling and necrosis were less severe in the males and fatty changes were practically nonexistent. Histopathologic damage progressed from outerlobular areas toward centrolobular regions with time.

Chemical analyses showed that female livers accumulated fat while male livers did not. The increased fat content of female livers was presumably neutral lipid since total phospholipid and cholesterol changed very little. Dietary and hormonal manipulations affect the degree of fat accumulation. Feeding glucose or an antioxidant decreases the fatty response, as did adrenalectomy and hypophysectomy. Choline and methionine administration had no effect.

The ability to oxidize palmitic acid- $1\text{-C}^{14}$  in vivo was decreased by  $\text{Np}^{237}$  in both females and males with females more severely affected. Incorporation of acetic- $1\text{-C}^{14}$  acid into liver lipids was stimulated two- to threefold in both males and females.

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