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Pathological Effects of Mercury

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For centuries mercury has been recognized as toxic. The lesions induced are related to the class of mercury compound administered and to a smaller extent to the species. Inorganic mercury (HgCl_2) causes acute damage to the gastrointestinal tract when given by mouth and, if the animal survives, necrosis of the proximal tubule of the kidney. After a single dose the acute renal damage is rapidly repaired, but repeated treatment causes fibrosis of the kidney (Dieckmann & Butler, 1970). In man repeated doses of the mercurial diuretic mersalyl {sodium *o*-[(3-hydroxymercuri-2-methoxypropyl)carbamoyl]-phenoxyacetate} may induce a nephrotic syndrome (Riddle *et al.*, 1958). The effects of methylmercury on the central nervous system have received much attention since the description of Minimata disease (Harada, 1968) and also poisoning from dressed grains (Jalili & Abbasi, 1961). Earlier Hunter & Russell (1954) described cortical and cerebellar necrosis as a result of industrial exposure. In the rat a similar pattern of damage is seen, affecting the cerebellum and sensory pathways, although, however, cortical lesions are not seen. The distribution of lesions differs from that of organophosphorus compounds, in that the entire sensory pathway is involved whereas in poisoning by organophosphorus compounds a dying back of sensory nerves from the periphery is seen.

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The Biological Properties and Distribution of Mercury

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The high affinity of mercuric cations for thiol groups imposes a severe logistics problem in considering the biochemical mechanisms of action of mercurial compounds. To quote from a recent review by A. Rothstein (paper presented at the 4th. Rochester Conference on Toxicity at the University of Rochester, Rochester, N.Y., U.S.A., in 1971) 'although the mercurials are highly specific to -SH groups, they are highly unspecific in terms of proteins. Almost all proteins contain -SH groups that are metal reactive. Furthermore, because -SH groups are important to most protein functions, mercurials can disturb almost all functions in which proteins are involved. Thus almost every protein in the body is a potential target'. In other words the mercurials are potent but unspecific enzyme inhibitors. Thus the view has developed that biochemical and cellular injury will be seen wherever mercury accumulates in sufficient concentrations, a view that has influenced much of the experimental work on the toxicology of mercury compounds. Thus considerable emphasis has been placed on studies of the kinetics and mechanism of transport and distribution of mercury. It is of interest to see to what extent this approach has been useful in leading to a better understanding of the toxicology of mercury.

Quantitative description of the processes of absorption, distribution and excretion have been greatly facilitated by the introduction of γ -ray scintillation counting making use of the isotopic tracer ^{203}Hg (Rothstein & Hayes, 1960). Compartmental analysis of the data revealed an important general property applicable to all mercury compounds studied to date, namely that, in experimental animals given repeated single doses of radioactive mercury, each dose behaved independently of the previous dose with respect to its kinetic parameters. This property greatly simplified mathematical treatment of the data. It allowed calculation of the cumulative body burden of mercury during chronic exposure, the determination of biological half-times of mercury and the efficiency of pulmonary and gastrointestinal absorption. Thus Rothstein & Hayes (1964) were able to determine the pulmonary absorption of mercury vapour to be 100%. The gastrointestinal absorption