$NADP+NADPH_2$ (Slater, Sträuli & Sawyer, 1964); the mechanism underlying this decrease has been studied in this investigation.

At 1–2hr. after dosing with CCl_4 there is no change in the total content of ATP in the liver or in total liver $NAD+NADH_2$, which are substrates for the NAD kinase reaction; NAD kinase is slightly increased in activity at this period of poisoning. These results suggest that there is no failure in the synthesis of NADP during the first 2hr. of poisoning with CCl_4, but this interpretation is complicated by intracellular shifts of ATP and the nicotinamide–adenine dinucleotides during this period.

The decrease in total liver $NADP+NADPH_2$ produced by CCl_4 *in vivo* is diminished by the concomitant administration of various free-radical scavengers with the CCl_4 (Slater, Sawyer & Sträuli, 1966). This indicates that the breakdown of the nucleotide is homolytic in character. This is further suggested by experiments *in vitro* that show that $NADPH_2$ is rapidly destroyed by u.v. irradiation in the presence of $CBrCl_3$ and, to a lesser extent, CCl_4. This rapid degradative reaction can be followed by fluorimetric or enzymic procedures, and is retarded by free-radical scavengers. The possibility will be considered that $NADPH_2$ is broken down *in vivo* as a result of the homolytic interaction of CCl_4 and the $NADPH_2$–cytochrome *c* reductase in the endoplasmic reticulum of rat liver.

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The Metabolic Fate of DL-[7-^{3}H]Isoprenaline in Man and Dog

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After intravenous injection of DL-[7-^{3}H]isoprenaline (90μc, 0·5μg./kg.) in the dog, plasma radioactivity fell biphasically, the initial rapid fall coinciding with a return of the pulse rate towards normal. Free amine represented about 85% of the total radioactivity, 3-*O*-methylisoprenaline making up the remainder. The findings were similar in man, intravenous dosage (40μc, 0·06μg./kg.) resulting in mostly free isoprenaline and a small amount of *O*-methylated metabolite in plasma. It is thus possible that the rapid termination of the pharmacological effect derives from a mechanism such as tissue uptake (Vane, 1969) rather than rapid *O*-methylation.

Urine samples collected in the first 24hr. after intravenous injection in man contained 80% of the administered radioactivity (40% free amine, 35% *O*-methylated amine). A progressively increasing proportion of 3-*O*-methylisoprenaline was excreted with time, and its sulphate conjugation also increased.

In contrast, after oral administration (70μc, 220μg./kg.) in man, peak concentrations of total plasma radioactivity (95min.) and maximum pharmacological effect (50min.) did not correspond. The major plasma metabolite was isoprenaline sulphate, with a small amount of *O*-methylated amine; 89% of the dose was excreted in the urine in 24hr., largely as isoprenaline sulphate conjugate, although 10% was the conjugated *O*-methylated derivative. A little free isoprenaline was also present in early urine samples. Intraduodenal administration in the dog (240μc, 600μg./kg.) gave a similar pattern; conjugated amine was largely responsible for plasma radioactivity, but a little 3-*O*-methylisoprenaline was detected. The main metabolite in the urine was isoprenaline sulphate.

Thus the pattern of metabolic degradation of isoprenaline, some aspects of which have previously been studied in the rat (Hertting, 1964) and the dog (Conway, Minatoya, Lands & Shekosky, 1968), varies with the route of administration.

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Regulation of Cytidine Aminohydrolase

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A possible regulatory role in nucleic acid synthesis for cytidine aminohydrolase (EC 3.5.4.5) has been suggested (Wisdom & Orsi, 1967) that implicates it in base conservation after nucleic acid breakdown. Further work on this enzyme has confirmed these conclusions and seems to indicate some rather novel characteristics for cytidine aminohydrolase from sheep liver.

The enzyme has been purified by the method of Wisdom & Orsi (1969) with slight modifications. The most important of these is the substitution of dithiothreitol (1mM) for 2-mercaptoethanol throughout the purification: this greatly increases the yield and stabilizes the enzyme enough to permit it to be freeze-dried or frozen for storage.