Investigation of the Accumulation of Fat in the Kidneys of Mice Poisoned with Carbon Tetrachloride

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Abstract. In mice carbon tetrachloride (3 μl/g i.p.) causes an increase in kidney weight, water and triglyceride content after 6 h, which is even more pronounced after 12 h. The increase in the renal fat content is closely paralleled by an increase in the serum non-esterified fatty acids. Since both the elevation of the non-esterified fatty acid level in the serum and the increase in the renal triglyceride content can be prevented by the antilipolytic drug β-pyridylcarbinol (500 μg/g i.m. every 6 h) it is assumed that the accumulation of fat in the kidneys produced by carbon tetrachloride is the result of enhanced lipolysis and uptake of fatty acids into the kidneys, with subsequent esterification of the fatty acids to triglycerides. β-pyridylcarbinol had no influence on the increase in the weight and water content of the kidneys and the morphological changes (albuminous swelling, constriction of the lumen of the tubuli, increased protein permeability) produced in the tubule system by carbon tetrachloride.

Key words: Non-Esterified Fatty Acids — Renal Triglycerides — Kidney Weight — Carbon Tetrachloride — β-Pyridylcarbinol.


Carbon tetrachloride is known to have toxic effects on the liver and the kidneys of man and experimental animals (von Oettingen, 1955; 1964). But, while carbon tetrachloride has become the most studied hepatotoxic agent, our knowledge of the renal effects of this drug is still very limited. One outstanding effect of carbon tetrachloride that has been established repeatedly by means of histochemical and biochemical methods (Moon, 1950; Smetana, 1939; Wong and DiStefano, 1966, 1968) is the accumulation of fat in the kidneys. However, in contrast to hepatic steatosis, the pathogenesis of the fatty infiltration of the kidneys is still obscure.

Two main mechanisms are involved in the development of carbon tetrachloride-induced fatty liver: an increased uptake of fatty acids from the blood with subsequent esterification (Brodie et al., 1961; Maling et al., 1962; Maximchuk and Rubinstein, 1963) and (probably more important) a decreased release of lipoproteins from the liver into the blood (Lombardi and Ugazio, 1965; Maling et al., 1962; Poggi and Paolelli, 1964; Recknagel et al., 1960). The present experiments proceeded from this observation and from the consideration that one or both mechanisms might also be responsible for the accumulation of fat in the kidneys. In these experiments, the inter-relationships between serum non-esterified fatty acids and renal triglycerides were studied in mice after acute administration of carbon tetrachloride and β-pyridylearbinol, a potent antilipolytic drug.

**Methods**

All the experiments were carried out on male NMRI mice of about 20 g body weight, kept at a room temperature of 25 °C and fed with standard diet (Altromin R) and tap water ad lib. before and during the experiments. They were divided into four groups which were treated as follows: Group 1: 3 μl/g carbon tetrachloride diluted with peanut oil to a final volume of 15 μl/g administered i.p., Group 2: 3 μl/g carbon tetrachloride in peanut oil i.p. + 500 μg/g β-pyridylearbinol (calculated as free base) administered i.m. In experiments exceeding 6 h in duration a second dose of 500 μg/g β-pyridylearbinol alone was given 6 h after the first dose, because of the short half-life of the drug, Group 3: 15 μl/g peanut oil i.p., Group 4: 15 μl peanut oil i.p. + 500 μg/g β-pyridylearbinol i.m. In the 12-h experiments a second dose of 500 μg/g β-pyridylearbinol was given 6 h later.

At various time intervals between 2 and 27 h after the injection of carbon tetrachloride the animals were killed by decapitation. Blood was collected for the determination of non-esterified fatty acids according to Duncombe (1964). The kidneys were removed and used for the enzymatic determination of triglycerides in accordance with the method of Eggstein and Kreutz (1966) or for microscopic examination. The water content of the kidneys was calculated from the difference between wet weight and dry weight of the organs. Mean values were calculated from 10 to 12 individual determinations and compared statistically by means of Student's t-test. Differences were regarded as significant if P < 0.05.

In preparation for the histological examination one kidney and the liver were fixed in 10% formalin. After fixation one half of the kidney and parts of the liver