76 (601)

The behavior of fat-soluble dyes in the organism.

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It is well known that the fat-soluble dye, Sudan III., is readily deposited in the adipose tissue of animals. An attempt was made by the authors to study the movements of the dye under conditions where fat transport takes place (*e. g.*, in starvation, phlorhizin- and phosphorus poisoning). The dye readily migrates into the blood with the fat under these conditions, but is rarely found in the liver tissue into which large quantities of fat enter (fatty infiltration). This is explained by the observation that the Sudan III. is abundantly excreted with the bile into the intestine from which it may be reabsorbed. Sudan III., which is insoluble in water, is not excreted through the kidneys except where alimentary lipuria is induced (in rabbits and rats). The elimination from the liver is not accomplished through the solvent medium of fat excreted in the bile (lipocholia); but the dye is soluble in bile as well as in solution of the isolated bile salts. *We have thus established a path of elimination for fat-soluble (or bile-soluble) substances through the biliary secretion.* An investigation of a considerable number of water-insoluble, fat-soluble compounds—mostly non-toxic aniline dyes and food colors—showed comparable conditions justifying the above general conclusion. It has further been established that these water-insoluble compounds do not experience absorption from the intestine in the absence of bile. Dissolved in fat-emulsion and introduced into the organism by alimentary, subcutaneous, or intravenous paths, these dyes are always eliminated with the bile into the intestine. When there is a paucity of fat in the diet the fat-soluble dyes may be absorbed through the agency of reabsorbed bile, but they are speedily eliminated again by the liver channels; with an abundance of fat to act as carrier, they travel with it through the lymphatics into the circulation. The distribution of fat-soluble dyes within the organism depends on the presence of fat and its migrations.

Thus they may be carried to or from adipose tissues, be deposited in the egg-yolk, or be secreted in company with fat in the milk of animals; they apparently do not traverse the placenta. The dyes have not been detected in the lipoids of the nervous tissue. We have failed to note any inability on the part of animals to utilize fats in which Sudan III. has been deposited.

77 (602)

Experimental studies on creatine and creatinine.

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The excretion of creatine induced by starvation in rabbits, is inhibited partially or completely by feeding a diet of carbohydrates alone. The creatine elimination is not reduced by feeding a diet of fat alone or by a diet of fat and protein.

Experimental interference with carbohydrate metabolism leads to the elimination of creatine. After phlorhizin diabetes, which depletes the store of carbohydrates, and during phosphorus poisoning, which disturbs the glycogenic functions, the output of creatine in dogs is decidedly increased.

An increase in the output of creatine plus creatinine (total creatinine) is always accompanied by an increase in total nitrogen elimination. This parallelism in inanition and with nitrogen-free diets, is ascribed to a common source,—namely, true tissue or endogenous metabolism. The metabolism of exogenous or reserve proteins is not accompanied by the production of creatine or creatinine.

Coincident with the increased elimination of total creatinine during fasting, a significant increase in the creatine content of muscle occurs in rabbits and hens. This indicates an increased production of creatine during the accelerated catabolic processes.

Creatine is a normal constituent of the urine of the young until the age of puberty. Possibly this is due to insufficient glycogenic functions. Though no direct evidence for such an assumption has been obtained, still the ease with which children develop