sucrose even after the dehydration produced by the previous injections. In the case of Dog 2, 100 ml. of Ringer's solution was given before both sucrose and sorbitol. Otherwise procedure as in Dog 1. In the experiment on Dog 3 Ringer's solution was injected before both sucrose and sorbitol in quantity to compensate for fluid lost.

In view of the apparent superior diuretic action of sorbitol, it would seem to hold promise of being a valuable clinical diuretic agent. Its possibilities are being further investigated.

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Utilization of the Arsenic Analogue of Choline Chloride in the Bio-Synthesis of Phospholipid.

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The mechanism by which choline chloride influences the deposition of fat in the liver is by no means clear. Best, Channon and others have shown that this nitrogenous component of lecithin is capable of preventing or curing the fatty infiltration of the liver which is produced in the rat on a high fat diet or in the dog on a lean meat-sucrose diet. The finding that diets essentially free of choline cause an infiltration of fat into the livers of rats, a condition curable by the addition of choline chloride to the diets, led Best, *et al.*, to suggest that choline may be an essential dietary factor.

The most obvious hypothesis as regards the manner in which choline produces its "lipotropic" effect would involve perhaps the formation of lecithins and other choline-containing phospholipids from fat, phosphate and ingested choline, thus favoring the transport of lipid materials. There are obstacles to the immediate acceptance of such a view, of possible significance among which is the lipotropic inactivity of aminoethanol, the nitrogenous constituent of the phospholipid cephalin. Of greater import is the finding (Best, *et al.*) that betaine, the naturally occurring acid corresponding to choline, is lipotropically active. This substance is incapable of entering into the formation of phospholipids unless it is first reduced to choline by the organism, a conversion which would be of considerable biochemical interest.

Pharmacological investigations of the phosphorus and arsenic

analogues of choline and acetylcholine,[1, 2] molecules in which arsenic replaces nitrogen as the nuclear element, suggested that the arsenic analogue of choline chloride ("arsenocholine" chloride) might prove useful in furnishing essentially a "tagged molecule," the assimilation of which by the organism might be followed.

It has been found that arsenocholine chloride† exerts no apparent toxic effects in the doses employed and is approximately as effective as choline chloride in preventing the fatty changes produced in the livers of rats on a high fat-low choline diet.‡ That the organism utilizes the arsenic analogue in the biological synthesis of lecithin is indicated by the following: A group of rats was fed a high fat-low choline diet, containing sufficient arsenocholine chloride to supply an average of 17 mg. per 100 gm. rat per day (equivalent to 11.8 mg. of choline chloride and containing 6.4 mg. of arsenic). After a period of 21 days on this diet, lecithin, in the form of the purified cadmium chloride complex,[3] was isolated from the brains and livers of the rats. Through the kindness of Dr. Gordon H. Scott, of the Department of Anatomy, carbon arc spectrograms of the materials were obtained and found to contain strong arsenic lines, while no such lines could be demonstrated in the spectrograms of lecithin similarly prepared from control animals.

Less intense but definite arsenic lines were seen in the purified mercuric chloride complex of sphingosine-phosphoryl-choline isolated, according to the technic of Booth,[4] from the kidneys of rats on a diet containing arsenocholine chloride.

Such tagging of phospholipid molecules suggests many applications in the study of phospholipid metabolism and in histochemical studies of cellular structures of a known or suspected phospholipid nature.

The mechanism of the lipotropic action of choline and betaine may possibly be approached through the administration of the arsenic analogue of betaine chloride; subsequent isolation of arsenic-containing phospholipids would evidence the ability of the organism to convert betaine to choline and support the hypothesis which suggests that these substances function lipotropically through the conversion of fat to phospholipid. Experiments of this nature are now under way.

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[1] Welch, A. DeM., and Roepke, M. H., *J. Pharmacol.*, 1935, **55**, 118.

[2] Roepke, M. H., and Welch, A. DeM., *J. Pharmacol.*, 1936, **56**, 319.

† The arsenocholine chloride was generously supplied by F. Hoffmann-La Roche and Co.

‡ Yeast concentrate kindly supplied by E. R. Squibbs and Sons.

[3] Levene, P. A., and Rolf, I. P., *J. Biol. Chem.*, 1927, **72**, 587.

[4] Booth, F. J., *Biochem. J.*, 1935, **29**, 2071.