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Effect of Sorbitol and Sucrose on Cerebrospinal Fluid Pressure and Urine Output.

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The intravenous administration of hypertonic sucrose has been shown to have distinct advantages over glucose in promoting diuresis and reducing cerebrospinal fluid pressure.[1-4] Bullock, Gregersen, and Kinney[1] demonstrated experimentally that the reduction of cerebrospinal pressure lasted for 5-8 hours following injection of 3-8 g of sucrose per kg of body weight. No secondary rise was noted. In their animals, an active diuresis was induced, lasting about 3 hours, during which time the kidneys eliminated about 4 times as much fluid as was given. Masserman,[2] in a clinical study of 35 patients, found that the injection of more than 100 cc of 50% sucrose resulted in an initial rise in cerebrospinal fluid pressure, which persisted for 20-80 minutes; subsequently reduction of pressure occurred which lasted for 2½ hours or more. In his series, there was very little reduction following 100 cc of the 50% solution; more marked reduction occurred with 300 cc. In 5 out of 17 cases, after injection of 500 cc fall in pressure was followed by a mild secondary rise. Masserman found that within 4 hours, 63% of the sucrose was eliminated in the urine; in 24 hours, 78-92% could be recovered from the urine. It is believed that the efficacy of sucrose as compared with glucose, depends upon the fact that the former is almost completely eliminated by the body, without passing the hemato-encephalic barrier;[1] theoretically, therefore, a secondary rise of cerebrospinal pressure does not occur.

In cases of arterial hypertension, the use of sucrose has been found to promote diuresis and relieve symptoms of increased intracranial pressure.[3] Hahn, *et al.*,[4] have reported favorably on its use in the treatment of head injuries.

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1 Bullock, L. T., Gregersen, M. A., and Kinney, R., *Am. J. Physiol.*, 1935, **112**, 82.

2 Masserman, J. H., *Bull. Jchns Hopkins Hosp.*, 1935, **57**, 12.

3 Murphy, F. D., Hershberg, R. A., and Katz, A. M., *Am. J. Med. Sci.*, 1936, **192**, 510.

4 Hahn, E. V., Ramsey, F. G., and Kohlstaedt, K. G., *J. A. M. A.*, 1937, **108**, 773.

West and Burget[5] compared the diuretic effect of sorbitol and sucrose. The former was found to be a much more efficient diuretic than sucrose in 3 dogs. According to their description, the hexahydric alcohol, sorbitol, is non-toxic, has enormous water-binding capacity, is rapidly excreted by the kidneys after intravenous injection, and has 1.88 times the osmotic pressure of sucrose. Solutions of sorbitol are stable to heat sterilization. Sorbitol has been used effectively in anuria.[6]

In attempting to determine the relative merits of sorbitol and sucrose as agents for the reduction of cerebrospinal fluid pressure and for diuresis, we have run parallel experiments on 9 pairs of dogs. The animals weighed between 8 and 12 kg. In each experiment, anesthesia was induced with nembutal (0.5 cc/kg) intravenously; at hourly intervals thereafter an additional 0.5 cc was given subcutaneously, to assure fairly constant depth of anesthesia. Under aseptic precautions, a needle was introduced into the cisterna magna and connected to an Ayer manometer. A catheter was inserted into the bladder. Preliminary observations were made for periods from ½ to 1½ hours, until we were satisfied that a basic level of pressure was present. Subsequently, each of the pair of animals was given 50% sucrose and 50% sorbitol respectively. The substances were given intravenously in a dosage of 2½ cc of the 50% solution per kilo. In preliminary experiments we had found that too-rapid injection almost always resulted in an initial rise. This fact has been noted by others in connection with sucrose.[1, 3] One of us (H.G.S.) had also observed this when sucrose is given too rapidly to patients suffering from neurosurgical lesions with increased intracranial pressure. Accordingly, we have made the intravenous injections simultaneously at a speed of 7 cc/min.

The chart demonstrates the average results in 9 dogs following sucrose injection, and 9 following administration of sorbitol. Changes in cerebrospinal fluid pressure were recorded every 3 minutes. Urine output is charted on the basis of cc eliminated in half-hour periods, calculated on the basis of 10 kg of body weight.

It is apparent that sorbitol is a much more efficient agent than sucrose in reducing cerebrospinal fluid pressure and promoting diuresis in dogs. The peak of diuresis and pressure reduction is reached at about the same time within the first half-hour after administration. With sorbitol the basic level of spinal fluid pressure was reached after 2¾ hours and was followed by a slight secondary rise. The

[5] West, E. S., and Burget, G. E., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 105.
[6] Strohm, J. G., *West. J. Surg. Obst. and Gyn.*, 1938, **46**, 200.

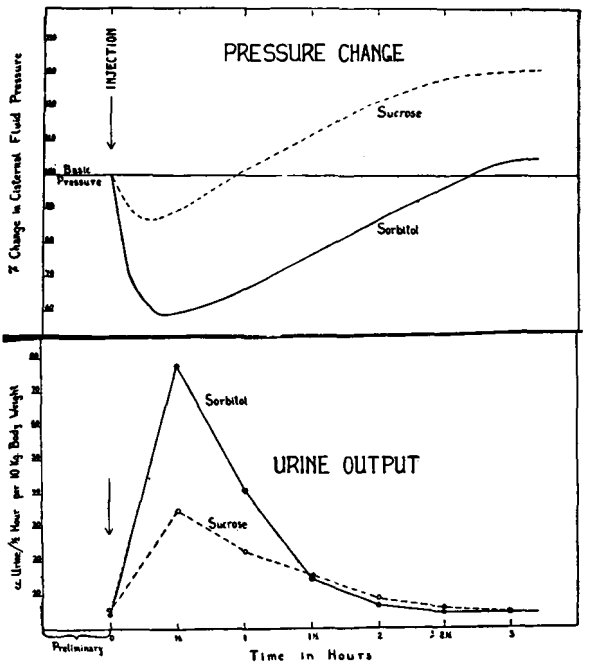

FIG. 1.

Average changes in cerebrospinal fluid pressure and urinary output following intravenous injection of 50% sucrose (- - - -) and 50% sorbitol (———) in 9 pairs of dogs.

fall in pressure following sucrose lasted only 1¼ hours, and the secondary rise was pronounced. The presence of a secondary rise with sucrose in our experiments may seem surprising. It should be pointed out that the dosage which we have injected is much smaller than other investigators have used in animals.[1] This dosage, however, compares with the amounts of sucrose which we have used clinically. We, like Hahn, *et al.*,[4] have customarily given 100 cc doses of the 50% solution to patients. This amount is less than that given by Masserman[2] and Murphy, *et al.*[3]

Summary. Parallel experiments have been carried out on 9 pairs of dogs. 50% sorbitol, in a dosage of 2.5 cc/kg, injected intravenously at a rate of 7 cc/min causes a more marked and protracted fall in cerebrospinal fluid pressure, and a greater diuresis, than does an equivalent amount of sucrose.