The Rebound Phenomenon and Hypertonic Solutions*

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THE TERMS secondary rise in cerebrospinal-fluid pressure or rebound phenomenon after administration of hypertonic solutions should be defined as a significant increase in tension of cerebrospinal fluid following the period of maximum reduction of cerebrospinal-fluid pressure and caused by mechanisms related directly to the use of the hypertonic solution.

In 1920, 1 year after Weed and McKibben introduced hypertonic solutions for reduction of cerebrospinal-fluid pressure, Ebaugh and Stevenson reported a "terminal rise" in intracranial pressure after oral administration of 200 cc. of 19 per cent Ringer's solution to a patient.

Prior to the clinical introduction of hypertonic solution of urea, a number of papers had appeared in the literature reporting a secondary rise in cerebrospinal-fluid pressure or rebound phenomenon following administration of hypertonic solutions of sodium chloride and glucose. Factors reported to cause increased cerebrospinal-fluid pressure include irritation of the meninges as the result of the presence of the needle, meningitis, pleocytosis ascribable to a solution in the manometer made from compressed tablets of sodium chloride dissolved in distilled water, and administration of barbiturate anesthetics.

Since 1954 we have carried out studies on cerebrospinal-fluid pressure with prolonged periods of control prior to the injection of hypertonic solutions. Our experience with hypertonic urea includes 1500 patients and several hundred experiments in rhesus monkeys and dogs. After administration of urea a rebound of pressure to levels above maximum levels of cerebrospinal-fluid pressure, during an adequate duration of the period of control, was not observed. This finding was confirmed by many investigators including Stubbs and Pennybacker, and Keegan and Evans. Wise and Chater reported absence of rebound after administration of hypertonic solution of mannitol. Bullock et al. found no secondary rise in pressure with 50 per cent solution of sucrose.

During the past 3 years reports have appeared in the literature describing secondary rise in cerebrospinal-fluid pressure in dogs and in human subjects after administration of urea. Wise and Chater reported no secondary rise with either urea or mannitol in dogs, but after ligation of all renal vessels, increases were noted which were greater with urea than mannitol. McQueen and Jeanes reported rebound after administration of mannitol to dogs. In a paper by Shenkin et al. 4 of 5 curves of cerebrospinal-fluid pressure following administration of mannitol to patients showed pressures above pre-injection levels.

After a review of the literature, we find that the majority of authors reported only short periods of observation of pressure before or after the injection of hypertonic solutions. In most of these papers the terms rebound phenomenon or secondary rise in pressure have been used to describe any increase in the cerebrospinal-fluid tension above maximum pressure before injection of the hypertonic solution. The authors of most papers dealing with human subjects reported short duration of periods of control.

Since studies which reported secondary rise in cerebrospinal-fluid pressure were done in dogs with short or no periods of control, studies on cerebrospinal-fluid pressure were carried out in dogs for a prolonged period before and after administration of hypertonic solutions in order to evaluate the earlier studies.

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Materials and Methods

In this investigation 110 mongrel dogs weighing 12–15 kg. were used. All animals were fasted for 12 hrs. prior to the start of the experiment. The initial anesthetic in all dogs was 25 mg./kg. sodium pentobarbital administered intravenously with subsequent supplementary doses of 30 mg. given as necessary through a cut-down in the femoral vein. Some dogs received 4 mg./kg. morphine sulfate and 0.6 mg. atropine 45 min. before administration of 15–20 mg./kg. sodium pentobarbital. The animals were placed in a prone position and allowed to breathe room air through an endotracheal tube with an inflatable cuff. An indwelling urinary catheter was placed for measurement of urinary output. A 20-gauge needle was inserted under sterile conditions into the cisterna magna. The needle was connected either to a water manometer, a strain gauge or a Gilson recording manometer. The manometers were provided with pyrex tubing, the inside diameter of which was 1.5 mm. The strain gauge and manometers were filled with sterile nonpyrogenic isotonic saline with the zero base line at the level of the cisterna magna.

The dogs were divided into 6 groups: Group I—50 control dogs whose cerebrospinal-fluid pressure was recorded for periods ranging from 12–36 hrs. Group II—35 dogs received 1 gm./kg. body weight of 30 per cent urea in 10 per cent invert sugar. Group III—8 dogs received 20 per cent mannitol. Group IV—6 dogs received 48 per cent glycerol. Group V—5 dogs received 15 per cent glycine. All agents in Groups III-V were given on an equimolar basis with 1 gm. urea per kg. body weight. Group VI—6 dogs received 0.5–1.0 gm. of sodium chloride in a 30 per cent solution. All solutions were given over a period of 30 min. With the exception of 6 animals in Group II in which 5 per cent dextrose in 0.2 per cent saline was administered intravenously in an amount equal to the urinary output of the previous 5 min., none of the dogs received any fluid other than the hypertonic solution and the anesthetic during the experiment. Cerebrospinal-fluid pressure was recorded continuously from 5 to 15 hrs. prior to and 15 to 34 hrs. following the administration of hypertonic solutions.

Results

Continuous measurements of cerebrospinal-fluid pressure over extended periods have shown that the pressure varies considerably. The mean cerebrospinal-fluid pressure and standard error are plotted every 30 min. for the 50 control dogs in Fig. 1. No fluids other than anesthetic were administered during the 12-hr. period. There is an obvious increase in the mean cerebrospinal-fluid pressure during the first 5 hrs. The mean pressure remains elevated with a slight tendency to decrease during the remainder of the 12-hr. period. The mean increase in pressure of all dogs in this study during the first 5-hr. period of control was 12 mm. of water per hr. The control animals had a mean variation of 174 mm. of water (SE ± 13.0) between maximum and minimum cerebrospinal-fluid pressure. Fig. 2 shows two representative curves of control pressure with the gradual increase in pressure com-