OSMOTIC THERAPY IN GLAUCOMA

BY

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DESPITE the fact that the possibility of lowering the tension of the eye by altering the osmotic condition of the blood has been known for some considerable time, the literature of cases so treated is scanty. To Cantonnet⁽⁹⁾ (1904) belongs the credit of first employing this method of therapy in glaucoma. Under the influence of the work of Winter⁽²²⁾ (1896) who, contemporaneously with Starling⁽¹⁸⁾ (1896), was the first to show the importance of chlorides in the maintenance of the equilibrium of the body-fluids, and stimulated by the investigations of Achard⁽¹⁾ (1903) and Loeper⁽¹³⁾ (1903) on the upset of that equilibrium caused by deranged renal excretion, he treated 17 cases, with good results in 12, by the oral administration of salt.

The experimental work of Hertel⁽¹⁰⁾ (1914) has already been referred to: in 1913, he published three cases, and again, in 1915, a further small series treated successfully by the injection of 150 to 200 c.c. of a 10 per cent. solution of salt.

Following his technique, Pletnewa⁽¹⁵⁾ of Moscow, (1923), described a series of 20 cases treated intravenously with good results; one of three cases to which salt was given orally (30 gms.) reacted.

Weekers⁽²¹⁾ (1923) has tried the method. At an earlier date (1912), following on the work of Chiari and Januske⁽⁴⁾ on the inhibitory action of the calcium ion on exudation and transudation, he had used calcium chloride subconjunctivally in glaucoma, an idea which was followed up by Tristaino⁽²⁰⁾ (1913), Gowland⁽⁸⁾ (1916), Alt⁽²⁾ (1918) and Kleiber⁽¹¹⁾ (1922) with subconjunctival and systemic administration of this salt; but the results were inconclusive (Weekers⁽²¹⁾, 1920). Giving up its use in favour of sodium chloride administered intravenously on osmotic principles, the latter (1923) treated 13 cases by the injection of 5 c.c. of the 30 per cent. solution: in 7 acute glaucomas the tension was markedly reduced for a period of two to three days, but the response in the other varieties of the disease was not so marked. Considering the smallness of the dose employed this is not to be wondered at.

By the prolonged and continuous intravenous injection of sugar, Sansum⁽¹⁹⁾ (1917) succeeded in obtaining a marked reduction of tension in two cases.

The following is a short note of an initial series of four cases of glaucoma, treated by an intravenous injection of concentrated salt solution. I am indebted to Mr. A. C. Hudson for the

privilege of availing myself of them from his clinic at Moorfields Hospital.

(1) Female, aged 47 years. Chronic glaucoma, L. T.R.=30 mm. Hg. (Schiötz), T.L.=45 mm. Hg. 35 c.c. 30 per cent. NaCl. intravenously in 10 mins. T.L. in 30 mins. became 12 mm. Hg.: in 1 hour=11; in 6 hrs.=8: next day=16: the following day=20 mm. Hg. T.R. in 30 mins. became 15 mm. Hg., and remained so up to 6 hours: next day=18 mm.: the following day=29 mm. Thereafter, L.E., trephine: R. eserine.

(2) Male, aged 54 years. Subacute glaucoma, R. T.R.=53 mm. Hg. T.L.=29 mm. 50 c.c. 30 per cent. NaCl. intravenously in 10 mins. In 45 mins., T.R. and T.L.=27 and 15 mm. Hg.; in 75 mins.=25 and 18 mm.: next day—T.R.=30 mm.

(3) Female, aged 61 years. Acute glaucoma, L. L.V.=p.l. Much pain. L. cornea hazy: fundus not seen. T.L.=95 (approx.) mm. Hg. 50 c.c. 30 per cent. NaCl. intravenously in 10 mins. In 30 mins. T.L.=80: in 1 hour=52 mm. Hg. L. cornea clear; retinal haemorrhages seen: L.V. 6/36: (pain away). In 6 hours, T.L.=38 mm. Hg. Later, trephine, L.

(4) Male, aged 29 years. Trauma L. eye—traumatic glaucoma. Cornea hazy; aqueous turbid, with floating red cells (by slit-lamp); iris showing several small haemorrhages on anterior surface; lens, position normal, iris pigment on anterior surface. Much pain. T.R.=25, T.L.=58 mm. Hg. (Schiötz). Three days later, despite eserine, leeches, etc., condition unchanged. 50 c.c. 30 per cent. NaCl. intravenously in 10 mins. 15 mins. later—T.R. and T.L.=10 and 30 mm. Hg. respectively. In 1 hour=10 and 15 mm.: in 6 hrs.=5 and 12 mm.; in 10 hrs., 5 and 14 mm.; in 48 hours 15 and 20. Three days later, 25 and 30 mm. at which level the tension remained for some months. The long-continued (? permanent) improvement here may have been due, either to the fluid traffic set up washing away red cells and other detritus from the filtration angle, or to the relief of tension allowing the recovery of tone in a possible vaso-motor paralysis induced by the trauma.

Technique used. Since the effect is a general one depending on increased molecular concentration independent of the nature of the molecules, the injection substance used is of secondary importance. Common salt would appear to be the most suitable, because of the ease and cheapness with which it is obtained and can be sterilized, because of its high osmotic power, and because it is comparatively non-toxic: normally its function in the economics of the body is that of the currency of water traffic, in that, without being in itself of intrinsic metabolic value, it

regulates and permits of the exchange of fluid. A 30 per cent. solution was employed, instead of the 10 per cent. solution used by most of the previous investigators. The former is better, since being a concentrated solution (the solubility of NaCl. is one in three) it is easily prepared without weighing, and can therefore be made up in any emergency, and the smaller bulk of water introduced makes the desired effect of dehydration the more powerful. That the standard of injection must be a relative velocity-weight has been pointed out in the previous communication, and the experimental lethal dose in cats obtained at about 1.5 gms. of salt per kilo. body weight introduced at the rate of 1 c.c. per minute. A dose of 1 c.c. per kilo. body weight (that is, an average adult dose of about 50 c.c.) of a 30 per cent. solution, injected slowly and evenly over 10 minutes, keeps within this value, gives the desired therapeutic effect, and has never given rise to anxiety.

The injection was made with the patient lying down, in case of any fall in blood pressure, and the salt solution was given (finally) through a needle attached to a rubber tube and funnel. It is difficult to feed regularly and slowly from a syringe, and, syringes of sufficient size not being usually available, it is easy to allow the point of the needle to leave the lumen of the vein in repeated recharging. This is important, for the presence of concentrated salt in the connective tissue is exceedingly painful, and leaves a brawny, indurated, painful swelling which persists for many weeks. For this reason the needle and lower end of the tube were filled first with normal saline, so that on its introduction none of the concentrated solution reaches the tissues, and if the funnel be held just at the level of the vein, a sufficiently slow and uniform flow is ensured with no disturbance whatever. After the injection the patient can get up at once. He will express the desire to drink, but no water should be given him; and he will suffer from polyuria.

The lowering of intraocular pressure thus obtained is transitory, lasting at most a day or two. There is no contra-indication to a second injection, but if any more prolonged effect is desired, the exhibition of salt by the mouth in cachet form, or by the rectum might be considered. Much larger doses would require to be given; the effect is less certain and less marked; and, in the usual type of glaucomatous patient, it would be advisable in any prolonged medication to estimate the renal efficiency and the chloride threshold as a precautionary measure.

The Dangers of Hypertonic Injection. The dangers of hypertonic injection are two-fold: the initial sudden drop in blood pressure, and the subsequent dehydration of the tissues. The

first can be overcome, as has been demonstrated experimentally and experienced clinically, by ensuring that the injection be made slowly enough. With this precaution not one of the patients that have been injected experienced any discomfort. The danger may be entirely obviated by adopting the alimentary route of administration, but the disadvantages of this method have already been pointed out.

The second danger—that of general dehydration—is a necessary effect of the success of the method of therapy. Considering the elaborate and delicately adjusted mechanism for the maintenance of the water-balance, it is surprising how little discomfort is felt after an injection within the limits proposed, beyond a sensation of thirst. Pushed to extremes, however, serious consequences ensue. Rubner⁽¹⁷⁾ (1907) has shown that, while an animal can lose practically all its glycogen and fat, 50 per cent. of its protein, and 40 per cent. of its body weight and yet live, a loss of 10 per cent. of its water content results in serious disorders, of 20 per cent. in death. The premonitory signs of too great water starvation are a general restlessness and tremor, a feeling of numbness and tingling followed by twitching and cramps in the limbs, a sinking in the abdomen, a vague sense of fear, and a rise of temperature—a condition easily combated by the free administration of fluid. It is seen clinically in the febrile attacks (“inanition fever”) Crandall⁽⁵⁾ (1899) of dehydration states in infancy, a condition dealt with by Heim and John⁽⁹⁾ (1910), and Peteri⁽¹⁴⁾ (1914) from the clinical standpoint, and studied experimentally by Finkelstein⁽⁷⁾ (1908) by the massive injection of glucose, and by Woodyatt and Rowntree⁽¹⁶⁾ (1922) by the injection of salt, the latter observers causing coma, convulsions, and death, with a final temperature of 110° F.

The opposite condition induced by hypotonic injections is of less clinical interest (*cf.* Weekers⁽²¹⁾, 1924). The initial danger is one of haemolysis, the subsequent one, of water intoxication. The latter is seen clinically in the effects of diabetes insipidus, and its nature and effects have been largely studied by Rowntree⁽¹⁶⁾ and his co-workers (1922).

Clinical Indications. It would appear that osmotic therapy might be indicated:

(1) In conjunction with miotics as a means of tiding over an acute case of glaucoma until such time as operation can be undertaken conveniently. An emergency operation is in many cases undesirable in that a skilled operator is not always immediately available, the most propitious surroundings are not always obtainable, and the condition of the patient is not always suitable

for a major surgical procedure. A measure simple in its application and efficacious in tiding over a crisis would seem to have something to be said in its favour.

(2) In conjunction with miotics, as a preliminary to operation. In conditions of high tension operation is often difficult owing to vascular congestion, and bears an element of risk from accidents (expulsive haemorrhage, etc.), while local anaesthetics are absorbed with difficulty, a circumstance often rendering general anaesthesia with its attendant discomforts advisable. With the tension lowered beforehand a difficult procedure becomes an easier one, and the risks and discomforts are minimized.

(3) In conditions of raised tension with iritis where hesitancy is felt in ordering atropin.

(4) As an aid to diagnosis when the clouded cornea of raised tension precludes ophthalmoscopic examination.

(5) As a possible aid to therapeutics. This is suggested by the observations of Knapp⁽¹²⁾ (1909), Crondstedt⁽⁶⁾ (1924), etc., who found that the ocular fluid re-formed after paracentesis, that is, under the changed conditions of lowered tension, contained a much higher percentage of bactericidal substances than the normal aqueous. That the aqueous re-formed under these conditions contains a higher proportion of protein is well known. All recent work tends to show that the various substances concerned in immunity are of a colloid nature and are susceptible to the laws that govern the behaviour of colloids, while the size of the particular units of at least one of them (diphtheria toxin) has been estimated* to be very nearly approximating to that of serum albumen (of the order of 3×10^{-6} mm.) Therefore, in common with protein, while under conditions of normal tension they are present in the aqueous only in negligible amount, their more ready entrance into the eye from the blood stream is to be expected on the provision of a steeper pressure gradient. Even in an eye with normal tension, and much more so in conditions of raised tension (iritis, corneal ulcer, etc.), when pressure conditions militate against the access of any substances in colloidal aggregation, such a procedure might be indicated, acting after the manner of a therapeutic paracentesis. It might also be suggested that therapeutic substances, such as arsenic, which normally find their entrance into the eye with difficulty, might gain access to the

* By ultra-filtration; see Bechold, *Zeitschr. Physik. Chem.*, lx, 257, 1907; lxiv, 328, 1908; also Ostwald, *Kolloid Zeitschr.*, xxii, 72, 143, 1918; Zsigmondy, *Zeitschr. Anorg. Chem.*, ciii, 119, 1918. This deduction should not be taken too literally, since, in addition to an atomic sieve action, other factors must be taken into account in the mechanism of the permeability of membranes; capillarity, adsorption, preferential solubility, chemical affinity, etc.

intraocular fluids the more easily under the influence of the increased fluid traffic set up after an osmotic dehydration.

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THE SCLERAL STITCH IN ADVANCEMENT OPERATIONS

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STOKE-ON-TRENT

THE modification in the grip of the needle-holder shown in the illustration, combined with the use of Worth's straight cutting scleral needle, will be found to enable the scleral stitch to be inserted with lightness and ease.

The grip is as in holding a pen, with the exception that the middle finger takes no part in it. The holder used is the one