

restores the balance, so that the nutrition of the parts concerned is maintained. In this specimen we have positive evidence that the nutrition of the uterus and tumour was not diminished, although both ovarian arteries had been cut off. Other cases in my hands also bear me out. Again, in the great majority of cases of large tumours, it is impossible, as I have already said, to get at the ovaries. But that there are certain cases in which oöphorectomy should take the place of hysterectomy I am free to admit. Such a case is that of a small or very moderately sized intramural fibroid. In such a case oöphorectomy will, I believe, render us good service, and should be preferred because of its small risk. But when the tumour is large, I believe oöphorectomy to be as dangerous as, and in some cases even more dangerous than, hysterectomy has now become under improved methods of performing the operation.

## CONCERNING THE EFFECTS OF DILUTION AND CONCENTRATION ON THE ACTION OF POISONS.

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THE persistence of the effects of drugs varies considerably. For instance, very soon after discontinuing the administration of chloroform consciousness returns, whilst after dropping into the eye a minute dose of atropia the pupil remains dilated for days. It is evident, then, that the changes induced by chloroform on the brain are obviated much more readily than the changes induced by atropia in the structures of the eye.

From experiments with the frog's heart, presently to be described, I find that the effects of one drug that completely arrests function are readily removed, whilst with another drug its effect is got rid of with much more difficulty, whilst in the case of a third its influence cannot be got rid of at all. The experiments were performed with Roy's tonometer, by means of which an artificial circulation can be maintained through the ventricle by a syphon action. In each experiment I employed 100 cc. of blood mixture, made by dissolving bullock's blood in saline solution. I took tracings first of the heart's contractions with this mixture, and then added to the whole circulating mass dose after dose of the substance experimented with, until the ventricle lost its contractility and failed to respond to a strong induction shock; then to the whole mass of the blood mixture I added an equal quantity of saline or an equal quantity of blood mixture, so that the same quantity of poison circulated through the ventricle, but in a much diluted form. In case neither dilution restored contractility, I replaced the poisoned blood with fresh unpoisoned blood mixture. These experiments show that the action at least of many poisons depends on the degree of their concentration. A given quantity administered in a concentrated form will act more energetically than a larger quantity in a more dilute form. For example, experimenting with the frog's ventricle, on adding a potash salt to the circulating fluid, the contractility grows less and less, and at last disappears; so that a strong induction shock fails to contract the ventricle. When, however, the circulating fluid is diluted with an equal quantity of saline solution, good contractility speedily returns. In this experiment the contractility returns although the ventricle receives the same quantity of potash only in a more dilute form. Indeed, in the case of the inorganic salts in the blood, this arrangement must prevail, otherwise the functions of the body would soon be all arrested.

In my experiments with the frog's heart, I find that with some salts dilution with saline solution is adequate to remove the depressing effect. With other salts dilution with blood mixture is necessary; and in some cases the poisoned blood mixture must be replaced with unpoisoned blood, producing thus, of course, a very large dilution. For instance, simple dilution with an equal amount of saline, solution will restore good contractions in a ventricle arrested by potassium, ammonium, and sodium salts, extract of opium, ethylic alcohol, extract of muscaria, and liquid extract of jaborandi. Very free dilution—i.e., threefold dilution—with blood mixture removed the effects of veratria;

but the substitution of fresh blood mixture for the poisoned blood of course made the experiment far more effective. The substitution of fresh blood for poisoned blood mixture restored good contractions to a ventricle arrested by arseniate of soda. On the other hand, the substitution of unpoisoned blood for poisoned blood mixture failed to restore contractions to a ventricle arrested by aconitia, arseniate of soda, chloral hydrate, and strophanthin. I have thoroughly investigated the effect of dilution on the action of potassium chloride, and now give in detail my experiments.

On April 13th, 1882, I added in one dose 2 cc. of 10 per cent. solution of chloride of potassium, a larger dose than is required to arrest the ventricle, for previous experiments show that on an average 1.5 cc. will suspend contractility (both spontaneous and excited). In about fifteen seconds after the addition of this dose the ventricle stopped beating, and strong faradaic shocks failed to induce any contraction. This dose produced some spasm, which lasted about ten minutes, gradually growing less, and finally disappearing. After an interval of forty-eight minutes, during which time the ventricle did not beat spontaneously nor respond to very strong induction shocks, I added to the circulating blood 100 cc. of saline. In a little over four minutes induction shocks with the secondary coil at 0 excited weak contractions, which grew gradually stronger, and could then be induced by a weaker excitation. Ten minutes after the first addition of saline I added another 50 cc.; fifteen minutes after the first addition the ventricle beat good spontaneous contractions, almost as good and quite as frequent as before the operation. However, on applying continued faradisation to the ventricle, the secondary coil standing at 2, I arrested the spontaneous contractions and brought the ventricle to a standstill, but on discontinuing the faradisation it at once resumed contraction. Although, then, the ventricle had to a great extent recovered itself, and gave good and frequent spontaneous beat, it was still so far under the influence of the potash salt that strong continued faradisation, instead of exciting tetanus as in an unpoisoned heart, arrested the spontaneous beats. I then added another 100 cc. of saline, and the contractions continued as strong and as frequent as before, but still continued faradisation arrested the ventricle. I then substituted some fresh blood mixture for the previous circulating fluid, and the contractions became more frequent and not quite so strong, but at this point continued faradisation produced imperfect tetanus.

On April 12th I added 3 cc. of 10 per cent. solution. This arrested contractility, notwithstanding the application of a strong induction shock, in about twenty seconds. This large dose induced more marked and more persistent spasm than in the previous experiment. In thirty-three minutes I added 100 cc. of saline solution, and in four minutes a similar quantity. In ninety seconds after the last dose contractions returned, and became good, but, as happened in the last experiment, continued faradisation arrested them. On another occasion, after suspending contractility by the addition of 1.5 cc. of the chloride of potassium solution, I allowed an hour to elapse before adding 100 cc. of saline. In a few seconds good and frequent spontaneous contractions set in, though less strong than before the addition by the salt. At another time, after the addition of 1.3 cc. of potassium solution, the ventricles remained for twenty-four minutes incapable of contraction, when I added 100 cc. of saline, and in a few seconds good spontaneous contractions ensued, contractions as good and as frequent as before the experiment. I then adopted another testing method. I employed the usual 100 cc. of the blood mixture, but diluted it with 100 cc. of saline, and then from time to time in small quantities added a 1 per cent. potassium chloride solution till strong induction shocks could no longer be produced. In two experiments I found that 37 cc. and 36 cc. were required to arrest the ventricles. I used double the amount required, when only half the quantity (100 cc.) of circulating blood is used. On another occasion I employed 100 cc. of blood mixture with 200 of saline; 52 cc. of the 1 per cent. solution were needed to arrest contractility, or rather more than three times the quantity required to arrest contractility when only 100 cc. of circulating blood is employed.

I next tried a third method. By the addition of 1.5 cc. of 10 per cent. solution in successive doses I arrested the contractility, and then added 100 cc. of saline; good spontaneous contractions ensued. I then again arrested the contractility by the further addition of the potassium chloride solution and in the addition of another 100 cc. of saline good spontaneous contractions returned a second time. I

then a third time arrested contractility, adding more potassium solution, so that in all 5 cc. were added (more than three times the quantity necessary to arrest the ventricle when added to only 100 cc. of circulating blood). I then added another 100 cc. of saline, and again good spontaneous contractions returned, which became arrested on the application of continuous faradisation. That the arrest of contractility is due to the concentration of the dose, and not to the amount sent by the ventricle, is shown by the rapidity of the loss of contractility. Thus, on adding to the circulating fluid a single large dose of potassium chloride, enough to arrest or greatly weaken the ventricle, in a few seconds, even before many drachms can have passed through the ventricle, its contractility is suspended, and cannot be re-excited even by a strong induction shock.

The effect of a strong percentage dose is also shown in the following experiment, performed by Dr. Sainsbury. He injected a small dose of potassium solution into the afferent tube leading to the ventricle. It thus was very little diluted with blood, and reaching the ventricle in a concentrated condition, arrested it. The blood, however, following, diluted the potash solution in the ventricle, and contractions soon returned.

It is interesting to note that potassium, sodium, and ammonium salts will suspend for an hour or longer not only spontaneous action, but contractility, so that a strong induction shock will not excite a contraction, and yet on dilution good spontaneous contractions recur. The action of these salts on the heart may be compared to the action of anæsthetics on the central nervous system.

It is probable that substances which affect the heart, according to the degree of concentration, act in the same way on other tissues. If so, then it is obvious that in cases of poisoning by any of these salts, we should give the patient abundant supply of fluids to dilute the poison, and to act on the kidneys and skin, and thus help to carry off the poison from the system. It is feasible, too, that in certain cases this dilution of the blood may be aided by bleeding the patient, and, if necessary, by both bleeding and transfusion, a mode of treating which has been successfully adopted in poisoning by phosphorus, &c. This effect of dilution is, I am told, well known to some who, on getting drunk, speedily sober themselves by drinking very freely of water.

By the light of these experiments we can readily explain Aubert and Dehn's observations. They arrested the heart of a dog by injecting a solution of potassium chloride into the jugular vein, and then restored contractions by connecting the crural artery of another dog with the jugular vein of the poisoned dog. Here the transfused blood of the unpoisoned dog diluted the blood of the poisoned animal, and so obviated the effect of potash to arrest the heart. I find that cane sugar weakens the contractility of the ventricle, and in large doses will even suspend contractility; but the dilution of the circulating fluid with saline solution restores good spontaneous contractions. In this fact we seem to have an explanation of the use in storing up glycogen in the liver; for if after every meal the sugar were at once poured into the general circulation, the excess of sugar would depress the functions of the body.

The foregoing observations seem to me suggestive of rules for guidance in prescribing medicines. For instance, when giving powerful drugs, like curare, conia, or physostigma, in toxic doses to produce paresis, as in chorea, tetanus, and other paroxysmal diseases, it is better to give small and frequent doses, rather than large and less frequent doses. Should the stomach be empty at the time large and infrequent doses are given they might be absorbed quickly, and produce more marked effects than we might desire. I have seen this occur, I think, in the case of conia. Again, in administering alkalies, &c., to render the urine neutral, or in epilepsy, especially in the case of potassium salts, it is better to give smaller doses frequently, and so prevent the percentage of potash in the blood becoming large enough to depress the heart.

In cases of poisoning we can dilute the blood by drinking fluid, or if that method is impossible, the fluid may be injected into the rectum, or even into a vein or the abdominal cavity. The fluid to be employed should be of such a character that it will not destroy the red corpuscles of the blood, and be the best adapted to sustain the functions of the tissues. Certain experiments recorded in the *Journal of Physiology*, vol. iv., No. 1, show that the heart's contractility can be sustained only by an alkaline fluid containing lime and potash salts—namely, potassium chloride 1 part

in 10,000 to 15,000, chloride of calcium 1 part in 5000 to 10,000. Any other combination of the salts of the blood without lime is incapable of sustaining the heart's contractility. It is fair, I think, to conclude that the salts needful to sustain the heart's contractility are likewise necessary to sustain the contractility of the skeletal muscles, and possibly may be likewise indispensable to the performance of nervous function. I would then suggest as a useful fluid 100 cc. of a saline solution containing 75 per cent. of common salt, with potassium chloride 1 cc. of 1 per cent. solution, sodium bicarbonate 5 cc. of 1 per cent. solution, and calcium chloride 2.5 cc. of 1 per cent. solution. In a recent number of THE LANCET, vol. ii., p. 437, 1882, Mr. C. E. Jennings recommends as "an almost perfect substitute for blood transfusion" the following solution: Water 20 ounces, sodium chloride 50 grains, potassium chloride 3 grains, sulphate of soda 2.5 grains, carbonate of soda 2.5 grains, phosphate of soda 2 grains, containing two drachms of absolute alcohol. By means of Roy's tonometer I have tested the action of this solution on the ventricle of the frog's heart, both with and without alcohol, and in the strength recommended, and in double that strength, and find that the ventricle fed with this solution rapidly grows weak and soon loses its contractility, so that it neither beats spontaneously, nor will it respond to a strong inductive shock.

Now I find that on adding 2 to 2.5 cc. of 1 per cent. solution of calcium chloride, spontaneous contractions soon recommence and become good. I would advise, therefore, the addition of calcium chloride to Mr. Jennings' solution; but as his solution on the addition of calcium chloride becomes cloudy from the formation of calcium carbonate, it is better to use sodium bicarbonate instead of sodium carbonate. In a case of poisoning, after washing out the stomach the patient should drink very largely of one or other of these fluids. If he is insensible, it may be introduced by a tube; but as absorption from the stomach may prove too slow, then, I think, in certain cases it may be warrantable to inject the fluid at a temperature of 100° into the abdominal cavity or directly into a vein. If in a place where no defibrinated blood can be obtained, or if in insufficient quantity, the free ingestion of this fluid will of course dilute the poison in the blood, and get rid of some of it through the kidneys and skin. Whilst we thereby dilute and diminish the poison circulating in the blood, we have got another resource in venesection, which will not only run off some of the poison with the blood, but will also assist the absorption of the saline solution.

#### REMARKS ON THE REMOVAL OF THE ENTIRE TONGUE WITH SCISSORS BY THE WHITEHEAD METHOD.

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HAVING made use of the above method in two cases, I wish to state my experience of it, as the safety and extreme simplicity of Mr. Whitehead's operation do not appear to be as yet sufficiently recognised.

The ages of my patients were forty-nine and fifty-seven. In both "soreness" of the tongue had existed for a very long period. Thus in the first case a small sore had been produced twenty-eight years before the operation by a pipe being broken in the patient's mouth. Since this time the tongue had always been sore off and on, especially after smoking too much, or after indulging in wine. A long, valley-shaped, ulcerated fissure occupied the middle and posterior thirds of the tongue on the left side; with this coexisted numerous smooth bald patches and others of a "leucomatous" nature. The ulcer extended so far back, and was so intensely painful, that before an anæsthetic was given it was impossible to define its posterior limit. Thus it would have been a matter of great difficulty to get the loop of an écraseur behind it; and even when this was done, the loop, when tightened, would certainly have come dangerously near the ulcer. In this the superiority of Mr. Whitehead's method was strikingly shown, as it enables the surgeon to place his