

for certain periods of time in the stomach. After acidification the gastric contents enter the small intestine. Alkaline digestive juices are secreted into the lumen of this part of the tract. Hydrolysis and absorption rapidly take place. When these processes pursue their usual involuntary or automatic course, there is a definite relationship established between the acid and base substances. This indicates a normal reaction of the material in contact with this part of the body surface. Alteration in the acid-base balance indicates abnormality. In our experience this is an index of maladjustment. The loss of the ability of this body surface to control the bacterial life in contact with it, is another index of changed biological function. We have been able to show experimentally in this brief report that a change in the reaction of the contents of the upper part of the small intestine from a slightly acid to an alkaline reaction is accompanied by a change in the susceptibility of the animal to *V. cholerae* infections.

The *V. cholerae* used in these experiments has been constant. The rabbit has been changed from a resistant to a susceptible experimental animal by changing the reaction of the material within the lumen of the duodenum and jejunum. The influence of diet upon health is becoming so well known that mention only needs to be made of this important subject. A population in a poor state of nutrition will be made more abnormal by climatic changes than they would be if their metabolic functions were normal. These changes in the population can play an important rôle in the epidemics of cholera in India. The equilibrium between the host and the *V. cholerae* will be disturbed to the advantage of the parasite and the detriment of the host, if the latter loses the power of disinfecting its body surface covering the alimentary canal.

Summary.

1. *V. cholerae* injected into the duodenum of rabbits in saline does not cause diarrhoea. Such animals remain healthy.
2. *V. cholerae* injected into the duodenum of rabbits in alkaline buffered phosphate solutions cause diarrhoea and death. The *V. cholerae* can be isolated from the intestinal tract and various organs of the animals.
3. One half of the minimal lethal dose of *V. cholerae* injected intravenously in rabbits does not cause diarrhoea.
4. One half of the minimal lethal dose of *V. cholerae* injected intravenously in rabbits and followed by an intraduodenal injection of sterile saline does not cause diarrhoea.
5. The same dose of *V. cholerae* intravenously followed by intraduodenal injection of sterile alkaline buffered phosphate solution causes diarrhoea and death in rabbits. The *V. cholerae* can be isolated from the fæces before

death, from the intestinal tract and various internal organs after death.

6. If sterile alkaline phosphate solution is injected into the duodenum up to 18 hours after one half of the lethal intravenous dose of *V. cholerae* has been injected, the rabbits develop diarrhoea and die after 24 to 48 hours. The *V. cholerae* can be isolated from the various organs after death.

7. Host susceptibility to *V. cholerae* infection has been changed or modified in these experiments by changing the reaction of the upper part of the intestinal tract.

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INTRAVENOUS CALCIUM CHLORIDE IN THE TREATMENT OF CHOLERA.

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LOOKING to the morbid anatomy and blood changes in cholera, one finds that the coagulability of the blood is diminished, there are extensive hæmorrhages into the tissues of the kidneys—especially in the cortex after suppression of urine, and petechial hæmorrhages in the stomach and visceral pericardium. It was these indications which, I believe, led Sir Leonard Rogers to use calcium chloride as one of the ingredients of his hypertonic saline solution. His solution contains 4 grains of calcium chloride and 120 grains of sodium chloride to the pint.

It seemed to me that the former dose was too small and the latter too large. Even if 4 pints be given, this contains only 12 grains of calcium chloride; in my experience it is always best to stop the transfusion when rigor occurs, and in many late and severe cases one cannot introduce as much as 4 pints before rigor sets in. Accordingly, last year I increased the proportion of calcium chloride by 1 to 2 grains to the pint, and found the results most gratifying in many respects. In 1927, 1928, and the first two months of 1929, I treated cases according to Sir L. Rogers' method; but during the last two months of 1929 by increased doses of calcium chloride without alkalis. This year (1930) I have kept up the increased dose of calcium chloride in the hypertonic saline infusion, combining it with separate transfusions of sodium bicarbonate, 160 grs. to

the pint of normal saline. The results are shown in Table I.

neglected. A cure rate of 77.8 per cent., effected by increasing the strength of calcium

TABLE I.

Results with different forms of treatment of cholera in the collapse stage by the intravenous method.

Period.	Treatment.	Cases.	Deaths.	PERCENTAGE OF		
				Deaths.	Recoveries.	
A.	1927, 1928, and first 2 months of 1929.	Hypertonic saline, CaCl ₂ gr. 4 to pint.	38	13	34.2	65.8
B.	Last 10 months of 1929	Hypertonic saline, CaCl ₂ gr. 5 or 6 to pint.	28	5	17.8	82.2
C.	First 20 days of 1930 epidemic.	Hypertonic saline, CaCl ₂ gr. 5 or 6 to pint, with sod. chloride gr. 105. Also sod. bicarbonate gr. 160 to the pint separately.	18	4	22.2	77.8

The figures given in Table I refer only to patients admitted in the stage of collapse and in urgent need of transfusion, the pulse at the wrist being either very feeble or imperceptible.

A study of Table I might make it appear that the second line of treatment gave the best results, but the cases treated in the early part of 1930 were the very worst that I have ever come across in my 18 years of practice, and in at least 700 cases of cholera seen. I am not sanguine about the efficacy of the increased calcium chloride treatment alone in old persons over 50. Six out of the 18 cases treated this year with treatment C were more than 50 years of age, and only one died—a very successful result for the onset of epidemic conditions.

Other advantages in increasing the amount of calcium chloride which I have found are:—(i) rectal salines are not so frequently needed to stimulate the kidneys; in the severest cases rectal salines every 6 hours for one day are sufficient, including cold salines for controlling pyrexia. (ii) Vaso-constricting drugs are required with much less frequency. (iii) Excepting in the most severe cases, only one intravenous saline transfusion is required; at the most a subcutaneous hypertonic saline is sufficient to make up for the deficiency in fluids.

Rogers states that with the addition of the oxidising drug, 68 per cent. of 69 transfusion cases were saved, and in patients in whom no pulse could be felt at the wrist, or where the blood pressure was too low to be measured at the wrist, no less than 58 per cent. were rescued from certain death, during 12 months. Adding the 7.5 per cent. extra gained by him by the introduction of alkaline treatment, the success rate is 65.5 per cent. or even 75.5 per cent. under epidemic conditions when dealing with severe cases. The mortality is high at the commencement of an epidemic and then progressively decreases, so that drugs found useful in the early stage of an epidemic cannot be

chloride, among the first cases in the epidemic of April 1930 is therefore satisfactory enough to be given further trial.

Technique.—My technique is as follows:—

The solution consists of calcium chloride 5 or 6 grains, sodium chloride 120 grains, to the pint; and two pints are rapidly introduced, followed slowly by alkaline normal saline—sodium bicarbonate 160 grains, sodium chloride 60 grains, to the pint. One pint or as much as possible of the calcium chloride-increased solution is then introduced again before rigor sets in. Pituitrin 1 c.c. and digitaline and atropine gr. 1/100th are injected subcutaneously after the first transfusion. Calcium permanganate drink, gr. 1 to the pint, is given in small quantities as often as necessary. After the febrile reaction is controlled, if the patient's pulse gets feeble, the specific gravity of the blood is observed, and if it is found to be high, the transfusions are repeated in the following order:—(i) one pint of hypertonic saline containing increased calcium chloride; (ii) alkaline normal saline; (iii) hypertonic increased-calcium chloride saline again; until the specific gravity of the blood has been restored to normal.

It is premature to come to final conclusions on 18 cases observed, but the indications all seem to point to the necessity for an increase in the calcium chloride content of the injection. It is needless to add that successful results can only be achieved by the closest and most patient personal attention by the physician himself, with the help of subordinates who must be honest workers.

Conclusion.—Of the three lines of treatment shown in Table I, the third appears to be the best method for severe cases of cholera asiatica.

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