An Address

ON THE

USE AND ABUSE OF THE LIME SALTS IN HEALTH AND DISEASE.

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BY

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LADIES AND GENTLEMEN,—I am here to-day to deliver the opening address of your session, in response to your kind invitation which has been twice extended to me. My presence here is to me specially gratifying, as it renews old reminiscences of my residence in this Infirmary thirty-seven years ago under my revered teacher, the late Sir William Gairdner. Many of my friends of those days are still alive, and perhaps as youthful as ever, though some, I regret to say, have joined the great majority.

In selecting a subject for my address worthy of this occasion, I had to recollect that it was going to be delivered before an intelligent and critical Scottish audience, who would expect something new or something true. It is always my habit to adhere to the latter condition, and it will be for you to judge as to the newness or freshness of the presentation.

It occurred to me that as Loch Katrine water was supposed to be very deficient in lime, and when I was here this deficiency was blamed for the prevalence of rickets, you might take some interest at least in the use of the lime salts. The subject of the lime salts has interested me for over thirty years, first from a pathological standpoint, next as therapeutic agents, and finally from a physiological point of view. Perhaps the order should have been reversed, but I studied the questions intermittently as they presented themselves to me, and not in any systematic manner.

In 1876 I published a paper on the effects of overwork on the heart and aorta.¹ I showed how chronic high arterial tension led to atheroma of the aorta. At that time I had not the advantage of any of the numerous blood-pressure instruments which are now on the market. My observations were made with my finger-tips and the sphygmograph. I have still plenty of faith in my fingers; with proper training they become very sensitive instruments of precision. In a paper which I read at the Liverpool Medical Institution on February 17th, 1881, on the etiology of aneurysm,² I showed that calcification of the aorta was due to the deposition of lime salts in the atheromatous patches which occurred in the subendothelial layer of the intima.

Between 1882 and 1890 Sydney Ringer³ performed a series of classic experiments on the physiological effects of the various inorganic constituents of the blood. He showed that for the continuous contraction of the ventricles of the frog's heart the presence of minute quantities of a calcium salt was absolutely essential. Calcium increases the efficiency of the beat but delays dilatation: "The effects produced by lime salts in dilatation, and even the persistent spasm induced by the alkaline preparations, are completely removed by a minute trace of a potassium salt—1 in 10,000 to 15,000."

The ventricle continued to beat perfectly when supplied with a neutral normal saline solution containing minute quantities of calcium and potassium chloride, and therefore alkalinity of the circulating fluid is not necessary for contractility. The alkaline reaction of the blood is no doubt necessary indirectly for contractility, for muscular contractions develop acidity, and this must give an acid reaction to a neutral fluid, and the heart cannot contract when supplied with an acid-circulating fluid.

Sodium bicarbonate added to normal saline broadens the beat and rounds its summit, and slightly prolongs both contraction and dilatation. Owing to the increased breadth of the beat, if the contractions are frequent, there occurs partial fusion of the beats. Sodium bicarbonate also induces some persistent spasm (contracture) if the contractions are frequent. All these effects of sodium bicarbonate are obviated by a physiological quantity of potassium chloride.

He showed the antagonism between the potassium and calcium salts, and that the presence of both in proper

proportions was necessary for regular and efficient cardiac systoles. He also showed that this antagonism between calcium and potassium existed even in toxic doses, though the antagonism was somewhat modified by temperature, as hot weather caused much tonic contraction, which was not entirely obviated by the effects of potassium in hastening dilatation.

He found that sodium phosphate and sodium bicarbonate accelerated dilatation without sustaining the contractility of the ventricle, and of the calcium salts the phosphate was the most efficient.

He experimented on fishes, and found that the presence of lime in the water was necessary for the maintenance of life.

I draw attention to the interesting fact that those lime salts most efficacious in sustaining function of cardiac tissue are those best adapted to sustain life in ova and tadpoles, phosphate of lime being far more efficacious than sulphate, and the sulphate somewhat more efficacious than chloride. It would appear that those salts of lime in which the lime atom is least saturated by the acid are the most capable of sustaining function.

It must be remembered, however, that in the human subject where drugs are administered by the mouth the sulphate and tribasic phosphate are practically insoluble, and therefore useless. The glycerophosphate of calcium is very soluble, and a very effective drug. I recollect being very much amused a few years ago by the statement of a professor of therapeutics that the phosphate of lime cured the toothache of pregnancy. His idea as to the cause and cure of the toothache in a pregnant woman was, to say the least of it, original, but it is to be hoped the idea will die with him.

Dr. Ringer, in association with Dr. Dudley Buxton, showed that the effects of the salts of sodium, potassium, and calcium on skeletal muscles are somewhat different from their effects on the heart. The contractility of skeletal muscles perfused with normal saline solution lasts longer, but when exhausted there is a great delay in relaxation. The contractions are strengthened and the relaxation delayed by potassium salts. On the other hand, the lime salts accelerate both contraction and relaxation. Personally, I have usually found that patients liable to cramp, especially of the calf muscles, have a deficiency of lime in their blood, and thus the remainder-contraction so apt to occur in exhausted muscles is not counteracted by a sufficiency of calcium.

In the present day, when the effect of sodium chloride in the causation of dropsy is so widely recognized, it is worth remembering that Dr. Ringer made experiments on the swelling of laminaria when immersed in water, and he found that sodium and potassium chloride retarded but did not lessen the amount of fluid taken up; on the other hand, even minute traces of the chloride or other soluble salt of calcium greatly and persistently restricted the swelling of laminaria. In the treatment of dropsy the chloride of sodium should be excluded, while the calcium salts are beneficial.

I have given this long summary of the work of Sydney Ringer because in the present day it is practically unknown, or does not receive the recognition to which its great merits entitle it. If it had come from Germany it would have been in every textbook on the circulation. Its clinical importance was not sufficiently recognized because only the few took the trouble to inquire as to whether there was too much or too little lime in the blood, and all estimations on this score were purely guess-work, as there was no method known of estimating the amount of lime in less than a litre of blood, and there was no patient who would spare that amount for the mere sake of knowing how much lime it contained. Sir Almoth Wright used a moderately convenient, but not very reliable, method based on the strength of a solution of oxalate of ammonium required to prevent blood clotting. Since the work of Ringer and Sainsbury⁴ and others it has been universally recognized that the presence of calcium was necessary for the clotting of blood and milk. More recently, Blair Bell has shown that the setting of gelatine is also due to the presence of calcium. Recently, in a series of very careful experiments, Dr. T. Addis⁵ has controverted the work of Wright, and he concludes:

(1) The coagulation time of the blood is unaffected by the administration by the mouth of soluble calcium salts or of citric acid. (2) The amount of ionizable calcium in the blood is

increased by the administration of soluble calcium salts by the mouth, and is diminished by the administration of citric acid, but the increase or decrease which is thus brought about is considerably less than the degree of variation in the calcium content which is necessary before any appreciable effect is produced on the coagulation time.

In 1907 Blair Bell⁶ devised a most ingenious and reliable method of estimating the amount of ionizable calcium in a few drops of blood. Briefly stated, he mixes in a small capsule 250 c.mm. of an aqueous solution of oxalic acid (1 in 30) and 100 c.mm. of blood. After the oxalic acid has had time to combine with the calcium and magnesium in the blood, he adds 250 c.mm. of a weak solution of acetic acid and glycerine, which dissolves the magnesium salts. He next adds 100 c.mm. of the mixture to 500 c.mm. of distilled water. Of this final dilution he places a drop on a glass slide of a Thoma haemocytometer. He counts the number of calcium oxalate crystals in 250 squares, and an average of one crystal per square gives his calcium index 1.0. Blair Bell now considers the normal healthy maximum to be 0.8. This excellent method has not caught on as it should, simply from the fact that it involves trouble, and the ordinary Britisher will not take trouble. When Blair Bell showed the powerful effect of the pituitary extract on involuntary muscular fibre, and its great value in shock, uterine inertia, and intestinal paresis, he had any number of followers, because it is a very simple matter to give a hypodermic injection, so that the drug has been used in all manner of diseases for which it is in no way suited, and Blair Bell has had to complain of its abuse.

When you see a patient in consultation you have usually to make up your mind pretty quickly not only as to diagnosis, but also as to treatment. As to the question whether a patient has got too much or too little calcium in his circulation I have got a good many devices of my own which help me in arriving quickly at a conclusion. These devices I am not going to put down categorically, because they require a good deal of practical experience, but if you are very attentive to this address you may discover them. I frequently have my opinion corroborated or corrected by Pantland Hick, who conducts my blood examinations after Blair Bell's method. For many of the beneficial effects of calcium in health and disease I can strongly recommend my readers to the work of Blair Bell and Pantland Hick on calcium metabolism.

In the following remarks on the use and abuse of the lime salts it will save time and space if I deal with health and disease together.

The Effects of the Calcium Salts on the Circulatory System.

I have referred to the work of Sydney Ringer on the necessity of calcium for the maintenance of the action of the heart and of life. On several occasions I have shown that most chronic diseases of the heart arise from causes acting on the periphery. In my Toronto address⁷ I described my methods of estimating the velocity of the blood in the arteries, capillaries, and veins. I also dealt with the viscosity of the blood as the chief cause of the resistance to the flow in the capillaries. Since then I have come to the conclusion that the principal cause of this viscosity is the lime salts, especially the fixed lime. The viscosity can be accurately estimated by the viscosimeter of Du Pre Denning and Watson, and clinically by watching the freedom of flow from a lancet-needle puncture. I determine it by watching the velocity of the capillary circulation in the dorsal surface of a warm finger or hand held at the level of the heart. It is necessary to take the capillary circulation at the level of the heart because the velocity is about doubled by lowering the hand 320 millimetres.

I measure the capillary velocity by gently expressing the blood out of a flat plexus of capillaries in the back of the finger or hand with a rod 10 mm. in diameter, and then watch the time it takes the blood to return with a stop-watch recording fifths of a second. A spot must be selected where the return current comes from all parts of the circumference of the compressed area. In a capillary the axial velocity is double the mean velocity; now the red cells occupy the centre and fill about four-fifths of the lumen of the capillaries, so the actual velocity is about four-fifths of the observed velocity. I therefore put the radius of my rod down as four, although it is actually five millimetres.

From repeated observations I have come to the conclusion that when the capillary velocity is 4 mm. in one second or less there is no excess of lime salts in the blood, but the converse does not hold good.⁸ I have recently seen a case where the capillary velocity was only 4 mm. in one and two-fifths seconds, but the calcium index was only 0.5; the patient was 74 years of age, suffering from arteriosclerosis, with lesions of his aortic, mitral, and tricuspid valves. I felt confident that there was too much fixed lime in his blood and tissues; accordingly I put him on a calcium-free diet and large doses of phosphoric acid. In a week the free calcium ions in his blood had so increased that the index had risen to 1.2, and at the same time the velocity had increased to 4 mm. in one second. In the chilblain circulation the capillary velocity may fall to 4 mm. in two or three seconds, but in this condition almost every one believes that the lime salts are deficient. This is quite true of the free calcium ions, but not necessarily so of the fixed lime. In these cases the fingers and toes are much swollen from the congestion of the large capillaries, but there is no true oedema of the tissues, which would undoubtedly occur if the fixed lime in the blood was deficient. The large molecules of calcium albuminate do not readily transude, and, as Sydney Ringer showed, the oedema of the tissues is inhibited by the presence of the lime salts. On the other hand, in orthostatic albuminuria there is a marked deficiency in the fixed lime, and so the albumen readily transudes through the glomeruli under the increased pressure from the erect posture.

From repeated observations I have come to the conclusion that it is the fixed lime which is concerned in the viscosity and in the coagulation of the blood, and with both these phenomena the free calcium ions which are revealed by Blair Bell's method have directly nothing to do.

The viscosity of the blood in the capillaries increases the work of the heart, but this is merely the second line of resistance, and owing to the large capillary bed it cannot raise the arterial pressure much unless there be also contraction of the arterioles. So far as the lime salts are concerned, this contraction and the action of the heart are due to the free calcium ions. Of course, the secretions of the infundibular portion of the pituitary body and of the suprarenals also lead to such contraction of involuntary muscular fibre, but we are not at present concerned with their excess or deficiency in the circulation. In many cases of orthostatic albuminuria, although there is a deficiency in fixed lime, there may be no defect in free calcium ions, so with the increased capillary velocity there may be contracted arterioles and raised arterial blood pressure. In the maintenance of the arterial blood pressure both the free and fixed lime salts play a very important rôle, both in the input from the heart and in the regulation of the output through the arterioles and capillaries, but I do not wish you to get any exaggerated ideas of their importance, because the secretions of the pituitary and suprarenal glands are also necessary for the regulation of this pressure and the maintenance of life. In Addison's disease, where the vasomotor nerves have not got their natural stimulus, you cannot sufficiently maintain the blood pressure, no matter how much lime you administer. Again, in Landry's paralysis, when you get paralysis of vasomotor nerves with dilatation of the arterioles, the viscosity of the blood may be great, and for a time the heart may act powerfully in order to maintain the blood pressure, but there is an enormous fall in the pressure gradient, and the heart soon gets exhausted pumping blood into the unfilled arteries. There is a great waste of energy and the force of the heart is poorly represented at the periphery. When the capillary velocity falls to about 1 mm. in the second or less, the blood gets charged with carbonic acid; this increases the viscosity and further enhances the work of the heart, but, apart from contraction of the arterioles, it does not raise the arterial blood pressure.

"Good healing flesh," of which many people are very proud, simply means that there is a sufficient or excessive amount of calcium cement in the tissues. This is very useful if you are going to get cut up in strips with a bowie knife, or bruised by a Johnson or Jeffries, as might happen in some parts of America, or if you are going to fall into

⁸ Dr. Haig uses a capillary dynamometer for estimating the amount of purin bodies in the circulation.

the hands of the surgeons, which is a very great risk in this country; but if you are going to preserve the even tenor of your way and live a healthy life to a good old age then you had better not have any unnecessary amount of lime in your blood or tissues. It is one of those cases where you can have too much of a good thing.

My conclusions are that the fixed lime, or that which is linked on to the molecules of albumen, increases the viscosity and coagulability of the blood, while the free calcium ions in association with the suprarenal and pituitary secretions increase the tone and contraction of the arteries and arterioles, heighten the blood pressure, and maintain the force and efficiency of the cardiac contractions. In this latter effect the ions of potassium and sodium play an important part. Lime is by no means the only agent in the production of the viscosity of the blood, which is a moderately viscous fluid, being about five times more viscous than distilled water. The viscosity is augmented by an increase in the number of the corpuscles and in the density, by cold and carbonic acid. It is also important to note that the suprarenal and probably infundibular (pituitary) secretions lead to the retention of lime salts in the blood and tissues, while the thyroid and ovaries increase calcium metabolism, diminish the free and fixed lime in the blood, and thus lessen the viscosity. This has been well shown by Blair Bell, and, on his recommendation, I have for the last three years used with great advantage the calcium salts in the treatment of exophthalmic goitre. However, in many cases the great metabolism leads to an excessive amount of free lime in the blood, and hence calcium is not the only factor in treatment. What part the purin bodies play in the viscosity of the blood I am not prepared to say, and at present it is not my business to inquire, but there can be no doubt that lime may be united with uric acid in the blood, tissues, urine, and urinary calculi.

It is very difficult to prove experimentally the part played by calcium in producing and maintaining high arterial pressure, because it is a slowly acting drug; it is absorbed with difficulty by many people, the blood can only hold a limited amount in the free state, and the more alkaline the blood the less it will hold. There are some people, like myself, who absorb lime very readily, but fortunately excrete it almost as quickly. Within two hours of drinking a glass of milk there is a marked increase in the lime in my urine. While we cannot show with the sphygmomanometer that a dose of lime markedly raises the blood pressure, we have the indirect evidence that decalcifying agents quickly and markedly lower the blood pressure and lessen the viscosity of the blood. These agents do not always lessen the free calcium ions, because they take up a good deal of the loosely fixed lime in the blood vessels and other tissues. Under the free use of phosphoric acid I have seen the free calcium ions increase in the blood, while coarse valvular murmurs abated, and in some cases even disappeared. The blood is the agent for carrying the calcium to the tissues, and from them to the excretory organs.

Sir Almroth Wright has shown the great value of decalcifying agents in the treatment of thrombosis; on the other hand, when you get capillary haemorrhages, whatever treatment the blood pressure may demand, the viscosity of the blood should be increased by the lime salts. When using decalcifying agents the lime salts should be as far as possible eliminated from the diet, hence milk, cheese, the numerous milk foods in the market, animal jellies, and hard water should be interdicted. Five years ago I sounded a note of warning against the indiscriminate use of sour milk, on account of the lime which it contains; but now the craze has sufficiently developed to attract a discussion at the last meeting of the British Medical Association, and to merit the attention of the daily papers. The craze will soon die out, no doubt to be replaced by some other equally absurd, when people find that they are not going to live to the age of Methuselah. Exercise rapidly increases calcium metabolism, and no doubt the Bulgarian peasant can quickly get rid of the excess of lime which he takes in, but it is quite a different matter with the town dweller. Milk is essential for children, and is useful in many diseases where we wish to increase the amount of calcium in the blood, such as cases of haemorrhage, many cases of pneumonia, and the acute stage of typhoid fever, etc., but for the ordinary adult its utility is somewhat limited.

There are many who assert that the tissues will only take up what lime they require, but I am afraid the tissues have often no discretion in the matter. The lime salts are very apt to get deposited in any part of the body which is not properly functioning. I have seen ossification of the costal cartilages in a man of 27 years of age produced by long-continued fixing of the chest with a spinal support.

Arteriosclerosis.—I here use the term "arteriosclerosis" in its widest sense, to include all thickening and hardening of the arteries. However high blood pressure is brought about it eventually leads to degenerative changes in all the coats of the vessels. Very many years ago I showed how chronic high tension led to degenerative changes, with subsequent atheroma and calcification of the deep layers of the intima of the aorta, and lately Oskar Klotz* has found that the degenerative changes in the muscular arteries begin in the media. He has also shown that the lime salts are always deposited in the form of calcium soaps, and afterwards the fatty acid is replaced by phosphoric and carbonic acids.* Dr. Klotz has experimentally demonstrated in corroboration of the previous work of Dr. Josué, that the intravenous injection of adrenalin led to degeneration and subsequent calcification of the media. He also suspended rabbits by the hind legs for a few minutes daily, and thus brought about advanced lesions in the aorta. In this connexion it is worthy of note that in rabbits the calcium index is usually high, and in the human being the arteries of the lower extremities, which are usually subjected to the highest blood pressure, are the most prone to arteriosclerosis. In all the aortas from subjects over 25 years of age examined by Dr. Klotz he found more or less calcareous degeneration.

As the degenerative changes proceed the arteries, especially the aorta, gradually lose their elasticity; consequently the energy imparted by the heart to the blood is not properly stored up, there is a great fall in the pressure gradient between the systolic and diastolic pressures—this leads to longitudinal straining of the arteries, the arch of the aorta gets dilated, and the muscular arteries become tortuous. The best way to prevent and improve these degenerative conditions is to maintain a low systolic and a relatively high diastolic pressure. You may not be able to regulate the secretions of the pituitary and suprarenal glands, but you certainly can control the high-pressure effects which they produce. You can stimulate or add to the secretion of the thyroid gland, which increases calcium metabolism and lowers the blood pressure.

In this indirect manner the iodine preparations act. If the degenerative changes in the aorta have not proceeded too far—and this is most readily measured by the difference between the systolic and diastolic pressures—it is really wonderful what the free and long-continued use of decalcifying agents can accomplish. I have seen aortas considerably dilated so that the arch could be easily felt in the suprasternal notch, and the elasticity much impaired, as indicated by the loud, clear, clanging second sound, diminish in size and the second sound become quite normal. I have seen coarse, rough valvular murmurs and cardiac intermissions permanently disappear. Healthy exercise increases calcium metabolism and lowers blood pressure, and for good health a considerable amount of exercise is absolutely essential. At the last meeting of the Association of Physicians a couple of gentlemen detailed their experiments in exercising rabbits in order to cause cardiac hypertrophy. Of course, the rabbits' hearts did not hypertrophy, as any one should have been able to forecast. The way to bring about hypertrophy of the heart is to raise the arterial blood pressure; if they had given the rabbits some digitalis they would have succeeded better.

Women are not so liable to arteriosclerosis as men, because they eat less, are more temperate in all things, and, as Blair Bell has shown, they get rid of a good deal of calcium with each menstrual period. When it does occur in women, apart from kidney disease, it chiefly occurs in those who have borne large families and in those liable to emotional disturbances—emotion acts like suddenly turning a stopcock in a water-pipe connected with the main; it sets up waves of pressure, the chief stress of which is thrown on the aorta. Blair Bell has shown

* I am now informed that over twenty years ago, in the Glasgow Royal Infirmary, David Newman taught that the lime is always deposited in the blood vessels in the form of a calcium soap, and afterwards the fatty acids are replaced.

that many of the ailments of pregnancy and menstruation appear to be due to calcium deficiency.

It may be inferred from what I have previously said that I am not an advocate of the numerous milk foods in the market. It is only fair to state that Dr. Francis Bond of Gloucester is a strong advocate of cheese and the skipping-rope for the maintenance of health, and he has, I think, about skipped into the Eighties. May he long continue to skip and enjoy his cheese! If a man takes plenty of exercise he can easily get rid of any excess of lime. It does not matter much what a healthy man eats so long as he does not eat too much and takes a large variety. It would be a great advantage to the community if there were better cooks and fewer artificial foods. Sydney Smith said:

Man could direct his ways by plain reason, and support his life by tasteless food; but God has given us wit, and flavour, and brightness, and laughter, and perfumes, to enliven the day of man's pilgrimage, and to charm his pained steps over the burning marl.

Although I am anxious to direct your lives according to the dictates of reason, I have no wish to deprive you of all the sweets of life for the mere sake of prolonging existence.

Angina Pectoris.—There has been a great deal written on this subject of late which I suppose you have all read. I think I have read all the papers and learnt to forget the most of them. I am not going to weary you with any further dissertation, except to point out two types from a therapeutic point of view. There is, first, the spasmodic type or true angina, where the patient is pale, cold and haggard, anxious, and suffering severe pain, with great oppression in the chest. There is a feeling of want of air, though no real respiratory distress; the skin may be dry, or there may be a cold, clammy sweat. The pulse is usually slow, infrequent and firm, though it may be frequent and rather feeble, and is often intermittent. In these cases there is an excess of lime in the heart muscle and also to a less extent in the blood. The following illustrative case may be here recorded.

On June 18th, 1910, I was asked by my friend, Dr. J. Herbert Sykes, to see a lady with whom he had been suffering for six months from angina pectoris. Lately the attacks had been increasing in number and severity, and now there were at least a dozen attacks in each twenty-four hours. All the usual remedies had been tried without much avail, and a very grave view was taken of the case. Mrs. C., aged 66, a thick-set, well-nourished woman, pale face, anxious expression, great pain and intense feeling of oppression in region of heart. The attacks are now so frequent that she has scarcely any rest night or day. Heart's area large, 2 in. to the right and 5½ in. to the left of the mesial line; marked tenderness over the front of the chest. Heart sounds fairly clear, and action regular, except for an occasional intermission; at the aortic area there is a long, rough, loud systolic murmur; a low-pitched systolic murmur at the mitral and tricuspid areas; marked pulsation in the veins of the neck, and the liver large and tender; the superficial arteries thickened and tortuous, and the aorta dilated. Pulse 120, fair volume, an occasional intermission, raised tension. Capillary circulation sluggish, 4 mm. in 1½ seconds. Skin at present dry, but she has often cold sweats.

I explained my view to Dr. Sykes, that the patient had too much lime in her blood, and more especially in the cardiac muscle. I recommended that all lime should be excluded from her diet, including the hard Southport water; that she should have plenty of acid fruit, half a drachm of dilute phosphoric acid every four hours; also small doses of morphine and atropine until the pain was relieved. Dr. Sykes had never heard of phosphoric acid for angina pectoris, but was quite willing to try it on my recommendation. Pantland Hick found the calcium index of her blood 1.1. I was afraid to tell Dr. Sykes at the time that the free calcium in her blood was only a point over Blair Bell's unit, for fear he might lose faith in the phosphoric acid, and I had not time to enter into a long explanation, so I simply wrote to him that the calcium content in her blood was more than twice that of mine, without mentioning that my friend Hick thought mine at that time (0.5) too low, and also that I had seen the index over 2.0 without any cardiac symptoms. I advised him to continue the phosphoric acid until her tissues were well decalcified, and that I had no objection to nitroglycerine, so long as he recognized that it was a mere palliative. The treatment seemed to have been almost too successful, as I was not asked to see her again. However, in reply to my inquiry, Dr. Sykes wrote me on August 16th: "Mrs. C., the angina patient, has done exceedingly well. Up to the time that you saw her she required to take twelve to fourteen tablets of nitroglycerine daily, so frequent were her attacks. Afterwards the attacks became much less frequent, perhaps one in three or four days. I kept her in bed for about a month; she then got up, but was very weak, shaky, and pulse apt to be intermittent. I stopped the acid mixture, and put her on strychnine and tincture of strophanthus, continuing the same diet. She improved in strength and appetite, so that

she was enabled to walk out without any discomfort. About two weeks ago she went with her husband to Bournemouth, and the latest report is very satisfactory. She is exceedingly pleased with her progress, and thankful that so much relief has been gained. Certainly the increased amount of lime salts was the cause of the trouble."

The second type of angina to which I wish to draw your attention is really not a true angina, but is often mistaken for such and disastrously treated as such. The distress and danger are equally great. These cases are marked by dilatation of the heart, especially of the right side, and increased intracardiac pressure. There is no increase of lime salts, but rather a deficiency. The respiratory distress is real and extreme; there is a feeling of suffocation and great oppression about the chest. The patient is dusky and bathed in a cold, clammy sweat. The lungs get rapidly oedematous. If such a patient is treated with nitroglycerine, nitrite of amyl, or alcohol, his fate is certainly sealed. I have seen many such cases, but a recent one will suffice. It was the case of a stout, flabby lady, aged 56 years, suffering from a much-dilated heart with congestion of the lungs after a protracted attack of rheumatism. When I entered the room she made an effort to raise herself in bed, and was seized with an acute attack of cardiac failure. She gasped for breath, could not speak for the oppression in her chest; her pulse was frequent, quick and small, feeble, and scarcely perceptible at the wrist. She became livid and bathed in a cold perspiration and appeared to be dying. I have no doubt she would have died in less than half an hour if assistance had not been at hand. Before examining her I at once gave her hypodermically $\frac{1}{10}$ grain of strychnine and $\frac{1}{10}$ grain of atropine. There was marked congestion of the lower lobes of both lungs, with commencing acute oedema. She afterwards got a hypodermic injection of $\frac{1}{10}$ grain of strychnine and $\frac{1}{10}$ grain of atropine twice daily; also a mixture of the iodide of calcium and tincture of iodine. She made a good recovery.

Stokes-Adams Disease.—You all know the modern hypotheses as to how the rhythmic function of the heart is started and maintained; how a stimulus is generated at the sino-aortic node, and somehow or other travels through the auricles down the bundle of His to the apex of the ventricles and the papillary muscles, and back again to the base of the ventricles. What is the nature of this stimulus and how it is propagated God only knows, as the nearest approach to a definition which I have heard is that a stimulus is a stimulus. In this case it is not Scotch whisky, but just a stimulus to contraction. As to its mode of propagation, nothing definitely is known except that it is supposed to travel along the auricular-ventricular bundle, and at the Stannius bridge, between the auricles and ventricles, it moves very slowly, like an old flint gun which often misses fire. Some have supposed that this stimulus has got a wave of contraction of its own, which wave is picked up and reinforced by the ordinary cardiac muscle. On the other hand, Engelmann has shown that it can be propagated apart from any contraction. There are various embellishments of this theory, such as *positive* and *negative chronotropic*, *dromotropic*, *bathmotropic*, and *inotropic* influences. This stimulus runs the risk of being more or less frequently blocked by disease and drugs, so it has been necessary to assume that every healthy muscle cell of the heart has the power of producing a stimulus of its own, which it constantly does, and this is as constantly used up with every contraction, so that after every systole the heart is bankrupt of stimulus. From a therapeutic point of view, as far as I can see, this apparently learned jargon leads only to the grave. It seems to be forgotten that rhythmic action is the function of all muscle; even the skeletal muscles act rhythmically under certain pressure or strain—witness an ankle or patellar clonus. While the myogenists are settling these matters I would advise you to pay some attention to the inorganic constituents of the heart muscle and blood. I have not yet made up my own mind as to the proper treatment of this affection, but I will point out to you the lines along which I think observations should be made. These cases are, perhaps fortunately, few and far between, so that the number which any individual sees is not great. The last case I saw was a lunatic, and he absolutely refused to take any physic. His relatives were quite content to leave the matter to Nature.

In these cases the contraction of the left ventricle,

although very infrequent, is powerful and fairly regular; the systolic arterial blood pressure is high and the diastolic low. There may be two or three ineffective contractions of the right ventricle between the powerful systoles of the left. In these cases you should try to increase the irritability of the cardiac muscle, lessen the remainder-contraction of the ventricles, hasten ventricular diastole, and increase the intracardiac pressure. On this last account this is about the only cardiac affection where a liberal allowance of beer or stout does good. To hasten diastole and lessen the remainder-contraction, active potassium ions are necessary, while the sodium salts should be diminished. For the maintenance of efficient cardiac contraction, free calcium ions are essential, hence all agents which increase calcium metabolism do good, such as thyroid gland and iodine. I have found a combination of calcium iodide, potassium chloride, and tincture of iodine useful. Also phosphoric acid with the glycerophosphates of potassium and calcium.

In this connexion the work of George Ralph Mines⁹ is very interesting and instructive. He showed that "the chlorides, nitrates, and sulphates of lanthanum, cerium, and yttrium (unlike those of aluminium) form neutral aqueous solutions. Such solutions added to Ringer's solution made up without alkali will, when perfused through the frog's heart, stop it in diastole when the mixture contains only a hundred-thousandth or even a millionth gram molecule of the rare earth in a litre. The effect is very slowly removed by washing out with neutral Ringer's solution, but the beat is instantly restored by the addition of a little alkali". . . "The close parallel between the action of acids and of the salts of the rare earths on an artificial membrane and their actions on the living heart seems to have a special significance in view of the strong probability that the rhythmic activity of the heart depends on the relations which obtain between the ions within and without the cells."

My text covers a very large area, and I have occupied so much time with a small portion of the field that I am afraid in the remainder of my address I cannot give you much more than headlines; you must fill in the details. I do not wish you to get the idea that the maintenance of health and the treatment of disease consist only in the regulation of the lime salts, but this is merely the part of the subject with which we are at present dealing.

Diseases of the Lungs: Pneumonia—This is the disease in which I first began the systematic use of lime salts about twenty years ago. I had noticed that in the acute stage of pneumonia the more scanty and the more sticky the expectoration, the more viscous the blood, the more lime salts and leucocytes it contains, *ceteris paribus*, the more favourable the prognosis; on the other hand, the more fluid and haemorrhagic the expectoration, the more liquid the blood, the less the lime salts and leucocytes the worse the prognosis. Dr. Auld¹⁰ has also shown

that pneumonic consolidation is Nature's method of localizing the morbid process and curing the disease. . . . Moreover, in cases of pneumococcus infection showing little or no tendency to pulmonary hepatization—when the pneumococci run riot in the organism, so to speak—the result is always grave, and indeed generally fatal.

Asthma.—In the attacks there is an excess of free calcium ions in the blood, and in the treatment, both during and between the paroxysms, the intake of calcium in the diet should be strictly regulated. During the paroxysm not merely antispasmodics, but also decalcifying agents should be freely prescribed. A milk diet should be rigidly excluded.

Bronchitis and Emphysema.—In chronic throat cough, bronchitis, and emphysema alcohol and tobacco should be strictly interdicted. The individual should, as far as possible, live in a dry atmosphere and have a dry diet. There is not, as a rule, too much free lime in the blood, but in later stages there is too much fixed lime; you get rigid costal cartilages and a fixed chest wall. One writer thinks that a large rigid barrel-shaped chest is an advantage in emphysema, because it increases the size of the chest, and he thinks exercises a constant suction, thus assisting the heart. This idea is about as absurd as an individual hanging on to the handle of a pump and expecting the instrument to go on working. The practical person would keep moving the handle of the pump,

so I would advise you never to let your costal cartilages become rigid if you can help it, but if they do, increase their function by respiratory gymnastics, use decalcifying agents, and lessen the intake of lime.

Acute Infectious Diseases.—Recently Major W. D. Sutherland and Captain D. McCay¹¹ have shown the inhibitory influence exerted by hypertonic saline solutions and calcium chloride on the action of specific haemolysins, and in blackwater fever they recommend large intravenous or subcutaneous transfusions of a solution containing sodium chloride 12 grams and calcium chloride 0.25 gram to the litre of distilled water. In septicæmia, pyæmia, and infective endocarditis the lime salts do good. They are also useful in pernicious anaemia.

Acute Rheumatism.—In this disease there is an excess of free calcium ions in the blood, and a tendency to fibrin formation. The increase in calcium raises the blood pressure, and this increases the liability to heart mischief. The valves which are subjected to the greatest strain are those which are affected. In valvulitis and pericarditis decalcifying agents should be freely used. A milk diet always does harm, whereas plenty of red meat, which increases the ammonia in the tissues and thus neutralizes the sarcolactic acid, is beneficial. In gout there is more frequently an excess of lime in the tissues and urine than in the free state in the blood; a decalcifying agent like phosphoric acid is useful.

The Nervous System.—It seems to me that those lapsed cranks who constitute the Food Reform Association must have a good deal of lime in their brains, as their ideas seem as firmly fixed as if they were set in plaster-of-Paris. However, there are some of them who have got an axe to grind that are not such fools as they look. If you want to think quickly, speak quickly, and act quickly, you had better not have too much lime in your nervous tissue, but, on the other hand, for stability and tenacity a certain amount of lime is necessary. I sometimes think it might be worth while to have a typically slow, deliberate, solid Aberdonian chopped up to see how much granite is in his composition. Their salvation seems to rest in oatmeal and Scotch whisky, and thus the calcium is never allowed to reach the cement stage, so you never meet one who is stolid; even the ubiquitous and versatile Jew has no chance against an Aberdonian. Scotsmen, as a rule, do not sink with their gravity or rise with their levity.

Epilepsy.—All the soluble calcium salts do good in this disease, but their administration is not sufficient, you should also lessen the sodium salts, which increase excitability and conductivity of nerve; hence I allow epileptics very little table salt in their food. You should also avoid all decalcifying agents, such as acids, acid salts, and acid fruits, and you should correct any acid fermentation in the stomach. All kinds of milk foods are good. The magnesium salts have a somewhat similar effect to that of calcium, and they constitute the best purgative in this disease. If you wish to use a bromide, which is not always necessary or desirable, then the strontium bromide is the best. Of the calcium salts, I am inclined to think that the iodide is the most efficient in this disease, and it is effective in much smaller doses than any of the other lime salts.

Disseminated Sclerosis.—The lime salts are useful in this disease and the sodium salts injurious, and all acids should be avoided. However, I prefer the salts of zinc, especially the sulphate, with which I have had some excellent results. In this connexion I may mention that in England, to any one who has been in a railway accident, or who wants something out of the Workmen's Compensation Act, exaggerated knee-jerks are a valuable asset; it is often painful to listen to the exaggerated importance which is frequently attributed to this simple sign, which can be readily developed, and is not of much consequence when it is developed. If the knee-jerks are exaggerated in a person who is not taking strychnine, and is not suffering from any obvious nerve lesion, there is usually a deficiency of lime. When the knee-jerks are excessive, or there is other evidence of nerve irritability, you should not prescribe strychnine—a drug which is about as much abused in the present day as digitalis.

Locomotor Ataxia.—The lime salts in this disease are in excess. The treatment from which I have seen the best results has been phosphoric acid and strychnine, Fraenkel's exercises, and the avoidance of a milk diet

Some wonderful results—real or imaginary—have lately been ascribed to mercury, contrary to all former experience. It is supposed that the mercury destroys the *Spirochaeta pallida*, or their toxins, but I am inclined to agree with those who think that the spirochaetes and their toxins have disappeared long before the appearance of locomotor ataxia. Any good effect which the mercury may have must, therefore, depend on the influence of the metal on the nerve tissue, though I should scarcely expect any of the heavy metals to prove advantageous in this disease.

Neurasthenia and Hysteria.—These are protean or nondescript diseases, a refuge for the destitute. The lime salts are very variable, but, as a rule, deficient, and, at any rate, the metabolism is defective, hence when you wish to give a calcium salt it should be in an active form, such as the iodide, chloride, or glycerophosphate.

Migraine.—As a rule, the lime salts are in excess, and there is also some intestinal toxæmia. Cutting off the lime salts in the diet and giving a course of sulphate of magnesium in the mornings do good.

The Skin: Eczema, Urticaria, etc.—I believe nowadays dermatologists look upon the majority of cases of eczema as microbic in origin, but I think the irritation may come from within as well as from without, and that in many cases the germ lies in a deficiency of lime and in a dilated stomach. The old gouty eczema is not such a myth as some suppose it to be. In urticaria, enema and serum rashes there is a deficiency of lime in the blood.

Muscular System.—In myalgia, or the so-called muscular rheumatism, there is a deficiency of lime and an effusion into the muscular sheath. Any dilatation of the stomach or acid fermentation should be corrected. The diet should be fairly salt-free, contain no acids, and not much starch. I prefer a meat diet, and in place of milk the lime can be taken as medicine. There should be no sour milk given.

Tetany and Cramp.—Tetany, and cramp of the calf muscles which usually occurs at night, are often associated with dilatation of the stomach and acid fermentation; in both the lime salts are defective. The treatment is best conducted by attention to the intestinal tract.

Wounds.—Wounds of all kinds heal best when there is a fair amount of calcium in the tissues affected. On the other hand, you may have too much lime and more repair than is either necessary or desirable. Blair Bell has shown that there is a large amount of lime in all scar tissue. All the operations of the surgeons in Dupuytren's contraction have ignominiously failed, and as a rule only made matters worse. I have found an excess of lime in the blood in such cases, and lately I have been treating them—with what success remains to be seen—by increasing the function of the part affected and by using general decalcifying agents.

The Digestive Tract.—In the so-called congenital hypertrophic stenosis of infancy I believe the causal agent to be the excessive amount of lime in cow's milk setting up first spasm and then hypertrophy of the pyloric walls. If this be so the disease is not congenital, and the treatment is largely a question of diet. If there be no mother's milk and the cow's milk must be used, then it should be well diluted and contain a considerable quantity of citrate of sodium. Olive oil is useful as a nutrient and to relieve the spasm.

Lime is absorbed into the system through the intestinal mucous membrane, and this is also the most active agent in excreting it.

Professor Benjamin Moore¹² says:

It is now generally accepted that the neutral fats of the food are completely split up in the course of intestinal digestion, by the lipase of the pancreatic juice, into free fatty acids and glycerine, and that the fatty acids are then rendered soluble by the bile salts and lecithin, either in the form of free acids or as alkaline soaps. So that all the constituents formed in fat digestion are finally taken up by the columnar cells in soluble form.

He also holds that the absorbed fat is re-synthesized to neutral fat in the intestinal mucous membrane, and while

the detached cells of the pancreas, mucous membrane of the intestine, and mesenteric lymphatic glands have a powerful action in setting fatty acid free from soap, no synthesis of neutral fats has been obtained by the action of such cells or their extracts upon solutions containing soap and glycerine.

Dr. O. T. Williams,¹³ who has done some important work on fat digestion and assimilation, has shown that—

there are conditions in the intestines in which certain soaps or other insoluble compounds of fatty acids are not absorbed by the intestinal mucous membrane, and that with the presence of these conditions certain diseases of the alimentary tract are related. The analyses here given show that true intestinal sand, appendix concretions, and some bodies formed in the intestines are largely formed of fats and calcium soaps. The fats and soaps present are compounds of saturated fatty acids. The constitution of these bodies and their relation to each other in chemical constitution throw, in my opinion, much light upon the etiology of appendicitis and mucous colitis, and possibly upon the underlying factors in certain diseases accompanied by colic.

Dr. Williams¹⁴ has also shown that in countries such as Italy, Greece, and Spain, where large quantities of unsaturated fatty acids, such as olive oil, are taken, appendicitis is comparatively rare. My own experience corroborates the views of Dr. Williams. In my opinion, if people were more careful in their diet and kept their bowels freely open—thus preventing the *Bacillus coli* assuming a malignant type—appendicitis would be a rare disease. The more acid the contents of the colon, the less the putrefaction and the less the liability to appendicitis and colitis.

Some persons absorb lime very badly, and this is perhaps due to the form in which it is presented to the mucous membrane. The insoluble fats, stearin and palmitin, which constitute the greater part of beef and mutton fat, can be extracted from the faeces to the extent of 80 per cent. or more. When these fats are split up their acids readily combine with calcium, forming insoluble soaps which irritate the mucous membrane. On the other hand, cod-liver oil, olive oil, butter and bacon fat contain a large quantity of unsaturated fatty acids, which even with lime form soluble soaps. When, therefore, a person is on a milk diet, or for any reason taking lime, the fat which he takes should largely consist of olein. Butter is much better than margarine, because it contains more unsaturated fatty acid.

Colitis.—In some cases of obstinate constipation there is too much lime in the blood and in the intestinal wall; the same remark applies to the spasmodic form of colitis where there is very severe colicky pain, but where the mucous membrane is to a slight extent involved in the colitis there may be attacks of diarrhoea alternating with the constipation. In such cases there is also intestinal sand in the form of insoluble calcium soaps.

In mucous colitis the calcium index is frequently low, though not invariably so, owing to defective absorption of lime on account of the formation of insoluble calcium soaps, and owing to excessive excretion of lime. In such cases there is diarrhoea, but where there is a fair absorption of lime with a moderately high calcium index the diarrhoea may alternate with constipation. The colitis in dysentery, typhoid fever, tuberculosis, and summer diarrhoea is, of course, microbic in origin, but the forms with which we are here dealing are due to dietetic errors.

In the treatment of spasmodic or mucous colitis or muco-entero-colitis, milk, cheese, all milk foods, animal jellies, and hard water should be forbidden. The fats should be of the unsaturated type, and I usually order a wineglassful of olive oil at bedtime each night. If there be diarrhoea, the acid sulphate of sodium is an excellent drug, while if there be constipation the ordinary sulphate with the citrate of sodium answers better.

Cirrhosis.—In cirrhosis of the liver the calcium index is generally low owing to the catarrh of the stomach and intestines set up by the alcohol. The first part of the treatment is to stop the alcohol and cure the catarrh.

The Urinary Tract.—Dr. Mackarell, Professor B. Moore, and Professor Thelwall Thomas¹⁵ have recently shown that in a preponderating number of renal calculi—at least in Liverpool—there is a large amount of oxalate and phosphate of calcium. This is no more than might be expected anywhere, as healthy kidneys always excrete a certain proportion of lime, though not so much as is excreted by the bowel. The excretion is greatest when the blood is most alkaline; hence the excretion, even under ordinary diet, is greater during the day than it is at night, and on a milk diet the increase is often very marked. Blair Bell and Pantland Hick found the calcium index of the blood to fall gradually during the day, and I think this apparent periodicity is due to the increased excretion. When the kidneys are diseased the defective excretion often leads to retention in the system. The late Dr. J. H. Bryant and Dr. W. Hale White¹⁶ recorded a

unique case of calcification of the arteries, and obliterative endarteritis associated with congenital hydro-nephrosis, in a child aged 6 months. The right foot was gangrenous, and the changes in the anterior tibial artery extreme. The child was fed at the breast for the first two months, and on cow's milk for the last four. In chronic Bright's disease and in advanced granular kidneys the excretion of lime is very defective, and yet in these diseases milk is almost universally prescribed by the medical profession. In the albuminuria of adolescence or orthostatic albuminuria there is no defect in the excretion of lime, and in such cases milk is beneficial.

As a matter of ordinary routine in my examination of the urine I always precipitate the lime. This helps me to estimate not merely the activity of the kidneys, but also the calcium content of the blood. If there be no excess in the blood there is not likely to be any excess in the urine, but in all these examinations the condition of the kidneys and the specific gravity of the urine must be taken into account—in *urina potius* you do not expect to find much lime or anything else.

In conclusion, ladies and gentlemen, I must thank you for a very patient hearing. I feel that the address has been very long, but I could have made it much longer without exhausting the subject. However, I think I have said enough to show you that I attach considerable importance to the lime salts in health and disease.

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A SIMPLE CURATIVE TREATMENT OF CHOLERA.

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THOSE who have had to deal with cholera cases in the tropics must often have felt great disappointment at the absence of any material improvement in the treatment of the disease as a direct result of Koch's discovery of the causative organism. The lack of power to check the copious evacuations and prevent the onset of collapse in the acute stage, and the no less helplessness in the presence of later continued suppression of the functions of the kidney, with slow but sure uraemic poisoning, make cholera a terrible disease to contend with. Feeling convinced that a careful study of the changes in the blood would yield valuable indications for its treatment, I have carried out a long series of researches on these lines,¹ especially during the past three years. The first result was the reduction of the death-rate to barely one-half by the use of hypertonic saline intravenous injections in the collapse stage, and blood-pressure-raising measures as a preventive of later uraemia. These have already been published elsewhere,² so they will only be summarized here as a preliminary to an account of a more directly curative treatment, which has yielded still more remarkable results during the last twelve months.

THE BLOOD CHANGES AS AN INDICATION FOR THE USE OF HYPERTONIC SALINE INJECTIONS.

I first studied the loss of fluid from the blood and the degree of its concentration by measuring the volume of corpuscles and serum respectively by means of the haemocrite. Table I gives the results, which show that in the mildest cases, not requiring transfusion, an average of one-third of the fluid had been lost from the blood; in severe cases recovering after hypertonic injections, one-half of the fluid had been lost; while in the most severe fatal cases no less than two-thirds of the fluid of the blood had escaped. There was thus a very definite relationship between the amount of fluid lost and the severity of the case, although the rapidity of the loss is doubtless also a factor of great importance, as pointed out by Wall. These

observations clearly indicate the necessity of replacing the lost fluid in the collapse stage of cholera.

TABLE I.—Blood Changes and the Effects of Hypertonic Saline Injections in Cholera.

	Normal.	Average of 7 Fatal Cases.	Average of 12 Cases Recovering after Transfusion.	Average of 5 Mild Cases not Transfused.
Percentage of corpuscles	45	71	63	56
Percentage of serum...	55	29	37	44
Loss of serum...	—	64 per cent.	52 per cent.	35 per cent.
Pints of saline injected	—	3.7	3.6	—
Serum after injection	6	61 per cent.	61 per cent.	—
Blood pressure before injection	110	0.50 mm.	51 mm.	71 mm.
Blood pressure after injection	—	97	107	—
Chlorides before injection	0.8	0.79	0.90	0.92
Chlorides after injection	—	0.95	1.07	—

Of equal importance is the discovery that in cholera, in addition to the loss of fluid from the blood, there is also a great loss of the salts. Thus, instead of the percentage of chlorides becoming increased with the concentration of the blood, it remains comparatively low, and may even be below normal in the worst cases, the loss of salts being in some degree in proportion to the severity of the case, as shown in Table I. This change accounts for the comparative failure of injections of normal salines in cholera collapse, and furnishes an additional reason for the use of hypertonic solutions in order to replace the chlorides, as well as the fluid, lost from the blood in cholera. Raising the salts in the blood appears to check to some extent further loss of fluid from the blood, and so hypertonic injections are not often rapidly followed by an increase of the watery stools, as is so usually the case after normal salines, with rapid recurrence of collapse.

The results of this treatment during two years at the Calcutta Medical College Hospital, compared with the records of the same hospital during eleven years before the revival of intravenous injections by me, are shown in Table II.

TABLE II.—Results of Different Forms of Treatment of Cholera.

Period.	Treatment.	Cases.	Deaths.	Percentage.	
				Deaths.	Recoveries.
1895-1905 ...	Rectal and subcutaneous salines	1,243	783	59.0	41.0
1906 ...	Normal salines intravenously	112	57	51.9	49.1
1907 ...	Rectal and subcutaneous salines	153	94	59.5	40.5
1908-1909 ...	Hypertonic intravenous salines	294	96	32.6	67.4
Aug., 1909, to July, 1910	Hypertonic plus permanganates	103	24	23.3	76.7

During the eleven earlier years the death-rate was 59 per cent. In 1906, when normal salines were used intravenously by Captain Megaw, I.M.S., and myself, it fell slightly to 51 per cent., but on their being given up once more in 1907 as of little use, it rose again to 59.5 per cent. The hypertonic solutions were commenced early in 1908, and during two years' observations the mortality among 294 cases was only 32.6 per cent., or but little more than one-half the previous rate, thus affording most conclusive evidence of the great life-saving value of the new method.

The technique of the injections has been fully described by me in the *Indian Medical Gazette* of November, 1909,³ including a simple method of regulating the rate of flow, so only the following points need be mentioned here: The hypertonic solution consists of 120 grains of sodium chloride, 6 grains of potassium chloride, and 4 grains of calcium chloride to one pint of sterile water, so as to approximate in its composition to Ringer's fluid. Both Burroughs and Wellcome and Parke, Davis and Co. stock soluble tablets of this formula, such that four to a pint make my hypertonic solution (1.35 per cent.), while three in the same amount of water (0.95 per cent.) is suitable for rectal