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

injections. Down Brothers make my stopcock cannula and graduated transfusion bulb for regulating the rate of the flow into the vein. In marked collapse in an adult male with little or no pulse at the wrist, three or four pints should be given intravenously at the rate of not more than 4 oz. per minute, being slowed at once to 1 oz. per minute if any distress or severe headache is caused. The specific gravity of the blood is a valuable guide, as, if it is raised to 1062 or over, the above quantities may safely be given. If it is not above normal the collapse is probably not due to cholera, and such copious intravenous injections may be dangerous by producing oedema of the lung. A patient admitted to my ward as cholera, with marked collapse and epigastric pain, was found to have a blood specific gravity of only 1048, so was not transfused, although obviously dying. *Post-mortem* haemopericardium from perforation of the aorta was found, in which condition transfusion would have only hastened her death.

If collapse recurs after a hypertonic injection for cholera the same strength should be repeated. A marked rise of temperature follows these injections, which occasionally goes on to hyperpyrexia. I have found that this grave complication occurs most commonly in patients whose rectal temperature is above normal on admission, even if the surface of the body is cold. In such cases the fluid should be given at only just blood heat, or, better, a little below. In a recent case of cholera with complete loss of pulse, an axillary temperature of 101° and a rectal one of 105°, an intravenous injection was given at a temperature of only 86° F., and with external applications of cold the hyperpyrexia was controlled, the circulation restored, and the patient safely tided over the collapse and reaction stages, recovering completely.

THE PREVENTION OF POST CHOLERAIC URAEMIA BY MAINTAINING A HIGH BLOOD PRESSURE.

Another very important fact brought out by my researches is the close relationship between continued deficient blood pressure and fatal post-choleraic uraemia. Daily observations on a large number of cases have shown that every adult whose blood pressure remained continuously below 95 mm. died of uraemia, while if it is raised to over 105 mm. urine is almost invariably freely secreted. Moreover, in fatal uraemia *post-mortem* saline perfusions through the renal circulation revealed very evident obstruction to the flow through the organ, due to the great congestion and haemorrhages into the organ, which was clearly the cause of the suppression of urine. Daily manometer observations have enabled the danger of uraemia to be foreseen, and by using all means to raise the blood pressure to the necessary height I have been able to reduce the proportion of deaths from uraemia to the total admissions to one-half of the former rate, and that, too, in spite of having tided so many severe cases over the collapse stage by hypertonic transfusions, to face the dangers of continued suppression of urine. In fact, I regard this discovery as only second in importance to the value of the strong salt solutions. The measures used include rectal, subcutaneous, and occasionally slow intravenous injections of normal salt solution (0.95 per cent.), cardiac tonics, such as digitalin and strophanthin (the latter intravenously), and the vaso-constrictors, adrenalin and pituitary extract.

By the above means the circulation is usually rapidly restored to such a degree as to lead to the free excretion of the toxins through the kidneys, which is far safer and more satisfactory than Johnston's attempt to eliminate them by purgative treatment. Although by these various measures the mortality of cholera has been reduced by nearly one-half, yet even this system of treatment frequently fails in the most severe and late cases, and especially in immigrant Europeans, whose attacks are more serious than those of native inhabitants of the endemic areas of Lower Bengal. If collapse recurs after a hypertonic injection, repetitions also often fail to save the patient. In some very severe cases the restoration of the circulation by salines is followed by absorption of a lethal dose of toxins from the bowel with high fever, which, in my experience, is always fatal if unconsciousness ensues. Yet to neglect transfusion in these cases is only to allow the patient to die of collapse. I therefore became convinced that any further reduction in the mortality could only result from some more directly curative means, while the power to greatly prolong life, even in very serious cases of cholera, by the hypertonic

injections led me to hope for further progress in such a direction.

THE DESTRUCTION OF TOXINS IN THE BOWEL AS A CURATIVE TREATMENT OF CHOLERA.

Since the discovery of the comma bacillus, innumerable intestinal antiseptics have been used in the treatment of cholera with a view to destroying the causative organism in the bowel. The simple fact that none of these have come into general use, taken with the sustained mortality of the disease for many years past (the death-rate of cholera in the British army in India, for example, having during recent years been nearly 80 per cent.), is sufficient evidence that such antiseptics have no specific action against the disease. Their failure may best be explained in the following manner. We know that the comma bacilli are practically limited to the interior of the bowel, and only penetrate slightly into the mucous membrane. The symptoms of the disease are therefore largely due to the absorption of the specific toxins from the intestinal contents. Now these toxins are mainly, if not entirely, intracellular in nature, and are only set free from the bodies of the bacilli after their death and disintegration in the alkaline bowel fluids, for the rice-water stools of cholera are distinctly alkaline. This being the case, it is easy to conceive that the extensive destruction of comma bacilli in the bowel by intestinal antiseptics may actually result in the more rapid absorption of the deadly intracellular toxins, and so aggravate instead of curing the disease. In this connexion it is worth recalling the observations of Gotschlich and Weitgang that in agar cultures of forty-eight hours' incubation only 7.43 per cent., and after sixty-eight hours only 0.8 per cent., of the cholera spirilla present at the end of the first twenty-four hours were still alive. This tendency of the organisms to quickly reach their maximum numbers, and then as quickly die out and liberate their endotoxins, best explains the short but sharp nature of an attack of cholera, as pointed out by Strong. It at once becomes clear, from these considerations, that an effectual cure of cholera—apart from any specific anticholeraic serum—is most likely to result from some simple method of destroying or rendering harmless the toxins within the bowel itself, thus preventing their absorption in fatal doses. I therefore set to work to find such an agent of a non-poisonous nature.

THE ACTION OF OXIDIZING AGENTS IN RENDERING BACTERIAL TOXINS INNOCUOUS.

A consideration of the close affinities in their chemical nature and physiological actions between bacterial toxins and snake venoms led me to test the effects of oxidizing agents on the former. The remarkable power of permanganates in destroying the toxicity of snake venoms was shown by Lacerda as long ago as 1881, and confirmed by Brunton and Fayer soon after. In 1903 I tested the action of potassium permanganate on a number of Indian, African, and American venoms, and found a small quantity of this drug was equally effective against each of them, since which many lives have been saved by the local use of this remedy by means of Sir Lauder Brunton's snake lancet. I have recently carried out a number of experiments which demonstrate an equally remarkable action of permanganates in rendering harmless certain bacterial toxins. Those relating to cholera toxins may be briefly referred to here.

Although dead cholera bacilli containing the intracellular toxins are not fatal to pigeons when injected subcutaneously, I have found that a quarter of a culture tube injected intravenously kills these animals in from twelve to eighteen hours. Yet I have been able to inject three-times that amount, previously mixed for half an hour or less at blood heat with 3 mg. of calcium permanganate, without death resulting, although some immediate dyspnoea may result from the effect of the precipitate formed in the mixture. The toxin thus appears to have been destroyed by the oxidizing agent. I have not been able to use larger doses, as 5 mg. of the permanganate salt intravenously caused rapid death of pigeons with convulsions. I was also unable to test the action of the toxins given intraperitoneally in guinea-pigs, as unfortunately the salt here also proved to be poisonous, while of course they cannot be given intravenously with safety in sufficient amounts to be of therapeutical value in larger animals or in man.

ADMINISTRATION AND DOSES OF PERMANGANATES.

Although in cholera the bowels are so completely cleared out of their normal contents, and the watery stools contain very little albuminous matter, still, it is not to be expected that the usual small doses of 2 to 3 grains at long intervals, as given in amenorrhoea, could exert much influence in destroying toxins in the small intestine. On coming into contact with unstable animal albumens the oxygen is set free in a nascent form and manganese dioxide precipitated, which appears to be largely inert in the bowel. I have already given up to 50 grains within a day or two, without the slightest indication of any harm having resulted from it, and intend to push it still further in bad cases in the future.

The permanganates are given in two different ways. First, in solution, to drink *ad libitum* in the place of water. Beginning with $\frac{1}{2}$ to 1 grain to the pint, on account of the unpleasant astringent taste, the strength is rapidly increased up to 4 to 6 grains in 1 pint, or even stronger if the patient will swallow it. Fortunately, in severe cases the thirst is so great that no difficulty is usually experienced in pushing the drug in this way. Vomiting may occur, but does no harm. On the contrary, it probably helps to remove some toxin. I have even known obstinate vomiting in cholera relieved by the permanganate drinks, doubtless by destroying some irritant substances in the stomach. Calcium permanganate is the best salt for this purpose, being somewhat less astringent than the potassium one, while as it is divalent it will exert a greater oxidizing action. The calcium element may also possibly lessen the effusion through the bowel wall. The other method of administration is in pill form, for which purpose the potassium salt is more easily dispensed on account of the very hygroscopic properties of the calcium and sodium compounds. The simplest method is to mix two grains of potassium permanganate with a little kaolin powder and vaseline, and make as small a pill as possible. It is then coated with salol one part, in sandarach varnish five parts, or with keratin so as to only dissolve on reaching the alkaline small intestine, where its action is wanted. It is important to see that the pills readily dissolve as they sometimes become hard and inefficient after being kept some time, and may then pass through the bowel unchanged. Two leading firms are investigating the best way of putting up the permanganates at my suggestion, so a thoroughly efficient preparation is sure to be available very shortly. I now give one pill every quarter of an hour for the first two hours, and then every half-hour until the stools become coloured green and less copious, which usually occurs in about twelve hours. In mild cases they need only be given during alternate four-hourly periods. Barley water may also be administered to maintain the strength, as it is not readily acted on by the permanganates. At the beginning of the second day eight more pills are given, and in severe cases this is repeated on the third day in order to avoid relapses which have occurred in three cases. They all promptly yielded to a renewal of the permanganate treatment, thus furnishing an additional reason for believing its action to be directly curative.

RESULTS OF THE PERMANGANATE TREATMENT.

The internal administration of permanganates in cholera for the purpose of destroying the specific toxins within the alimentary tract was commenced in August, 1909. By the end of the year 17 cases, including 10 severe attacks requiring transfusion, had been treated, with only 1 death. The mortality at that season, however, is usually lower than in the first quarter of the year, when I felt sure such a phenomenal recovery-rate could not possibly be maintained. I therefore contented myself with mentioning the new treatment in a lecture to the Calcutta Medical Club in December, 1910,⁶ and determined to pursue it for a complete year before fully analysing the results obtained, which are as follows:

In the first quarter of 1910 several very severe cases were lost, but the mortality was still 15 per cent. below that of the same period of the previous year. During this time the proper dosage and best methods of administration were being worked out, and the knowledge so gained may bear further fruit in the future. The mortality for a complete year from August, 1909, to July, 1910, inclusive, has been 23.3 per cent. among 103 cases, against 34.7 per cent. in the first complete year of hypertonic transfusions

alone, and 59 per cent. in the eleven years before the revival of transfusion. Thus, the mortality, which had been reduced by nearly one half by the hypertonic saline injections, has now been reduced by the addition of the permanganate treatment to but little more than one-third of the old rate. This further great gain is particularly satisfactory, as it can only be due to saving very severe and previously hopeless cases. It is still possible that slight further improvement may result from pushing the treatment, which necessarily had to be used with considerable caution at first. That the drug is not very toxic in nature will be clear from the following case, which was under the care of Captain J. W. D. Megaw, I.M.S., at the European Hospital: A young adult male swallowed half an ounce of solid potassium permanganate crystals in an attempt to commit suicide. When he came under observation, it was already too late to wash any of the salt out of the stomach, yet he made an excellent recovery after only a fairly acute pharyngitis and a very mild gastritis.

Before accepting the reduced mortality of the last twelve months as due to the new line of treatment adopted, it is necessary to be certain that the cases dealt with were not milder than usual. That they were undoubted cholera is beyond question, for, in the first place, the typical symptoms of the disease were present, all clinically doubtful cases having been excluded. Secondly, the diagnosis has been confirmed bacteriologically in almost every case by finding large numbers of comma bacilli in the stools, while in many they were also isolated and found to give the serum reactions in high dilutions, commonly as high as 1 in 10,000. Regarding the severity of the disease, we fortunately have an admirable control in the figures of the neighbouring Campbell Hospital, which for a number of years previously to the use of transfusion ran closely parallel with those of the Medical College. Until the last three months my methods have not been used there, and the mortality in the first quarter of this year was no less than 71 per cent., the disease having thus been of at least average, or somewhat over average, severity. From May to July, however, hypertonic transfusions and very weak permanganate drinks have been regularly used at the Campbell Hospital, and the mortality has fallen to 34 per cent., against 64 per cent. in the same months of the previous year, the assistant surgeons in charge attributing the great improvement to these measures.

A new cholera ward at the Medical College Hospital was opened in April, 1909, and was placed under my care, thanks to the kindness of Surgeon-General C. P. Lukis, I.M.S. The blood pressure has been taken in every case on admission, and, as a rule, transfusion has only been performed if it has fallen to below 70 mm., which means a very feeble or no pulse at the wrist. All the other conditions have been the same, except the addition of the permanganate treatment in August, 1909, while 9 cases were treated with another similar oxidizing agent, namely, sodium peroxide. The latter drug was found, however, to be more irritating and less convenient for making into pills than permanganates. Experience has shown that the mortality among cases not requiring transfusion is very small and due to complications. The proportion of admissions requiring transfusion will, therefore, furnish the most reliable test of the severity of any series of cases, and the percentage of recoveries among those patients showing such serious collapse as to necessitate intravenous saline injections will give the clearest indication of the life-saving effect of any given treatment, for very few such cases recovered in Calcutta before the introduction of hypertonic transfusions by the writer in 1908. Tested in this way I find in the first place that during the last twelve months intravenous injections have been required in no less than 67 per cent. of the admissions, which is a larger proportion than at any previous period. The proportion of severe cases during the last year has, therefore, been actually higher than usual, so that the reduced mortality under the permanganate treatment is all the more striking.

We may next consider the mortality among the severe transfusion cases. During a year and a half of hypertonic injections without permanganates, the death-rate among 170 transfusion cases was 47 per cent., leaving 53 per cent. of recoveries. In the first year the precise blood pressure and other indications for transfusion were being worked

out, and a larger number of moderately severe cases were given intravenous salines than at later periods, cholera having been also somewhat milder in Calcutta in 1908 than usual. A fairer comparison would be obtained by taking the results in the new ward before and after the addition of permanganates under otherwise identical conditions. From April to July, 1909 (a season when the mortality is somewhat below the yearly average), 28 cases were transfused, with 46.4 per cent. of recoveries. Against this we have, during the last twelve months of permanganate treatment, 69 transfusions with 68.1 per cent. of recoveries, leaving only 31.9 per cent. of deaths in these serious cases. Such a result in the collapse stage of cholera, with a blood-pressure below 70 mm., speaks volumes for the new method.

An even more severe test may be obtained by considering the extremely severe cases requiring more than one transfusion, which is only exceptionally necessary with hypertonic solutions. Before the addition of permanganates, only 38 per cent. out of 50 such cases recovered. Since the toxin-destroying drug has been added, 15 out of 24, or 62.5 per cent. have been repeatedly saved from impending death.

EFFECT OF THE PERMANGANATE TREATMENT IN DIFFERENT PERIODS OF THE DISEASE.

If my contention that the permanganates actually destroy some of the cholera toxins in the bowel is correct, then it should have most effect in those cases which come early under treatment. In testing this it is necessary to bear in mind that there is a marked variation in the mortality of the disease in relation to the time which has elapsed after the onset of the symptoms before admission to hospital. As some of the older Anglo-Indian writers have pointed out, and contrary to what at first sight might be expected, the mortality of cholera is highest among those coming under observation within the first twelve hours of the onset of the disease, and considerably lower among later admissions. It may rise again among patients coming after more than forty-eight hours, as these latter are commonly brought on account of the occurrence of the deadly uraemic complication. The simple explanation of these facts is that the more virulent the disease, the more rapidly collapse requiring removal to hospital will set in. Table III illustrates this point, the first line giving the results of cases treated by hypertonics alone, and the second similar figures for the last twelve months under permanganate treatment.

TABLE III.—Relation of Period of Admission to Death-rate in Cholera.

Hours after Onset.	Up to 12 Hours.			12 to 48 Hours.		
	Cases.	Deaths.	Per-centage.	Cases.	Deaths.	Per-centage.
Hypertonic only ...	74	33	44.6	94	19	20.6
Hypertonic with permanganates	46	9	19.6	36	8	22.2

These figures are very striking, and show that the further reduction in the death-rate by the administration of permanganates is essentially due to their favourable action in the severe rapidly developing class of cases coming early under treatment—that is, just those whom early destruction of the toxins in the bowel might be expected to most benefit. In cases in which the disease develops slowly there is more time for the formation of antitoxins in the system as a result of the continued absorption of less overwhelming quantities of the poison. In these the hypertonic salines alone may raise and maintain the blood pressure sufficiently high to allow of rapid elimination to the toxins through the kidneys, thus preventing the accumulation of a fatal dose in the blood.

Again, if the toxins are really rendered harmless to any marked extent in the bowel, then a smaller number of patients admitted with a blood pressure over 70 mm. should subsequently collapse and require transfusion after they have been some hours under treatment in hospital. An analysis of my cases from this point of view shows with the hypertonic injections alone 21.5 per cent. of the transfusions were required for failure of the blood pressure some time after admission; while since the permanganates

treatment was added only 12.8 per cent. of such cases have occurred, or but little over half as many. Moreover, in nearly all these the collapse came on within four hours of admission—that is, before the permanganates had time to fully act.

PROPORTION OF DEATHS AT DIFFERENT PERIOD STAGES OF THE DISEASE.

Among the 103 cases the 24 deaths were distributed as follows:

Collapse, 11; reaction with fever, 4; late uraemia, 7; other complications, 2; total, 24.

These figures may be compared with the deaths among 136 cases during 1907, before I introduced the use of hypertonic salines. The percentages then were:

Collapse and reaction stages, 46.3 per cent.; uraemia, 13.2 per cent.; total, 59.5 per cent.

The notes in 1907 were not sufficiently detailed to allow of a separate estimation of the deaths in the collapse and reaction stages, but it will be seen the combined figures are just over three times as high as those of the last twelve months, while the deaths to admissions from uraemia were twice as many. The present death-rate from uraemia of 6.8 per cent. is nearly as low as is likely to be reached, for 5 per cent. of all *post-mortem* subjects in Calcutta show some degree of organic disease of the kidneys, which would leave little or no chance of recovery from a severe attack of cholera. Three of the 7 fatal uraemic cases were in opium eaters—a significant fact. The reduction of the death-rate in the collapse and reaction stages to only 15 per cent. in the last year is very noteworthy, especially if we take into account the condition of admission of the fatal cases. Thus of the total twenty-four fatalities no less than eleven of the patients were admitted with absolutely no pulse to be felt at the wrist, so that the blood pressure could not even be estimated, and in three more it was less than 50 mm., the pulse only just being perceptible. Even such cases, however, are very far from being hopeless, for out of 36 pulseless cases in the last twelve months, no less than 21, or 58 per cent., were saved. Three of the fatal cases were of the very virulent haemorrhagic type and 2 had severe abdominal pain, which is a very bad prognostic sign. Still, I believe that with my present experience several more cases might have been saved, and I am hopeful that another year even 80 per cent. of the Calcutta Medical College cholera patients may possibly be saved.

Clinically the good effects are equally marked, and were particularly striking in several very severe cases, requiring two transfusions within a few hours. Formerly, in the rare occurrence of recovery in such patients, they remained in a critical condition, with marked toxæmic symptoms, for several days. With the permanganate treatment I have repeatedly been astonished to find such patients practically convalescent within twenty-four hours, and showing very little signs of the terrible ordeal through which they had passed. In ordinarily severe transfusion cases the copious rice-water stools become changed to small green evacuations in twelve to twenty-four hours of admission in collapse, in a manner formerly rarely observed. The number of comma bacilli in the stools becomes greatly reduced at the same time. Thus, everything points to permanganates having a definite specific curative action in cholera, and I have no hesitation in recommending its adoption as a routine method of treatment, in combination with hypertonic salines when necessary, as superior to any other therapeutical measure yet subjected to a prolonged and critical trial.

At the same time, I am very far from claiming the new treatment as an infallible remedy for cholera. On the contrary, the more I see of this terrible disease, the more fully I realize the impossibility of saving certain very virulent types, especially if brought late when a fatal dose of toxin has been absorbed. In the future, intravenous injections of a powerful anticholeraic serum may be available for their treatment, while I am about to try oxygen inhalations in the hope of destroying some of the toxins in the blood. Further improvement is most likely to result from these measures and from giving the permanganates in still larger doses than I have yet ventured to use. In trying my methods it should also be borne in mind that the mortality at the beginning of an epidemic is very much higher than at the end, or it may at once be con-

demned on account of its apparent failure in the early hopelessly severe cases, although, if persevered with, it can scarcely fail to reduce the total mortality in a parallel manner to the Calcutta results. Due allowance should also be made for the greater mortality in epidemics than among sporadic cases in an endemic area, such as Calcutta. Of course the permanganates alone will be of little or no use without the addition of hypertonic intravenous salines in those patients who come under observation in a state of marked or complete collapse.

In conclusion, I would point out that the clearest idea of the real life-saving effect of the new methods can be conveyed by the following consideration of the foregoing data. Since the new cholera ward has been open, and an assistant surgeon and a nurse have been available day and night (to whom I owe my best thanks for their ungrudging labours under trying conditions, to which so much of the success of my treatment is due), only 2 per cent. of the admissions have died without being transfused, including a young child in whom a large enough vein could not be found. During nearly three years' experience, 63 per cent. of the admissions have required intravenous injections. This leaves 37 per cent. of mild cases not passing into the collapse stage, 35 of whom might be expected to recover in any case. Now, in the eleven years preceding my investigations, during which intravenous salines were very rarely given, the total recovery-rate was 41 per cent. If cases not showing collapse were in the same proportion as latterly, then 35 of the 41 per cent. of recoveries must have been mild cases, leaving only 6 of the 63 per cent. of collapse cases who were saved, or just under 10 per cent. If we compare this figure with the recovery-rate of 68 per cent. in transfusion cases during the last twelve months, we obtain a seven-fold increase of the cures among severe and formerly nearly always fatal attacks of cholera. Such a result, obtained by a system of treatment based on a close investigation during several years by modern scientific methods of the blood and circulatory changes in cholera, is very gratifying, and should encourage the provision of greater facilities for research work in connexion with large hospitals in the tropics.

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NOTES ON CHOLERA.

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CHOLERA reigns again in Russia. It has appeared in a sporadic form in several spots in Turkey, and cases have been reported from the northern provinces of Persia, especially Ardabile. Before long, many of the readers of the BRITISH MEDICAL JOURNAL may have the misfortune to face the disease for the first time in the East. I have, therefore, thought it useful to publish a few notes. I remember the cholera epidemic of Ispahan in 1869. I studied the disease in the cholera ward of the medical hospital of Bengal under the late Drs. Smith and S. Partridge during the years 1878-9 and 1880. I had much to do with the terrible epidemics of 1892 and 1903 in Teheran. Personally, and indirectly through my former pupils, I had perhaps more to do in the fight against it than any of my colleagues. My full notes, statistics, etc., are in Teheran; I cannot avail myself of their assistance. I shall mention only such points as have appeared to me new or suggestive.

Cholera is not one disease, since a series of many conditions differing very widely in their clinical features, and demanding different lines of treatment, are grouped under the name of cholera. The disease I saw in Calcutta was so mild as to look contemptibly ridiculous when placed side by side with the Persian form of it. The epidemic of 1892 was different from the epidemic of 1903; the last was dangerous mostly on account of the uraemic symptoms it produced early in the attack, rendering all preparations of opium, so useful in the epidemic of 1892, dangerous agents in the cholera of 1903.

It is impossible to determine the period of the occurrence of the first cases of cholera in a large city. Teheran was

officially declared cholera-stricken at the end of June in 1892, but I have notes of mysterious cases of much earlier date. An old lady died about the end of May, 1892, after a short attack of vomiting, constipation, and uraemia. Later on during the cholera I saw many similar cases, and no doubt was left on my mind that this old lady died of cholera with unusual symptoms long before cholera was officially pronounced as existing in Teheran. The two epidemics I have watched in Teheran have generally run a course like this: The earlier cases were mild; most of them recovered by taking a few doses of salol, benzonaphthol, naphthol-β, salicylate or nitrate of bismuth, etc. I am sure any mild intelligent course of treatment would cure 80, 90, 95 per cent. of these cases; gradually the type of disease changed, severer forms became more frequent, until we reached a period of several days when nearly every one attacked by cholera was carried off rapidly. In 1892 this period lasted a week, in 1903 it was three days. Then the type of disease changed, without a diminution in the number of cases attacked; recoveries were seen, they became more frequent, and lastly, most of the cases recovered. In the same epidemic we can watch side by side widely different types of cholera. In 1892 Ekbalah Saltaneh left Teheran during the epidemic with a host of his followers, and took refuge at Davoudieh, a garden of ten minutes' drive from the British village of Gulhak. I passed two nights among the cases at Davoudieh. Some brought a mild form of cholera from the town, and many who took cholera (I suppose from them) in Davoudieh had this mild form. But a niece of the gentleman took severe cholera in Tadjrishe, was carried to this garden, she became pulseless and black and died rapidly. Her father and a woman who nursed her, living, eating, and drinking, Persian fashion, freely with the patient, took cholera from her, became rapidly pulseless, livid, and died within ten to twelve hours of the attack. In all, 26 people took cholera in this camp, and only these three of Tadjrishe source were so severe, most of the other type of cholera running side by side with this recovered. The importance of drinking water was brought out again and again. In the epidemic of 1892 I published a brochure in Persian, wherein I stated the evidence of the propagation of cholera through water, and insisted on the boiling of drinking water. The Persians first laughed at this; Persian colleagues and priests on purpose had cholera subjects washed in running drinking water to disprove European theories. Some of the older school of European colleagues thought it wise to keep a close tongue. But facts are hard things. Persians saw how, on placing the springs of two dirty, wall-closed Armenian villages under strict control, we absolutely controlled the epidemic; only a few imported cases were seen in these villages, Dahrousse and Vanak. Meanwhile cholera was rife in the neighbouring royal camp and in all the Persian villages round under Persian, English, and Russian control. None could control the water so absolutely as the Armenian communities, because they had to deal with a different population. The Armenians were ready to take suggestions from Europe, willing to accept and act upon advice coming from us; the Persians opposed our ideas on the mere ground that they came from Europe. But gradually they saw hard facts; they then found that in their several writings and traditions it was stated that cholera spreads by drinking water. Appropriate sound texts were found or quoted, and in 1903 very few intelligent Persians took cholera. Every family of any note adopted the rule of using only boiled water for drinking, and although the type of disease in 1903 was very fatal, its total ravages were much less than in 1892, because many people had found out the secret of protecting themselves from it.

Cholera finds favourable conditions for its propagation in Oriental promiscuous living. In 1892, early one morning, Sapahdar, then one of the Bakhtiari chiefs, passed through the Russian village of Zerghendeh to tell me to call on his family in Teheran. He had abandoned them and was moving to the mountains in the north. I arrived at his residence about 11 a.m., found twenty to thirty women and children grouped in one hall over their breakfast spread on the ground. Some were eating, others howling with cramps, others vomiting, all forms of intestinal and gastric filth spread on the same carpet from which this host fed most philosophically. No doubt visitors were received all day in the same hall, invited to