AN EPIDEMIC OF CHOLERA

Treated by

INTRAVENOUS SALINE INFUSION

G. DUNCAN WHYTE, M.B. (Edin.)
D.T.M. & H. (Cantab.)

C O N T E N T S.

AN EPIDEMIC OF CHOLERA

Treated by

INTRAVENOUS SALINE INFUSION

"Hippocrates, Celsus, Aretaeus, Caelius, Aurelianus and other Greek and Roman physicians are reported to have seen and described cholera; all the Arabian writers on medicine mention the disease"[1] and even in China the symptoms of cholera were recognised in those far away times as is shown by the following quotation from a Chinese contemporary of Hippocrates:- "The Ho-luan (Cholera) is a sudden attack of pain in the heart and abdomen with vomiting and purging, a dread of cold and a desire for warmth.....when the pain attacks the heart first vomiting comes on first, when the pain commences in the abdomen the purging precedes; when the disease is severe the patient has spasms, and when these enter the abdomen death ensues."[2].

The first invasion of China by cholera of which we have a reliable report was during the course of the pandemic 1817-1826; and Dr. Hirsch suggests that the above description may have referred to a disease that was not true cholera. As, however, scarcely a year passes without some

part of China being attacked by cholera, one is reluctant to believe that the disease had not made its appearance there before the first great pandemic, and, as the term "Ho-luan" is used in China to-day exclusively to denote epidemic cholera, it seems quite likely that the Chinese writer was indeed describing a true case of cholera.

During the last fifty years authoritative accounts have been published of cholera epidemics in the following treaty-ports:- viz, Shanghai (1863[3] and 1897[4]) Amoy[5] (1877-78) and Hankow[6] (1882), as well as the adjoining territory of Macao[7] (1862) and the Island of Formosa[8] (1884-5). Since cholera has occurred so frequently in China in epidemic form one naturally asks 'What is the explanation of these frequent epidemics?' 'How does the disease so quickly assume epidemic form?' and the answer must be - so far as the South of China is concerned - that both the physical configuration of the country and the habits of the people assist in the spread of the disease. Much of what is hereafter stated of the port of Swatow can be applied mutatis mutandis to most seaport towns in the South of China.

The adjoining Map (Map I) shows that the town of Swatow (in which the epidemic took place) is situated in the South of China in the eastern part

MAP I.


CHINA & JAPAN
WITH
COREA
YELLOW SEA
EAST CHINA SEA
SOUTH CHINA SEA
SEA OF JAPAN
SEA OF OKHOTSK
BAY OF BENGAL
PACIFIC OCEAN

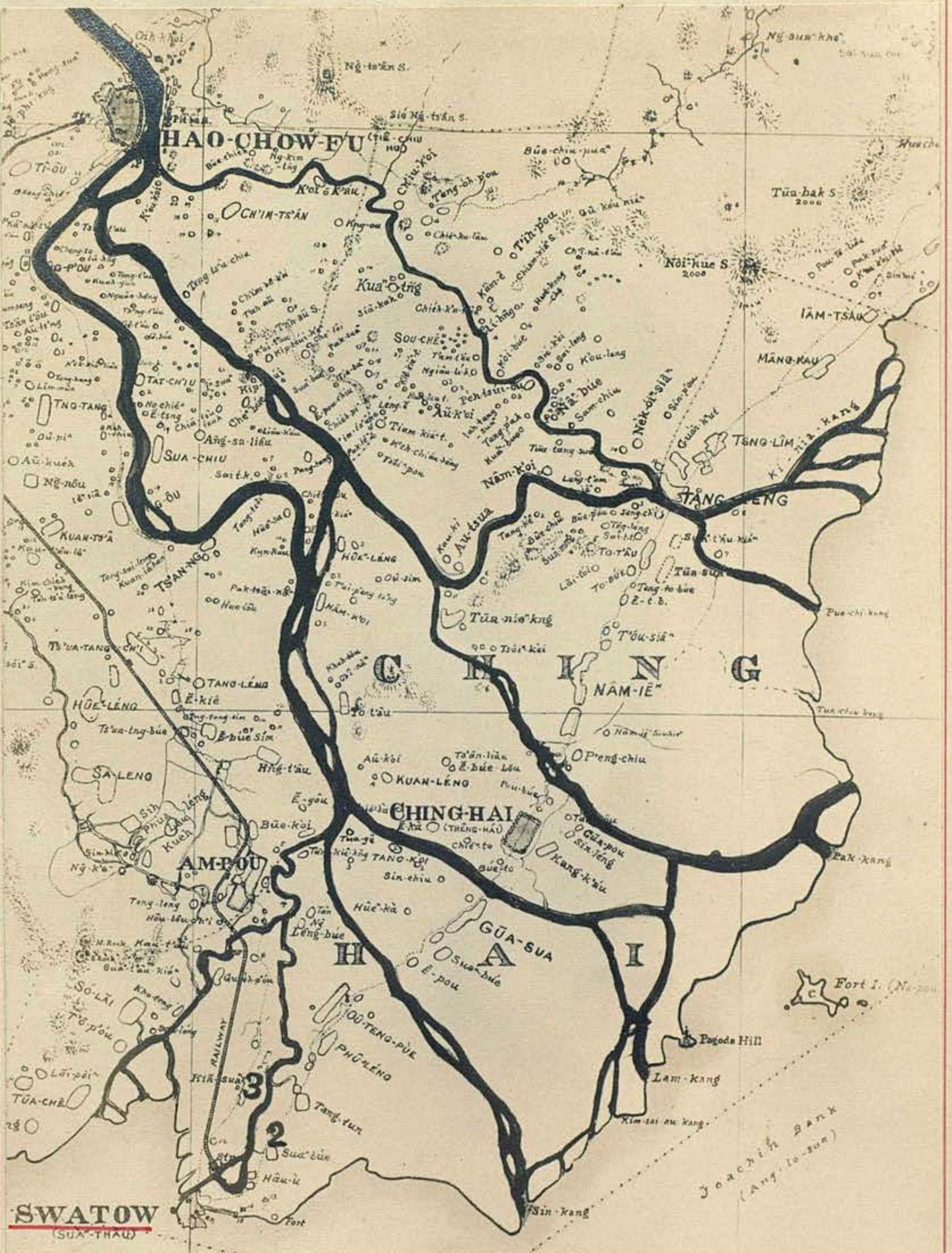
of the Kwang-tung province. The tropic of Cancer passes about twenty miles North of the town, so it will be readily understood that for many months of the year the temperature is so high as to facilitate the rapid growth of vegetable life, including the multiplication of bacilli.

From a study of the large scale map (Map II) of the neighbourhood of Swatow, it will be readily seen that the port is only one of many towns and villages built on a delta over 150 square miles in extent which is formed by the branching of the Han river and is everywhere intersected by water channels. Both to the west and the north-east of the delta hilly country will be noticed, but within the area enclosed by the branches of the river there are practically no hills, the land being composed of alluvial soil carried by the river from the three provinces through which it flows, viz: Kiangsi, Fuhkien and Kwangtung.

The following quotations from a recent text-book on Tropical Diseases[9] will show that the natural conditions of Swatow are those which render a place especially liable to be severely attacked by cholera:

"Cholera attains its greatest intensity on "soils which are permeable to water, and are at the "same time capable of retaining a certain degree of "moisture."

MAP II.



HAO-CHOW-FU
CHING-HAI
AM-POU
SWATOW
(SUA-THAU)
C H I N G
H A I
TSAN-NG
TANG-LENG
TSANG-LIM
IAM-TSAU
MANG-KAU
KUAN-LENG
GUA-SUA
SUA-CHIU
TAT-CHIU
SA-LENG
HUE-LENG
Nam-koi
Au-tsua
Tua-sua
Pak-kang
Pagoda Hill
Lam-kang
Sin-kang
Fort I.
Joachim Bank
Double Is.
(Ma-su)
KAK-CHIEH MUDDY BAY
Flower Is
Ng-sua-khe
Noi-kue S.
Tua-hak S.
RAILWAY
1
2
3

"Low-lying areas are much more apt to suffer."

"It attacks places on the banks of rivers with "special severity."

It must not be forgotten that "the infection of cholera must be swallowed,"and it is not enough that the physical conditions of the district supply almost every condition to facilitate the spread of cholera if the habits of the people do not supply what has been called "the chief condition - the liability of the water supply to be contaminated with infected excreta."[9]

As far as the Chinese* are concerned the three main sources of water supply are the river, ponds and wells.

The city of Chaochowfoo and the numerous towns and villages on the banks of the river do not drain into it, so that the river water is comparatively free from sewage contamination as is shown by the following analyses of samples obtained at the points marked "2" and "3" on Map II.

	Suabue	Kiasua
Total Solids	6.8	5.5
Chlorine	1.4	.25
Hardness	2.	1.5
Ammonia	0.	0.
Albuminoid Ammonia	.0014	.0028

* The European community uses water obtained from wells on the mainland opposite Swatow (See "1" on Map II) but such water is too expensive for the Chinese.

But even if the water were not free from chemical impurities it might still be bacteriologically clean, for it has been shown that a river cleanses itself from pathogenic bacteria in the course of twelve miles.[10] The river water-supply for Swatow is brought in boatloads from Suabue and Kiasua, from the latter, only when owing to exceptional conditions the river at Suabue contains an undue admixture of sea-water.

Ponds are found only in the outlying parts of Swatow; some communicate by deviating channels with the river, while others are only filled when the whole countryside is flooded.

There are many wells in Swatow but owing to its close proximity to the sea and the soft porous nature of the soil on which the wells are dug, it is impossible to obtain from them a good supply of fresh water.

These last two sources of water-supply - ponds and wells - are very liable to become infected with cholera vibrios, the contamination taking place in one of the following ways:-

(a) The latrines which abound throughout the town also act as cess-pools and so have to be of considerable size, and as they are built of lime and sand without any adequate foundations, there are always cracks through which the contents find access to the soil

and thus to the neighbouring wells and ponds. The photograph shows the massiveness of quite an ordinary latrine.

PLATE I.

Photograph of a latrine and cesspool in Swatow. Such a massive building, erected without adequate foundation, is bound to crack below the surface of the ground, and therefore to leak.

(b) Clothes and other domestic articles are as a rule washed at home, but if a large amount of clothing has to be washed, or if the articles are so repulsively soiled as to be deemed too dirty for the wash-tub, they are carried to the mouth of the well or to the edge of a pond and washed there. Similarly, a bed, when soiled with cholera evacuations, would also be washed at a well or pond. Thus all the most infective materials are taken to the place where they can do most harm.

(c) A bucket that has stood on a floor wet with the vomiting and evacuations of a cholera patient may be used to draw water from the well.

It has been shown that cholera bacilli can live in common tap water for forty-two days[11], and in harbour water for forty-seven days[12] - in spite of the presence of other bacilli - and it is probable that they will live as long as in well or pond water.

Having traced the vibrios from the cholera patient to the water-supply we have now to discover how the infection is conveyed back again to man. Those who are familiar with the habits of the Chinese know that they never drink unboiled water. The coolie who sweats under his load in

the hot sun and earns thereby from 200 to 500 cash a day has many opportunities of buying a cup of tea at a cost of one cash, and so has no temptation to drink unboiled water. But although the contaminated water is not drunk, it is a source of infection in other ways.

(1) Not only is it theoretically possible that the washing of bowls, chopsticks, etc. with infected water may convey the disease, but in India an attack of cholera has been actually traced to the use of a dish-cloth on which cholera vibrios were found, the cloth having been washed in a stream near an infected area.[13]

(2) Unboiled water is regularly used to give a "fresh" look to fruit exposed for sale; whether pieces of sugar cane, slices of melon or the Chinese arbutus*, they all alike look dry and uninviting after a few hours' exposure to the hot sun on a dusty road, so the vendor improves their appearance from time to time by pouring water over them, - with results that may prove fatal to the

---

* Polak has shown[66] that vegetable contaminated with cholera vibrios may retain their infectivity for as long a period as 29 days, if sufficient moisture is present to prevent their dessication.

purchaser. (See photo.)

PLATE II.

Boy selling sugar cane.
NOTE.- The dipper ("1") with which he pours water over the sections of sugar cane on his tray.
The bucket ("2") which contains a reserve supply of water.

Up till a few years ago it was believed that water was the only source of cholera infection, so that even in 1905 we read "the cholera vibrio outside the human body only lives and reproduces in water;" 14 and Manson uttered the epigram "for plague the rat-trap, for malaria the mosquito net and for cholera the kettle." But such views were really old-

fashioned even then, for Sir William Moore, writing to the medical press twelve years earlier, had been able to congratulate himself that the correctness of the views he had long held as to the conveyance of cholera-infection by flies had been demonstrated by Sawtschenko,[15] and nine years earlier than that an Italian book had been published[16] to prove that cholera infection could be conveyed by flies.

It has now been placed beyond dispute that flies can carry the living cholera vibrio for 24 hours after contact with the source of infection, and this has been demonstrated in North China[17] and the Dutch Indies[18] as well as elsewhere.[19] In South China not only are there large swarms of flies during the cholera season but there seems no reason to doubt that they are assisted in the mechanical conveyance of the infection by such other insects as mosquitoes, cockroaches, etc.

The extreme poverty of a large number of the people increases the likelihood of their being infected by food which has been contaminated by flies. They can afford neither to throw away the food remaining over from one meal nor to protect it from flies, and they even grudge the trifling cost of cooking it again. Further, some vegetables and all fruits they prefer to eat in an uncooked and therefore

unsafe condition. In this connection it may be of interest to note the case of an old woman whose greed or poverty led her to finish the food remaining over from the last meal of a neighbour who had died of cholera. Two days later she herself developed cholera and died.

In addition to water and flies there is a third possible source of infection, namely fingers that have been soiled either from direct contact with cholera patients or from handling garments fouled with their discharges. Although the dexterity of the Chinese with chopsticks makes it unnecessary for them to finger their food, yet it is probable that infection through soiled fingers is of not uncommon occurrence.

Before leaving the question of the spread of infection, something should be said on the subject of Cholera Carriers, who may be either convalescents from cholera or healthy people in the entourage of cholera patients. The frequency with which these "carriers" may be met with is shown by the fact that in from one-third to one-half of the cases of cholera which recover the vibrio may be detected in the stools for more than ten days, and that 1% of apparently healthy passengers examined at New York in 1911 were shown to harbour the vibrio of Koch;[20] but it is generally accepted that there are very few

instances of chronic carriers, for the vibrios almost always disappear within fifty days.[21, 22.]

There is some divergence of opinion, however, as to the practical importance of these cholera carriers. On the one hand Dr. Vay of the Suez Quarantine Office maintains that "no epidemic of cholera followed on the cholera vibrio carriers," and that in spite of "cholera vibrio carriers..... mixing with others.....in the general Hospital... ....not a single case of cholera occurred."[23] On the other hand Macrae has recorded an outbreak amongst the nurses of a Hospital in Calcutta in which the contamination was traced to certain servants who were proved to be vibrio-carriers,[24] and similar outbreaks have been traced to cholera carriers at the Bilibid prison in Manilla.[25] The fact that cholera can be carried by a person who shows no sign of the disease makes it essential that even in the absence of an epidemic the strictest precautions must be taken to secure an uncontaminated water supply, freedom of food etc. from infection by flies, and strict cleanliness of all hands that come in contact with cooked food.

As we have now completed our examination of the various routes by which the infection of cholera can be conveyed, a short account will now be given

of the epidemic that occurred in Swatow in the summer of 1912.

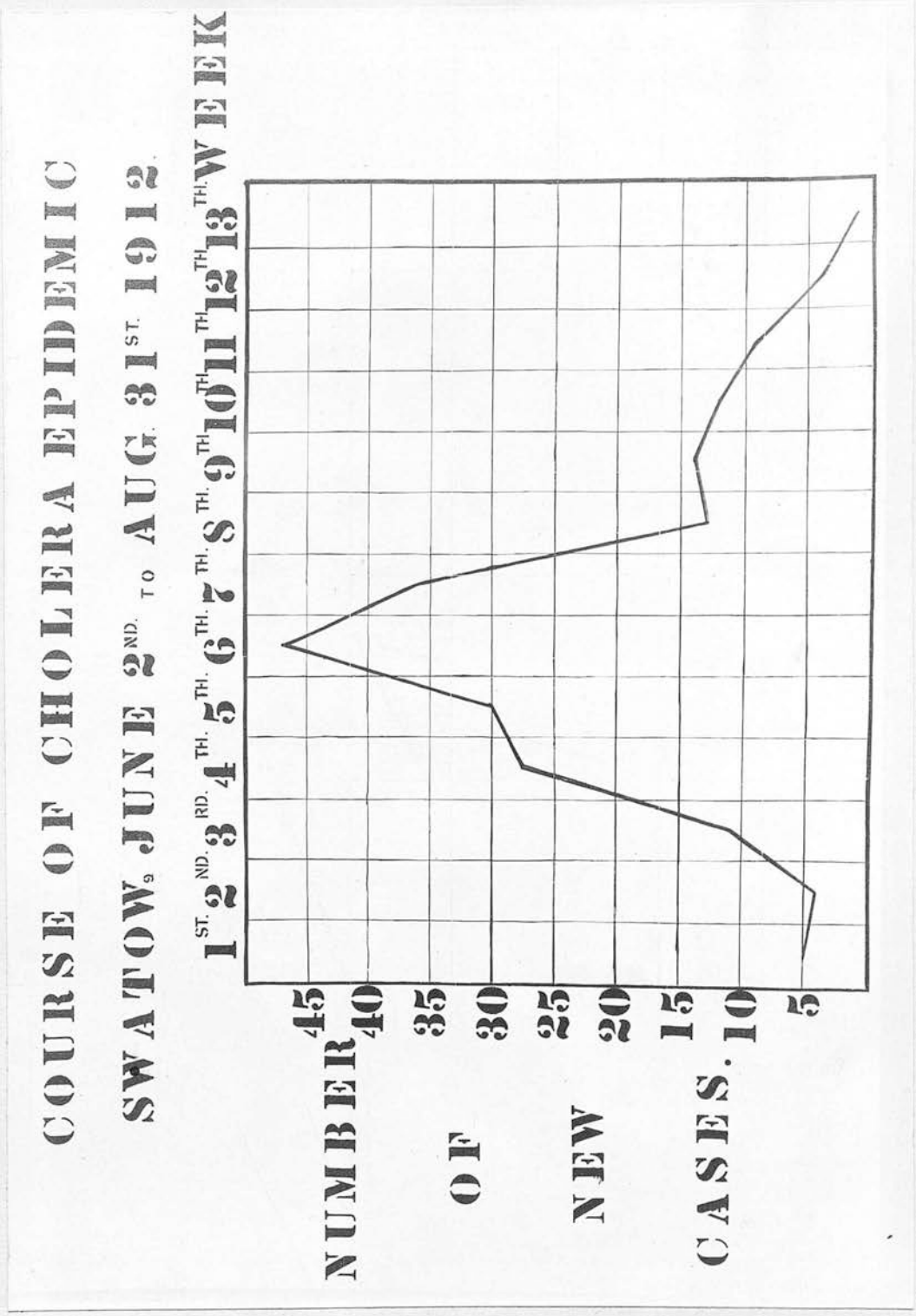
The first summons to attend a cholera patient came on the 2nd June, and as during the two following weeks only eight more patients were treated it was not anticipated that there were going to be more than a few sporadic cases. During the third and fourth weeks, however, 38 cases were treated, and it was evident that the port was being visited by a moderately severe epidemic.

Although several definite centres of the disease had been revealed (e.g. 12 cases from one street of 16 houses - which all obtained their water from the same well - and four cases from three households opening on a courtyard with a common well) yet there was a large number of cases which were separated from one another by considerable distances. As will be explained later on (pp. 37 to 41) each case required to be revisited at frequent intervals after infusion and when, in the 5th week, there were as many as 9 new cases in one day, apart from old cases, all of whom required frequent visiting and treatment, the work became so heavy that it was impossible any longer to treat the patients in their own homes. It was fortunate that the 8 patients from amongst the prisoners and employees at the central police

station who were undergoing treatment at that time, all recovered, as this was the means of attracting the attention of the commissioner of police who, to show his gratitude, placed at our disposal, for the accommodation of cholera patients, an empty and dismantled fort in close proximity to the Mission Hospital. A trifling expenditure made this quite suitable for our purposes, and by July 11th we were able to enter into possession. After that date it was required that all male patients desiring treatment should be brought to the old fort, the women being taken to a temple where accommodation is provided "for the dying."

Previously, when the patients were allowed to stay in their own homes, each was a source of infection to his neighbours so that it was not surprising that, simultaneously with the new patients all being taken to the fort and temple, there came a check in the spread of the epidemic. The weekly number of new cases immediately fell from 48 to 37, and continued steadily to diminish so that at the close of the thirteenth week, i.e. after the 31st August, no case requiring intravenous injection came under treatment.

FIGURE I.



The diagram (Fig. 1) shows the number of those cholera patients each week who were so severely ill

as to require the intravenous injection of saline; and a chronological table is appended giving details of each case thus treated.

The total number of patients receiving intravenous infusion was 212, but many other patients were treated whose condition never became so dangerous as to make this necessary. These latter all recovered, some with subcutaneous infusion, some with saline enemata, some even (especially towards the close of the epidemic) after treatment with drugs by the mouth.

It is of interest to consider the influence of the climatic conditions upon the course of a cholera epidemic. "In India a constant phenomenon of cholera is its increase directly after a fall of rain that has succeeded a period of drought" (Wall)[65] and this is doubtless true of places other than India, but the effect of a fall of rain that has <u>not</u> "succeeded a period of drought" is quite uncertain. An examination of the deaths from cholera in Calcutta during two periods (1830-1860[26] and 1865-1876[27]) shows that during the dry season (November to April) with a monthly rainfall of less than 3" and an average temperature of 74°F. there were 86,000 deaths, whereas during the wet season (May to October) when the rainfall was never less than 5" and rose as high as 13" in a month, there were only 48,000 deaths,

although the average temperature was 83°F. This shows how difficult it is to determine the influence that a heavy fall of rain, or a period of bright dry weather may have upon the course of a cholera epidemic. Theoretically, longer duration of sunshine means more thorough dessication and destruction of those bacilli exposed to its direct rays; but the greater warmth of the atmosphere which results from this increase of sunshine facilitates the rapid multiplication of bacilli, and by increasing the thirst of the populace leads to a greater demand for fruits, cold drinks and ices, all of which are especially to be avoided in cholera time. It might be thought that a heavy rainfall would assist the spread of the disease by washing infective material into the wells, but, on the other hand, the cleansing of the streets causes a diminution in the number of flies and the cooling of the atmosphere leads to a lessened demand for dangerous refreshment.

The following table (Table I) has been prepared with a view to showing, for each week of the epidemic, the rainfall, the hours of sunshine and the thermometric readings.

T A B L E I.

Showing climatic conditions during the Epidemic

				Temperature			
				Dry Bulb		Wet bulb	
Week of epi-demic	No.of new cases treated	Rain-fall in inches	Weekly total of hours of sun-shine	Weekly average of daily maxima	Weekly average of daily minima	Weekly average of daily minima	Weekly average of daily maxima
1st	5	2.9	8	84	75	75	79
2nd	4	5.2	32	84	74	74	80
3rd	11	7.1	4	87	77	76	80
4th	27	6.2	57	91	78	76	83
5th	30	.3	65	90	79	77	83
6th	47	.5	84	92	79	78	84
7th	36	.3	84	91	79	78	84
8th	13	3.2	36	87	78	77	81
9th	14	3	52	91	79	77	81
10th	12	5.4	69	87	77	77	81
11th	9	1.3	32	87	77	75	80
12th	3	1.8	50	88	78	76	80
13th	1	.7	68	90	77	76	80

It will be seen that, on the whole, an increase in the temperature was attended by an increase in the number of cholera cases, a fact which is brought out better in the following diagrams (Figs.II, III and IV)

F I G U R E II.

Diagram showing the relation between the course of the Cholera Epidemic from week to week and the total number of Hours of Sunshine recorded each week.

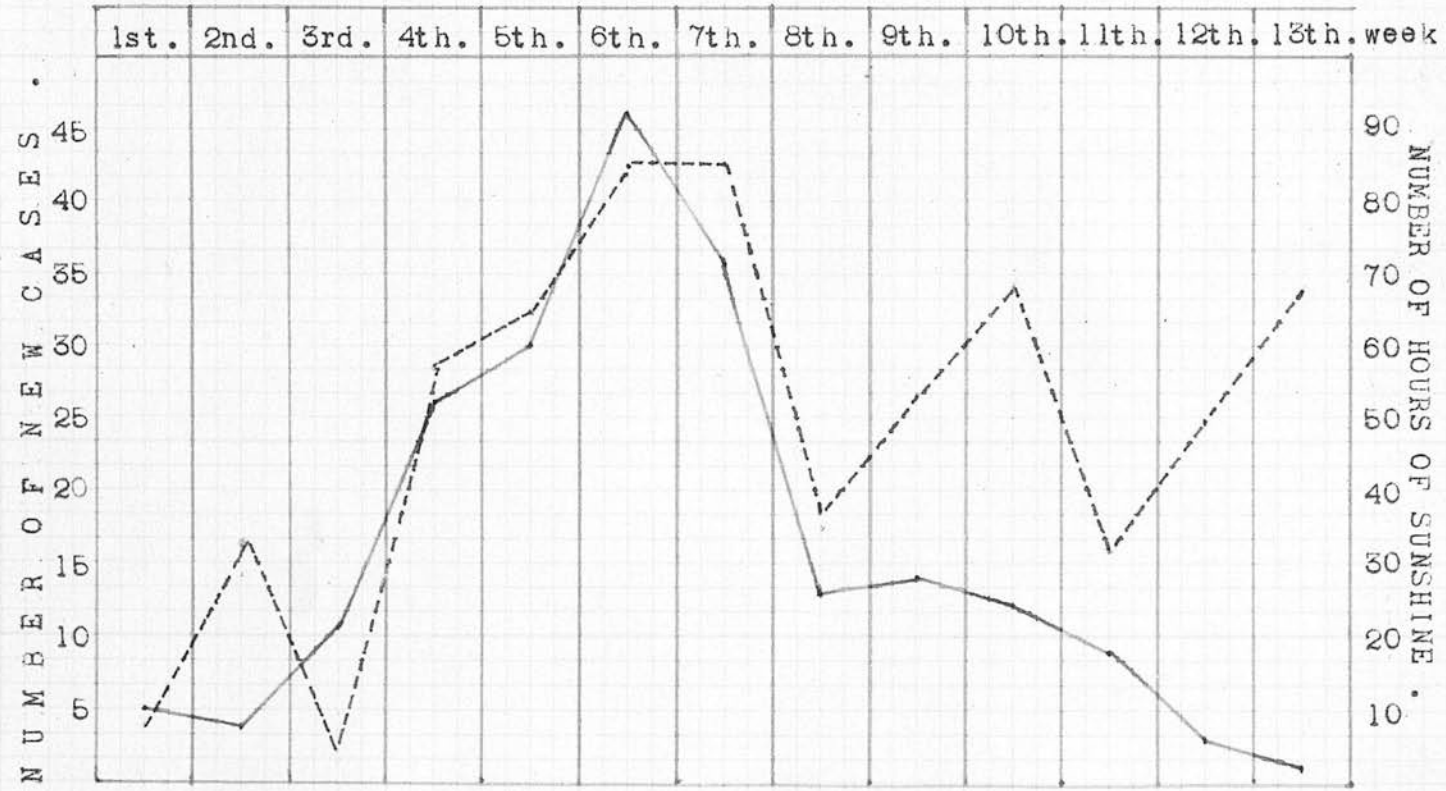


Diagram showing the relation between the Course of the Cholera Epidemic from week to week and the average , for each week , of the daily maximum Temperatures (dry bulb) Fahrenheit Scale .

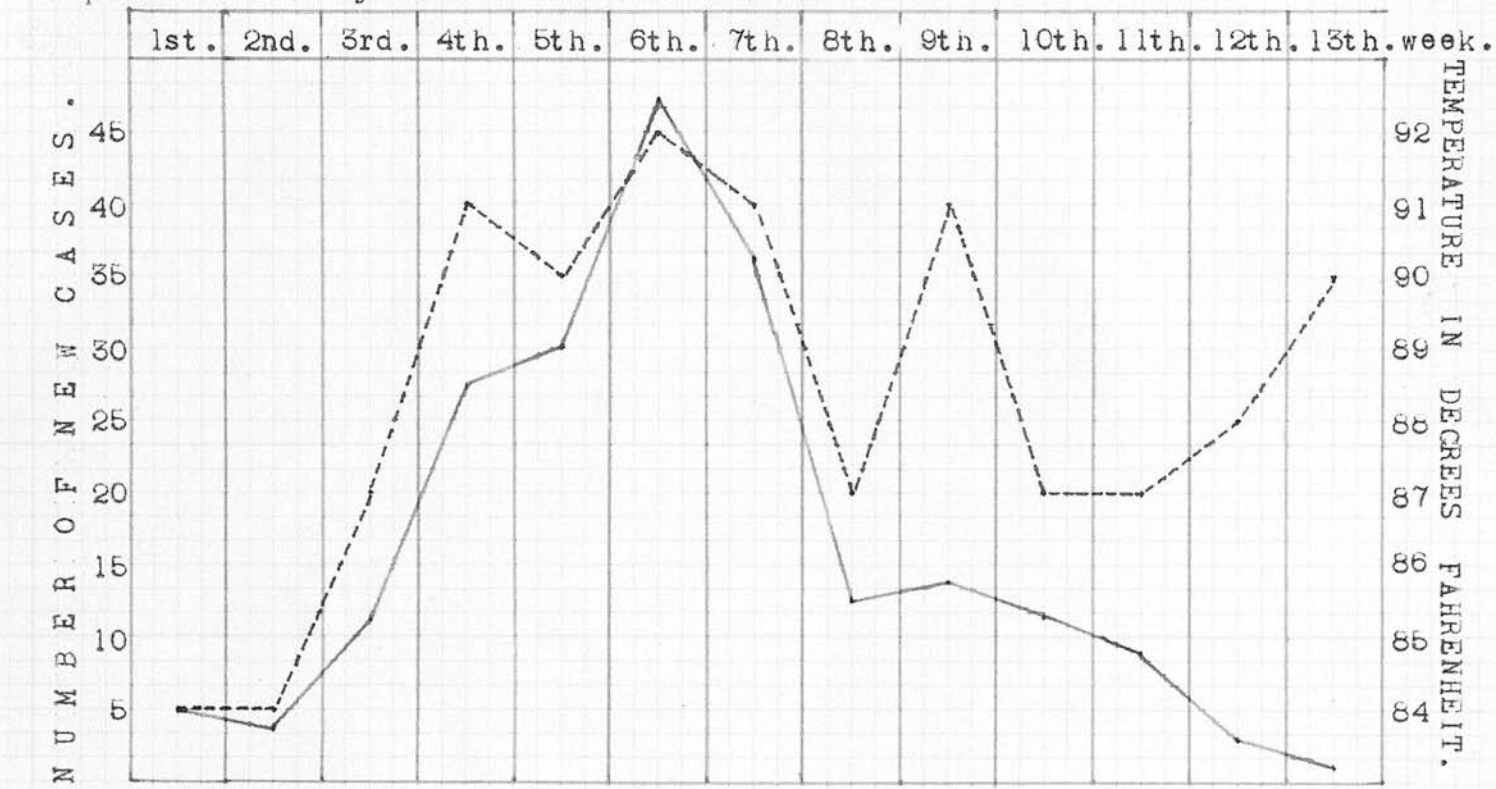
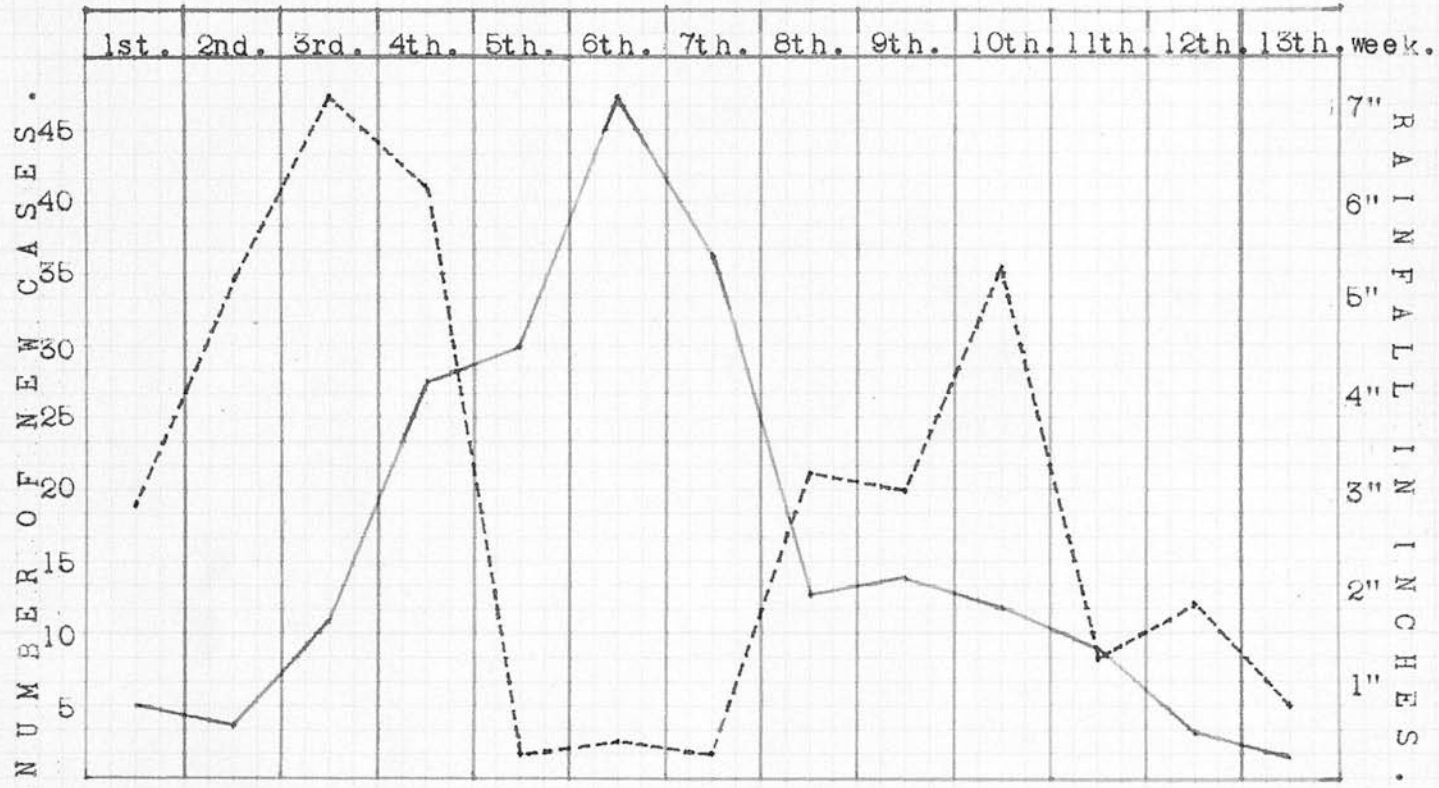


Diagram showing the relation between the Course of the CholeraEpidemic from week to week and the total rainfall in inches for each week.



Before we go on to the question of how this epidemic was treated, it may be as well to deal with the question that some critic may ask - "Was this an epidemic of true cholera? Was it caused by the vibrio of Koch?" It is impossible to answer this question for though it is true that the clinical picture of a case of cholera is sufficiently striking to be easily recognisable,* yet it is desirable to have a bacteriological diagnosis, and as we face this many difficulties meet us for science is progressing so rapidly that the tests that would have been thought specific ten years ago are now known to be merely group reactions. Further, it appears that one may have a cholera epidemic and no cholera vibrios, and, at other times, vibrios which "sont tout identiques avec le vrai vibrion de cholera de Koch"[22] and yet meet with no case of cholera.

In fact a vibrio may resemble the true cholera bacillus in giving a positive Pfeiffer reaction and even a positive agglutination test, and the only way

---

* "The copious, painless passage of watery motions, devoid of bile colouring, resembling rice-water and exhaling a characteristic odour; the profound nausea and frequent vomiting of watery material; the suppression of urine; the muscular cramps; the cyanosis and shrinking of skin; the cold breath and whispering husky voice; the dyspnoea and restlessness; the prostration, torpor and failing pulse; the cold sweats and depression of the surface temperature with a tendency to rise of internal temperature. These constitute a group of symptoms which..... are seldom identical with those of any other flux." 9

in which one can show that it is not a true cholera bacillus is because an emulsion of the vibrios gives a haemolytic reaction.[28] It is obvious that a practitioner whose whole time is occupied in the treatment of a cholera epidemic is compelled to neglect this clinically unimportant point of the presence or absence of a vibrio which even bacteriologists with well equipped laboratories, devoting the whole of their time to scientific research, may fail to identify as the true cholera bacillus.

And so we leave on one side the question of diagnosis, and proceed forthwith to consider the treatment of an epidemic of cholera.

It is obvious that the ideal method of dealing with a bacterial disease is to destroy the causal bacillus <u>in situ</u>. Attempts have been made to achieve this end in cholera by the use of such antiseptics as Calomel,[29] Carbolic acid,[30] Chlorine,[31] Creasote,[32] Cyanide of mercury,[33] Izal,[34] Salol[35] and, more recently, Creolin;[36] but all these methods are passing into disuse (save perhaps the use of calomel) since the good results that were reported in one epidemic were rarely obtained - even by the same doctor - in subsequent epidemics.

At the Bombay Medical Congress in 1909 Pant[37] mentioned that he used solutions of potassium

permanganate in the treatment of cholera, and Rogers,[38] having satisfied himself - both by laboratory experiments and at the bed-side - of the value of permanganates in destroying the toxins formed by the bacilli, has regularly used them since either in the form of a solution of the Calcium salt, or as pills of potassium permanganate. Unfortunately this line of treatment did not prove acceptable to the Chinese patients, the unpleasant astringent taste, when given in solution; frequently brought on exhausting vomiting, and the same result followed the administration of permanganate pills. Rogers does not make any reference to the use of these salts in his account of "The treatment of cholera at Palermo"[39] and it may be that this permanganate treatment is unsuitable for those with more sensitive stomachs than his Indian patients.*

If, then, treatment directed against the bacilli is ineffective, and treatment intended to destroy the

---

* The subject of treatment directed against the bacilli, and treatment intended to neutralize their toxic products, should not be left without a reference to the views enunciated 35 years ago by Sir George Johnson,[40] ("Med. Lectures and Essays, Churchill, 1887) who opposed the administration of opium, and advocated the use of Castor Oil as the safest method of "sweeping the morbid secretions from the intestine." The elimination of the bacilli and their products which he promoted with a purgative is - in cases treated by saline infusion - carried on by nature, the physician merely providing the watery and saline elements which constitute the medium in which the bacilli etc. pass from the body.

bacterial toxins cannot be carried out, what is left for the physician to do? He must obey the old injunction to "avert the tendency towards death," and in order to do this he must in the first place ascertain the methods in which cholera brings about the death of the patient. According to Liebermeister the patient's vitality is diminished by (1) "the loss of water from the blood and tissues," (2) "the absorption of ..... poisons" and (3) "the severe disease* of the intestinal membrane may cause ..... heart failure."[41] Presuming that the above poisons exert their most serious action on the heart, these three factors may be resolved into two, viz.- the degree of concentration of the blood, and the failure of the heart. Treatment by the intravenous injection of saline solution exactly meets these conditions, for on the one hand large quantities of fluid are supplied to diminish the concentration of the blood (and incidentally to dilute the toxins), and on the other hand the heart is powerfully stimulated.‡

---

* The severity of the disease of the intestinal membrane may be gathered from the following description of the post mortem findings in a case of cholera:- "The mucous lining of the jejunum and ileum . . . had "been so completely cast off that it is difficult to understand how regeneration ever takes place."[60]

‡ The value of intravenous infusion in combating shock due to <u>surgical</u> causes is too well known to require further reference, but it is only rarely employed to overcome collapse in <u>medical</u> cases. A case described by Bradley & Smith[42] shows the great value of intravenous infusion in overcoming very severe prostration following a sudden fall of temperature.

The interest of a brief survey of the history of intravenous infusion may be sufficient justification for a short digression. An Edinburgh physician was the first to practise this method of treating cholera, and within eight months of the disease being imported into the British Isles (Sunderland, October 1831) Dr. Latta of Leith was able to describe in the Lancet[43] the results of his treatment with intravenous saline injections. It is interesting to note the steps that had led to his very prompt adoption of such a scientific method of treatment. Careful analyses of the blood serum and of the dejecta had been published by Dr. Thomas Thompson in the Philosophical Magazine,[44] but his work was not made use of by the physicians who were treating cholera till an article by Dr. O'Shaughnessy, embodying Dr. Thompson's findings, appeared in the Lancet.[45] This paper showed that in cholera cases "the dejections were alkaline and albuminous, and "contained the water and soluble salts in which the "serum of the blood was deficient." The way in which the analyses published in this article helped Dr. Latta and Dr. Murphy (independently of one another) to carry out the intravenous injection of saline may be best described in their own words. Dr. Latta wrote: "As soon as I learned the results "of Dr. O'Shaughnessy's analysis, I attempted to

"restore the blood to its natural state by injecting
"copiously into the large intestine warm water hold-
"ing in solution the requisite salts ... but by this
"means I produced no permanent benefit ... I at length
"resolved to throw the fluid immediately into the cir-
"culation."[43] Dr. Murphy's letter contained the fol-
lowing:- "My first idea was to return into the
"system the alvine dejections by injecting them into
"the veinous system.....but as the dejections are
"seldom preserved, it occurred to me to make an arti-
"ficial serum from the analysis of Dr. O'Shaughnessy."[46]

The almost miraculous improvement in the patient's condition that follows the use of saline infusion quickly led to this line of treatment being generally adopted; and one of the earliest notes thereon is an account of "A trial of saline venous injection in malignant cholera at the Drummond Street Hospital, Edinburgh."[47] The extraordinary effect of intravenous infusion in the collapse stage of cholera must be seen in order to be realised. "You have be-
"fore you a man cyanosed, ice-cold, entirely pulse-
"less, with half-open eyes sunk deep in the sockets,
"exhibiting no reflex of the cornea, which may be
"already dried up; unconscious and without feeling.
"You lay open a vein, but the pain of the cut calls
"forth absolutely no reaction. The cannula is

"fastened into the vessel and the warm solution "poured in. From 200 to 300 gms. have scarcely "been introduced when the effect begins to show it- "self, and before the ordinary amount of 1000 to "1500 gms is reached the picture is entirely changed. "The lips are again cherry red, the cheeks of healthy " colour, the eye regains its lustre, sensation re- "turns, the blood streams through the arteries with "a full strong pulse, the breathing becomes deep and "quiet, consciousness is again present, the patient "shows signs of intelligence."[41]

Unfortunately, however, the improvement that follows infusion with normal saline is generally transient, the diarrhoea and vomiting recommence, or become more severe, and in a few hours the patients again collapse and often fail to rally. In the six months that followed the publication of Dr. Latta's report, the medical press contained the records of 105 cases of cholera that had been treated with intravenous injections: 78 of these cases had terminated fatally, in 22 the result was uncertain at the time of publication, and in only 5 cases was it possible to announce a definite cure.[48] Thus, in spite of the improvement that always followed intravenous infusion, the final result was so disheartening that this method of treatment very largely fell into

disuse. Although it formed the subject of a discussion[49] at the Medical Society of London during the second European epidemic, yet in a list of 170 "Proposed cures for cholera"[50] published in 1850 intravenous saline infusion finds no place. Since then there have always been some practitioners who have carried out this line of treatment, and doubtless in borderline cases it has sometimes sufficed to turn the scale on the side of recovery. The difficulty, however, of retaining the saline fluid in the circulatory system prevented intravenous infusion from yielding permanently satisfactory results until Leonard Rogers in 1908 overcame this obstacle by the use of saline solution double the normal strength, and so established intravenous saline infusion as the most successful as well as the most scientific method of treating cholera. It may be said that no real advance had been made in the treatment of cholera from the time of Latta (1832) till Rogers made this discovery.

It is not enough to know the best method of treating cholera unless one also knows how to determine which cases are so severe as to require this form of treatment. Mild cases of cholera occur during an epidemic which it would be absurd - and might even be dangerous - to treat with intravenous

infusion, while in other apparently mild cases the progress of the disease is so rapid that only immediate intravenous injection can save the patient's life. The line of treatment to be carried out in each particular case can only be determined by the accurate measurement of the degree of concentration of the blood, and of the amount of cardiac failure.

The degree of concentration of the blood in cholera was first accurately measured by Hermann in 1830 during the first invasion of Europe by cholera. He found that while the normal specific gravity of the blood serum was 1.028, it rose to 1.036 in a case of cholera which he investigated; similar results, with even higher specific gravity figures were obtained two years later in Glasgow and Belfast. The specific gravity of whole blood was not taken till 1850 when Schmidt found that, in the particular case of cholera he tested, it was 1.072 as compared with the normal about 1.056.[41] O'Meara, in reporting the treatment of a cholera epidemic in 1908 recommended that the specific gravity of the blood should be taken at the bed-side;[51] and this important advance is a feature of the line of treatment carried out in Swatow.

According to Rogers it is advisable to have a series of small stoppered bottles each holding a few

drachms of a mixture of glycerine and water representing every other degree of specific gravity between 1.040 and 1.076. "The estimation can now be "rapidly carried out by placing a small drop of "blood in the middle of one of the bottles of gly-"cerine solution of about the specific gravity which "is expected to be found. If it rises, it is light-"er than the fluid, and another drop is placed in a "bottle of lower specific gravity until either the "one in which it just floats for a second or two is "found, or it has been noted to rise slowly in one "and sink in the next one, in which case the correct "figure will be between those on the two latter "bottles. The estimation does not take more than "two minutes."[38]

I found this method of estimating the specific gravity of the blood to be distinctly unsatisfactory, and that for two reasons. In the first place a drop of blood placed "in the middle of one of the bottles of glycerine solution" does not remain a definite drop but at once diffuses itself into the glycerine and water to form an ill-defined cloud (See Plates III, IV, V & VI); this makes it difficult to determine exactly the upward or downward movement of the blood drop. In the second place, even if the blood is of lower specific gravity than this testing solution, the blood-drop only rises to the

surface for a very few seconds before it begins to sink (See Plate IV): and if the specific gravity of the blood and of the solution are approximately the same, it is almost impossible to be quite sure that the drop of blood did indeed "float for a second or two" before it subsided towards the bottom. The indefinite results obtained by the glycerine and water mixture led me to give up that method of determining the specific gravity of the blood; for, as the question of giving or with-holding saline solution depends upon the test, it is of supreme importance that the results obtained should be accurate.

Another method of testing the specific gravity is that of Hammerschlag in which a mixture of chloroform (Sp.gr. 1.490) and benzene (sp.gr. .670) is employed. When a blood-drop is expelled into this, it is not diffused into the fluid but remains a definite but shapeless mass (See Plate V). If the blood-drop rises, more benzene must be added, and if it sinks, more chloroform till the blood just floats. The specific gravity of the mixture will then be the same as that of the blood. The accurate determination of the specific gravity of the blood by this method entails the expenditure of considerable time at each case, and therefore makes the method quite impracticable in an epidemic.

In view of all these difficulties I endeavoured

to find a simpler method and obtained the most satisfactory results with a mixture of oil of wintergreen (i.e. methyl-salicylate Sp.gr. 1.180) and castor oil (Sp.gr. .950). In this the blood remains as a definite globular drop, which will keep floating at the surface of a mixture of higher specific gravity, and will definitely sink to the bottom in a mixture of lower specific gravity. The examination is rapidly made at the patient's bed-side if bottles of the testing mixture are prepared beforehand representing the different specific gravities desired - a plan which cannot be carried out if chloroform and benzene are employed on account of their extreme volatility.

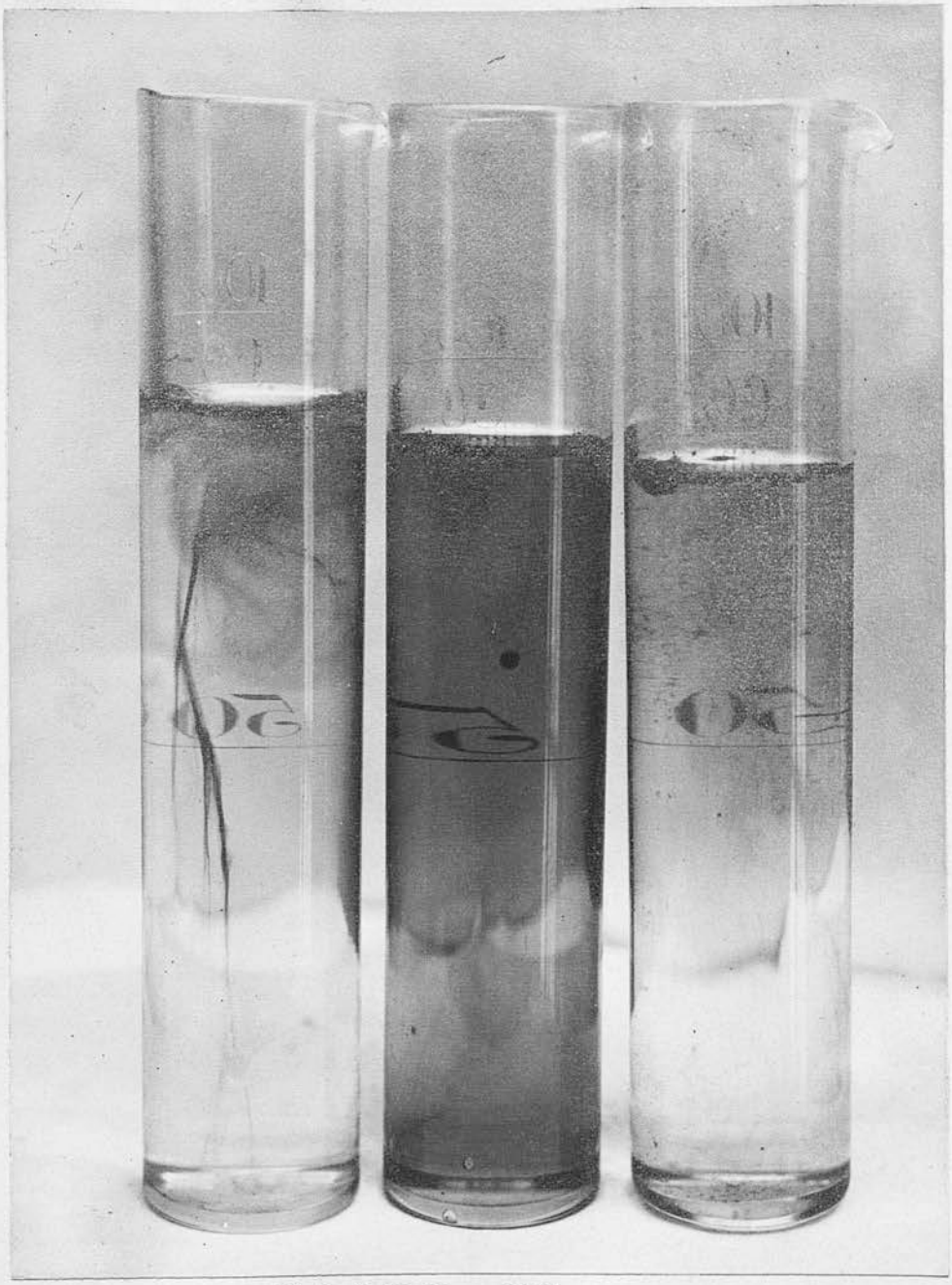


PLATE III.

Left-hand glass - Mixture of glycerine and water. In this the blood-drop diffuses to form an indefinite cloud.

Middle Glass - Mixture of oil of winter-green and castor oil. In this the blood is seen as a definite globular drop.

Right-hand glass Mixture of chloroform & benzene. In this the blood-drop appears as a definite but shapeless mass.

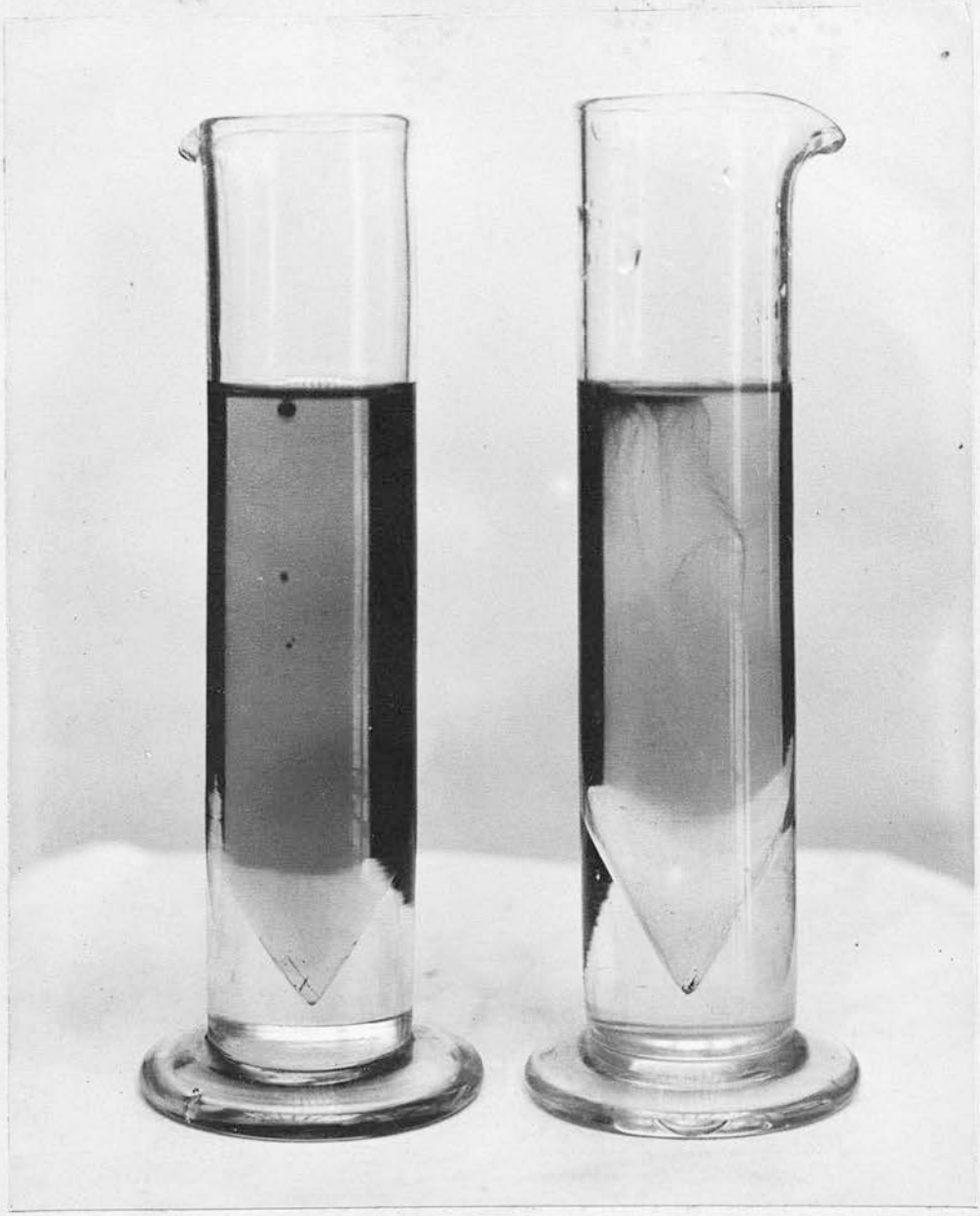


PLATE IV.

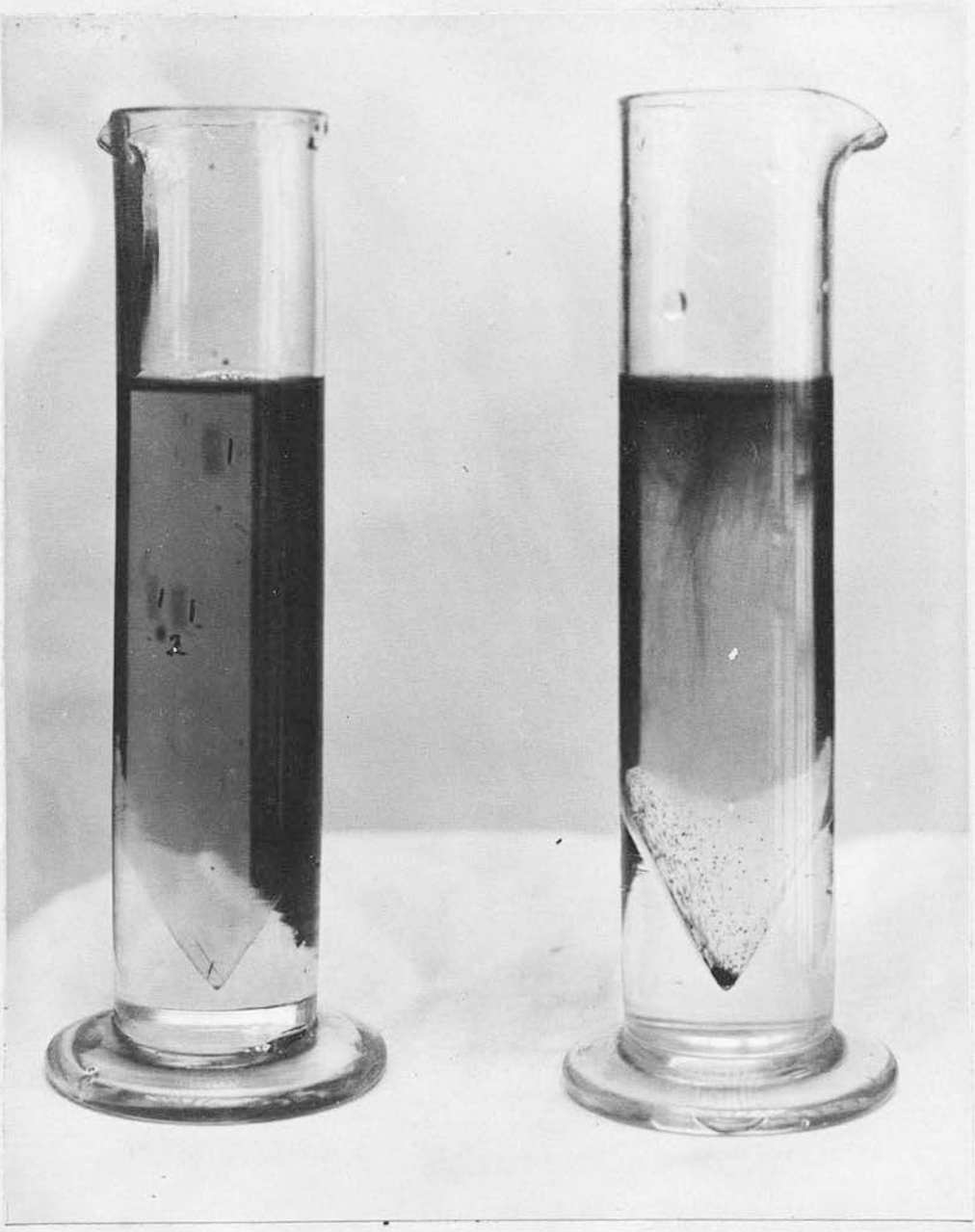
Left-hand glass - Oil mixture.

Right-hand glass -Glycerine-water mixture.

The specific gravity of both is the same and is higher than that of the blood-drops which were expelled into the fluids immediately before the photograph was taken.

On the left the blood-drop has risen to the surface and remains floating there.

On the right the blood-drop after rising to the surface has already begun to sink.



P L A T E V.

Mixtures and position as in Plate IV, this photograph being taken only a few minutes later.

On the right the blood-drop shown in Plate IV is seen as a granular precipitate at the bottom of the glass, while a second drop, which was expelled immediately before the photograph was taken, is already seen to be sinking.

The glass on the left has been shaken so displacing the drops seen floating on the surface in Plate IV The patches ("1") are due to these drops being in the act of rising towards the surface while the plate was exposed. The darker mark ("2") is a blood drop that is so small that owing to the friction on its surface it is rendered almost stationary.

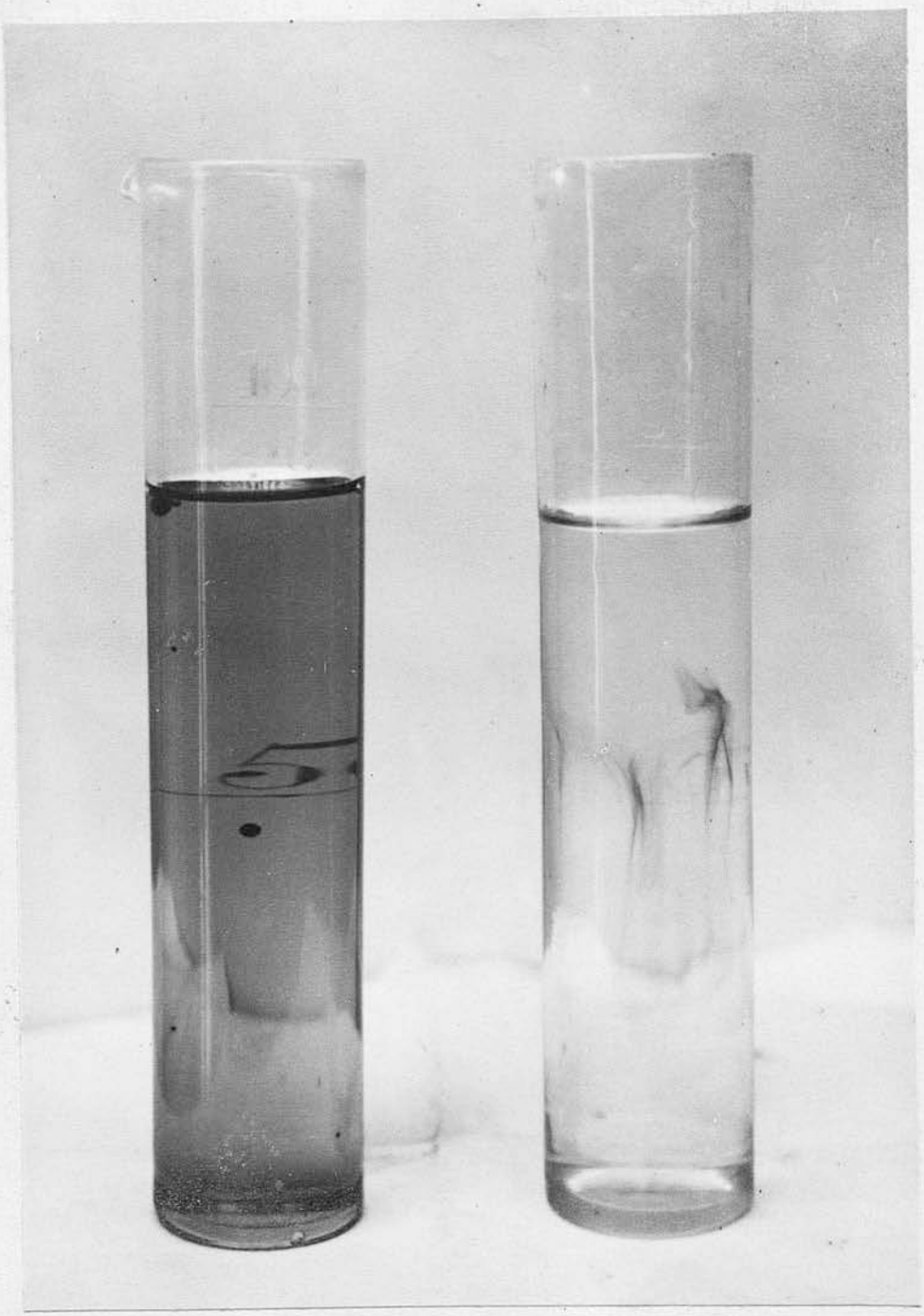


PLATE VI.

Left-hand glass - Oil mixture.

Right-hand glass - Glycerine-water mixture.
The specific gravity of both the mixtures is the same and equals that of the blood examined.
Contrast the definite motionless globule of blood in the oil mixture with the diffuse cloud that is sinking towards the bottom of the glycerine-water mixture.

In the use of this oil mixture two points must be noted: in the first place a drop not smaller than 5 cubic millimetres should be employed as, if the specific gravities of the blood and the oil do not differ greatly, drops smaller than this will neither rise nor fall, but, owing to the friction of the fluids, will remain stationary. (See Plate V).

In the second place, the heavier ingredient of the mixture (the oil of winter-green) is more volatile than the lighter, so that, if the bottle is frequently opened, the specific gravity of the mixture will become appreciably lower after a few days; in any case, however, a new supply of oil will be required by that time on account of the accumulation of blood-drops in the testing fluid. In the case of the glycerine and water mixture there exists the same need for a fresh supply at frequent intervals, owing to the increasing turbidity produced by the repeated addition of blood-drops.

The important effect of <u>temperature</u> upon specific gravity must be borne in mind in the preparation of these mixtures for testing the blood. The contents of a specific gravity bottle may weigh 1000 grains in the temperate climate of Europe and only 997 grains during the hot season in Swatow. The same difference of specific gravity will be shown if an hydrometer is used. It is essential

that the apparent specific gravity should be corrected as otherwise one's standard testing solutions will be so inaccurate that saline infusions may be administered too often and in too large quantities. The amount of correction required is easily found by testing the specific gravity of distilled water at the same temperature as the standard solution one is preparing.

Rogers has shown that two specific gravity figures stand out as of special importance in cholera, viz. 1.062 and 1.066; if the specific gravity of the blood is below 1.062 the injection of saline is not required, whereas if it is over 1.066, one hundred and twenty ounces must be administered at once; between these two figures 80 ounces of saline should prove a sufficient amount. In treating this cholera epidemic, I found these two figures of incalculable value, for in place of measuring the exact specific gravity of the blood of each patient, it is only necessary to determine its relation to these two standards. This only requires <u>two</u> bottles of solution in place of the series of nineteen employed by Rogers.

But the proper line of treatment to be adopted cannot be learned from a study of the specific gravity of the blood alone, the condition of the heart must also be examined. The sphygmomanometer

enables the degree of cardiac failure to be accurately measured so that instead of depending upon one's estimation of the strength of the pulse, as made out by digital pressure, one obtains an exact figure representing the number of millimetres of mercury required to obliterate the pulse. Here again Rogers has established a standard figure for the guidance of those engaged in the treatment of cholera. He writes: "As a result of prolonged experience, I have "come to regard a blood pressure below 70 mm. of mer-"cury as an indication of the presence of a dangerous "degree of collapse necessitating an intravenous "saline injection.....I have several times had occa-"sion to regret having postponed transfusion in cases "with a pressure a little below 70 mm. on account of "their general condition appearing to be fairly good."[38] Subsequent experience in India led him to adopt for Europeans 80 mm. of mercury as the figure below which the blood pressure should not be allowed to fall, but after treating the Italians at Palermo he advised that the standard for Europeans should be 100 mm.[39] Although in healthy Indians "the blood-pressure is often on a much lower scale than is the case in Europeans"[52] yet this does not apply to Chinese - as I have shown elsewhere.[53] In treating cholera amongst Chinese intravenous injection is often required - as in Europeans - while the blood pressure is between

70 mm. and 100 mm. of mercury. It sometimes happens that in a patient with quite a good blood pressure (e.g. over 100 mm. of mercury) the blood is so concentrated as to demand the administration of saline solution. In such a case the injection should not be given intravenously, but may be administered under the skin or per rectum.

The sphygmomanometric estimation of the blood pressure yields more reliable information as to the strength of the heart than any other method, but if only the systolic pressure is estimated one will occasionally be led to wrong conclusions in patients in whom there is an abnormal difference between the diastolic and systolic blood pressures. Although it may be more difficult to determine exactly the diastolic pressure - i.e. the sustained pressure between the beats - yet it is upon this, rather than upon the systolic pressure, that the carrying on of vital functions depends. As a rule the difference between the systolic and diastolic pressures is about 30 mm. but in various abnormal conditions it may be either greater or less. The difference is, for instance, much greater in aortic incompetence; and in the case of a cholera patient (Case 182) aged 35, who was also suffering from aortic incompetence, his high systolic pressure led to the postponement until too late of the intravenous infusion that might

have saved his life. On the other hand, when the difference between the systolic and diastolic pressures is less than usual, the patient may make a good recovery without intravenous infusion, although the low systolic pressure may have suggested that this was necessary. This was exemplified in the following case (Case 172): A woman 27 years of age, an opium smoker who was menstruating*, was admitted with a blood pressure of 70 mm. of mercury. The pressure remained between this figure and 90 mm. for the five days that she was under observation, although after the first 24 hours the blood was not unduly concentrated and a reasonable amount of urine was being secreted each day. It is important that one should be on the watch for these cases in which the cause of the misleading systolic pressure can only be discovered by a thorough and careful examination of the patient's general condition.

Those who have treated epidemics of cholera in the past, without the guidance afforded by the accurate determination of the concentration of the

*Dalmahoy Allen has found that the blood pressure usually falls at the commencement of the menstrual period and does not reach the normal again till the period is over. (From a private letter).

blood and the degree of cardiac failure will remember the anxiety with which they often had to consider the question of the necessity or otherwise of saline infusion - an anxiety which is now done away with.

Having considered in detail the indications for intravenous infusion, we now pass to an account of the treatment of cholera as it was actually carried out in the Swatow epidemic of 1912.

It is unnecessary to describe minutely the technique of giving an intravenous infusion; it is enough to note that seven Chinese assistants and senior students quickly mastered the simple routine of injecting a local anaesthetic, sterilizing the skin, and exposing and opening the vein with antiseptic precautions: they learned to administer the saline without permitting the entrance of air bubbles etc. and then ligatured the vein and closed and dressed the wound; the whole being carried out so carefully that not a single case of phlebitis, thrombosis or embolism occurred throughout the epidemic. Save in very thin people the internal saphenous vein, lying just in front of the internal malleolus, was generally selected for the first infusion; or, if that was inconvenient, one of the veins on the back of the hand was chosen. One

assistant was set aside to prepare the saline solution* for injection, and sterilise the instruments as they were brought back from each case. The solution was filtered into glass flasks holding 20-30 ounces each, and these were plugged with sterile wool and boiled for ten minutes. The infusion was administered by means of Horrock's apparatus which consists of a simple glass funnel into which the saline is poured, and a rubber tube through which it makes its way to a cannula which is inserted into the vein. It was found advisable to interrupt this tube a few inches from the vein by the insertion of a simple piece of apparatus which not only acted as a trap for any air bubbles that might otherwise have found their way into the circulatory system, but also enabled the temperature of the saline to be measured as it was about to enter the patient's body. During the height of the epidemic, four complete outfits were required, each consisting of Horrock's apparatus, the necessary instruments, lotions and dressings and the flasks of solution with a spirit lamp and tripod to enable the saline to be warmed to the proper temperature at the bedside.

In actual practise I always paid the first visit to each patient myself, taking the two standard

---

* R. Sodii Chloridi oz. 1
Potassii Chloridi grs. 24
Calcii Chloridi grs. 16
Aquam Distill. ad ozs. 80.

specific gravity bottles and the sphygmomanometer with me in order to determine whether the injection of saline was required and if so by which route - vein, skin or rectum. If the patient was at a distance I was accompanied by an assistant with a complete outfit, so that an injection in any of these three ways could be given at once. Before the administration of the intravenous infusion had been completed, the patient had passed from "the stage of collapse" to "the stage of reaction;" the surface temperature had risen and the patient expressed a desire for more bed clothes.

About two hours later I again visited the patient and took his temperature in the rectum - the only accurate method of measuring the temperature in cholera.* A certain degree of fever was always met with in the stage of reaction, but this cannot be regarded as abnormal for even in the collapse stage the rectal temperature is frequently above normal.** Even in untreated cases the internal as well as the surface temperature usually rises when

---

* Temperatures taken under the patient's tongue were found to be so unreliable as to be worse than useless, and the axillary temperature has been shown to be from 3 F. to 4 F. below the rectal temperature. 41

** This is due to the feebleness of the circulation on the surface of the body which hinders the adequate dissipation of the body - heat that is being continuously generated in the muscles and internal viscera.

the patient enters the reaction stage, and in cases in which an early reaction is artificially induced by the use of saline, this rise of temperature is constant and is much more marked. If the temperature remains above 106°F. for any length of time, the probability is that all efforts to diminish the fever will prove fruitless and the patient will die of hyperpyrexia. If these deaths are to be avoided therapeutic measures must be energetically carried out as soon as the rectal temperature reaches 104°F. It is true that many of these cases might recover without treatment, but as it is impossible to tell in which cases the temperature will subside if left to itself, and in which it will rise to uncontrollable heights above 106°F, it would be unjustifiable to with-hold treatment from a patient who might benefit thereby.

Cold sponging and the application of ice to the head would probably prove the most effective means of reducing the temperature, but in Swatow treatment could only be carried out in so far as it received the approval of the patient's friends, and, as they did not generally approve of cold sponging, etc. it was often impossible to give the patients the benefit of what one believed to be the best treatment. As, however, the administration of an iced enema was entirely beyond their comprehension,

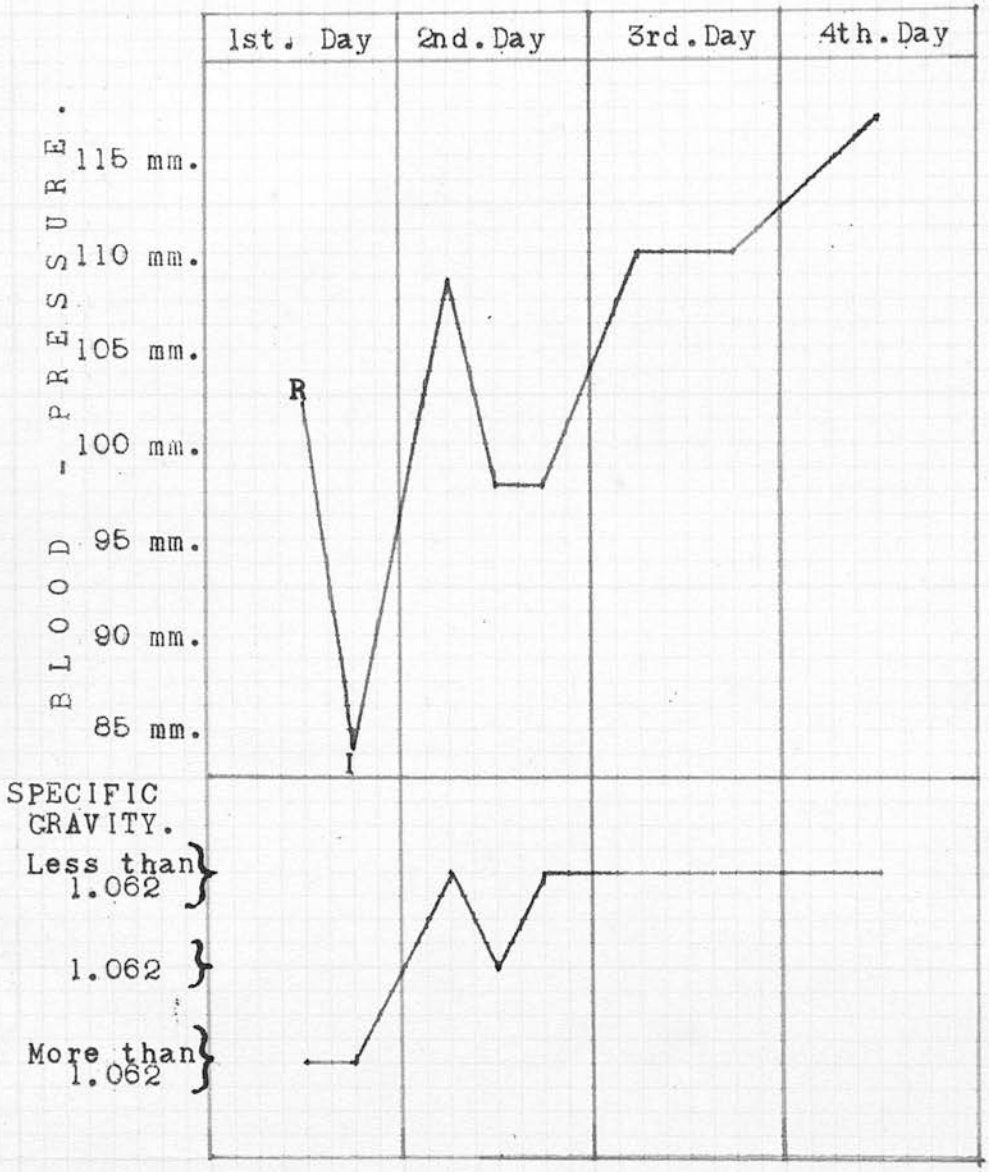
they generally made no objection to this line of treatment, which gave very satisfactory results. The actual method used to reduce the temperature is relatively unimportant; the essential point is that ample warning should be obtained of the threatened onset of hyperpyrexia so as to enable suitable measures to be taken for the patient's relief. If the patients are being treated in hospital, the temperature may with advantage be taken two or three times an hour, but if they are in their own homes such constant watchfulness is impossible; sufficient warning can generally be secured by a visit paid about two hours after the injection has been given. If the temperature does not then exceed 104°F. no treatment will be required and the patient need not be revisited till 4-6 hours later.

On the occasion of this third visit, the blood pressure and the specific gravity must again be measured, and treatment carried out according to the indications thus obtained. The importance of this visit is shown by the fact that, during the first six weeks of the epidemic, in more than one quarter of the patients who had been treated with intravenous injection, the blood pressure subsequently fell so low as to necessitate a second injection within eight hours of the first.

The patient should be visited twice daily for four or five days or until a copious flow of urine and the absence of any disturbing symptoms show that all danger is past. Saline solution must be re-administered whenever the specific gravity of the blood is too high or too little urine is being secreted; but unless the blood pressure is below 100 mm. the saline should be given under the skin or into the rectum and not into a vein. The need for these repeated visits was often exemplified. The accompanying charts (See Figs.V, VI & VII) show the course of illness in three cases:- Case 138, a man of forty with a very mild attack and no complications; Case 129, a young man with a moderately severe attack; Case 115, a man of fifty in whom there was difficulty in securing a sufficient secretion of urine. In the first of these cases no attention was required after the intravenous infusion, but in the others it was only by constant attention that the patients were safely brought through the different dangers that threatened them.

F I G U R E V.

Diagram showing Daily Variations in the Blood Pressure and in the Specific Gravity of the Blood.



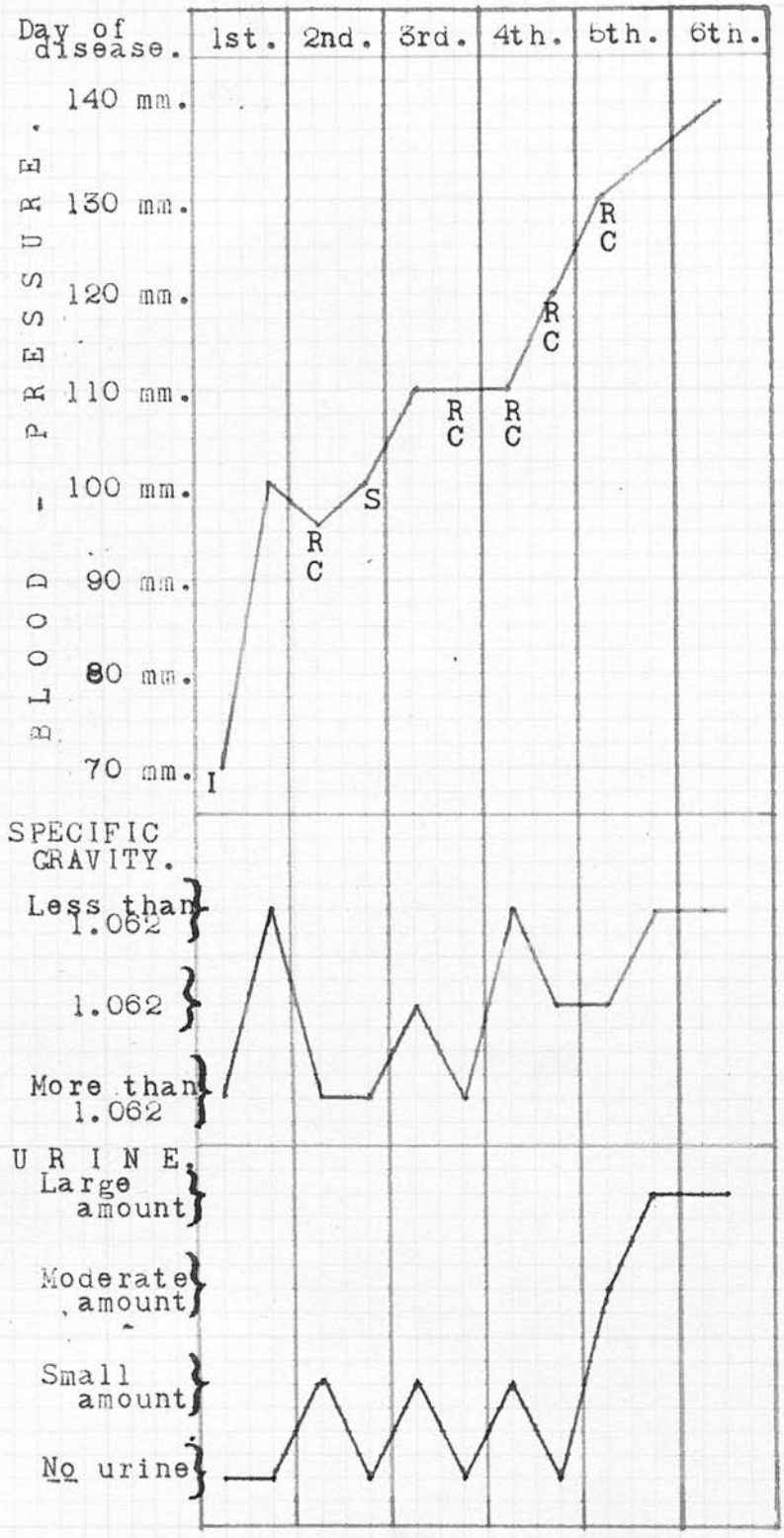
I = Intravenous infusion of 80 ounces of "double-strength" saline solution .

R = The administration per rectum of 30 ounces of "normal" saline solution .

Case No. 138 , male , aged 40 .

F I G U R E VI

Diagram showing Daily Variations in the Blood Pressure and in the Specific Gravity of the Blood.

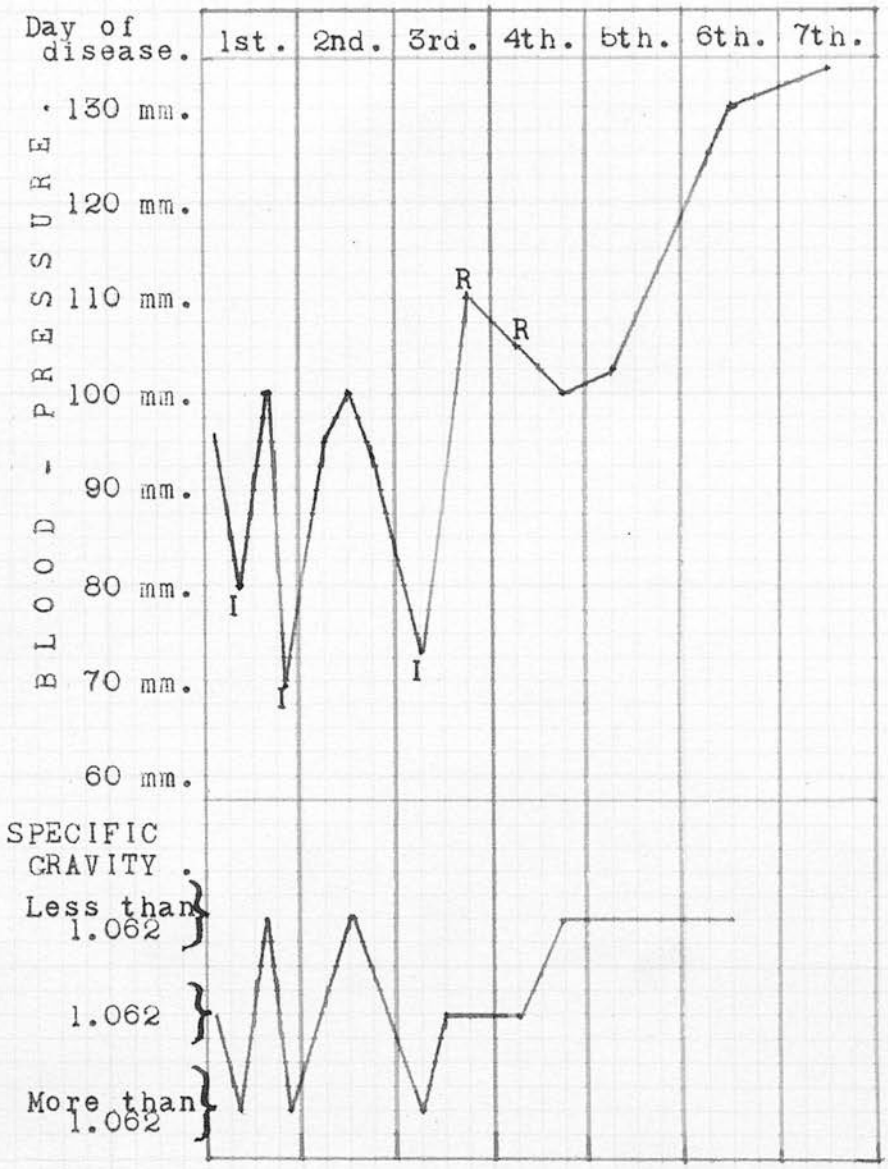


I = Intravenous infusion - as before.
R = Saline per rectum - as before.
C = Dry Cupping over the kidneys.
S = Subcutaneous injection of 40 ounces of "normal" saline solution.

Case No. 115, male, aged 50.

F I G U R E VII .

Diagram showing the daily Variations in the Blood Pressure and in the Specific Gravity of the Blood.



I = Intravenous infusion of 80 ounces of "double-strength"saline solution.

R = The administration per rectum of 30 ounces of "normal"saline solution.

Case No.129, male , aged 26 .

Apart from this use of saline solution very little was done in the way of routine treatment. If the blood pressure was low and the blood was not unduly concentrated, vaso-constrictors were given, either infundibular extract or adrenalin chloride hypodermically or, when all vomiting and nausea had ceased, the fluid extract of apocynum cannabinum by the mouth. The use of the sphygmomanometer showed that the use of these drugs was almost always followed by a rise in blood pressure and an increase in the flow of urine.

After the acute stage of the illness has passed, some patients are troubled with persistence of the vomiting or of the diarrhoea. For the former, cocain,[29] menthol[54] and iodine[55] have been recommended; but in cases treated with large salines the vomiting is rarely so persistent as to require such special treatment. Throughout this epidemic no patient was troubled with long-continued nausea and vomiting, a result that may be attributed, in part at least, to the almost routine use of calomel in doses of one-sixth of a grain every hour. In the few patients who were troubled with frequent small stools so late as the third or fourth day after the onset, immediate relief followed the use of a small starch enema containing one or two drachms of bismuth subnitrate and half a drachm of the tincture

of opium.

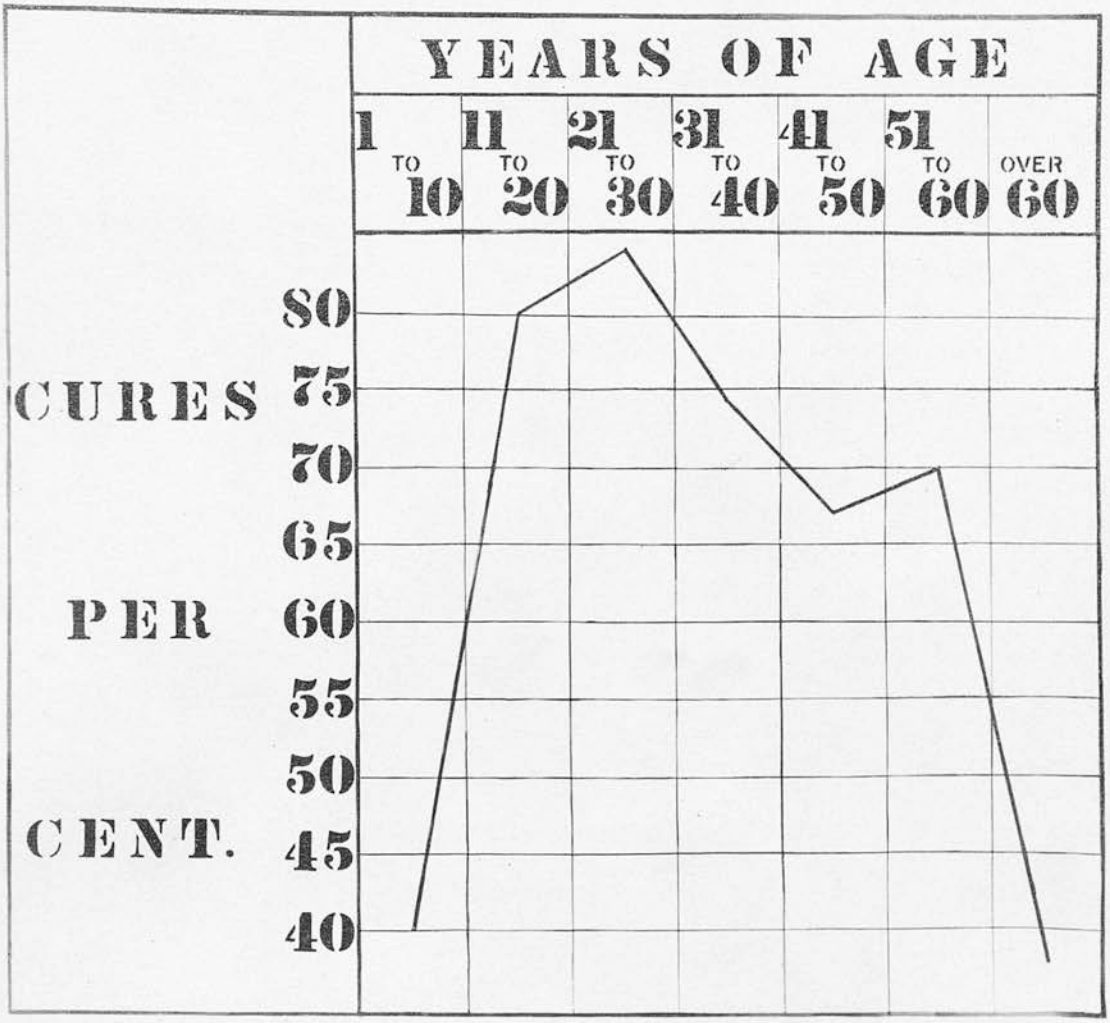
A difficult problem in the treatment of cholera is the question of how to sustain the patient's strength. The persistent vomiting and diarrhoea prevent the giving of nourishment either by the mouth or in the form of nutrient enemata, and even after the vomiting is relieved, the patient has but little appetite and only feeble digestive power. The administration of dextrose dissolved in the saline solution is advisable in very severe cases; for, although it may increase the tendency to hyperpyrexia, it certainly helps to sustain the patient's strength while he is in a very critical condition. The most important point that was insisted upon was that the patients must remain in a recumbent position. The attendants soon learned that any infringement of this rule was likely to be followed by fatal results.

It was on these lines that the Swatow epidemic was treated, and the results varied according to the age, sex, and habits of the patients.

The influence of age in determining the result of treatment is shown in the diagram (Fig.VIII) which gives the percentage of recoveries in each age period. The results obtained in Swatow confirmed the truth of the dictum "Children under ten show a high mortality.... After fifty the prognosis

FIGURE VIII.

SHOWING EFFECT OF AGE ON RATE OF RECOVERY.



is very unfavourable."

The results amongst the women were not so good as amongst the men, death ensuing in one-third of the female and in one-fourth of the male cases. This is partly to be accounted for by the occasional complication of pregnancy which "greatly increases the danger" and partly by the fact that owing to the strictness of Chinese etiquette and the absence of women nurses it was usually impossible to obtain the rectal temperature, so that no sufficient warning could be obtained of the threatened onset of hyperpyrexia. Similarly Chinese etiquette frequently forbade the administration of an iced enema which might have saved the patient's life.

In the case of chronic opium smokers the results were unsatisfactory, for not only was their vitality diminished by long continued indulgence in this habit, but it was found that they were especially liable to develop hyperpyrexia, and if that danger were surmounted there was considerable risk of their succumbing to uraemia.

But it is unnecessary to consider in more detail the results obtained in each of the groups into which the patients might be divided by age, sex, etc. Taking the epidemic as a whole, it may be stated that of the 212* patients who were treated

---

* This number - as has already been stated - does not include the large number of cholera cases in whom, though the concentration of the blood may have required the use of saline, the state of the

(Contd)

with intravenous saline injection 154 recovered, i.e. 72.7%.

It would be unreasonable to contrast this eminently satisfactory figure with the percentage of recoveries obtained in the days before Rogers had published the results of treatment carried out with hypertonic (i.e. "double strength") saline solution; but comparison may fairly be made with the results obtained in epidemics treated since that date.

The following table (Table II) has been prepared from the most recently published reports of cholera epidemics.

TABLE II.

Date	Place	No. treated.	No. of recoveries	Percentage of recoveries	Physician in charge.	
1910	Puglia	14	3	21%	Casbarrini	56
1911	Tunis	688	229	33.2%	Conseil	57
1911	Toulon	466	241	51.7%	-	58
1911	Palermo	67*	40	58.2%	Rogers	59
1911	Calcutta	94*	59	62.8%	Megaw	60
1911	Madeira	319	206	64.6%	Stevens	
1911	Toulon Fleet	18	12	66.6%	-	
1912	Swatow	212*	154	72.7%	Whyte	61

* These figures only include those cases which were so severely ill as to require the intravenous injection of saline.

(Contd.) heart was such that it was not necessary to administer this intravenously; these cases all recovered. 14 patients were taken home before their treatment had been completed. Some of them are known to have recovered, but as in other cases the final result could not be ascertained none of these fourteen is included in the total of 212 cases. On the other hand this figure does include the cases that were brought to the hospital in a moribund condition, for no case was considered too ill to receive treatment, so that there were no deaths in those who remained under our treatment that are not included in these statistics.

In the course of the Swatow epidemic 58 patients died and the main causes of these deaths were, Collapse, Hyperpyrexia, Uraemia and Asthenia.

The following table (Table III) shows the number of deaths that occurred at each age period and the causes to which these were due; for purposes of comparison the causes of death in the Palermo and Madeira epidemics are also shown in the table.

T A B L E III.

Causes of death in the Swatow epidemic compared with the causes of death in other epidemics.

Swatow Patients	Collapse	Hyper-pyrexia	Uraemia	Asthenia	Other causes
Age 1-15	3	8	0	0	1
" 16-40	6	10	2	3	4
" over 40	4	7	5	2	4
Total at Swatow	13	25	7	5	9
Palermo	15	2	7	1	2
Madeira	104	0	2	3	4

These causes must now be carefully examined seriatim so that one may learn how to anticipate, and if possible avert, the tendency to death.

Collapse accounted for death in 6% of the cases treated. In anticipating the probability or otherwise of a patient becoming collapsed great assistance is derived from a reliable history of the duration of the illness. The more acute the onset, the more likelihood there is of the patient becoming suddenly collapsed.

Example: Two members of the same family (Cases 79 and 80) were seen at 9.30 one Sunday morning; one had been ill since the previous evening, and had a blood pressure just below 70 mm., the other had a blood pressure just above 70 mm. but had only been ill since sunrise. Although the blood pressures differed but little, the history showed that the latter patient was more acutely ill and would require closer attention. The subsequent course of the cases showed the accuracy of this judgment, for although both alike received 80 ozs. of saline into a vein, six hours after the former patient had a blood pressure of 86, while the latter was still in a semi-collapsed condition, and the blood pressure remained as before. A second infusion was then administered, raising the blood pressure to 86, and

the patient made an uneventful recovery. This shows that in a patient with a history of rapid onset the blood pressure requires to be estimated at short intervals, till the acute stage has drawn to a close; and in dealing with cases in which no history can be obtained equally frequent observations are required until the rate of progress of the disease has been estimated.

The following extracts from the case records show the rapidity with which the blood pressure may fall, and the consequent importance of taking frequent readings with the sphygmomanometer.

TABLE IV.

Case No.	Sex.	Age.	Hour	Specific Gravity *	Blood Pressure	Treatment
103	M.	49	9 a.m.	-	110 mm.	
			12 noon	+	88 mm.	Intravenous
138	M.	40	6 p.m.	+	102 mm.	Rectal
			9.30 p.m.	+	84 mm.	Intravenous
151	F.	30	2.30 p.m.	-	120 mm.	-
			6.30 p.m.	+	84 mm.	Intravenous
180	M.	42	7 a.m.	-	110 mm.	-
			11 a.m.	+	84 mm.	Rectal
			1 p.m.	+	74 mm.	Intravenous

* The negative sign (-) in this column indicates that the specific gravity of the blood was less than 1.062. The positive sign (+) means that that figure was exceeded.

The lesson taught by such cases is obvious, if death from collapse is to be avoided, frequent

estimation of the systolic blood pressure must be made and intravenous saline must be injected as often as this falls to a dangerous level. I agree with Rogers, however, in acknowledging the impossibility, in spite of all watchfulness, of saving certain extremely virulent forms.

The second great cause of death was hyperpyrexia, which accounted for death in 11.5% of the cases treated. This figure, though high, is a marked improvement on the deathrate from hyperpyrexia (23%) which obtained amongst the Europeans treated in Calcutta from 1895 to 1906 before the use of hypertonic saline solution had been introduced.

If deaths from this cause are to be avoided, careful attention must be given to the composition and amount of the saline solution to be injected and to the temperature at which the injection is to be made. McIntosh and others[62] have shown that the infusion of saline solution, which has been sterilised but from which the dead bodies of the bacilli have not been filtered, is sure to be followed by the development of pyrexia. They suggest that if these bodies are got rid of, little or no fever will result, More recently, however, Hart and Penfold[63] have shown that there may be present, even in bacillus-free water a substance "pyrogen" the injection of which into a patient's circulation will assuredly be

followed by the development of fever: this substance can neither be removed by filtration nor destroyed by heat.[64] A further point is that the saline solution must not be unduly concentrated. Rogers has shown that as a result of raising the saline content of the blood by the use of hypertonic solutions, the tendency of the osmotic currents is to carry fluid from the intestines into the blood stream. Consequently, if the saline solution injected is too concentrated, the salt content of the blood will be raised so high that a dangerously large amount of toxic fluid will be absorbed from the intestines.* Repeated sterilisation of the saline solution by boiling may render it so concentrated as to be dangerous; sterilised distilled water should, therefore, be added after each boiling in order to restore the saline solution to its original volume.

It has been shown experimentally[63] that the greater the volume of fluid injected the greater will be the degree of fever produced, so it is obvious that in order to prevent an undue degree of fever the amount of saline solution injected must not exceed the limit appropriate to each case. Some

* The pyrogenetic power of cholera toxins may be gathered from the frequency with which fever used to be brought about by the re-absorption of the bowel contents consequent upon the sudden checking of the diarrhoea in cholera by large doses of opium.

light is thrown on this question by the table on Page 46 (Table III) which shows that hyperpyrexia was the cause of a larger proportion of the deaths that occurred under the age of 16 than of those at either of the other age periods. In dealing with children it must be borne in mind that the normal blood pressure is low (in a child of 3 it is only 70 mm. of mercury) and varies with each year of age, so that Rogers' standard figure here becomes inapplicable. In view of this variation in the normal one may sometimes be led to administer saline solution to children by the intravenous route when a saline enema would have met the requirements of the case. In such a case even a very small amount of saline may prove to have been too large and hyperpyrexia may ensue.* Further, in those cases in which an intravenous infusion is really necessary, sufficient allowance must be made for the much less body-weight and much smaller circulatory system of children, and a correspondingly small infusion must be given.

In regard to the temperature at which the saline is administered, Rogers[38] has shown that, in the case of patients who are febrile in the collapse stage, hyperpyrexia will almost certainly develop if saline is administered at the ordinary temperature (98-100°F);

---

* It will not be forgotten that the heat-regulating centres are remarkably unstable in small children.

whereas, if the temperature of the saline is reduced to 70-80°F. the fever will in all probability not increase to any dangerous extent.

But even when we have done all that lies in our power to prevent the development of hyperpyrexia, there still remains one difficulty - the presence of pyrogen in distilled water - which has not yet been surmounted. One may hope, however, that ere long the laboratory workers will have conferred upon the clinician the further benefit of showing him how to prepare saline solution which will be free from this substance.

The third main cause of death was Uraemia. Seven patients died from this cause, i.e. 3% of those treated; two of these were under forty years of age, and most were over fifty. To avoid death from Uraemia one must secure and maintain a copious flow of urine, and treatment directed to this end must embrace three distinct lines: the blood pressure must be raised, the concentration of the blood must be diminished, and congestion of the kidneys must be relieved.

The importance of a high blood pressure has been shown by Rogers[38] who found by experiment on kidneys obtained at post mortem examinations that, whereas in normal organs a pressure of 20 to 30 mm.

of mercury sufficed to run a good stream through the renal circulation, yet in the case of kidneys obtained from patients after death due to the uraemic complications of cholera, a pressure of 80 to 100 mm of mercury was required for the same purpose. Theoretically the blood pressure can be raised by intravenous saline infusion, but often the patient seemed too well for such severe treatment, so a drug was prescribed for this purpose. The preparation which yielded the best results as a vaso-constrictor was the liquid extract of Apocynum cannabinum, in doses of 2 minims every three or four hours.

For diminishing the concentration of the blood water must be given - into the vein, or under the skin, into the mouth or into the rectum. When one is dealing with a case of threatening suppression of urine, the less salt introduced into the body the better, so that once the initial collapse stage has been passed, the amount of salt added to the water to be administered should be reduced to its lowest possible limits. If the fluid is for intravenous or subcutaneous use then "normal saline" - i.e. one drachm of salt to the pint - should be employed, while if it is proposed to give the fluid <u>per rectum</u> no salt at all need be added to sterile tap-water.

The third line of treatment in uraemia is to relieve the congestion of the kidneys, and this is best secured by cupping. In many cases this was practised twice daily and although it occasioned some discomfort to the patient the passage of urine, which so frequently followed the cupping, more than compensated him for the discomfort he had undergone. In cases that proved fatal it would have been well if as a last resort the capsules had been stripped off the kidneys, but neither the patients nor their friends would consent to this operation.

Unfortunately, however, the battle with uraemia is not won when the kidneys have begun to secrete a little urine; if the secretion is not maintained, deaths will occur from delayed uraemia. The following may represent the history of a case in which this threatens:- A patient has got over the stage of collapse and has not developed hyper-pyrexia, he has passed urine, the vomiting and diarrhoea have practically stopped and no anxiety is felt either by the friends or the physician, but the patient has little desire for food and his friends do not insist on his taking it; and so day by day less nourishment is taken. The patient does not complain of any discomfort and he still gives a prompt and cheery response to enquiries for his welfare. After a few days a certain delay is noticed in the response;

work of last summer, that many of the earlier deaths would have been avoided if only one had possessed at the beginning of the epidemic the knowledge that one acquired during its course. One can but hope that the knowledge thus obtained may enable one in dealing with future epidemics to achieve even better results than a recovery rate of 72.7%.

B I B L I O G R A P H Y

1. August Hirsch, "Handbook of Geographical and Historical Pathology." London 1883.

2. Livingstone, "Observations on the Epidemic Cholera as it appeared in China" Trans.Med. & Phys. Soc. Calcutta 1825, Vol.1.

3. Home, "Report on the sanitary condition of Shanghai and on the epidemic of cholera which visited that station in 1863" Army Med.Dep., London 1863.

4. Crawford, Rep.Surg.Genl. Navy, Washington, 1897.

5. Manson (D.) "Epidemic of Asiatic Cholera at Amoy" Chin.Imp.Cust.Med.Rep., Shanghai,1877-78.

6. Aldridge, "Asiatic Cholera in Hankow" Chin.Imp. Cust.Med.Rep., Shanghai 1882.

7. Uplersperger, "Die cholera Epidemie zu Macau im Jahre 1862" Aerztl.Intl.Bl., München 1864.

8. Bahier "Formosa et les Pescadores, le cholera pendant l'occupation de ces deux iles 1884-5" Paris 1888.

9. Allbutt and Rolleston, "System of Medicine," Art. Cholera, 1907.

10. Hankin, Ann.de l'Institut Pasteur March & Sept.1896.

11. Klein,Centralb.f.Bakteriol. Nov.5th 1896.

12. Jacobsen, Cen.f.Bakt. Orig.Bd.LVI. 1910.

13. Hankin, Brit.Med.Journ.Dec. 26 1896.

14. Duke, "The Prevention of Cholera and its Treatment" 1905.

15. Moore, Brit.Med.Journ, June 3, 1893.

16. Cornoldi, "La Mosca e il colera" Venezia, 1884.

17. Tsuzuki,A.F. Schiffs u.Trop.Hyg.1904.

18. Ganon, Geneesk Tijdschr v.Nederl.Indie 1908.

19. Chantemesse et Borel "Mouches et Cholera" 1906.

20. Ledingham and Arkwright, "The carrier problem in Infectious Disease" London 1912.

21. Pfeiffer, Klin.Jahrbuch, 1908.

22. Gotschlich, "Report to the Conseil Sanitaire et Quarantenaire d'Egypte."

23. Vay. Journ. Trop. Med. Aug.1 1908.

24. Macrae, Ind. Med. Gaz. Oct. 1909.

25. New York Med.Journ. 1911, Vol.1. p.115.

26. Macpherson, "Cholera in its Home" London 1866.

27. Lewis & Cunningham, "Cholera in relation to certain physical phenomena."

28. Ruffer, Brit.Med.Journ. March 23 1907.

29. Reiche, Medical Annual 1893.

30. Lowe, "Carbolic Acid in Choleraic Diarrhoea" Madras Monthly Journal of Medical Science, 1871.

31. Dobie, "On the use of chlorine in the treatment of Cholera" Edinburgh 1867.

32. Cain, "The use of creosote in Cholera morbus," Charleston Med.Journ & Review,1852.

33. Choksy, Lancet, April 20, 1907.

34. Indian Medical Gazette, December 1905.

35. Nicholson, "Treatment of Cholera with Salol." Ind.Med.Gaz.1889.

36. Basil, Brit.Med.Journ. 24 Sept.1910.

37. Pant, Trans. Bombay Medical Congress, 1909.

38. Leonard Rogers, "Cholera and its Treatment," London 1911.

39. Leonard Rogers, Brit.Med.Journ. Nov.18 1911.

40. Johnson,"Medical Lectures and Essays," Churchill,1887

41. Nothnagel, "Encyclopedia of Medicine" Art. 'Cholera' Liebermeister, English Translation, London 1902.

42. Bradley & Smith, Journal of the Royal Army Medical Corps, August 1912.

43. Latta, Lancet, June 2.1832.

44. Thompson, "Chemical Pathology of Cholera" Philosophical Magazine, May 1832.

45. O'Shaughnessy, Lancet, May 26. 1831.

46. Murphy, Lancet, June 23. 1832.

47. Meikle, Lancet, September 15. 1832.

48. Wright, Lancet, February 9. 1833.

49. Transactions Med.Soc. London, No. 11, 1848.

50. Bushman, "Cholera and its cures" London 1850.

51. O'Meara, Indian Medical Gazette, Oct. 1908.

52. McCay, "Standards of Constituents of the Urine and Blood in Bengalis," Calcutta.

53. Duncan Whyte, "The need for physiological standards in Clinical Research," Trans. Far Eastern Ass.Trop.Med.1912.

54. Marnii, Jour.de Prat, May 16. 1905.

55. Semaine Medicale, October 2. 1907.

56. Gasbarrini, "L'Epidemia Colerica nelle Puglie" Policlinico Oct. 1912.

57. Conseil, "L'Epidemie de Cholera de Tunis et de sa Banlieu pendant l'Annee 1911" Arch.de l'Inst.Pasteur, Tunis 1912.

58. Lancet, Jan. 4. 1913.

59. Megaw, "Note on Major Leonard Rogers' Method of Treatment of Asiatic Cholera," Lancet, Nov. 23. 1912.

60. Stevens, "Analysis of 326 cases of Asiatic Cholera" Brit.Med.Journ. March 25. 1911.

61. Archives de Medecine et Pharmacie Navales, Aug. and Sept.1911.

62. McIntosh and others, Lancet, March 9. 1912.

63. Hart & Penfold, "Micro-organisms and their relation to Fever," Journal of Hygiene, October 1912.

64. Hart, "Vaccines and Fever," Brit.Med.Journ. Feb.8th 1913.

65. Wall, "Asiatic Cholera: its History, Pathology, and Modern Treatment," London, 1893.

66. Pollak, "Ueber die Lebensdauer und Entwicklungsfahigkeit von Choleravibrion auf Obst und Gemüse" Centralbl. f. Bakt. 1 Abt. Orig. 1912 Oct.

A P P E N D I X.

No. of Case	Date	Sex	Age	Specific Gravity of Blood *	Blood Pressures	Results
1	June 2	F.	28	+	?	Recovery
2	" 4	M.	29	+	?	"
3	" 5	M.	58	+	?	"
4	" 6	M.	30	+	?	"
5	" 7	F.	56	+	?	"
	Total for first week FIVE Cases					
6	" 9	F.	42	+	?	Death
7	" 9	M.	52	+	?	Recovery
8	" 11	M.	22	+	?	"
9	" 11	F.	46	+	?	Death
	Total for second week FOUR Cases					
10	" 17	F.	63	+	?	Death
11	" 17	M.	8	+	?	Recovery
12	" 18	F.	40	+	?	Death
13	" 20	F.	47	+	?	Recovery
14	" 21	M.	28	+	?	Recovery
15	" 21	M.	29	+	?	"
16	" 22	M.	52	+	?	"
17	" 22	M.	39	+	?	"
18	" 22	M.	25	+	?	"
19	" 22	F.	29	+	?	Death
20	" 22	M.	10	+	?	Recovery
	Total for Third week ELEVEN Cases					

* NOTE.- + = Specific Gravity over 1.062
++ = " " " 1.066

No. of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
21	June 23	M.	5	+	?	Death
22	" 23	M.	7	+	?	Recovery
23	" 24	M.	10	+	?	"
24	" 24	F.	28	+	?	"
25	" 24	M.	33	+	?	Death
26	" 24	M.	7	+	?	"
27	" 24	M.	28	+	?	Recovery
28	" 24	F.	26	+	?	"
29	" 24	M.	42	+	?	"
30	" 25	F.	28	+	?	Death
31	" 25	F.	33	+	?	Recovery
32	" 25	M.	4	+	?	Death
33	" 25	F.	13	+	?	Recovery
34	" 26	F.	81	+	30	Death
35	" 26	F.	28	+	?	Recovery
36	" 27	F.	32	+	90	Death
37	" 27	F.	33	+	110	Recovery
38	" 27	F.	34	+	35	"
39	" 27	M.	41	+	35	"
40	" 28	M.	47	+	0	Death
41	" 28	M.	28	++	0	Recovery
42	" 29	M.	25	+	85	"
43	" 29	M.	29	+	60	"
44	" 29	F.	18	++	56	"

No. of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
45	June 29	F.	41	+	60	Recovery
46	" 29	F.	38	+	62	"
47	" 29	M.	63	+	0	Death
	Total for Fourth Week			TWENTY-SEVEN	Cases	
48	" 30	F.	14	+	?	Recovery
49	" 30	F.	10	+	20	"
50	July 1	M.	36	+	80	"
51	" 1	F.	9	+	0	Death
52	" 1	M.	71	+	20	Recovery
53	" 2	F.	10	+	0	Death
54	" 2	M.	41	+	0	Recovery
55	" 2	M.	39	+	65	"
56	" 2	F.	43	+	0	"
57	" 3	M.	39	+	64	"
58	" 3	M.	38	+	40	"
59	" 3	M.	6	+	0	Death
60	" 3	M.	53	+	60	Recovery
61	" 3	M.	39	+	80	"
62	" 4	F.	55	+	62	"
63	" 5	M.	6	+	40	Death
64	" 5	F.	38	+	0	Recovery
65	" 5	M.	45	+	62	"
66	" 5	F.	19	+	66	"

No.of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
67	July 5	F.	27	+	0	Recovery
68	" 5	F.	38	+	90	"
69	" 6	F.	20	+	0	Death
70	" 6	M.	13	+	0	Recovery
71	" 6	F.	40	+	94	Death
72	" 6	M.	8	+	40	"
73	" 6	F.	34	+	60	Recovery
74	" 6	M.	28	+	70	"
75	" 6	M.	55	+	60	"
76	" 6	F.	20	+	50	Death
77	" 6	F.	55	+	0	Recovery
	Total for Fifth Week THIRTY Cases					
78	" 7	F.	12	+	60	Recovery
79	" 7	F.	38	+	64	Death
80	" 7	F.	17	+	74	Recovery
81	" 7	M.	13	+	60	"
82	" 7	M.	13	+	54	Death
83	" 7	F.	16	+	72	Recovery
84	" 7	M.	28	+	80	"
85	" 7	M.	38	+	92	"
86	" 8	F.	16	+	94	"
87	" 8	M.	32	+	80	"
88	" 9	F.	13	+	80	"

No.of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
89	July 9	M.	38	+	83	Recovery
90	" 9	M.	19	+	0	"
91	" 9	M.	31	+	0	Death
92	" 9	M.	37	+	60	Recovery
93	" 9	F.	17	+	60	"
94	" 9	F.	33	+	82	"
95	" 10	M.	14	+	90	"
96	" 10	M.	36	+	100	"
97	" 10	F.	48	+	92	Death
98	" 10	M.	50	+	50	Recovery
99	" 10	M.	41	+	96	"
100	" 10	M.	62	+	30	"
101	" 10	M.	30	+	82	"
102	" 10	M.	35	+	0	"
103	" 10	M.	49	+	88	"
104	" 10	F.	8	+	20	Death
105	" 10	M.	26	+	70	Recovery
106	" 10	F.	26	+	65	"
107	" 11	M.	47	+	0	Death
108	" 11	F.	28	+	80	Recovery
109	" 11	M.	20	+	90	"
110	" 11	M.	24	+	80	"
111	" 12	M.	30	+	80	"
112	" 12	M.	28	+	0	Death

No.of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
113	July 12	F.	37	+	70	Death
114	" 12	F.	77	+	42	"
115	" 12	M.	50	+	70	Recovery
116	" 12	M.	22	+	70	Death
117	" 12	F.	37	+	0	"
118	" 12	M.	29	+	70	"
119	" 12	M.	19	+	62	Recovery
120	" 12	M.	21	+	60	"
121	" 13	F.	33	+	72	"
122	" 13	F.	17	+	0	"
123	" 13	M.	50	+	18	"
124	" 13	M.	44	+	0	Death
	Total for Sixth Week				FORTY-SEVEN	Cases
125	" 14	M.	30	+	40	Recovery
126	" 14	M.	36	+	72	"
127	" 14	M.	64	+	72	"
128	" 14	M.	25	+	74	"
129	" 14	M.	26	+	80	"
130	" 14	M.	53	+	50	"
131	" 14	F.	11	+	20	Death
132	" 14	M.	33	+	?	Recovery
133	" 14	M.	29	+	90	"
134	" 15	M.	37	+	16	"

No.of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
135	July 15	M.	12	+	0	Death
136	" 15	M.	38	+	70	Recovery
137	" 15	M.	30	+	0	Death
138	" 15	M.	40	+	84	Recovery
139	" 16	F.	31	+	25	Death
140	" 16	M.	26	+	62	Recovery
141	" 16	M.	36	+	?	"
142	" 16	M.	32	+	56	"
143	" 16	M.	53	+	70	"
144	" 16	F.	44	+	80	"
145	" 16	M.	56	+	62	Death
146	" 17	F.	39	+	74	Recovery
147	" 17	M.	21	+	40	"
148	" 17	F.	26	+	80	"
149	" 17	M.	45	+	0	Death
150	" 17	M.	24	+	72	Recovery
151	" 18	F.	30	+	76	Death
152	" 18	M.	32	+	60	Recovery
153	" 18	M.	37	+	94	"
154	" 18	M.	24	+	100	"
155	" 19	M.	15	+	72	"
156	" 19	M.	50	+	70	Death
157	" 19	F.	40	+	98	Recovery
158	" 19	M.	9	+	40	"

No.of	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
159	July 20	M.	54	+	62	Death
160	" 20	M.	40	+	0	"
	Total for Seventh Week THIRTY-SIX Cases					
161	" 21	M.	13	+	78	Recovery
162	" 22	M.	29	+	70	"
163	" 22	M.	14	+	?	"
164	" 22	M.	45	+	0	Death
165	" 23	M.	27	ǂ	90	Recovery
166	" 24	M.	62	+	110	Death
167	" 24	M.	22	+	96	Recovery
168	" 24	M.	24	+	90	"
169	" 25	M.	14	+	40	"
170	" 27	M.	18	+	70	Death
171	" 27	M.	53	+	30	"
172	" 27	F.	27	+	70	Recovery
173	" 27	M.	18	+	36	"
	Total for Eighth Week THIRTEEN Cases					
174	" 28	M.	36	+	0	Death
175	" 28	M.	41	+	24	Recovery
176	" 29	M.	37	+	40	"
177	" 29	M.	21	+	44	"
178	" 29	M.	43	+	0	Death

No. of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
179	July 29	M.	27	+	68	Death
180	" 30	M.	42	+	74	Recovery
181	" 30	M.	32	+	0	"
182	" 30	M.	35	+	76	Death
183	" 31	M.	26	+	40	Recovery
184	Aug. 1	M.	31	+	70	"
185	" 1	M.	19	+	60	"
186	" 2	M.	47	+	60	Death
187	" 3	M.	31	+	70	Recovery
	Total for Ninth Week FOURTEEN Cases					
188	" 4	M.	19	+	80	"
189	" 4	M.	60	+	50	Death
190	" 5	M.	32	+	60	"
191	" 5	F.	55	+	?	Recovery
192	" 7	M.	42	+	60	"
193	" 7	M.	41	+	80	"
194	" 8	M.	26	+	70	"
195	" 8	M.	27	+	?	"
196	" 9	M.	30	+	70	"
197	" 10	M.	16	+	80	"
198	" 10	M.	49	+	70	"
199	" 10	M.	51	+	80	Death
	Total for Tenth Week TWELVE Cases					

No.of Case	Date	Sex	Age	Specific Gravity of Blood	Blood pressures	Results
200	Aug.11	M.	39	+	80	Recovery
201	" 11	M.	37	+	80	"
202	" 11	M.	34	+	60	"
203	" 12	M.	16	+	?	Death
204	" 12	M.	51	+	60	Recovery
205	" 13	M.	36	+	70	"
206	" 13	F.	27	+	70	"
207	" 13	F.	56	+	80	"
208	" 13	M.	27	+	70	"
	Total for Eleventh Week NINE Cases					
209	" 19	F.	13	+	60	"
210	" 19	M.	17	+	80	"
211	" 22	F.	48	+	70	"
	Total for Twelfth Week THREE Cases					
212	" 26	M.	51	+	76	"
	Thirteenth Week ONE Case					