THESIS

For the DEGREE of M. D., EDINBURGH UNIVERSITY, on

CHOLERA ASIATICA,

CLINICAL OBSERVATIONS on One Hundred and Twenty-five Cases of the DISEASE, with special reference to the Beneficial Effects obtained in its treatment by INTRAVENOUS INFUSIONS of a normal (isotonic) SALINE SOLUTION,

BY

ARCHIBALD LANGHILL, M.B., F.R.C.S. Ed.
GENERAL INDEX.

Introductory remarks. 5

Incidence of cholera, compared with that of other communicable diseases. 6

Variability of the annual incidence of cholera. 13

Variability of the annual case mortality of cholera. 22

Seasonal incidence. 26

Influence of age on the incidence and case mortality. 39

Influence of race on the incidence and case mortality. 42

Influence of Anti-cholera inoculation:-

1) On the case mortality. 44

2) On the degree of severity of a subsequent attack. 52b

3) Relationship between the time which had elapsed since the last anti-cholera inoculation and the severity of the cholera attack (including the case mortality). 55

Influence of the duration of the disease prior to admission to hospital upon the ultimate fate of the cases. 62

Sources of cholera infection. 68.

Symptomatology of the various stages of the disease:-

1) Incubation period. 71.

2) Invasion period (the stage of 'premonitory diarrhoea'). 72

3) Evacuation period (the true choleraic attack). 75

4) Algide period (the asphyxial stage) 108

5) Reaction period. 121
Morbid anatomy.

Diagnosis.

Prognosis:

1. Immediate.

2. Remote.

Treatment:

1. General remarks.

2. The rôle of permanganates.

3. The rôle of atropin.

4. Methods of replacing the fluid and salts which have been lost from the blood:

A. Rectal infusions of saline solution.

B. Subcutaneous (intra-cellular) infusions of saline solution.

C. Intravenous infusions of saline solution:

   a) Indications for.

   b) Some practical points in the technique of the operation.

   c) The quantity of saline solution to be infused.

      i) Average quantity infused at the initial and at each of the subsequent infusions.

      ii) Average quantity infused at all infusions.

      iii) Mortality amongst the infused cases, and the average quantity infused in these fatal cases at the initial and at each of the subsequent infusions.
3.

(iv) Average quantity infused on each occasion in those infused cases which recovered.

(v) Note on the total quantity which may be required in an individual case.

D. Number of cases infused and number of infusions.

(i) Total number of infused cases.

(ii) Number of cases requiring different numbers of infusions.

(iii) Total number of infusions given to the total infused cases.

(iv) Number of infusions given as initial and subsequent infusions.

(v) Average number of infusions given to each of the fatal cases, each of the recoveries, and to the total infused cases respectively.

E. The salt content of the infused fluid:

(i) The advisability of infusing an isotonic rather than a hypertonic saline solution.

(ii) Strengths of the solutions actually infused in the present series of cases.

(iii) Effects of varying strength of the infused fluid:

(I.) On the artificial reaction thereby induced.

(II)
usually

(II). On the mortality as a whole. 241

(III). On the mortality from different causes.

F. The rate at which the saline solution should be infused.

G. The temperature of the infused fluid. 246

H. The duration of the interval between two consecutive infusions.

(5). Diet in Cholera. 258

(6). Treatment by drugs, with special reference to treatment of uraemia by alkalis.

Complications and Sequelae. 265

Causes of death. 274

Case Mortality, both annual, and as a whole. 277

Duration of the patients' stay in hospital, with some remarks on the period of infectivity of cholera. 282

Ultimate distribution of the recovered cases. 287

Summary of conclusions. 289

Concluding remarks. 304

References. 306
INTRODUCTORY REMARKS.

The following observations were made by me while I was serving as a Captain in the R.A.M.C. with the Mesopotamia Expeditionary Force. Shortly after my arrival in Mesopotamia, in May 1916, I was sent up River to Amara, which is a town situated on the left bank of the River Tigris, about 76 miles up River from Basrah.

During 1916, when the British Front Line was situated below Kut-el-Amara, Amara acted as Advanced Base, and was, therefore, from a military point of view, of greater importance than during the following years, when it became merely a station along the long line of communication from Basrah to Baghdad.

There I was attached to a small unit which was, in reality, a detached section of a British General Hospital - namely Section 'D', 2nd British General Hospital. Its function, at that time, was confined to the care of British troops who were suffering from communicable diseases, such as Enteric Group infections, Dysentery, Diphtheria, and the like.

Early/
Early in August 1916, our unit was detailed to take over the treatment of Cholera. This entailed the moving of the whole of the personnel and equipment to what was then known as 'The Cholera Camp', at the same time relieving the Field Ambulance which had been in charge there.

In addition to the care of all Cholera cases, we were to continue to receive all cases of communicable disease - except enteric group infections, and dysentery - occurring in or brought to the Amara area. Both British and Indian troops came under our charge, and accordingly our unit was renamed 'The Isolation Hospital'.

The capacity of the Hospital was 250 beds, 125 beds being allotted to the British Section and 125 to the Indian.

With the exception of four huts (50 beds in all) in the British Section, the whole Camp was composed of tents (E.P.) each tent accommodating 6 beds fairly comfortably.

The four huts in the British Section were far from ideal, from the point of view of the treatment of a disease such as Cholera.

In the first place, they were mere shells of matting made locally, by the Arabs and known as 'chittai'.
'chittai'. The roofs too, were composed of this fragile material and consequently it was possible to spread only a thin layer of mud and straw - (Bhoosa) on top, providing but the slightest opportunity to keep the temperature lower than that of the outside air.

It will be appreciated, therefore, under what adverse conditions those who suffered from high temperatures in the reaction stage of cholera, attempted to pass safely through that critical period of the malady.

As to the staff of the unit, there were at first (up to November 1916), three Medical Officers, including the Commanding Officer, sixteen British Nursing Orderlies, and some eighty Indians (Nursing Orderlies, Ward Boys, etc.).

The nursing of all patients was carried out by men. This, I think, is as it should be, when one considers to what an extraordinary degree the nursing of cholera demands physical strength to move these helpless, collapsed patients.

INCIDENCE/
INCIDENCE of CHOLERA

COMPARED with that of other COMMUNICABLE DISEASES.

Before confining my attention to the subject of Cholera, it will be interesting to tabulate the various diseases and the numbers of cases of each admitted to the Isolation Hospital, Amara, from August, 1916, till the end of 1918.

**TABLE 1.**
<table>
<thead>
<tr>
<th>Diseases</th>
<th>1916</th>
<th></th>
<th></th>
<th></th>
<th>1917</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>1918</th>
<th></th>
<th>TOTAL for the 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EOS</td>
<td>BORs</td>
<td>IOS</td>
<td>IORs</td>
<td>Total</td>
<td>EOS</td>
<td>BORs</td>
<td>IOS</td>
<td>IORs</td>
<td>Total</td>
<td>EOS</td>
<td>BORs</td>
</tr>
<tr>
<td>Arsenical Poisoning</td>
<td>1</td>
<td></td>
<td>31</td>
<td>64</td>
<td>96</td>
<td>1</td>
<td>28</td>
<td>29</td>
<td>4</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilharziasis</td>
<td>2</td>
<td></td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chicken Pox</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>28</td>
<td>29</td>
<td>4</td>
<td>4</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholera Asiatica</td>
<td>4</td>
<td>1</td>
<td>64</td>
<td>31</td>
<td>96</td>
<td>1</td>
<td>21</td>
<td>22</td>
<td>10</td>
<td>29</td>
<td>39</td>
<td>157</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>5</td>
<td>1</td>
<td>26</td>
<td>12</td>
<td>36</td>
<td>2</td>
<td>100</td>
<td></td>
<td>9</td>
<td></td>
<td>9</td>
<td>136</td>
</tr>
<tr>
<td>Dyentery</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>20</td>
<td></td>
<td>5</td>
<td>25</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>Eczema</td>
<td>7</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteric Group</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erysipelas</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
<td>3</td>
<td>4</td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastro-enteritis</td>
<td>10</td>
<td>1</td>
<td>5</td>
<td>10</td>
<td>16</td>
<td>1</td>
<td>3</td>
<td>21</td>
<td>25</td>
<td>35</td>
<td>39</td>
<td>80</td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>German Measles</td>
<td>11</td>
<td>5</td>
<td></td>
<td></td>
<td>5</td>
<td>12</td>
<td>36</td>
<td>4</td>
<td>52</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Heatstroke</td>
<td>12</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leprosy</td>
<td>13</td>
<td>8</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>14</td>
<td>5</td>
<td>4</td>
<td>9</td>
<td>3</td>
<td>7</td>
<td>3</td>
<td>10</td>
<td>2</td>
<td></td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>Measles</td>
<td>15</td>
<td>2</td>
<td>7</td>
<td>21</td>
<td>4</td>
<td>17</td>
<td>16</td>
<td>37</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>52</td>
</tr>
<tr>
<td>Meningitis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebro-spinal fever</td>
<td>16</td>
<td>3</td>
<td>3</td>
<td></td>
<td>3</td>
<td>51</td>
<td>54</td>
<td>57</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute pneumo-coecal</td>
<td>17</td>
<td>2</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute suppurative</td>
<td>18</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td>B.O.</td>
<td>B.O.R.</td>
<td>I.O.</td>
<td>I.O.R.</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>------</td>
<td>--------</td>
<td>------</td>
<td>--------</td>
<td>-------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Mumps</td>
<td>1</td>
<td>27</td>
<td>28</td>
<td>2</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 Plague (Bubonic)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 Relapsing Fever</td>
<td>1</td>
<td>12</td>
<td>42</td>
<td>55</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22 Sandfly Fever</td>
<td>6</td>
<td>20</td>
<td>26</td>
<td>26</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 Scabies</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 Scarlet Fever</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 Scurvy</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 Smallpox</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>79</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27 Tonsilitis (acute)</td>
<td>11</td>
<td>11</td>
<td>6</td>
<td>1</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 Typhus</td>
<td></td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>6</td>
<td>130</td>
<td>89</td>
<td>225</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>230</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>759</td>
<td>1037</td>
<td>33</td>
<td>131</td>
<td>141</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>305</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1567</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B.O. = British Officer.
B.O.R. = Other Ranks.
I.O. = Indian Officers.
I.O.R. = Other Ranks.
It will be seen that, occurring in the list of diseases, there are a few which are not of an infectious nature. Of such are Nos. 1, 2, 7, 12, 14, 22, and 27, and the reason that they were admitted at all is, that in the majority of cases, they were sent in as suffering from one of the strictly communicable affections.

There is no object in this monograph in detailing in each case how such an erroneous diagnosis had been arrived at, but it is interesting and instructive to note here, that those patients suffering from Dysentery, Enteric Group infections and Acute Gastro-enteritis, (Nos. 6, 8, and 10, in Table I.) had been sent to us as possible cases of Cholera. And, in an area where these four diseases co-exist, such mistakes will certainly on a few occasions occur, for sometimes cholera is very closely simulated by these three conditions. Especially is this true with regard to Acute Gastro-enteritis, or, to give it its more generally used title - Cholera Nostras.

To what extent these and other conditions may resemble Cholera, will be discussed more fully under the heading of 'differential diagnosis'.

In Table I. the figures for a certain number of the diseases are not complete for the year/
year 1918, as these statistics were compiled about the month of September of that year. But, from certain notes which I was able to bring home with me in February 1919, I am able to give exact figures for the incidence of Cholera, Acute Gastro-enteritis, and Smallpox, during the whole year, and these are quoted in the Table. Notwithstanding this slight deficiency, the Table is instructive to the reader, as it shows at a glance what proportion the incidence of Cholera bore to the whole, during the two and a half years, - namely, out of a total of 1567 admissions, 157 were cases of cholera (10 per cent).
VARIABILITY of the ANNUAL INCIDENCE of CHOLERA.

TABLE I. shows that during the latter half of 1916, a total of 96 cases of cholera was reached - all being admitted during the acute stage of the disease.

Of these 96 cases, 1 was that of a British officer - who, by the way, recovered, - while 64 cases occurred amongst British troops; 31 Indians were admitted suffering from cholera during 1916.

During 1917, there were admitted a total of 22 cases, only one of these occurring amongst British troops.

During 1918, 10 British cases and 29 Indian cases were dealt with, making a grand total for the two and a half years of 157.

Apart from those admitted during the acute stage of cholera, there was, probably, double that number admitted during the same period in a more or less convalescent state, having been brought down from the Front Area for segregation purposes.

Unfortunately, after a very strenuous but fruitless effort to obtain the case notes, which I had/
had made upon the 31 cases of cholera occurring amongst Indians in 1916, I am compelled to leave these out from the series to be considered in this monograph. The case notes of the British Officer, already referred to, are also not to hand. Leaving out of account, therefore, these 32 cases of the total of 157 cases of Cholera, I have the case notes and Charts of 125, and it is to these that I shall confine my attention in the following pages.

TABLE II. shows what proportion each of the 3 years contributes to the total:

<table>
<thead>
<tr>
<th>YEAR</th>
<th>BRITISH</th>
<th>INDIAN</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1916</td>
<td>64</td>
<td>-</td>
<td>64</td>
</tr>
<tr>
<td>1917</td>
<td>1</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>1918</td>
<td>10</td>
<td>29</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>75 +</td>
<td>50</td>
<td>125</td>
</tr>
</tbody>
</table>

It will be seen that the year 1916 contributes by a very large majority to the total, and if to its quota were added the 32 cases already referred to, along with the cases dealt with by our predecessors, i.e./
i.e. up to the beginning of August - the very marked incidence of cholera in 1916 as compared with that in 1917 and 1918, becomes all the more striking.

In explanation of this, one might put forward the following as factors:

(a) The fact that before the British advance to Baghdad in the early months of 1917, Amara was the Advanced Base of the Expeditionary Force, and, therefore, there was probably, a greater number of troops in the station than during the following years.

(b) Although every year the climatic conditions during the hot season in Mesopotamia are trying, there is no doubt that in 1916, when our Force was slowly but surely increasing in numbers, the arrangements for their proper accommodation, protection from the fierce heat of the sun, a pure water supply from wells, and even, in some cases, a food supply sufficient and suitable to maintain health, were lacking.

(c) Not until the latter part of 1916 was Anti-cholera Inoculation practised on an extensive scale; moreover, on account of the only too apparent futility of the earlier inoculations in reducing both the incidence and the case mortality, it was decided to use a vaccine which had been /
been prepared from the Mesopotamian strain of the Cholera vibrio. (See page 45). To what actual extent, anti-cholera inoculation influenced the incidence of cholera amongst those so treated, I am unable to state, but its influence in reducing the mortality amongst those who, in spite of it, became infected by Cholera, will be discussed later.

(d) Lastly, it is unfortunately the case that, during the hot weather of 1916, cholera broke out amongst the patients in certain other medical units, and that these outbreaks accounted for as many as 51 of the 64 admissions into the British Section.

No fewer than 48 of the 51 cases were admitted during the comparatively short period 24-8-16, to 4-9-16.

These 48 cases were drawn from two hospitals in Amara, one of these sending us 18 cases, while the other contributed the remaining 30.

The source of the infection in the case of the first hospital was, I understand, never discovered, but, owing to the circumstantial and bacteriological evidence, the milk supply of the second hospital was incriminated.

It/
It is worth recording both how the milk came to be infected and how it was allowed to be distributed to patients in an otherwise well conducted hospital. It can readily be imagined how, in a country such as Mesopotamia, where the Front and lines of communication are dependent entirely on the River as a means of transport of food supplies, - as they were during 1916 - every effort was made to ease the transport difficulty by drawing on local resources when these could supply desirable, and indeed, essential articles of diet. Milk was, of course, one of these, and, to supplement the available supplies of tinned milk, a large quantity of fresh milk was purchased daily from the natives, - Arabs. Naturally, instructions were issued to the hospital cooks that all milk must be boiled before it left the cook house for consumption, and they were warned of the disastrous consequences, should they neglect these instructions. Milk has been the source of cholera in other epidemics, and this is little to be wondered at, as it provides an almost ideal culture medium, provided it is still in a fresh state; for the cholera vibrio is not robust and quickly dies out once the milk "turns", owing to the lactic acid ferment. There are various ways in which the milk supply might/
might have become infected.

1. The Arab dairyman is doubtless as alive as the dairyman in other countries, to the fact that his income will increase as he increases the bulk of his supplies by judicious watering, and this he certainly did, as was proved time and again by the lactometer and other tests. When detected, the faulty milk was rejected. But if dilution of the milk were carried out, even to the slightest extent with polluted water - and the Arab knows none other - it is not difficult to see how the vibrio should multiply rapidly in the diluted article and in a short time provide a lethal source of infection.

2. The Arab dairyman, and any other person handling the milk, might themselves have been 'carriers' of various kinds, e.g. ambulatory, precocious, convalescent, chronic, etc. Contaminated hands, therefore, might easily infect the milk itself or the receptacles.

3. Pollution of the receptacles by washing them in infected water.

4. Lastly, infection of the milk by flies. These pests are everywhere in the tropics, and it requires the utmost care and vigilance to protect milk and other articles of diet from them.

In whichever one of these ways infection
of the milk occurred, the fact remains that it was the locally obtained supply which was ultimately found at fault. The rest of the story is short and sad in the extreme, for the cook, on whom the responsibility for the thorough boiling of the milk rested, neglected to obey orders, with the result that 30 of the patients in that hospital contracted cholera and were transferred to the Isolation Hospital, most of them in a terribly collapsed state; of these 30 cases, 13 ultimately died.

One might also note, in passing, that of the 18 cases admitted from the other hospital, 8 deaths occurred.

Thus 21 deaths out of the total of 24 deaths of this 1916 series, are accounted for. The remaining 3 deaths occurred in cases of men who were presumably, in a more or less fit condition when the symptoms of cholera set in. As to the effect which the superadded infection of cholera on top of a previously debilitated state had, on the case mortality, I shall again refer to later, at greater length.

In contrast to the conditions which held in 1916, the hot seasons of the two following years provided, not only a distinct fall in the incidence of cholera, but, in addition, a very marked lowering of the case mortality. That is to say, during the cholera/
cholera seasons of 1917 and 1918, the conditions were less favourable to an extensive spread of the disease, and very distinctly in favour of recovery amongst those who chanced to become infected.

Briefly, these improved circumstances fall under four headings:-

(i) Fewer Troops in the Station:-

After the British occupied Baghdad on 11th March, 1917, the importance of Amara as a Military station diminished very considerably, and, in consequence, there was not the same concentration of troops in the district as held in 1916.

(ii) Improved Sanitary Arrangements:-

After the 'Mesopotamian Scandals' of 1916, enormous improvements were effected with regard to the quarters provided for both officers and men. Substantial hutments were substituted for tents, wells providing a pure water supply were sunk by each individual unit, and, latterly, a well-appointed town water supply, conducted by pipes to several of the larger units, was introduced.

Other comforts, such as soda-water factories, and ice factories, did a great deal to reduce the discomforts of the very trying hot seasons of 1917 and 1918, and to maintain the health of the troops at a higher level than formerly.

(iii)/
(iii). *Anti-cholera Inoculation:*

This was much more widely practised, and a more potent vaccine was employed, during the years 1917 and 1918.

(iv). *Resistance of the Individual:*

Although, in a few cases, infection of men already in Hospital - and, therefore, with lowered vitality - did occur in 1917 and 1918, yet no such wholesale spread of cholera occurred in hospitals as was the case in 1916.
VARIABILITY of the ANNUAL CASE MORTALITY
During the three Years.

The high incidence of Cholera in 1916 has been accounted for, and as the case mortality of the three years is intimately associated with the incidence, it might be wise, even at this early stage, to discuss the former.

TABLE III, shows not only the high incidence in 1916, but also how very much more fatal the disease proved to be in that year. Apart from the influence of anti-cholera inoculation, slight changes in the mode of treatment etc. to account for the very decided fall in the case mortality in the later years - viz; - 18.18 per cent in 1917 and the extraordinary low figure of 10.25 in 1918 - it must be remembered that out of the total of 64 cases admitted in 1916, no fewer than 51 were already in a distinctly debilitated state, and when the onset of cholera occurred, were under treatment in other hospitals. Some of these men were already in the poorest possible condition to resist such a virulent disease as cholera. They were in many cases anaemic/
anaemic and emaciated to a degree, having been confined to bed for weeks, suffering from such affections as dysentery, paratyphoid, malaria, various septic states.

TABLE III.

<table>
<thead>
<tr>
<th></th>
<th>BRITISH</th>
<th></th>
<th>INDIAN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Dths.</td>
<td>Case</td>
</tr>
<tr>
<td>1916</td>
<td>64</td>
<td>24</td>
<td>37.5%</td>
</tr>
<tr>
<td>1917</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>1918</td>
<td>10</td>
<td>1</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>26</td>
<td>34.6%</td>
</tr>
</tbody>
</table>
TABLE IV. shows at a glance how many were already suffering from some other complaint when cholera became super-added; it also shows in many cases, what the nature of that previous malady was, and how it affected the case mortality. The exact nature of the original malady has, unfortunately, not been inserted in the notes in 21 cases, but, like the others in this series, there is no doubt that the majority were much reduced in general vitality, accounting for the very high mortality (nearly 50 per cent,) amongst these.

In only 13 cases, did the onset of cholera occur, while the men were fit enough to be able to do duty.

Taking into consideration the low resisting power of the 1916 series, as a whole, the wonder is that the case mortality (37.5 per cent) is not even higher.
### TABLE IV.

**CASES & DEATHS IN 1916**

<table>
<thead>
<tr>
<th>PREVIOUS DISEASE</th>
<th>CASES</th>
<th>DEATHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ANAEMIA &amp; DEBILITY.</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>DIARRHOEA.</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>DYSENTERY</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>ENTERIC GROUP</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>FURUNCULOSIS</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>GASTRITIS</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>HEAT EXHAUSTION</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>INSANITY (Delusional)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>JAUNDICE</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>MALARIA</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>SEPTIC FINGER</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>SYPHILIS</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>NATURE OF ILLNESS NOT NOTED</strong></td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td><strong>NO PREVIOUS DISEASE</strong></td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>64</td>
<td>24</td>
</tr>
</tbody>
</table>
SEASONAL INCIDENCE.

The study of the epidemiology of Cholera in the Tropics, proves that, with few exceptional instances, the outbreaks of the disease are most violent during the hotter months of the year, provided that the conditions of both temperature and moisture are favourable to the continued existence of the vibrio as a saprophyte - i.e. outside the body.

It is known that the vibrio is, after all, a feeble organism, and exerts but a trifling resistance to circumstances in its environment, which are not suitable. Of such, desiccation is, probably, the most injurious to the life of the germ. This drying process is brought about very rapidly and thoroughly in tropical countries such as Mesopotamia, and the greater part of India, and if it should be allowed to come into operation - as when the highly infective dejecta of cholera patients are exposed for quite a short time to the scorching heat of sun, the vibrio is quickly killed. Thus the possibility of individuals contracting the disease from dust swept up into the air by the wind, by fans and other agencies is negatived. Such a state of affairs holds good in Mesopotamia to a very high degree. Why/
Why, then, when one comes to consider the incidence of the disease, as illustrated by these 125 cases, is it found that like most other epidemics, the disease is so much more prevalent during the hottest and dryest months of the year?

In Mesopotamia - speaking generally - the atmospheric temperature begins to rise appreciably during April, and this increase is steadily maintained through May and June, until a maximum is reached in July, when the heat is intense. It will give the reader some idea of how fierce is the heat of the sun when I state that, on several occasions, shade readings of 130° F. were attained in my own tent on several occasions during the months of June, July and August, which are always the most trying months of the year.

There is an appreciable fall of temperature in September, and October is still cooler. Not until November can the weather be truly described as cold. The coldest months of the year are those of December, January and February. March ushers in the hot season, which progresses throughout the following seven months, the acme being reached in July, as already described.

Referring to the present series of cases, it will be seen from the graphs on page (28) that I have plotted out the admissions during the three years on three separate Charts.
CHART I.

SEASONAL INCIDENCE of CHOLERA in YEAR 1916.

(64 BRITISH CASES).
CHART II.

SEASONAL INCIDENCE of CHOLERA in year 1917.

(22 BRITISH and INDIAN CASES).
CHART III.

SEASONAL INCIDENCE of CHOLERA in YEAR 1918.

(39 BRITISH and INDIAN CASES).
Each month has been subdivided into five separate portions (vertical columns) each of the first four columns representing a weekly portion, the remaining column representing the few days required for completing the calendar month after the 28th day, a period which, of course, varies according to the particular month under consideration. None of the series was admitted before the fourth week in May (25-5-1917), although it has to be remembered that I have already explained why I am unable to supply any information regarding the incidence of Cholera in Amara prior to August 1916.

The latest date on which a case of Cholera occurred was during the second week of December - (9-12-17). So that, as far as this series is concerned, Cholera prevailed for a longer spell during 1917 than during the preceding or ensuing years.

During 1916, the very high incidence shown on the Chart for the ten days 29th August to 7th September (a total of 51 Cases), is accounted for by the patients in two neighbouring hospitals, to which I have already referred. (See p. 16). (Of these 51 Cases, 44 were of the 46 Cases which came from these hospitals.)

In Chart IV. the number of admissions each day during this ten days' period are plotted out, from/
from which it will be seen that within 48 hours no fewer than 26 cases were admitted. Such a rapid influx of profoundly collapsed patients, taxed the resources of our small unit to the utmost, more especially when the cases arrived in batches of five or more, and all required immediate intravenous infusions of saline solution.

During 1917, the greatest number of admissions occurred in July (10 Cases), while in 1918, June shows the highest incidence (17 Cases).
CHART NO. V. gives the sum of the admissions of Cholera Cases in separate months for the three years 1916 to 1918.

CHART V.

SEASONAL INCIDENCE of CHOLERA ADMISSIONS during the separate months for the three years 1916, 1917, and 1918.

(125 CASES).
These statistics, therefore, support those of other observers in that they prove that cholera is most prevalent during the hottest season of the year. Certainly, the influence of temperature on the saprophytic life of the vibrio is of great importance, as it is only during those months which are associated with high thermometer readings that the temperature is favourable to the continued existence of the vibrio outside the body. But, to come to a well-reasoned conclusion, as to the effect of season upon incidence, one must remember that the question is not merely one of temperature, but that, intimately associated with this factor, is the question of atmospheric and ground moisture.

There is no doubt that in Amara, at any rate, the surface soil is absolutely dry and parched for quite 6 months in the year (May to October). The first rains appear towards the end of October or early in November and continue irregularly till April. It thus follows that cholera is prevalent when temperature is at its maximum and moisture is at its minimum. At first sight, this seems rather inexplicable, since we know that moisture is essential to the extra-corporeal existence of the vibrio. These facts, however, are easily reconciled, for although the moisture, both atmospheric and in the ground, is at its minimum during the hottest months, the subsoil/
soil water is really not more than a few feet from the surface, even though soundings be made at a considerable distance from the banks of the rivers and canals. The soil is alluvial, and the whole country is perfectly flat. The conditions, then, are practically identical with those obtaining in certain low-lying districts of India where cholera is rife. Davidson in his article on Cholera in the "Encyclopaedia Medica" states:

"Cholera shows a special predilection for the low lying parts of a town. Farr laid it down as a law 'that the proportion of deaths from cholera is inversely as the elevation of the ground'. As an endemic disease, cholera is limited to altitudes not exceeding 1,500 feet."

From the points of view of both temperature and moisture, therefore, the high incidence of cholera during the hottest months can be explained.

The explanation for the gradual disappearance of the disease, during the cold and wet months of the year, rests on the same two factors but, in exactly opposing directions, for, while the incidence of the disease varies directly with the temperature, it varies inversely with the moisture of the ground soil. We know that a certain degree of moisture is essential, if the vibrio is to survive/
survive at all. Such is present in sufficient amount during the greater part of the year in Mesopotamia. But after the onset of the rains, the ground being low lying, soon becomes water-logged and for quite 5 months (November to March) the countryside becomes a veritable quagmire. To quote again from Davidson's article (Encyclopaedia Medica):

"The inability of the vibrio to live for any length of time in fluids deficient in nutritive material, as well as the effect of excessive moisture of the soil in reducing the oxygen at the disposal of the organism, explains the subsidence of the disease in endemic areas when the heavy rains dilute the water in tanks and wells, submerge large tracts of land, and displace the air from the soil that remains uncovered".

In addition to the facts already given regarding -

1. Temperature
2. Moisture
to explain the high incidence of cholera during the hot season in Mesopotamia, one might very rightly add -

3. During the hot season, the River Tigris runs/
runs very low in comparison with its volume after the onset of the rains. In consequence, the chances of infection from water obtained from this source is proportionately increased. The Arab knows no other source of drinking water, and since he takes no steps to sterilise it before he himself consumes it, it is not likely that he will abstain from using it in its original state for other purposes - for example, the washing of feeding utensils, dilution of milk for selling purposes, the keeping of fruit and vegetables in a 'fresh' state by submerging these overnight in polluted water. I shall speak of this again later under "Sources of Infection".

With the establishment of the rains, however, - and this a heavy rainfall over a comparatively short wet season - conditions are vastly changed; The volume of water in the Tigris is probably doubled during the rains, and this is most apparent after the melting of the snow on the mountains nearer its source, sets in. Dilution of the vibrios occurs as a result. Again, the heavy rainfall and the accompanying rise in the ground water level flush out storage tanks and wells and so diminish very considerably the chances of individuals swallowing a potent dose of the virus of cholera.
4. The broiling heat during the hot months provokes intense thirst, and the daily consumption of fluids by the individual is enormous. If a pure water supply is not forthcoming at frequent intervals it can be imagined how great is the temptation to run the risk of even cholera, by partaking from a polluted source.

5. The rôle played by flies as vectors is possible only during the hotter months. For quite 3 or 4 months during the cold season, one never sees a fly. This is in marked contrast to what obtains during the hot weather. With the filthy native quarters so close at hand, innumerable breeding grounds are afforded for these death-dealing insects. Numerous observers have proved beyond question that the cholera vibrio does continue to live during and after its passage through the alimentary canal of flies which have fed upon either the vomit or stools of cholera patients. Both PASSEK and BARBER have found that the vibrio of cholera may be recovered from the intestines of the fly, as long as 72 hours after feeding the insect on infected material. Not only by the regurgitations and excrement of these creatures may they inoculate food stuffs, but it is quite possible for them to actually convey the virus on their exterior (e.g. fouled feet) to food stuffs, after/
after they have alighted on material containing the germ.
Since these 125 Cases were drawn from amongst men of military age, it is obvious that little useful information will be obtained by an analysis of the prevalence and mortality of cholera as it affected the different age periods. However, for the sake of completeness, Table No. V., has been compiled. The age of the youngest patient admitted suffering from cholera, was 18 years, while the oldest patient was 46 years. For convenience, and in order to compare my statistics with those supplied by Rogers (2), the cases have been subdivided according to the particular decade in which each should be placed. Consequently four decades come under consideration, viz: - the age periods: 11 to 20, 21 to 30, 31 to 40, and 41 to 50.

It will be seen that I am unable to supply the ages of 13 of the patients. This is due to the fact that in some few cases, the patient himself did not know his age - even approximately - and in the remainder, it was impossible to converse with them, owing to our being unable to obtain the services of an appropriate interpreter. Practically all of the 13 cases were those of men from the most out-lying districts of India and, in a few cases, were Kurds.
TABLE NO. V.

<table>
<thead>
<tr>
<th>Writer's Series</th>
<th>Rogers's Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st Series</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td>11-20</td>
<td>25</td>
</tr>
<tr>
<td>21-30</td>
<td>61</td>
</tr>
<tr>
<td>31-40</td>
<td>23</td>
</tr>
<tr>
<td>41-50</td>
<td>3</td>
</tr>
<tr>
<td>?decade</td>
<td>13</td>
</tr>
</tbody>
</table>

Note: The table shows the distribution of cases and deaths in different age groups for Writer's Series and Rogers's Cases, with a comparison between the 1st and 2nd Series.
Referring to the TABLE, although one is compiling statistics from a trifling number of cases in comparison with the material at ROGERS' disposal in Calcutta, it is nevertheless curious that, confining our attention to the same four decades in the two series, the case mortality varies in exactly opposing directions, for ROGERS' figures show very distinctly that, in his own words:

"... the lowest mortality occurs in the second decade from 11 to 20 years of age, and it steadily rises with each subsequent decade to reach an exceptionally high figure among those of over 50 years of age".

My series shows entirely contradictory results in that the case mortality for the 11 to 20 decade is highest, and that the case mortality diminishes as the decades progress. I am unable to put forward any theory to explain these antagonistic findings,

INFLUENCE/
INFLUENCE of RACE on the CASE MORTALITY.

Since I am unable to furnish figures to give an idea as to the relative numbers of the different races from which the cholera cases were drawn, it is possible only to state how the members of the different races fared after they became infected.

In TABLE NO. VI. this is demonstrated.

<table>
<thead>
<tr>
<th></th>
<th>TOTAL CASES</th>
<th>DIED</th>
<th>CURED</th>
<th>RACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindus</td>
<td>27</td>
<td>(3=)11.1%</td>
<td>88.9%</td>
<td></td>
</tr>
<tr>
<td>Mohammedans</td>
<td>23</td>
<td>(3=)13.0%</td>
<td>87%</td>
<td>See Roger</td>
</tr>
<tr>
<td>Europeans</td>
<td>75</td>
<td>(26=)34.6%</td>
<td>65.4%</td>
<td>p.145%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>125</strong></td>
<td><strong>25.6%</strong></td>
<td><strong>74.4%</strong></td>
<td></td>
</tr>
</tbody>
</table>

With reference to the influence which Race exerts on the Case Mortality of Cholera amongst the people in Calcutta, ROGERS states:

"... figures show the highest mortality among Hindus/"
Hindus, who are so largely vegetarian in their diet, a slightly lower one among flesh-eating Mohammedans with slightly greater resisting powers, and a still lower one among Europeans and Eurasians with greater stamina and longevity.

The knowledge gained from the above Table is instructive only, so far as the present series is concerned, and these results must in no way be compared with those of Rogers, firstly, because the whole aspect of the question is altered by the unusual state of affairs, which held amongst the British patients in 1916, and, secondly, the very small number of cases admitted to the Indian Section - (only 50 Cases in all) hardly provides sufficient material from which to gain an accurate idea of the mortality amongst Hindus and Mohammedans.

It will be observed, however, that, again, these figures are, in every respect, contrary to what has been found from the study of this particular point, over a very large number of cases of the disease.
Influence of Anti-Cholera Inoculation on the Case Mortality.

I have already pointed out that owing to the apparent failure of inoculation during the earlier stages of the campaign in Mesopotamia, in mitigating both the incidence and the fatality of cholera, an 'autogenous' vaccine was subsequently prepared for administration.

The cholera vaccine employed in 1916 was put up in 50 c.c. bottles, each c.c. of vaccine containing 4,000 million microbes. Two injections at an interval of from 7 to 10 days was recommended to be given, the first of $\frac{1}{2}$ c.c. and the second of 1 c.c.

As in anti-typhoid inoculation, a reaction, manifesting itself in malaise, slight fever, and a local inflammation, might be expected; these, however, were very much less pronounced with anti-cholera than with anti-typhoid inoculation. To lessen the inconvenience arising from such symptoms, it was recommended that the injections be given before the treated person retired to rest.

The injections were given subcutaneously, suitable sites being beneath the middle of the clavicle/
clavicle, or the arm at the level of the insertion of the deltoid.

Instructions were issued to all medical officers to record each inoculation on the inside right-hand cover of Army Book 64 (Soldier's Pay Book) as follows:

(1st injection) \( \frac{\text{Ch.V}}{1} \) - date - initials of Medical Officer.

(2nd injection) \( \frac{\text{Ch.V}}{2} \) - date - initials of Medical Officer.

The afore-mentioned vaccine was used up till March, 1917, when a fresh vaccine was introduced. This was again put up in 50 c.c. bottles, and the doses were, as before, \( \frac{1}{2} \) c.c. and 1 c.c. respectively. But it differed from the 1916 vaccine in two respects.

(1) Each c.c. of vaccine now contained 8000 million microbes.

(2) It was prepared from the actual Mesopotamian strain of the cholera vibrio.

It will, therefore, be apprehended that this later vaccine was likely to provoke a more intense immunity to cholera than was its predecessor.

Amongst the present series, it is possible that a very few cases amongst those tabulated under the heading of "No history of protective anti-cholera inoculation available" - had actually received such protection, but, owing to the fact that no such information was definitely stated in the man's pay-book or other document, and, as is usually the case, the man himself was uncertain what the nature/
nature of any injection which may have been administered to him, really I have included under those so protected patients, only those, from the pay-books of whom definite records of anti-cholera inoculation could be obtained.

To the third category - namely "Never inoculated" - are relegated all those concerning whom such information is known to be definitely true; of such are 'conscientious objectors' and a few Arab and Persian coolies from neighbouring Labour Corps.

Owing to the importance which was attached even from the earliest days of the War, to the immediate and accurate filling in on the inside of the cover of the soldier's 'pay-book' of all information concerning protective inoculations of various kinds - e.g. against small-pox, enteric group, infections, cholera, and the like, I feel certain that the vast majority of those men, whose paybooks showed no record of their having received prophylactic inoculation, did never receive such protection, and should rightly be included under the category "Never inoculated" in the accompanying tables.

Nevertheless, in order that the whole question be gone into thoroughly, I have drawn up in the first of the tables - TABLE NO. VII. - a detailed analysis of the cases, to indicate how
## TABLE VII

<table>
<thead>
<tr>
<th>125 Cases</th>
<th>Inoculated</th>
<th>Recovered</th>
<th>Died</th>
<th>Survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1919</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1920</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1921</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1922</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1923</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1924</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1925</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1926</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1927</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1928</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1929</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1930</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: No. VII
the mortality occurred amongst British and Indian patients during the different years, as classified according to the above-mentioned three categories.

It is seen that, even in 1916, when grave doubts were cast upon the efficiency of the anti-cholera vaccine, there is a very striking difference between the mortality amongst the inoculated, (13.8 per cent) and that amongst patients with no record of having received inoculation (79.1 per cent). It is true that of the four cases on whom inoculation was definitely not practised, no deaths occurred, but the number is so small that this fact can be disregarded.

What has just been stated with regard to the 1916 cases is shown by the Table, to apply also to the 1917 cases, though the disparity is less pronounced.

The 1918 cases, both British and Indian, would seem to demonstrate in no undecided manner, that, although, as already stated, these figures give almost no indication how effective anti-cholera inoculation may be in preventing the disease from occurring, the administration of this vaccine does materially influence the prognosis for the better, amongst those who, in spite of it, contract the disease.

It is of great interest that of the 10 British
cases which occurred in 1918 (See TABLE VII.) only one death occurred - that of a man in whose pay-book was recorded the fact that he was a 'conscientious objector' to Anti-cholera Inoculation'. The eight men who definitely had been inoculated, all recovered, as did the 1 man with no record.

The Indian cases in 1918 also show results which are in favour of inoculation.

The left hand half of TABLE NO. VIII shows how the mortality amongst the total cases (125) was affected under the three categories.

Assuming that practically all those patients with no record of inoculation were never protected in that way - and one may rightly do so, I am convinced - it is permissible to combine the 'no record' cases with the definitely 'not inoculated', This has been done, and the result is shown on the right hand side of TABLE NO. VIII. - namely a mortality of only 10.6 per cent amongst the inoculated, and the high figure of 42.5 among the uninoculated.

If one takes these statistics and studies them only from the point of view of the relationship between inoculation history and mortality, a conclusion must be inevitably arrived at that an increased power/
### TABLE NO. VIII

<table>
<thead>
<tr>
<th></th>
<th>TOTAL CASES</th>
<th>TOTAL DTHS.</th>
<th>CASE MORT.</th>
<th>TOTAL CASES</th>
<th>TOTAL DTHS.</th>
<th>CASE MORT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoculated</td>
<td>66</td>
<td>7</td>
<td>10.6</td>
<td>66</td>
<td>7</td>
<td>10.6</td>
</tr>
<tr>
<td>No information re Anti-Cholera Inoculation</td>
<td>42</td>
<td>22</td>
<td>52.3</td>
<td>59</td>
<td>25</td>
<td>42.3</td>
</tr>
<tr>
<td>Never Inoculated</td>
<td>17</td>
<td>3</td>
<td>17.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td>125</td>
<td>32</td>
<td>25.6</td>
<td>125</td>
<td>32</td>
<td>25.6</td>
</tr>
</tbody>
</table>
power of resistance is afforded by anti-cholera inoculation to those who contract the malady.

But it is worth recording here that such eloquent testimony to the potency of anti-toxin inoculation in reducing the case mortality has not always been forthcoming from other observers. ROGERS states that:

"The published statistics regarding the efficacy of cholera inoculation in greatly lessening the liability to infection with cholera within a few months of the injection is so conclusive that it has even stood the test of mathematical enquiries, which are not always readily applicable to the complicated problems of biochemical reactions in the human subject. On the other hand, there is greater difficulty in deciding whether the case mortality in those who are attacked after inoculation, is reduced or not. Most authorities and some extensive statistics, such as the Batavia ones in the table, show no reduction in the case mortality. On the other hand, the Greek Army statistics did reveal a reduction in the case death-rate, but the outbreak was a comparatively mild one. It is, however, clear that the case mortality is far less reduced than the incidence of the disease in the inoculated, while in severe outbreaks, such as that at Batavia, the lethal powers of the disease may/
may not be reduced at all in the case of the few in-
oculated persons who succumb to infection, probably
on account of the antigens resulting from the vac-
cines being bactericidal, but not to any material
extent antitoxic".  

On the other hand, VINCENT & MURATET State
"Gowadiaa has stated that during the epidemic
which broke out in the Greek Army at the time
of the last Balkan War, his cholera patients
included:

82.5% of non-vaccinated subjects.
10.6% of incompletely "  "
6.7% of completely "  "

Among the non-vaccinated, there were 21 per
cent of deaths; among the vaccinated patients,
2 per cent.

Arnaud has published similar data".

If, as seems undoubtedly to be the case,
anti-cholera inoculation does lessen the liability
to infection with cholera, it may, perhaps, seem
strange at first sight, that the admissions for the
disease, as it affected this series, includes a
higher proportion of inoculated persons than uninoc-
culated. But it must be remembered that the proba-
bility is high that the admissions amongst those
inoculated, comprise only a fraction of the protect-
ed, while quite a high proportion of the uninoculat-
ed/
uninoculated troops contracted the disease. I put this forward as a feasible explanation of the results recorded on TABLE IX., because it is likely that only a small minority of the troops were denied prophylactic inoculation at some time or other.

<table>
<thead>
<tr>
<th></th>
<th>CASES</th>
<th>PERCENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoculated</td>
<td>68</td>
<td>52.8</td>
</tr>
<tr>
<td>Uninoculated</td>
<td>59</td>
<td>47.2</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>125</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Closely/
Closely associated with the influence which inoculation has upon case mortality, is the relationship which exists between inoculation and the degree of severity of a subsequent attack of cholera.

In order to show this relationship, I have utilised a classification of the 135 cases, according as these were, from the clinical standpoint, 'very mild', 'mild', 'severe', or 'very severe'. It should be stated that such a classification was made before I had worked out the inoculation history of the cases, and, therefore, a quite unbiassed estimate of the severity of each case was arrived at.

As far as it is possible to classify the cases into these four degrees of severity, their grouping depended chiefly on their condition when they first came under observation - in other words, on the degree of collapse present, severity of cramps, mental state, etc. and, to a less extent, on the way in which each patient responded to treatment, e.g. the number of intravenous infusions administered, etc.

TABLE NO. X. shows the complete series arranged as I have explained. In the left hand portion of the Table, the "No record of inoculation" cases have been kept apart from the definitely "inoculated" cases, while in right hand portion of the Table these two types have been combined.
<table>
<thead>
<tr>
<th></th>
<th>INOC.</th>
<th>NO RECORD</th>
<th>UNINOC.</th>
<th>TOTAL</th>
<th>INOC.</th>
<th>UNINOC.</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>V. M.</td>
<td>20</td>
<td>3</td>
<td>=</td>
<td>23</td>
<td>20</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>M.</td>
<td>14</td>
<td>8</td>
<td>2</td>
<td>24</td>
<td>14</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>S.</td>
<td>16</td>
<td>11</td>
<td>5</td>
<td>32</td>
<td>16</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>V. S.</td>
<td>16</td>
<td>20</td>
<td>10</td>
<td>46</td>
<td>16</td>
<td>30</td>
<td>46</td>
</tr>
<tr>
<td>S.</td>
<td>66</td>
<td>+</td>
<td>42</td>
<td>+</td>
<td>59</td>
<td>=</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>66</td>
<td>+</td>
<td>125</td>
</tr>
</tbody>
</table>

TABLE NO. X

<table>
<thead>
<tr>
<th></th>
<th>INOC.</th>
<th>UNINOC.</th>
<th>TOTAL</th>
<th>INOC.</th>
<th>UNINOC.</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>V. M.</td>
<td>20</td>
<td>3</td>
<td>23</td>
<td>20</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>M.</td>
<td>14</td>
<td>8</td>
<td>24</td>
<td>14</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>S.</td>
<td>16</td>
<td>11</td>
<td>32</td>
<td>16</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>V. S.</td>
<td>16</td>
<td>20</td>
<td>46</td>
<td>16</td>
<td>30</td>
<td>46</td>
</tr>
<tr>
<td>S.</td>
<td>66</td>
<td>42</td>
<td>125</td>
<td>66</td>
<td>59</td>
<td>125</td>
</tr>
</tbody>
</table>
The Table shows that amongst the inoculated, as would be hoped for, the disease, in the greater number of the cases, was of less severe type, even though their numbers exceed the most severe cases, by only a trifling majority. But it is amongst the uninoculated that one finds greatest support to the belief that not only does anti-cholera inoculation reduce case mortality, but it also, to some extent, modifies the severity of the attack. In both the right and left hand portions of the Table, it is seen that amongst the uninoculated as the Table progresses from the 'very mild' cases to the 'very severe', there is an appreciable increase in numbers at each step.
RELATIONSHIP OF THE SEVERITY OF THE CHOLERA ATTACK to the INTERVAL of TIME between the last INOCULATION and the ONSET of the DISEASE.

It is known that the duration of the protection against cholera afforded by prophylactic inoculation is short - i.e. when compared with the effect of certain other vaccines, e.g. smallpox, typhoid. - Six months is the commonly accepted period, and it is admissible to argue that even within this period of six months - the longer the time which has elapsed since the last dose of anti-cholera vaccine was received, the greater is the probability that a subsequent attack of cholera will be of a severe type. In order to see if this series conforms to the above reasoning, I have again utilised the classification of the cases into 'very mild' (V.M.), 'mild' (M.), 'severe' (S), and 'very severe' (V.S.).

Referring to TABLE NO. AI., it is seen, first of all, that the total cases inoculated numbered 66.

In one of the 16 severe cases and in three of the 16 very severe cases, the date on which the preceding inoculation had been carried out was not stated/
stated in the pay-books, it only being recorded that anti-cholera vaccination had been administered. These 4 cases then, have had to be disregarded, and as a result only 62 of the 66 inoculated cases are available for the further calculations. In each of these 62 cases, the interval between the last inoculation and the onset of the subsequent attack of cholera has been calculated in weeks, the number of weeks recorded denoting that inoculation had been administered just within that period, - for instance 12 weeks indicates that the onset of cholera occurred during the 12th week after inoculation.
Column 3 shows quite distinctly that if a man were inoculated within the comparatively short period of 13 to 12 weeks, (about 3 months), the subsequent cholera attack tended to be of a milder type, whereas, if a longer time had elapsed - namely 16.3 to 20.7 weeks, (or about 3½ to 5 months), - there was more likelihood that the subsequent attack would be severe.

It is curious that in 2 of the 20 'very mild' cases, the inoculation had been carried out quite a long time previously - viz: 48 and 59 weeks respectively. With these two exceptions, the interval varied from 1 week as a minimum, to 21 weeks as a maximum. Since these two cases are so exceptional to the other members of their category, and as possibly some factor other than inoculation was operating to reduce the severity of their illness, it is interesting to see what the effect is, when they are left out of the calculation. The results of this modification are shown in columns 4 & 5 of TABLE No. XI.

These 60 Cases show in rather a striking manner that if cholera patients had been inoculated within 2, 3, 4, or 5 months, the degree of severity of their illness would accordingly be 'very mild', 'mild', 'severe', or 'very severe' respectively.

Theoretically/
Theoretically, the case mortality also should be in direct proportion to the latter factor, but, as regards this series, it is difficult to give evidence of any weight on this point, for the following reasons:

(a) In the first place, only 7 cases out of the total of 66 inoculated cases (See TABLE NO. XI.; column 1.), ultimately succumbed, and statistics based on such a small number would not prove very convincing.

(b) I have already stated (p. 36) that only 62 of these 66 cases are 'available' as data from which deductions may be drawn, owing to the fact that, in 4 instances, the date of anti-cholera inoculation was not recorded in the 'pay-books'; and it is rather a strange coincidence that these 4 cases should all ultimately prove fatal. It follows, therefore, that in only 3 of the fatal cases is it possible to estimate the duration of the period between inoculation and the cholera attack. For what it is worth TABLE NO. XII. is inserted to show the effect of the above period on the 7 fatal cases.

TABLE/
TABLE NO. XII.

<table>
<thead>
<tr>
<th>DEATHS</th>
<th>DURATION of PERIOD between inoculation and onset of CHOLERA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4 weeks</td>
</tr>
<tr>
<td>1</td>
<td>8 weeks</td>
</tr>
<tr>
<td>1</td>
<td>12 weeks</td>
</tr>
<tr>
<td>4</td>
<td>Duration unknown.</td>
</tr>
<tr>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

It is seen that the average duration of the three available deaths, works out at 8 weeks, which is very considerably shorter than both that of the total available cases (15.2 weeks) and even that of the mildest cases, 13 weeks (TABLE XI, column 3), a result which is, of course, not what one would expect.

The cause of such a paradoxical finding is, however, exposed on further enquiry, for it is then found that all the three available fatal cases had already been in hospital for some other debilitating condition when cholera set in. Hence, a fatal termination occurred in spite of comparatively recent inoculation having been given.

Recapitulating the findings of the effects of anti-cholera inoculation, as illustrated in these 125 cases, it seems probable that:-

(1)/
(1) Case mortality is diminished.

(2) So also is the severity of the subsequent attack.

(3) The severity of the subsequent attack is directly proportionate to the time which has elapsed since the last administration of anti-cholera inoculation.
When one recollects how very urgent are the clinical features of cholera - complete collapse taking place in a very few hours in the more severe forms - it is natural to assume that it is of the utmost importance to get such cases under treatment at the earliest possible moment, and that if this is accomplished, the prognosis becomes all the more favourable. Such an assumption is justified and is supported by facts. If, then, it were possible to have under treatment a large series of cases, all exactly comparable in initial and progressing severity, but admitted to hospital for treatment at varying periods from the exact moment of onset of symptoms, one would find that the mortality was considerably greater amongst those admitted 'late' than amongst the 'early' cases. By getting the cases as soon as possible after the onset, and commencing treatment at once, it is possible in the great majority of them, to prevent the more profound degrees of collapse from ever being reached. Further, as ROGERS has shown by his statistics, compiled from an enormous number of cases, the chances of that most deadly complication - namely uraemia - setting in, become very great, if, owing to a prolonged collapse stage, suppression of urine has occurred.
occurred, and persisted for several hours. With regard to this ROGERS says:

"Suppression of urine for over twenty-four hours is, therefore, of serious prognostic import, which becomes increasingly grave as each day passes without restoration of the renal functions."

Fortified with this knowledge, it is not unnatural that the theorist should expect that if an analysis of any series of cases be made, it should be possible to show, in tabulated form, that the severe cases - including the fatal ones - were, on the average, sent in to hospital for treatment later, than the bulk of those who ultimately recovered. In point of fact, however, that is exactly what does not happen, and the explanation of it is not far to seek.

A study of TABLE NO. XIII., shows the reader that in 92 out of the 125 cases, it was possible to elicit, with a considerable degree of accuracy, the exact time at which the onset of symptoms occurred and thus to estimate the duration of the disease prior to admission. These 92 cases are, therefore, referred to in the Table, (Column 5), as available for the further calculations. Of these, 63 recovered, while 29 succumbed, (Columns 6 & 7).
TABLE NO. XIII

<table>
<thead>
<tr>
<th></th>
<th>9.3</th>
<th>12.7</th>
<th>11.6</th>
<th>11.7</th>
<th>69</th>
<th>+6+</th>
<th>98</th>
<th>22</th>
<th>32</th>
<th>93+</th>
<th>125</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.8</td>
<td>12.0</td>
<td>11.8</td>
<td>11.8</td>
<td>18</td>
<td>17</td>
<td>35</td>
<td>20</td>
<td>26</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.0</td>
<td>12.7</td>
<td>11.7</td>
<td>11.7</td>
<td>8</td>
<td>21</td>
<td>29</td>
<td>8</td>
<td>24</td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.0</td>
<td>13.1</td>
<td>12.1</td>
<td>12.1</td>
<td>3</td>
<td>15</td>
<td>18</td>
<td>4</td>
<td>20</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>12.6</td>
<td>12.6</td>
<td>12.6</td>
<td>0</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>22</td>
<td>23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* In hours. In hours. In hours. In hours. In hours. In hours. In hours. In hours. In hours. In hours.

(10) (6) (8) (7) (6) (5) (4) (3) (2) (1)
Columns 8, 9, & 10 show that, while the average duration of the disease prior to admission was 11.6 hours amongst the total available cases, that period was actually longer amongst the recoveries (12.7 hrs) than amongst the fatal cases (9.3 Hours), a difference of 3.4 hours. One who has never seen a case of out-spoken cholera, and who is, therefore, not in a position to realise to what a desperate condition the patient may be rapidly reduced, might be tempted to remark that a delay of less than 3½ hours is surely of little significance.

Were these 92 cases all of equal severity, actual experience of the treatment of such - or statistics relative to this question - would soon convince him how valuable is each hour that passes, during which time treatment might have been instituted.

But although TABLE No. XIII., shows that the period in question was longer in those who recovered, it is accounted for by the fact that cases of cholera, which are sudden in onset, which become rapidly and markedly collapsed, and concerning which from the start, there is little scope offered to miss the diagnosis, are transferred to hospital with the utmost dispatch. Not so concerning those cases which conform to a milder type of the disease - and their numbers are, in many epidemics, not inconsiderable/
inconsiderable. Here the diagnosis of cholera is often not arrived at for, it may be, a day or two, and these cases are looked upon and treated as 'diarrhoea', 'enteritis' and the like, until, perhaps, the symptoms become gradually but progressively more disturbing to both patient and medical attendant. This is especially prone to occur under active service conditions in tropical climates, where cases of 'diarrhoea', and mild cases of dysentery are not uncommon. When active treatment has been begun in such cases, quite a large percentage of them ultimately recover, - indeed, they are often prevented from becoming 'severe' cases at all.

This, then, is the explanation that the fatal - and presumably more serious - cases were admitted on the average 3.4 hours sooner than the recoveries.

Further, it is rather interesting to observe, that the more severe the case appeared to be, the sooner was it transferred to hospital. This is shown - with appreciable emphasis - in column 8 from which it is learned that, while the very mildest cases came in 12.5 hours after the onset, the most severe were admitted after 11.2 hours.

The recovery cases (Column 9) are less conclusive. The fatal cases (Column 10) appear at first sight contradictory, but the reason the period for the/
the 'mild' cases (7 hours) is shorter than that for the 'very severe' cases (9.8 hours), is due to the fact that 2 of the 3 deaths which occurred amongst the mild cases (from which the calculation of 7 hours is derived) were accountable to late complications. Broncho-pneumonia (9th day), and dysentery (24th day), while the third died on the 5th day from sheer asthenia, and would have died no matter how soon or how late he was brought to hospital. So that, disregarding this item, Column 10 may not differ from its neighbours.

Apart from averages, the duration of the disease prior to admission to hospital varied throughout the total 'available' cases from 2 to 48 hours. It must be remembered, however, that in a very few instances, diarrhoea had existed sometimes for a few days before symptoms of any urgency supervened, and, as it is always doubtful whether this should be regarded as a stage in the disease,—in other words, a true 'premonitory diarrhoea'—or as only a factor predisposing to the invasion of the vibrio, these few cases have not been included in the calculations.

SOURCES/
As happens in many other diseases which are attributable to organismal invasion, so apparently with regard to cholera, the origin of the infection was seldom found, for it is surprising that, with the exception of those 30 cases which were admitted from another hospital, and which undoubtedly owed their origin to infected milk (See P.16), in not a single other case could the source of the cholera virus be traced conclusively.

Suspicion, however, was rightly cast on certain food stuffs or drinks in a small number of the remaining 95 cases.

In spite of repeated warnings, issued to the troops, both in lectures and in printed matter - on no account to eat certain articles of diet which were for sale in the Arab Bazaars or to drink anything of which the nature and source were unknown, there is no doubt that often such wise counsel went unheeded, and both foods and drinks were not only purchased from the natives, but were actually consumed there and then. In a very few instances, the patients admitted to having eaten or drunk certain articles of diet which they had purchased in the native bazaar, and very rightly, suspicion was cast on these as the source of their malady. Of such were the following:-

1./
1. MILK. All authorities are agreed that milk is, par excellence, the most dangerous article of diet. I have already referred to this and tried to show how it may become infected by the cholera vibrio. (See page 18).

2. For the same reason, coffee, if not boiling, may provide an undoubted harbouring ground for the vibrio, if infected milk be added to it.

3. WATER. There is no need to explain the importance of avoiding all drinking water from an unknown source. Yet, one of these patients actually made a practice of drinking quantities of water from one of the native 'Persian coolers' in the bazaar.

4. ICE. After the British occupied Baghdad, and comforts became a little more plentiful along the lines of communication, even the Arabs and Jews reaped the benefit of the British regime. They too, were ambitious, purchasing and erecting their own ice plant and factory. In consequence, ice was to be had in the native shops, and drinks were cooled by inserting pieces of ice into the drinks. It has been found that the vibrio can survive for a considerable time in ice.

5./
5. FRUITS & VEGETABLES.

Certain fruits and vegetables, especially if ripe and uncooked, may harbour the vibrio for several days. The melon is notoriously a source of cholera in the East. The Arab custom of keeping both fruit and vegetables 'fresh' by immersing them in water over night is, I believe, in many cases responsible for the contamination of these articles, and this is especially true where only portions of the fruit are thus treated. Also, it is conceivable that if the melon skin is not absolutely intact, the interior of the entire fruit may be reached by organisms living in the water used for immersing purposes. In one or two cases, corroborative evidence in the form of melon seeds occurring in the cholera stools, pointed to the patient having taken the fruit, and as such was not a ration to Indians at that time, it followed it owed its origin to the native bazaar.

Dates, as sold in the Eastern bazaar, are most likely to become contaminated, as, during the hot weather, they are swarming with flies all day long.

Apart from these few instances just enumerated, no light was thrown on how, exactly, the infection had been contracted.
SYMPTOMATOLOGY.

It is the custom when describing the clinical features of cholera, to divide the course of the disease into several stages. These stages, though undoubtedly arbitrary, are apparently more or less easily distinguished one from another in many cases. It is possible in such to recognise the following phases.

I. THE INCUBATION PERIOD.

With regard to this, VINCENT & MURATET state:

"The Constantinople Conference adopted the opinion that this period does not, in the majority of cases, exceed a few days. In reality its duration is variable. According to Thoinot, it varies between a minimum of a few hours and a maximum of five or six days; it may, however, exceed this".

Did it not so happen that these few patients, to whom I have just referred under 'Sources of Infection', as having consumed questionable food or drink, had made a practice of committing such folly, it might have been possible to estimate with considerable accuracy, the duration of the incubation period of cholera. But all had partaken unwisely over a comparatively/
comparatively prolonged period, so that this series of cases contributes no corroboration to the generally accepted view of the duration of the incubation period - namely between 2 and 5 days.

During the summer of 1916, a large number of cholera 'contacts' were sent to the Isolation Hospital, and for purposes of safety, the minimal quarantine period to be undergone by these men was fixed by the authorities at 7 clear days. That 7 days probably covers the great majority of cases is supported by the fact that, although in 2 or 3 instances contacts did develop cholera during their period of quarantine, I am not aware of a single instance where a contact was attacked by cholera subsequent to the completion of the prescribed quarantine period.

II. THE PERIOD of INVASION.

(Initial or Prodromal or Premonitory Period)

This stage is characterised by diarrhoea usually. The stools are loose and frequent, though not to the same extent as during the height of the next phase. In addition to diarrhoea, other indefinite symptoms may be present, such as malaise, headache, epigastric uneasiness and nausea. Diarrhoea may be absent altogether, and these latter features then constitute the prodromata. According to various observers/
observers, the duration of this period may vary from 1 to 7 days, but 2 or 3 days is most usual.

The present series provides but a few instances in which the premonitory stage could be recognised at all, for of the 125 cases, it was present in but 9 of them, or 7.2 per cent.

But it is recorded of many epidemics that the premonitory stage is conspicuous by its absence. When such is the case, the choleraic diarrhoea and vomiting set in with lightning suddenness. VINCENT & (1) MURATET state:

"Diarrhoea is the dominant symptom of the period of invasion. In temperate countries, it is observed in two cases out of three (Guerin); in hot countries it is rarer, the disease often commencing at the first onset with the choleraic period"

Again ROGERS (2) states that:

"This stage is ------- completely absent in the majority of cases seen in the tropics", and that "According to MACNAMARA, premonitory DIARRHOEA is the exception rather than the rule in India, although it is said to be present in at least half the cases seen in Europe".

One may take it then, that the occurrence of this stage in only 7.2 per cent of this series is what is to be expected. As to the duration of the period in/
in those 9 cases, it is found that an average of 3.8 days obtained. The exact duration of the period for each case is given in -

**TABLE NO. XIV.**

<table>
<thead>
<tr>
<th>DURATION of PREMONITORY PERIOD</th>
<th>NO. of CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 days</td>
<td>1</td>
</tr>
<tr>
<td>(2x) 2 &quot;</td>
<td>2</td>
</tr>
<tr>
<td>3 &quot;</td>
<td>1</td>
</tr>
<tr>
<td>(2x) 4 &quot;</td>
<td>2</td>
</tr>
<tr>
<td>5 &quot;</td>
<td>1</td>
</tr>
<tr>
<td>6 &quot;</td>
<td>1</td>
</tr>
<tr>
<td>7 &quot;</td>
<td>1</td>
</tr>
<tr>
<td>34.5 &quot;</td>
<td>9</td>
</tr>
</tbody>
</table>

I have already stated that it must often be difficult to decide whether an attack of diarrhoea prior to the onset of urgent symptoms of frank cholera is really due to the action of the specific vibrio, or whether, owing to the alimentary derangement associated with quite a simple diarrhoea, an opportunity is offered to the vibrio to attack and invade the mucous lining of the intestine. Only by bacteriological examination of the stools can such a problem be solved in any individual case, and it is /
is significant that three of the 9 cases under consideration had been admitted to other hospitals solely on account of diarrhoea, and after having been under treatment there for 2 or 3 days, the sudden onset of symptoms of typical cholera necessitated their immediate removal to the Isolation Hospital. A thorough routine examination of the stools of all cases of diarrhoea was made by hospitals as soon as possible after the cases were admitted, and yet these other hospitals apparently found nothing in the examination of these patients' stools to suggest that their condition was of choleraic origin.

(2) ROGERS and other authorities point out that "the stools, early and atypical form" (of cholera) "will contain the cholera bacillus". From this, one can only argue that either the presence of the vibrio was not suspected and consequently certain bacteriological procedures were not adopted to demonstrate it; or, at the time when the stools were examined, the cholera vibrio had not as yet superimposed itself on a pre-existing 'simple' diarrhoea.
III. EVACUATION PERIOD.
(The True Choleraic Attack).

It is the severity and persistence of this stage on which are dependent almost entirely the ultimate progress and fate of the patient.

The clinical features of well-marked cases of cholera are so strikingly uniform that the descriptions of the disease which are to be found in practically all writings on the subject of cholera, are applicable to the majority of the writer's series, and, therefore, it would seem unnecessary to include here a detailed account of the features of an average case. It will, nevertheless, not be unprofitable to enumerate the symptoms and signs characteristic of this stage of the disease, and, at the same time to mention in what respects certain of the cases broke away from convention.

(a). DIARRHOEA.

This was the first symptom complained of, in all the cases, without one single exception. Nearly all observers agree that the earliest features of true cholera asiatica, are diarrhoea and vomiting, and that the onset of diarrhoea usually precedes the vomiting. Such was the case in the present series.
This is an important point to remember, from the point of view of diagnosis, for there is no doubt that in certain cases of acute gastro-enteritis ("cholera nostras" or "food poisoning") in which the predominating features are, again, diarrhoea and vomiting, the time of onset of these two symptoms is reversed, vomiting often occurring before diarrhoea sets in.

A fulminant form of cholera, is often described in text books. In this, the patient is so rapidly overcome by the action of the cholera toxins that he succumbs before time has been afforded even for diarrhoea to manifest itself; hence the appellation "cholera sicca". Cf. "cholera sicca", (4) LIEBERMEISTER writes -

"The amount evacuated is of less importance than the amount of exudation poured into the intestine. In fact, the worst cases are those, in which, on account of paralysis of the intestine, the fluid is no longer spontaneously evacuated, but remains in the intestine and flows out only after pressure on the abdomen".

"It is common to hear of 'cholera sicca'. If, by this, are understood cases in which the exudation is not evacuated, but remains in the intestine, the term is probably hardly applicable/
"applicable; but such cases are seen, and, especially in feeble persons, death may occur before evacuation of the exudation.

But if, under this name, cases are cited in which no pathologic exudation into the intestines has taken place, then it is likely that a wrong diagnosis has been made".

"The aged, consumptives, and those otherwise enfeebled, may die of cholera before characteristic symptoms appear".

No such condition occurred amongst this series. When one reads that "cholera sicca" is apt to occur amongst persons who are already feeble and debilitated, it is indeed curious that not even one of all those men, who in 1916, were attacked by cholera while they were already reduced to skin and bone by some other exhausting disease, should provide an instance of this fulminant 'dry cholera'.

The onset of diarrhoea was in most cases strikingly sudden, and if a premonitory diarrhoea had already existed, it was noticeable to the patient himself that there was a well defined juncture at which the diarrhoea became aggravated in intensity. Once the diarrhoea is established, the evacuations follow one another in quick succession - often every few minutes, and appear to become more and/
and more copious until the patient shows signs of collapse. Then, there occurs an obvious diminution both in the frequency and bulk of the watery stools.

What impresses one very much is the frequency with which there is entire absence of any abdominal discomfort when the evacuation stage is at its acme; there would appear to be neither colic nor tenesmus, while the alvine evacuations literally pour from the patient.

The situation, however, is changed during the latter portion of this stage, for then the extraordinary loss of fluid, from both the circulating blood and the tissues generally, provokes excruciating muscular cramps in which the abdominal varieties share. Only a few of the patients complained of a sense of burning in the abdomen, chiefly referred to the epigastric region.

Another striking feature is the precipitateness with which the desire to use the bed-pan comes on at each occasion, for while at one moment the patient is lying more or less at ease, in a second, the call to stool is urgent and must not be denied.

CHARACTERS of the EVACUATIONS:—

Little need be said in regard to the appearances of the stools except on one or two topics.
Of chief interest is the presence or absence of blood. I cannot help thinking that the appearance of blood in the motions - i.e. blood in sufficient quantity to be apparent to the naked eye - must be quite the exception in uncomplicated cholera asiatica - even in the most severe cases. One reads that sometimes the stools are "red, sanguinous, and dysenteriform in appearance, resembling meat-scrapings (Petit, Lesage)". or again, that "Not rarely red blood corpuscles are present, and when very numerous the fluid has the appearance of water in which raw meat has been steeped".

Notwithstanding these statements, I am of opinion from the experience of my cases, that the occasions on which blood is recognisable in the stools are very rare, and that this fact should be emphasised. That there are grounds for holding such an opinion is undeniable, for only in 4 cases of cholera (3.2 per cent) was it possible to detect blood in the stools by the unaided eye. One of these cases showed only blood-stained flakes of mucus, and ultimately proved to be suffering from amoebic dysentery as well. The other three passed watery evacuations of a pinkish hue. In contrast to cholera, it is worth recording that amongst 63 cases of acute gastro-enteritis (cholera Nostras) sent/
sent into the Isolation Hospital as probable cases of cholera asiatica, blood was apparent in the stool in no less than 11 cases, or 17.4 per cent. So often did it occur that, when stools, obviously containing blood, were sent to the Laboratory for bacteriological investigation, a report was returned to us stating "No cholera vibrios found", it was latterly possible to foretell the negative nature of the case with a fair degree of certainty, and to provisionally diagnose that the condition was one of 'cholera nostras'. And further, in the event of the common bacillus being recovered from blood-tinged stools, one is justified in at least suspecting, that there is, in addition, some complicating condition - dysentery, for example.

No other character of any significance was recorded with regard to the naked eye appearance of the stools. The usual sequence in the changes of consistence and colour of the stools was adhered to - namely that after the first few evacuations, the alimentary canal is emptied of its faecal contents and there follows watery material which, at first, is of greenish or yellowish tinge (bile), but which rapidly loses even this source of colour. From then on, till recovery is setting in, the evacuations are entirely devoid of colour - or at most greyish/
greyish white - and conform to the apt description of 'rice-water' stools.

It is this striking absence of bilious colouration in the stools of fully-developed cholera asiatica which lends weight to the belief that the disease which the most ancient writers on medicine (Celsus and others) described as cholera, was in reality what we now call "cholera nostras". For, it is understood that these physicians of antiquity derived the name from the two Greek words "χολή", bile, and "ῥέω", to flow. As it is undeniably true that the stools in cases of cholera nostras are quite often deeply bile-stained, while in cholera asiatica, bile is mostly absent, it is highly probable that "cholera nostras" was indicated by these old writers, accordingly, the view that the word 'cholera' when employed to indicate cholera asiatica, is derived from the sources already quoted is, from an etymological standpoint, untenable. (5) As "J. MOORE, rather pointedly refers to the question:

"The term cholera involves a principle, but that principle is repugnant to the disease. The term cholera signifies a flow of bile, but the want of bile is usually one of the most prominent peculiarities. The term cholera, therefore/
therefore, cannot be used without pointing out the absurdity of an expression which literally implies not what it ordinarily is, but what it ordinarily is not".

More acceptable theories as to the etymology of the word when used to indicate cholera asiatica, are those of ALEXANDER of TRALLES (κολάδες, the intestine, and ἰέω, to flow) and of some recent authorities (κολέρα, the gutter of a roof).

Possibly it is worth while mentioning that there were five cases, amongst Indians, which provided curiosities on examination of the stools. They are as follows:

One case showed the ova of ankylostomum and trichocephalus dispar.

Another, the ova of trichocephalus dispar and necator americanus, -

A third passed a large ascaris on the 6th day of the disease, while two others, late on in the disease, commenced to pass greenish-blue motions which proved to be heavily infected with B. pyocyaneus. One of these latter eventually died of septicaemia from this organism, and will be referred to later under 'Causes of Death'.

Finally/
Finally, it need only be said that all the cases included in the writer's series were found to harbour the specific cholera vibrio, and that all other cases of acute diarrhoea and vomiting going on often to complete collapse, but from which the cholera vibrio was not recovered, were, according to an order from the Army authorities, not diagnosed as Cholera Asiatica, but were diagnosed and sent in on the daily 'returns' as 'Acute Gastro-enteritis'. I am not in a position to speak authoritatively on the bacteriological findings of the large number of cases of so-called 'acute gastro-enteritis' which were clinically indistinguishable from true and severe cholera asiatica and which I had the opportunity of treating; but in spite of the investigation of their stools having proved negative to cholera, I still believe that a certain proportion of them were, in reality, cases of cholera asiatica, and this view of the matter is backed by the experience of certain experienced bacteriologists, who informed me that it is sometimes impossible to isolate the common bacillus from cases which are otherwise identical to cholera asiatica, and that, provided no other organism can be recovered to explain the urgent nature of the case, the diagnosis might legitimately be based on the clinical picture present. Such a loop-hole, however, was not taken advantage/
advantage of in any of the writer's series, which embodies only those cases which conformed to the stipulation of the Army Order, I have referred.

As to the duration of diarrhoea, this symptom persisted in my cases for 5.06 days as an average. In the severe pulseless cases, the average was 5.42 days, and in the milder cases, the average was 4.96 cases. (See TABLE XVIII., page 248.)

(b). VOMITING:

With the exception of diarrhoea, the most constant and important symptom is vomiting. It is, compared with the diarrhoea, a more distressing feature to the patient.

But though it is such a very characteristic symptom, it should be realised that it is not constantly present, even in cases where the stools are actually 'rice watery' and contain the sholera vibrio in almost pure culture. Five of my cases (4 per cent) apparently did not vomit throughout their illness, but, as would be expected, such cases never proceeded to an alarming degree of collapse, and consequently are members of the 'very mild' group. So that apparently absence of vomiting is indicative of a mild infection and therefore of good prognostic import.

The best description of the vomiting of cholera is conveyed in the word 'easy', for one is struck/
struck by the absence of retching or voluntary effort. Without the slightest warning, even to the patient himself, he is disturbed at frequent intervals by the sudden desire to vomit. The force with which the gastric contents are ejected is also a noticeable feature, the vomited matter seeming to be 'pumped' out under great pressure; accordingly, this fluid, often containing the vibrios in great numbers, is shot quite a considerable distance from the patient, contaminating not only his surroundings but also those who are attending to him. These are points of practical importance, for on two occasions I have had the rather alarming experience of receiving the full force of the vomited material in my face. This, of course, is only likely to occur when the patient is in a highly restless and almost irresponsible state of mind, distracted by agonising cramps, and careless of what is going on around him. When such cases are being attended to - e.g. during the process of saline infusion - it is, therefore, advisable to obtain the services of an assistant whose sole duty it will be to steady the patient's arm and insure that if he (the patient) should suddenly vomit, the stream will be directed away from those near him and preferably towards a suitable receptacle.
The quantity of fluid brought up by the patient is enormous, even when only a few minutes elapse between the successive bouts. Since at the same time, diarrhoea is profound, one is forced to wonder at the large quantity of fluid which must be normally contained in the blood vessels and tissues.

As to time of onset, I have said that in all my cases, diarrhoea preceded the onset of vomiting. Usually this interval was about 2 hours, but as long as 3 or 6 hours was recorded. Again, vomiting followed within an hour in a few cases.

The material ejected was, in almost every case, very similar to the watery material passed per rectum, and is best described as 'rice water' vomit.

As a curiosity, it is worth recording that one patient - an Arab - vomited two large Ascarides during the 3rd day of his cholera attack.

None of the patients vomited blood or blood-stained material.

Vomiting persisted for 3.292 days as an average for all cases, for 3.272 days in the severe pulseless cases, and for 3.296 days in the milder cases. (See TABLE XVIII. page 148.) Thus vomiting ceased earlier in the course of the disease than diarrhoea by 1.768 days on the average in all cases.
(c). HICCOUGH.

This was noticed in four cases (3.2 per cent). Apart from the annoyance and distress which it brings to the patient, owing to its persistence in spite of all attempts to check it, it is only natural that I should regard the appearance of this symptom with dread; for, all of these 4 patients eventually died. Some other writers apparently agree that persistent hiccup is a symptom of ominous import and makes the prognosis worse.

On the other hand, such an eminent authority as ROGERS observes:-

"Hiccup may exceptionally be a very troublesome symptom and persist well into the stage of convalescence; but my own experience is in agreement with that of MUIRHEAD, WALL, and others, in regarding it as not a particularly unfavourable sign".

Nevertheless I cannot be persuaded that a mortality of 100 per cent amongst those cases in whom the symptom was present is merely a coincidence.

(d). THIRST.

This would appear to be very distressing to the cholera patient, if diarrhoea and vomiting are of more than an hour or two in duration. He is constantly clamouring for water, and more water, and his thirst is unquenchable. The hopelessness of/
of trying to relieve his distress by supplying him
with unlimited drinks is apparent, when one knows
that both his stomach and intestine are already
filled to overflowing with fluid, and yet no absorp­
tion is taking place. However, I see no contra-in­
dication to supplying such patients with water ad
libitum, for thereby two important ends are attained,
- first, the mental anxiety of the patient is, to a
certain extent, diminished, while, second, the toxic
products in the alimentary canal are diluted, and
even although the patient vomit immediately afterward
wards, the not undesirable effects of gastric lavage
are obtained. How well founded is the belief that
absorption of fluid from the alimentary canal entirely
ceases during the stage of cholera when collapse
is at hand, is demonstrated immediately after a
sufficiently copious infusion of saline solution has
been given intravenously; it is only then that the
patient will tell you that thirst has ceased to tor­
ment him.

I have never been able to satisfy myself
that the drinking of plain water excites vomiting in
cholera cases, as some people would appear to be­
lieve, and, therefore, deny their patients fluid of
any kind by the mouth. In regard to the signific­
ance of vomiting as a symptom and the inadvisability
of/
of taking steps to check it, I shall speak again, when treatment falls to be considered.

(e). MUSCULAR CRAMPS.

Little is to be said about this symptom, except to emphasise the excruciating agony which they caused those patients at the height of the cholera attack.

The smaller muscles of the hands and feet seemed to be first involved, while, as the loss of fluid from the tissues proceeded and the pulse became more feeble, the muscular spasms progressed centripetally, i.e. the calves and forearms were next affected, and lastly the muscles of the anterior abdominal wall and back. Although it is, of course, difficult to be quite certain on the point, I am inclined to believe, that when a patient complains of marked "pain in the stomach", it is to painful contraction of the abdominal parietes that the cause must be assigned in most cases, and not to intestinal colic.

Like so many other symptoms and signs of cholera, this, probably the most distressing of them all to the patient, speedily disappeared after intravenous infusion of saline solution.

(f)
(f). RESTLESSNESS.

Even in this stage, restlessness may be extreme, and it is little to be wondered at, for the mental state of the patient is as yet such that the torment of the cramps and the seriousness of his condition are appreciated by him, only too readily.

The perpetual turning over in bed, the waving of the arms, and the drawing up of the knees all indicate his distress, and that collapse from sheer draining away of fluid, is at hand.

(g). FACIES CHOLERICA.

As the fluid continues to be poured from the patient, his whole appearance becomes altered. Amongst the large number of very severe cases which I had the opportunity to treat, it was possible in only a few to notice how markedly and how rapidly the facies changed during the choleraic period. The scarcity of such opportunities was due, of course, to the immediate administration of intravenous infusions which usually arrested the further progress of changes in the outward appearances.

Although not confined to cholera asiatica entirely, yet the "facies cholerica" is a very real and helpful phenomenon as it indicates the extreme degree of desiccation at which the tissues have arrived./
91.

arrived.

The eyeballs sunk deeply in their sockets, the pinched nose, the sunken cheeks, and the prominent malar and jaw-bones together compose a picture which is so highly characteristic that it has earned the title of "facies cholerica".

(h). THE SKIN.

The whole body seems to shrink owing to the marked diminution of the tissues. In consequence the skin, as a whole, is loose and wrinkled, flabby and inelastic, and when pinched up between the finger and thumb, the crease so formed takes an unduly long time to subside.

Highly characteristic also is the corrugated, shrivelled, and wrinkled skin of the fingers (washerwoman's fingers.)

Many of the patients in this stage were covered by a clammy sweat, though in quite a number it was the extreme coldness and dryness of the skin which was the outstanding feature.

In all but the mildest cases, cyanosis is apparent in varying degree. An earthy-gray hue of the whole body is extremely common, while in cases of marked severity, the skin assumes a bluish or purplish tint, especially over the extremities. I have/
have noticed that this purple colouration is often not evenly distributed, but is patchy or more accurately described as "dappled". This was particularly noticeable amongst the Indian patients.

(i). VOX CHOLERICA.

The voice of a patient suffering from well-developed cholera is at first high pitched and piping ("broken") and husky, and becomes later more and more feeble ("vox choleria") until absolute aphonia occurs. All the cases which were so prostrated as to require intravenous infusion exhibited in varying degrees this characteristic alteration in the voice. It is said to be due to a "drying" of the vocal cords combined with weakness of the muscles of the larynx.

(j). MENTAL STATE.

Not until collapse is present to a degree which is just consistent with the preservation of life is consciousness lost. At least so it would seem from the study of my cases.

To well nigh the end, the patient seems to be fully aware of things going on around him, though, from pain and anxiety, he is apathetic towards them. I refer here only to those cases in the stages of collapse, and do not include patients who are already in/
in the reaction stage, when from hyperpyrexia, coma may supervene quite a considerable time before death occurs.

In only one case did delirium occur. So wild and violent was this patient, that it was only with the greatest difficulty that he could be sufficiently controlled to allow the intravenous infusion of saline to be administered.

Other features, indicative of the loss of body fluids, are not amongst those, concerning which any points of peculiar interest can be recited. They are, none the less, of the greatest importance.

Again, since certain therapeutic procedures are dependent on their presence, it might be as well to mention certain points with regard to them.

(k). THE GRADUALLY INCREASING FAILURE of the PULSE.

Several factors unite to bring this about, but by far and away the most influential are;

(1). The loss of the fluid constituents of the blood by which the circulating fluid is greatly diminished in bulk.

(2). The greatly weakened action of the heart, which in turn is due to,

(a). Smaller volume and higher viscosity of the blood, with the result that the heart is provided less "purchase" to contract, and its action is impeded respectively.

(b). The inspissated state of the blood does not allow of sufficient nourishment reaching the heart muscle.

(6).
(c). Reflex action from the Intestine. In this connection LEIDERMISTER (4) rightly points out that, "the heart weakness is in part due . . . . to the severe and extensive disease of the intestinal mucous membrane, which acts in the same way as an extensive burn of the skin, or as the shock occasioned by severe wounds of the abdominal organs. As in intestinal strangulation or other lesion of the peritoneum, in perforation, in acute peritonitis, in poisoning by corrosives, a reflex heart weakness or paralysis, which may present symptoms of severe collapse, may be produced through the medium of the nerves, so in cholera the wide-spread and serious lesions of the intestinal mucous membrane may be responsible for the same".

(d). Degenerative processes in the heart musculature brought about by the cholera toxin.

(l). FALL in BLOOD PRESSURE.

For the same reasons that the failure of the pulse occurs, the blood pressure is also diminished in proportion to the severity of the case. All degrees of fall in pressure were met with from only a few degrees below normal in the very mild cases to absolute absence of pulse in the most severe.

The/
The exact numbers of those who were admitted in a pulseless condition will be recorded when discussing the next phase of the disease — namely the algide or asphyxial stage. Amongst those in whom the pulse was still perceptible on admission readings of 50 or 60 m. m. Hg. were recorded frequently by the sphygmomanometer.

(m). THE TEMPERATURE.

As the algide stage is approached, one of the most interesting phenomena is the gradually increasing disparity between the superficial (skin) temperature and that recorded internally (rectum). For, as the former sinks lower and lower, the latter tends to rise. (See Table, XVI. Column IV., page 119.) Such an occurrence is, I imagine, peculiar to cholera asiatica — at least in this respect — namely, that the difference in the two readings is greater than obtains in other conditions, "cholera nostras," for instance. The difference in the two readings, as it occurred in the present series, will be recorded and discussed in treating of the next — or algide — stage, and again in speaking of differential diagnosis. In the meantime, it is well that the reason for such a phenomenon should be understood. The most probable explanation seems to be that, in cholera,
cholera, toxins elaborated by the vibrio in the mucosa of the bowel are absorbed, and, as in other toxæmias of bacterial origin, pyrexia is brought about. Owing, however, to the depressed state of the circulation, - for which I have already accounted, - the flow of blood through the peripheral parts of the body practically ceases, while it is still maintained, however imperfectly, through the vital internal organs. By peripheral parts, I refer not only to the extremities but also to the surface of the whole body. Consequently the body is deprived of one of its most effective means of heat loss, while heat production presumably continues as usual - indeed, it is highly probable that heat production exceeds the normal, owing to disordered metabolic processes. It is thus easy to see how the internal temperature gradually rises while the superficial temperature falls, especially when, owing to evaporation of moisture from the skin, the cooling of the superficial parts is still further promoted.

Even though one disregards excessive heat production as an influential factor in bringing about an unusually high internal temperature, it is still a simple matter to explain the disparity between/
between "skin" and "rectal" readings, and I cannot do better than quote Liebermeister (4) who in a masterly fashion makes out a very fair case for deficient heat loss as being the sole aetiological factor. He says,

"Even in health, much more heat is dissipated from the extremities, especially the peripheral parts, than is generated in them. They retain their normal temperature only by the constant flow of arterial blood through them, which brings heat from the interior of the body. Therefore, if the circulation is depressed, they become cooler and approach more closely the temperature of the surrounding air. In fact, if the circulation in an extremity ceases entirely, the temperature may fall below that of the surrounding air, on account of the continued evaporation of water from the surface. And so it happens in the asphyxial stage, if the circulation is markedly depressed, that the peripheral parts come to feel so cold to the observer's hand that the coldness is aptly described as death-like, or frequently/
frequently as marble-cold, or, again, hyperbolically, as icy-cold. The thermometer, too, shows an abnormally low temperature in these parts.

It is otherwise with the interior of the body. There, heat is continuously produced, and its dissipation takes place only through the medium of the arterial blood in the act of conveying heat to the surface. Consequently, the feebler the circulation, the greater the accumulation of heat in the interior; and it is to be expected that since heat production remains the same, every decrease in the general circulation must cause a rise of temperature within. Therefore, if in the asphyxial stage, as frequently happens, with a coldness at the periphery, the temperature of the interior rises, this is not necessarily to be looked upon as fever, since it may possibly be simply the result of a defective equilibrium of the temperature as a consequence of the slowed circulation. And if, as is seen less frequently, the temperature/
temperature is found normal or lower in this stage, it is a positive proof that the heat production in the whole body is decidedly below normal."

Nevertheless, the fact that during the "reaction stage" of the disease - even in cases where this is not brought on artificially by intravenous saline infusions, - high temperature readings are recorded both in the axilla and in the rectum for sometimes two or three days would serve to indicate that the element of toxaemia, as a potent factor in the cause of the internal pyrexia during the collapse stage, cannot be disregarded entirely. For I think it is unlikely that the time required for the normal equilibrium between external and internal temperatures to be regained, would extend to more than a few hours at most after the peripheral circulation has been reestablished, were the question merely one of "defective equilibrium" as Liebermeister would argue.

It is also of practical importance to remember that in cholera, unlike what happens in other diseases, the temperature of the mouth of a cholera patient is even more misleading than that of the skin, for it was found that a reading of 103° or 104° may be recorded/
recorded in the rectum - and this, after all, is the true temperature of the body - and one of 95° or 96° is recorded at the axilla, the mouth gives a still lower reading - as low as 80 F. Apparently the mucous membrane of the mouth shares with the peripheral parts of the body the effects of diminished blood supply.

(n). THE RESPIRATIONS.

Coincidently with the rising pulse rate and temperature, the number of respirations per minute also increases. The highest recorded number, amongst my cases, was 35 per minute, while the average was 23.3 per minute. Such observations were, of course, made during the choleraic period of the disease and before any treatment had been begun.

(o). DISORDERS of the SECRETIONS.

Owing to the blood supply being deficient both in quality and quantity, as also to toxic action, all secretions except those from the intestinal mucous membrane are considerably diminished. In the worst cases, they are in complete abeyance. Of first importance is the diminution of the kidney function.

As the patient becomes more and more prostrated through loss of fluid, the amount of urine secretion/
secreted per hour steadily diminishes, until, when the pulse is almost imperceptible, it would appear that absolute anuria occurs. In studying the pathogenesis of this very serious feature of the disease, it is reasonable to assign the cause to several factors: -

(1). It is obvious that if the fluid portion of the circulating blood is reduced to almost a minimum, less fluid remains to be transformed into urine by the kidneys.

(2). The blood is so inspissated - i.e. of such high consistency - that its circulation through the kidney tissue becomes a difficult matter, and, therefore, it is unable to come into sufficiently close relationship with the secreting epithelium.

(3). Undoubtedly the marked fall of blood pressure in the renal arteries must be responsible in a marked degree to diminished flow of urine. The several causes of the reduction in blood pressure have already been enumerated. (See page 93.)

(4). Lastly, there seems no doubt that the highly sensitive secreting tissue of the kidneys undergoes degenerative processes, for which the following are probably responsible: -

(a)/
(a) Its own blood supply is deficient.

(b) The circulating cholera toxins must almost certainly exert a harmful influence on such highly organised and sensitive epithelium.

(c) Retained products of metabolism in turn damage the secreting tissue.

Closely allied with this is the condition of acidosis, or as Rogers and Shorten have shown, is more correctly described as a "diminished alkalinity of the blood", which still further aggravates the condition.

I have enumerated these various factors which contribute to the aetiology of suppression of urine, in the order in which, most likely, they come into operation, during the progress of a case of cholera, but it must be realised that although Nos. 1, 2 & 3, probably come into operation early on - say after a few hours - No. 4 may not add its quota for several days. Accordingly, the necessity of beginning treatment at the earliest moment is obvious. The suppression of urine which results from circulatory disturbances alone (Factors 1, 2, & 3.) is usually overcome by giving intravenous infusions, whereas once toxic or other causes of 'cholera nephritis' have come into force, the resulting uraemia is almost certain to bring about a fatal termination, as/
as will be shown when the treatment of uraemia is being discussed. Apparently, there occurs a critical period after which the possibility of the kidney function being restored is only remote, the first step in the process being mechanical stasis of the renal circulation, which, if not counteracted by timely intravenous infusion of saline solution, will be succeeded by a toxin nephritis and permanent cessation of kidney function.

According to ROGERS, the naked-eye and microscopical changes seen in the kidneys of fatal cholera cases are very variable, for he found that while, in some cases after suppression of urine, the epithelium of the convoluted tubes showed some cloudy swelling and granular degeneration, these changes were by no means constant and were sometimes altogether absent in spite of fatal uraemia having ensued.

It is, therefore, quite possible for uraemia to prove fatal in spite of an entire absence of actual toxic degeneration of the secreting epithelium, and, an account of this, together with the success which has attended the use of methods, to raise the blood pressure in the prevention and cure of post choleraic uraemia, ROGERS (2) thinks that the trouble is more mechanical than due to direct action of the toxins on the renal epithelium.

Such a theory, however, does not explain
those deaths from uraemia in cases where quite an appreciable blood pressure is maintained, and here we are driven to the belief that a true toxic degeneration of the epithelium has occurred.

This theory of a toxic nephritis is supported by so eminent an authority as MacCallum. His own observations on the microscopical changes in the kidneys, are to the effect that "in severer cases there are profound destructive changes in the epithelial cells of the convoluted tubules. Even in the less advanced, certain tubules are partly lined by cells which are swollen and contain large hyaline droplets, but in those which have passed through several days of anuria, the convoluted tubules are choked throughout their whole course with masses of necrotic cells. The necrosis of the renal epithelium has the appearance of a toxic process, especially since the cholera vibrios have been so rarely found in the urine, although so carefully searched for".

There is little doubt, therefore, that although a certain number of cases may die anuric apart from an actual nephritis, many others owe their fatal termination to this cause. We shall see when treatment falls to be discussed, how important, therefore, it is that, in obviating a fatal termination/
termination from initial collapse, no measures should be adopted which will tend to unduly encourage toxic absorption from the bowel. I believe that the giving, intravenously, of a distinctly hypertoxic saline solution, such as ROGERS recommends, does unduly promote toxaemia and, as a result, toxic changes in the kidneys, an occurrence which is less probable if an isotonic saline solution be used.

(p). BLOOD CHANGES.

(1). INCREASE of the SPECIFIC GRAVITY of the BLOOD.

The whole question of specific gravity will be discussed in full in the section on Treatment. It is only necessary to state here that, as the fluid portion of the blood diminishes, the normal ratio between the volume of the corpuscles and of the plasma is disturbed at the expense of the latter. Since the sp.gr. of the corpuscles is higher than that of the plasma, the result is that the sp.gr. of the blood as a whole becomes increased as the plasma is lost. How this variability in the sp.gr. of the blood in cholera influences the treatment will be explained.

(ii) ALTERATIONS in the SALT CONTENT of the BLOOD.

Inseparably bound up with the alteration in the sp.gr. of the blood, is the question of the variation/
variation in the quantity of its dissolved salts. Apparently it is still unknown how exactly the fluid constituent of the blood is forced to transude into the lumen of the intestine - i.e. in what way the presence of the cholera vibrio or its toxins, or both, in the intestinal mucous membrane, exerts its specific action. The fact remains, however, that the fluid which escapes from the circulation is unlike any normal intestinal secretion, in that it holds in solution such a high concentration of salts, chiefly chlorides. EDMUND PARKES estimated that the rice water stools of cholera contain from 0.5 to 1 per cent of chlorides, and this has been confirmed by ROGERS, who found that on an average, 0.53 per cent was the figure, (or about 46.2 grains to the pint). These investigations are of great importance because they prove conclusively that along with loss of water from the blood, there is an accompanying loss of its dissolved salts. Rational treatment, should, therefore, aim at replacing both water and dissolved salts.

One, naturally, is anxious to know what effect the loss of both water and dissolved salts has on the blood, for both, of course, come from it. It is, necessary, that we should know this, for our aim/
aim must be to replace those constituents, which have been diminished, only to such an extent that the circulating blood shall be once more normal, both in quantity and quality. This matter will be taken up in full in the 'Treatment' Section, as will also -

(iii). The Reduction in the Alkalinity of the Blood.

IV./
IV. ALGIDE PERIOD.
(Stage of Collapse; Stage of Asphyxia.)

No hard and fast line can be drawn to distinguish this from the previous phase of the disease. All that can be said is, that as the patient's strength steadily diminishes, a period is sooner or later reached which is characterized by symptoms differing from those of the evacuation period only in degree. The two stages merge insensibly the one into the other. Only in one respect is it possible to differentiate them - a procedure which is not universally adopted - namely, to define the algide period as that in which collapse has reached such an extreme degree, that the pulse is no longer perceptible at the wrist. It must be realised that algidity is a progressive feature, as I have tried to point out, when treating of the choleraic period, and consequently does not show itself at any well defined juncture. If, then, by the 'algid stage' in cholera, one wishes to convey the impression that extreme collapse and pulselessness have occurred, then it seems to me that the term 'asphyxial stage' is more descriptive when applied to it. As LIEBERMEISTER (4) observes:

"The expression asphyxia, commonly but wrongly employed/"
employed to indicate cessation of breathing, is in this case thoroughly appropriate, since it properly signifies failure of the pulse. (ἀσφυκτικ in Galen, from ἀσφυκός, 'pulse').

For convenience, I shall adopt this suggestion as it will be more helpful in discussing certain aspects of cholera as illustrated by the present series.

The appearance of a patient in the 'asphyxial' stage of cholera is one not quickly forgotten. When after a little experience such a case is met with, one is overcome by impatience to begin treatment at the earliest possible moment, for the knowledge that every minute is of value and that it is in many cases, possible to literally snatch a patient from death itself, is at once stimulating and encouraging.

I have explained with what serious consequences a prolonged depression of the circulation is fraught, how every organ and tissue of the body suffers from the primary defect in its blood supply and from the secondary degenerative changes in structure owing to toxic agencies. The longer the collapse is allowed to continue, the greater is the probability that actual stasis will occur in highly important structures, such as the heart and kidneys. There is no doubt that frank, out-spoken cholera, is/
is one of the most urgent emergencies met with in the realm of medicine, and demands attention from the physician quite as urgently as do many acute abdominal conditions from the surgeon.

Amongst my 125 cases, 35 were admitted to the Isolation Hospital in an absolutely pulseless condition.

An enquiry into the history of the illness of these 35 cases is interesting in showing, not only how long they had been ill, but also how soon a person may be reduced to a pulseless condition by cholera. The shortest recorded time to elapse between the onset of the illness and the patient's admission to hospital in a completely pulseless state was 3 hours, the longest time was 24 hours and the average for all the cases was 10.2 hours. These three figures would certainly be even smaller did they represent the interval between the onset and the moment when the pulse became imperceptible.

I will not go into minute details as to their clinical condition, because this would entail much repetition of what has already been said with regard to the choleraic period. Rather will I be content to state that all showed the features characteristic of the evacuation stage in an extreme degree with the following reservations:

(1)/
III.

(1) DIARRHOEA:

It will be apparent that profuse diarrhoea and vomiting cannot continue indefinitely, if no replenishment of the circulation is taking place, either by absorption from the alimentary canal higher up, or by fluid introduced directly into the blood-vessels. Consequently, diminution in both the frequency and the copiousness of the evacuations becomes a more and more marked feature, after a certain climax has been reached. In short, the circulation has been depleted to its uttermost. So it is quite noticeable that while a patient is still possessed of a moderately strong and not excessively rapid pulse, the passage of 'rice-water' material occurs, say, every 3 or 4 minutes, whereas, when the pulse is extremely feeble and, it may be, imperceptible, that interval may be prolonged to half an hour or longer. In several instances, a patient was admitted in a very collapsed state, with a history of frequent and copious 'rice-water' evacuations, but, no specimen forthcoming, treatment was begun, and it was not until the circulation was revived that diarrhoea recommenced.

(2) VOMITING.

To a certain extent, this symptom also ceases to be so frequent as in the earlier stages of the disease, but its absolute cessation would seem to be longer delayed than that of diarrhoea. Although/
Although less frequent, it becomes increasingly trying to the patient, for now the act is no longer a forcible and apparently involuntary ejection of fluid, but is more or less transformed into a process of retching, while almost nothing is brought up on each occasion. The quantity of the vomited material increases once more after the intravenous infusion of fluid.

(3). MENTAL STATE.

Anxiety, having given place to apathy, during the later phases of the choleraic period, the mental condition of a patient, once the asphyxial stage is arrived at - becomes rapidly less and less receptive, until coma, and very often death, supervenes. But it is extraordinary how near the end consciousness may be maintained, for though the patient lies moribund, he may still be aroused by the excruciating pain of a cramp, or even sometimes by speaking to him or interfering with him in any way. The rapidity with which even such comatose patients are revived by intravenous saline, is one of the most dramatic events which I can imagine. For, while one is still holding the cannula in his vein, he will open his eyes, speak to you of his own accord, and often jocularly remark on his condition.

The initial improvement, however, is not always/
always maintained and relapse is prone to occur, necessitating repetition of the infusion.

Again, the mortality, as would be expected, is high, if treatment has not been begun before the patient is rendered pulseless. I have said that 35 of my cases were admitted in this condition. It is true that death claimed a bigger proportion of them than of those who arrived in a less collapsed state, but it is indeed gratifying to learn that the majority recovered under treatment.

TABLE NO. XV. shows that of the 35 pulseless algid cases, no fewer than 21 recovered, (60 per cent), while 14 succumbed (40 per cent).

<table>
<thead>
<tr>
<th></th>
<th>NUMBERS</th>
<th>PERCENTAGE amongst Total Pulseless Cases.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recoveries</td>
<td>21</td>
<td>60 per cent</td>
</tr>
<tr>
<td>Deaths</td>
<td>14</td>
<td>40 per cent</td>
</tr>
<tr>
<td>TOTAL</td>
<td>35</td>
<td>100 per cent</td>
</tr>
</tbody>
</table>

It is an interesting fact that a very similar recovery rate has been recorded by Rogers amongst/
amongst his pulseless cases (38 per cent), although before 1905, when improved methods of treatment, had, as yet, not been introduced, the recovery rate amongst patients who were admitted at all collapsed, was only 10 per cent.

(d.) TEMPERATURE READINGS. (Rectal and Axillary on Admission. (See TABLE XVI.) p. 119

The average rectal temperature of all cases on admission was 99.83°F. (TABLE No. XVI. Col.1.), the highest recorded being one of 104.8°F., and the least, 93.6°F.

The average axillary temperature 97.52°F. for all cases on admission, the highest record being 101.4°F., and the lowest, 95°F.

Therefore, the difference between the average rectal (99.83°F.) and the average axillary temperature (97.52°F.) amounted to 2.31°F.

It will be agreed that a difference of 2.31°F. is distinctly less than one is led to believe is typical of cholera, as seen in other countries. But I think one can explain such deviation from the usual. Mesopotamia is, unquestionably, a super-tropical country. When the circulation fails to reach the peripheral parts of the body in the collapse stage of cholera, the temperature of the skin becomes adjusted to that of the surrounding atmosphere/
atmosphere. Provided the skin is not unusually ac-
tive so that cooling of the skin from evaporation of
the sweat is unlikely, the tendency will be for the
skin temperature to approach that of the atmosphere.
If then, the atmospheric air registers — as it often
does — anything between 110 and 125° F., it will be
understood why those extremely low skin temperatures,
cited by other writers, as typical of cholera, were
not met with in my series.

With such a heat in the atmosphere, the
skin of an algid patient is prevented from rising to
a similar temperature only by evaporation from sweat.

Before discussing the significance of tem-
perature observations as affecting the prognosis, it
might be profitable to discuss when pyrexia is to be
expected, and to what degree. We may take it that a
certain degree of pyrexia is to be expected in cho-
lera, as in other acute infectious diseases, and that
such is an indication that the body is reacting to
the toxaemia. Other things being equal, the more in-
tense the toxaemia, the greater also the necessity
for reaction on the part of the patient, and conse-
quently the higher the pyrexia. Associated with this
intense toxaemia and high rectal temperature, there
is a proportionate fall in the skin temperature, which
reaches its minimum in the asphyxial stage of the dis-
ease/
disease. Great difference between internal (rectal) and external (skin) temperatures is, therefore, an indication that, although the infection is a heavy one nevertheless, the patient is reacting to the toxaemia and is striving to overcome it.

With these considerations in view, it is permissible to formulate a few general rules as to the utility of temperature observations in indicating a favourable or an unfavourable prognosis.

Points of favourable prognostic significance are the following:-

1. Very slight disturbance of temperature either per rectum or in the axilla, in a patient who is not otherwise sorely distressed.

2. Moderate pyrexia (rectal) and only slight falling (1° to 2° F.) in the axillary temperature, even though the diarrhoea and vomiting be urgent and copious: such indicates that although the attack is severe, the resistance of the patient is equal to the occasion.

Points of unfavourable prognostic significance are:-

1. Very high rectal temperature, especially if associated with an unduly low skin temperature, for such will indicate that although resistance is being offered to a severe infection, the powers of overcoming such an intoxication are being taxed to the utmost. In general, the greater the/
the difference between the rectal and the skin temperature, the more unfavourable the prognosis.

In order to prove this last statement, I have calculated the average temperature in the rectum and of the skin respectively amongst only those cases which were admitted in the asphyxial (pulseless) stage of the disease, and which I have already shown were associated with a higher case mortality than obtained amongst the less collapsed patients. The figures are these:

The average rectal temperature in the pulseless cases (TABLE No. XVI. Col. II.) was exactly 100° F. with a maximum of 104.6° F. and a minimum of 97.6° F.

The average skin temperature amongst the same cases was 95.95° F. with a maximum of 99.4° F., and a minimum of 95° F.

Accordingly the difference between these two averages was 3.05° F.

It will be remembered that I have said that the difference between the rectal and skin temperature for all cases was 2.31° F., and therefore the pulseless cases show an increase in the difference amounting to 0.74° F.

It is an interesting fact that the asphyxial
asphyxial case which gave the highest rectal temperature also gave a skin temperature reaching below the average, namely 104.6°F. and 96.3°F. respectively, giving a difference of no less than 8.3°F. (TABLE NO. XVI., Col.IV.). The curious thing about this particular case, however, is the fact that the patient ultimately recovered. One argues from this that the patient's resistance was exceptionally high and was able to overcome a severe infection in the end.

Carrying the investigation still further, I have calculated the average rectal and skin temperatures of the non-asphyxial cases, so that one may see a still greater contrast with the asphyxial cases. In the non-asphyxial cases, (TABLE NO. XVI., Column III) the average rectal temperature was 99.76°F. (or 0.24°F. below the asphyxial cases) while the average skin temperature was 97.71°F. (or 0.76°F. above the asphyxial cases). Consequently, it is found that in the severe asphyxial cases, the average difference between the rectal and skin temperatures amounted to 1°F. more than in the non-asphyxial cases.

For convenience, the average temperature readings in cholera nostras are also included in TABLE XVI. Columns V, VI, VII., and these will be discussed later under Differential Diagnosis.
<table>
<thead>
<tr>
<th></th>
<th>2.16</th>
<th>2.17</th>
<th>2.30</th>
<th>2.35</th>
<th>2.37</th>
<th>2.38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axilla</td>
<td>98.3°</td>
<td>98.0°</td>
<td>96.3°</td>
<td>97.7°</td>
<td>96.9°</td>
<td>97.0°</td>
</tr>
<tr>
<td>Rectum</td>
<td>100.1°</td>
<td>100.1°</td>
<td>104.6°</td>
<td>99.7°</td>
<td>100.0°</td>
<td>99.8°</td>
</tr>
</tbody>
</table>

Skin temperatures during the collapse stage of cholera.

To show the difference between the average rectal and average abdominal skin temperatures during the collapse stage of cholera.

Table No. XI
The most unfavourable sign of all, I believe, is a falling of the internal temperature or - what comes to the same thing - an insufficient rise of it, during that stage of the disease when asphyxia is threatened, and when the skin temperature is at the same time unduly low. Such will indicate that the patient's powers of reacting to an exceedingly virulent infection are far from equal to the occasion, and that the infection has gained the upper hand. Such was very apparent among the present series of cases.
V. THE REACTION STAGE.

If a cholera patient does not succumb during the algid or asphyxial stage, either from collapse resulting from excessive loss of fluid, or from intense toxaemia, a critical phase is reached when signs of returning vitality become obvious to the observer. What exactly affects this transformation is not quite known, but, from a consideration of the progress of other bacterial diseases, with which a 'crisis' is associated, it is natural to assume that the onset of the 'reaction period' of cholera is analogous to the 'crisis' of—say pneumonia, typhus, or relapsing fever. It is, in fact, a manifestation that a sufficiency of antibodies has been elaborated by the patient to counteract the amount of toxin in his blood, so far as present requirements are concerned. This, however, must not be taken as implying that from this point onwards the quantity of antibodies present in the patient's blood will continue to be sufficient to neutralise the available supply of toxin; for, owing to the circulatory disturbance, which is peculiar to cholera, the ushering in of any revival of the circulation is promptly accompanied by a greatly aggravated toxaemia, as a result of the commencement of re-absorption/
absorption from the bowel. Consequently, the temperature, both internal and external, rises suddenly and often excessively.

As happens immediately after the crises of the diseases mentioned above, the 'reaction stage of cholera may be the starting point of many of the dangers of the disease, although its existence at all is indicative of a certain degree of resistance offered by the patient to the infection.

The 'reaction period' of cholera may be entered at any stage during the previous two arbitrarily defined periods of the disease. The severity of the infection may not be such that the patient is brought to the asphyxial stage at all, and it is quite possible for a patient to show signs of reaction after a rather sharp attack of diarrhoea and yet his condition at no time approached a state such as one could recognise as 'algidity'.

Such cases do occur naturally - i.e. without artificial aid, such as from saline infusions, intravenous or subcutaneous.

As one would expect, reaction which sets in early, before the patient is reduced to a state of collapse, is characterised by a mildness and freedom from further complications which are altogether foreign to that which supervenes upon a well marked/
marked asphyxial stage.

The clinical features associated with reaction vary in degree according to the profundity of the preceding collapse, and, speaking generally, the stage is one in which the symptoms and signs of returning vitality occur in the reverse order in which indications of steadily diminishing vitality appeared. For, although imperceptibility of the radial pulse was practically the last sign of collapse to be appreciated, its return is the first sign of revival. The heart beats more strongly and regularly and the pulse accordingly is also stronger, more regular, and often slower, if it had not actually gone before. From this moment onwards, the observer is struck by the rapidity with which the appearance and general condition of the patient improve. The skin becomes warmer and pink once more and perspiration is often profuse, the intellect becomes more acute, the facies cholerica slowly disappears, the voice improves, and so on. There is no need to describe further the lines along which the return to the normal is conducted, but such a description will be conveyed in the statement that undesirable features gradually disappear, and, in favourable cases, convalescence is begun.

Modern/
Modern treatment ought to prevent one from being able to study the natural course of cases of cholera which are at all marked, for cases which show any degree of collapse demand instant aid in the shape of saline infusions, which, of course, accelerates the onset of reaction, but, in this case, an artificial one.

However, whether the reaction be the result of natural or artificial causes, two important features should be kept in mind in all cases, namely the degree of reactionary pyrexia and the rate at which the secretion of urine returns to normal.

Observations on the present series of cases are of value in showing how natural reaction affected these two clinical features in mild cases only. This is, of course, due to the fact that every patient who, on admission, showed from examination of the pulse, blood pressure, and estimation of the specific gravity of the blood, that the circulation had been appreciably depleted, received an immediate infusion of saline solution, usually intravenously. Very exceptionally, intracellular infusions were relied on to maintain the circulation. Since such cases contributed to the vast majority of the series, and therefore in them only an artificially produced reaction period could be studied/
studied, it will be more convenient to record such observations, after I have described the treatment by saline infusions.

I shall confine my remarks at this stage to the natural reaction as evidenced in the present series, and include all those cases which were treated otherwise than by intravenous or intra-cellular infusions.

When cases were admitted in such a condition that immediate intra-venous - or even intra-cellular infusion of saline was deemed unnecessary, certain other routine therapeutic procedures were adopted and these will be described in detail later, but it is only necessary to point out here that I believe they are not such as to influence materially the reaction period, either as regards its time of onset or its characteristics.

A study of, TABLE XVII. will show that a more or less natural reaction period can be investigated in only 27 out of the total of 125 cases (or 21.6 per cent). All the others were treated by intravenous or intracellular infusions of saline solution, with the exception of but 1 case, that of a man who was admitted in a gasping moribund state, and died even before the intravenous infusion could be begun.

TABLE/
Table XVII. showing the proportions of the case series treated by different methods and the mortality amongst them.

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>CASES</th>
<th>PERCENT.</th>
<th>DEATHS</th>
<th>DEATHS Percent of cases treated by different methods.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous</td>
<td>93</td>
<td>74.4</td>
<td>26</td>
<td>27.9 per cent</td>
</tr>
<tr>
<td>Intracellular</td>
<td>4</td>
<td>3.2</td>
<td>1</td>
<td>23.0 &quot;</td>
</tr>
<tr>
<td>Otherwise</td>
<td>27</td>
<td>21.6</td>
<td>4</td>
<td>14.8 &quot;</td>
</tr>
<tr>
<td>Nil.</td>
<td>1</td>
<td>.8</td>
<td>1</td>
<td>100.0 &quot;</td>
</tr>
<tr>
<td>TOTAL</td>
<td>125</td>
<td>100.0</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

The natural reaction period as it occurred in these 27 cases will be described under four headings:—

1. Time of onset.
2. Degree and duration of the pyrexia.
3. Re-establishment of the Renal Function.
4. Termination.

1.) Time of onset.

It will be obvious that in cases of only moderate severity, the alteration of the body temperature from the normal is not so marked as occurs in/
in more severe infections, nor is the disparity between the internal (rectal) and the surface (axillary) temperatures anything like so appreciable. Again, we must presume that the available quantity of toxin is less in these cases, and that, therefore, less pyrexia is to be anticipated when reaction does set in. Accordingly, it becomes a difficult matter for the observer to say with precision from a study of the temperature chart alone, at what time the reaction period was entered. Such a state of affairs does not exist when a well-marked case is allowed to continue its course untreated, for one is led to believe, from the writings of others, that a certain proportion of severe cases do ultimately recover without saline treatment, and the temperature records of these would, I imagine, indicate the time of onset of the reaction period.

But, as I have said, all except the mildest of my cases received either intravenous or intracellular saline infusions, because I believe that one is not justified in denying even a very slightly collapsed patient the benefit of such treatment; the risk of losing a case is too great if one wastes valuable time by carrying out utterly useless procedures, such as saline infusions per rectum.

Another factor which contributes to the impossibility/
CHART VI.
To show the degree & duration of a typical reactionary pyrexia, ending in recovery.

Name

Age

Disease Cholera.

DAY OF DISEASE 1 2 3 4 5 6 7

TEMPERATURE FAHRENHEITS SCALE.

RED = RECTAL
BLUE = AXILLARY

Pulse

Resp.

Motions

Urine, ozs.

Sp Gr

Reaction

Chlorides

Albumen

Day of Dis.
impossibility of stating the time of onset of the reaction period amongst my non-infused cases is the delay which often occurred before these mild cases reported sick. Consequently reaction had in many cases set in before they reached hospital.

Of the 27 non-infused cases, 9 showed no temperature changes to indicate reaction.

The other extreme is exemplified by one of the remaining 18 cases. His chart (Chart VI) shows that while the skin temperature on admission had dropped to 97°F, that in the rectum was 100°F. Reaction set in about 24 hours after the onset, as indicated by the slight rise in both skin and rectal temperatures. The fall by lysis of the rectal temperature during the succeeding 4 days indicates the duration of the reaction period. Between these two extremes, various degrees of abruptness in the onset of reaction occurred, and where it can be more or less accurately detected, seemed to occur as early as during the first 48 hours of the disease.

2. DEGREE of DURATION of the REACTIONING-PYREXIA.

The highest recorded rectal temperature during natural reaction was 101.8°F. with an accompanying axillary temperature of 101.4°F.
Reaction here again occurred during the first 24 hours.

As to the duration of the pyrexia, this varied fairly uniformly between 3 and 5 days, the fall to normal being, in practically every case, by lysis.

3. REESTABLISHMENT of the RENAL FUNCTION during REACTION.

In describing the symptomatology of cholera, I have explained why the secretion of urine fails in proportion to the degree of collapse reached. If the reasons for failing secretion are appreciated, there will be no difficulty in understanding why most of these mild and non-infused cases of mine show neither an initial fall in the daily output of urine to any noticeable degree, nor a supervening reactionary rise. Probably the best idea of altered kidney function is imparted by quoting the facts of a typical case.

An Indian patient was admitted at 5 p.m. suffering from mild cholera. Pulse good. Had passed 5 watery motions that day, and vomited about 9 times. No urine was passed from admission till midnight. Next day, only 2 stools, and vomiting had ceased. During this 24 hours, reaction set in and /
and 11 ounces of urine were passed. On the third, fourth and fifth days, he passed 20, 50 and 50 ounces respectively. Such a case illustrates what is ordinarily to be expected in a mild and non-infused case. This reactionary increase in the urinary secretion is, of course, due to the rise in blood pressure within the renal arteries, along with the disappearance of those other abnormal features which I have already enumerated as being aetiological factors of diminished urinary secretion (oliguria) or of total suppression (anuria) during the collapse stage of cholera.

In none of these 27 non-infused cases did the renal function fail to be re-established.

I wish to draw attention to a point of practical importance - namely, that in tropical countries, the daily output of urine, even of healthy persons, during the hot dry weather, is very considerably below that quantity which is recognised as normal in more temperate climates. This is due to the enormous quantity of water lost from evaporation of the sweat. Accordingly, in arriving at a decision as to whether the renal function has or has not been sufficiently recovered, the volume of the daily output/
output of urine is only one factor to be noted; while the temperature and humidity of the atmosphere, the activity of diaphoresis and the concentration of the dissolved constituents of the urine must all be duly taken into consideration. In other words, one must not conclude, that because a cholera patient is not passing the normal 50 ounces of urine per diem, the renal function is necessarily at fault, unless the atmospheric conditions, inactivity of the sweat glands, or chemical examination of the urine corroborate such a diagnosis.

4. TERMINATION of those CASES which experienced a NATURAL REACTION.

It might be expected that, since the greatest care was observed in actively treating every case whose condition was in the least collapsed, the recovery rate amongst the non-infused mild cases would be 100 per cent. These 27 cases of mine prove otherwise, for 4 of them (14.8 per cent) ultimately died. (See Table XVII, p.186). This, however can be said for such an apparently erroneous presumption, namely that 3 of the 4 deaths are attributable to sequelae and not to cholera per se. One died of broncho-pneumonia on the 14th day of his illness, another from dysentery (24th day), and another from broncho-pneumonia (24th day). The fourth/
fourth death was that of an Arab of poor physique, who died on the eighth day apparently from sheer exhaustion (asthenia); at any rate, the post mortem examination revealed no concrete lesion to explain the death otherwise.

Twenty three of the twenty seven non-infused cases recovered (85.2 per cent). Fourteen of these twenty three cases continued to make an un-interrupted recovery after reaction had set in, and therefore experienced a true normal convalescence. Such cases are described in books as having a "regular" reaction period. Nine cases developed complications or sequelae which will be dealt with under those headings later.

We see, therefore, that even those cases which experience the mildest attack of cholera do not invariably recover, nor do they invariably recover to normal health without the development of complications or sequelae. Still, one may truthfully say that death after a natural reaction in suitably chosen cases is the exception, and that if it should occur, it is usually attributable to complications or sequelae, which, I should imagine, are wholly unavoidable.
MORBID ANATOMY.

For several reasons, the practice of performing post-mortem examination on cases of cholera was discouraged by the medical authorities, who advised that a sectio be made only in such cases where the cause of death was not completely accounted for clinically.

In the first place, the conveniences at one's disposal for the proper carrying out of a post-mortem examination were inadequate. The procedure had to be conducted in a tent at a time of the year when the temperature within was anything up to 120°F. Further, it was quite impossible to prevent the influx of flies, which swarmed in thousands about the viscera and discharges of the cadaver, with the consequent risk of the conveyance of the infection to other persons in the camp. The experience, also of other observers, in showing that, in the average cases of cholera, the post mortem appearances are very similar, proved the futility of examining the anatomic changes in all cases.

Accordingly, an autopsy was performed in but three instances. The first case was that of a British/
British soldier who died in a comatose state after only 18 hours illness. He had received an intravenous infusion of 4 pints of hypertonic saline in another hospital prior to his being transferred to the Isolation Hospital. Shortly after arrival, he died of hyperpyrexia, in spite of all efforts to reduce the temperature. Nothing very peculiar was revealed at the sectio. The usual appearances, congestion etc. in the lower coils of small intestine were noted. The spleen was not enlarged. The heart muscle was infiltrated with fat a little more plentifully than is consistent with health.

The sectio in the second case revealed early consolidation of lobar pneumonia in both lungs, while in the third case, no gross changes were found, death on the eighth day being due apparently to exhaustion.

The remarkable attitudes assumed by the limbs of those dead from cholera and due to extensive post mortem rigidity were not witnessed at the Isolation Hospital. This is probably due to the fact that little delay is incurred in the burial of the dead in tropical countries.

DIAGNOSIS/
DIAGNOSIS.

The occurrence of symptoms which are characteristic of epidemic cholera - such as urgent rice-water diarrhoea and vomiting, cramps and collapse - will usually lead one to at least strongly suspect that a patient is suffering from cholera asiatica. The probability that such a diagnosis is correct will be the greater, if other cases of the disease have occurred in the same district and at the same time, and the cholera bacillus has been recovered from their discharges.

Many are the pathological states which are said to closely resemble cholera infection, and, indeed, to be often indistinguishable from cholera, when considered from a clinical standpoint alone.

It is said that Symptoms of an acute gastro-enteritis resembling true cholera may occur when the patient is in reality suffering from one or other of the following pathological conditions: -

1. Acute arsenical poisoning, when the poison is taken by the mouth. (The case which occurs in Table No. I was not sent to the Isolation Hospital as a possible case of cholera, but as scarlet fever, on account of a rash which followed the administration of a dose of salvarsan/
salvarsan given intravenously).

"White arsenic" (acidum arseniosum) is often the form in which the drug is taken. Shortly after it has been swallowed, violent gastro-enteritis with vomiting and diarrhoea, cramps, collapse and other symptoms bearing a close resemblance to those of cholera set in.

2. Acute antimony poisoning, when the poison is taken by the mouth. 'Tartar emetic' (antimonium tartaratum) is the usual form in which it is taken. The symptoms, though less pronounced, are not unlike those of acute arsenical poisoning, the so-called 'stibial cholera'.

3. Acute mercurial poisoning, when the salts of mercury are taken by the mouth in poisonous doses. 'Corrosive sublimate' (hydrargyri perchloridum) and 'white precipitate' (hydrargyrum ammoniatum) are the usual salts taken, and these cause intense gastro-enteritis.


5. Cholera nostras, including -

(a) Cholera infantum, which is a very acute summer diarrhoea occurring in young children.

(b) 'Food poisoning' of exogenous origin ('Ptomaine poisoning')
6. Mushroom poisoning, which is an example of "food poisoning" of endogenous origin. The poisonous mushroom, Agaricus muscarius, contains a very powerful poisonous alkaloid called muscarine. Its action is practically the same as that of pilocarpine in poisonous doses, exciting copious secretion of alimentary fluids and purging, vomiting, profuse secretion of sweat, and therefore the secretion of urine is lessened. A marked fall in the skin temperature also occurs. Its action therefore produces a clinical picture not unlike that of true cholera.

7. Very acute bacillary dysentery with profuse watery stools and collapse.

8. Typhoid and paratyphoid fevers.

9. Malignant malarial fever (the so-called "pernicious algid access" of malaria.

10. Sunstroke, when associated with diarrhoea.

11. Trichinosis in its early stages.

12. Certain forms of acute intestinal obstruction or peritonitis with vomiting and serious collapse. Such cases may possibly be confused with "cholera sicca".

Further/
Further, owing to the difficulty which sometimes may occur in discovering the cause of various collapsed states, one may also include -

13. Certain conditions associated with a comatose state, e.g. moribund persons dying of various diseases, and about whom no history is forthcoming.

I do not propose to discuss the differential diagnosis between all the above pathological states and cholera asiatica, as such can be found in most text-books. My present aim is rather to treat only of certain amongst them which occasioned difficulty to me in arriving at a correct diagnosis from a consideration of clinical features alone.

The disease which caused by far the greatest confusion in diagnosis, prior to bacteriological investigation of the stools, was cholera nostras.

Some idea of the frequency with which this form of acute gastro-enteritis was mistaken for cholera asiatica, can be gleaned from TABLE I pages 9\&10. It will be seen that during the three years, no less than 80 cases of acute gastro-enteritis were sent to the Isolation Hospital under the supposition that they were suffering from cholera asiatica. In other words, over a third (80) of the cases admitted with choleraic symptoms (237), ultimately were proved, on bacteriological/
bacteriological examination to be free from true cholera infection. Such a state of affairs is in my experience most natural and justifiable, for certainly in many respects, the two conditions are clinically indistinguishable. Mildness of the choleraic symptoms proved time and again, to be of no aid in arriving at a diagnosis of cholera nostras, for while all degrees of severity were met in cholera asiatica cases, the same is true of cholera nostras.

I have said that many of the cases of cholera asiatica were of so mild a type that saline treatment was found to be unnecessary. On the other hand, I have in my possession the case notes of 63 of these cases of acute gastro-enteritis and amongst these, no fewer than 25 (39.7 per cent) were so collapsed, on admission that immediate intra-venous saline infusion was indicated. The average quantity infused in these cases on admission was 4.56 pints, the minimum quantity being 3 pints and the maximum 9 pints. Seventeen of these cases were given isotonic saline (80 grains of sodium chloride to the pint), while the remaining 8 cases received hypertonic saline (120 grains of sodium chloride to the pint). In only two cases was it necessary to repeat the intra-venous infusion. The first of these was re-infused after 10 hours, 4 pints of normal saline being given. The/
The other case was so obstinate that he had to be reinfused twice, the second infusion was given $1\frac{3}{4}$ hours after the first, and consisted of a pint of hypertonic saline, while the third infusion, given $1\frac{1}{2}$ hours after the second, consisted of 9 pints of isotonic saline. We see, then, that cholera nostras may be an alarming condition and every bit as influential as cholera asiatica in the production of prostration in those affected.

There are many other points of resemblance in the two diseases, such as:

(a) The occasional occurrence of cholera nostras among groups of people. Such is particularly liable to happen amongst units on field service, and did actually happen amongst a large number of the men of an Indian regiment at Amara. These patients were sent in, in a collapsed state and, clinically, conformed to the picture of cholera asiatica. Bacteriological tests, however, proved negative to cholera asiatica. One can say, however, that the absence of all tendency of the malady to spread beyond the particular little community affected, and thus to assume epidemic proportions, is in favour of the disease being other than that associated with Koch's vibrio.

In/
In this regard, the synonym of 'sporadic cholera' applied to cholera nostras seems particularly appropriate. Certainly, the disease refrained from transgressing its initial bounds as regards the regiment in question.

(b). The Seasonal Incidence. Here again, the two diseases are alike, for both reach their highest incidence during the hot summer months.

CHART NO. vii., shows the monthly incidence of the 63 cases of cholera nostras. It is seen how the disease was confined to the hot season of the year, reaching its maximum incidence in July, the hottest month of all. No cases of cholera nostras occurred during the cold months of December, January, February and March.

A comparison of this with CHART NO. V proves how alike the two diseases are in their seasonal incidence, and how useless this factor is as an aid in distinguishing the one from the other.

(c) Age, Sex and Race, are factors which, from all accounts, exert no material influence on the susceptibility of persons to either cholera Asiatica or cholera nostras.

It may be asked, then, are there any symptoms or signs, prior to the commencement of treatment/
CHART NO. VII.

To show the seasonal incidence of Cholera Nostras.
(Compare with CHART NO. V. page 32) 63 CASES.
treatment, and excluding the recovery of the cholera vibrio in the stools, which might tempt one to predict that a given case is cholera nostras rather than cholera asiatica?

I think that this question may be answered in the affirmative. For, from a consideration of my cases, I believe that the diagnosis of cholera nostras, may be favoured when any of the following clinical features is present;

(1) The onset of vomiting preceded that of diarrhoea. This certainly did hold in a few of my cases of cholera nostras, but in none of the cases of cholera asiatica.

This matter has already been discussed when speaking of symptomatology. See page 75.

(2) The presence of blood or blood-tinted watery motions. (see page 79).

(3) The temperature is less disturbed. This point is conveniently discussed under two headings:

(a) The degree of pyrexia, as indicated by the estimation of the true body temperature per rectum.

(b) The disparity between the internal (rectal) and the external (axillary) temperatures.

(a) PYREXIA.
The average rectal temperature of those cases of cholera nostras in which such was recorded on admission — i.e., prior to the beginning of any treatment (53 cases) is found to be $100.14^\circ F.$, the highest temperature being $102.8^\circ F.$ and the lowest being $97^\circ F.$ See Table No. XVI page 119.

In cholera asiatica, my cases showed that the average rectal temperature was $99.83^\circ F.$ or only $0.31^\circ F.$ lower than that in cholera nostras (See Table XVI, Columns I and V).

The average axillary temperature is found to be $98.27^\circ F.$ (Table XVI, Column V.) the maximum record being $100.8^\circ F.$ and the minimum being $95^\circ F.$

From this it will be calculated that in cholera nostras, the difference between the average rectal ($100.14^\circ F.$) and the average axillary temperature ($98.27^\circ F.$) amounted to only $1.87^\circ F.$

In cholera asiatica I have shown that my cases showed an average axillary temperature of $97.52^\circ F.$ or as much as $0.75^\circ F.$ lower than that in cholera nostras.
Comparing the disparity between the rectal and the axillary average temperatures in the two diseases, one finds that this is greater in cholera asiatica, to the extent of $0.44^\circ F$, when all cases are considered, (Table XVI, Columns I and V), but that the difference is even greater ($0.39^\circ F$) when only the worst cases of the two diseases are considered (Table XVI, Column II and VI).

My contention, therefore, is that a marked difference between the rectal and axillary temperatures is more characteristic of cholera asiatica than of cholera nostras, provided that the patient is, at the same time, in a state of collapse, partial or complete. Conversely, if these two readings approach one another in a collapsed patient, the diagnosis is in favour of cholera nostras.

(4) Persistence of a bilious tinge in the stools is often a characteristic of cholera nostras, but is quite an exceptional feature in cholera asiatica. See page 81.

(5) I think that, on the whole, cases of cholera nostras seem to experience more abdominal discomfort, probably of a colicky nature. I am not referring to the muscular cramps which occur in the abdominal parietes during the latter/
latter stages of cholera asiatica and which are so distressing.

Are there any further points which help to differentiate the two diseases after treatment has been begun?

The following features are characteristic of cholera nostras, according to the notes of my cases.

(6) No matter how serious a patient's condition may appear, the great majority of cases of cholera nostras improve from the moment at which intra-venous infusion is begun. So much is this the case, that it is seldom necessary to repeat the infusion. I have already referred to this (See page 140).

(7) The duration of the dominant symptoms, namely diarrhoea and vomiting, is much shorter in cases of cholera nostras, even when severe, than in cases of cholera asiatica, even in the milder cases.

Reference to Table No. XVIII will show that this is so. The table also shows that in both diseases, vomiting ceases before the diarrhoea does so.

(8) The freedom of cholera nostras from complications is really very striking. Amongst my/
<table>
<thead>
<tr>
<th></th>
<th>Mid Cases</th>
<th>Severe Cases</th>
<th>All Cases</th>
<th>Mid Cases</th>
<th>Severe Cases</th>
<th>All Cases</th>
<th>Mid Cases</th>
<th>Severe Cases</th>
<th>All Cases</th>
<th>Mid Cases</th>
<th>Severe Cases</th>
<th>All Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.990</td>
<td>2.040</td>
<td></td>
<td>1.610</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.298</td>
<td>3.272</td>
<td></td>
<td>3.292</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.960</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.77</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE NO. XVIII**

<table>
<thead>
<tr>
<th>Duration (in days) of Nystagmus</th>
<th>Duration (in days) of Vomiting</th>
</tr>
</thead>
</table>

Showing the average duration (in days) of diarrhea and vomiting in both cholera asiatica and cholera no. XI. 38.
my 63 cases, only one caused any real anxiety, namely, a patient who had received an intravenous infusion of 3 pints of hypertonic saline. Hyperpyrexia supervened; but, with appropriate treatment, he ultimately recovered. No cases of uraemia, or even of more than an evanescent oliguria were noted.

Another striking fact about cholera nostras is that a fatal termination is very exceptional. My own experience is, that of 63 cases not a single one was lost. When it is remembered that 25 of these (39.7 per cent) were sufficiently collapsed as to require immediate intravenous saline treatment, it will be admitted that a recovery rate of 100 per cent is both highly significant and gratifying. Further, I am not aware of a fatal termination having occurred amongst those other 17 cases of the disease, whose case notes I have unfortunately been unable to obtain. From this, I argue that the element of toxaemia is decidedly less pronounced in cholera nostras than in cholera asiatica; for to take an example of a condition of toxic causation, namely, persistent suppression of urine/
urine which may supervene during the course of a mild case of cholera asiatica, such never occurred once in cholera nostras - even in the most collapsed patients. One might cite also the less pronounced reactionary fever - whether natural or artificial - in cases of cholera nostras.

Lastly, when all other characteristics fail to allow of a differential diagnosis being made, the final decision must rest on a careful and thorough bacteriological investigation of the dejecta.

I do not intend to go into this question in great detail. It has already been said that when the specific cholera vibrio (or KOCH'S bacillus) was found in the stools, the case was pronounced as one of cholera asiatica; when, on the other hand, it was not recovered, the case was returned officially as "acute gastro-enteritis". In the great majority of those cases where the cholera vibrio could not be found (63), the bacteriological investigation revealed no other variety of micro-organism which was present in such proponderating numbers that it could/
could be definitely pronounced as causal.

Only in 6 cases (9.52 per cent) did the bacteriological report throw any light on the flora of these stools which were found to be negative to cholera".

These six cases are as follows:-

1. *E. pyocyaneus*.
2. *E. enteritidis* of Gaertner.
3. Lactose fermenters ("Food poisoning group")
4. Lactose non-fermenters.

Whether the clinician must accept a diagnosis of cholera nostras (or acute gastro-enteritis") where neither the cholera vibrio nor any other obviously causal organism can be isolated from the stools, I am unable to say, but I do believe that sometimes a patient's symptoms may actually be the result of infection by the cholera vibrio, and yet such cannot be isolated. I hold this view for several reasons. First, my own experience has shown me that, on several occasions, the cholera vibrio was not isolated from a patient's stools during a particular stage of the evacuation/
evacuation period, and yet on sending another specimen to the Laboratory, a few hours afterwards, the vibrio was recovered in almost pure culture. Repeated examinations of the stools would appear to be essential before we must satisfy ourselves with the bare diagnosis of cholera nostras in a case whose stools show no vibrio on a first examination. In other words, the finding of the cholera vibrio is sure proof that the patient is suffering from cholera asiatica, but a negative result does not necessarily indicate that he may not still be so infected.

(8)

As KOCH says,

"We may now, I think, regard it as an ascertained fact that the cholera-bacteria are the inseparable concomitants of Asiatica cholera, and that the demonstration of their presence is an infallible proof of the presence of this disease. This does not imply, however, that the absence of the cholera bacteria, or rather the failure to find them, in a case suspected to be one/
one of cholera, proves under all circumstances that the disease in question is not cholera. In cholera, just as in other infectious diseases caused by microorganisms, cases may occur which one must, owing to their other symptoms, regard as indubitable cases of cholera, in which, however, owing to the defective qualification of the investigator, or to the circumstance that they are investigated at an unsuitable time, cholera bacteria are not found."

Again Sir Patrick Manson observes:

"The detection of the common bacillus in the stools is now regarded as a positive indication of cholera. It would be rash, however, to affirm that a negative result, from bacteriological examination of a single case, is conclusive against its being cholera/
cholera". ---"A few cases of what, from a clinical point of view, appears to be true cholera, have been observed in which the most careful and prolonged bacteriological examination failed to detect the common bacillus. Therefore, it has been advanced—as cholera can occur without the common bacillus, the common bacillus cannot be the cause of cholera. Against this, it has been said—

(a) that these observations were defective"----"such examinations, to be trustworthy, have to be made by a skilled bacteriologist"----

(b) that although the bacillus was not found, it by no means follows, that the bacillus was not present at some time in the case.

That the bacteriological investigation of
my cases was most skilfully carried out, there is no question, for the stools were examined by a bacteriologist of the highest repute. Further, the specimen from each case was sent to the Laboratory with the utmost dispatch so as to eliminate any chance of the cholera vibrio dying out before steps could be taken to cultivate it in suitable media.

(4) Liebermeister, too, apparently agrees that bacteriological examination is not absolutely infallible, for he says - with regard to the question of diagnosis -

"---it is as bad to call every suspicious case cholera, and thereby cause unnecessary uneasiness among the population, as to overlook a true case and leave the way open for an epidemic. Fortunately we possess today in the examination for cholera bacilli a means of decisively recognising almost all cases. When the result of the examination is positive, there is/"
is no doubt about the disease being cholera; when, after correct and careful examination, it is negative, though there is not the same certainty, it is highly probable that the presence of Asiatic Cholera may be denied."

It is thus possible that some of my cases of cholera nostras were in reality cases of cholera asiatica owing to the impossibility of recovering the vibrio in all cases, for which anomaly, the reasons are not yet fully understood. If this be the case, the recovery rate amongst my cases of cholera asiatica is actually even higher than the figures indicate.

I have devoted most of my remarks regarding differential diagnosis, to cholera nostras, because I should imagine it is the chief stumbling block amongst the conditions which may resemble true cholera, and obstruct the path to an accurate diagnosis.

Fortunately, the treatment of these two diseases is very similar, and, from the patient's point of view, it matters little whether differentiation is ever accomplished. But it is obvious that it is highly desirable to come to a correct decision, as soon as possible, in order to avoid the/
the danger to other patients in a ward of admitting amongst them, a cholera patient under the supposition that the case is one of simple gastro-enteritis. Moreover, it is possible that, unless the greatest care is taken to prevent cross infection, a case of simple gastro-enteritis, mistaken for cholera and admitted to a cholera ward, may, subsequently contract the more serious infection.
PROGNOSIS.

The following circumstances were found to be favourable towards the immediate prognosis - i.e. the ultimate recovery - of the cholera patients admitted to the Isolation Hospital.

1. Previous inoculation with cholera vaccine. (See page 44.)

2. Freedom from preceding or coincident disease acute or chronic. (See page 22.)

3. Admission to Hospital at the earliest possible moment after the onset of symptoms so that treatment may be instituted before the asphyxial stage is reached. (See page 6.)

4. Mildness of the clinical features irrespective of the duration of the disease prior to admission to Hospital.

5. Adequate, but not excessive, reaction following treatment.

6. Absence of all important complications & sequelae, especially hyperpyrexia, prolonged suppression of urine, and the typhoid state.

Points of unfavourable significance as to the immediate prognosis, are the respective converses of the foregoing, not omitting the importance of persistent hiccups, as an omen of impending death. (See page 87.)

As to the remote prognosis of these cases, that is to say, the question of future immunity or increased susceptibility to cholera infection of/
of those who recovered - it is interesting to record the progress of one case:-

J.H. Age 25. On 6/9/16, diarrhoea and vomiting began suddenly at 5 a.m. Sent into Isolation Hospital at 10 a.m. as a probable case of cholera. On admission, he was somewhat sunken in appearance. Pulse = 92, regular, and of quite good force. Temperature in rectum = 96.6° F, in axilla = 95° F. Respirations 18. No cramps. Routine treatment by pills of potassium permanganate, hypodermic injections of atropine sulphate etc. begun at once. Infusion of saline solution not considered necessary. Diarrhoea and vomiting continued mildly for three days, during which period the secretion of urine continued satisfactorily. Thereafter convalescence set in and he made an uninterrupted and uneventful recovery.

This case was considered as one of the "very mild" class. He had received prophylactic inoculation against cholera - ½ c.c. in 9/6/1916, and 1 c.c. on 17/6/1916 - that is to say, about 12 weeks prior to the onset of his symptoms. Except for an obstinate slight looseness of the bowels, he was quite fit for duty when he was discharged to rejoin his unit on the 5/11/1916, having completed/
completed the then prescribed segregation period of "42 days after the passage of a normal formed motion". He volunteered the statement that he had been subject to "looseness in the bowels" for years, and that he had often been treated for "chronic diarrhoea". As an additional safeguard against the possibility of his being a "convalescent carrier" of the cholera vibrio, a specimen of a diarrhoeic stool was sent to the Central Laboratory on 31/-10/1916 for investigation. No vibrios were found and therefore the question of his being a "carrier" was answered in the negative.

After only 8 days, he was again sent to the Isolation Hospital in a hurry (on 13/11/1916). The history was to the effect that at 2 a.m. on that date, violent diarrhoea and vomiting set in very suddenly. He was on guard duty at the time, and so weak that he was forced to go off duty. Reported sick at 6 a.m. He was so collapsed that the Medical Officer administered 1½ pints of saline solution (tonicity unknown) intravenously. Relapse again occurred and he was transferred to the Isolation Hospital at 4 p.m. on the same day. On admission, purging and vomiting extreme, cold, sunken and
and collapsed. Cramps in muscles of calves and abdomen. Pulse 93 and of poor quality. Blood pressure 97 m.m. of Hg. Temperature per rectum = 98.4°F and in axilla = 96.6°F. Specific gravity of the blood = 1069.

He was immediately given an intra-venous infusion of 6 1/2 pints of slightly hypertonic saline solution (98 grains of sodium chloride to the pint) and the other routine therapeutic measures taken, i.e. potassium permanganate pills, atropin injections etc. Reaction set in at once, rectal temperature rose to 100°F and the axillary temperature to 98°F, at 11 p.m. that same night.

My notes on this case made at 11 a.m. on the following day, are as follows. "Much improved. Pulse good, 80 per minute. Blood pressure = 94 m.m. of Hg. Rectal temperature = 98°F. Axillary temperature = 98°F. Has not vomited since he did so a few minutes after the infusion had been given last night. Two stools this morning. Passing plenty of urine".

From this date onwards, he again progressed through an uneventful convalescence, except that chronic looseness of the evacuations persisted in spite of all preventative treatment. Stool specimens/
specimens were sent for examination on the 23rd and 28th December 1916, and both were negative to cholera, both in film and on culture. Since he continued to have this troublesome diarrhoea, and as he was somewhat debilitated, his discharge to India was considered advisable. Accordingly, he was dispatched down river to Basrah on 5/1/1917.

This is the only case which I am able to record of a patient's suffering from two distinct and separate attacks of cholera. One must look upon the facts as indicating that, in this particular instance, the patient had acquired practically no immunity to cholera by the first attack of the disease, thus allowing either a re-infection or a re-crudescence of the disease to very seriously affect him. The negative report on the examination of the stools prior to his discharge after the first attack, lends weight to the theory of re-infection. Since, however, this case is so exceptional to the series, I think that there is little doubt that one attack of cholera seems to excite an accidentally acquired immunity from a future attack, for a time at least, as is generally held to be the case.

The satisfactory results obtained from anti-cholera inoculation in diminishing not only
the incidence but also the mortality of cholera, by provoking an artificial (intentional or purposeful) acquired immunity, of varying degree, also support the belief that the remote prognosis of the disease is highly favourable.
Before taking up the question of unusual methods of treatment in individual cases, it is necessary at this stage to describe the routine procedures carried out upon a cholera patient on his admission to the Isolation Hospital.

I. GENERAL REMARKS.

Immediately on a patient's admission, all his clothing was rapidly removed and he was placed in bed on a mattress which was covered completely by thick waterproof sheeting.

Depending on the atmospheric temperature and on the patient's own comfort, the bed clothing consisted of merely a single sheet or an additional blanket or two. The pulse, respirations and temperature, both rectal and axillary, were then taken and charted. At this point, special notice was taken of the rectal temperature, for on it depended whether heat should be applied externally to the collapsed patient. The natural thing, it would seem to do to an algid patient with cold clammy skin, would be to surround him with hot bottles and heap blankets upon him. A very little experience, however, is sufficient to show how useless and/
and dangerous such a practice might be, for in taking the rectal temperature, it may be found that the thermometer registers over $102^\circ$ F. Further, it is very striking how a patient with markedly sub-normal skin temperature and high rectal temperature apparently is unable to tolerate externally applied heat, for he becomes more restless and resents the heavy blankets. Only in cases where both rectal and skin temperatures were below normal did I allow hot water bottles and heavy blankets, and such patients only too readily indicate how grateful they are for such comforts.

No patient was allowed anything by the mouth but plain boiled water until he had been thoroughly examined, and until a specimen of the stools had been obtained. I have spoken at length about the debatable point of whether a cholera patient should be allowed to drink _ad libitum_, but I repeat that all my patients were given a large vessel containing cool drinking water at their bedsides, from which they were at liberty to drink liberally if they so wished.

The huts in which these cholera patients were treated were of the lightest construction and afforded but little comfort or scope to protect the patients/
patients from a prostrating atmospheric heat, dust storms, flies etc. There was no flooring of any kind, the beds being placed on the hardened desert earth. This, however, I believe was, under the circumstances, an advantage, as it was an easy matter to saturate the ground of these huts with an antiseptic, e.g. cresol solution. This was done several times a day, not only to keep down dust, but also to kill the cholera vibrios which reached the patient's surroundings during vomiting, etc.

(2) THE ROLE of PERMANGANATES.

With a view to destroying the cholera toxins by oxidation, ROGERS introduced his "permanganate treatment" in August of the year 1909. The whole subject is very fully discussed in his book. It only remains to be said here that the instructions, issued by ROGERS with regard to the giving of permanganates in cholera were followed very closely. Practically every case received this treatment, so that I am unable to compare the effects of giving or denying this drug. The greatest care was taken not to begin the administration of either the pills or the solution till a stool specimen had been obtained for bacteriological investigation.
investigation. Once such had been procured, and the case was pronounced to be cholera on clinical grounds, the permanganate treatment was begun. The patient was encouraged to drink \textit{ad libitum} a solution of calcium permanganate in a strength of 5 grains to the pint, while a course of permanganate pills was also begun. Each pill consisted of 2 grains of finely powdered potassium permanganate, made up with kaolin or vaseline, and coated with either keratin or a varnish composed of salol (1 part) and sandarach varnish (5 parts). Such a coating protects the permanganate within it until the pill reaches the small intestine where the coating becomes dissolved by the alkaline intestinal contents. In this way, the action of the pills is concentrated upon a segment of the alimentary canal where probably the cholera toxins are most plentiful. It is believed that the readiness with which permanganates give up their oxygen in the presence of organic matter is the potent factor in rendering the cholera toxins innocuous. No danger of poisoning occurs, owing to diminished absorption characteristic in cholera; indeed, ROGERS has shown that the drug, per se, is not by any means a dangerous poison when taken even apart from cholera.
The prescribed course was as follows - Two pills were given every \( \frac{1}{4} \) hour for 2 hours (=18 pills or 36 grains of potassium permanganate) Then two pills were given every \( \frac{1}{2} \) hour until the stools diminished in quantity and frequency and showed a distinctly greenish tinge which is evidence of oxidised bile. Once the green colouration in the stools appeared, the giving of pills was stopped, for it was found that by this time the patient's general condition also was very much improved.

(3) THE ROLE of ATROPIN.

Again ROGER'S teaching was followed and all my patients who were at all collapsed received a hypodermic injection of \( \frac{1}{100} \) grain of atropin sulphate night and morning until their condition ceased to give cause for alarm.

Although there is no doubt that ROGER'S statistics have shown the efficacy of atropin in reducing the mortality from cholera, since its introduction by him in 1915, it is difficult to fully understand how the remedy is efficacious. It is of course, known that atropin, in small doses, tends to paralyse the terminations of the vagus in the heart, and, in this way, the heart's action is quickened.
quickened. Although the heart's action is accelerated, its force is not diminished, and thus the blood pressure is raised. It is this raising of the blood pressure to which the beneficial effects of the drug in the treatment of cholera are in all probability entirely due. Other drugs could also raise blood pressure, but it is the particular way in which atropin accomplishes this action which signals this drug out from the others as peculiarly desirable in the treatment of cholera. ROGERS tells how Sir Lauder Brunton, in 1894, suggested the use of atropine in cholera on the grounds that, first of all, the actions of the cholera toxins are very similar to those of the highly poisonous alkaloid muscarin which can be shown to have a local stimulating influence on the terminations of the vagus in the heart (HALE-WHITE). Atropin, being exactly antagonistic to muscarin in its effect on the heart, therefore naturally suggested itself as a likely antagonist to cholera toxin.

The other beneficial effects, claimed by ROGERS for atropin, would seem to be secondary to and dependent on the raising of the blood pressure.

We see, therefore, that although the subsidiary/
subsidiary effects of atropin in cholera are not completely explained, the use of the drug seems justified, and can not be considered as entirely a measure of empirical therapeutics.

A point of practical importance to be noted is that more than one injection of any drug hypodermically should not be given to an algid patient. The slowing or actual cessation of the peripheral circulation associated with the algid stage of cholera provides little or no means for absorption of a drug given subcutaneously. If then more than one dose of the drug be so given, absorption of a toxic and possibly fatal dose may take place when the reaction stage sets in. This is a danger which should always be borne in mind and may occur no matter what the drug may be, whether atropin, morphine, or energetic stimulants.

(4) METHODS of REPLACING the FLUID and SALTS LOST from the BLOOD.

Reference to Table XVII, page 126, shows to what a large extent my cases were treated by intravenous infusions of saline solution, namely 93 out of a total of 125 (or 74.4 per cent).
A. RECTAL INFUSIONS OF SALINE SOLUTION.

During the cholera season in 1916, the cholera section was under the care of another medical officer and myself, and, at that time, a few of the milder cases were treated by rectal injections of normal saline solution (80 grains to the pint). It was during this period that I began to feel dissatisfied with the method as a means of replenishing the circulations. First of all, one knew that absorption is very slow when fluid is administered in such a way, and that, if it is absorbed from the lower bowel, it will also be much more quickly absorbed if the patient be allowed to drink ad libitum provided vomiting is not so persistent as to render such a channel impossible. Further, if vomiting is so persistent that the patient can retain nothing in his stomach, I believe that very soon his condition will become much more serious, and that by relying on rectal salines, much valuable time is lost.

Another objection to rectal injections in cholera is the frequency with which the fluid is returned. This is certainly a most troublesome matter to deal with, more especially when, owing to the/
the strain of vomiting, it becomes almost impossible for a patient to retain even quite a small quantity of fluid in the lower bowel. And, after all, what is the object of giving rectal injections? Presumably in the hope that the administered fluid and its dissolved salt will be absorbed. But in cholera the bowel, from end to end, is full of fluid, so much so, indeed, that it can not be retained. It seems to me, therefore, that it is an aimless procedure to run in still more fluid. The only benefit which I can see is to be derived from rectal saline treatment, is that the concentration of cholera toxins within the bowel are diluted and that even if the diluted intestinal contents are not promptly ejected again, a less intense toxaemia will ensue when the circulation is once more revived.

The giving of saline intravenously is a very simple little procedure, and anyone who has had to carry out the actual nursing of many cholera patients at one time, will bear testimony to the fact that treatment by the rectal route is not only very trying to all concerned, but infinitely less satisfactory from the point of view of the patient's progress.
My experience convinced me that if diarrhoea is not so urgent that retention and absorption of the injected fluid is a possibility, there is no necessity to supply fluid by this route at all, and that permission to the patient to drink ad libitum will accomplish more marked improvement, and that in a more pleasant manner. These observations and reflections very soon forced me to abandon rectal injections of saline solution as a method of treatment, and during the cholera seasons of 1917 and 1918, when I was in sole charge of the section, I never once adopted it. The mildest cases were treated by permanganate and atropin, while all others, with the exception of 4 cases, received intravenous infusions in addition.

B. SUBCUTANEOUS SALINE INJECTIONS.

A great many of the remarks which I have made concerning rectal injections are applicable also to the intra-cellular route of administering the required fluid. Absorption is slow; the procedure is undoubtedly a source of much discomfort - in many cases, actual pain - to the patient; only a negligible diminution in the trouble occasioned to the nursing staff is effected by preferring intra-cellular/
intra-cellular to intra-venous treatment. These disadvantages impressed me very markedly. One can understand that occasions may sometimes arise when the intra-venous method is impracticable—for instance, in very young children—or where there is no one at hand who possesses even the little skill required to perform the trifling little operation. In such cases, the intra-cellular method may be adopted as a dernier resort.

But the present series in no single instance forced the adoption of the intra-cellular method. It will be seen from Table XVII, that in only 4 cases, was the method used. One of these patients ultimately died from asthenia on the 9th day, so that, inefficient though I consider the method to be, the fatality cannot really be attributed to it.

Nevertheless, I quickly became alive to the fact that, when collapse is threatened, and replenishment of the circulation is indicated, by far and away the best mode of treatment is immediate and sufficiently copious infusion of saline by the intra-venous route.
C. INTRA-VENOUS INFUSION of SALINE SOLUTION.

The whole question of the treatment of cholera by this method must be studied from the following aspects:-

(a). The indications for replacing the lost blood fluid by intra-venous infusions.

(b). The technique of the actual operation.

(c). The quantity of saline to be infused.

(d). Number of cases infused and number of infusions.

(e). The salt content ("tonicity") of the infused fluid; the relationship between this and the subsequent artificial reaction, and its influence on the mortality.

(f). The rate at which the saline is infused.

(g). The temperature of the infused fluid.

(h). The duration of the interval between two consecutive infusions.

(a). INDICATIONS that LOST BLOOD-FLUID should be replaced.

In coming to a decision as to the necessity for giving an intravenous infusion, one has only to consider to what degree of progress towards collapse the patient has been already carried. An intimate knowledge of the symptomatology and of the pathogenesis of cholera is essential in order that/
that a correct conclusion may be drawn from the condition of a given patient.

What, then, are the clinical features, which, if presented by a choleraic patient, strongly indicate that the circulation has become so far depleted of its watery constituents as to demand speedy replenishment?

I intentionally devoted a deal of attention to the clinical features associated with the "evacuation" and the "asphyxial" stages of the disease, in order that the answer to this question might be given now the more readily. So far as I can see, after only a short experience of the treatment of cholera, one instinctively knows when it is imperative to infuse and when one may safely delay.

It is obvious, of course, that if any one of the clinical features of cholera in its acute stages, is well marked, one may as a general rule be fairly certain that such a patient is suffering from inspissation of his circulating blood. But it is my experience that not one but quite a number of features arise which point to the necessity for early administration of saline intravenously, and I should like to point out here that it was my custom to infuse in a questionable case rather than delay.
I do not believe that the slightest harm can accrue from the giving intravenously of one or two pints of physiological saline to a patient whom, I know, many other medical officers would treat in a more expectant fashion. On the contrary, I believe that my practice was based on logical grounds, as it is wiser to prevent the patient's reaching the collapse stage than to put off until such is threatened.

The following are the signals which I recognise as calling for intravenous infusions:

(a) A FAILING PULSE:

This, of course, is probably the most obvious sign of all. A rapid flabby pulse, even when quite regular, was always a significant indication of distress. I need not repeat what I have already said as to the explanation of the poor quality of the pulse in cholera, but refer the reader to page 93.

(b) A LOW BLOOD PRESSURE.

In regard to this, ROGERS takes a reading of 70 m.m. of Hg. as the very lowest point to which the blood pressure may be allowed to fall with safety. This, I consider, cannot be trusted as an unerring guide to treatment, for it was an occasional/
occasional experience of mine to find the blood pressure not so appreciably low in a patient who otherwise showed only too apparently that his circulating blood had become dangerously concentrated, for instance by extreme thirst, agonising muscular cramps, and subnormal skin temperature. Therefore, I looked upon a fall in blood pressure as an indication for infusion, but upon its absence as not necessarily contra-indicating such treatment. Fortunately, it so happened that nearly all my cases with other signs of deficient circulation showed a proportionate fall in blood pressure; nevertheless, the fact that I had met with exceptions to this rule impressed upon me the necessity to take all the clinical features of the case into consideration and to refuse to be guided by one alone.

(c) INCREASED SPECIFIC GRAVITY of the BLOOD.

I have explained (page 177) why, in cholera, the specific gravity of the blood rises in proportion as the blood fluid is lost, and therefore it is apparent that the higher the specific gravity reaches, the stronger becomes the indication for intravenous infusion of saline. Theoretically/
Theoretically, any rise at all in the sp.gr. calls for a proportionate addition to the blood fluid being made, and I am inclined to believe that, in practice, one is attaining the ideal most nearly by being guided by this theory. With this, however ROGERS is not in entire agreement, for he states most emphatically that a specific gravity of under 1062 indicates that less heroic treatment may be persisted in, e.g. subcutaneous saline treatment. There is no doubt that when the blood is as yet not unduly concentrated, saline solution infused intracellularly, is ultimately absorbed, but since I had resolved latterly to treat all cases which required additional fluid to the circulating blood, by intravenous infusions alone, the reader will understand why I did not recognise an arbitrary specific gravity figure as deciding for or against intravenous infusion.

Many of my cholera patients were already weak and debilitated subjects from recent acute illness, while others were men - both British and Indian - who suffered from chronic malaria. It was among such persons that contradictory indications were found on estimating the specific gravity of their blood, for sometimes readings of normal, or only/
only slightly raised sp. gr. were obtained and yet the patient's circulation had become seriously depleted as indicated by other clinical features, sunken appearance, cramps, flabby pulse etc. From this one argues that these patients must have had an abnormally low specific gravity before cholera set in, owing to an alteration in the corpuscle to plasma ratio, which normally, according to ROGERS is 9 to 11. Now the specific gravity of the blood is always in proportion to the haemoglobin. If, therefore, one is confronted by a cholera patient who was already debilitated and anaemic, a normal or only slightly increased sp. gr. of the blood might be found in spite of his having lost a considerable proportion of his blood fluid by choleraic exosmosis. The danger of obeying the dictates of a specific gravity estimation alone in such a case is obvious. My argument, therefore, is that since it is impossible to know in a given case whether the specific gravity owes its present degree, normal or abnormal, to an abnormality in the corpuscle factor or in the plasma factor, or both, it is courting disaster to be guided by rules which state

(a) Intravenous infusion shall not be given until the specific gravity is found to have risen to a specified figure.

(b).
(b). Such and such a specific gravity demands that only such and such a quantity of saline be infused, owing to the danger of inducing oedema of the lungs or other undesirable conditions, if such a quantity be exceeded. I shall refer at greater length to this latter "rule" when treating of the quantity of saline to be infused.

The reader will gather from the foregoing remarks that in regard to increased sp. gr. of the blood, as with an appreciable fall in blood pressure, presence of the sign is an indication for infusion, but its absence does not contraindicate such treatment.

(d). OTHER INDICATIONS.

Under this heading I consider all those features which proclaim threatening collapse, and which are really the other features associated with the evacuation and "asphyxial" stages of the disease. Such are,

(I) Persistence of frequent and copious evacuations and vomiting.

(II) Increasing thirst.

(III) The slightest suspicion of muscular cramps in the feet or hands.

(IV) Restlessness.

(V) Commencing fall in the axillary temperature.

(VI) Cyanotic tinge in the lips, ears, or finger nails.

(VII)/
(VII) Corrugation of the skin of the fingers
(VIII) Facies cholerica, even though not pronounced.
(IX) Vox cholerica.
(X) Oliguria, not otherwise accounted for.

All these, individually, should cause the physician to, at least, seriously consider the expediency of giving to the cholera patient some saline solution intravenously. Where, as most usually happens, several of such signals are present synchronously, I believe that intravenous infusion is imperative, for, a continuation of the steady loss of fluid from the circulation will shortly reduce the patient to such a low state that actual stasis of the blood-flow through certain vital organs - above all the kidneys - will likely occur.

Summing up, I repeat that, in order to decide whether or no a patient should be infused, a careful and complete clinical examination of his every symptom and sign is of the utmost necessity, and that as regards certain individual features, attention to these alone may prove misleading.

(b). SOME POINTS of PRACTICAL IMPORTANCE in the TECHNIQUE of the OPERATION of INTRAVENOUS INFUSION of SALINE.

Owing to the depletion of the circulation associated with cholera the veins are more or less collapsed/
collapsed, and it is only in exceptional circum-
stances that the subcutaneous venous system can be
made to become sufficiently distended to allow of
insertion of the infusion needle by puncturing the
vein wall through the intact skin. Still I was
able to satisfy myself that such a procedure is
sometimes possible, especially in cases admitted
before collapse is extreme, yet in whom indications
for infusion are presented. But such a method de-
mands a certain degree of distention of the veins,
and I found that the maximum distention can be got
in cases with a minimum of 'vis a tergo' in the ven-
ous return by using the pneumatic armlet of the
sphygmomanometer. In this way, one is enabled to
so carefully adjust the pressure that the maximum
effect is brought to bear on the veins with a
minimum effect on the arteries, the result being,
of course, that the veins fill up distally to the
armlet.

The pneumatic tourniquet devised by Mr. G.
Grey Turner of Newcastle-on-Tyne would also suit
admirably for such a purpose, but is not so likely
to be at hand.

This is an apparently trifling point, but
I have found the procedure to give satisfaction
when it is possible to employ it. Less pain is occasioned, time is saved, and no further attention is demanded as with an incision to expose the vein.

If the patient's arm be allowed to hang over the side of the bed while the armlet is in action, an additional agency of venous engorgement is called into play, namely, gravity.

However, in cases admitted in a severely collapsed state, it is practically always necessary to incise the skin overlying the chosen vein, and after cutting a tiny V-shaped flap in the wall of the vein (the apex of the V directed distally) to slip into its lumen a blunt-pointed cannula. Sometimes it is extremely difficult even to detect the position of the subcutaneous veins. Here again, I have found the pneumatic armlet, along with the aid of gravity, of the greatest assistance. Such is especially required in dark-skinned races in whom the superficial veins are completely obscured unless they are distended.

If even by taking advantage of such aids, still no indication is forthcoming as to the exact situation of the veins, one must fall back on one's anatomical knowledge and incise where a superficial vein is known to be constantly present.

In order to cause as little disturbance to/
to the venous system of the arm, as well as to use as unimportant a tributary as possible in view of the probable necessity to repeat the infusion several times, I always made a practice of choosing a vein as near the wrist as possible. By following this method, I economised in my destruction of many named subcutaneous veins by thus providing numerous opportunities of opening the same vein, each future opening being made just proximally to the point of confluence of successive tributaries.

In several cases, I utilised the same vein for two, three or even four infusions, so that the patient had a corresponding number of tiny incisions between the wrist and elbow of one arm.

In every case, I stitched up the skin incision with horsehair immediately after the infusion had been given, as I believe that primary union is more satisfactory than delaying to appose the skin edges and hoping for secondary union. In other words, the practice of some of leaving a surgical knot around the vein proximal to the opening in it, and which can be unloosened at the next infusion was not followed. Moreover, I believe there is always a danger of thrombosis occurring within the vein just proximal to the ligation.
ligature and where stagnation of the blood flow must be absolute. By again opening this short segment of vein during the next infusion, an embolus might be carried away to the lungs.

Very few of my skin incisions became septic, and this I attribute to the freedom with which I constantly dabbed the exposed tissues with 1 in 20 carbolic acid solution while I exposed and isolated the desired length of vein.

Further the use of 1 in 20 carbolic serves not only as a reliable antiseptic, but also as an admirable local anaesthetic. Before incising the skin, I always placed on it, just over the chosen site, a pledget of cotton wool saturated with the solution, allowing this to remain in situ for 2 or 3 minutes, during which time the armlet was adjusted. I found that the numbing effect of the carbolic diminished very considerably the discomfort occasioned on incising the skin, while the frequent mopping of the wound with the carbolic during the process of isolating, the vein had a similar analgesic action.

For ligaturing the vein, I invariably employed the finest silk, and found it to be completely satisfactory.

Full/
Full details as to the technique of intravenous infusions can, of course, be found in most surgical handbooks, and an excellent description is given in ROGER'S book. But those details which I have picked out for special remark, I consider are sufficiently important to warrant particular attention being paid to them.

(c) The quantity of Saline to be Infused.

On being confronted for the first time by a severe case of cholera to whom one must give an intravenous infusion, a little doubt is bound to trouble the physician as to how much saline may be given to be sufficient and yet not unduly to exceed that amount. My experience is, that the error usually lay in not infusing sufficiently.

When I first took charge of the cholera section, I followed ROGERS' instructions as to deciding the quantity of saline required in each case. Very soon, however, I realised that, in some of my cases, at any rate, very much larger quantities than the sps.gr. estimations indicated were required to efficiently restore the pulse and blood pressure; as an experiment, I departed from the routine practice of Rogers, and obtained such satisfactory results that during the latter part of 1916, and during 1917 and/
and 1918, I never once allowed the treatment to be influenced by sp.gr. estimations.

I relied entirely on an accurate history of the patient's previous and present illnesses, along with a thorough clinical examination of his condition.

Such a disclosure may seem to the reader - to say the least of it - unconventional, in the light of ROGERS' recent work on cholera. I therefore feel compelled to state my reasons for not following the suggestions of one who has undoubtedly done more than anyone else to reduce the mortality from an epidemic disease which, till recently, was second only to plague in its fatality.

As I have said, practical experience convinced me that there is a fallacy somewhere in ROGERS' conclusions, and being extremely interested in the matter, I studied in numerous books the physics and the physiology of the blood, hoping to discover where the fallacy lay. I believe that I have discovered the fallacy, and in the following pages, I shall attempt to explain to the reader why, on physical and physiological grounds, I ceased to be guided by specific gravity estimations in deciding both when to begin and when to stop the administration of intravenous infusions in cholera.

The specific gravity of the human blood in health may vary within certain limits. The following/
following are the figures given by various authorities:

<table>
<thead>
<tr>
<th>Sp.gr.</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.055</td>
<td>Brodie p.264</td>
</tr>
<tr>
<td>1.060</td>
<td>Hutchison &amp; Rainy p.254</td>
</tr>
<tr>
<td>1.057 to 1.066 (man)</td>
<td>(12) Starling p.971</td>
</tr>
<tr>
<td>1.054 &quot; 1.061 (woman)</td>
<td></td>
</tr>
<tr>
<td>average =1.060</td>
<td>(13) Burton-Opitz p.163</td>
</tr>
<tr>
<td>1.053 to 1.062</td>
<td>(14) Halliburton p.440.</td>
</tr>
<tr>
<td>1.054 (Indians)</td>
<td>Rogers p.90.</td>
</tr>
</tbody>
</table>

This absence of uniformity may be accounted for in several ways:

(1) The specific gravity of either of the component parts of blood, namely, the corpuscles and the plasma may vary in health.

Regarding the specific gravity of the blood corpuscles and of the blood plasma, the following are the figures given by different authorities:

Sp.gr./
As to the effect which variations in the corpuscles may have, it is significant to read what HUTCHISON and RAINY say with regard to this point:

"The normal specific gravity of the blood is about 1060. Variations are not of much clinical value. The specific gravity is always in proportion to the amount of haemoglobin - a low specific gravity means little haemoglobin. The ratio is so constant that one can tell the percentage of haemoglobin by taking the specific gravity".

The specific gravity of the blood plasma may also be variable owing to differences in concentration of dissolved salts etc.

The relative volumes of corpuscles and plasma may vary even in health.

The specific gravity of the blood as a whole is dependent very largely on the proportion of corpuscles in the suspension, since the specific gravity of the corpuscles is greater than that of the plasma/
plasma. The higher the proportion of corpuscles (and accordingly the lower the proportion of plasma) the higher will be the specific gravity of the blood as a whole. It follows, therefore, that if the proportion of corpuscles varies even in healthy people, the specific gravity of the blood will also vary. It would seem that the proportion of corpuscles does vary even in health, since the following are the proportions stated by different authorities:

<table>
<thead>
<tr>
<th>PROPORTION (Volume) of CORPUSCLES</th>
<th>PROPORTION (Volume) of PLASMA</th>
<th>AUTHORITY.</th>
</tr>
</thead>
<tbody>
<tr>
<td>33\text{%} per cent</td>
<td>66\text{%} per cent</td>
<td>(13) GULLAND &amp; GOODALL p.10</td>
</tr>
<tr>
<td>40/48 &quot;</td>
<td>60/52 &quot;</td>
<td>(11) BAII pp. 264 &amp; 266</td>
</tr>
<tr>
<td>46/54 &quot;</td>
<td>52/46 &quot;</td>
<td>(12) STARLING p.968</td>
</tr>
<tr>
<td>average = 50%</td>
<td>average = 50%</td>
<td></td>
</tr>
<tr>
<td>35 to 40%</td>
<td>65 to 60%</td>
<td>(13) BURTON-OPITZ p.160</td>
</tr>
<tr>
<td>45 per cent (in Indians)</td>
<td>55 per cent (in Indians)</td>
<td>(2) ROGERS, p.87</td>
</tr>
</tbody>
</table>

By calculation, it is found that, accepting the specific gravity of the corpuscles and plasma as fixed respectively at 1085 and 1035, the specific gravity of blood composed of 45 per cent of corpuscles and 55 per cent of plasma, is 1057.5. But I have stated that ROGERS found the corpuscles and plasma (in Indians) to be present in these proportions and yet the specific gravity of the blood was only 1054. The only/
only explanation for this is, of course, that the figures given by BRODIE, as to the specific gravity of the corpuscles, or of the plasma, or of both, are slightly over estimated for application to natives of India.

It is worth noting as a ready means of reckoning the specific gravity of the blood from estimations by the haemocrite of the proportions of corpuscles and plasma that, (again assuming the specific gravity of the corpuscles and the plasma to be 1085 and 1035 respectively), each increase of 1 percent in the proportion of corpuscles in the blood will bring about an increase in the specific gravity of the blood as a whole, amounting to 0.5; for instance, when the corpuscles represent only 45 percent of the blood, the specific gravity of such blood is 1057.5, whereas when the former figure is 50 percent, the latter figure is 1060.

In his researches on the blood of cholera patients, ROGERS found by the haemocrite that, as

*The 'haemocrite' or 'haematocrit' is an instrument used to determine the relative volume of corpuscles and plasma in blood. It consists of a graduated capillary tube and centrifuge. The method is known as the 'direct' method of Blix, and, for clinical purposes, is much more convenient than the 'indirect' method of Hoppe-Seyler, which is analytical in nature.
would be expected, the proportion of the blood corpuscles increases per unit of volume, as the plasma diminishes, by transmudation of fluid from the blood vessels into the intestinal lumen. Accordingly the specific gravity of the blood is increased in cholera. He showed that whereas normal blood (in Indians) is composed of 45 per cent of corpuscles and 55 per cent of plasma, an equal volume of the blood from a severe case of cholera may be composed of as much as 71 per cent of corpuscles and only 29 per cent of plasma, representing a loss of 36.5 per cent of the volume of the total blood, or of 66.5 per cent of the fluid portion of the blood.

By carrying these investigations still further and estimating in a given case, the percentage of corpuscles and plasma both before and during the intravenous infusion (rapidly administered) of saline solution, one is able to run in to the circulation only so much saline solution as will be necessary to restore to the normal the ratio of corpuscles to plasma.

Several difficulties and fallacies, however, creep in here. In the first place, although one were to find, on examining the blood by the haemocrite, immediately after the infusion has been given that the normal ratio of corpuscles to serum has been restored/
restored, such a relationship is bound to be short lived owing to the eagerness with which the desiccated tissues will withdraw fluid from the circulating blood and thus upset again the normal ratio.

Second, it is perfectly obvious, that if this method were adopted to decide how much fluid is to be infused, the body weight of the patient (in his original healthy state) would, of necessity, have to be taken into consideration; for it is inconceivable that if the haemocrite indicates that a huge male adult and a young child have lost a similar percentage of the fluid portion of their bloods, the same quantity of saline must be administered in both cases. For the capacity of the blood vessels plus that of the body tissues to accommodate fluid must differ enormously in two such patients.

Consequently, although the haemocrite is able to demonstrate the scientific fact that in cholera, the proportion of corpuscles to plasma is altered from the normal - and to what extent at a given moment - its utility as a means of indicating what volume of fluid must be infused in a given case, is almost nil unless certain conditions are fulfilled. These are:

1. The body weight of the patient (in health) should be known.
2. Either a series of observations must be made at intervals during the infusion in each case in order neither to over-reach/
overreach nor fail to reach the proper degree of dilution of the blood, or a table compiled from observations made on a large number of cases of similar body weight must be used on which would be readily indicated how much saline would be required once the preliminary ratio of corpuscles to plasma has been estimated.

(3). Such a table must have been formulated from observations which were made not after rapidly administered infusions, but after infusions occupying a sufficient time to allow a certain amount of fluid to pass into the tissues.

It will be agreed, therefore, that such a method will give, even at its best, only approximate information, for it is impossible to accurately estimate, either the amount of fluid which is likely to pass into the tissues or the speed with which such a process occurs.

(2)

ROGERS adopts the following method in order to allow for a re-disturbance of the restored ratio owing to passage of blood fluid unto the tissues. From numerous observations by the haemocrit, he has "been able to ascertain the quantities ordinarily required to dilute the blood to the normal". In other words, this means, I presume, that for each degree of loss of blood fluid, he has estimated that a corresponding quantity of saline will be required to be given to a patient of average body weight. But such a quantity of saline, although it has restored the blood to the normal dilution temporarily, is quickly/
quickly taken up by the tissues, so, to overcome as far as possible the resulting increase once more in the concentration of the blood, he dilutes the blood to normal first of all by running in the required quantity of saline at a rapid rate and then continues at a slower rate "a little beyond that point so as to allow for some further loss of fluid". He states that "three to four pints were required fully to dilute the blood when given at this rapid rate". Surely, when the amount of fluid lost from the blood in cholera varies within wide limits, such information is not very helpful when one is confronted with an extreme case, for he states that "in extreme cases even the larger amount occasionally still left the blood more concentrated than normal". He then goes on to say,

"once the pulse has been restored by the injection of about three pints at a rapid rate, then, in severe cases, another one or two more pints can be given at the rate of one ounce a minute, without further materially diluting the blood, as it will have time to pass largely into the tissues and thus create a valuable reserve of fluid in the body".

There/
There is no doubt that a finger kept constantly on the pulse during the administration of intravenous saline is of the very greatest assistance, and is, in my experience, a sure guide as to the quantity of fluid required. I have never met an instance where there was difficulty in deciding when to stop the infusion, provided that the administration is conducted slowly, and only two or three pints are given after the pulse (and blood pressure) attain near the normal.

Lastly, as ROGERS observes, "the haemocriote observations above described require a laboratory for carrying them out", and therefore the method is of little clinical value when a rapid decision must be come to as to how much saline should be infused in a given case of cholera.

Another more direct method of estimating the specific gravity of the blood - and one which is quite simply and rapidly carried out at the patient's bedside - is that based on the principle that if a drop of the patient's blood be submerged below the surface of a fluid of known specific gravity, it will do one of three things depending on the relationship between the respective specific gravities. It may sink to the bottom of the solution/
solution, indicating that the blood is of higher specific gravity than the solution; it may rise to the surface, indicating a lower specific gravity of the blood; or it may remain stationary at the level at which it was introduced by the pipette, indicating that the sp. gr. of the blood is the same as that of the solution, which is already a known quantity. Such a procedure gives a very accurate result, if the observation is made immediately the drop of blood is introduced into the fluid, for then no time is given for any of the constituents of the blood to diffuse into the surrounding fluid which would, of course, vitiate the observation.

The two best known procedures are those of HAMMERSCHLAG and LLOYD-JONES. The principle involved is exactly the same in both, but while HAMMERSCHLAG employs a mixture of chloroform and benzol as the solution of known sp. gr., LLOYD-JONES uses a graduated series of glycerine dilutions, and that dilution in which the blood drop remains suspended indicates the sp. gr. of the patient's blood. It is unnecessary here to give a detailed description of the technique in these two methods, as such can be found in textbooks.
ROGERS' prefers the method of LLOYD-JONES, and in the Isolation Hospital this was adhered to.

It will readily be appreciated how much more convenient is this method than is that carried out by the haemocrite.

By carrying out simultaneous observations by the haemocrite and by the LLOYD-JONES technique, ROGERS' found that he obtained closely parallel results. That is to say, he was able to show that, in a given case of cholera, while the haemocrite indicated that a certain quantity of saline was required to restore the normal ratio of corpuscles to plasma, if the sp. gr. of the blood were estimated (by LLOYD-JONES method) at the same moment, a very similar quantity of saline, whereby the blood might be sufficiently diluted to restore the normal sp. gr., was indicated.

As a means of determining how much saline is required to restore the blood to normality as regards its sp. gr. the practice of making observations on the point before treatment is begun and at various intervals during the infusion process is certainly of the greatest interest. For one is thereby informed when to stop the injection, if restoration of the normal sp. gr., per se be the aim/
aim in view. But here again, as has been said of the haemocrit observations, the sphere of usefulness is to a certain extent limited, though to a much less extent than in the latter.

First, the same difficulty in deciding accurately how much saline should be allowed for loss from absorption by the tissues creeps in, unless very frequent observations are made and the infusion given very slowly. Granted these conditions, it is possible to give to the cholera patient a quantity of saline solution which will not only restore the blood to normal sp. gr. but will also ensure that it will remain of normal sp. gr., although fluid is passing into the tissues.

The observations are so simple to carry out, that estimations of sp. gr. at intervals during the infusion are possible. Short of this, I am inclined to believe that observation of the sp. gr. is not a real foundation on which to base an opinion as to the quantity of saline which should be infused. The statement that, from a single preliminary estimation of the sp. gr. of the blood, it is possible to state exactly how much saline should be given, not only seems to me to be based on a guessing principle, but is also, in my experience/
experience, misleading, in that in many cases con-
current observations on the pulse indicated that if one gave merely the quantity indicated by the primary estimation of the sp. gr. of the blood, the marked improvement both in the "feel" of the pulse and in the blood pressure (as estimated by the sphygmomanometer) was not obtained to the same extent as when these two latter clinical methods were relied on. In other words, I feel that if the physician relies on giving the so-called "average" amount of saline which a primary sp. gr. estimation denotes, it will frequently occur that an insufficient quantity is given. Such is of more serious import than the giving of a pint or two more than an estimation of the sp. gr. would indicate, for an excess of saline, especially if it be isotonic is quickly taken up by the tissues and the balance restored.

My objections to being guided by specific gravity estimations in deciding how much saline to infuse, may therefore be summarised -

(1). The normal sp. gr. is admittedly a variable quantity - indeed within wide limits.

(2). Other diseases, apart from cholera, affect the specific gravity.

(3).
(3). Even although by diluting the blood, a questionable "normal" figure is reached the quantity to be allowed in addition for loss by passage into the tissues is impossible to estimate.

(4). The method takes no notice of the body weight of the patient, and therefore since adults have often very different body weights, the capacity of their blood vessels and especially of their tissues to receive fluid must also vary widely. Consequently, similar sp. gr. findings in two patients of very different body weights can not possibly indicate a similar quantity of saline to be infused even to within a pint or two, while the whole object of the method is to decide the quantity required.

Such being so, I find it difficult to be persuaded that a difference of a very few degrees from an arbitrary "normal" specific gravity is any indication that either infusion is necessary or in what amount. For instance, ROGERS' insists that sp. grs. of 1063, 1064, 1065 etc. demand respectively 3, 4, and 5 etc. pints of saline. When a person, even in health, may possess a sp. gr. of anything from 1054 to 1060 or more, and if ROGERS' instructions be followed, cholera cases, who in health possessed the above sp. gr. figures, will, obviously receive the same quantity of saline, should their blood concentration exceed 1063; which is absurd, for these patients must have lost totally different quantities/
quantities of blood fluid, amounting to pints, as can be proved by simple calculation.

I am convinced that estimations of the sp. gravity of the blood per se. can never be of any real aid in helping one to decide when to infuse and what quantity to infuse, unless it were possible to know what the particular patient's sp. gr. was before he lost any blood fluid from cholera. Such, of course, is quite impossible.

Therefore, provided the physician has already had a little experience of the treatment of cholera, I feel that it is in the interests of the patient that he should be guided by more trustworthy signs than sp. gr. estimations - and, among these, I consider the pulse, and blood pressure as the most important. After these, I would place disappearance of all the patient's anxiety and discomfort as a certain indication that sufficient saline has been infused in the meantime.

As regards the actual quantities of saline infused in my 125 cases, table No. XVII shows that 93 of these (74.4 per cent) received treatment by intravenous infusion of saline. In many cases, however, the infusion had to be repeated on one or more occasions. The figures on this point are shown in Table No. XIX.

TABLE/
We thus see that in the treatment of the 93 cases, 176 intravenous infusions were administered, or 1.89 infusions per case.

In order to calculate the average quantity of fluid given at the first infusion and at each repetition of the treatment, it is necessary to represent these 176 infusions in yet another way.

### TABLE XIX.

<table>
<thead>
<tr>
<th>Infusion Type</th>
<th>Cases</th>
<th>Infusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 infusion only</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>2 infusions</td>
<td>28</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td>51</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
<td>176</td>
</tr>
</tbody>
</table>

### TABLE XX.

<table>
<thead>
<tr>
<th>Infusion Type</th>
<th>Infusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st infusions</td>
<td>93</td>
</tr>
<tr>
<td>2nd</td>
<td>51</td>
</tr>
<tr>
<td>3rd</td>
<td>23</td>
</tr>
<tr>
<td>4th</td>
<td>6</td>
</tr>
<tr>
<td>5th</td>
<td>2</td>
</tr>
<tr>
<td>6th</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
</tr>
</tbody>
</table>

It
It is necessary, however, to state here that in 5 of the few cases which had received their first intravenous infusion in another medical unit prior to being sent to the Isolation Hospital, the actual quantity of the fluid given was not discovered, and therefore, such cases must be left out of the calculation.

Further, for some unknown reason, it so happens that in 4 of the 51 cases receiving 2nd infusions, no record has been kept as to how much saline was given on that occasion.

The infusions which are available for calculation are therefore as follows:

<table>
<thead>
<tr>
<th>TABLE XXI.</th>
</tr>
</thead>
</table>

| 1st infusion | 88 |
| 2nd infusions | 47 |
| 3rd " | 23 |
| 4th " | 6 |
| 5th " | 2 |
| 6th " | 1 |

167

The average quantity of fluid given at the first and each subsequent infusion is as follows.
This table shows that between 5½ and 6 pints was generally administered intravenously in my cases. Such a quantity is greater than ROGER'S is in the habit of giving, especially when one remembers that the cases so treated included all degrees of collapse, while, at the same time, ROGERS' mentions that "about 4 pints of fluid are required in an averagely severe collapse stage of cholera in an adult male, in order to replace the loss from the circulation and to give a slight excess in order to allow for some further loss".

The following additional facts may be of interest:

(1) Of the 93 cases treated by intravenous infusions, 26 ultimately died (= 27.9 per cent). See table No. XVII, page 126.
The average quantity of fluid infused on each occasion amongst these 26 fatal cases is as follows:

TABLE XXIII.

<table>
<thead>
<tr>
<th>Infusion</th>
<th>Pints</th>
<th>Ounces</th>
<th>Drams</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>6</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>2nd</td>
<td>5</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>3rd</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>4th</td>
<td>5</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>5th</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>6th</td>
<td>2</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>All</td>
<td>6</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

From this it is seen that the average quantity infused at each of the total occasions in the fatal cases amounted to 6 pints, 0 ounces, 1 dram.

I find that the average quantity for the 67 recoveries given at each of the total occasions amounts to 5 pints 10 ounces 2 drams, showing that the fatal cases received on the average 9 ounces 7 drams more than them.

(3). Each of the 26 fatal cases who were treated by infusions received on the average 2.05 infusions, while each of the 67 recoveries were infused an average of 1.65 times. It will be remembered that I have said that the total 93 infused cases received an average of 1.89 infusions per case. See page 204.

(4).
(4) One of the most remarkable cases of all is that of an Indian patient who required to be transfused 5 times within 3 days, and who ultimately recovered. During this period, he received no less than $22\frac{1}{2}$ pints of saline intravenously.

(e). **THE SALT CONTENT (tonicity) of the INFUSED FLUID.**

Under this heading it is necessary to study:

(I) The advisability of infusing either a hypertonic or a true isotonic saline solution.

(II) The strengths of the solutions actually infused in the present series of cases.

(III) Effects of varying tonicity of the infused fluid on  
   (I) The subsequent reaction.  
   (II) The mortality as a whole.  
   (III) The mortality from different causes.

(1) **THE ADVISABILITY of INFUSING either a HYPTONIC or a true ISOTONIC SALINE SOLUTION.**

The writer believes that isotonic saline is more likely to give satisfactory results in the treatment of cholera. Such a belief is held, on account of not only the higher recovery rate associated with the isotonic treatment, but also the theoretical grounds for preferring such a method.
In the following pages, I shall attempt to explain why on theoretical grounds - apart altogether from the results obtained in the present series - I preferred to use an isotonic saline solution (i.e., "normal" or physiological saline) for intravenous infusions.

THE LOSS of DISSOLVED SALTS from the BLOOD and its BEARING on TREATMENT.

According to CASTELLANI and CHALMERS, the toxin (intracellular, or endotoxin) of the vibrio in some unknown way causes great gastro-intestinal disturbance, leading to the passage of substances from the blood to the interior of the bowel in the following order,

(1) Water.
(2) Inorganic salts, especially sodium chloride.
(3) Organic substances.

Such exosmosis cannot be gauged except by chemical examination of the blood, or, when the patient is drinking nothing, by the stools.

To the loss of water, I have just referred. Such a loss would bring about an extraordinary concentration of the dissolved salts in the patient's blood, did not the salts leave the circulation at or about the same rate as the fluid which holds them/
them in solution. ROGERS' has conclusively demonstrated that the percentage of chlorides in the blood in cholera may or may not be higher than the normal, but, in any case, no increase occurs proportional to the great loss of blood fluid, as might be expected. He found, however, that the loss of salts was in no sense comparable to the loss of fluid, for even in some of the most severe fatal cases of case, the chlorides in the plasma were only slightly lower than normal. It is important to note, however, that in some of his worst cases, as low as 0.6 per cent of chlorides was met with, while haemolysis of the erythrocytes had set in.

On the other hand, "in all except the most severe cases of cholera, the percentage of chlorides in the blood becomes slightly increased". This is to my mind, a most significant statement, as on the information which it conveys is - or should be - dependent the concentration of the salts in the saline to be administered intravenously.

The belief that the blood of cholera patients usually possesses a higher salt content than normal, might at first sight seem to receive additional support from the suggestive observation of ROGERS' who found that the rice water stools of cholera/
cholera gave an average of 0.53 per cent of chlorides (or about 46 grains to the pint). Now, if both the fluid and the dissolved salts in rice water stools were derived entirely from the blood, and if each left the circulation with equal rapidity, one would expect the salt content of stools and blood to be very similar. We know that the chlorides in the normal blood amount to 0.9 per cent (or about 80 grains to the pint). ROGERS' observations on the stools might seem to show, that, if anything, more water leaves the blood than do chlorides; but we must remember that although vomiting may be a prominent feature, nevertheless a certain amount of fluid taken by the mouth does ultimately reach the intestine, and there dilutes the salt content of the stools. So that we really cannot conclude that because the salt content of rice water stools is lower than in normal blood, the salt content of cholera blood must therefore be higher than the normal.

Knowledge as to the salt content of the blood in a given case of cholera is of the utmost importance, for very serious consequences are possible, if not indeed probable, should one cause the salt content of the blood to depart from the normal too markedly in either direction.
(1) **CHANGES in the RED CORPUSCLES.**

It is well recognised that the red corpuscles are extremely sensitive to variations in the salt content of the plasma. If the dissolved salts are reduced in concentration either by actual loss of salts outstripping the loss of the blood fluid, or by the addition to the blood of a too markedly hypo-tonic saline solution, there is a danger of wholesale destruction of the red corpuscles from haemolysis. For these cell elements then find themselves under conditions far from normal, and, obeying the dictates of the law of osmosis, water promptly proceeds to pass from the blood plasma through their outer coating (membrane) into their interior, with the result that they swell up so enormously that they ultimately burst, and their haemoglobin is discharged into the surrounding plasma, a process known as "laking" of the red cells. The danger then of such a serious state of affairs arising is possible under two circumstances in cholera, the one where, in the very worst cases, the loss of blood salts outpaces even the enormous loss of blood fluid, the other where, even in cases in which the blood salts are not so markedly reduced, the physician attempts/
attempts to administer intravenously a hypotonic saline solution. So that, so far, we see there is no place for hypotonic saline in the treatment of cholera. Apparently its use is contra-indicated even in those milder cases where the salt content is slightly higher than normal, when, by diluting the blood, a hypotonic solution might seem advisable. In such cases, the concentration of salts does not seem to rise to such a dangerous level that the red cells are affected in a way to be described shortly, and, besides, as ROGERS' observes the slightly increased concentration of the blood salts "would have the advantage of tending to retain the remaining fluid in the circulation". For it would seem that the process of osmosis is all important in the explanation of the symptoms of cholera and, to a certain extent, guides the treatment.

A significant statement made by ROGERS' in his advocacy of hypertonic treatment, is to the effect that "the use of hypertonic saline transfusions in cholera . . . . has produced a very remarkable reduction in the death rate in cholera. The failure in so large a proportion of cases (70 to 86 per cent in different recorded series) of injections/
injections of "normal" saline solutions is now easily understood, for they commonly contained only 60 grains of sodium chloride to the pint, or 0.65 per cent, although we now know that the healthy blood contains 0.9 per cent, or about 80 grains of sodium chloride to the pint.

Apparently such failures are not attributable to "normal" (isotonic) saline at all, but to saline which was very decidedly hypotonic, according to recently adopted standards. The evidence, therefore, for the defence of a true isotonic treatment is not in any way weakened.

Having discussed the effect of hypotonic surroundings, on the erythrocytes, let us consider for a moment the influence of an unduly hypertonic plasma.

Here the direction of the passage of fluid is reversed, for the osmotic tension of the plasma is now greater than that of the contents of the red cells, and accordingly, water is attracted towards the plasma from the interior of these elements. This leads to a shrinkage of each red cell, its outline becomes irregular, jagged and shrivelled-looking. Such a process is termed "crenation", and, one would imagine, is bound to bring about profound effects on the ease with which it passes along/
along in the circulation and in its capacity as an "oxygen carrier".

Hyper-tonicity of the blood plasma may occur in cholera under two circumstances, the one where the passage of water into the bowel is more rapid than that of the blood salts, as happens, (2) ROGERS' tells us, "in all except the most severe cases of cholera"; the other, when the physician intentionally infuses into the veins a hypertonic saline solution, the hyper-tonicity of which is not counterbalanced by a sufficiently hypo-tonic state of the blood plasma already existing. It seems to me that with the knowledge that even "in the most severe fatal cases (of cholera cases)" in which on the average two-thirds of the fluid (2) of the blood has been lost, ROGERS' found that the chlorides in the plasma were only slightly lower than normal, the giving of the necessary large quantities of saline solution intravenously in a hypertonic state may not be without detriment to the red cells. I am unable to provide proof of this statement, so I merely suggest the possibility of its veracity.

(2)
(2) **INFLUENCE of the CONCENTRATION of the BLOOD SALTS on the COPIOUSNESS of the EVACUATIONS and on the TOXAEMIA in CHOLERA.**

The process of osmosis is, it would seem, one which is called into operation by the hyper-tonic saline treatment of ROGERS! As we have seen, the rice-water stools often contain chlorides in less concentration than these occur in the blood, and, therefore, the agency which brings about the marked and persistent transudation of water from the blood into the intestine can hardly be one dependent on osmotic tension. The passage of fluid from blood to bowel is probably dependent on some specific action of the cholera toxin.

During the evacuation stage of cholera, the current of the fluid is very decidedly from blood to bowel, and we must assume that dissolved in this fluid is a large amount of the soluble cholera "exo-toxin" picked up during the passage of the fluid through the submucous and mucous coats of the intestinal wall. Having reached the lumen of the gut, the "toxin content" of this fluid is still further added to by the intra-cellular toxin (endo-toxin) which is set free on the death and dissolution of those vibrios whose vitality is on the wane. The/
The rice-water stools, therefore, constitute a highly toxic solution, and, even in the face of the tendency to collapse as a result of their evacuation, it should be the aim, I consider, to do all in one's power to aid in ridding the patient of such a formidable source of poison, and, above all, to prevent, in the meantime, such conditions arising as will tend to bring about a reversal of the current which is flowing from blood to bowel.

There is no reason to suppose that because the copious stools of cholera are not dependent on an osmotic process, it is impossible to bring such an agency into force, and thus cause fluid to pass back once more from the intestine into the blood stream. I refer to the practice of raising the salt content of the blood by the giving of large quantities of a distinctly hypertonic saline solution. I do not doubt that osmosis is set up under such circumstances, and that a certain amount of "reabsorption" of fluid takes place from the interior of the gut. As a result, toxins may temporarily flood the whole system and bring about very serious consequences by damaging sensitive and highly specialised organs - none more so than the kidneys. I believe that the dominant factor in/
in bringing about a fatal termination in cholera, is toxaemia and its effects on vital tissues. Collapse from loss of fluid is to my mind only of secondary importance as a cause of death, if such cases be got in time. One can immediately rectify this by the timely administration of saline solution intravenously, but I fear that once toxaemia has reached a certain degree, little is of any avail in avoiding a fatality. How important is it, then, to avoid at any cost, measures which tend to increase the toxin content of the blood?

I shall show from a study of my cases that toxaemia seemed to reach a higher degree after the administration of hyper-tonic saline than after a purely isotonic solution. Reactionary temperatures were higher after hypertonic than after isotonic treatment, and in some cases death resulted from hyperpyrexia. Again, the much dreaded uraemia seemed to cause more fatalities amongst the hypertonic cases.

The 'Reaction Stage' of cholera is in nearly every case characterised by some degree of pyrexia, which varies in different cases, both in degree and duration. What is the explanation of this pyrexia? I have already stated, when speaking of the temperature during the evacuation stage, that the skin, which is singularly cold during the choleraic period/
period regains its warmth on the revival of the circulation through it, on the onset of the reaction stage.

I have also explained why it is that, even without a toxaemia, the internal temperature would rise very markedly while the skin temperature falls, by adopting Libreriester's view, that there is during the evacuation stage deficient heat loss. When to this is added the effect of excessive heat production, there will be no difficulty in appreciating the reason for the rise of temperature - often excessive and prolonged - characteristic of the reaction stage. But the fact that the pyrexia is appreciable both in the rectum and in the skin for often two or three days after reaction sets in, points to toxaemia as being the cause. For, were it merely the result of a previous temporary defect in heat loss, the rectal temperature would fall - and that as rapidly - as the skin temperature rose. So that there is little doubt that reactionary pyrexia is due to toxaemia; moreover, the pyrexia would seem to be proportional to the degree of the toxaemia. Up to this point, I have been referring to the reaction period as it is observed in cases where it occurs 'naturally', in contradistinction from the reaction which is brought about 'artificially' in an immediate and rapid manner by the intravenous infusion of salines, whether hyper- or iso-tonic.
The source of the toxæmia, which becomes a more obvious feature in the reaction period is the intestinal mucous and submucous coats. With the revival of the circulation, a more vigorous absorption of cholera toxins from the bowel is promoted, and, if excessive, the pyrexia, too, is excessive. Death from uncontrollable hyperpyrexia is, therefore, not an uncommon eventuality in this stage. If such may occur 'naturally' - and, from all accounts, has occurred many times in the past, it is surely incumbent on the physician to, as far as possible, obviate this tendency of the circulation to take up the cholera toxins, and not encourage it by the administration of hypertonic saline infusions.

When the reaction period in cholera sets in 'naturally', the process, of revival of the circulation takes a little time, and the influx of toxin to the systemic blood is, therefore, not so overwhelming as when such reaction is 'forced' by artificial means. For, by intravenous saline, the pulse returns within a matter of seconds and becomes increasingly forcible during the succeeding minutes. As a result, the temperature charts of such treated cases record much higher readings than do those of patients in whom the reaction is allowed to take place in sua sponte. We must assume, therefore, that, it is the suddenness of the reaction and the rapidity with which the toxins are/
are reabsorbed in the infused cases which account for the difference in the 'natural' and 'artificial' reaction. I am not aware that a rigor is a common feature of the 'natural' reaction, but this I do know, - the frequency - indeed the almost universal occurrence - of a rigor during, or immediately after, the administration of intravenous saline. It would be difficult to explain this phenomenon in any way other than by assuming that a sudden and plentiful influx of toxins has invaded the system.

(2)

Even ROGERS himself is prepared to admit (1) that even in the naturally-occurring reaction period, reabsorption of toxins from the bowel does occur with possibly disastrous consequences, for, he says in accounting for the mortality amongst a series of cases treated before the revival of intravenous injections (1906) - "when the mortality was no less than 81.6 per cent. Of the 94 deaths, 62 per cent took place in the collapse stage, 23 per cent during reaction and 15 per cent from uraemia. Thus, after collapse, excessive reaction was the principal cause of death, being half as fatal again even as the dreaded uraemic complication. Much light is thrown on the causation of this high mortality by a study of the temperatures recorded, all of which are axillary or mouth readings/
readings, mainly the former. These figures are very striking, for they show that in no less than nineteen out of the twenty-two cases proving fatal in the reaction stage, the temperature rose to 103° F. or over, while in ten it reached the hyper-pyrexial point of from 105° to 106.8° F., although only one of these last had received any saline injection. Thus excessive febrile reaction was the most frequent cause of death in those Europeans who survived the collapse stage of cholera, even when no saline injections had been given, and actual hyper-pyrexia caused 28 per cent of the deaths in the reaction period. This mortality is clearly due to absorption of a fatal dose of toxins from the bowel with the revival of the circulation, for apart altogether from hyper-pyrexia, every European patient, during the eleven years under review, whose temperature rose to 103° died in the reaction stage."

(2). That when the artificial reaction is brought about by intra-venous infusions, the resulting toxaemia is proportional to the hyper-toxicity of the infused fluid, for he says:—

"By the use of hypertonic solutions, on the other hand, the saline content of the blood, is immediately raised very considerably, with the result that the osmotic currents will tend to/
to carry more fluid into the blood rather than allow it to escape from it, and thus the diarrhoea is checked instead of encouraged, as by normal salt solutions. There is, however, a very definite limit beyond which it is not advisable to go in this direction, for too high a salt content of the blood might possibly give rise to a reabsorption of fluid which has been poured out into the bowel which may contain a large amount of toxins. The marked temperature reactions following hypertonic solutions may in part be due to this factor, but with due care excessive reaction can almost always be avoided, and if the blood pressure be fully restored, rapid excretion of the toxins by the kidneys takes place.

Again, in referring to the hypertonic solution which he advises - namely 120 grains of sodium chloride to the pint (or about 1.4 per cent), he states "I have not seen any advantage in using still stronger solutions, while I am inclined to think that they may produce a more violent reaction with greater danger of serious hyperpyrexia, possibly due to temporarily increased absorption of toxins from the bowel".

It is true that, by carrying out those most valu-
valuable instructions of ROGERS with regard to the
temperature at which the hypertonic saline solution
is infused, "with due care, excessive reaction can
almost always be avoided, and if the blood
pressure be fully restored, rapid excretion of
the toxins by the kidneys takes place".

Nevertheless, such a statement is practically an ad-
mission that the question of increased toxaemia
during the artificially produced reaction period
is a very real entity and has to be reckoned with.

If so much is admitted, why should one
adopt a method of treatment which confessedly
throws an extra burden on the already sadly devita-
lised kidneys? For we know how intensely disappoint-
ing is the not infrequent experience of pulling a
cholera patient safely through the collapse stage,
but losing him in the end from suppression of urine
and uraemia, which supervene, it may be, days after
reaction has set in, although in the intervening
period quite satisfactory quantities of urine per
diem may have been passed. Surely such a state of
affairs points to the late onset of suppression of
urea being due to a gradually increasing structural
and functional alteration in the kidneys; and
how else is one going to assign the cause for such
changes but to a toxic agency, whether this toxin
be/
be the actual cholera toxin, or some other poisonous substance in the blood which might have been encouraged to pass out of the system by being excreted by the intestine? In other words, one is probably correct in attributing suppression of early onset to stasis and the other factors which I have already given, but, when setting in after the collapse had been recovered from, such suppression is the result of toxic degeneration of the renal epithelium ("cholera nephritis").

Further, ROGERS is prepared to admit that when mere isotonic saline is used as the infused solution, a more copious flow of fluid escapes from the blood stream into the intestine than obtains after hypertonic solutions. With this I fully agree, but whereas ROGERS holds this up as a point of great discredit to isotonic treatment, I firmly believe that, on the whole, it is in its favour. I, of course, admit that, thereby, the fluid, which has been infused, is more quickly lost and that one may have to repeat the infusion somewhat more frequently in bad cases, but what matters this, if one has the satisfaction of knowing that the treatment being carried out is attaining a most worthy ideal - namely, to flush the cholera toxin out of the intestinal wall in the proper direction - and not to encourage its absorption first and thereafter to optimistically wait/
wait for its excretion by the kidneys?

Moreover, since one can always replace the lost fluid by timely intravenous infusions, the practice of encouraging the reinforcement of the circulation by absorption of toxic laden fluid from the bowel is, to my mind, both unnecessary and harmful.

I have stated that copious evacuations are not by any means to be discouraged, provided one can keep pace with the loss of fluid by giving sufficiently frequent and copious intravenous infusions. (2) It is admitted by ROGERS that such is more likely to occur after isotonic infusions than after hypertonic infusions. Therefore, the following extracts (2) from ROGERS' writings, indirectly, but surely, bear testimony to the beneficial effects of isotonic infusions in eliminating toxins.

(1) In speaking of the management of cases when uraemia has occurred after reaction has set in he says; -

"Diarrhoea may persist, and I agree with Good- eve's advice that it should not be checked, as it may carry off some toxic substances, although it has the disadvantage of tending to lower the blood pressure. I have seen lead acetate given for late diarrhoea in a patient passing/
passing somewhat scanty urine, followed by complete and fatal suppression of urine, although the original attack of cholera had not been a particularly severe one".

(2) Again he says:

"Do not check diarrhoea in the after-stage of reaction. Astringent remedies have frequently been recommended at this period to stop finally the now greatly diminished diarrhoea. Experience, however, has convinced me that this is wrong, owing to its leading to an increased absorption of toxins through the damaged intestinal mucous membrane. I therefore make no attempt to check the diarrhoea at this stage, but leave the reparatory processes in the bowel entirely to nature".

If such is said concerning the reaction stage, how much more forcibly do these remarks apply to the critical stage of the disease, when toxic substances in the bowel must be considerably more plentiful?

Provided a patient is in hospital and one has a sufficient staff to cope with the work, I fail to see that the necessity for the repetition of the infusion at reduced intervals is any real argument against isotonic saline treatment when it possesses admirable/
While I am dealing with this question of toxaemia and the desirability of taking every precaution to reduce it to a minimum, I would like to take this opportunity to express my opinion on the significance of the vomiting of cholera. It is not known exactly how the act is stimulated — whether the 'focus of irritation' lies in the stomach itself or in the bowel, or again whether the 'vomiting centre' in the brain is stimulated directly by the cholera toxin. DAVIDSON in his article on cholera in the "Encyclopedia Medica" states that:

"Among the toxic substances isolated from cultivations of the cholera bacillus, no emetic principle has been discovered, so far as we know. Yet such a principle is probably present".

Be that as it may, it is admissible to believe that the material which the stomach rejects is highly charged with cholera toxin. It is because I believe this to be so, that I deprecate exceedingly the practice of those who would take steps to check the vomiting of cholera in all cases. I need not here enumerate the various medicinal substances prescribed, nor the other procedures adopted to attain this end. Only one method of trying to check vomiting is/
is, I consider, permissible, because it at the same time aids in the elimination of cholera toxin from the body by the shortest route, namely, gastric lavage. But, as can be imagined, such meddlesome interference is most trying to the wretched cholera patient, and in addition is wholly uncalled for, because, by allowing him to drink his fill of water, such will be returned if vomiting be persistent, bringing with it quantities of cholera toxin. In this way, much distress to the patient is avoided, while the stomach is efficiently washed out.

From these considerations, I believe that both by the diarrhoea and by the vomiting, Nature is striving to rid the body of harmful products, and that she should be aided and not resisted.

I am unable to say with precision that vomiting was more copious after isotonic infusions than after hypertonic infusions, but from analogy, it is possible that this was actually so. It is certainly very noticeable, how promptly a patient will vomit a large quantity of fluid shortly after receiving an intravenous infusion, but this should constitute no cause for disappointment or alarm, as we know that it implies so much less available toxin.

Why then, it will be asked, has isotonic treatment found disfavour in ROGERS' eyes, and what?
what is the evidence in favour of hypertonic treatment?

1. First and foremost, of course, is the fact that the mortality amongst cases treated by hypertonic saline is distinctly lower than occurred formerly amongst those who were given mere 'normal saline'. This is undoubtedly the case, and ROGERS' figures are arresting in their significance. In the year 1906, he treated his cases by repeated copious intravenous infusions, using a solution, the strength of which was that usually recommended up to that time namely, 60 grains of sodium chloride to the pint (0.667 per cent). In other words, he used not a true 'normal' or isotonic solution, but one most decidedly subnormal or hypotonic, as we now interpret these expressions.

The result obtained from such treatment, as regards mortality, was only a slight reduction, for whereas during the previous 11 years, when rectal and subcutaneous salines were relied on entirely, the case mortality was 59 per cent, in 1906, it was 51 per cent.

In 1908, he commenced to use hypertonic saline intravenously (120 grams to the pint, or 1.375 per cent), with the immediate result of reducing the death-rate from cholera in a large number of cases to 33.6 per cent. It would be highly interesting if/
if one could determine whether the same or even a still more remarkable reduction in case mortality could not have been effected had ROGERS employed 'normal' (isotonic) saline as we now know it — namely 0.9 per cent or almost 80 grains to the pint.

In explanation of the only slight benefit derived from the 'normal' saline treatment carried out in 1906 (60 grams to the pint), I must refer the reader to what I have already said about the objections to the giving intravenously of hypotonic solutions. (p. 212.)

It will be appreciated why a fatal termination was rendered highly probable in a very severe case when, as we have seen, the blood plasma is sometimes hypotonic already to such an extent that haemolysis has commenced. What benefit is to be derived from the pouring into such a person's circulation of a large quantity, of equally hypotonic saline solution? Surely, very little.

(2) ROGERS tells us that, in some of his worst cases, the haemolytic process was already found to have commenced if the chlorides in the blood were as low as 0.6 per cent, which strength is not much lower than that of the saline solution which he used for infusion in the treatment of his 1906 series, — namely 0.68 per cent (or 60 grains to the pint).

These/
These statistics of ROGERS, therefore, do not prove at all conclusively that hypertonic treatment possesses powers of reducing mortality which are not possessed by true isotonic infusions. (2)

2. ROGERS claims that the mortality from collapse is markedly reduced by hypertonic infusions as compared with that associated with isotonic solutions. I do not see that this argument is any stronger than the preceding, for the same reason.

If one recognises the fact that, owing to a less tonic state of the blood plasma and consequently a slightly more rapidly continued transudation of fluid into the intestine following isotonic infusions, the repetition of such infusions may be necessary at shorter intervals and possibly more frequently, there is little difficulty in conducting the patient safely through the collapse stage. I believe that where a patient dies from initial collapse, in spite of timely and sufficiently copious infusions of isotonic saline, such a death is attributable not to a lack of either blood fluid or blood salts, but to a coincident toxaemia of overwhelming intensity and that had one infused hypertonic, and not isotonic, saline, the result would have been the same; indeed death might have been
even more speedy.

3. Probably the only occasion on which hypertonic treatment possesses a real advantage over isotonic treatment is that when the blood salts are reduced to a dangerously low point. Here, of course, there is not the slightest doubt that by supplying to the hypotonic blood a quantity of hypertonic saline, the resulting mixture becomes more nearly isotonic; surely a most laudable object. But even granting that such is attained in certain cases, there are certainly some aspects of cholera which must be considered before one blindly accepts the statement that hypertonic treatment is the best - or, indeed, even suitable - in all cases. HOGHSH states that this marked reduction in the blood salts occurs in only the very worst cases, and that in practically all others, the salt content of the blood, is higher than normal.

The danger, therefore, of infusing hypertonic saline in cases all and sundry is that the majority of patients will have their blood rendered unduly hypertonic, with the result that reactionary toxaemia is induced to an unnecessarily high intensity.

It must be realised that when one talks of 'hypertonic' saline, it is not merely a solution whose salt content is slightly higher than 'isotonic' which/
which is referred to. For the former contains as
much as 40 grains to the pint (or almost 0.5 per cent)
in excess of 'isotonic' saline.

Now, keeping in view the points which I have
put forward to the discredit of hypertonic saline, it
seems to me that the average case will more likely re-
cover under isotonic regime than under hypertonic.
And, after all, it is the average case one must cater
for, since, only by carrying out estimations of the
salt content of the blood in each individual case,
could one say with certainty what the salt content of
the solution for intravenous infusion should be. By
giving to the average patient only isotonic treatment,
the odds are in favour that he will die neither from
initial collapse nor from disastrous complications at-
tributable to toxaemia after reaction has set in —
notably hyperpyrexia and uraemia. If, on the other
hand, hypertonic saline had been administered, the
probability of death from initial collapse owing to
loss of fluid would be equally remote, but the chances
of totally preventing toxaemic manifestations would be
fewer.

Any other arguments raised by the advocates
of hypertonic saline in favour of the method and
against true isotonic treatment will, I feel sure, have
been met already at some time or another in the fore-
going pages.

ii./
It has already been seen from TABLE No. XVII, page /26, that 93 cases were treated by intravenous infusion, the latter numbering 176. It now remains to show what proportions of these 176 infusions were represented by

A. Hypertonic saline infusions.

B. Ictonic saline infusions.

It is necessary that I should here state that, having become dissatisfied with the immediate and remote results of hypertonic treatment, I began to try to improve these by giving a less hypertonic solution in some infusions and an exactly isotonic solution in others, and to compare the effects produced from these three graded strengths.

What is meant by an isotonic solution?

Under normal conditions, the contents of the erythrocytes and their immediate environment, namely the blood plasma, are in a state of osmotic equilibrium, and under such circumstances each red blood corpuscle maintains a fairly constant shape and size. Alteration in the concentration of the salt content of the plasma determines a flow of water either into, or out of, the erythrocytes.

In cholera, the direction is variable according/
according to the severity of the case (See page No 210) for only in the very severest cases is the flow directed into the erythrocytes while in the other cases, which constitute the great majority, the flow is from erythrocytes to plasma. In other words, the plasma is hypotonic in the first case, and hypertonic in the second. An isotonic solution is one which, when constituting the immediate environment of a red corpuscle in health, will ensure that the healthy osmotic balance is maintained, and therefore in disease will tend to re-establish it under all circumstances.

Physiologists tell us that a solution of sodium chloride in distilled water in strengths varying from 0.85 per cent to 0.9 per cent will form an immediate environment for the red cells which is isotonic with them in health - in other words, this solution possesses a "tonicity" similar to healthy blood plasma. It is, indeed, a physiological fluid, and hence is designated "normal saline solution".

Calculating from the above percentages, we find that saline solution in order to be isotonic must not contain less than 74.1 grains, nor more than 78.6 grains to the pint.

HALE WHITE states that a 0.91 per cent solution/
solution is isotonic with the normal blood. This works out at about 79.4 grains to the pint.

Both for convenience, and in order to ensure that, at any rate, a hypotonic solution would not be administered to the patients, I fixed on 80 grains of sodium chloride to a pint of sterile distilled water, as fulfilling the function of an isotonic solution for intravenous administration. The "intermediate strength" was obtained by running into the patient's vein the first few pints as hypertonic saline (120 grains to the pint) and then by continuing with isotonic saline (80 grains to the pint) until the desired quantity of fluid had been given. Since, of course, it was impossible to foretell how much saline would ultimately be required, the proportions of the two solutions varied in different cases, and accordingly also the tonicity of the total volume infused. For instance, if 4 pints of hypertonic saline (120 gr. to the pint) were first run in, and then a further 2 pints of isotonic saline (80 grains to the pint), the strength of the total 6 pints infused would be 106.6 grains to the pint. If, however, the total quantity of the infusion consisted of equal parts of hypertonic and of isotonic saline, its strength would, of course, be 100 grains to the pint.

Table/
Table No. XXIV shows that 24 infusions of such intermediate strengths were given varying from 93.3 grs. to the pint to 110 grains to the pint.

### TABLE XXIV.

<table>
<thead>
<tr>
<th>Infusions of intermediate strength</th>
<th>Grains per pint.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>93.3</td>
</tr>
<tr>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>100.8</td>
</tr>
<tr>
<td>1</td>
<td>103.3</td>
</tr>
<tr>
<td>4</td>
<td>104</td>
</tr>
<tr>
<td>1</td>
<td>105</td>
</tr>
<tr>
<td>11</td>
<td>106.6</td>
</tr>
<tr>
<td>2</td>
<td>108</td>
</tr>
<tr>
<td>1</td>
<td>108.5</td>
</tr>
<tr>
<td>1</td>
<td>110</td>
</tr>
</tbody>
</table>

24

The average of these 10 graded strengths is found to be 103.9 grains to the pint, and hereafter the use of the words "intermediate strength" implies/
implies this average.

In 13 of the infusions, I am unable to state the strengths given, either owing to the infusion having been given at another hospital prior to the patient's admission, or owing to such a record having been omitted to be made.

**TABLE XXV**

shows how these 176 infusions are shared by the different strengths:-

<table>
<thead>
<tr>
<th>STRENGTH</th>
<th>NUMBERS of INFUSIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertonic (120 grs.)</td>
<td>81</td>
</tr>
<tr>
<td>&quot;Intermediate strengths&quot;</td>
<td>24</td>
</tr>
<tr>
<td>Isotonic (80 grs.)</td>
<td>58</td>
</tr>
<tr>
<td>Unknown</td>
<td>13</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>176</strong></td>
</tr>
</tbody>
</table>

### Effects of Varying Strengths of the Infused Fluid

(I) on the artificial reaction thereby induced.

I have analysed these 93 infused cases from the point of view of the skin and rectal temperatures which occurred after the infusions of different strengths, and the results are given in **TABLE/**
**TABLE No. XXVI**

<table>
<thead>
<tr>
<th>Infusion Type</th>
<th>Average Skin Temp</th>
<th>Average Rectal Temp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertonic infusions (81)</td>
<td>100.2</td>
<td>101.9</td>
</tr>
<tr>
<td>Intermediate infusions (24)</td>
<td>100.4</td>
<td>102.3</td>
</tr>
<tr>
<td>Isotonic infusions (58)</td>
<td>100.2</td>
<td>101.7</td>
</tr>
</tbody>
</table>

I admit that these figures do not give much support to my contention that hypertonic infusions tend to induce a more severe type of reaction than that which follows isotonic infusions. But these very important points must be taken into consideration, namely that, in spite of the greatest care being taken to give the infusions at a temperature appropriate to the rectal temperature, two cases of hyperpyrexia occurred, and ultimately died from this cause. In both instances, the excessive reaction followed hypertonic (120 grains to the pint) infusions, and as the temperature could not be recorded, these two cases are left out of the foregoing calculations. Could they have been included, the average temperatures for the hypertonic series would, of course, be still higher.

Not a single case of hyperpyrexia followed isotonic saline infusion.

Further/
Further, after having met with these two cases, the experience is one which is not easily forgotten, for it would seem that once a hyperpyretic state is reached, nothing is of the slightest avail to avert a fatal termination. Therefore to ensure that the artificial reaction after hypertonic infusions would not another time be excessive, the saline solution was cooled down to a lower temperature than that when isotonic solutions were given; accordingly no further cases of hyperpyrexia occurred, but the procedure had the inevitable effect of lowering the average temperatures for the hypertonic series, while the isotonic series required no such precautions to be taken.

**EFFECTS of VARYING STRENGTHS of the INFUSED FLUID on**

**(ii) the MORTALITY as a whole:**

It is difficult to construct a suitable table to show this, since many of the cases received both hypertonic and isotonic infusions. Nevertheless, Table No. XXVII shows how these 176 infusions were shared by the 93 cases which received them, namely 67 recoveries and 26 deaths.

TABLE/
It will be seen that as the strengths of the infusions are reduced from hypertonic to isotonic, there is an accompanying rise in the percentage in the number of those infusions associated with the recovery cases.

**EFFECTS/**
EFFECTS of VARYING STRENGTHS of the INFUSED FLUID on

III the MORTALITY from DIFFERENT CAUSES.

This will be discussed more conveniently under "Causes of Death".

(f). The rate at which the Saline Solution should be infused intra-venously.

When a cholera patient is admitted in a markedly collapsed state, not an unnecessary moment's delay should be permitted before treatment by intravenous infusion of saline is begun. It is just in such cases that one is tempted to run in the solution very rapidly, although a moment's consideration of the effect of this procedure should restrain one from doing so.

We know that in such cases the heart beat is at its minimum as a propulsive force, and we have seen why this is so. Accordingly, it is highly undesirable to suddenly establish circumstances which demand from the heart an effort, which, for the moment, it may not be able to put forth. I believe that by infusing the first few pints at a rapid rate, as is recommended, one runs the risk of throwing an unduly great strain on the as yet enfeebled heart, and before sufficient time has been given for the diluted - and therefore more easily circulated - blood to perfuse the heart muscle itself/
itself and so allow it to regain an activity equal to the effort demanded.

My practice was to run in the first 2 pints very slowly — say about 2 ounces every minute — and after noting that the force of the pulse had satisfactorily returned, to continue the remainder at twice that speed, i.e. a pint in 5 minutes.

From this, it will be seen that the giving of an infusion of 5 pints occupied over a \( \frac{1}{2} \) hour. But I consider that such care is necessary and the time is well spent. Moreover, by not unduly hurrying the infusion, one is able to study more minutely the alterations in the various clinical manifestations — the gradual return of the pulse, the extraordinary relief given to the patient from the torturing cramps, and from the intense thirst, the dramatic way in which not only consciousness but even a feeling of pleasurable exhilaration is established. Having noted these, one is enabled to continue the infusion process as long as the pulse remains satisfactory and the patient's general condition improves. Once the patient shows the slightest sign of experiencing any sense of fulness in the chest or at the epigastrium, the infusion should be stopped in those cases where observations on the pulse rate and blood pressure have not already indicated.
indicated that sufficient saline has been given.

Further, and this I consider equally important - the practice of extending the infusion process over a prolonged period allows the physiological fluid to pass into the desiccated body tissues, and in this way a larger capacity is offered for available saline solution. In other words, at the conclusion of a slowly administered intravenous infusion, not only has the circulation been replenished, but also that very considerable storehouse of reserve fluid - the body tissues - has received a satisfying supply of the saline, and, accordingly, relapse from continued loss of fluid into the bowel is all the longer delayed.

It is by the slowness with which I administered the saline that I account for both the fact that I was enabled to give larger quantities (2) than ROGERS' would seem to consider necessary, and for a satisfactorily prolonged interval between two consecutive infusions, when repetition of the treatment was demanded.

Lastly, it is obvious that the more fluid one is enabled to infuse, the greater will be the effect of diluting the cholera toxins which have already/
already been absorbed into the general circulation a not insignificant advantage to be sought.

It may be asked, how was this prolonged infusion process carried out in each case when I was in sole charge of the cholera section during 1917 and 1918, and when severely collapsed patients were sometimes admitted in batches of 3 or more? This difficulty was overcome by my carrying out the actual insertion of the cannula into the vein and allowing a highly competent nursing orderly to temporarily continue the administration of the infusion while I attended to the next patient.

(g). The TEMPERATURE of the INFUSED FLUID.

I cannot speak too highly of the value (2) of ROGERS' instructions with regard to this matter, being especially privileged to speak on the subject. Mesopotamia is probably about the last place one could wish in which to conduct a patient through the reaction stage of cholera, owing to the terrific atmospheric heat which thus reduces to a minimum any chance of a patient's losing bodily heat, especially when at the same time humidity of the air is high.

It, therefore, requires the utmost vigilance on the part of all concerned to prevent that most disastrous complication - hyperpyrexia - from occurring/
occurring; such care was imperative not only in the giving of the infusion but in the after treatment of these patients.

One must realise the important fact that the skin temperature in the collapse stage of cholera is no indication whatever as to the body temperature. The rectal temperature is the only guide as to the true temperature of the body; as LIEBERMEISTER observes "accurate conclusions as to the internal temperature can be drawn only when the bulb of the thermometer is inserted far into the rectum".

When what I have already said as to the explanation of this fact, and what occurs during the reaction stage, are appreciated, it is not difficult to understand why special precautions should be observed when artificial reaction is brought on.

Often, the temperature of saline solution as it stood in the stock Winchester quarts, was found to be over 110° and therefore had to be cooled to the desired temperature. This was accomplished by standing the bottle in cold water and rubbing its exterior with ice.

I need not discuss the matter more than indicate how the temperature of the infused fluid was adjusted according to the rectal temperature, for ROGERS' describes the procedure amply in his book.
Table No. XXIX shows at a glance how the saline should be infused at a low temperature when that in the rectum is high, and vice versa.

**TABLE No. XXIX.**

<table>
<thead>
<tr>
<th>Rectal Temperature</th>
<th>Suggested Temp. of Infused Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>95</td>
<td>102</td>
</tr>
<tr>
<td>96</td>
<td>101</td>
</tr>
<tr>
<td>97</td>
<td>100</td>
</tr>
<tr>
<td>98 (Zero)</td>
<td>99</td>
</tr>
<tr>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td>100</td>
<td>94</td>
</tr>
<tr>
<td>101</td>
<td>90</td>
</tr>
<tr>
<td>102</td>
<td>86</td>
</tr>
<tr>
<td>103</td>
<td>82</td>
</tr>
<tr>
<td>104</td>
<td>78</td>
</tr>
<tr>
<td>105</td>
<td>74</td>
</tr>
<tr>
<td>106</td>
<td>70</td>
</tr>
</tbody>
</table>

This table, based on ROGERS' directions, was drawn up by me for use at the Isolation Hospital and proved to be of the utmost value. The fact of only two cases of hyperpyrexia occurring amongst 93 cases requiring intravenous infusions, and under most trying climatic conditions is surely attributable,
attributable to these valuable suggestions of

(2) ROGERS'!

It must not be forgotten that the mere infusion of saline solution intravenously - even in a healthy person - will induce a certain degree of pyrexia, and acting on this knowledge, I usually refrained from giving to a collapsed patient whose rectal temperature was very high - say 103° F. or over - just as much saline as I would have, had that record been lower. It is better practice, I believe, to give to such patients only a moderate amount of saline at the first infusion, and to repeat the administration only when one is satisfied, from frequent rectal temperature observations, that hyperpyrexia is not likely to occur.

There is one more precaution, which must be taken, if one is to avoid troublesome high temperatures in the artificial reaction induced by intravenous saline. The matter is so important and is referred to so concisely by ROGERS' (2) that I will be excused if I quote his remarks.

"Another important practical point, which is too often neglected, is that as intravenous injections are always followed by a febrile reaction, it is not only unnecessary, but is actively injurious/
injurious, to surround the patient with hot-water bottles during the process. I have several times seen a patient, whose temperature was rapidly becoming hyper-pyrexial during or soon after transfusion covered with very hot rubber water bottles, while the increasing restlessness, due to the rise of temperature, was being locked on as an indication for continued saline injections. Personally, I hold that the external application of warmth to the body, even during the cold collapse stage is nearly always harmful, except perhaps in the few cases in which the rectal temperature is markedly subnormal. When we bear in mind the great loss of fluid from the body in cholera, it becomes clear that the coldness of the surface and extremities during collapse is very largely a conservative process, in order to retain the small remaining supply of blood for the vital internal parts, and, by drawing the blood to the distal parts, the collapsed condition can only be increased. For these reasons
I never allow the use of hot-water bottles, etc., in my cholera ward, except only where the rectal temperature is subnormal.

These directions were also observed at the Isolation Hospital.

When a patient had received an intravenous infusion during the day, it was found to be to his advantage to carry his bed out into the open in the evening, owing to the merciful concession of Providence in that such a distinct drop in the atmospheric temperature occurs at sun-down in Mesopotamia. In this way, the patient was enabled to lose heat by the skin, and high fever was diminished. Fanning of these patients by Indian "boys" proved most helpful, both in keeping them comfortable, and aiding regulation of their temperatures when the warm atmospheric air was absolutely stationary, as it often was.

(h). The DURATION of the INTERVAL between two CONSECUTIVE INTRAVENOUS INFUSIONS.

This is a very interesting subject to study, as it brings out several instructive points. First of all, an analysis of a fairly large series of cases such as this indicates what one is to expect.
expect in the treatment of cholera with regard to frequency of necessary intravenous infusions in each case, and how soon one may have to repeat the treatment after a first, second, third etc. infusion.

The analysis also demonstrates how actually the strength of the saline infusion influenced the duration of the interval between a given infusion and its successor - or, in other words, how soon after a hypertonic, intermediate, and isotonic infusion respectively, the patient again became so collapsed that repetition of the infusion became necessary.

Referring to Table No XIX page 204 we see that 93 cases received amongst them a total of 176 infusions. Obviously, 93 of these infusions could not be followed by an interval, included in this number being the 42 cases which received only 1 infusion, and 51 others with terminal infusions. Thus there are 176-93 = 83 intervals on which apparently we may base calculations.

**TABLE No. XXX**

shows how these 83 intervals are distributed amongst the 51 cases.
<table>
<thead>
<tr>
<th>Cases requiring</th>
<th>data on which to calculate the</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd infusions = 51</td>
<td>1st interval = 51</td>
</tr>
<tr>
<td>3rd infusions = 23</td>
<td>2nd interval = 23</td>
</tr>
<tr>
<td>4th infusions = 6</td>
<td>3rd interval = 6</td>
</tr>
<tr>
<td>5th infusions = 2</td>
<td>4th interval = 2</td>
</tr>
<tr>
<td>6th infusions = 1</td>
<td>5th interval = 1</td>
</tr>
<tr>
<td></td>
<td>= 83</td>
</tr>
</tbody>
</table>

We thus see that we have 83 intervals distributed amongst the 1st, 2nd, 3rd, 4th and 5th intervals. Further the 2nd, 3rd and 4th infusions given to one case were necessary, not from cholera collapse but from B. pyocneus infection, and these three infusions have been omitted in the calculation, reducing the 1st, 2nd and 3rd intervals each by 1 item. Again in one instance the 1st interval is not recorded, and in another, the 2nd interval.

Now, disregarding these 5 intervals which I have just referred to, we have the following number of intervals to calculate from:

Table/
TABLE No. XXXI.

<table>
<thead>
<tr>
<th>Interval</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>49</td>
</tr>
<tr>
<td>2nd</td>
<td>21</td>
</tr>
<tr>
<td>3rd</td>
<td>5</td>
</tr>
<tr>
<td>4th</td>
<td>2</td>
</tr>
<tr>
<td>5th</td>
<td>1</td>
</tr>
</tbody>
</table>

78 data.

Table No. XXXII shows the average duration of these intervals, and also how the duration of the various intervals was influenced by the salt content of the fluid given at the preceding infusion.

On account of the fact that the strength of the infusion is unknown in 5 first infusions, and 2 second infusions, there are accordingly 7 fewer data on which to base calculations as to the effect of salines of different strength on the succeeding interval.

From Table No. XXXII we learn that -

(i) About 18.5 hours is the period which is likely to elapse before a second infusion becomes indicated.

(ii) Speaking generally, the interval became longer and longer as the preceding infusion was a 1st, 2nd, 3rd, 4th or 5th infusion respectively.

(iii)
(iii) The interval between 1st and 2nd infusions, when isotonic solution was used as the 1st infusion, is slightly shorter (by 1½ hours) than when hypertonic saline (120 grains to the pint) was given.

(iv) Under the same conditions, the second interval was also shortened (by as much as about 10½ hours).

As to the other facts shown by Table No. XXXII, no conclusions of any value can be drawn from them, as it is seen on how few data the results are based.

What I should like to emphasise, is the fact that one may be driven to re-infuse a patient a little sooner after an isotonic infusion than after a hypertonic one. I have already pointed out (See page 225) that such an eventuality is to be expected from a consideration of the action of these two solutions which possess different osmotic values.

I also explained why I believe that such is not at all an undesirable phenomenon, namely, that the more copious evacuations which tend to follow isotonic infusions tend also to diminish the quantity of cholera toxin which is available for absorption from the bowel, and which is so potent a factor in the production of toxaemic complications, such as hyperpyrexia, and toxic suppression of urine.

The/
The reader will surely admit that the increase, by a fraction, of the interval between two consecutive infusions - and therefore a corresponding reduction in the attention demanded by each case - is a very trifling advantage to be gained, for, provided one has the necessary apparatus and assistance available, the patient can be given the isotonic re-infusion when he has reached no greater a degree of collapse than had he been originally given hypertonic saline.

Admittedly, the necessity to reinfuse is delayed by hypertonic infusion, but if, as I have said, one doesn't allow a patient to reach an unduly pronounced collapsed condition after an isotonic infusion, I believe the results obtained by the latter treatment are even better. This belief is founded on,

(1) The statistics shown throughout this thesis.

(2) Reasoning as to the physical and physiological properties of the two solutions.

(3) Lastly, but not least, of all, the observations made at the time on the patients in the wards. In this connection it is an interesting fact that my 16 British nursing orderlies, the majority of whom were well-trained, keen and observant fellows, were in entire agreement.
agreement with the belief that by giving isotonic saline at the infusions, less anxiety as to the patient's future condition - immediate and remote - was occasioned, than when hypertonic solutions were given.

THE DIET of CHOLERA PATIENTS.

I have said (page 65) that from the moment at which a patient was admitted, no food of any kind was given to him. If the case was one of very urgent diarrhoea and vomiting, no steps were taken to prevent the patient from drinking as much plain water as he wished, in order to, in some measure, help to quench the intolerable thirst, during the preparation of the apparatus for intra-venous infusion.

An unlimited supply of this was put at the patient's bedside, from which he was at liberty to drink as often as he wished. On no account whatever was anything else given to a cholera patient, during the cholera attack and during the artificial reaction stage.

On the appearance of features which indicated return of the digestive juices and a certain degree of absorption from the bowel - for instance, return of a bilious tinge in the stools, and much less copious and less watery evacuations - barley water/
water and farinaceous foods were added. Very thin arrowroot was what was usually given.

The greatest care was taken not to increase the diet too rapidly and to give small feeds very frequently - e.g. hourly. On the slightest sign of the diarrhoea again becoming more marked, barley water alone was resorted to.

The reduction of the evacuations to only 2 or 3 per diem was taken as a safe stage at which to still further increase the diet - e.g. custards, a little milk.

When at length a semi-solid, faecal stool had been passed, the patient was given, every three hours, a small quantity of one of the following - thin vegetable soups, - thin bread with butter, cocoa, a little very weak tea, corn flour.

When diarrhoea had ceased for at least three days, fish, eggs, and the like were carefully added, until a nourishing full diet was attained.

The danger of causing choleraic symptoms to return, by allowing a patient to climb the dietary ladder too rapidly, cannot be exaggerated. On several occasions, the enforced abstinence of a patient from nourishment for a prolonged period, tempted one to increase both the frequency and the quantity of his feeds accordingly; nothing, however, was gained by the procedure, for diarrhoea returned, and was/
was checked only when the diet was once more restricted to barley water. Against the giving of nourishment of any kind during the acute stages of cholera there are the following weighty arguments:—

(1) All the secretions - alimentary and otherwise - are in abeyance, and therefore digestion is at an absolute minimum.

(2) Even though the nourishment given could be digested, it would not be absorbed.

(3) The nourishment given may provide a medium in which the cholera vibrio can grow and multiply as a saprophyte.

(4) Further irritation of the already harassed intestinal mucous membrane is likely to occur, with the result that diarrhoea is still more strongly stimulated.

(5) Lastly - and I think quite as important as the former - the fact that the permanganate salts are so readily deoxidised in the presence of organic matter. When our aim is to concentrate this oxidising action of the permanganate salts upon the cholera toxin in the bowel, it is obvious that by providing other substances which will share in the oxidation change - if they don't entirely monopolise it - our therapeutic agent is in like measure rendered impotent.

Although/
Although it is true that barley water is probably the least oxidisable of the articles of diet which I used, I did not encourage its administration during the acute stage of cholera when, at the same time, the patient was undergoing the course of permanganate treatment. Otherwise, it was the one form of nourishment relied on, until indications for a more liberal diet presented themselves.
With the exception of atropin (page 168) the permanganates (page 166) and intravenous infusions of sodium chloride solution, no other drugs were utilized in the routine treatment of the present series.

The occasions on which other medicinal substances were called on, were indeed few, so strongly did I believe in the theory that by restoring the circulation and encouraging the elimination of toxin, one is doing almost all there is to be done to encourage the rapid recovery of the patient.

Such drugs as digitalis, ammonium carbonate, adrenalin, brandy and other stimulants were given in a few cases, but no useful purpose is to be derived from an account of the indications for them. These substances were given in the reaction or convalescent stage and took no active part in the bringing of the patient through the more anxious stage of the disease.

There is, however, one method of treatment which was adopted on not a few occasions - namely the giving of sodium bicarbonate solution intravenously.

I have referred to the occurrence of 'acidosis', or, as it is more correctly described - diminished alkalinity of the blood, in cholera (pages 102).

In order to counteract this tendency, intravenous infusions were given to these patients whose daily output of urine fell very considerably and did not/
not increase in spite of raising the blood pressure by intravenous saline solution.

At the next repetition of the intravenous infusion, 160 grains of sodium bicarbonate were added to the first pint of saline given, this initial pint being in every case isotonic with normal blood. Seven cases received this treatment. It is interesting to record the ultimate fate of these 7 cases in the light of the other treatment which they received.

Table No. XXXIII. shows how many were being given only hypertonic treatment at the same time, and how many were given only isotonic saline; it also shows not only how indications for alkaline treatment occurred much more frequently amongst the hypertonic series, but also that, associated with these, death occurred in 4 out of the 5 cases, while the two isotonic cases both recovered.

<table>
<thead>
<tr>
<th>CASES RECEIVING ALKALINE INFUSIONS.</th>
<th>RECOV.</th>
<th>DEATH</th>
<th>TOTAL CASES.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertonic Cases</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Isotonic Cases</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

Of/
Of these 4 deaths, all occurring in the hypertonic series, 2 died of uraemic symptoms, one died of exhaustion having recovered from temporary suppression, while the fourth case was an extremely collapsed patient to whom it was deemed advisable to administer the alkaline solution at the second infusion, but who, nevertheless died of collapse.

Apart from these 7 intravenous alkaline infusions, two patients received the alkaline infusion intracellularly, and five rectally. But it is impossible to determine whether any benefit was really derived from such procedures, since they were adopted in bad cases to supplement other modes of treatment. The fact remains that no cases recovered in which they were employed. I imagine that the only method of administering alkalies in cholera with any hope of effecting real improvement in the state of the patient's blood is by the intravenous route.

COMPLICATIONS/
Complications & Sequelae.

The following complications and sequelae were observed amongst the total 125 cases:—

1. PNEUMONIA.

This occurred in 4 cases, three of which died from this cause. The lung consolidation was of broncho-pneumonic type in 3 of the cases, lobar, in the fourth. One of the broncho-pneumonia cases recovered. (See also 'Causes of death').

2. PAROTITIS.

This occurred in 6 cases, three times in the right gland and three times in the left. The swelling of the gland was first noticeable on the 6th, 9th, 11th, 12th, 19th, and 25th day of the disease amongst the six cases respectively. Suppuration occurred in 3 cases and the abscess was incised and drained. In two cases, the inflammation subsided under fomentations, while the sixth case died from a relapse of choleraic symptoms before suppuration had time to occur. The only other death occurring amongst these cases which developed parotitis (non-suppurative) was that of an Indian patient who developed a secondary enteritis from Bacillus pyocyaneus infection and ultimately died from septicaemia.

3. CONSTIPATION.

This has been referred to before. I pointed/
pointed out that, in a few cases, the cessation of copious evacuations is succeeded by a very obstinate constipation, no action of the bowel occurring sometimes for many days. This troublesome but not serious sequel occurred in 12 convalescent patients, but ultimately yielded to energetic treatment, e.g. high enemata.

4. **PERSISTENT Oliguria.**

This was noted in 11 cases, 7 of whom ultimately died with symptoms of what was taken to be uraemia. I should, however, like to emphasise what I have already said as to the comparative insignificance of greatly diminished output of urine per diem, as a sign of defective renal function, when such is noted in a tropical country such as Mesopotamia. For, even a healthy person passes only a matter of a few ounces of urine during the hotter hours of the day. Accordingly, it was extremely difficult to decide whether oliguria - or even apparent anuria - was consequent on pathological or mere physiological processes, without laboratory-conducted examination of the urine.

Under the circumstances, therefore, it is possible that a few of the so-called 'uraemic' deaths may be really attributable to a toxaemia other than that associated with defective renal function. The fact/
fact that these deaths occurred almost entirely amongst cases which were treated by hypertonic saline was one of the chief means of arresting my attention to the possibilities of isotonic saline. When the causes of death are discussed, it will be shown how very striking is the association between deaths of toxic origin and a preceding hypertonic treatment.

The remaining 4 cases in which a rather pronounced oliguria was observed, ultimately regained an efficient renal function under appropriate treatment, two of them making complete recoveries, while the other 2 died of exhaustion.

5. HAEMORRHAGIC RASH.

An interesting case is that of a British soldier who, on the 17th day after the onset of cholera and while in a thoroughly convalescent state, suddenly developed a peculiar haemorrhagic, blotchy eruption over the greater part of the anterior abdominal wall. He was rather anaemic. It was unlike purpura in its distribution, and there were no other signs of scurvy. The patient was given calcium chloride in 10 grain doses thrice daily, and the ecchymosis gradually cleared up, disappearing completely in just under three weeks.

from/
From observations on just under 160 cases of cholera, I should think that this type of skin eruption is very exceptional. Still it is interesting to note that LIEBERMEISTER draws attention to the occasional occurrence of small haemorrhages (petechiae) or larger ones (vibices and ecchymoses) into or under the skin.

6. FURUNCULOSIS and other ABSCESS FORMATION.

It is well known how susceptible the cholera patient is to infection by the organisms of ordinary suppuration, and that such susceptibility is usually shown by the occurrence of boils and other septic states, during the convalescent period.

The present series, however, provides only 4 instances where boils or other superficial abscess formations were noted. The various situations where suppuration took place were,

<table>
<thead>
<tr>
<th>1st case</th>
<th>(a) Left buttock (20th day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(b) Anterior abdom. wall 23rd day.</td>
</tr>
<tr>
<td>2nd case</td>
<td>Right buttock.</td>
</tr>
<tr>
<td>3rd case</td>
<td>Left forearm.</td>
</tr>
<tr>
<td>4th case</td>
<td>Over lumbar spine (6th day).</td>
</tr>
</tbody>
</table>

The septic process appeared to begin as small superficial pustules which eventually formed abscesses of moderate size in the subcutaneous tissues. All these patients ultimately recovered.

7./
7. HERPES ZOSTER.

An unusual case is that of a patient who, on the 6th day of the disease, developed a herpetiform eruption on the palm of the right hand. From 8 to 10 small rounded vesicles, each a little smaller than a 3d piece, appeared on the thenar and hypothenar eminences and along the palmar aspect of the roots of the fingers, and were so arranged that an almost perfect circle was described by them. Under ordinary treatment to ensure cleanliness, the eruption quickly disappeared. LIEBERMEISTER (page 363) notes that "True herpes labialis orfacialis is very infrequent", but makes no reference to herpetiform eruptions elsewhere.

8. BED SORE.

It is highly praiseworthy that in only one instance a pressure sore occurred, especially when one recollects what a large number of helpless and emaciated patients the nursing orderlies had to attend. As would be expected, the case was a severe and prolonged one, requiring no fewer than 5 intravenous infusions before all danger was past. Although a suppurative parotitis also developed, the patient made a good recovery. The pressure sore was situated in the usual place, over the sacral region.
9. "CHOLERA TYPHOID".

Obscure, indeed, is the pathology of this condition. It, however, would seem to indicate a toxic state. This "typhoid" state was noted in but 2 instances, both the patients who exhibited it dying on the 4th and 6th day respectively of the disease. Further reference will be made to the condition under "causes of death".

10. HYPERPYREXIA.

Beyond noting that this accounted for 2 deaths, little more need be said here owing to the fact that the condition has been freely discussed under "Symptomatology" and will again be referred to under causes of death.

11. ENTERITIS from SECONDARY B. PYOCYANEUS INFECTION

Two cases of this occurred. The first case was quite a mild infection. The bluish-green stools were passed for only a few days and no further invasion took place.

The other case, however, was of a different stamp. The cholera attack was satisfactorily recovered from, and about a week after the vomiting and diarrhoea had ceased, and about the 10th day of the disease, the typical bluish green stools appeared. Soon an exhausting diarrhoea returned, each stool exhibiting B. pyocyaneus infection. The patient ultimately/
ultimately developed a septicaemia from the same organism, and, after a prolonged illness, died on the 63rd day of his disease.

12. EVANESCENT PARESIS of all the LIMBS.

No explanation can be given for this extraordinary condition. The patient was an Indian who, on the 9th day of the disease, suddenly became so helpless that he had to be fed. After two days his strength returned, and he was able to walk about. I believe that it was a manifestation of hysteria.

13. CHRONIC DIARRHOEA.

One case of obstinate diarrhoea following the choleraic attack occurred. This case has been referred to already (See page 76/).

Other conditions complicating the course of the cholera infection need only be mentioned -

14. BRONCHITIS (1 case).
15. DRY PLEURISY (1 case).
16. PARATYPHOID A. (1 case).
17. MALARIA. (3 cases).
18. DYSENTERY. (3 cases).
19. SANDFLY FEVER (3 cases).

The only case, amongst these latter, which died is that of a patient who had been suffering from dysentery and contracted a superadded cholera infection. He, however, did not die from the/
the cholera attack, as he lived for 12 days after its onset, succumbing at last from dysenteric symptoms.
**TABLE XXXV**

<table>
<thead>
<tr>
<th>INFUSED CASES</th>
<th>TOTAL DEATHS</th>
<th>DURATION</th>
<th>NUMBER</th>
<th>DURATION OF ILLNESS</th>
<th>NUMBER</th>
<th>DURATION OF ILLNESS</th>
<th>NUMBER</th>
<th>DURATION OF ILLNESS</th>
<th>NUMBER</th>
<th>TOTAL dts.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Showing the causes of death amongst the differently treated cases.
CAUSES OF DEATH.

Table No. XXXIV is sufficiently comprehensive to show the reader at a glance how the total deaths (32) of the present series of cases (125) are accounted for.

It will be seen that the various causes of death have been arranged in the order in which death occurred after the onset of symptoms. For instance, collapse caused death earliest, on the average 21.4 hours after the onset of symptoms, hyperpyrexia = 35 hours, and so on.

The most striking feature of the table is the very high proportion of the total deaths which is contributed by those cases which received intravenous infusions of hypertonic strength only.

Only in one instance did a case treated with isotonic infusions only succumb, - that of a patient who, having recovered from the cholera attack, died of secondary B. pyocyaneus enteritis and septicemia (See page 270).

That such results are not explained by the fact that the hypertonic series was proportionately larger is clearly shown by the last three columns of the table. It will then be seen that out of the 53 cases heated by hypertonic saline only as many as 18 (or 33.9 per cent) died, while, of the/
the 23 members of the purely isotonic series, only the one death, which has just been alluded to, occurred, or only 4.3 per cent.

In the last line of the table, is shown for what percentage of the total deaths each of the different causes is accountable, and it is interesting to compare these percentages with the figures given by Rogers’ for the fatal cases in his wards from 1914 to 1917. He classifies the causes of death under 3 headings, namely, collapse, uraemia, and other causes.

Doing the same with the present series, a comparison can be made.

Table No. XXXV shows how much smaller is the percentage of deaths both from collapse and from uraemia.

**TABLE NO. XXXV.**

<table>
<thead>
<tr>
<th></th>
<th>COLLAPSE</th>
<th>URÄEMIA</th>
<th>OTHER CAUSES</th>
<th>DEATHS from all CAUSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases per cent.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROGERS</td>
<td>95</td>
<td>42</td>
<td>21</td>
<td>158</td>
</tr>
<tr>
<td>PRESENT SERIES.</td>
<td>8</td>
<td>7</td>
<td>17</td>
<td>32</td>
</tr>
</tbody>
</table>

Although, of course, the remainder of the percentage,
percentage must be made up by a proportionate increase in the percentage of deaths from "other causes" the instructive fact remains that the deaths from uraemia are of smaller proportion in the present series. This I attribute to a diminution of the toxaemia consequent on the method of treatment adopted, namely the large number of isotonic saline infusions administered.
THE MORTALITY AS A WHOLE.

In order to study the case mortality of the present series, it is only right that the subject should be discussed from the aspect of the mortality during the different years separately, owing to the unusual circumstances under which the great majority of the British cases in 1916 became infected. Naturally, the death rate among these already exhausted patients was comparatively high, and if one looks at the case mortality when such deaths are included, quite an erroneous estimate of the effects of isotonic saline treatment will be found.

Table No XXXVI shows how very greatly this high death rate in 1916 affects not only the case mortality amongst the British cases during the 3 years, namely 34.6 per cent as against the low figure of 12.0 per cent amongst the Indian patients, but also the total case mortality amongst British and Indian patients for the 3 years (25.6).

TABLE/
Let us therefore for a moment disregard the influence of these wholly unusual cases of 1916, and consider the mortality of the 1917 and 1918 cases by themselves.

### TABLE NO. XXXVII

<table>
<thead>
<tr>
<th>Year</th>
<th>BRITISH</th>
<th>INDIAN</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Dths.</td>
<td>C.M.</td>
</tr>
<tr>
<td>1917</td>
<td>1</td>
<td>1</td>
<td>100.0</td>
</tr>
<tr>
<td>1918</td>
<td>10</td>
<td>1</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>2</td>
<td>18.18</td>
</tr>
</tbody>
</table>

Analysing/
Analysing these, it is seen from Table No. XXXVII that the series which gives the lowest case mortality is that of the 10 British patients in 1918, namely the very low rate of 10 per cent. Now such a strikingly low death rate can not be attributed to a mild type of infection being present, for all the cases, with one exception, were severe, requiring to be infused on one or more occasions.

The solitary British case in 1917 died, so that the mortality of 100.0 per cent in the table is not so alarming as might appear at first sight.

Leaving this case out of account, it is interesting to note that no matter which batch of cases one chooses out of these 1917 and 1918 series, the case mortality is always lower than the latest results obtained by ROGERS', namely those under purely hypertonic treatment for the year 1919, when the deaths amongst 479 cases amounted to 22.6 per cent. Arranging these batches in order of diminishing case mortality.
TABLE XXXVIII.

<table>
<thead>
<tr>
<th>BATCH</th>
<th>CASE MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Total cases in 1917</td>
<td>18.18</td>
</tr>
<tr>
<td>2. Total British cases in 1917 and 1918</td>
<td>18.18</td>
</tr>
<tr>
<td>3. Indian cases in 1917</td>
<td>14.28</td>
</tr>
<tr>
<td>4. Total cases in 1917 &amp; 1918</td>
<td>13.11</td>
</tr>
<tr>
<td>5. Total Indian cases in 1917 and 1918</td>
<td>12.0</td>
</tr>
<tr>
<td>6. Indian cases in 1918</td>
<td>10.34</td>
</tr>
<tr>
<td>7. Total cases in 1918</td>
<td>10.25</td>
</tr>
<tr>
<td>8. British cases in 1918</td>
<td>10.0</td>
</tr>
</tbody>
</table>

The proportion of severe cases of any one of these batches was always sufficient to eliminate the factor of mildness of the cholera attack in reducing the case mortality, for I have just drawn attention to the fact that 90 per cent of even that series with the lowest case mortality, namely, the British cases in 1918 with a case mortality of 10 per cent, comprised 90 per cent of severely collapsed patients.

It must be admitted, of course, that one is dealing here with only 10 cases. On the other hand an equally gratifying result is obtained by combining with these ten British cases the 29 Indian cases for the same year, when the case mortality, notwithstanding/
notwithstanding the almost quadrupled number of cases, remains practically stationary, namely 10.25 per cent.

It is seen, then, how successful modern methods of treatment have proved in reducing the death role from a disease, which, only a few years ago, was appalling in its deadliness.
DURATION of the PATIENT'S STAY in HOSPITAL.

This subject is of interest, as its study throws some light on the duration of the infectious period of cholera.

During the year 1916, the practice of retaining cholera patients in hospital for a minimum period of 42 days was adhered to. At that time, the official instructions were —

"The following period of segregation has been fixed as the minimum required to be undergone in the case of patients convalescent after cholera, viz, the patient is to remain in hospital for a minimum period of 42 days (6 weeks) after the date on which is first passed a stool which is normal both in consistence and colour".

Such a period was fixed on account of the fact that previous observations had shown that in the great majority of cases, the "carrier" state in recovered cholera cases is not continued for anything like so long as 42 days. This prolongation of the segregation period, was, however, considered an insurance against the danger of discharging "convalescent carriers" of the vibrio.
The whole question of the "cholera carrier" is an extensive one, and can not be discussed here, but it is worth noting the following facts in regard to it, as recorded by different authorities.

"In the majority of recovered cholera patients the specific organisms disappear from the stools within a very few days."

(2) (ROGERS')

"Analysing the researches conducted by writers, . . . . it follows

(1) that the cholera vibrio may persist after the complete recovery of the patient in about 30 to 35 per cent of cases;

(2) that this persistence is not as a rule, very prolonged, but continues at most for thirty or forty days, rarely more . . . " (1)

(VINCENT and MURATET)

"Cholera vibrios often disappear from the faeces of patients in 3 or 4 days and rarely persist in them for longer than 20 days, but the healthy cholera carrier may go on passing vibrios for a period of two months, a gall bladder infection having become established. As a rule, however, the carrier only excretes vibrios for a week or ten days".

(10)

("Memoranda on Some Medical diseases in the Mediterranean War Area, with some Sanitary Notes" 1916).
From such information, we see that a segregation period of 42 days should have eliminated practically all risk of disseminating infection.

As it was, there was little chance of our being able to discharge the majority of the 1916 series under that period owing to the weak state in which they were left after their double infection (See page 24). I have calculated the average duration of these patients' stay in the Isolation Hospital and the figures are given in

TABLE NO. XXXIX

<table>
<thead>
<tr>
<th>YEAR</th>
<th>CASES</th>
<th>Average DURATION of stay in HOSPITAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1916</td>
<td>Recoveries 40</td>
<td>53 days.</td>
</tr>
<tr>
<td></td>
<td>Deaths 24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total cases 64</td>
<td></td>
</tr>
</tbody>
</table>

It is seen how, even had the bacteriological examination of their stools proved negative much earlier, the patients would, nevertheless, have had to remain in Hospital for almost 8 weeks, on the average.

In 1917, however, the conditions under which the medical services were able to carry out their duties, were vastly improved, and it was then possible.
possible for the Laboratories to cope with the extra work entailed by bacteriological examination of the stools of recovered cholera patients prior to their discharge. Accordingly, a new segregation period was decided on, namely, "The patient to remain in hospital until the stools have been bacteriologically negative on two successive occasions with a minimum interval of 3 days".

Such a concession allowed of the discharge of cholera cases much earlier than had previously obtained, as will be seen from

**TABLE NO. XL**

<table>
<thead>
<tr>
<th>YEAR</th>
<th>CASES</th>
<th>AVERAGE DURATION of stay in HOSPITAL.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1917 &amp; 1918</td>
<td>Recoveries 53</td>
<td>34.9 days.</td>
</tr>
<tr>
<td></td>
<td>Deaths 8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total cases 61</td>
<td></td>
</tr>
</tbody>
</table>

It is seen how such a procedure allowed the patients to go out of hospital in 5 weeks, on the average.

From this one is, of course, unable to know how much sooner these cases might have proved to be vibrio-free, for the stools were not sent for examination until convalescence was well advanced.
At the same time, the value of recording these figures lies in the fact that, in every instance, the patient was found to be vibrio-free on the first investigation undertaken to decide whether he might or might not be discharged. We may calculate that the first stool was sent for examination about a week prior to each patient's discharge, which, of course, points to the fact that these 53 patients were vibrio-free after, at most, 4 weeks, while the truth of the statement that the carrier state after recovery from cholera persists usually for only a few days is supported.
ULTIMATE DISTRIBUTION of the RECOVERED CASES.

Both from a scientific and from a military standpoint, it is worth recording how many of these patients who recovered from cholera were sufficiently fit to return to their units for duty, how many were somewhat debilitated and required further recuperation in convalescent depots, and how many were so exhausted that their transference to the Base en route for India was deemed advisable.

TABLE NO. XLI
shows the figures in this point.

<table>
<thead>
<tr>
<th>Year</th>
<th>British</th>
<th>Indian</th>
<th>To duty</th>
<th>To Convalescent Depot</th>
<th>To India</th>
</tr>
</thead>
<tbody>
<tr>
<td>1916</td>
<td>40</td>
<td>-</td>
<td>1</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>(British)</td>
<td>(Indian)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1917</td>
<td>-</td>
<td>18</td>
<td>8</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>(British)</td>
<td>(Indian)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1918</td>
<td>9</td>
<td>-</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>(British)</td>
<td>(Indian)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total Recoveries = 93
Per cent = 100% 29% 36.6% 34.4%
The table is interesting in showing

(a) What a large proportion of the 1916 cases had to be sent out of the country to recuperate after their trying illness. Only one man was able to return direct to duty.

(b) How few of the 1917 and 1918 cases were debilitated to the same extent.

(c) That the proportion of the cases distributed in the three stated directions do not differ very widely, namely, 29%, 36.6%, and 34.4%.

SUMMARY/
SUMMARY of CONCLUSIONS.

The conclusions, arrived at by a study of these cases, have already been discussed at length in the foregoing pages. The most important of them may be summarized in a very few words.

I. The marked variability of both the annual incidence and the annual case mortality was consequent on a serious outbreak of cholera amongst the patients in certain hospitals during the summer of the year 1916, an influence almost wholly absent in the two subsequent years.

II. As in the case of many other outbreaks of cholera, the source of infection amongst these hospital cases was milk; the milk had been procured locally from the natives (Arabs).

III. The seasonal incidence of the cases of this series was strictly comparable with that associated with the disease in other tropical countries, namely, its marked prevalence during the hottest months of the year.

IV. Anti-cholera inoculation did seem to provoke the elaboration of anti-bodies within persons so dealt with, and, thereby created a certain degree of immunity to the disease. Although, by the study of these cases, it cannot be proved that/
that the incidence of cholera was actually diminished by the practice of giving prophylactic cholera vaccine to the troops, it is shown that both the case mortality and the severity of a subsequent attack of the disease were decidedly diminished. Sir LEONARD ROGERS and other observers would seem to be doubtful that previous inoculation is at all effective in reducing the case mortality, though they are agreed that the disease is less prevalent amongst the inoculated.

V. Amongst those persons who had received anti-cholera inoculation, and who, in spite of such protection, contracted the disease, the severity of the attack was directly proportionate to the duration of the period which had elapsed since the last inoculation.

VI. With a fulminant disease, such as cholera, the gravity of the prognosis was proportionate to the interval between the onset of the actual cholera attack and the admission of the case to hospital.

VII. Although, in many cases, it was impossible to discover the source of the infection, there seems little doubt that the disease was frequently contracted by indulgence in articles of food or drink/
drink procured from the native Arabs in the bazaars. Above all milk, water, and uncooked fruits and vegetables (e.g. melons, dates and lettuce) seemed to be the chief offenders.

VIII. Owing to the patients' having run the risk of contracting the disease for an indefinite period prior to the onset of symptoms, no definite information as to the duration of the incubation period of cholera can be gathered from a study of these cases. Incubation, however, must occupy at most, only a few days, because of many contacts who underwent a 7 days' quarantine, none developed cholera after his release, while a few did develop the disease during their segregation. Moreover, the outbreak of cholera in a certain hospital owed its origin to an omission on the part of the cook to boil the cholera-infected milk on a particular day, certainly well within a week, before the first patient developed symptoms.

IX. The history of an initial stage of cholera (the stage of 'premonitory diarrhoea') was obtained on only a very few occasions. This is in entire accordance with the observations of other writers, for example, ROGERS, who states that "this/
"this stage is ... completely absent in the
"majority of cases seen in the tropics". In
other words, the onset of the disease in the
cases under review, was characterized by its
suddenness and its immediate severity.

X. Diarrhoea was the first symptom complained of,
being followed by the onset of vomiting in every
case, a sequence which is a characteristic fea­
ture of cholera asiatica, and not of other cho­
leraic infections - e.g. food poisoning, - in
which the sequence is reversed.

XI. "Cholera sicca" - i.e. cholera unattended by
diarrhoea, and often by vomiting in addition -
must indeed be a rare form of the disease. Not
an instance of it was provided by the cases
dealt with, though many of them were at the time
in hospital and enfeebled from other diseases,
the very circumstances with which, according to
text-books, this 'dry cholera' is generally asso­
ciated.

XII. Marked abdominal discomfort in the early stages
of a choleraic disease is more suggestive of
cholera nostras than of cholera asiatica.

XIII: The occurrence of blood in the stools of cholera
is/
is singularly rare - that is, in an amount sufficient to be recognised as such by the unaided eye. The presence of blood to such an extent should suggest that one may be dealing with a case, either of cholera nostras, or of true cholera complicated by dysentery.

XIV. The persistence of bile-tinged evacuations throughout a choleraic malady, favours a diagnosis of cholera nostras rather than of cholera asiatica.

XV. (a) The absence of vomiting appears to be a sign of good prognostic import.

(b) When vomiting was present, it always ceased before the diarrhoea did so.

XVI. Persistent hiccough was a sign of evil omen, as all four cases which exhibited it, proved fatal. This is contrary to ROGERS' experience.

XVII. It is undesirable to check the vomiting, as, I believe, the patient may thereby be denied an effective means of ridding the alimentary canal of cholera toxin, which would probably be absorbed on the induction of artificial reaction by treatment.

XVIII./
XVIII. Provided circumstances are such as to allow immediate intravenous infusion of saline solution to be given, it is unnecessary to attempt to relieve the pain of muscular cramps by other means. As the patient's agony ceases almost immediately after even a pint or two of saline has been administered, we have a further incentive not to delay such treatment a moment longer than can be avoided.

XIX. Speaking generally, all untoward features rapidly disappear after a timely and sufficiently copious intravenous infusion of normal saline solution (80 grains to the pint).

XX. Amongst other valuable information to be gained from a study of the internal (rectal) and the external (skin) temperatures, a marked difference between these two readings, or a coincident fall in both is an unfavourable sign with regard to prognosis.

XXI. As a general rule, in collapse associated with choleraic symptoms, the greater the disparity between the rectal and the skin temperatures, the greater the probability that the case is one of cholera asiatica rather than of cholera nostras.
XXII. In dealing with patients in a tropical country such as Mesopotamia, Oliguria - even when marked - must not be taken as an infallible indication of defective renal function, as even in health, only a few ounces of urine may be passed during the hotter part of the day. This is true even of the 'reaction stage' of cholera.

XXIII. In spite of quite a number of characteristic points of difference which often help the physician to distinguish cholera asiatica from cholera nostras, it would appear that many cases cannot with certainty be diagnosed as one or the other, except by a skilfully-conducted bacteriological examination of the dejecta.

XXIV. In both cholera asiatica and cholera nostras, diarrhoea persisted for a longer period than did vomiting. In cholera asiatica, both symptoms were of longer duration than in cholera nostras.

XXV. The absence of a single fatality amongst 63 cases of cholera nostras - many of them of marked severity - is very striking - and it would seem that the prognosis in a severely collapsed case of cholera nostras is decidedly more favourable than even a less collapsed case of cholera asiatica.
asiatica. This supports my belief that the element of toxaemia in cholera asiatica is as potent a cause of a fatal termination as is initial collapse from loss of fluid from the blood vessels and body tissues. Consequently, the treatment in cholera, while by all means directed to the restoration of fluid to the circulation, should not be such that the slightest avoidable increase of toxic absorption from the bowel is encouraged. By replenishing the circulation with intravenous infusions of an isotonic saline solution, one is doing all that is necessary. At the same time, the osmotic tension within the blood vessels of the intestinal wall is not so unduly increased as to induce endosmosis of a highly toxic fluid from the bowel into the general circulation, giving rise to manifestations of toxaemia - e.g. hyperpyrexia, and consecutive nephritis. Such highly undesirable complications were associated only with those cases which were treated by hypertonic saline infusions, an occurrence, for which, I believe, toxic absorption, which was excessively encouraged by the high tonicity of the infused solution, is accountable.
XXVI. The remote prognosis of cholera is favourable in that one attack of the disease does appear to give a certain degree of protection from further attacks, for a time at least. Since anticholera inoculation provokes an artificially acquired immunity, it is only to be expected that accidentally acquired immunity should follow the actual disease.

XXVII. The temptation to raise the skin temperature in the collapse stage of cholera - by hot bottles blankets and the like - must be sternly resisted, since possibly a hyperpyretic internal temperature may already exist. An intravenous infusion at appropriate temperature is the only justifiable means of attempting to restore the external and internal temperatures to the normal ratio.

XXVIII. The treatment of cholera by rectal injections of saline solution was highly unsatisfactory because, first, the constant desire of the patient to empty the lower bowel interfered greatly with the efficiency of the method, and second, I found that if diarrhoea was not so urgent as to interfere with this method of treatment a more rapid absorption of fluid, and that less toxic, was/
was simultaneously obtained by allowing the patient to drink ad libitum, while if the procedure was impracticable the collapse was usually such that more heroic measures to replace lost fluid were indicated - I refer to intravenous infusions.

XXIX. The method of treating cases of cholera by subcutaneous (intracellular) infusions of saline solution, while certainly beneficial, is not followed by the immediate and rapid improvement consequent upon intravenous administration. The method is almost useless in those pulseless (asphyxial) cases in which absorption from the subcutaneous cellular tissues has practically ceased. Subcutaneous infusions should not be looked upon as anything more than a method of giving a fillip to a moderately impoverished circulation.

XXX. Estimations of the specific gravity of the blood in cholera, though an aid in determining when intravenous infusion is necessary, did not seem to indicate correctly, how much saline solution should be given. From a consideration of first - the numerous factors, apart from cholera, which may influence the specific gravity of the blood, second, variability of the specific gravity/
gravity within fairly wide limits, even in apparent health, and, third, the fact that when given in greater quantity than an abnormal specific gravity estimation would indicate, the administration of saline produced much more marked and lasting improvement, I gradually ceased to follow the dictates of such estimations in deciding the quantity to be given in an individual case. For instance, if two cholera patients are admitted, both with blood specific gravity of 1.064, it is inconceivable that, as ROGERS' believes, both ought to receive 4 pints of fluid intravenously, when it is quite possible that these two patients in health possessed blood specific gravities as widely apart as 1.055 and 1.062. It is obvious that these two patients have lost very different proportions of their blood plasma, and therefore, it follows that different quantities should be given at the intravenous administration. A previous careful and thorough clinical examination of the patient, and the utmost attention to the rapidity with which improvement takes place during the infusion, are, I believe, the most trustworthy guides regarding the quantity of fluid to be given.
The actual operation of intravenous infusion in cases of cholera, though a simple procedure if certain points be attended to, may, on occasion, give rise to a little trouble both during and after the treatment, if these points be neglected.

Of the total infusions administered - i.e. both isotonic and hypertonic - a larger percentage of the isotonic than of the hypertonic infusions were associated with the recovery cases.

Slow administration of the intravenous infusion is of the greatest importance, as time should be allowed for fluid to pass back once more into the desiccated tissues and thus, both the general circulation and the tissues are sufficiently replenished at the end of the administration.

Attention to ROGERS' suggestions regarding the temperature of the infused fluid will be repaid by an almost complete avoidance of that most disastrous complication, hyperpyrexia, during the artificially induced reaction period.

Where the rectal temperature is unduly high (over 103°) in the algide stage, it is better to refrain from giving a copious intravenous infusion owing to the danger of inducing an uncontrollable/
uncontrollable hyperpyrexia. I believe it is wiser to give for the time being, just a sufficient quantity to restore the circulation, and repeat the administration after a short interval—say an hour or two.

xxxvi. When, by a timely intravenous infusion, the restoration of the circulation has been accomplished, great care is required to ensure that opportunity is provided for the patient's temperature to become adjusted once more to the normal. Therefore, once the initial rigor is passed, all hot water bottles, plentiful blankets, and a complete absence of movement of the surrounding air are distinctly harmful. Bodily heat loss ought to be encouraged at this stage, and not prevented, as is brought about by the agents mentioned.

XXXVII. About 18½ hours was the time which elapsed after an initial intravenous infusion was given, and before repetition of the treatment became indicated. This is instructive, as it demonstrates how successful the treatment is in restoring the circulation. It also proves how richly one is repaid for the little extra attention demanded by the universal adoption of intravenous treatment rather than futile rectal, or slow and painful subcutaneous methods.
XXXVIII. Nothing but barley water should be given to patients in the acute stage of cholera, and, indeed, even this should be given only in small quantities, so that the maximum oxidising action of the permanganates upon the cholera toxin may be obtained.

XXXIX. As universally recommended by ROGERS, both permanganates and subcutaneous injections of atropin sulphate (--- gr.) were administered to all of these patients, so that a comparison with 'controls' cannot be made. It would seem, however, that the beneficial effects claimed by him for these two therapeutic measures were fully realised.

XL. ROGERS' practice of giving intravenous infusions of sodium bicarbonate solution (1.8 per cent) in all cases which were threatened with uraemia, was adhered to, and seemed to influence for good. It is a striking fact, that such treatment was perforce resorted to more frequently among cases treated by hypertonic saline than among the isotonic series.

XLII. Complications and Sequelae were frequent and various. Many were of trivial import, such as parotitis, boils, and obstinate constipation, while/
while others were the cause of much anxiety, for instance, pneumonia. Others again actually brought about a fatal termination; among these were hyperpyrexia, uraemia, and that peculiar toxic state, 'cholera typhoid'.

As regards the case mortality, brought out in the various tables throughout this thesis, the salient features are these:

(a) The total case mortality for the three years was 25.6 per cent.

(b) The case mortality of the successive years shows a steady reduction. In 1916 (when as already explained, the majority of the cases were already hospital patients) the result was 37.5 per cent. In the following year, (1917) the case mortality was reduced to 18.18 per cent; while, in the final year, (1918) a reduction to the low figure of 10.25 per cent was attained.
To Sir Leonard ROGERS - more, by far than to anyone else, - the world at large should be immeasurably grateful for the years of devotion which he has bestowed on the devising of efficient methods of combating an otherwise disastrous disease. For it is he, who was most active in reviving intravenous saline infusions, and it is he who introduced the standard treatment by permanganates and atropin, WHILE HIS STUNNING RESEARCHES INTO THE ACIDOSIS of cholera provided for us a means of counteracting to a great extent the mortality from uraemia.

It may seem that I have laid myself open to the charge of inconsistency, when, in the face of this eulogy of one who is undoubtedly the greatest authority on the subject of cholera, I depart from the narrow path along which he would direct those who would strive to be so successful as he in treating the disease. But I trust I shall not be so accused, when the reader recollects that the treatment which I adopted for my cases was based very largely on the teaching of ROGERS, and that my preference for an isotonic solution for intravenous administration is founded on the knowledge that such a/
a solution had not been experimented with previously. I felt, and still am persuaded, that because the trial given to a hypotonic, - and therefore an unphysiological - fluid, did not produce as successful results as was anticipated, the desire to go to the other extreme by employing an equally unphysiological hypertonic fluid might be unwarranted, unless, at the same time, one had been previously convinced that the physiological had been found wanting.

So far as I know, no other series of cases of the same proportions has received exactly similar treatment. In view of the disheartening conditions under which one laboured in attending to these patients, the adverse circumstances under which many of the patients themselves contracted their infection and, notwithstanding, the encouraging results I have been enabled to record, I trust that my venturing to depart from convention to the extent to which I have done will not be devoid of an influence for good, and that, at least, attention has been sufficiently drawn to methods which may possibly still further 'obviate the tendency to death'.
REFERENCES


2. ROGERS: "Bowel Diseases in the Tropics" 1931. Pp. 54, 143, 144, 145, 72, 137.


10. "MEMORANDA on some Medical Diseases in the Mediterranean War Area". (Reprinted with Amendments, 1917). P.


12. STARLING: "Principles of Human Physiology" 1912.


