

PARENTERIC FEVERS IN EGYPT.

By Z. KHALED,

Bacteriologist, Hygienic Institute, Cairo.

(With 3 Charts.)

INTRODUCTION.

IT is the common experience of all workers in the Tropics to have to record negative (typhoid-paratyphoid) agglutination results in cases that are clinically of the Enterica group. The statistics of different laboratories show that the figures for positive findings centre somewhere around 15 per cent. and usually do not exceed 20 per cent. of the total. During the Great War there were many cases amongst the British troops on the Western Front that could not be bacteriologically classed as typhoid or paratyphoid, though they were clinically enterica-suspects; the comparative incidence of such cases in the eastern war zone was even much higher. And yet these negative cases, though varying greatly in virulence and intensity of symptoms, give the same clinical picture as the typhoid-paratyphoid fevers, *i.e.* continued fever with slow pulse in relation to temperature, abdominal symptoms due to involvement of the small intestines, dulling of the nervous system, etc.; in the same way they are not influenced by climate, are widespread, and occur sporadically or in epidemic form. There seems no doubt that in their mode of infection, in pathology and in mechanism there is no difference, in kind, between the enterica and these enteric-like cases; and that the only difference lies in the causal organism. It was in an attempt to elucidate the aetiological germs in these cases that the present investigation was undertaken.

CLINICAL NOTES.

Case I. Early in October, 1921, the serum and stools of a child were sent to me for enterica examination. Though the fever was clinically typhoid, yet its duration was 32 days, and the spleen was not enlarged. The serum was negative for typhoid and paratyphoid agglutination. From the stools an organism was isolated which agreed culturally and biochemically with *Bacillus asiaticus* (Castellani, 1912). This organism was agglutinated by the patient's serum in a dilution of 1 : 800, thus raising the possibility of its being the offending germ. The fever continued for nine weeks, broncho-pneumonia set in and the child died.

Case II. Two weeks later the following case came under my notice:

A. M., boy ten years old, with a rather delicate constitution, admitted to hospital with simple fracture of both bones of right fore-arm. Temperature

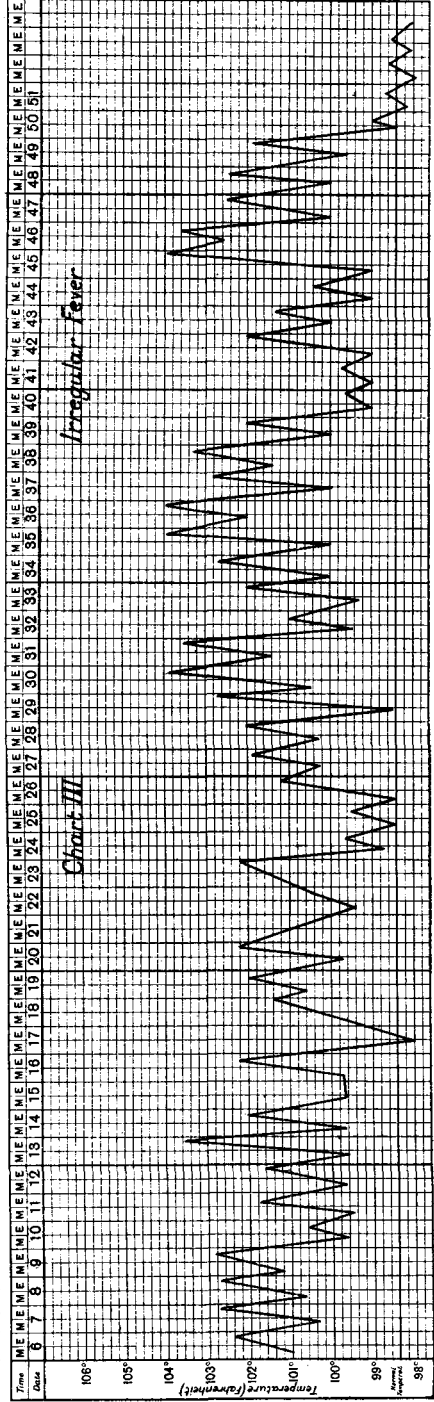
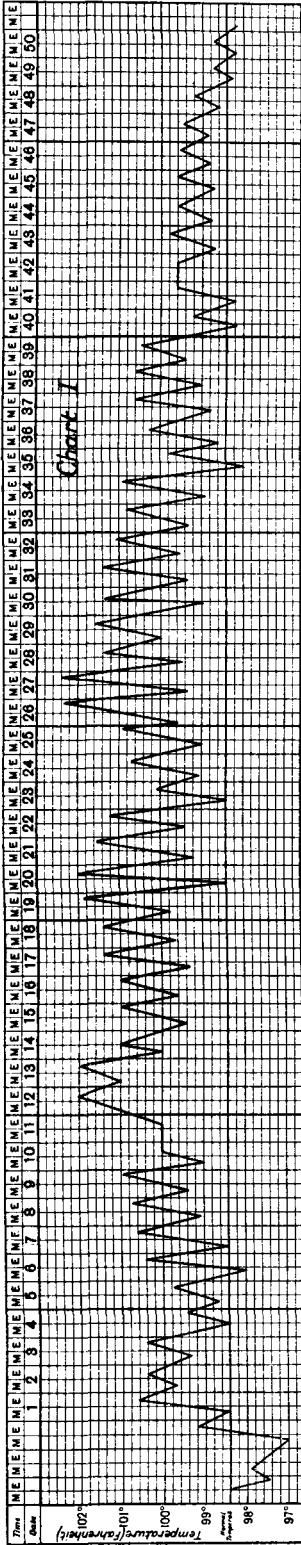


Chart I. Name A.M. Age 10. Disease, Asiaticus Parenteric Fever. Admitted 10. x. 21.
 Chart III. " M.Z. " 30. " " " 12. ix. 22.

rose on third day and ran an irregular course. No rash appeared; slight pain in right iliac fossa. Tympanites and borborygmi marked, but spleen and liver were not enlarged. No meningeal symptoms present. Stools normal, rather more constipated than loose; urine normal. Fever continued six weeks before any drop began, and then came to normal in a week's time (Chart I). Patient, though slightly delirious in the later stages of the disease, did not develop any other untoward symptoms or complications.

Bacteriological Examination. On the ninth day of the fever, there being nothing surgical to explain the rise of temperature, the blood was sent for culture and for enterica agglutination. The latter was absolutely negative; from the blood *B. asiaticus mobilis* (Castellani) was isolated in pure cultures. The patient's serum agglutinated this organism strongly (1 : 400).

At the end of the second week of fever the stools were examined and the same organism isolated. At that time the titre of the serum towards *B. asiaticus* rose to 1 : 800 and attained 1 : 1600 at the end of the third week of the disease.

It was then thought desirable to test the incidence of *B. asiaticus* as a causal agent in producing fever. All sera sent to this Institute for Widal examination were tested against an emulsion of the organism isolated from Case II (*B. asiaticus*, strain Shawki) and those that gave a positive result were examined again, together with the blood and stools, for further data. The results of these findings will be mentioned later.

The following two cases are also illustrative:

Case III. D. H., a girl 14 years old, suffering from fever of 35 days' duration; the temperature sometimes reaching 40° C. Abdomen distended, spleen not enlarged; stools solid, enemata often necessary.

The serum was negative for typhoid, paratyphoid, melitensis and paramelitensis infection, but positive for *B. asiaticus*. From the stools *B. asiaticus* was grown. The doctor in charge wished to try autogenous vaccine therapy. Doses of 15, 30, 60 and 120 millions were given with three days' interval between injections. The first dose was without effect, the second was followed by a drop of the temperature from 39.8° C. (in the evening) to 38° C.; after the third dose it came down to 36.8° C. and it remained there ever afterwards.

Case IV. A. H., boy 16 years old, brother of former case; began to have fever two days after his sister took her third dose of vaccine. His prodromata and initial symptoms were described by his mother as being the same as his sister's. The blood showed no malarial parasites or relapsing fever spirochaetes. Consequently a blood culture was made on the fifth day of the fever, giving a pure growth of *B. asiaticus*. On the eighth day his serum agglutinated this organism in a dilution of 1 : 400. On that day a dose of vaccine (30 millions) was given. Three more doses of 60, 120 and 150 millions were administered. The first three injections were followed by a drop in the temperature to normal (see Chart II). There is no doubt that the disease was contracted, in this case, through infection from the girl. The incubation period, however, could not be determined owing to obvious reasons.

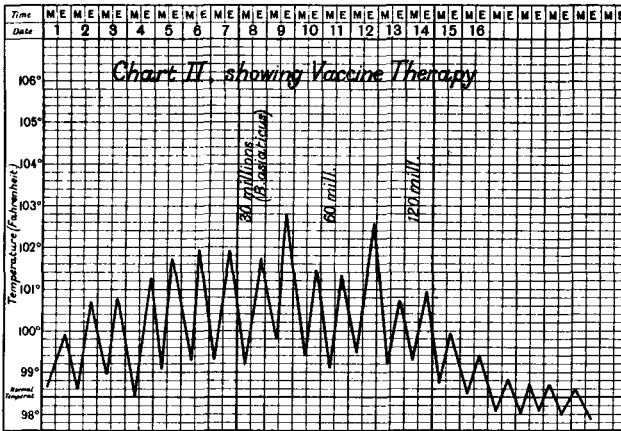


Chart II. Name A.H. Age 16. Disease, Asiaticus Parenteric Fever. Admitted 17. v. 22.

SYMPTOMATOLOGY OF ASIATICUS PARENTERIC FEVER.

Summing up my colleagues' as well as my own experience of the clinical aspects of the fever, the picture is as follows:

The fever begins with a feeling of malaise, head-ache and a rise of half to one degree in the evening. The patient can, during the first week, attend to his work. The tongue becomes furred but the "fur" never becomes thick in an uncomplicated case. There is some pain in the abdomen, but tympanites is a very common feature. The spleen is frequently not enlarged. The stools are usually solid, though in very few cases dysenteric symptoms with blood and mucus marked the onset of the disease.

During the first week of the fever the temperature ranges between 37.5°C . and 39°C . in the evening and is almost normal in the morning. From the beginning of the second week it runs a remittent course, though some cases are intermittent, the temperature reaching 40°C . in the evening and 38.5° – 39.5°C . in the morning. Sometimes the course is a very irregular one (see Chart III). A marked feature about this fever is that in spite of the high range of the temperature the patient usually does not seem much the worse for it. Notwithstanding the emaciation resulting from prolonged starvation, the patient can sit up and talk while the thermometer is running high. There is lack of toxæmia; as a matter of fact the "typhoid condition" is rarely, if ever, met with.

The pulse is small but the heart stands the attack fairly well and requires little in the way of cardiac stimulants. There is a slight dullness of the senses after the third week but no marked delirium. The duration of the fever is usually more than three weeks; five to nine weeks is the common period. In two cases, however, it was 15 and 19 days respectively.

Diagnosis. Distension of abdomen (tympanites), constipation, absence of enlarged spleen, prolonged pyrexia and a good general condition of the patient

in spite of the high temperature are points suggestive of Asiaticus Parenteric. The ultimate diagnosis, however, rests with the bacteriologist.

Prognosis. The prognosis is generally favourable. Complications are rare. The rate of mortality was not worked out because many of the cases diagnosed were not traced. Those that have been traced (60 cases) showed 4 deaths, a rate of 6.6 per cent., but it may be a little higher than this.

Pathology and Morbid Anatomy. The examination of a blood film does not show any particular evidence in favour of Parenteric diagnosis apart from slight leucopenia of the lymphoid type. The following is an example:

| | |
|------------------------|----------------|
| Total leucocytic count | 6000 per c.mm. |
| Polymorphonuclears | 51 per cent. |
| Lymphocytes ... | 43 ,, |
| Large mononuclears... | 4 ,, |
| Eosinophils | nil |

The organism can be isolated from the blood during the first 10 days of the fever. Agglutinins appear at the end of the first week and show a rising titre, with some stationary phases, till the end of the fever, after which they begin to fall. Thus a case showing a titre of 1 : 3200 on the fortieth day of the illness gave only 1 : 200 agglutination after 4 months of convalescence. The organism can be isolated from the stools and in some cases from the urine.

Unfortunately no post-mortem examinations were made on any of the cases that ended fatally.

Treatment. Only a word need be said about treatment by autogenous vaccines. The prolonged fever and the generally satisfactory state of the patient are points that indicate a trial of vaccine therapy. In the few cases in which it has been tried, the results were very encouraging. Not only did a fall in temperature follow the injections but they seemed to cut short the fever as well. I do not mention Case III as an example, because in this case the temperature would probably, in any condition, have come down. But Case IV is illustrative. Instead of the temperature keeping high for 40 to 50 days, it came down to normal in a fortnight. The method, I believe, is well worth trial.

BACTERIOLOGICAL METHODS.

PROCEDURE.

I. *Blood Culture.* 5 to 10 c.c. of blood drawn aseptically from the arm vein are immediately placed in 50-100 c.c. of trypsinised broth (Douglas, 1914) and incubated for 24 hours, at the end of which loopfuls are spread on Endo-agar plates for identification.

II. *Stools.* Being usually solid, a thick emulsion is made in a small volume of broth. Two loopfuls are spread, in succession, on four Endo-plates by means of a bent glass spreader. After 24 hours' incubation suspicious colonies are picked up and each inoculated into 2 c.c. of sugar-free peptone water. After

4 hours' incubation there is usually sufficient turbidity (growth) to supply a sufficient inoculum in a loopful for Durham tubes charged with lactose, saccharose, dulcitate, mannite and glucose—the five sugars recommended by McConkey as most suitable for bacterial differentiation. This method economises at least 24 hours—a valuable consideration when many cases have to be dealt with at the same time. If, however, there is any suspicion about the purity of the individual colonies on the Endo-plate, these (the colonies) must be plated again and pure colonies picked up from the second series and treated as above.

Bouillon tubes and litmus milk are also sown at the same time as the Durham tubes.

III. *Indol Test.* Carried out according to Ehrlich's method with paramethylaminobenzaldehyde after extraction with ether.

IV. *Motility.* Tested in the ordinary way in hanging-drop preparation.

V. *Agglutination Test.* Carried out in small tubes 5 cm. × 5 mm. The dilutions are made in series 1 : 50 up to 1 : 6400. The tubes are incubated at 37° C. for two hours and then put at room temperature for 18 hours, after which they are read. The positive tubes usually show sedimentation.

VI. *Absorption Test.* The same technique used as in a previous communication¹.

DESCRIPTION OF *BACILLUS ASIATICUS*.

A. *Morphology.* A Gram-negative motile delicate organism, 4 microns by 1 micron thick; does not show polar staining with carbol-thionin or old Loeffler's methylene blue but is on the contrary quite a homogeneous rod.

B. *Biological Characters.* Grows best aerobically at 37° C., but can grow at 25° and at 40° C. though growth is scanty. The growth is also meagre if grown anaerobically.

C. *Cultural Characters.* Grows luxuriantly and rapidly on ordinary media and best on tryptic media. On broth it produces uniform turbidity usually without a pellicle. On agar it forms raised, round, whitish colonies. Gelatine is not liquefied but a white growth is produced mainly along the track of the stab. On fuchsin-sulphite agar (Endo's media) the colonies simulate those of paratyphoid or dysentery, though in some cases they are much bigger than either. Litmus milk is slightly changed on the acid side without any clotting. No fluorescence or pigment is produced in any of the media.

D. *Indol and Carbinol Production.* Most of the strains are indol producers, though, judging by the colorimetric test, the amount of indol produced cannot be great. The carbinol (Voges-Proskauer) test is always negative.

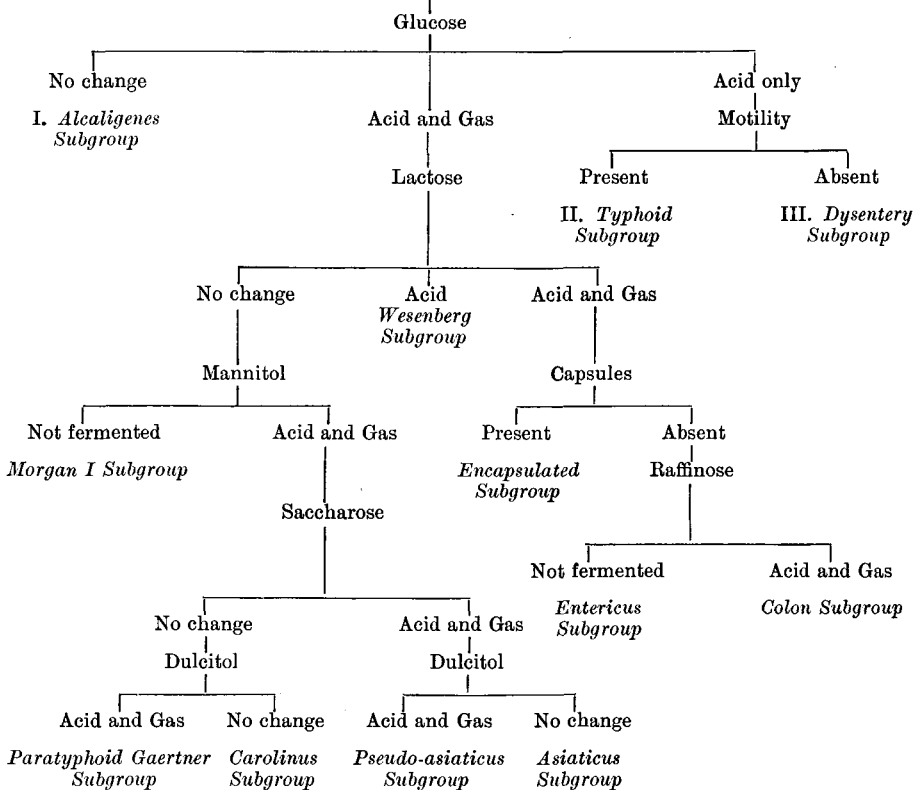
E. *Fermentation of Carbohydrates.* There is fermentation of saccharose, mannite, and glucose, with production of acid and gas. The full production of gas may take 48 to 72 hours or even longer. *There is no change whatever in lactose or dulcitate.*

¹ *Journ. of Hygiene*, Dec. 1921. "Comparative study of bovine abortion and undulant fever."

Summing up, *B. asiaticus* is an organism that grows well on ordinary laboratory media, does not form endo-spores, is Gram-negative, uniform, non-capsulated, grows aerobically and sometimes anaerobically and, in growing, does not produce fluorescence or pigment. This description places it in the typhoid-colon group.

Further, from consideration of its biochemical character it is seen that *B. asiaticus* belongs to the paratyphoid-Gaertner subgroup—a fact which is shown serologically (see Tables I and II).

Table I.
Typhoid Colon Group



F. *Pathogenicity.* Tested on a series of guinea-pigs it was found that 1 c.cm. of an 18-hours' broth culture of a recently isolated strain injected intra-peritoneally kills a guinea-pig in 18 to 24 hours. Compared with a recently-isolated typhoid strain, it was found to be of about the same virulence to guinea-pigs, though, in human cases, the fever it produces is milder than typhoid. If inoculated in smaller quantities or injected subcutaneously, the guinea-pig apparently gets over it in 5-7 days and is quite happy again.

G. *Serological Tests.* Specific serum was prepared against the standard strain, *B. asiaticus*, strain "Shawki" (isolated from Case II), by immunising

a rabbit with four doses of 500 millions, 1000, 2000, and 4000 millions respectively at five days' intervals. The first two doses are from cultures killed by heating at 60° C. for half an hour, the other two are living organisms. The serum, tested a week after the last injection, agglutinated the homologous strain fully in a dilution of 1 : 6400 and slightly in 1 : 12,800. It kept its powers remarkably well in ice, and, tested 9 months after its preparation, showed only a slight fall (1 : 3200 full agglutination).

1. All strains that reacted culturally and biochemically like *B. asiaticus* were tested against this specific serum. The result as mentioned in Table III shows a remarkable response of the different strains to the homologous serum. Some were agglutinated to full titre, others to titres ranging between 200 and 1600, and only three were not agglutinated at all.

2. Other intestinal organisms were tested against this serum. The results were as follows:

Table II.

| Organism | Titre of agglutination × anti-asiaticus serum |
|-----------------------------|--|
| <i>B. typhosus</i> | 1 : 10 |
| <i>B. dysenteriae</i> Shiga | nil |
| <i>B.</i> " Flex. | nil |
| <i>B. paratyphosus</i> A | 1 : 50 |
| <i>B.</i> " B | 1 : 20 |
| <i>B.</i> " C | nil |
| <i>B. Gaertner</i> | 1 : 20 |
| <i>B. Morgan</i> No. 1 | 1 : 10 |
| <i>B. proteus</i> "X 19" | nil |

Absorption of anti-asiaticus serum with the above organisms did not affect the amount of agglutinins for the homologous strains, thus showing that the above agglutination is only a group effect.

3. The organism was repeatedly tested against antityphoid, paratyphoid A, paratyphoid B, dysentery and Gaertner sera, and, though these sera agglutinated the corresponding laboratory strains to a very high titre, *B. asiaticus* was agglutinated only by antiparatyphoid B serum (1 : 50) and anti-Gaertner serum (1 : 20) and this again is only group-agglutination as shown by absorption.

4. The organism was also tested against normal human and rabbit's serum. For this purpose some of the sera sent for Wassermann test as well as the sera of persons perfectly normal at the time of examination and for some time previously, were tested. 150 specimens were examined in all, and of these 3 agglutinated the organism, one in a dilution of 1 : 800, another in 1 : 400 and the third in 1 : 100. *B. asiaticus* is not agglutinated by normal rabbit's serum.

SCOPE OF THE INVESTIGATION.

As mentioned above, as soon as the incidence of asiaticus parenteric fever was suspected to be a fairly common occurrence, all sera sent for enterica examination were examined against *B. asiaticus* as well. The Hygienic Institute constitutes the central examination station for all parts of Egypt except

Alexandria, and this fact gives the results obtained a special significance. It was not possible, however, to examine all sera sent to the laboratories, mainly because of insufficiency of quantity. Those sera that agglutinated *B. asiaticus* to a high titre (1 : 400 or above) were tested again after 4 to 7 days to see if there was evidence of rising titre and a specimen of stools was examined as well in an attempt to isolate the offending organism.

The stipulation of a high agglutinating titre for a positive conclusion is liable to under-estimate the number of actual parenteric cases since a serum taken at the end of the first week of the disease and for a few days afterwards may only agglutinate the causal organism in low dilutions (1 : 50 or 1 : 100). But it was believed that a reliable index of positivity could only be arrived at in this way. Moreover *B. asiaticus* isolated from the stools of a febrile case, was considered the cause of the fever, only if the patient's serum agglutinated the standard strain in a high dilution.

As the investigation proceeded, some physicians in Cairo became willing to supply blood for culture from enteric-like cases in the early days of the disease. Twenty specimens were examined in this way; two grew *B. typhosus*; two, *B. paratyphosus* B; three, *B. asiaticus*; one, *B. faecalis alcaligenes*, the rest were sterile.

The investigation comprises 1078 cases, most of whose sera were examined twice, apart from one or two stool examinations; some were having haemoculture as well. The cases from which the organism was isolated from the stools alone and where no blood or sera were examined, are not included in the series. *The presence of specific agglutinins in high dilution is considered fundamental for a positive result.*

The number of positive cases in this series of 1078, is 112, *i.e.* about 10 per cent. of the cases suspected to be enterica, prove to be asiaticus parenteric.

Table III.

| Date | Serial number | Sex | District | Titre of patient's serum | Titre of agglutination of organism by specific serum | |
|-----------|---------------|------|--------------|--------------------------|--|---------|
| Feb. 1922 | 1455 | F. | Cairo | 1 : 400 | Not isolated | |
| | 1734 | M. | Abu Hommos | 1 : 800 | 1 : 400 | |
| | 1794 | M. | Nag Hamadi | 1 : 400 | 1 : 400 | |
| | 1795 | M. | " " | 1 : 3200 | 1 : 800 | |
| | 1799 | M. | " " | 1 : 400 | 1 : 400 | |
| | 1940 | M. | Deshna | 1 : 800 | Not isolated | |
| | 1963 | F. | Cairo | 1 : 800 | 1 : 400 | |
| | 2184 | M. | Abu Hommos | 1 : 800 | Not isolated | |
| | 2186 | F. | " " | 1 : 400 | " " | |
| | 2187 | F. | " " | 1 : 800 | " " | |
| | 2538 | M. | Cairo | 1 : 400 | 1 : 400 | |
| | March, 1922 | 2560 | M. | Fashn | 1 : 1600 | 1 : 800 |
| | | 2635 | M. | Deshna | 1 : 400 | 1 : 400 |
| 2684 | | M. | Cairo | 1 : 1600 | 1 : 1600 | |
| 2705 | | M. | Faraskour | 1 : 800 | 1 : 800 | |
| 2753 | | M. | Tala | 1 : 3200 | 1 : 3200 | |
| 2778 | | F. | Deshna | 1 : 400 | 1 : 800 | |
| 2780 | | M. | Nag Hamadi | 1 : 1600 | 1 : 800 | |
| 2783 | | M. | Kous | 1 : 800 | 1 : 400 | |
| 2803 | | M. | Shibinel Kom | 1 : 400 | 1 : 800 | |

Table III—*continued*.

| Date | Serial number | Sex | District | Titre of patient's serum | Titre of agglutination of organism by specific serum | |
|---------------|---------------|------|----------------|--------------------------|--|--------------|
| March, 1922 | 2804 | M. | Zagazig | 1: 800 | Not isolated | |
| | 2862 | M. | Cairo | 1: 3200 | 1: 1600 | |
| | 2864 | M. | " | 1: 400 | 1: 1600 | |
| | 2953 | M. | " | 1: 1600 | 1: 400 | |
| | 2976 | M. | " | 1: 3200 | 1: 400 | |
| | 2995 | M. | Nag Hamadi | 1: 1600 | 1: 800 | |
| | 3028 | F. | Cairo | 1: 800 | 1: 1600 | |
| | 3126 | M. | Deshna | 1: 1600 | 1: 3200 | |
| | 3140 | M. | Nag Hamadi | 1: 1600 | 1: 3200 | |
| | 3182 | M. | Cairo | 1: 1600 | 1: 200 | |
| | 3195 | M. | Abu Hommos | 1: 400 | Not isolated | |
| | 3368 | F. | Cairo | 1: 800 | 1: 400 | |
| | 3378 | M. | Mit Gamr | 1: 800 | nil | |
| | 3387 | F. | Deshna | 1: 400 | 1: 200 | |
| | 3548 | F. | Cairo | 1: 400 | 1: 200 | |
| | 3647 | M. | Fashn | 1: 800 | 1: 200 | |
| | 3721 | M. | Tura | 1: 800 | 1: 1600 | |
| | April, 1922 | 3726 | M. | Cairo | 1: 800 | 1: 3200 |
| | | 3774 | M. | Fayoum | 1: 800 | 1: 400 |
| | | 3810 | M. | Shubrakheet | 1: 800 | Not isolated |
| 3907 | | M. | Tala | 1: 1600 | " " | |
| 3951 | | M. | Luxor | 1: 400 | " " | |
| 3979 | | M. | Abu Hommos | 1: 3200 | 1: 3200 | |
| 4012 | | M. | " " | 1: 800 | 1: 6400 | |
| 4056 | | M. | Shubrakheet | 1: 800 | 1: 400 | |
| 4080 | | M. | Nag Hamadi | 1: 3200 | 1: 800 | |
| 4115 | | F. | Cairo | 1: 400 | nil | |
| 4711 | | M. | " | 1: 400 | 1: 200 | |
| May, 1922 | | 5178 | M. | Nag Hamadi | 1: 3200 | 1: 200 |
| | 5187 | F. | " " | 1: 1600 | 1: 400 | |
| | 5273 | M. | Kafr el Sheikh | 1: 400 | 1: 6400 | |
| | 5893 | M. | Nag Hamadi | 1: 400 | 1: 200 | |
| | 5987 | M. | " " | 1: 800 | Not isolated | |
| | 6043 | M. | Assiut | 1: 400 | " " | |
| | 6132 | M. | Port Said | 1: 400 | " " | |
| | 6170 | M. | Cairo | 1: 400 | 1: 200 | |
| | 6403 | F. | " | 1: 800 | 1: 400 | |
| | 6623 | F. | Mansura | 1: 800 | 1: 1600 | |
| | June, 1922 | 6815 | M. | Cairo | 1: 400 | 1: 800 |
| | | 6839 | M. | Deshna | 1: 800 | 1: 400 |
| 6854 | | M. | Mit Gamr | 1: 1600 | 1: 800 | |
| 7300 | | M. | Luxor | 1: 800 | 1: 200 | |
| 7335 | | M. | Benha | 1: 400 | 1: 400 | |
| 7423 | | M. | Nag Hamadi | 1: 1600 | 1: 400 | |
| 7430 | | M. | Cairo | 1: 1600 | 1: 400 | |
| 7497 | | M. | Nag Hamadi | 1: 3200 | 1: 1600 | |
| 7518 | | M. | Bagour | 1: 800 | 1: 200 | |
| 7636 | | F. | Barrage | 1: 400 | nil | |
| 7666 | | M. | Teh Baroud | 1: 400 | Not isolated | |
| 7711 | | M. | Girga | 1: 1600 | " " | |
| 7794 | | M. | Cairo | 1: 800 | 1: 200 | |
| July, 1922 | | 9208 | M. | " | 1: 800 | 1: 800 |
| | | 9209 | M. | " | 1: 1600 | 1: 800 |
| | 9273 | M. | " | 1: 1600 | 1: 1600 | |
| | 9282 | F. | Assiut | 1: 800 | 1: 200 | |
| August, 1922 | 9470 | M. | Cairo | 1: 400 | Not isolated | |
| | 9536 | F. | " | 1: 1600 | 1: 800 | |
| | 9575 | M. | " | 1: 800 | Not isolated | |
| October, 1922 | 11233 | M. | " | 1: 1600 | " " | |
| | 11234 | M. | " | 1: 400 | " " | |

Explanation of Table III.

Table III contains the asiaticus parenteric findings amongst some of the enterica-suspect cases that have been sent to these Laboratories during the period from February to mid-August and from mid-August to the end of October, 1922. It was during this period that most of the work was carried out.

(1) The series comprises 912 enterica-suspect cases and 1130 different examinations.

(2) Of these 912 cases:

| | | | |
|----------------------|-----|-----|---------------------------------------|
| Typhoid | ... | ... | 74 |
| Paratyphoid A | ... | ... | 22 |
| Paratyphoid B | ... | ... | 13 |
| Total Enterica | ... | ... | 109 cases, <i>i.e.</i> 11·7 per cent. |
| Asiaticus parenteric | | | 92, <i>i.e.</i> 10 per cent. |

The rest (711 cases) are negative for either.

(3) The positive cases are distributed all over the country, upper Egypt contributing 35; lower Egypt, 20; and Cairo (including Abbassia Fever Hospital), 27 cases.

(4) It was not always possible to get exact data regarding the age of patients but there have been positive cases in children in their second year of life and in persons 50 years old.

(5) There were 75 males and 17 females, but this does not mean that more males get infected than females. It is due, I believe, to the fact that women decline admission to hospitals and cordons.

(6) The seasonal incidence was also not easy to determine, but judging from the incidence in March-June, both enterica and parenteric seem to follow the same curve.

DISCUSSION.

The classification of febrile diseases in the tropics has always been a most baffling problem. Apart from obscure fevers due to tubercular processes, visceral syphilis, amoebiasis, helminthiasis, urinary infection, chronic malaria, etc., there are enteric-like cases, which, despite repeated and careful bacteriological investigation, fail to show indication of any member of the typhoid-paratyphoid group as being the offending organism.

There has been a conviction for years that these cases are due to bacillaemia with "intermediate organisms," but no serious attempt was made to identify or classify these organisms except of late years. The literature is, therefore, very meagre, though the number of such cases is large and the distribution widespread. Castellani, as far back as 1905, described *B. columbensis* and others, but the first thorough description is that of Archibald (1911), who recorded four cases in the Sudan due to bacilli of the cloacae-group. The cases were successfully treated with autogenous vaccines. Taylor (1914) described four cases of "anomalous fever," enteric-like with constipation and tympanites and

negative Widal reaction. Gauducheau (1915) described a case in Indo-China where blood culture showed a Gram-negative motile bacillus that did not liquefy gelatine or kill rabbits or monkeys. Spaar (1915) described a case where *B. columbensis* was isolated from the stools and was agglutinated by patient's serum (1 : 80), though the latter did not agglutinate *B. typhosus* or *B. paratyphosus* A or B.

Wanhill in Mhoa (1915) during three years of laboratory work isolated "intermediate organisms" from the blood of enteric-like cases. Sixteen such organisms are described and of these, six conform biologically, culturally and biochemically with *B. asiaticus*, though the author did not give them a name. Chalmers and McDonald (1916), in a masterly paper, described their experience of enteric-like cases in the Sudan, where they isolated *B. khartoumensis*.

Shearman and Moorhead (1917), Hirst (1917) and Thomson and Hirst (1918) described bacillaemia due to *B. faecalis alcaligenes*. They substantiated the views first put forward by Petruschky (1889 and 1907) that this organism is capable of entering the blood-stream and causing fever of a mild type. Their work was carried out for the most part on British soldiers invalided to Egypt from the eastern war zone (Salonica, Mesopotamia and Egypt).

Archibald (1919), in investigating enterica in the Sudan, described six cases due to bacilli of the Wesenberg type and to a bacillus which he designated *B. vivax*. Lastly, Castellani (1914) described cases due to *B. asiaticus*, and at another date (1917), in describing the tropical diseases met with in the Balcanic and Adriatic war zones, classified these enterica and parenterica cases into groups according to the different offending so-called "intermediate organisms."

The present investigation is, however, believed to be the first serious attempt, on a large scale, to tackle the problem of the incidence and classification of parenteric fevers in Egypt. It also substantiates *B. asiaticus* as the causal organism of parenteric fever. It has been isolated from some of the cases by haemo-culture, from practically all the cases by stool-culture, and the serum of the patients agglutinated, to a high titre, this organism.

Regarding the mode of infection in these cases, it is thought to be the same as the typhoid, *i.e.* by ingestion of food or drink contaminated with excreta of a patient or a carrier. There is, however, another view, namely that *B. asiaticus* (and others) may exist in the intestines as harmless germs and that, if for some reason or other the intestinal mucosa is damaged, they gain access through fissures or ulcers to the blood stream causing bacillaemia and fever. In order to get an idea about the carrier problem in asiaticus parenteric, fifty stools obtained from persons apparently quite healthy were examined with a positive result in one only. In this connection attention may be called to the small number (3 out of 150) of normal persons' sera agglutinating this organism.

B. asiaticus, apparently, cannot play the rôle of a perfectly innocuous guest. Thus, examining 20 stools of cases of chronic intestinal trouble (colitis,

diarrhoea, etc.), two showed *B. asiaticus* as the only abnormal germ; one, *B. asiaticus* with *B. Morgan No. 1*; three, *B. Morgan No. 1*; four, *B. dysenteriae* Shiga; five, *B. dysenteriae* Flexner; and five, cysts of *Entamoeba histolytica*.

The next question to be considered is whether or not there are parenteric cases in Egypt due to organisms other than *B. asiaticus*. The answer is unhesitatingly in the affirmative. Referring to the statistics mentioned above, it is seen that in every 100 clinically typhoid cases, 11·7 proved to be enterica, 10 asiaticus parenterica by bacteriological examination, while the rest (78) were negative for either. Making allowance for errors in clinical diagnosis and in bacteriological technique, there will remain at least 50 to 60 per cent. of the cases which are enterica-like and which I have no doubt belong to the parenterica group due to some one or other organism that has either been described or awaits description and nomenclature. Three of these organisms must be mentioned in this connection, viz. *B. pseudo-asiaticus*, *B. faecalis alcaligenes* and *B. carolinus*. The first and second were isolated by haemo-culture each from two cases, whilst the third, though isolated from the stools alone, was the only organism agglutinated by the patient's serum.

It is intended to investigate, in the near future, the incidence of these germs as causal agents of disease on similar lines to those of the present work. The number of the causal parenterica germs may prove to be large and the responsibilities and difficulties of the bacteriologist will correspondingly increase. The serological test will become a lengthy procedure. The cooperation of the physician is earnestly needed and the adoption of early haemo-culture as the diagnostic method *par excellence* must be pressed.

It is only by thorough, laborious and extensive bacteriological research that the parenteric fevers can be successfully classified, and, by such grouping, the so-called "Unclassified Fevers of the Tropics" would diminish to a minimum.

SUMMARY.

(1) Bacteriological examination of 1078 enterica-suspect cases showed that 112 (*i.e.* 10 per cent.) were due to *Bacillus asiaticus* Castellani. In the same series 12 per cent. were found to be due to *B. typhosus* or *B. paratyphosus* (A or B).

(2) The distribution of cases is widespread, both in time and space, and there is no special incidence on sex or age-group.

(3) The symptomatology of asiaticus parenteric fever is detailed and a description is given of the causal organism.

(4) There is some group-(agglutination) relation between *B. asiaticus* and the paratyphoid-Gaertner subgroup.

(5) Parenterica due to "intermediate organisms" other than *B. asiaticus* is believed to exist in Egypt. These will be dealt with in a later communication.

(6) Early haemo-culture in all enterica-suspect cases should be considered the diagnostic method *par excellence*. If the blood develops immune bodies as well, the diagnosis becomes definite.

In conclusion I wish to express my gratitude to Dr C. Todd, Director of the Institute, for his help and criticism. It is through his encouragement and the interest he has shown from the beginning that the work was carried to a successful issue. My thanks are due to Dr I. Shawki, Dr M. Abu Allam and others, for giving me access to their cases and allowing me to use their clinical notes. I also thank all the M.O.H.'s and P.M.O.'s who have helped in supplying material for the investigation.

BIBLIOGRAPHY.

- ARCHIBALD, R. G. (1911). Four cases of pyrexia due to infection with bacillus of the cloaca type. *Fourth Report Wellcome Tropical Research Laboratories*, p. 231.
- (1918). Enterica in the Sudan. *Journ. Trop. Med. and Hyg.* XXI. 229.
- CASTELLANI, ALDO (1907). Notes on cases of fever frequently confounded with typhoid and malaria and due to *B. Ceylonensis*. *Journ. Hygiene*, VII. 1-12.
- (1912). Cases of fever probably due to *B. asiaticus*. *Journ. Trop. Med. and Hyg.* XV. 161.
- (1917). Notes on Tropical Diseases met with in Balcanic and Adriatic war zones. *Ibid.* XX. 181.
- CASTELLANI and CHALMERS, A. J. (1919). Parenteric Fevers. *Manual of Trop. Med.* 3rd edition, p. 1404.
- CHALMERS and McDONALD (1916). An enteric-like fever in the Anglo-Egyptian Sudan due to *B. khartoumensis*. *Lancet*, II. 139.
- DOUGLAS, CAPT. (1914). *Ibid.* II. 891.
- GAUDUCHEAU, A. (1915). Bacilles trouvés dans le sang au cours d'une fièvre indéterminée. *Bull. Soc. Méd. Chirurg. Indochine*, VI. No. 7.
- HIRST, L. F. (1917). Observations on the pathogenicity and specific characters of *B. faecalis alcaligenes*. *Journ. Royal Army Med. Corps*, XXIX. 476.
- HIRST and THOMSON, J. G. (1918). Reports from the bacteriological lab. of No. — Hospital, Alexandria. *Lancet*, I. 566.
- PETRUSCHKY (1889). *B. fecalis alcaligenes*. *Centralbl. für Bakteriologie*, Bd. VI. 657.
- SHEARMAN and MOORHEAD, T. G. (1917). Bacillaemia due to *B. faecalis alcaligenes*. *Journ. Royal Army Med. Corps*, XXVIII. 104.
- SPAAR, ERIC (1915). Notes on a case of fever due to *Bacterium columbense* Castellani. *Journ. Trop. Med. and Hyg.* XVIII. 281.
- TAYLOR, SEYMOUR (1914). Some cases of anomalous fever. *Lancet*, II. 1300.
- WANHILL, MAJOR C. F. (1915). Notes on organisms isolated from the blood of cases suffering from symptoms simulating mild enteric fever or paratyphoid fever. *Journ. Royal Army Med. Corps*, XXIV. 482.
- The *Trop. Dis. Bull.* (1912-1921) also contain abstracts under: "Enteric Fevers" and "Unclassified Fevers."