P A R A T Y P H O I D F E V E R

including

" A Discussion of the Relationships and Charact-"
"-eristics of the Intermediate Members of the "
" Typhoid-Colon Group of Bacteria . "

being

A T H E S I S

for the

D E G R E E of M . D .

by

Harry Overy

M.B., Ch.B.(1902)

The matter contained in the following Thesis is based on cases of which I have had personal knowledge, and have investigated; and also on the literature which I have been able to collect, especially :-

1. Observations on the Bacteriology of Paratyphoid Fever and on the reactions of Typhoid and paratyphoid Sera, by A. E. Boycott, M.A., M.D. in the Journal of Hygiene, January, 1906.

2. Pathogenic Micro-Organisms, by W.H. Park, M.D.1906.

3. Paratyphoid Fever, by Edmund Cautley, M.D. Cantab F.R.C.P. Lond.

4. The pathological anatomy of "Paratyphoid Fever" journal of Infectious Deseases, Vol. 1., P.72. 1904 by Wells & Scott.

5. Paratyphoid Fever, by Lorrain Smith, in The System of Medicine by Allbutt & Rollston, 1905.

These writers will be referred to by name only, unless there is some special reason for mentioning the exact page .

I have personally carried out all the simpler Bacteriological work, including the agglutination tests at all dilutions, the examination of many of the reactions and cultural qualities of the strains 'Paratyphoid A. (Shottmuller) and Paratyphoid B. (Schottmuller); the cultures being obtained from the Lister Institute of Preventive Medicine. The strain of Bacillus Typhosus I have used was also obtained from the Lister Institute, and is their regular Laboratory strain for carrying out the Widal reaction. I am also personally responsible for the different tests and examinations; the results of which are incorporated in the cases quoted at the end of this Thesis

Paratyphoid Fever is a continued Fever resembling in many respects Typhoid Fever. The clinical features indicate a wide spread infection which is practically a Bacterial Septicaemia. At present the term denotes an infection by one of two, possibly three or four organisms, allied on the one hand to the Bacillus Typhosus and on the other to the Bacillus Coli Communis.

It is possible that some of the Indian Fevers which are not at present definitely allocated or in amny cases described as separate entities may prove to be due to infection by one of the Typhoid-Colon group. A considerable amount of work is being done there now, but is not yet published. That there are , in India, various Fevers corresponding to no known type or infection, and which are not hybrids(e. g. Typhoid-Maliria) cannot be doubted . See Mackie "Paratyphoid Fever" Lancet vol ii 1905 page 875

History. Achaude and Bensaude (1896) apparently are the authors of the word "Paratyphoid" for they published in the Bulletins Et Mémoires de la Société Médicale des Hôpitaux de Paris, vol. 13. a communication called "Infections paratyphoidiques." They isolated, from 2 patients, an organism allied to B. Typhosus, but differing in several important respects. One case was that of a woman who had an attack of what appeared to be a somewhat atypical Typhoid Fever . It ran an unusual course and was complicated by phlebitis and cystitis. No agglutination tests were carried out, but

the organism was isolated from the urine. The second case was one of continued Pyrexia in an infant, followed by suppuration in the sterno-clavicular joint. In this case a similar organism was cultivated from the pus, but no agglutination tests were attempted. As will be seen subsequently the agglutination tests are by no means without suspicion, and these cases may be accepted as 'Paratyphoid'. The next advance was the cultivation of a 'Para-colon' bacillus from the blood of a patient by Gwyn in 1898. This patient was to all appearances suffering from a typical attack of typhoid fever. Nearly 200 cases have been described and the most trustworthy are the following:-Schottmuller, who studied the cultural differences between the paratyphoid and typhoid bacilli and also between the different members of the typhoid-colon group. He adopted the method of systematic blood culture from the patients: Pratt who obtained the bacillus from the gall-bladder in a case of cholecystitis; de Feyfer and Kayser (1902); Craig & White(1902) who cultivated the bacillus from the spleen; and Kurth, Lipman, Johnston, wells, who in each case obtained the bacillus from the blood or other fluid or from an organ.

Cases have been reported by many observers, but in many of them the identity of the organism had not been definitely and conclusively proved. As will be seen later there is without doubt a series of closely allied organisms, varying in lesser cultural and pathogenic properties, bewteen B. Typhosus and B.Coli Communis.

Etiology. The disease has been reported in all parts of the world i.e. Great Britain, United States, Germany, France, Holland, Phillippines, the West Indies, India and Egypt. It occurs sporadically or in an epidemic form: ~~Defayfer~~ de Fayfer and Kayser, Eiberg, Holland, 1902, 38 cases; Fisher, 1903; Hünermann; 1902; Conradi etc, in Sarrbruck 1902: Schottelius 1905; and van Ingen and Frissell, 1904. It is usually a mild form of fever and deaths are rare.

Infection is conveyed by the excreta and soiled clothes etc., as in typhoid fever; the organism being present in the urine and faeces.

It shows little preference for either sex or age; an infant of 4 months and a woman of 60 being among the cases reported. The B. Bacillus is much more frequently found than the A.; being present in at least 80% of cases. Apparently 3 to 10% of the registered cases of typhoid are paratyphoid. Boycott found five in 176 cases; Schottmuller in Hamburg found five in 68 or 7%; Zepnik 7 %; Wells of Chicago, and Kolle in Germany put it at 10%.

Bacteriology. It is impossible to discuss the specific organisms adequately without considering the typhoid-colon group of organisms as a whole, and com--paring the various members of this group of bacteria, of which the most prominent are the B. typhosus and the B. coli Communis, Tabulating them in their order of relationship they are approximately as follows:-

I. The Typhoid Group

Bacillus Typhosus (Eberth)

II. The Paratyphoid Group

Bacillus Paratyphosus A. (Schottmüller)

III. The Paracolon Group

(a) Bacillus Paratyphosus B. (Schottmüller)

(b) Bacillus of Hog-cholera. (Aertryck)

(c) Bacillus Enteritidis. (Gaertner)

(d) Bacillus Psittacosis.

IV. The Colon Group

Bacillus Coli Communis , and its varieties .

In the compilation of this table I have had considerable assistance from the writings of Lorrain Smith; Boycott ; and Park .Nevertheless it is a more complete clasification than is given by any of these writers separately .

Morphologically they are motile, flagellated organis-
-ms, 2-3 u in length and ·5 u. in breadth. They have
rounded ends, may show polar staining and in old
cultures frequently show aberrant and involution forms
which stain irregularly and often appear vacuolated.
In young cultures filamentous forms may be seen, but
the great majority of the organisms in young cul-
tures stain deeply, and uniformly, giving a plump
appearance to the bacillus. They stain with ordin-
ary dyes but are decolourised by Grams
method. The flagellae vary in different species
from 4 to 12 or more in number
The B. typhosus has usually 10 or 12 long wavy
filamentous flagellae. Paratyphoid A. and the para
colon group have from 6 to 10 which are shorter,
more delicate and stained less easily than those of
the B. Typhosus. The Flagellae of the bacillus coli
-communis are shorter and straighter than any of the
above and are fewer in number, usually four (4) or six.
The para-colon group are the most actively mostile
and then the para typhoid A.. The B. typhosus is
more motile than the colon baccilus which is the least
active of them all.
Their growth is aerobic; facultative anaerobic. They
grow on all ordinary media. They produce uniform
turbidity in broth, ferment sugars, may produce gas,
do not liquefy gelatin, and some tend to produce indol
in greater or less quantity. They are differentiated

by various reactions into the four groups mentioned above. These will now be considered:-

Growth on Agar. The B. typhosus produces on Agar when"stroked" a blueish gray almost transparent film with slightly wavy margins.

The paraeolon group especially paratyphoid B. produce a thick luxurient growth whilst paratyphoid A. grows more like B. typhosus and the growth is clear and thin and tends to be arranged in colonies rather than a general covering.

The B. coli-communis as is well known produces a luxuriant thick, white, and opaque growth. Stroke cultures on gelatine have much the same appearance but in no case does liquefaction take place. In broth they all produce uniform turbidity, especially marked in B. C. In the latter there is occasionally a pellicle on the surface and distinct sedimentation. Paratyphoid B. produces near-ly as much turbidity as the colon bacillus. Paratyphoid A. in my experience gives the least turbidity of any. Even 48 hours incubation at 37 ' C. may only cause slight cloudiness.

Indol Production. This phenomenon so characteristic a distinction between the colon bacillus and B. typhosus appears as follows:-

B. typhosus. Indol never appears in ordinary peptone solution to which the typhoid bacillus has been transfered, but if re-transfered repeatedly, after a few generations of three days each it may acquire this property.(Peckham, Journal of Experimental Med

Medicine vol. 2. page 549).

As regards the paratyphoid A. bacillus the occurance has never been noted, but several observers state that the paracolon group produce indol. I have been unable to obtain it with paratyphoid B.(Schottmuller). Morgan (1905); Libman, (1902); Buxton; Cushing; and Savage have noted it; but Schottmuller 1901; Kranepuhl, (1905); Kayser, (1904); and Korte (1903) who have reported many cases have not observed it. Boycott says small amounts are frequently found in old broth cultures of paratyphoid B. and hog cholera, and very rarely in similar cultures of Gaertner. On the other hand Lorrain Smith states that paratyphoid B. does not produce indol while B. Enteritidis does to a slight extent. It is hardly necessary to mention that the colon bacillus produces indol in quantity.

Chemical Activities. Passing on to more definite differences the most reliable distinctions are met with in their respective actions on the Carbohydrates. Among these the more important are the sugars and the higher alcohols.

Hexoses ($C_6H_{12}O_6$) including dextrose laevulose mannoese fructose galactose are fermented by the typhoid bacillus with the production of acid but no gas. With the paratyphoid A. and paratyphoid B. acid and gas are formed as they are with the colon bacillus.

Pentoses ($C_5H_{10}O_5$) e.g. arabinose and xylose. These are unaffected by B. typhosus but with the paratyphoids and paracolons acid and gas are formed similarly to the B.C.C.

Binoses or Disaccharides ($C_{12}H_{22}O_{11}$) e g Saccharose lactose, maltose. The B. typhosus produces fermentation with acid production in maltose but no gas. Lactose and Saccharose are unaffected. The paratyphoid and paracolon groups vary in their actions:- Acid & Gas are produced in maltose, but lactose is only affected by the paracolon group and then only slowly (Kayser). According to Lorrain Smith paratyphpid B. produces acid and gas with lactose whilst the A.bacillus only produces acidity.
Saccharose is unaffected by either group, ~~all are fermented~~ All binoses are fermented by the colon bacillus.

Hexatomic Alcohols e.g. mannite, dulcite, sorbite. The B. typhosus causes acid reaction without gas in mannite and sorbite but no change in dulcite.
The paratyphoid and paracolon groups produce acid and gas in all.

The Pentatomic Alcohols e.g. erythrite are unaffected by either the B. typhosus or the paratyphoid and paracolon groups; but they are fermented by most strains of the colon bacillus. Salicin is not affected by the typhoid bacillus ~~but is~~ nor by the paratyphoids and paracolons but it is by the colon bacillus

With regard to the technique of fermentation tests the following points must be bourne in mind. There must be nitrogenous substances present to be used as food by the bacteria; a suitable temperature 30 -35 C; and absence of deleterious substances. A. 1 - 2 per cent

solution of the carbohydrate in broth is the best medium to use. The products formed are lactic acid both levo-rotatary (B. Typhosus and paratyphoid A.) and dextro-rotatary (paracolon and colon bacilli); alcohol; acetic , formic, and succinic acids; gaseous substances chiefly carbonic acid gas and hydrogen. (Anders)

The Action on Milk. Bacillus typhosus produces no clotting; produces a definite acidity in 24 hours which slowly becomes alkaline in from ten to 30 days. B. paratyphoid A. produces permanent acidity without clotting.

The paracolon group produce an initial slight acidity which is succeeded in a short time(2 - 14days) by definite and increasing alkalinity; the milk is clarified but there is no coagulation as with B. Coli.

Growth of Potato. The B.typhosus, if the patato is acid shows no obvious growth, but on scraping the surface the bacili are found in large numbers. If the potato, be alkaline a faint brown colour is produced. The growth of paratyphoid A. is quite colourless. Paratyphoid B. produces a brown colour whilst the growth of the colon bacillus is markedly brown, moist and thick.

Another useful medium is the neutral red agar. It is not affected by B. typhosus. Paratyphoid A. first turns it yellow and then later it becomes red again. Paratyphoid B. and paracolon group turn it yellow and so does the colon bacillus.

Sugar Litmus Agars. Lactose remains blue with B. typhosus. Becomes Red with the para-colon and colon bacilli. Dextrin violet blue with B.typhosus and blue with the colon bacillus.

Summing up:- The main differences are as follows:- The paratyphoid A. bacillus grows less luxuriantly and the growth is transparent even on paper; it produces no change but acidity in milk, forms no bubbles of gas with lactose although it acidifies it?; and does not show terminal alkalinity in milk. It ferments dulcite. It first turns neutral red agar yellow and later red.

Paratyphoid B. and the para-colon group grow very abundantly, are brown on potato, clarify milk with clotting, produce a terminal alkalinity in milk, ferment lactose broth, with the production of gas.

It is thus seen that with the possible exception of B. Gaertner the members of the para colon group are indistinguishable, and there agglutination reactions must be depended upon. When this is done they are readily separated.

In addition, between these organisms the clinical symptoms of an infection are usually quite sufficient to distinguish them. It may be well before discussing the paratyphoid A. and B. organisms further to refer briefly to the other three organisms, and their pathogenic effects.

Bacillus of hog cholera; the bacillus Aertryck. (Aertryck) This was isolated by Prof. van Ermengem from an outbreak of food poisoning (Kolle and Wassermann's Handboch). Although the distinction between this organisms and paratyphoid B. appears slender it is real for while paratyphoid B. causes a disease resembling typhoid the Aertryck bacillus gives rise to a sudden acute illness---a food poisoning. It is characterised by severe vomiting and abdominal pain, followed rapidly by severe prostration, and marked nervous symptoms resembling bulbar paralysis. It is apparently conveyed from pork, or sausages, and is probably synonymous with "sausage poisoning"

Bacillus Enteritidis or the Gaertner Bacillus. This organism resembles paratyphoid B. in its cultural and morphological characteristics, and there is hardly one point on which authorities are agreed that they differ. It ferments lactose (denied by Park) and seems to form indol in small quantities in old cultures (denied by Boycott). It is very pathogenic to animals and may be acquired from eating diseased meat. There are a number of cases reported in man. There is intense enteritis with intestinal haemorrhages

Swelling of the lymphfollicles but apparently no ulceration. There is marked prostration. The symptoms usually begin in 24 hours. It is noteworthy that during recovery there is desquamation of the skin.

Bacillus Psittacosis. This is a short actively motile bacillus, closely allied to the para colon group. Its growth on potato resembles the colon bacillus. It does not ferment lactose, does not curdle milk, and gives no indol reaction. It is clumped by a typhoid serum in one in twenty dilution; thus completing the proof of its being a member of the group under consideration. It is a disease of parrots of a septicaemic nature in which haemorrhagic enteritis is marked. There is intense congestion of all the organs and peritoneal ecchymoses. It attacks parrots when imported from the tropics in large numbers. It may also attack most domestic animals and appears readily transmissable to man and probably from man to man. Several small epidemics have occurred in Paris and the organism has been isolated from the blood of the heart and from the solid organs. It is a serious affec-tion. The death rate being at least 30 %.

N.B. The description of the Bacillus Psittacosis is drawn from Muir and Ritchie's Manual of Bacteriology. Park also gives a brief description of this organism.

Agglutination Reactions of the Paratyphoid and allied organisms. These are very deceptive unless carried out most carefully. The points to be borne in mind in separating the organisms are as follows:- Agglutination per se is of little value, the relative vaule of the results alone are of importance, unless the reaction is given by one strain only and at a dilution of at least one in 50. As Boycott puts it '---it is not enough to show that an unknown organism reacts at some arbitrary dilution with a known serum; the ultimate limits of agglutination should be determined for each serum with both the unknown organism and the strain and organism homologous with the serum. The diagnosis depends on the relative , not the absolute , value of the figures so obtained'. (Page 40)
This is well shown by a table in the same paper which is here reproduced. Nine sera were taken and the agglutination limits estimated for the three organisms. The figures represent the greatest dilution at which the reaction was obtained.

Serum	SchottmullerB.	Aertryck	Gaertner.
Paratyphoid B; human	20,000	20,000	100
" "	1,000	1,000	50
" "	5,000	1,000	200
Schottmuller B.rabbit	5,000	1,000	200
" "	5,000	200	200
Aertryck; rabbit	100	5,000	50
" "	2,000	2,000	20
Gaertner original A; rabbit	100	50	20,000
" "	20	20	5,000

With regard to what constitutes a positive reaction it is necessary to speak with caution. Unfortunate-ly it must remain to some extent indefinite. Boycott makes five grades as follows:- completely clumping = +++ ; nearly complete but some free bacilli = ++ a fait number of small clumps with many free bacilli = + ; a few clumps of not more than 3 or 4 organisms = ± ;and lastly the same as controls = 0.

Another factor is the time taken, most observers make the observation in half to one hour; so long as the control is used and simultaneous observations be made either time will do. It is nec-essary to maintain the temperature of the sur-round-ing air at not less than 60 F. for I find the reactions are more distinct, and spontaneuos agglutination and loss of activity are not so marked as when the temperature falls to 50 F.

Again it must be borne in mind that B.Gaertner and paratyphoid B. do not clump so densely as B. typhosus. The former form large loose open aggregations, which are very distinct from the dense clumps of B. typhosus, but when these organisms react with typhoid serum the clumps follow the typhoid type and appear as tight masses (Boycott). This may be of considerable practical diognostic value.

Secondary Agglutinations. These must be considered in detail. As has been shown above, this is what for want of a better term is called Group Agglutination in distinction to specific agglutination. That there are distinct agglutinations for each bacillus would be a bold statement to make, but the results of absorption experiments are interesting, and are referred to later.

Taking my own figures I find that secondary agglutinations occurred as follows:-

Typhoid sera giving secondary agglutinations with B. paratyphoid B. 60%.

Typhoid Sera giving secondary agglutinations with paratyphoid A. 8%.

Paratyphoid B. sera giving secondary agglutinations with B. typhosus 25%.

Boycott gives the following:-

Typhoid sera with paratyphoid A. 10. 8 percent.
" " " paratyphoid B. 31. 2 "
" " with Aertrycke 30. 7 per cent.
" " with Gaertner 51. 2 per cent

His conclusions may be summarised as follows:-

The typhoid strength in the different sera is the cause of the variation in the presence and degree of the subsidiary agglutinations, but there are variations which do not come under this heading. The secondary agglutinations are not a function of the strength of the primary agglutinin, for the secondary agglutinations may be entirely removed by the homologous subsidiary organisms while the strength of

of the primary agglutinins is much the same. The explanation may be that most typhoid agglutinins are possessed of combining groups for other bacilli, in quantities which are very variable but in most cases far less than for typhoid.

Boycott has also shown that with increasing agglutination, the relative amount of subsidiary agglutinins decreases.

Secondary agglutinations are much more prominent in the early stages and on several occasions I have suspected a paratyphoid infection which later results have shown to be typhoid. In my own work, I have found paratyphoid B. show secondary or subsidiary agglutination more frequently than paratyphoid A. although Boycott states the opposite.

Absorption Tests. These are necessary to decide the question of double or multiple infection and for a more definite knowledge of secondary agglutination. I have no practical acquaintance with this procedure. What follows is mainly obtained from the writings of Castellani , Park & Collins, and Boycott.

Boycott adopts a fairly rapid method by saturating the diluted serum with excess of bacilli until it ceases to react with the absorbing bacillus. It may be stated that in an infection by one member a specific agglutination is produced for that organism, and group agglutinins for that and allied organ-isms and when there is a double infection, specific

agglutinins are produced for each organism and group agglutinins in addition. Castellani considered the following conclusions warranted. Firstly, the serum of an animal immunised against a certain microbe organism, when saturated with that organism looses not only its agglutinating power for that organism but also for all other varieties that it formerly acted on. Saturated with the others its action upon the first is reduced little or not at all (? vide Boycott as quoted below) Secondly, the serum of an animal immunised against two micro-organisms A & B. loses its agglutination (ion) when saturated with A. only for A. Saturated with A & B it loses its agglutinating power for both. Park points out that these conclusions are not entirely warranted, for bacteria absorb group agglutinins produced by other varieties of bacteria and which agglutinins may not affect them. Park (page 183) sums up as follows:- " the absorption method simply proves, therefore, that when one variety of bacteria removes all agglutinins for a second, the agglutinins under question were not produced by that second variety!" It is also important to carry out absorption experiments after the agglutination limits of a serum have been determined and the type or types of infection suggested by this method; otherwise a second infection may easily be missed by the absorption method (vide Park & Collins, and Boycott)

Isolation of the Bacillus. The bacilli have been obtained from the urine , faeces, blood, bile, and rose spots during life; from the pus of suppurating lesions; and after death from the spleen and lymph glands.

Isolation from the Blood. The simplest method and the surest is to take 5 to 10 c. c. from the median basillic vein. This can only be done in certain cases. The organism grown readily in the mixture of broth and blood and sub-cultures can be made on the special media which serve to differentiate the bacillus.

Isolation from the Stools. This method described by Boycott at length is as follows:-
Dulcite Broth is used as a differential medium, because this encourages the growth of B. paratyphoid B. and apparently discourages the growth of the colon baccillus. As pointed out before the whole group of paratyphoid and para-colon organisms, ferment dulcite freely. Dulcite-Bile-Salt-Peptone-Water was introduced by MacConkey. The result is that the paratyphoid organisms far out-number the colon bacilli. The process is carried out as follows:-
The dulcite broth is inoculated with the infected faeces and after twenty hours incubation at 37°C plates are made. The great majority of colonies varying from 80 to 90 per cent in different cases are paratyphoid where this organism is present. When direct plating may give no result this method is successful. Another method which has been used and which may give good

results, is to inoculate a guinea pig with infected faeces or a culture of faeces in dulcite broth when the organism may be obtained from the hearts' blood in abundance.

Morbid Anatomy. Accounts of this are conflicting Death from paratyphoid is uncommon probably not more than 2 to 3 per cent. Only 6 fatal cases have been described. There is general blood infection. The spleen is enlarged and presents much the same appearances as in typhoid fever, the bacilli can be cultivated from it. The intestines rarely if ever, show ulceration resembling typhoid ulceration. In my fourth case there is evidence of very definite ulceration in so much as sloughs were passed. The post-mortems reported give the following details. Ulceration was found in 2 cases, healing ulcers in another, but in neither was the lesion typical of typhoid ulceration. In one (van Ingen) the ulcers were situated above the ileo-caecal valve and presented a deep punched out appearance, extending in some cases to the peritoneal ~~cope~~ coat. In the other (Wells & Scott) there was superficial, ragged ulceration without ~~infiltration~~ infiltration, extending some distance above the ileo-caecal valve. In

Berg and Libman's case healing ulcers were found. In ~~Court~~ Cautley's opinion this was a case of mixed infection. In Longcope's case no ulceration was found. In Tuttle's case a few erosions above the ileo-caecal valve were seen. In Strong's case there were a few superficial haemorrhages and some moderate catarrh. The Peyer's patches and the solitary follicles were healthy.
The mesenteric glands were unaltered in five cases enlarged in the other.
Cloudy swelling of the Liver and the Kidneys and patches of Focal necrosis were found in two cases (Longcope & Wells and Scott.)
For a full account of the post-mortom changes see the article mentioned at the beginning of this thesis by Wells & Scott.

Symptoms and Course.

The Incubation period is said to be shorter than that of typhoid fever, probably only some three or four days. The onset is more abrupt in the majority of cases. According to Cautley the attack is sometimes ushered in by vomiting and abdominal pains. In some cases (vide cases 1 & 3) the onset may be gradual and resemble that of typhoid. The disease in the majority of cases seems to be ushered in by three to six days of malaise accompanied by anorexia, pains

in the back and limbs, and headache. The latter is in some cases very marked and is almost of diagnostic value. As regards the temperature; apparently there is not the step ladder phenomenon of typhoid; the temperature throughout being irregular In some cases rigor has been reported, but, this is not common although slight shivering seems to be so common. The vomiting is in many cases a marked feature. Drowsiness is present comparitavely early in the disease e.g. fifth day or even earlier as in case 2. It is a marked sympton sooner or later. Epistaxis is frequently observed. Herpes is present in many cases; The tongue is more or less furred, but rarely is the typical typhoid tongue seen, for it is usually moist, and the lips are dry. Constipation is usually present but by no means always (de Feyfer & Kayser) Undigested stools may be passed, and occasionally sloughs (vide Case 4) Haemorrhages are reported but are usually slight although they may be repeated. The Abdomen may or may not be distended and the same uncertainty applies to tenderness on palpation. Usually these symptoms are not marked. Rose spots are present in many cases. The spleen is enlarged in practically every case and is usually palpable. Some affection of the lungs is usually present, generally there is nothing more than a slight pulmonary catarrh. Pleurisy has been recorded. Wasting and Anaemia are usually present and in some cases marked.

The temperature remains irregular for ten , twelve , or more days, oscillating between 101 and 103 and then drops either by lysis or a crisis.

The pulse is soft often dicrotic and not very rapid.

Blood. Leucocytosis is never present early in the disease but there is often a leucopenia. In some cases the mononuclear cells are increased during the period of infection. A slight leucocytosis is present in some cases later on in the disease, but if marked it is an indication that suppuration has taken place some-where. The haemoglobin percentage is lowered as the disease progresses and there is diminution in the number of red cells. Eosinophylls are increased during convalescence. These blood changes are well shown in a case reported by Lieut Mackie in the Lancet of Sept. 23rd, 1905.

The urine occasionally contains albumen and Ehrlichs Diazo reaction may be present. Indican has been present in quantity in several cases reported.

Relapses are by no means uncommon. According to Lorrain Smith they occur in 10% of cases. They are usually less severe and of shorter duration than those of typhoid fever.

Various forms of the disease are described clinically. Kurth describes the condition which used to be called "Gastric Fever" in which there is vomiting and diarrhoea with very liquid stools containing mucus and blood; and this he attributes to the paratyphoid or para-colon organisms.

Another form described by Walker resembles pyaemia, in which there are ague like attacks with rigors, intermittent fever with wide oscillations and a termination by crisis with excessive sweating., in another form the abdominal pain and tenderness are very marked.

Complications are many and various. I can find no instance of perforation but intestinal haemorrhages occur in five to ten per cent. of cases. They may recur many times but are usually slight. The occurrence of peritonitis has not been reported, but the gall-bladder seems very prone to be affected. Cholecystitis hepatitis, cholelithiasis, have all been reported, and the bacilli isolated from the part. Bronchitis pleurisy, broncho-pneumonia are reported. Affections of the urinary tract appear to be common. Albuminuria is comparatively frequent, so apparently is Cystitis. Tube casts and blood have been found, so that a true nephritis may occur. Pyelo-nephritis is recorded in one case. Suppurative affections are frequent, especially arthritis and furunculosis; but osteo-myelitis, otitis media, and meningitis are described. Amongst other recorded affections are myositis, orchitis, ~~endocarditis, and femoral phlebitis.~~ endocarditis, and femoral phlebitis.

Diagnosis

Paratyphoid infection may be inferred from clinical signs and agglutination results, but it can only be definitely proved by isolating the organism from the blood, or some lesion, or from the stools. Even the cultivation from the stools is not absolutely conclusive (Lorrain Smith). When a patient shows signs of a mild typhoid fever often with few abdominal signs, the temperature oscillating Widal's reaction with typhoid cultures negative or only given at very low dilutions e.g. 1 in 20 then agglutination tests with the paratyphoid bacilli should be tried. As mentioned in the description of the bacilli various dilutions of the serum with the different cultures must be systemically tried and tabulated in order to find the bacillus which is agglutinated at the highest dilution. As Boycott has shown if this be done carefully the results may be relied on with a great amount of confidence. It must be borne in mind that paratyphoid B. has a considerable tendency to spontaneous agglutination; my own experience of the Schottmuller strain has convinced me of this, therefore a control should always be made. Boycott refers to this (page 54) and points out that the microscopic examination of the agglutination is far preferable to the macroscopic, where admixtures are made in capillary tubes and these suspended and a deposit watched for. In my own

cases I have alwayd used the microscopic method. Where spontaneous clumping is found to occur, it is well to make a fresh culture under different conditions such as lower temperatures or younger cultures. If possible, the reactions should be compared with sera prepared with known cultures. (Boycott)

Where it is possible cultures from the faeces in the manner before described should be made and these tested with known sera. Better still is the blood culture method, but this is not possible in many cases and unless five c.c. of blood be taken, or even more, it is apt to fail. It cannot be too strongly pointed out that a partial or more or less complete positive result with ordinary typhoid cultures at low dilutions is not proof positive of typhoid infection until the ultimate limits of agglutination have been determined, But if these be determined, with a serum tested with the different members of the group the result in the great majority of cases is reliable. With regard to mixed infections, the question is more complicated and absorption tests are necessary for the positive and negative diagnosis of these (Boycott). I have no practical acquaintance with this procedure. Again it must be remembered that conflicting results are sometimes obtained even when working with known sera from immunised animals and cultures of the bacillus with which the animal was immunised.(vide Boycott page 54,Park page 182)

In cases where the agglutination limits with typhoid and paratyphoid are approximately equal, there is in all probability a typhoid infection only.

Prognosis.

This is much more favourable than in enteric. Out of nearly 200 cases described only six have terminated fatally. Relapses are comparatively frequent and recur. The duration of the disease is very variable but is rarely as long as typhoid fever, 5 to 6 weeks being the limit. The intestinal lesions being usually slight, food can be given more easily and sooner, and so convalescence is hastened.

Treatment.

The treatment is practically that of typhoid fever with the additionthat diet may be more liberal provided abdominal pain and distension is not complained of and there is no evidence in the stools of serious intestinal lesions.

CASE No. 1. :-- J.S. September 24 1904. Aged 10. Boy

History . Patient had been ailing for six weeks; complaining of pain all over him, chilliness, pains in the head, and occasional abdominal pain . His mother noticed he was wasting. He had some blood-stained discharge from the nose . The bowels had been constipated not being moved without aperients . He had been feverish at night .

On examination .The boy appeared wasted and drowsy . The lungs were clear . The heart was slightly dilated and the first sound weak . There was no distension, pain , or tenderness on palpation, of the abdomen . No rose spots could be seen , but the spleen was easily palpated . The liver reached two fingers' breadth below the costal margin in the nipple line . The temperature was 102' F. and the pulse 120 .

Sept. 26. The patient was markedly distended and lay with his legs drawn up . He complained of tenderness when the abdomen was touched, but nothing could be felt either over the surface or per rectum . The pulse was running and the boy was obviously ill .

A blood-count showed 7000 leucocytes but no disproportion of the various kinds .

Sept. 27 . The boy was better, he had less distension but there seemed a little free fluid in the abdomen . There was some congestion of the bases of the lungs . Widal,s Reaction was negative with dilutions of 1 - 20, 1 - 50 , and 1 - 100 . Leucocytes 10000 .

Sept. 28 . Several rose-coloured spot were seen

Sept . 30 . Widal again negative .

Case No. 1.(contd.)

October . 4. Some fresh spots and the stools showed und digested material .

Oct . 12. Widal,s Reaction carried out with cultures of Typhoid Bacillus ,Paratyphoid A(Schottmuller), and Paratyphoid B (Schotmuller) .A positive reaction was obtained with Paratyphoid B.at dilutions of 1 - 30 and 1 - 100 ., and no reaction with either of the others.

Oct . 15. Temperature is falling and the boy is better

Oct . 17 .The above reaction was repeated and confirmed

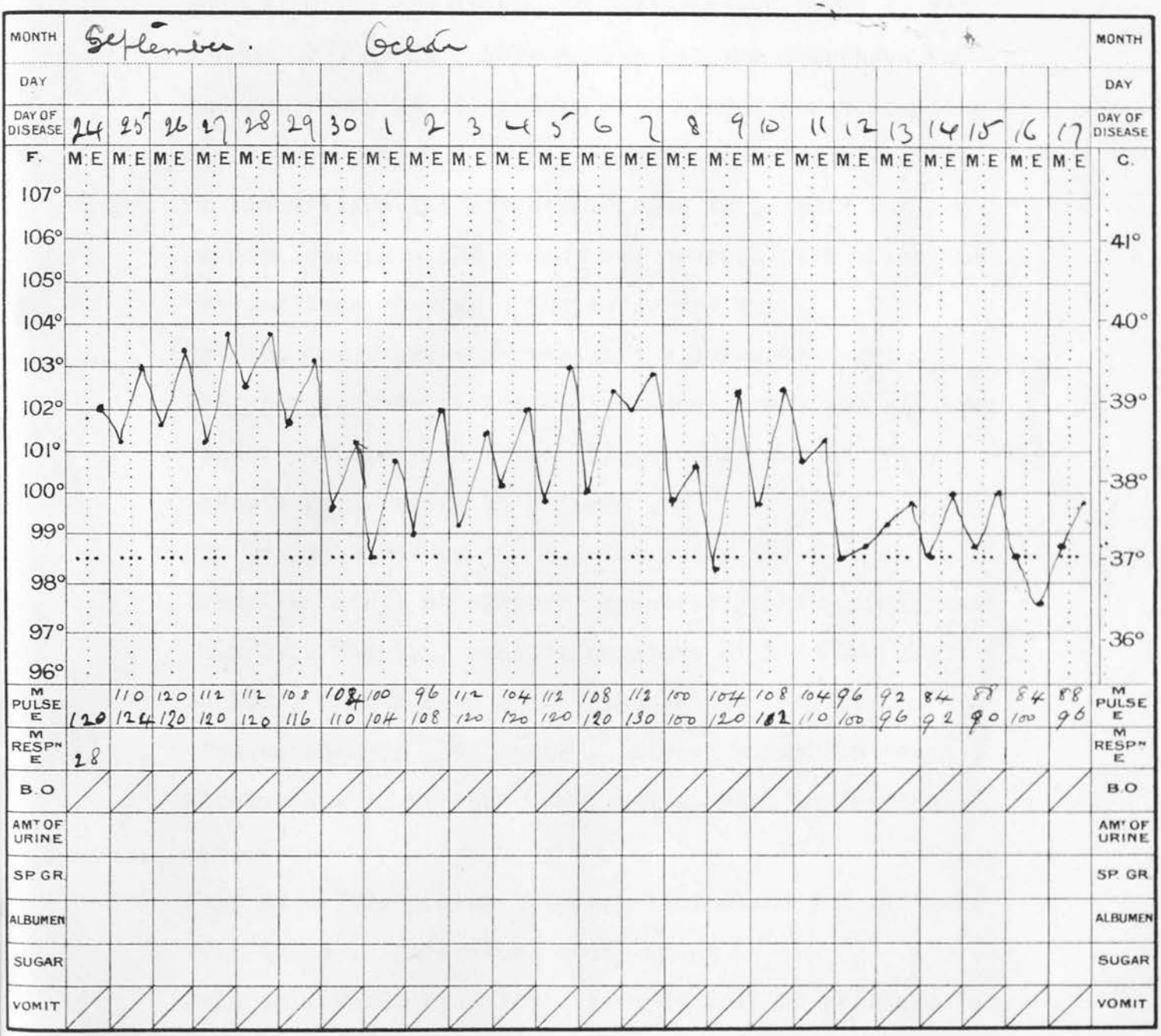
The temparature remained practically normal from this date , and the boy recovered slowly , getting up on NOV Nov. 5.

No attempt was made to make a culture from the blood or stools .

The treatment was the orthodox enteric treatment,and there were no relapses or complications .

METROPOLITAN HOSPITAL.

Patient's Name J. S. Reg. N° Ward



CASE No. 2. -- E.R. aged 9. female . July 25 1905.

History. Patient was quite well on the 19 July . On July 20 . she complained of severe headache and pain in the abdomen ; the child losther appetite and there was marked diarrhoea .

July 21 Still complained of headache and began to get drowsy . July 22 . More drowsy and the diarrhoea was better. July 24 .Diarrhoea recommenced and more pain was complained of . There had been no epistaxis .

On examination the child was found to be pale and an--aemic looking . The tongue was covered with white fur the papillae shewing . The lips were dry .

Nothing was found abnormal in the lungs or heart .

The abdomen was full and distended ; resonant all over tender on palpation ; the spleen could not be felt; there were no spots to be seen .

The temperature was 102'F., the pulse 124 .

Urine contained no albumen; specific gravity 1022; acid

July 27 . Widal,s reaction negative at 1 in 30, and 1 in 100 . Time 1 hour . Leucocytes 7500 .

Tongue cleaner . No spots . Abdomen still distended . Stools watery, profuse , but not showing undigested food .

July 28 . Very drowsy . Tongue furred and dry . Stools very loose . Temperature oscillating .

July 29 . Widal Reaction . Typhoid 1 in 30 positive in 1 hour, clumping not well marked . Paratyphoid B. 1 in 30 positive in 15 minutes; 1 in 100 positive in 20 minutes ; clumping well marked . Paratyphoid A. negative

Case No 2.(contd.)

July 31. Stools not digested . Abdomen still distended Weak breathing at base of left lung . Tongue furred an and dry . Leucocytes 8800 . No disproportion .

Aug. 2. Stools firmer, and digested .

Aug. 5. Agglutination tests repeated and confirmed.

One or two doubtful spots on the abdomen .

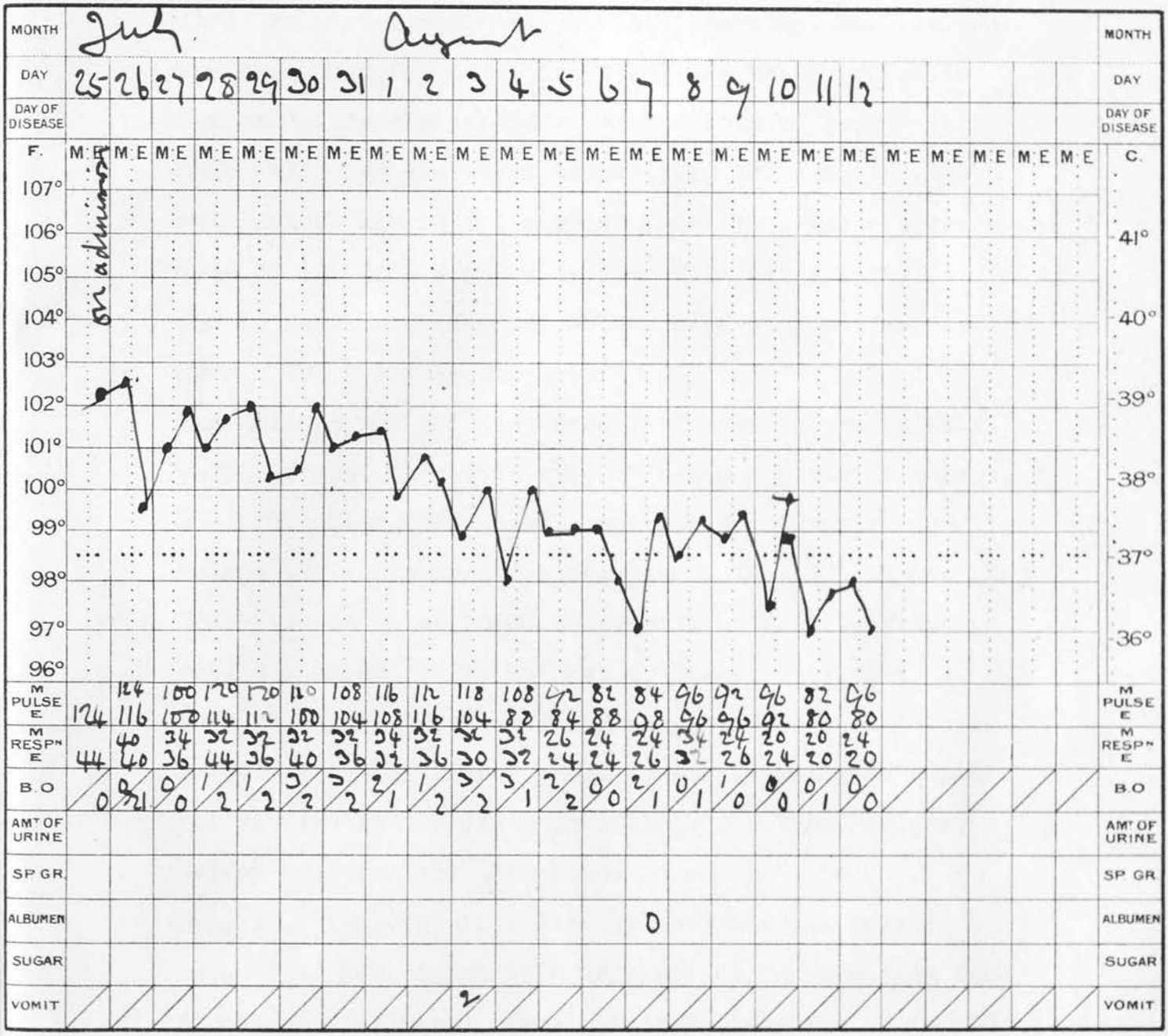
Aug. 10. Spleen palpable . Patient better in every way

Aug. 15. Agglutinations as follows ; B. Typhosus 1 in 30 positive in 40 minutes ; 1 in 100 some clumping in an hour ; Paratyphoid B. 1 in 30, marked reaction in ten minutes ; 1 in 100, complete reaction in 30 minutes

Patient made a good recovery and had no relapses .

METROPOLITAN HOSPITAL.

Patient's Name Ellen Ryan Reg. No. 352 Ward B. 3.



Case No. 3. E.P. aged 40, female . Dec. 19 1905 .

History . Three weeks ago she commenced to have pain in th in the back, which never left her .Shortly after she began to have continuous headache ,which is not localised but is'all over' . The bowels have been opened ~~ever~~ three or more times a day during this time. She vomited yesterday for the first time, but has had no appetite She had'pains all overher ' on the 15th of Dec.

On examination the woman looked ill, and anaemic . Her temperature was 100F , and her pulse 110, and respirations 30 . Tongue dry and covered with white fur .

The lungs showed slightly weaker breathing at the right apex . The heart seemed natural .

The abdomen was not distended . The spleen was easily palpable, but the liver was not below the costal margin.

Dec. 20. Temp. 102 ,bowels not moved, otherwise no change . Widal's reaction negative 1 in / 30 in one hou

Dec. 21.Leucocytes 10200 ch no evident disproportion .

Dec. 23. Enema result natural . Tongue very dirty .

Dec. 24. Agglutination with Paratyphoid B. 1 in 50 ; 1 in 100; 1 in 500 .Paratyphoid A. and Typhoidgave doubtful results with a dilution of 1 in 20 .Time 1½hours. Spleen much smaller Otherwise no change .

Dec. 26. Temperature falling , spleen still smaller .

Dec. 28 . Leucocytes 9800 .Agglutination reactions con firmed as follows : Paratyphoid B. positive 1 in 500 30 minutes . Paratyphoid and Typhoid doubtful.

Dec 30. Temperature is now domn to normal but is still swinging . Patient better .

Case No. 3 (contd.)

Jan. 1. Temperature going up; not so well .

There were some very faint sounds at the base of the right lung; friction? .

Jan. 4. Temperature reached 103.8 F

Jan .6. Temperature dropped rather suddenly.

Jan . 9. Temperature remaining down , w

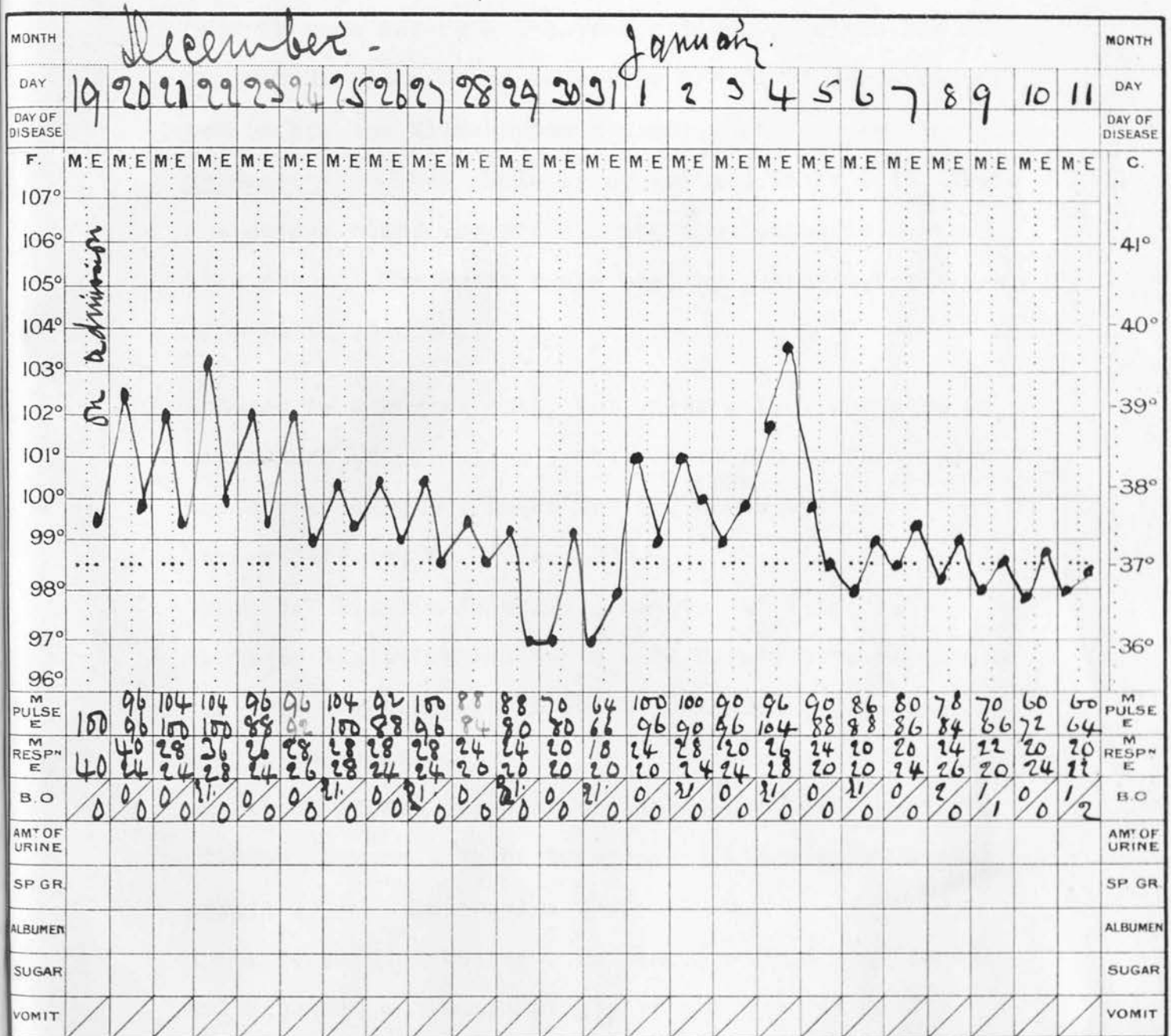
Agglutination reactions again confirmed, but little reaction at 1 in 500 .

Patient made a good recovery .

N.B. It will be noticed that this patient had a relapse.

METROPOLITAN HOSPITAL.

Patient's Name Emily P. Philpott Reg. No 612 Ward B. 3 -



CASE No. 4. E. W. aged 8 , female ,April 2 1906.

History. Illness commenced six days ago ,vomiting and pain in abdomen . She vomited as often as 3or four times a day. Bowels constipated till the end of the second day of the illness when she was given a pill. Next day the motions were watery and have continued so since.The child had been noticed to be'off her food' for a day or two before the illness was noticed.

On Examination the child is drowsy and looks ill , there are sordes round the mouth , and the tongue is covered with fur . The chest seems healthy , except for a few bronchitic sounds .

Abdomen is somewhat full, but moves well . There is no tenderness on palpation , the spleen can be falt under t the costal margin . There are two ~~spots~~ rose spots.

Temperature 102 F. Pulse 120 .

April 3. Widal's Reaction negative at 1 in 30.

April 4. Agglutination tests with Paratyphoid B. gave a positive reaction with 1 in 100 dilution ; ParatyphoidA. A.gave no reaction

April 5. Stools frequent,undigested,and very watery . Tongue cleaner . No distension . Spleen below costal margin . Leucocytes 9800

April 9. Patient better , no temp., stools well formed and digested . Lungs stillgive a few moist sounds

April 12. Agglutination reactions repeated at dilutions from 1 in 30 to 1 in 5000 with the three organisms Paratyphoid B. reacted at all , but very feebly at the higher dilutions . Paratyphoid A. showed no sign

CASE No. 4. (contd.)

of agglutinating in a 1 in 30 dilution after two hours . Typhoid showed definite clumping at 1 in 30 in 30 min. some clumping at 1 in 100, but no clumping at 1 in 200 in an hour .

April 16. Temperature normal ; bread and butter given

April 19. Temperature went up last night to 102 and is still high. The child does not complain , but is rather drowsy . There are no abdominal signs

April 20 Temperature coming down

April 21 Last night child had a profuse sweat , temp. dropped to 96F ,there was no pain , the pulse was small and only 70 . No abdominal distension or pain. This morning on an enema being given 5 or 6 sloughs came away

April 22 . General condition same . Blood culture attempted , but only a tiny quantity was obtained , which gave no growth.

April 23 Child better and more interested in things

Widal reaction again repeated with practically identical results . Leucocytes 15400

Differential count:-

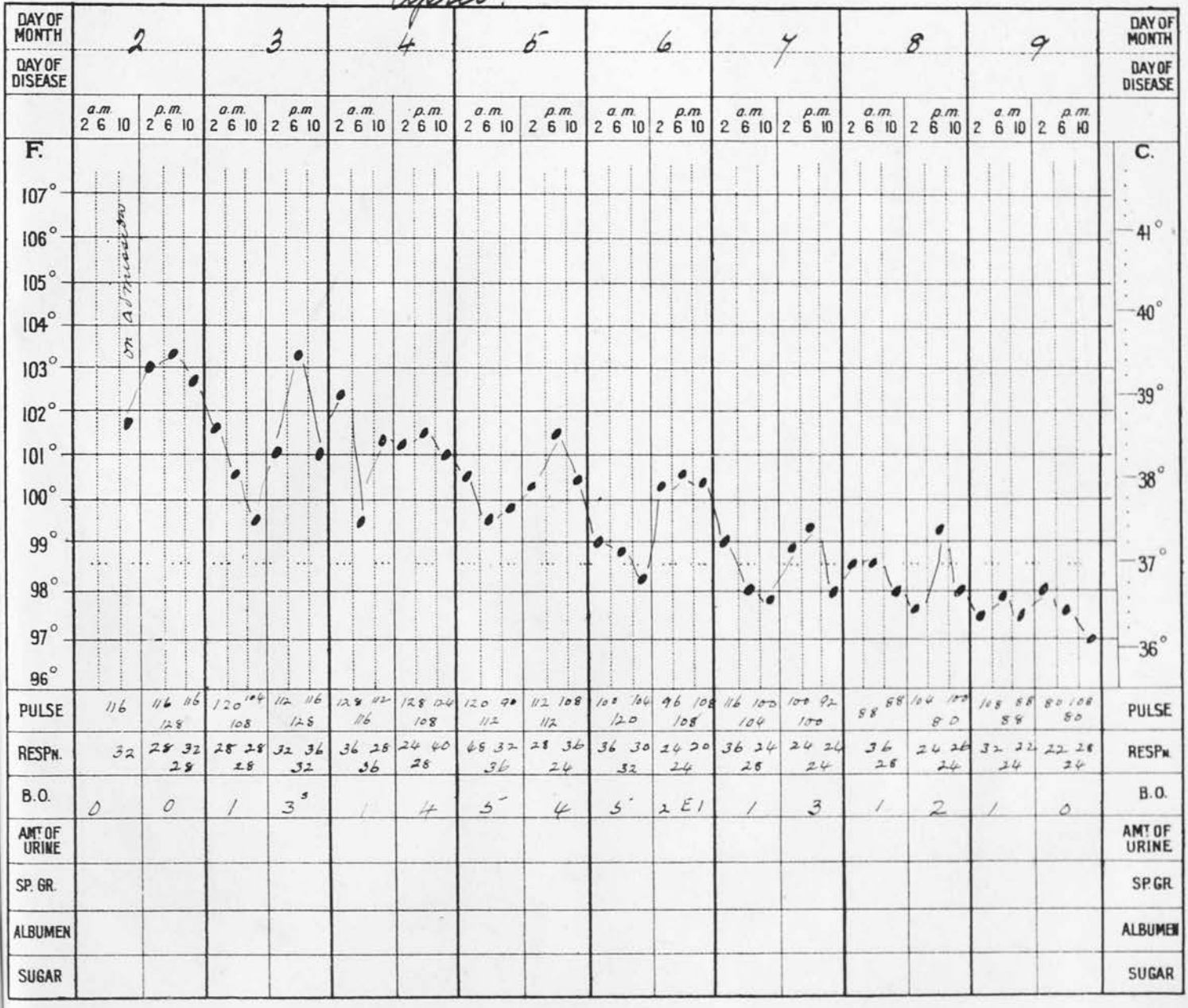
Polymorphonuclear	70 %
Eosinophylls	2 %
Large Mononuclear	10 %
Lymphocytes	18 %
Mast Cells	0 %

April 25 . Temp. still subnormal, but child is taking well, and seems going on well . No further passage of sloughs, nor any sign of haemorrhage

Metropolitan Hospital.

Patient's Name E. U. Reg N° Ward B. 3

April.



Metropolitan Hospital.

Patient's Name E. W. *Reg N°* *Ward* B 3.

April

DAY OF MONTH	10				11				12				13				14				15				16				17				DAY OF MONTH
DAY OF DISEASE																																	
	a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		a.m. 2 6 10		p.m. 2 6 10		
PULSE	76 84 72		80 76 84		60 72 80		88 68 92		76 84 92		80 64 80		88 76 84		76 88 64		76 88 76		62 76 80		100 80 72		64 72 80		76 100 76		88 80 72		68 72 72		88 72 66	PULSE
RESPN.	24 24 24		22 24 24		20 20 20		22 20 24		20 24 20		24 20 24		24 20 24		24 20 24		20 20 24		22 24 24		24 24 20		22 20 24		24 24 20		20 24 24		20 20		22 24 24	RESPN.
B.O.	0		0		0		E1		0		0		0		E1		0		0		0		E1		0		0		0		E1		B.O.
AMT OF URINE																																	AMT OF URINE
SP. GR.																																	SP. GR.
ALBUMEN																																	ALBUMEN
SUGAR																																	SUGAR

F. 107° 106° 105° 104° 103° 102° 101° 100° 99° 98° 97° 96°

C. 41° 40° 39° 38° 37° 36°

Cudlipp + Kelly.

Bruce + Tuttle

Metropolitan Hospital.

Patient's Name E. W. Reg N° Ward B3.

April

DAY OF MONTH	18		19		20		21		22		23		24		25		DAY OF MONTH
DAY OF DISEASE																	DAY OF DISEASE
	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	a.m. 2 6 10	p.m. 2 6 10	
PULSE	84 76 82 92 80 88		96 104 100 108 128 100		100 84 88 80 152 92		56 76 72 68 80 66		68 64 68 56 80 66		68 60 60 48 68 58		52 64 68 56 74 80		60 68 66 68 60 66		PULSE
RESPN.	24 24 20 20 20 24		28 24 24 28 28 24		28 22 20 24 24 20		16 20 20 20 18 24		18 18 20 20 20 18		24 20 22 16 24 18		16 18 20 16 20 20		18 20 20 18 20 20		RESPN.
B.O.	0 0		E1 2		0 0		E1 0		2 0		0 0		E1 0		0 0		B.O.
AMT OF URINE																	AMT OF URINE
SP. GR.												1015					SP. GR.
ALBUMEN												0					ALBUMEN
SUGAR																	SUGAR

F. 107° 106° 105° 104° 103° 102° 101° 100° 99° 98° 97° 96°

C. 41° 40° 39° 38° 37° 36°

Conclusions :--

Of my own cases the most interesting is No. 4. I still have hopes of cultivating the organism, for the reactions are very definite .

The passage of sloughs brings it into line with the cases reported by Wells and Scott, and mentioned above .

On my own showing not one of my cases are absolutely conclusive , but I have said enough to to show that they may be accepted with very good reason.

With regard to the general subject the work quoted goes to prove without doubt that there is a definite infectio with organisms resembling the bacillus of Eberth, but not identical and not provoking the same symptoms although the clinical type very closely resembles a mild attack of typhoid fever.

Bibliography; A complete list of the literature of the subject is given by Boycott ,and by Cautley in the works mentioned on the front page .

In addition to the five publications mentioned there I h have consulted the following:- MacConkey, Journal of Hygiene, vol. v. p.365 ;Anders' Practice of Medicine ; Savage , Journal of Pathology and Bacteriology ,Vol.X. p.341. ; Osler's Practice of Medicine , 1905. ; Park and Collins , Journal of Medical Research, Vol.XII.; Aand several which are referred to in the thesis.