Thesis for the degree of M.D. Edinburgh, by John Henry Aytoun M. B. C. M.

On the Clinical Characters of the Enteric Fever Rash, and the reasons for its Time of Occurrence and Distribution.

Probably more has been written about the Clinical Features of Enteric Fever, since it was first clearly recognised as a definite specific disease, than about those features of any other infectious fever in the same period of time.

This being so, one would expect that some degree of final-ity as regards the description of the characteristics of the Rash which occurs in most cases of Enteric Fever, and as regards the relationship which exists between the type of Rash and the type of disease associated with it,

would have been reached.

But this does not seem to have been arrived at yet, as the description of the rash and of its characters, and of the type of Enteric Fever which might be expected to be associated with a certain type of rash, varies to some extent in the works of different authors.

There are certain points about the rash of enteric fever upon which the great majority of authors are agreed. These are as follows: ——

I. That in a considerable proportion of all cases of enteric fever —— generally assumed to be about twenty three per cent. —— no rash occurs during the whole course of the illness.

II. That the total number of spots constituting the rash may vary from only one or

two up to several hundreds, and that generally they are not very numerous at one time.

III. That the spots are practically always discrete and circular (though Roberts (4) says that they are sometimes oval, and I have myself met with a case in which two of the spots were of large size and irregularly quadrilateral in shape): that they are of a rose red colour: are distinctly raised above the level of the skin and can be felt by the finger tips: that the colour of the spots dis-appears completely on pressure and reappears when the pressure is removed: that the spots come out in successive crops, so that, when the rash is at all abundant, spots of different ages are present at the same time: that each spot usually lasts from two

to five days, and then disappears, leaving a slight yellowish or brown stain in most instances: that commonly they continue to come out during the whole course of the febrile period, and to reappear during a relapse: and that the spots practically never become petechial.

IV. That when the rash is present, it usually first appears from the seventh to the twelfth day of the disease: but that it may appear sooner or be delayed even for a number of weeks.

The points about the Enteric Fever Rash and its associations upon which different authors are not altogether agreed, or which are ignored by them are: ——

I. The distribution of the rash.

II The size of the spots.

III The sensation conveyed to the finger on touching the spots.

IV. The relation, if any, which a scanty or abundant rash bears to the severity or mildness of the attack with which it is associated.

V. Whether vesiculation of the spots occurs; and, if it occurs, its relative frequency.

VI. When vesiculation of the spots occurs, causing each spot affect-ed to appear and to feel acumin-ated, whether it affects generally all of them or only a relatively small number.

VII. The relation, if any, existing between a generally acuminated rash and the severity or type of the attack associated with it.

VIII. Whether, if the infection from a case of enteric fever having a generally acuminated rash is conveyed to another person, the rash in the second case is likely to be acuminated also.

IX. Whether, if enteric fever should spread from one patient

to a second person, other things being equal, the attack in the second person, and the amount of rash present, will tend to be the same as in the first case.

X. What determines
(a) the time of occurrence of the rash in enteric fever:
(b) the distribution of the rash over the skin.

I propose to deal briefly with each of the points on which there is a difference of opinion, giving a few cases in support of my views; and finally to sum up the conclusions at which I have arrived.

A number of my earlier cases occurred before Notification became compulsory in some of the areas of my practice, and had to be treated at home, sometimes in small houses, and without trained nurses: so that I had an opportunity of

studying the disease as it oc-
-curred in several members
of the same family where,
from the period elapsing between
each case in a household, and
where the original source of
infection could be excluded, it
appeared to be almost certain
that the disease had been
contracted from the first case.
The opportunity of studying such
cases at the present time is,
owing to careful precautions,
not commonly available in
infectious diseases hospitals,
where the disease rarely spreads;
and for many years, owing to early
removal of cases to hospital, the
use of improved disinfectants, and
more knowledge on the part of
those nursing the cases, it has been
equally wanting in private practice
in this country.

The disinfectants used in my
earlier cases were nearly always

crude carbolic acid and chlorinated lime for disinfection of discharges &c: and permanganate of potassium or carbolic acid for hands &c. In nearly every instance where the disease spread through a house, there was a dry closet.

My experience of the disease has chiefly been gained by the study of a large number of cases occurring in a very large general practice in Midlothian between the years 1889 and 1911.

I. The distribution of the rash. Niemeyer (15) states that the roseola spots occur first at the upper part of the abdomen. Broadbent says (1) "the spots are usually few in number and are distributed irregularly over the abdomen and chest." He, later on, says that spots, if found on the back alone, cannot safely be assumed to be Typhoid spots,

because similar spots are of not uncommon occurrence on the backs of persons who have not got enteric fever. He thus practically admits that they may occur on the back.

Finlayson (2) says "the enteric fever eruption appears chiefly on the trunk, and especially on the abdomen, but an examination of the back sometimes discloses the only spots visible."

Bristowe (3), and Roberts (4), agree with Broadbent and Finlay-son that the spots are chiefly developed on the chest, abdomen, and back. They add that occasion-ally they are observed on the face and extremities, Roberts laying special stress upon their occurrence on the thighs and the rarity of their appearance on the face.

Eustace Smith (9) says of the eruption in children, "careful inspection of the chest, abdomen,

and back, will generally discover a few — it may be only one or two — of the characteristic spots. Sometimes they can be detected upon the limbs."
Sydney Phillips (19) says the spots "chiefly appear on the back, or surface of chest or abdomen. They are rarely seen on the limbs or face."
W. Cayley (5) says "the spots are generally confined to the abdomen, chest, and back. Sometimes the eruption is very copious and may then extend to the extremi-ties and even to the face."
Dr Dreschfeld (6) says "the spots appear chiefly on the abdomen and back, occasionally on the arms and thighs: rarely on the face." He does not mention the chest, legs, forearms, or hands; and in the first edition of the book quoted from the face was omitted also.

Osler, whose opportunities of studying the disease have been exceptional, says (7) "the spots appear usually at first on the abdomen." "The spots may be present upon the back, and not upon the abdomen. The eruption may be very abundant over the whole skin of the trunk, and on the extremities." He gives the following statistics of four hundred and twenty six cases in which the spots were looked for with particular care on the extremities and face. They were found on the arms in thirty nine cases: on the forearms in thirteen cases: on the thighs in nineteen cases: on the legs in eight cases: on the face in three cases: and on the hands in one case. Holt (8) says, in speaking of the disease in children, "the eruption is less constant, less abundant, and less characteristic than in adults. The typical eruption appears chiefly

or solely upon the abdomen at the beginning of the second week."

I have not personally seen the rash on the forearms, legs, face, or hands. From an analysis of my cases, I have found that the rash has occurred most frequently on the abdomen: rather less frequently on the front and sides of the chest: thirdly in order of frequency on the back of the chest and lumbar region: fourthly in frequency over the hips and outer sides of the thighs: and fifthly, over the shoulders and upper arms.

While the rash may be seen, rarely, in all these situations at the same time, it is usually limited to two or three of them.

While Holt's statement is, I believe, quite correct, I have seen a boy, aged six years, who had a widespread rash over the abdomen, chest, and back, associated

with a very severe type of the disease, and in whose case death occurred in the third week from intestinal perforation.

II. The size of the spots.

Broadbent (1) says that they are "small — about the size of a pins head." I have measured several heads of pins and find that the diameter is about two millimetres.

Finlayson (2) says that the spots are "small — not exceeding one eighth of an inch (that is 3·1749 millimetres) in diameter.

Bristowe (3) says that the spots "when fully formed vary from half a line to a line and a half (that is from 1·058 millimetre to 3·1749 millimetres) in diameter.

Roberts (4) incidentally mentions the fact that the spots may be oval in shape, — a shape which I do not remember to have observed, — and adds

that they vary from "one half to two lines (that is from 1·058 millimetre to 4·232 millimetres) in diameter."

Eustace Smith, (9) referring to the spots in children, agrees with Bristowe as to the length of the diameter of each spot.

W. Cayley (5) says that they "measure about two lines (that is 4·232 millimetres) in diameter", and that they are "uniform in size."

Dr Dreschfeld (16) describes them as being "about the size of lentils," and he, Sydney Phillips, and Osler, agree that they vary from two to four millimetres in diameter. (A lentil measures slightly over four millimetres in diameter.)

Holt merely states that they are "small scattered rose-coloured spots."

I believe that the spots, when

fully developed, are nearly all about three millimetres in dia-meter, and that they do vary slightly in size: sometimes some smaller spots are seen which do not increase in size: and in other cases every spot in the rash is larger than the average. The spots are difficult to measure as the colour disappears with the slightest pressure.

III. The sensation conveyed to the finger on touching the spots. Broadbent speaks of the spots as being "about the size of a pin's head, slightly raised and pointed." Such spots probably feel very slightly hard on touch-ing them; but in my experience such spots are not very common, and he himself does not mention the sensation produced by touch-ing them with the finger. Bristowe says that the spots are

"sensible to touch:" and Roberts that the spots "have a soft feel."

Drs. Cayley, Sydney Phillips, and Dreschfeld, do not speak of the sensation produced by touching or feeling the spots with the finger, nor does Holt mention it.

Coler says that the spots "can be distinctly felt by the finger."

I have always noticed that the ordinary rose spots, when pressed lightly by the finger, feel soft to the touch, and pro-duce a very slight feeling of resistance to pressure; and that no trace of sharpness at the apex of the spots can be felt. But that, when the spots are acuminated, each one feels rather firmer than the commoner form of rose spot, and has a distinct-ly pointed feeling, sometimes almost as if it were sharp. This

sharp feeling is most marked when the spot has been vesiculat-ed for about thirty hours, by which time the point has usually become dessicated.

IV. The relation, if any, which a scanty or abundant rash bears to the severity or mildness of the attack with which it is associated.

Neither Briotowe, Dreschfeld, nor Holt, gives any opinion on this point. Finlayson, Broadbent, Eustace Smith, and Osler, state that the amount of the eruption bears no relation to the severity of the attack. Osler however (7. p. 34), in describing the abortive and mild forms of enteric fever, says "the rose spots may be marked. Often they are very few in number."

Roberts (4, p. 135) says with reference to prognosis "abundant

eruption is not a bad sign in Typhoid."

W. Cayley says "while it is often considered that there is no relation between the amount of the eruption and the severity of the attack, in my experience, when the eruption is very profuse and dark, the case is usually a severe one."

Sir Joseph Fayrer (16) speaking of enteric fever in India, says "the eruption is sometimes absent, even in the Specific Enteric; but as it stands in direct relation to bowel ulceration, it may occur, nevertheless, as the latter condi-tion is established." He seems to believe that when the eruption is present, intestinal ulceration is also present.

Sydney Phillips (19, p. 510) makes two statements which do not seem to agree with each other. They are (1) "There is no relation-

-ship between the amount of the rash and the severity of the disease." (2) "Still, where profuse eruption repeatedly recurs the prognosis is less favourable than where the eruption is shortlived and slight."

Dr. Whitehead (14) describes fourteen severe cases of Enteric Fever each of which had intestin-al haemorrhage, sometimes repeatedly, as a complication. These cases were admitted to the Monsall Hospital at various stages of the disease. On the day of admission eight of these cases had distinct rose spots, three having a profuse rash. Of the remaining six cases which had no rose spots on admission or afterwards, only two could be definitely known to have no rose spots at all (admitted on the eighth and

ninth day of disease respectively). The remaining four cases were admitted too late in the disease for it to be known whether rose spots had been present or not.

Excluding these last four cases, there were thus ten cases of very severe enteric fever with marked haemorrhage from the intestine: in eight of these the rash was distinctly present, and in three it was profuse: only two of the cases had no rash at all.

Dr Whitehead states, in a letter, that in his experience where the rose spots are plentiful the type of the fever is a severe one.

It is well known also that in children, in whom the rash is less constant and less abund--ant than in adults, the disease is usually of mild character.

Some of the mildest cases of enteric fever that I have

met with have had no eruption at all, and I think it is probable that in some of these cases there has been no intestinal ulceration: while with some exceptions most of my cases of Grave Enteric Fever have had an abundant rash.

My own experience therefore is in agreement with Dr Cayley's statement, as I have usually found that, other things being equal, the greater the amount of the rash, the more severe the attack has been.

V. Whether vesiculation of the spots occurs; and, if it occurs, its relative frequency.

No author, whose works I have read hitherto, says that the spots never become vesiculat-ed.

Broadbent, Finlayson, Eustace Smith, and Holt, do not refer

to the occurrence of vesiculation. Bristowe says that the spots "occasion-ally become vesicular in the centre and thus more or less distinctly acuminated."

Roberts says "in very rare instances the spots are minutely vesicular."

W. Cayley also says "in rare cases the spots have been observed to be acuminated, with a small vesicle on the summit."

Sydney Phillips says "the spots may be slightly vesicular."

Dreschfeld says "in some cases a minute vesicle may be seen at the apex of the roseolar spot."

Osler says "of variations in the rash, frequently the spots are capped by small vesicles."

In my own practice I have been able to include every case of enteric fever rash in one of two classes:

(a) The ordinary form, in which each spot is a circular, raised papule, measures about three millimetres in diameter at the base, is of a rose red colour, has a somewhat flattened summit, feels soft to the touch, and lasts for from two to five days during which time the colour disappears on pressure. The papule then disappears leaving a slight yellowish stain.

(b.) A much more uncommon form in which each papule is of the same size, begins in quite the same way, and has the same colour and characters, as the commoner form of rose spot, but in which, within forty-eight hours, a tiny tense vesicle develops in its apex, causing the papule to be acuminated. Each spot lasts for from three to five days and then disappears, leaving a distinct brown stain,

much more marked than in the case of the ordinary rash.

This may be called the Acumin-ated Rash of Enteric Fever.
In my practice the rash of enteric fever has been of the acuminated type in about seven per cent of all cases having a rash.

VI. When vesiculation of the spots occurs, causing each spot affected to appear and to feel acuminated, whether it affects generally all of them or only a relatively small number.

There is practically no literature upon this point.
In my experience, when acumin-ation is present it generally affects nearly all the spots con-stituting the rash. I have noticed also that the acuminated rash is generally rather more abund-ant than in the case of the simple papular rash.

It is of some importance to remember that this acuminated rash sometimes occurs in Enteric Fever, as it has a somewhat different appearance from the ordinary rash. Indeed I was once called in consultation to see a woman, aged fifty-three years, who had been ill for eleven days with gastric symptoms, un-accompanied by any diarrhoea. Her pulse, when I saw her, was slightly quicker than normal: her temperature, however, was 102°F. when I took it: and the acuminated rash was present in abundance over the abdomen and chest: a few spots were also scattered over the hips. The tip of many of the spots was dark brown and looked like the tip of a thorn. Her ordinary medical attendant (who was also medical officer of health for the district) had not thought of enteric fever,

he having been deceived by the slow pulse and the presence of constipa-tion. The temperature had never been taken: and the spots did not appear to him to be typical, even when they were pointed out.

The patient died in Hospital about a week later, having had intestinal haemorrhage: and her daughter, who had nursed her during her illness, shewed symptoms of enteric fever a day or two after I first saw the mother. She had a moderately severe attack and made a good recovery; but, except that the rash in her case began as the ordinary rose coloured papules coming out on the abdomen and chest in small numbers, I cannot say very much about her case as she also went to Hospital. (Please refer to the note about these two cases on page 116.)

VII. The relation, if any, existing between a generally acuminated

rash and the severity or type of the attack associated with it.

As there seems to be no available literature upon this point I simply give the result of observations upon some of my own cases.

The generally acuminated rash is, in my experience, usually associated with a severe type of enteric fever, having a high temperature, slow pulse, tendency to constipation, and to the occurrence of serious complications.

Thus the case already referred to died from intestinal haemorrhage; while of two other cases which will be mentioned later (cases I and II), case I had an unusually severe type of enteric fever, with much delirium and very severe bronchitis, and the development of the typhoid state, followed by a relapse of the fever; this patient nearly died; and case II had a somewhat similar

attack of enteric fever, with much muttering delirium, and secondary pneumonia as a complication: the typhoid state developed, and the case terminated fatally.

My cases suggest to me the probability that in such cases a mixed infection has occurred, and that the Bacillus Typhosus, which has frequently been found in the ordinary rose spots (7, p. 4), and in the blood taken from the roseolar eruption, (Neuhaus, Roux, and Meisels, 6, p. 800; Krause, 17; and Neufeld, 18,) assisted probably by septic organisms, produces a more severe type of inflammation in the rash in the skin than occurs in the ordinary rose spots.

VIII. Whether, if the infection from a case of enteric fever having a generally acuminated rash is conveyed to another person,

the rash in the second case is likely to be acuminated also.

Here again I know of no literature upon the subject; but I think that a perusal of the three following cases will help to convince one that a generally acuminated rash tends to pro-duce a similar rash when the poison causing it, if not modi-fied by the action of antiseptics, infects a second person: and that the same poison, when modified by the action of anti-septics, tends to produce the ordinary papular rash by infec-tion: and also that the distribu-tion of the rash will tend to be the same in each case.

Case I. J. D., a man aged twenty-five years, residing at Bonnyrigg. He had always had good health, and weighed, early in January 1892, ten stones and seven pounds. During the first

three weeks of January 1892 he had worked as a stonemason at Preston, near Manchester. During that time he had drunk, with the other workmen, the water of a small stream nearly every day. While he was there several of the stonemasons who worked with him developed enteric fever, and at least one of them died from it.

He came home to Bonnyrigg on January 22nd, 1892, and started work as a weaver. He had never felt quite in his usual health since his arrival home, but had continued at work till February 6th, 1892, when he had to leave his work and come home as he felt very ill. He went to bed and had to remain there for many weeks. He had felt chilly for about four days before he gave up work: had lost his appetite: and had felt

frontal headache occasionally.

I first saw him on February 8th, at half past three in the afternoon, that being his third day in bed. He then had the following symptoms and physi-cal signs:

Severe pain in the lower part of the back, which was aggravated on movement: a feeling of weight and soreness in the epigastrium and lower part of the chest in front: aching pains in the limbs: severe frontal headache: total loss of appetite: great thirst: and sleeplessness — he having been awake all the previous night. He was lying on his back and had very flushed cheeks. His tongue was moist and thickly coated with white fur on the dorsum, the tip and edges being red. The abdomen was moderately distended, and was not tender on palpation. No

spontaneous gurgling in the abdomen had been noticed, nor was any present when I examined him. The bowels had moved on the previous day, after a dose of castor oil, but there had been no diarrhoea. No rash was present on any part of the skin.

He had had a cough with mucous expectoration for about a week before I first saw him; and examination of the chest shewed that marked bronchitis was present on both sides, and that the heart was healthy.

The urine was concentrated, and, on cooling, shewed a large deposit of dark pink urates. It contained no albumin.

The pulse rate was 86 beats per minute: the pulse was regular and well filled between the beats: and the vessel walls were healthy.

Respirations were twenty per

minute and regular.

The temperature was 104°7. The temperature in this and my other cases was always taken in the axilla and by myself.

He was put upon an entirely liquid diet; and a dose of a mixture containing nitrate of potash and acetate of ammonia was given every four hours. A five grain dose of acetanilid was given at irregular intervals, as noted in the chart, to relieve headache and aching in the back and limbs, and to reduce the temperature.

During the course of the case handkerchiefs soaked in iced water were continuously applied for an hour or two at a time to the head, chest, and abdomen, when the temperature was very high or delirium occurred.

The accompanying charts will give a good idea of the case.

Dr Aytoun, Bonnyrigg.

Case I

February / March

Date 1892 — 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 1 2 3 4 5 6 7 8 9 10

Day of Disease	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.
Temp. F.	V	V	V				IV																											
Pulse	86	86	88	85	80	84	84	80	72	84	72	84	80	80	80	84	80	82	92	80	84	84	98	84	97	102	88	100	94	96	94	108	90	92	88	120	92	84	102	108	88	92	78	76	88	88	96	88	84	88	88	92	95	96	76	96	80	92	78	96	86	96	98
Respiration	20	24	24	22	20	24	22	20	20	28	28	22	23	28	30	29	28	28	32	27	28	28	32	24	27	32	31	28	30	28	26	28	28	28	26	29	28	26	28	28	24	22	24	28	24	18	24	20	20	19	22	22	28	22	20	22	14	22	20	17	17	24	23
Motions /	0	0	0	0	1	0	0	0	2	0	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1	1	0	0	0	1	0	0	0	1	1	2	0	1	0	1	0	0	0	2	1	4	1	2	0

Acetanilid gr. V
Acetanilid gr. V
Acetanilid gr. V
headache better
Two rose spots
Acetanilid gr. IV
Spots mesiculated
Iced handkerchiefs applied
Iced handkerchiefs
Iced handkerchiefs
Glycerin Suppository
Iced handkerchiefs
Profuse sweating
Profuse sweating
Perspiring freely
Perspiring freely
Perspiring freely
Perspiring profusely
Glycerin Suppository
Blyderin Suppository
Perspiring
Relapse

Name J. D. (male) Occupation Carpet Weaver Diagnosis

Age 25 years. { S / M } Residence Termination

Dr Aytoun, Bonnyrigg. *Case I (continued)*

March

Date 1892	11		12		13		14		15		16		17		18		19		20		21		22		23		24		25		26		27		28		29		30	
Day of Disease / Temp. F.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.	M	E	M.	E.	M.	E.	M.	E.	M.	E.	M.	E.
Pulse	100	101	100		100	104	86	98	84	100	88	100	90	90	95	90	80	96	70	76	83	70	76	64	70	76	74	62	72	68	76	76	72	76	78	76	86	72	84	66
Respiration	22	24	20		21		24		18		18	26	20	24	20	20	26	20	24	20	19	20	21	20	24	20	16	20	20	22	20	22	19	20	20	20	20	20	20	17
Motions	1	0	0	0	0	1	0	1	0	0	0	0	1	2	2	1	0	2	1	1	1	1	3	1	1	1	2	0	0	0	0	1	1	0	0	0	1	1	2	1

Name *J. D.* Occupation Diagnosis

Age *25 years* S / M Residence Termination

Briefly stated, the temperature remained high till February 28th (the 23rd day in bed), when it came down, profuse perspirations having occurred once or twice a day from February 20th to February 28th, both days inclusive.

The temperature kept down for eight days: and on March 8th a relapse of the fever began, and lasted for twelve days, the temperature becoming normal on March 20th, and not rising again.

A peculiarity of the temperature for the first nine days that it was taken, was that it was of the inverted type, being higher in the forenoon (10 a.m.) than at night (9 p.m.), those being the hours when it was taken.

The rash appeared on the abdomen first, on February 12th, the seventh day in bed, and continued to come out in successive crops till the temperature came

down. The rash, which was very abundant, occupied the abdomen, chest, and back, and was also specially marked over both hip joints and the outer side of both thighs. It was first noticed over the hips and thighs on February 14th. Each spot began as the usual rose coloured papule, and in nearly every instance, within forty-eight hours of its appearance it had become vesiculated, with a pointed apex. Some of the later spots became vesiculated within an hour or two of their first appearance. It was noticed that each spot disappeared, after lasting about five days, leaving a deeply pig-mented mark. The spots had all disappeared by March 11th.

The pulse in this case was persistently slow during the primary attack and the relapse.

Spontaneous gurgling in the

abdomen was frequently heard during the second and third weeks of the primary attack and during the relapse. Constipation was present throughout the ill-ness till the relapse occurred when he had diarrhoea. The diarrh-oea was easily kept in check by salicylate of bismuth.

From February 15th to February 28th, muttering delirium occurr-ed every night and sometimes in the daytime. He once or twice micturated unconsciously. He became very deaf about February 28th, and this symptom lasted for a week.

He was, by February 28th, extremely emaciated, could hardly move in bed, and was covered all over the trunk with sudamina. It was with great difficulty that a bedsore over the sacrum was prevented from forming.

The urine remained free from

albumin throughout the whole illness.

The bronchitis, after persisting in a very severe form during the primary attack, gradually cleared up during the period of relapse and subsequent convalescence.

The patient was allowed to get up for a few minutes for the first time on March 29th, he having been in bed for fifty two days. He made a slow but per-fect recovery, the last sign of his illness to disappear being oedema of both feet and ankles which persisted for several months. He desquamated over the whole body, feet and hands included, during convalescence.

Case II. R. D., aged fifty three years, a stonemason, the father of Case I, and residing in the same house that his son was nursed in. He had generally

had good health, but had been troubled with a cough and loss of appetite for several weeks before he was laid up.

On March 25th 1892, while Case I was convalescing after his relapse, he went to work as usual, but felt chilly in the morning. The chilly feeling became worse during the day, and he had difficulty in walking home in the evening owing to weakness.

Shortly after reaching home, he had four or five severe rigors. He was put to bed at once.

I first saw him on March 25th, at eight o'clock in the evening. He complained of severe headache, pain in the back and limbs, tightness behind the upper part of the sternum, and a feeling of chilliness. He had total loss of appetite and felt thirsty.

His tongue was moist and had a white coating on the dorsum.

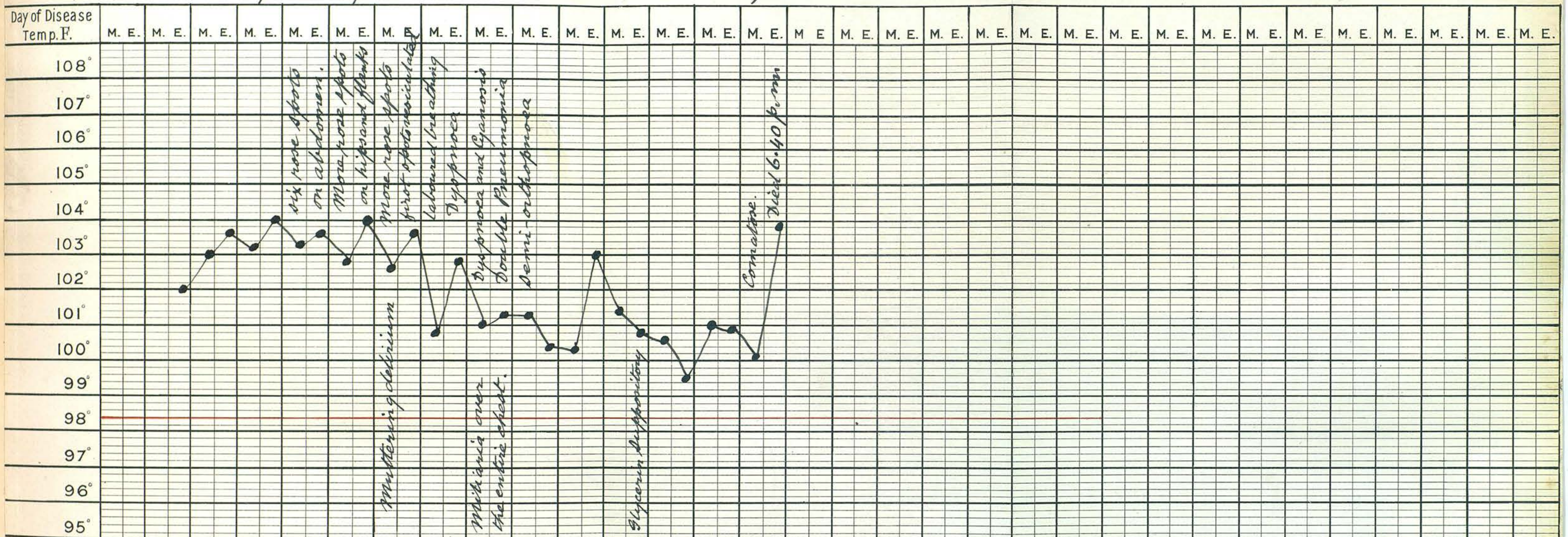
The fauces and pharynx were much congested. There were signs of marked bronchitis all over both sides of the chest.

The pulse was 78 beats per minute, regular, and full.
Heart sounds normal.
Respirations were twenty per minute and of natural character.
The temperature was 102°7.
The bowels had acted on the previous day, but not on March 25th.
There had been no diarrhoea.
The urine was concentrated, and on cooling had a large deposit of dark red urates. It contained no albumin.
There were no spots on the skin.

In this case, as the bronchitis was severe and the patient elderly, alcohol was given early, in the form of port wine at first. A mixture containing ammonium carbonate, nux vomica,

Dr. Aytoun, Bonnyrigg. *Case II*

Date *1892* — *March* 24, 25, 26, 27, 28, 29, 30, 31; *April* 1, 2, 3, 4, 5, 6, 7



	24 M	24 E	25 M	25 E	26 M	26 E	27 M	27 E	28 M	28 E	29 M	29 E	30 M	30 E	31 M	31 E	1 M	1 E	2 M	2 E	3 M	3 E	4 M	4 E	5 M	5 E	6 M	6 E	7 M	7 E
Pulse				78	76	86	78	90	74	77	80	70	76	92	90	92	96	86	92	96	90	104	102	102	117	108	118	117	160	150
Respiration				20	20	24	19	25	21	22	20	26	24	28	32	29	31	30	26	29	27	30	31	33	32	29	37	37		
Motions		1	0	0	0	1	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0

Name *R. D.* Occupation *Stonemason* Diagnosis

Age *53 years* { ~~S~~ / M Residence Termination

and senega was prescribed.

The temperature here kept continuously high till April 7th, when death occurred.

This patient generally slept well at night during his illness. The cough persisted throughout the whole attack, but was generally quite loose, and the expectoration continued to be free till towards the close of the case. The head-ache disappeared on March 28th, on which day, for the first time the rash appeared. It consisted of six ordinary rose spots over the abdomen. Spontaneous gurgling in the abdomen had now become very obvious, and it continued more or less every day till the case terminated. More rose spots came out on the hips, flanks, and thighs, on March 29th. On March 30th fresh rose spots had appeared, by the forenoon, on the chest and abdomen,

and it was noticed that every spot which had first come out was distinctly vesiculated. The vesicle at the apex of each spot was of a pearly white colour.

On March 30th, in the evening, the spots were nearly all vesiculat-ed, giving to the finger when drawn over them the sensation of passing over a mildly sharp point.

The patient was now much weaker, and muttering delirium began to be a prominent symptom: the delirium persisted throughout the rest of the illness. Strychnine was now added to his mixture, and brandy given instead of port wine.

On March 31st the breathing had become rather laboured and dyspnoea was present. The tongue was still moist, and was coat-ed with a yellowish fur.

On April 1st the dyspnoea con-

-tinued, and slight cyanosis was noticed about the lips and cheeks. The cough had now become very frequent and distressing. Physical signs of secondary pneumonia were present at the base of both lungs. The entire chest was covered with miliaria. The patient had hitherto taken liquid nourishment well.

April 2nd. The tongue was moist and coated as before. The physical signs of pneumonia had extended higher up the back of the chest and to the infra-axillary regions. Marked dyspnoea and semi-ortho--pnoea were present.

April 3rd The tongue was now dry. He was in a semi-comatose state from which he could be roused with difficulty. The breath--ing was stertorous and the lower jaw hanging down. The sputum was now black in colour and easily expectorated.

April 4th. The tongue was still dry and coated with brown fur. The teeth were thickly covered with sordes. He now refused all nourish-ment except milk and brandy. A glycerine suppository was used which produced one motion.

April 5th Patient had slept during the night and had had much muttering delirium. He was coma-tose. The sputum was now puru-lent

April 6th Patient was still coma-tose but could be roused. The tongue was dry and thickly coat-ed. Carphology was now present. The abdomen was markedly tumid. Seven rose spots were present on it, but the presence of sudam-ina made it impossible to deter-mine whether they were acumin-ated or not.

April 7th. The comatose con-dition was still present. The breathing was very rapid and

laboured. The pulse was very rapid and feeble, and could not be counted satisfactorily. In the afternoon it became intermittent: and he died at twenty minutes to seven in the evening.

I have given the notes of these two cases with some detail in order to shew the severity of the disease in each case, and the points in which they resembled each other.

Case I and Case II were examples of a severe type of Enteric Fever; and I think it is probable that their course would have been somewhat similar if Case II had not developed pneumonia. In both cases the pulse was persist--ently slow: the temperature high: constipation present: and there was great prostration, with mark--ed nervous symptoms. The rash in each case was acuminated, and had the same general distribution;

and it was practically the same in amount during the time that the two cases could be compared with each other.

Spontaneous gurgling in the abdo-men was marked every day in each case after the end of the first week. I do not here refer to gurgling on pressure over the right iliac fossa, a method of examination which I have never used, and which I believe to be without value.

It is interesting to note that Broadbent (1, p. 1682) says that gurgling on pressure over the right iliac fossa is only present in those cases which have diarrhoea as a symptom: and that Osler (7, p 25) says "gurgling in the right iliac fossa exists in a large proportion of all the cases, and indicates simply the presence of gas and fluid faeces in the colon and caecum." I have referred to many

works upon this point, and in none of them is spontaneous abdominal gurgling mentioned as a symptom, except that Eustace Smith (q) says, speaking of the early stage of the disease "borborygmi are frequent". One or two refer to the occurrence of gurgling in the right iliac fossa.

I have noticed in a large pro-portion of my cases that, about the end of the first week, both in cases having diarrhoea as a symptom and in those with constipation, a distinct clicking or gurgling sound, evidently due to bubbles of gas passing through liquid, can be heard over the abdomen, apparently coming from various parts of it; this usually persists through the second week, and is, I think, a symptom of some value in a doubtful case.

The attempt to elicit gurgling by pressure over the right iliac fossa is sometimes resented by the patient;

and if he knew the state of his intestine about this region he would be inclined to do so still more.

Case III. J. D., a girl aged four-teen years, residing in the same house as cases I and II. She was a sister of Case I, and daughter of Case II. She had always had good health till about the time of her father's death, which occurred on April 7th. Since then she had felt very weak and easily tired, had lost her appetite, and occasionally felt chilly and rather sick. Her mother had given her a dose of compound rhubarb powder on April 13th, which had acted freely but did not produce any improvement.

I first saw her on the morning of April 15th. She was doing household work at the time. She had slight headache, took little

Dr Aytoun, Bonnyrigg. Case III

April

Date 1892. 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

Day of Disease	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M E	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.
Temp. F.																												
108°																												
107°																												
106°																												
105°																												
104°																												
103°																												
102°																												
101°																												
100°																												
99°																												
98°																												
97°																												
96°																												
95°																												
Pulse									100	99	97	95	100	101	98	88	102	49	72									
Respiration									24	23	24	22	25	25	26	24	25	20	24									
Motions							2	0	0	0	0	0	1	1	0	1	1	0	0	0	1	0	1	0	1	0	1	0	0

Patients father died

Dose of Compound Rhubarb bowels

Three distinct rose spots on abdomen

Large raised rose spots on abdomen chest & hips

Rose spots quite distinct

Six Large raised rose spots on Abdomen, hips, and thighs

More rose spots.

Rose spots over right hip are very large: two quadrilateral.

Rapid and perfect recovery.

Name Janet D.

Age 14 years S

Occupation

Residence

Diagnosis

Termination

interest in anything, and fainted while I was examining her.

The tongue was moist and had a thin white coating on the dorsum. She had a slight cough with mucous expectoration.

Pulse 100 per minute. Heart normal. Respirations 24 per minute. Temperature 100·8°F.

There were no spots visible on the skin.

She was put to bed and ordered liquid nourishment.

The temperature continued to be raised till April 25th when it came down to normal: it was never at any time above 101°F. when taken in the forenoon.

The pulse rate varied from 72 to 102 beats per minute.

On April 17th several rose spots came out on the abdomen; and they continued to appear on the abdomen and chest, but in small numbers, for eight days. On April

19th the spots came out also on both hips and the outer part of the thighs.

A peculiarity of the spots was that they were nearly all of larger size than in cases I and II. I noticed on April 25th that the spots over the right hip were the largest of them all; and that two of them were of an irregularly quadrilateral shape — a shape that I have never seen since in an enteric fever rash. They all disappeared completely on pressure. None of these spots became vesiculat-ed.

Spontaneous abdominal gurgling was heard nearly every day while the temperature was raised. This patient had very slight diarrhoea during her illness and the tongue was never dry.

She felt well all the time that she was in bed, — so well in-deed that it was with some

difficulty that she was persuaded to remain there. She was allowed to get out of bed on April 26th; and she made an uninterrupted and rapid recovery. The cough disappeared during convalescence.

This is an example of an extremely mild attack of enteric fever, which presented a few of the characters of the disease as it occurred in cases I and II. Thus, the pulse was slow, there was little if any real diarrhoea, and the distribution of the rash was similar, notably occurr-ing over the hips and thighs.

IX. Whether, if enteric fever should spread from one patient to a second person, other things being equal, the attack in the second person, and the amount of rash present, will tend to be the same as in the first case.

This point, I think, requires

to be divided into two sub points—

(a) When no antiseptic precautions have been taken; and

(b) When antiseptics have been used before the second case became infected.

(a) When no antiseptic precautions have been taken between the occurr-ence of the first case and the infection of the second person, or their use has been discontinued for some time before the infection of the second person, I have noticed that the attack and the amount of the rash in the second case tend to be the same as in the first case, or even more severe.

Murchison long ago pointed out the resemblance which cases of enteric fever occurring in the same house bear to one another. This is due, I believe, to such cases being infected by the same strain of Bacillus Typhosus.

When Case I turned ill, anti-
-septic precautions were rigidly
enforced during the whole of
his primary attack, with the result
that no other member of the family
took the disease then. But I
have reason to believe that at the
time of his relapse the precau-
-tions were stopped for some
time as he was supposed to be
over his illness. It was at this
time that Case II became in-
-fected (during the practical
absence of antiseptics), and the
character of his attack and the
amount of his rash were almost
the same as in Case I.

In Case II the type of the rash
and its distribution were also
the same as in Case I. This will
be referred to later.

I will also mention the follow-
-ing instance of infection spread-
-ing through the members of a
household in the absence of anti-

- septics.

A boy, aged about fourteen years, developed enteric fever, having become infected while away from home. He came home feeling rather ill, but did not go to bed. No antiseptic precau-tions were taken till the tenth day of his illness. A fortnight after he came home three other members of the family were almost simultaneously attacked with enteric fever in a severe form and one of them died from it. The rash in all these cases was not very copious, was of the ordinary type, and was limited to the abdomen, chest, and back.

(b) When antiseptics have been used before the second case became infected. I have noticed that in such instances the second person has usually a milder

attack than was present in the first case, the disease being a somewhat abortive form of that in the first case: and that the amount of the rash tends to be rather less.

In both (a) and (b), the distribu-tion of the rash in the second case tends to be the same as that in the first case.

In the time intervening between the development of enteric fever by case II and the infection of Case III, the antiseptic precau-tions were again carried out.

Case III then became infected, but with organisms which had been subjected to the action of carbolic acid to some extent. Her attack was very much milder than that of either Case I or Case II, although some of the characters of the disease as it occurred in Cases I and II were present in her case. Her rash was

of the ordinary papular type, and was smaller in amount than in Cases I and II, but its distri-
-bution was the same as in these two cases.

The following short summary of three cases of enteric fever occurring in one house will also, I think, help to bear out my state-
-ment.

A boy, aged six years, residing at Lasswade, became rather gradually ill. He had no appetite, was very thirsty, and wanted to lie down often. His mother, know-
-ing that Enteric Fever had recent-
-ly appeared in the village, and being afraid of infection, used antiseptics in various parts of the house &c. from the time that he first turned ill.

I first saw him when he had been ill for about five days, and advised that the antiseptic pre-
-cautions should be continued.

A rather abundant rash came out on the abdomen, chest, and back. The temperature continued high till he died from intestinal perforation about the end of the third week.

The abdomen in this case was very tumid and diarrhoea was a marked symptom. The prostration during the course of this case was very great. When perforation occurred the abdomen became enormously distended, liver dulness disappeared, the pulse became thready and he died the same night.

This boy had swallowed a number of very small glass beads about the time that he turned ill. I was shewn one or two of these which had been recovered from the stools. I have never seen a fatal case of enteric fever in a child of this age since, and think that the beads may

have had some connection with the occurrence of perforation; but apart from that it was an unusually severe case all through.

A sister and brother of this boy shewed symptoms of enteric fever about a week after I first saw him. In each case the disease was of a somewhat mild type, having rather more rash than is usual in children, but smaller in amount than in the fatal case. They both recovered. The rash in each case was limit-ed to the abdomen, chest, and back.

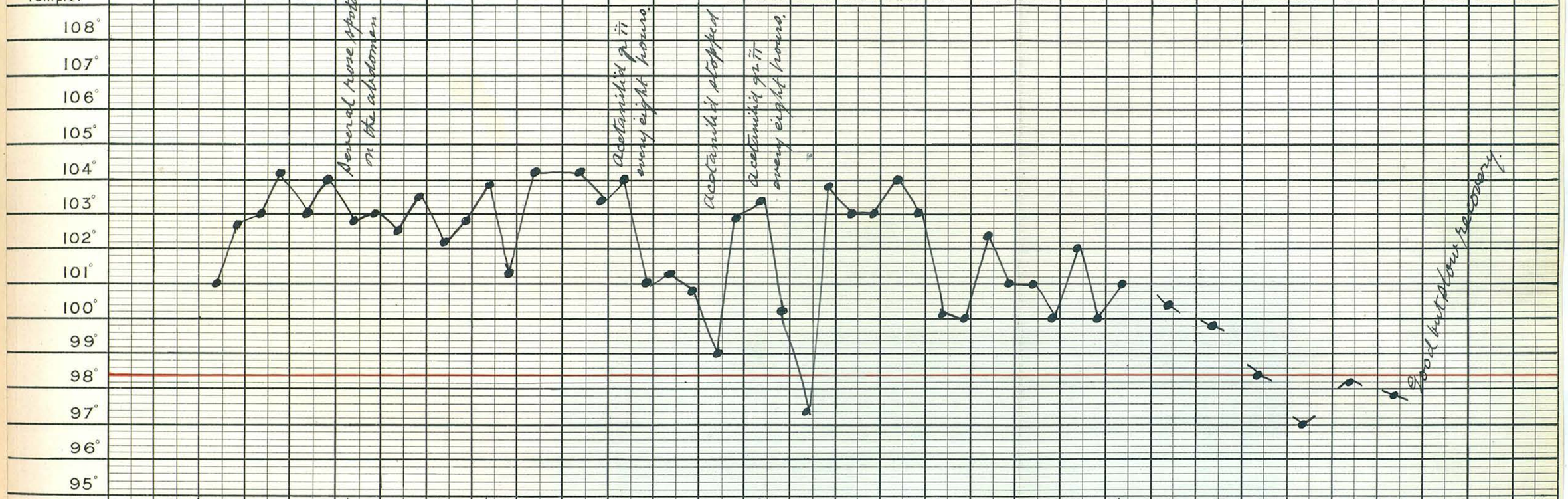
The two following cases also bear upon this point.

Case IV. M.S., a little girl aged eight years, residing at Bonnyrigg. On January 23rd 1892, having previously appeared to be quite well, she rather suddenly became very sick and vomited. She also had diarrhoea, some

Dr Aytoun, Bonnyrigg. Case IV

January. February.

Date 1892	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Day of Disease																														
Temp. F.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M E	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M. E.	M E	M. E.	M. E.	M. E.	M. E.	M. E.
Pulse			132 152	152	144	136	144	136	136		144	148	132	112	150	102	144	144	120	128	128	158	156	128	128	124	198	112	104			
Respiration			28 42	32	48	32	40	40	35		40	48	40	40	36	40	48	36	24	28	25	28	32	48	46	32	29	28	32			
Motions	2	3	1 0	1 0	1 0	2 1	2 0	2 1	3 0	0 1	0 1	1 0	2 0	2 2	3 1	1 3	2 0	1 0	2 0	0 0	0 0	1 0	1 0	0 0	0 0	1 0	0 0	0 0	0			



Name M. D. (girl) Occupation Diagnosis

Age 8 years { S / M } Residence Termination

headache, and thirst.

I first saw her on January 25th in the forenoon, that being her third day in bed. She had still headache, sickness, thirst, and diarrh-oea, the motions being light colour-ed and of pea soup appearance. The tongue was clean and moist. No spots were present on the skin and the abdomen was not tender. Pulse 132 per minute. Respirations 28 per minute. Temperature 101°7.

Antiseptic precautions were at once adopted, to, if possible, pre-vent the disease from spreading.

Diarrhoea was a marked symptom during the first three weeks of this child's illness.

January 28th. The previous symp-toms were still present. Her mouth was sore; the tongue was dry, and had a white coating on the dorsum in patches, the papillae being very prominent; and much spont-

-aneous gurgling in the abdomen could be heard. Several rose spots had now come out on the abdomen. A cough due to bronchitis had now become a marked feature of the case.

January 29th. The tongue was still dry and white, diarrhoea was still present, and the abdomen was very tumid. She was now complete-ly prostrated and looked perious-ly ill. She was very fretful and complained of pain in the abdomen. Pulse 144 per minute: respirations 40 per minute: temperature 102·5°F.

January 30th. She felt very sick. The tongue was moist with a thick coating on it. Gurgling sounds in the abdomen were still frequently heard. She cried occas-ionally as if in pain.

January 31st. She complained of pain over the abdomen. The cough was now much more

distressing.

February 2nd. The tongue was dry and white. The gurgling in the abdomen was very marked. The cheeks were very much flushed, being in marked contrast with the rest of the face. She had had a very restless night.

February 3rd. The tongue was now quite dry and hard. Fresh spots had continued to appear every day, chiefly over the abdomen and chest.

February 4th. The tongue was now moist, and she felt better.

February 6th. She had been very restless all night. The diarrhoea was more severe than before. She was rather deaf. Pulse 150 per minute: respirations 36 per minute: temperature 103·4° F.

The temperature in this case continued to be high till February 13th, when it was 102° F in the forenoon. The pulse was then

158 per minute, and the respira-
-tions 28 per minute.

The deafness improved on Feb-
-ruary 13th, and disappeared
soon afterwards. The tempera-
-ture came down by lysis,
becoming normal on February
17th, that being the twenty-sixth
day of her illness.

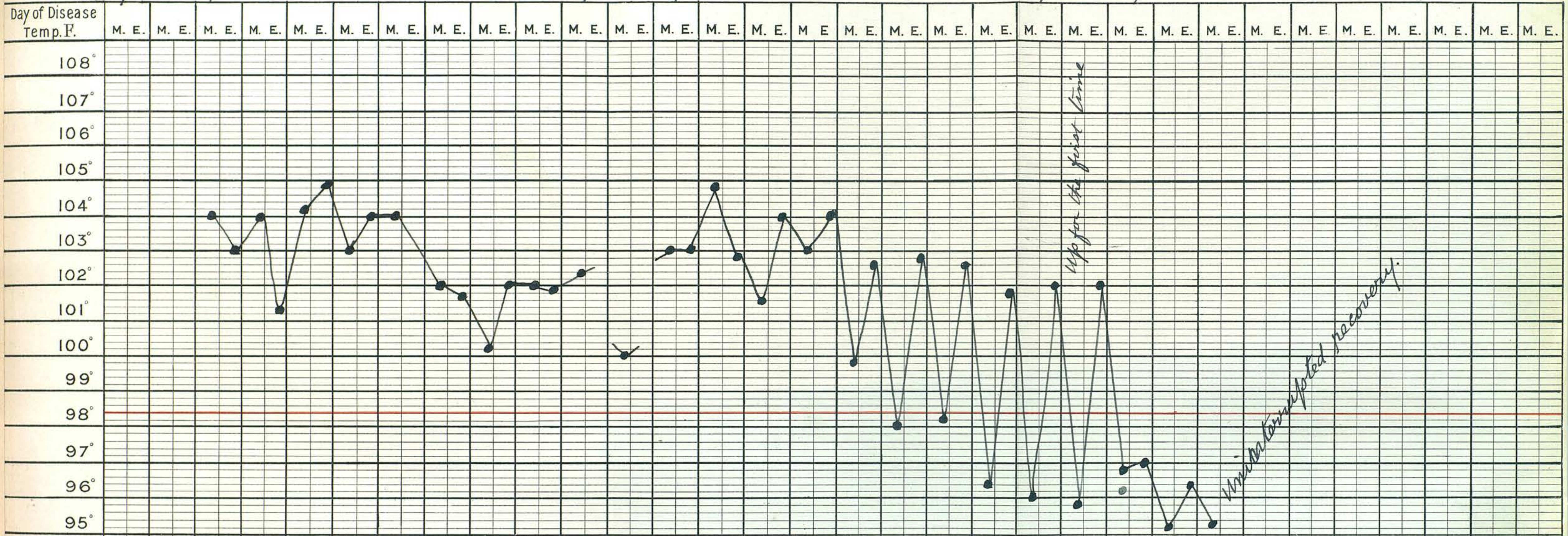
During the second and third weeks
of her illness acetanilid in two
grain doses was given every eight
hours while the temperature was
at or above 103° F. This may
account for some of the peculiar-
-ities in the temperature record
during that time.

The cough gradually improved
as the temperature came down,
and she felt better every day.
She made a perfect recovery, but
the pulse was rather long in
becoming normal.

Case V. Maggie S. aged nine

Dr. Aytoun, Bonnyrigg. *Case V*

Date *February 1892* — *March*



Date	Pulse M.	Pulse E.	Respiration M.	Respiration E.	Motions M.	Motions E.
Feb. 7						
8						
9	158	144	36	28	0	0
10	152		32		1	0
11	128		24		0	0
12	128		28		1	0
13	124		32		0	0
14	116				0	0
15	100		28		3	0
16	116		36		0	0
17	124		31		1	0
18	108		32		1	0
19	124		28		0	0
20	132		32		1	0
21	124		28		1	0
22	132		25		no diarrhoea	
23	108		26			
24	100		28			
25	98		28			
26	88		28			
27	84		26			
28	92		28			
29	96		24			
Mar. 1	104		24			
2	96		24			
3						
4						

Name *Maggie D. (girl)* Occupation .... Diagnosis ....

Age *9 years* { S / ~~M~~ } Residence .... Termination ....

years, a sister of Case IV and resid-
-ing in the same house as that
in which Case IV was nursed.

She seemed to be quite well
till February 7th, that being the
sixteenth day of her sister's illness.
On that day she felt chilly, com-
-plained of headache, had loss
of appetite, and was very thirsty.
No diarrhoea was present.
She was put to bed on February
8th. I first saw her on February
9th, the third day of her illness.
Her tongue was then moist, with
a thin white coating on the
dorsum. Constip-ation was present;
and this symptom continued
throughout her illness.

She had a dry cough. The pulse
was 158 per minute: respirations
36 per minute: and temperature
104°F. She was in good spirits
and her expression was quite placid:
she said that she was quite
comfortable. She did not complain

of headache. No rose spots were present.

A few rose spots appeared on the abdomen and chest a day or two later; the total number was smaller than in her sisters case.

She complained of hunger a day or two after going to bed, and felt hungry during the rest of her illness.

February 12th. She felt quite well and wanted to get up.

February 14th. She still felt quite well and wanted food. The cough was very slight. Very little spontan-eous gurgling was heard at any time in the abdomen, and she had never at any time pain or tenderness there.

Throughout her whole illness she was remarkably cheerful, and could laugh readily at any-thing in the least degree amus-ing. She had no prostration; and, but for the rise of temperature,

quickened pulse and respirations, and the slightly furred tongue, she really seemed to be quite well. The temperature began to fall on February 14th and came down by lysis, becoming subnormal on February 29th, the twenty-third day of her illness. The cough was very slight all through her illness. She wanted to get up so much every day after February 11th that I allowed her to rise on February 28th, and every day afterwards. Her recovery was perfect and rapid. Her illness seemed to be a mere shadow of the attack which her sister had suffered from, resembling in this respect Case III.

This case was certainly not an example of the Abortive form of enteric fever: neither was it a case of what is described as the Mild form of enteric fever, in which the temperature

does not exceed 103°7.
It was, I believe, an attack of enteric fever where all the symptoms resulted from an infection by a pure culture of Bacillus Typhosus, all septic organisms having been destroyed in the infecting discharges by the use of antiseptics before she became infected, — in other words a non septic case.

I believe that in most very severe cases of enteric fever, while the Bacillus Typhosus and its toxins are the cause of a certain amount of the rise of temperature, quickening of pulse and respira-tions, bronchial catarrh, inflamma-tory changes in the lymphoid tissues of the intestines, and of the appearance of the ordinary rash and of its distribution: many of the symptoms are much aggravated, and fresh ones develop-ed, by the absorption of septic

organisms and their products which have been present along with the Bacillus Typhosus in the infecting material, or have been previously in the intestine, and have gained an entrance probably through the intestinal lesions.

It is well known that in enteric fever the bile loses its normal slight antiseptic characters, and allows the bacilli typhosi to grow readily in it, especially in the duodenum and in the gall bladder: and that the normal resisting power of the intestinal secretions to the growth of pyogenic organisms in the intestines is reduced enormously, if not completely destroyed, so that such organisms multiply with great rapidity in the ileum and colon. This being so, it can be readily understood that the bacillus typhosus, against whose action the normal intestine can offer but little resistance, contributes

in more than one way to the occurrence of mixed infection, by permitting of the enormous development of adventitious organisms in the intestines, and by so damaging the lymphoid tissues in certain parts as to allow some of these organisms to enter the blood and tissues.

The poison contained in the discharges from such a case of mixed infection is of a most virulent nature, containing as it does the elements for producing a similar mixed infection. Dreschfeld (16, p.800) says "in the blood taken from the finger tip, or from a vein, (in a case of enteric fever) Eberths Bacilli have very rarely been found, and cultivations have either given negative results, or have shewn the presence of Streptococci or Staphylococci, indicating a mixed infection."

J. Lorrain Smith (6, p. 1087), writing a few years later, states that by using larger quantities of blood, 75 per cent of positive results as regards Bacillus Typhosus have been obtained.

Vincent (16, p. 802) observed that enteric fever is more severe when streptococci are found in the blood.

Dr J. J. C. Nash (13), who had charge of a large number of cases of enteric fever which were attri-buted to the consumption of shell-fish, found that his cases of enteric fever which followed on the eat-ing of raw shellfish, whether oysters, mussels, or cockles, were exceptionally severe in general clinical character: and that the cases which followed on the eating of cooked shellfish were clinically of a much milder type in general character.

As Dr Savage (13, p. 234) found

that a minutes boiling did not destroy all the bacilli in such shell-fish, it seems probable that the heating destroys the less resistant forms, just as carbolic acid might do, leaving the more resistant forms still alive and thus producing less of a mixed infection when swallowed.

The action of carbolic acid upon the discharges in a case of mixed infection, if used of insufficient strength, must be to destroy the vitality of those organisms which have a rather low resisting power to its action, leaving the Bacillus Typhosus, and other organisms of higher resisting power if present, undestroyed, but possibly modified to some extent.

Holtz (Zeitschr. f. Hygiene VIII, p. 143, 1890), quoted by R. Von Jaksch, (10,) found that the development of bacilli typhosi was suspended in presence of 0·1 per cent of carbolic

acid.

Osler (7, p. 4) states that bouillon cultures of bacilli typhosi are destroy-ed by carbolic acid, 1 to 200, (that is 0.5 per cent).

Dreschfeld (16, p. 799) says, "in isolating the bacillus typhosus from the faeces, it is usual to mix three volumes of the faeces with one volume of a one per cent solu-tion of phenol, in order to pro-vide a mixture containing a quarter per cent of phenol. It is found that phenol in this proportion generally kills those organisms which, by producing liquefaction of the gelatine, would interfere with the plate cultures, but does not hinder the growth of typhoid and some other bacteria."

In a series of experiments carried out by David Somerville and J. T. Ainslie-Walker (12), they found that a one per cent solution of phenol did not destroy bacilli

typhosi cultures in two and a half minutes, but did destroy them in five minutes; and that if a trace of solution of sulphuretted hydro-gen is present in the broth in which the subcultures are made, it requires seven and a half minutes exposure to a one per cent solution of phenol to destroy the bacilli typhosi.

It is well known that when an epidemic of enteric fever is draw-ing to its close, the later cases are usually of a mild character. The reason for this is, I think, well given by Dr Peters (11,) who says "when we reflect upon the possible origin of bacterial life from the vegetable world; upon the fact, of which we can now have no doubt, that its stay within the animal tissues can only be maintained by constant battle; it is not difficult to believe that continued passage from case to case must ultimately

exhaust its forces and necessitate a return to its true home in the sapro-phytic world, there to renew its depleted energies."

But in my cases the transition from a severe case to an exceedingly mild one was always much too sudden to be accounted for in this manner.

X. (a). What determines the time of occurrence of the rash.

The skin consists of the epidermis and the corium. The superficial layer of the corium is raised into minute papillae which penetrate into the deepest layer of the epidermis. Beneath the corium is the subcutaneous tissue.

Two main somewhat parallel plexuses of small bloodvessels and lymphatic vessels are situated throughout the whole extent of the skin and subcutaneous tissue. The deeper plexus is situated in

the subcutaneous tissue, and it follows the plane of the subcutaneous tissue throughout the body and limbs. The more superficial plexus is situated in the corium just below the bases of the skin papillae, and it follows the direction of the surface of the skin. Numerous small blood and lymph vessels connect the more superficial with the deeper plexus. The superficial plexus sends usually one or more loops of capillary blood-vessels and one or more lymphatic blind shoots or capillary loops to each skin papilla. The afferent capillary bloodvessels to the papillae emerge as efferent capillaries and join the small veins in the plexus. The lymphatic capillary blind shoots in the papillae join lymphatic vessels in the plexus at the bases of the papillae, and terminate near the apices of the papillae in rounded extremities which are

either closed, or, as Klein thinks, com-
-municate with surrounding lymph
spaces by means of true stomata.
The skin papillae vary in size, some
being simple and some compound.
My measurements of those on the
fingers give the average diameter
of each at the base as about ·2
millimetre. Over the skin generally
they are about ·1 millimetre in
diameter.

Intercellular lymph spaces occur
in the deepest layer of the epiderm-
-is which communicate in some
way with the lymphatic system
of the derma. Similar lymph
spaces and channels without inde-
-pendent walls are found in all parts
of the corium, and especially in the
interstices of the fibrous tissue of the
corium and between the cells of the
papillae (20). The hair follicles, sebace-
-ous glands, and sweat glands, have
their own systems of bloodvessels and
lymphatic capillaries (Neumann, Klein).

Involuntary muscle bands, arranged in various ways, are distributed universally in the skin and sub-cutaneous tissue. When the skin is exposed to a cold medium these muscles contract generally, and, aided by the muscular fibres of the walls of the skin arterioles which act in concert (21), lessen the amount of blood in the skin. Exposure to heat causes these muscles to relax, just as it causes the muscles in the arteriole walls to relax, reflex-ly. In this manner the skin capillaries react to heat and cold as if they had muscular walls.

The lymphatic capillaries in the skin are also compressed when the skin is cold and relaxed when it is warm.

As the cutaneous blood capillaries are, next to the capillaries of bone marrow, the largest in the body — being about one twelve-hundredth of an inch in diameter (22) — :

and as they are forcibly compressed by the neighbouring unstriped muscles when the skin is exposed to a colder medium, and are forcibly distended (their walls being somewhat elastic) by the blood pressure from dilated arterioles when the skin is exposed to a warmer medium: the difference in calibre of these capillaries when the skin is cold and when it is hot must be very considerable — greater probably than is the case with any other capillary vessels in the body.

Normally, the blood makes its way through the capillaries in a somewhat irregular stream, moving at a rate of about .5 millimetre per second, and having a pressure of between twenty and forty millimetres of mercury (23). The average length of a capillary is about .5 millimetre, so that any particle in the blood in a capillary, which

does not adhere to the capillary wall, remains in that capillary for about one second.

The capillary walls permit liquids to pass through them readily: lymphocytes and leucocytes can also pass through them, but normally not in large numbers: and lymph from lymphatic vessels sometimes contains a few red blood corpuscles which must have passed through the walls of blood capillary vessels. It is known that bacilli, especially motile bacilli such as bacilli typhosi, can pass readily through a capillary wall when they are single: and there can be little doubt that when such bacilli are agglomerated together into small masses, some of these small masses of bacilli may occasionally pass through the walls of blood capill--aries even when these capillaries are not much dilated.

When the skin is warm and

such small bacillary masses are circulating with the blood, the most favourable conditions are present for the escape of these little masses through the skin capillary walls because then (a) the capillaries, which are naturally of large size, are dilated and probably contain a larger number of such masses, (b) the intracapillary blood pressure is much increased, and (c) the capillary walls are tense and thinned.

In enteric fever each rose spot is the manifestation of a local inflammatory reaction due to the lodgment of one or more clumps of agglutinated typhoid bacilli in the small lymphatic vessels or lymph spaces of the skin papillae. These bacilli are thus shut off from the general circulation. As bacteriolytic substances accumulate in the blood, they penetrate to these bacilli and destroy them, and the

rose spot gradually disappears. The circulating blood itself is an unfavourable medium for such small masses of bacilli to survive very long in, and it is probably only when they reach very small lymph channels or capillary vessels, such as those of the liver, skin, kidneys, &c, that they can produce such a local reaction. As each rose spot is about three millimetres in diameter, and each skin papilla is not more than one or two tenths of a millimetre in dia-meter, it is probable that the bacilli multiply after lodgment so as to involve a number of papillae in the inflammatory process.

The rash generally first appears from the seventh to the twelfth day of the disease, that is, at the time that the agglutination reac-tion is usually first obtainable, and when the establishment of

immunity has begun. At this time the proliferative enlargement of the lymphoid tissues of the ileum and spleen is at its height, and typhoid bacilli exist in numbers in the centre of the follicles, in the lymph-atic vessels of the follicles, and in the submucous tissue, of the intestine. Large numbers of bacilli have long before this time reached the blood by means of the veins, thoracic duct, &c. The blood destroys a great many of these bacilli, the liberated toxins causing many of the symptoms of the disease. It is probably this destruction of bacilli in the blood that made most of the earlier attempts to isolate the bacilli from the blood unsuccessful. By now using larger quantities of blood — five to ten cubic centimetres — the bacilli have been cultivated from it in about seventy five per cent of cases by some observers.

The bacilli are more likely to escape rapid destruction when they occur in masses such as are formed when agglutination of them takes place, but even such clumps of bacilli are too quickly diminished in size or destroyed by the blood to permit of the formation of ordinary emboli.

It seems probable that when these agglutinated masses of bacilli are driven into the cutaneous capillary bloodvessels, some of them pass through the capillary walls and get caught by the minute origins of the lymphatic vessels and the lymph spaces in the skin papillae, where the more active strains may multi-ply by division, and thus cause the appearance of the rash.

That the bacilli in the rose spots are present in numbers, and are alive, can be shewn by pricking a rose spot and touching the

exuding fluid with a suitably pre-
-pared gelatine plate: in many
cases the bacilli will grow in the
gelatine. Agglutination causes them
to run together but does not des-
-troy their vitality.

The rose spots are thus merely
an accidental occurrence in the
course of a case of enteric fever,
but the accident is so likely to
happen that they do, in fact,
appear in about seventy-seven
per cent of all cases.

For the rose spots to develop,
then, it seems that agglutination
of a number of bacilli must
occur, as individual bacilli would
not produce such a local reaction.

The rash of enteric fever can
therefore only occur at that period
of the disease during which agglu-
-tinins and bacilli are both present
in the blood in considerable
quantities, and when at the same
time bacteriolytic substances are

not present in such excess as to destroy all the bacilli in the blood: in other words the rash can only come out after agglutinins have been formed in the blood and before complete immunity has become established.

When any specimen of blood serum gives a positive reaction to Widal's test, that serum (and therefore the blood of which it formed a constituent part) contains agglutinins.

A positive reaction to Widal's test has been obtained as early as the fourth or fifth day of the disease, shewing that agglutinins are sometimes present in the blood during the invasion period of enteric fever; but this is exceptional, and it is usually after the end of the first week that the positive reaction can first be obtained distinctly.

The enteric fever rash does not usually occur before the seventh day because then, although bacilli typhosi are present in the blood, the amount of agglutinins in the blood is insufficient to cause agglomeration of the bacilli into clumps (a condition which is necess--ary for the formation of rose spots), its tendency to cause agglutination being neutralized by the movement of the blood and the constant occurrence of bacteriolysis.

The rash first appears at that period of the disease when agglut--inins have accumulated in the blood to such an extent that agglutinated masses of bacilli begin to circulate in the blood stream without being all destroy--ed by bacteriolysis. This usually first happens between the seventh and twelfth days of the disease.

It continues to come out during the rest of the fastigium

and, though commonly to a less extent in my experience, during defervescence, because during these periods bacillary clumps are still circulating with the blood.

It, as a rule, ceases to appear when the morning and evening temperatures are at or below normal, because then immunity has been established, and no more bacillary masses circulate with the blood, which still contains agglutinat-ing and bacteriolytic substances.

According to Ehrlich's Theory (25 p. 156), the agglutinins consist of the thrust off cell receptors. The original cell receptors having been combined with the bacterial receptors, new cell receptors have been formed in excess and given off to the circulating blood. Thus agglutinins are formed while immunity is being established.

But the amount of agglutinins and of bacteriolytic substances

may vary greatly during the course of a case of enteric fever.

A relapse* in a case of enteric fever is due to (1), a breakdown of immunity, as regards the amount of bactericidal substances only, in the blood: and (2), a fresh invasion of the blood by typhoid bacilli, which are always present in the intestine and gall bladder for a considerable time after defervescence from the primary attack has occurred. It can probably only occur when some solution of continuity in the intestinal or gall bladder wall has occurred, or when bacilli are still present and alive in some capillary lymph space.

* See p. 119

When there is a marked deficiency in both agglutinins and bactericidal substances in the blood, and a relapse takes place, the relapse may

be unaccompanied by the development of any rash. Those authors who maintain that a rise of temperature occurring during convalescence from enteric fever, even if continued for days, is not a true relapse unless accompanied by the rash, might equally well say that a primary attack of enteric fever which had no rash could not be genuine enteric fever.

In health, the blood contains such an amount of substances which are antibacterial, as regards Bacillus Typhosus, that one cubic centimetre of normal blood serum can destroy ten million Bacilli Typhosi when they are suspended in an equal bulk of nutrient liquid (24). Normal blood,

however, contains practically no typhoid agglutinins.

Thus, at the beginning of a primary attack of enteric fever the blood contains bac-tericidal substances but no agglutinins; and this explains the non-occurrence of a rash during the first week of such an attack.

At the beginning of a relapse, on the other hand, the blood contains both bactericidal substances and agglutinins (the bactericid-al substances being in somewhat smaller amount than is usually the case), so that a rash may appear almost at the beginning of the rise of temperature, or it may even precede it.

The presence of agglutinins in the blood is merely a side issue in the establishment of

immunity: the agglutinins are formed, but are not essential to complete immunity. After enteric fever, in most cases, the agglutinating power of the blood, as regards typhoid bacilli, is rapidly lost, except to a very slight degree (26): and yet such a state of the blood is quite compatible with complete immunity.

X. (b.) What determines the distribution of the rash over the skin.

The rose spots generally first appear over the abdomen and the lower part of the chest. Here then there must be some local condition present to account for these clumps of bacilli, of every type of virulence, so frequently being lodged and producing the rose spots.

Dr Greenhalgh (6. p. 1105) suggests, in explanation of this occurrence, that in enteric fever this area of skin presents an inhibition of vasoconstrictor impulses reflexly set up by the intestinal and splenic lesions through nervous influence and that in consequence there is an abnormal facility for the lodgment of these clumps of bacilli in the skin over the abdomen and lower thoracic zone. This theory applies only to the regions mentioned.

I think that the frequency of occurrence of the rash in these areas of skin is due to the coincident action of two causes, which explains not only such local determination of the rash but also the distribution of the rash over the skin generally.

It is probably correct to say that, clinically, the rash is found most frequently over the abdomen,

and that the frequency of its occurrence in other areas of skin is almost in inverse ratio to the distance of such areas of skin from the epigastric region. Thus Osler, referring to the limbs and face, found that out of four hundred and twenty six cases the rash occurred on the upper arms in thirty nine cases, on the thighs in nineteen cases, on the forearms in thirteen cases, on the legs in eight cases, on the face in three cases, and on the hands in one case. In my own practice I have seen the rash more frequently on the hips and thighs than on the upper arms. The only notable exception to this general rule is in the case of the face which is very seldom the seat of the rash.

I need only point out here that the face is always exposed to the air during the whole course of a case of enteric fever: and that

a flushed condition of the face usually only occurs before the erup-
-tive period.

Shortly before the rash first appears the blood contains such an amount of agglutinins and bacilli that the bacilli in it begin to agglutin-
-ate into small masses which cir-
-culate with the blood.

When blood is flowing through an artery, the portion occupying the central part of the lumen of the vessel flows more quickly than that occupying the more peripheral part, and the column of blood becomes divided into the axial stream (containing the corpuscles, which have a higher specific grav-
-ity than the plasma, and some plasma) and the so-called inert layer, occupying the space between the axial stream and the vessel wall. The inert layer consists chiefly of plasma and a few of the white blood corpuscles.

When typhoid bacilli are circulating singly in the blood, many of them probably occupy the inert layer, as their mass is very much smaller than that of any of the corpuscles and their specific gravity is less than that of the red blood corpuscles. Such a situation must favour the occurrence of agglutination of the bacilli when sufficient agglutinins have been formed.

Such masses of agglomerated bacilli, when circulating with the blood, may be regarded as so many very small, slowly dissolving, foreign bodies in the blood. They will be propelled through those skin capillaries which are most dilated in larger numbers and under greater pressure than through capillaries which are less dilated; and in still smaller numbers, if at all, through those skin capillaries which are most

compressed by the contraction of the unstriped muscles of the skin when the skin is cool.

Those masses of bacilli which do enter the skin capillaries which are compressed or not dilated, are in small numbers, are under slight pressure, and are enclosed by capillary walls which are not stretched. The chance of any of them passing through the capillary walls is therefore very much smaller than in the case of well dilated capillaries.

In those skin capillaries which are most dilated the number of bacillary masses is much greater (increasing with the increase of diameter of the capillary), and, owing to the other conditions mentioned, the chance of some of the masses passing through the capillary walls is greatly increased.

It is extremely probable that many of these masses which do

reach ~~the~~ the lymphatic spaces and vessels are destroyed before they can produce any local re--action.

Those areas of skin therefore which are supplied by capillary bloodvessels and arterioles which are most constantly dilated during the eruptive period of the fever should exhibit the rash most frequently, and at the earliest period of the eruptive stage: and the rash should occur with less frequency and, if present, probably at a later date, in those areas of skin which are supplied by capillaries and arterioles which are continuously in a less dilated condition during that time: and with least frequency, or not at all, in areas of skin where, during this period of the illness, the capillaries are compressed and the arterioles are contracted.

The surface temperature, when

taken on the skin over various parts of the body of the same patient, is a good indicator of the state of the skin capillary bloodvessels and arterioles, as regards dilatation or the reverse, in the areas where the temperature is taken: the bloodvessels are most dilated where the surface temperature is highest, and least dilated where it is lowest.

Theoretically, therefore, we should expect to find the enteric fever rash come out with greatest fre-quency on those areas of skin which have, for each individual case, the highest average surface temperature during the eruptive period of the fever: with less frequency on those areas of skin which have a somewhat lower average surface temperature during that time: and with least frequency on those areas of skin whose average surface temperature

is lowest during the time that the rash continues to come out. And, were all strains of Bacilli Typhosi absolutely identical, this would be the case.

As it is, this is almost exactly what is found clinically to be the distribution of the enteric fever rash.

In health the surface tempera-ture is higher over the abdomen than over any other part of the body, it being generally between 93·2°F. and 95°F. (6. p. 834); and the next highest temperatures are usually over the trunk, the tempera-ture becoming lower as the extremi-ties of the limbs are approached unless some disturbing element is present.

It is known that in enteric fever a portion of the rise of internal temperature is due to a relatively diminished loss of heat from the surface, that is to say

although the actual loss of heat from the surface during the fastigium is increased, it is not increased proportionately to the rise of internal temperature.

In taking the surface temperatures of various areas of skin in a person in health, in order to compare them with the surface temperatures of the same areas of skin in a case of enteric fever during the eruptive period, it is necessary to have both persons in bed for an hour or two before taking the temperatures, with the face, neck, and hands, clear of bedclothes, and with the rest of the body covered with the clothes while the temperatures are being taken, as this is the usual state of the skin, as regards coverings, during the eruptive period of enteric fever. It is also necessary that all the surface temperatures should be taken on the same person

and at the same time, in comparing the temperature at one part of the surface with that at another part.

Under these conditions I have frequently found the surface temperature over the abdomen to be, in health, as high as 95·8°F. or even higher.

The following surface temperatures were taken recently in a neurotic person, who was otherwise well, under the conditions mentioned.

Abdomen,

Epigastric region	95·5°F.
Hypogastric region	95·6°F.

Thorax in front,

Right side	94·5°F.
Left side	93·6°F.

Back of thorax,

Right side	94°F.
Left side	93·8°F.

Lumbar region, posteriorly,
{ Middle 95.°7.

Thighs,
{ Right side 94.°7.
{ Left side 94.3°7

Upper arm,
{ Right side 94.4°7.
{ Left side not taken

Forearms,
{ Right side 92.°7.
{ Left side 93.4°7.

Legs,
{ Right side 91.4°7.
{ Left side 93.°7.

Face,
{ Right side 90.°7.
{ Left side 90.°7.

Back of hands,
{ Right side 90.3°7.
{ Left side 87.°7.

Palm of hands,

Right side	90°7.
Left side	90°7.

Feet

Left side	84°7.

(the feet happened to be very cold.)

The surface temperatures vary extremely in health, owing to mus-cular movements, differences in food, &c.

In enteric fever, during the fastigium, where the patient is in bed, and taking usually a fever diet, and where also the changes of internal temperature are generally not very great, some of the disturbing elements are eliminated.

A patient who has enteric fever is usually in bed during the whole of the eruptive period of the illness, and is covered with bedclothes.

The face is always exposed to the air, the hands very frequently, and the feet occasionally. The abdomen is practically always well covered with bedclothes, and in many cases a warm broad bandage is put round it to limit the amount of intestinal catarrh. It will be noticed that the bedclothes will tend to raise the surface temperature of all the parts covered with them equally, while those parts which are exposed to the air will have a lower surface temperature than if they were covered.

In the early period of the eruptive stage of enteric fever the difference between the surface temperature over the abdomen and that over the exposed parts of the skin is greater than in health, because at this stage the cutaneous capillaries react very readily to changes of external temperature.

During the rest of the fastigium the reaction of the cutaneous blood-vessels to changes of external temperature still continues, but is much more sluggish than is the case in health. It is found, however, that the surface temperature over the abdomen rises and falls more regularly with similar changes of the internal temperature than is the case with other areas of skin, and that its surface temperature is usually higher than that of any other part.

During defervescence, the cutaneous capillaries tend to dilate somewhat over the surface generally, and the surface temperature becomes rather higher than in the middle of the fastigium. The rash at this time may still come out, but it is often in small amount as the number of bacillary masses is now much smaller owing to active bacteriolysis and

the approach of immunity.

In a series of five cases of enteric fever quoted by W. Hale White, (6, p. 851) it was found that in each case, when the internal temperature was raised, the surface tempera-ture over the abdomen was always raised also, it being on an average seven degrees Fahren-heit lower than the temperature in the mouth. In the same patients when the temperature taken in the mouth had come down to about normal, the surface temperature over the abdomen had in each case become lower also, being on an average 5.2°F. lower than the temperature taken in the mouth.

Subject to the correction made in a subsequent paragraph in speaking of the effect which differ-ent strains of typhoid bacilli exert upon the distribution of the rash, I think that we can in this manner account for the fact that the

enteric fever rash occurs upon the abdomen more frequently and more early in the disease than upon any other region, and that all the other areas of skin on which it occurs with rather less frequency are situated on the trunk of the body, and that it occurs with least frequency on the areas of skin covering the limbs and face,— the rash becoming more infrequent as the extremities of the limbs are approached, so that it is practically never seen on the feet at all.

But if this were the sole explanation of the distribution of the rash, we should expect to find that in every case where the rash occupied some very unusual position such as the face, it would also be present on every one of the other areas which it more frequently occupies. That is to say, where the rash occurred in an

unusual situation it should only form, in that situation, part of a very extensive rash. This is sometimes the case; but the rash may occupy an uncommon site and be limited to that site.

I shall endeavour to explain how this happens.

I have hitherto spoken of the agglutinated masses of typhoid bacilli as if they acted merely as so many small slowly dissolving foreign bodies as regards their distribution in the small lymphat-ic vessels of the skin, and this, I think, is correct as regards every case of the disease; and I think also that it is almost certain that many of such clumps of bacilli which have become caught in the capillary lymphatics of the skin are destroyed by the blood serum before they can produce rose spots.

When the rose spots are very

numerous, the agglutinating action of the blood upon the bacilli is relatively in excess of its bacterio-lytic action.

When the rose spots are absent, the bacteriolytic action of the blood upon the bacilli is relatively in excess of its agglutinating action: and it is in such cases that I have found the agglutination re-action to be sometimes absent.

The increased dilatation of the capillaries in certain areas of skin, as compared with other areas, during the eruptive period of enteric fever, determines the areas of poten-tial rash, that is, the areas where the bacillary clumps are most likely to be, and frequently are, lodged (without necessarily rose spots developing): and these in a general way correspond with the areas in which the rash is found.

But every clump of agglutinat-

-ed bacilli, when caught in the cutaneous lymphatics, does not pro-duce a rose spot.

If each of two susceptible individ-uals, who were previously equally strong, becomes infected with a pure culture of bacillus typhosus, and if in one case the attack is of exceptional severity and in the other case it is of exceptional mildness, we may assume that probably the strain of bacillus in the severe case is more virulent to man than in the case where the attack was mild: that, in fact, there is a difference between the two strains.

So, I think, when agglutinated bacilli are caught in the cutaneous lymphatics in the areas of potential rash in any case, the individuality of the particular strain of bacillus which is present shews itself. The bacilli of some strains are so rapidly destroyed in every area that no rose spots result. In the

case of another strain of bacillus, those clumps which are deposited in the abdominal area can resist destruction there long enough to produce rose spots, while any clumps which may happen to be deposited in other areas are rapidly destroyed, as the conditions present in these other areas are not suitable for their development so as to produce rose spots. Certain strains of bacilli, which are probably of greater virulence, can not only produce rose spots in the usual situations, but can also survive in situations which are unsuitable for most strains to escape rapid destruction in, and cause the appearance of spots, thus producing a most widespread rash. And, in rare cases, a strain of bacillus occurs which can produce rose spots in exceptional situations, and whose clumps are destroyed by the blood serum when deposited

in the more usual situations.

Typhoid Bacilli from a case of enteric fever having a certain distribution of rash will tend, if inoculated directly (without modification by artifi-cial culture) into a susceptible person, to produce the same distribution of rash in that person. It is the individuality of the special strain of bacillus present in any case which determines the areas in which clumps of its bacilli can survive and produce spots, and the areas in which clumps of its bacilli are rapidly destroyed so that no spots are produced. But any area, such as the abdomen, which has a high temperature and where bacillary clumps are more frequently lodged than elsewhere, cannot be wholly unfavourable to the production of rose spots by almost any strain of bacillus typhos-us, as the supply of bactericidal

substances in the lymph there may be used up more rapidly than it can be replaced, while the supply of agglutinins in the lymph there will be augmented by the amount which the agglutinated bacilli bring with them from the blood.

The selective preference of certain strains of typhoid bacilli for certain special areas of skin can be traced when the rash in a case of enteric fever occurs in an unusual situation, for example on the hips or upper arms, and one or more people become infect--ed with the disease from that case. When this happens, the rash in the secondary case or cases has the same unusual dis--tribution as was present in the primary case.

This actually happened in three out of the few cases which I have previously given in detail (Cases I, II, and III). This Case

II was certainly infected from Case I, and therefore by the same strain of typhoid bacilli by which Case I was infected. The distribu-tion of the rash in Case I was the usual one as regards the trunk of the body, namely, the abdomen, chest, and back; and, in addition, the rather unusual one over both hips and thighs. The distribution of the rash in Case II was exactly the same as that which occurred in Case I, both as regards the areas of skin over the trunk and those over the hips and thighs.

Case III was infected from either Case I or Case II, and therefore by the same strain of typhoid bacillus which infected Cases I and II. Case III presented the same distribution of rash as occurred in Cases I and II, not only as regards the trunk areas, but also as regards the hips and

thighs, where indeed the spots were of exceptional size. Accident could not account for this very uncommon distribution of rash occurring in three consecutive cases of enteric fever each of which was infected by the same strain of typhoid bacillus.

The influence of heredity may also, I think, be excluded, although Cases I, II, and III, were related to each other.

Everything points to the exact nature of the living virus which infected these three cases as the cause of the unusual distribution of the rash in each case: and even assuming, as I do, that Cases I, and II, were examples of a mixed infection presenting an acuminated rash, and that Case III was an example of an infection by a pure culture of bacillus typhos--us, presenting the ordinary papul--ar rash and no symptoms of

mixed infection, then the only common element in the virus infecting these three cases was the Eberth's bacillus; and it must have been the exact strain of this bacillus which was present in all these three cases which determined the unusual distribution of the rash in these cases.

Case V was undoubtedly infected from Case IV, and by the same strain of bacillus as that which was present in Case IV. In Case V the distribution of the rash was the same as in Case IV.

As regards the two cases which I mentioned in point VI (p. 25), where a mother had the acuminated rash on the abdomen, chest, and hips, when I first saw her, and the daughter was infected by the same strain of bacilli as the mother: the spots on the abdomen in the mothers case looked dark

brown at the tips, and had evidently been acuminated for a day or two, while those on the hips were lighter in colour, and gave the impression of having become more recently acuminated. As the acuminated rash in Cases I, II, and III, came out on the hips at a later date than that on the abdomen and chest, it is almost certain that the spots, in the case of the mother just referred to, had come out on the abdomen and chest at an earlier date than those on the hips.

When the rash came out in the daughter's case, it occupied the abdomen and chest on the first day. I then lost sight of the case as it went to Hospital at Loanhead. But, so far as it was seen, it followed the same law: in both cases II and III the rash was limited to the abdomen and chest on the

Since writing this, I have to-day (March 5, 1912) received a letter from Dr Cameron, Loanhead, who had charge of this mother and daughter while they were in Hospital. He says:

"The name was Mrs Campbell: and after several attacks of haem--orrhage she died." —— "The spots on the daughter (Miss Campbell, aged twenty years) were also vesiculat--ed, and came out on the hips."

It will thus be seen that the distribution of the rash in the daughter's case was the same as that in the case of the mother: and that the rash in each case was vesiculated. The occurrence of vesiculation in these two cases has a direct bearing upon what I stated under Point VIII, pages 28 and 29.

first day of its appearance, coming out on the hips later.

In every instance that I have seen, where infection has spread from a case of enteric fever having a known distribution of rash to another person, the distribution of rash in the second person has been the same as that in the infecting case.

Abundance or scantiness of the rash depends upon the condition of the blood during the eruptive period, as regards the balance between the amount of agglutinins, bacteriolytic substances, and bacilli, which it contains. This balance may vary from day to day. The quality of the bacilli remains the same throughout, in any one case, but the amount may fluctuate. The amount of agglutinins and bacteriolytic substances varies also, owing to conditions which are not at present thoroughly

understood. It has, however, been definitely proved that there is a great increase in the amount of agglutinins in the blood within twenty four hours after a haemorr-hage (14), and that this increase is practically irrespective of the amount of blood lost.

It has also been shewn (25. p.4) that if a young dog be fed on typhoid cultures, the dog's serum will acquire agglutinating but not bacteriolytic properties.

Theoretically, the amount of agglutinins formed in any one case of enteric fever depends upon (a) the intensity of the stimulus (as regards agglutinin formation) supplied by the bacillary toxins which happen to be present in that case, and (b) the ability of the tissue cells to respond to that stimulus.

The amount of new bacteriolytic substances formed in any one

case of enteric fever depends upon the same two conditions, namely, (a) the intensity of the stimulus (as regards bacteriolytic substances formation) supplied by the bacilli and their toxins which happen to be present in that case, and (b) the ability of the tissue cells to respond to that stimulus.

The formation of agglutin-ins and of new bacteriolytic substances begins at the same time, and that time is when most of the bactericidal sub-stances, which were present in the blood at the beginning of the attack, is used up in the process of bacteriolysis.

For many years I have thought that the differences in the severity of the general symptoms, which are found in different cases of enteric fever, must be due (when mixed in-fection and other causes could

be excluded) to differences in the disease producing power of different varieties of the Eberth Bacillus. That is to say, that one strain of bacillus may produce an attack of enteric fever with severe general symptoms, while another strain will, other things being equal, produce a mild attack. I have also thought that each strain of bacillus tends to transmit its peculiarities to its successors. Both of these suppositions are generally held to be correct at the present time.

The breakdown in immunity, as regards bacteriolytic substances, which must occur when a relapse of enteric fever takes place, may happen in one of two ways: (1) From a diminution in the total amount of bacteriolytic substances in the blood during

the relapse. This, I believe, is what is generally supposed to happen.

(2) From a change in the bacilli which remain alive in some part of the tissues after an attack of enteric fever, by which they become able, after a period of rest, to survive and multiply in the blood in the presence of bacteriolytic substances which are not deficient in quantity. This I believe to be the usual cause of a relapse.

Franke (25, p. 683) infected a monkey with a particular strain of trypanosome. After waiting sufficiently long for immune substances to develop in the blood, he cured the monkey by an arsenic pre-paration. He then infected the monkey a second time with the same strain of try-panosome, in order to see if

the animal were immune. It proved not to be immune, as, after a prolonged incubation period, the disease reappeared. The blood of the monkey, during the second attack, was fatal to mice when inoculated. The serum of the blood destroyed the same strain of trypanosome as was twice inoculated into the monkey: but it did not, of course, kill the trypanosomes which were present in the blood drawn from the monkey.

The successors of the trypano-somes which were injected into the monkey the second time, had thus acquired the property of living in blood which con-tained substances which were fatal to the original strain. They, in fact, had formed a new strain which could re-infect an animal which was immune against the original

strain. This property lasted for many months, and persisted after repeated passage through normal animals.

The processes here are some-what analogous to those which occur during a relapse of enteric fever.

At the end of a primary attack of enteric fever, all the bacilli in the blood, and nearly all those in the tissues, have been destroyed by bacterio-lytic substances in the blood and lymph. But a few, pro-bably in agglutinated masses, may survive in some lymph spaces, shut off from the general cir-culation: only very small amounts of bacteriolytic substances reach-ing them. These bacilli may gradually become acclimatised to the action of bacteriolytic substances: their character becomes altered: and a fresh

invasion of the system by the new strain of bacillus occurs, causing a relapse.

If the bacilli from the blood of a patient suffering from a relapse of enteric fever, are subjected to the action of the serum of the blood of the same patient taken at the end of the primary attack, it will pro-bably be found that this serum will not destroy them. In that case it would tend to shew that the bacilli of the relapse attack have assum-ed the characters of a new strain.

If, on the other hand, the serum at the end of a primary attack of enteric fever does destroy the bacilli which are present during the relapse of the same case, it will shew that the bacilli have

not altered their character, and that the relapse is due to a deficiency in amount of the bacteriolytic substances in the blood at the beginning of the relapse.

I have never been able to decide this point, owing to want of material, a relapse of enteric fever being in my practice an occurrence of extreme parity.

Summary of the Thesis

I That the rash of enteric fever, when present, in the majority of cases occurs upon, and is limited to, the trunk of the body: that the regions upon which it appears are, in order of frequency, (a) the abdomen, (b) the front and sides of the chest, (c) the back of the chest, (d) the lumbar region, (e) the hips and outer sides of the thighs, (f) the shoulders and upper arms, (g) the forearms, (h) the legs, (i) the face, and (k) the hands.

II That while the size of the spots may vary from one millimetre to four millimetres in diameter at the base, in most instances the diameter of each spot is three millimetres.

III That the sensation conveyed to

the finger on touching the spots differs entirely when the rash consists of the common rose red papules from that which is felt when the rash is of the acuminat-ed type.

That when the rash is of the common type each spot feels soft and smooth, has no trace of sharpness at the apex, and gives a slight feeling of resistance to pressure; while in the case of the acuminated rash each spot feels firmer, and sharper on the summit, giving a greater feeling of resistance to pressure, the exact sensation varying somewhat with the age of the spot.

IV. That, while an attack of enteric fever may be most severe or even fatal, with either no rash or only a slight one: and while a case with an extensive rash may be mild: on the whole, the greater

the amount of rash present in any case at one time, the more severe is that case likely to be: but that the size of the individ--ual spots is quite independent of the severity or mildness of the attack.

V. That the rash becomes vesiculat--ed in about seven per cent of cases having a rash.

VI. That when the rash is of the acuminated variety, the acumina--tion affects the great majority of the spots constituting the rash.

VII That when a generally acuminated rash is present in a case of enteric fever, the attack will tend to be of a severe type associated with a considerable elevation of tem--perature, with a relatively slow pulse, with constipation as a

symptom, and with a greater than usual tendency to the occurr-ence of complications.

VIII. That when the infection from a case of enteric fever having a generally acuminated rash is conveyed to a second person, antiseptic precautions either not having been taken or having been stopped for some time before the second person becomes infected, the rash in the second person will tend to be of the acuminated type also, and to have the same dis-tribution over the skin as in the first case.

But that, in such a case, when antiseptics have been freely used before the second person becomes infected, the rash in the second person will not be of the acumin-ated type; but will have the same distribution as in the first case.

Also that acumination of the spots indicates the existence of a mixed infection.

IX. That when enteric fever spreads from one patient to another person, no antiseptics having been used before the second person becomes infected, the attack and the amount of the rash in the second person tend to be the same as in the first case, but the attack may be more severe and the rash more abundant.

And that when enteric fever spreads from one patient to an-other person, antiseptics having been used before the second person becomes infected, the attack in the second person and the amount of the rash tend to be of a milder character and smaller in amount respectively, than in the first case.

X. (a). What determines the time of occurr-

-ence of the rash.

The rose spots in enteric fever are caused by the accidental escape of small masses of agglutinated bacilli through the walls of the cutaneous capillary bloodvessels and their lodgment in the lymphatic capill--aries and lymph spaces of the skin papillae.

The eruptive period of enteric fever is that stage of the illness during which small masses of agglutinated bacilli are present in the bloodvessels, and are cir--culating with the blood.

It begins when agglutinins have formed in the blood to such an extent that for the first time agglutination of the bacilli occurs in the bloodvessels in excess of bacteriolysis, so that some of the agglutinated masses circulate with the blood. This in most cases first happens from the seventh to the twelfth day of

the disease.

It ends when such agglutin-
-ated masses have all disappear-
-ed from the blood. This usually
is the case when the morning
and evening temperatures have
become normal, indicating that
immunity as regards the pri-
-mary infection has been estab-
-lished.

A relapse of enteric fever
is due to a deficiency of bacteri-
-cidal substances in the blood
during convalescence, and a
reinfection by bacilli, which
are present in either the intes-
-tine, gall bladder, or some part
of the origin of the lymphatic
system.

At the beginning of a primary
attack of enteric fever, the blood
contains bactericidal substances but
no agglutinins: therefore the rash
does not appear until after the
first week.

At the beginning of a relapse, the blood contains both bactericidal sub-stances and agglutinins: therefore the rash may occur almost coincidently with the rise of temperature, or may precede it. The eruption during a relapse ceases to appear when agglut-inated masses of typhoid bacilli have completely disappeared from the blood, as in the case of the primary attack.

(b). What determines the distribution of the rash over the skin.

In every case of enteric fever during the eruptive per-iod there is a certain amount of leakage of clumps of agglutinated bacilli through the walls of the cutaneous blood capillaries, some of these clumps entering the lymph vessels of the skin papillae and lodging there. This leakage of bacillary clumps occurs chiefly in

those areas of skin which have the highest average surface temperature during the eruptive period: it is independent of the strain of bacillus which is present, and constitutes the Potential Rash, whose distribution is regulated by the average surface tem--perature over various areas of skin during the erupt--ive period; it being most constantly present in those areas which have the high--est average surface tempera--ture during the eruptive per--iod, and least frequently present in those areas which have the lowest average sur--face temperature during that time, for any one case.

Before being lodged in the lymphatic system of the skin papillae in some of

the areas of potential rash, the bacillary clumps play an entirely passive part, and act simply as if they were very small, slowly dissolving, foreign bodies.

But, after having been lodged in some of the areas of potential rash, the indi-viduality of the strain of bacillus typhosus which is the infecting agent in any one case, manifests itself in the behaviour of its clumps.

Taking any one strain of bacillus typhosus, only those clumps of that strain which, when lodged in the lymphatics of the areas of potential rash, find the surrounding condi-tions favourable for their multiplica-tion and resistance to rapid destruc-tion, can produce rose spots: all the other clumps are destroyed before

rose spots can be formed.

The bacillary clumps of any one strain of bacillus typhosus can only produce rose spots in those areas of the potential rash in which the surrounding condi-
-tions are favourable to their growth: any clumps deposited in areas unfavourable to them being destroyed by bacteriolysis, and no rose spots being formed. It is the individual peculiarity of the strain of bacillus present in any one case which determines in which of the areas of the potential rash a visible rash will appear.

Each strain of bacillus tends to perpetuate its peculiarity in this respect, its successors tend-
-ing to produce the same distri-
-bution of rash. This is proved by the distribution of the rash in Cases I, II, and III, and in others which have come under

my notice.

There are thus two factors present in every case of enteric fever, each of which is invariably in action in determining the distribution of the rash: —

(1) The average surface temperature, during the eruptive period, over various localised areas of skin. This factor determines the areas of potential rash in any one case, and affects all strains of bacilli typhosi alike:

(2) The individual peculiarity of the strain of bacillus which happens to be present in any case. This factor determines upon which areas of the potential rash the visible rash will appear.

Any area of skin which is the most frequent seat of the potential rash, must also be a frequent seat of the visible rash, because bacteriolytic substances in the lymph there tend to be used

up, while agglutinins tend to accumulate.

A scanty rash means relative excess of bacteriolysis: an abundant rash relative excess of agglutination.

It is the strain of bacillus which determines whether a rash will be widely distributed or strictly localised.

It is the state of the blood which determines whether it will be abundant or scanty.

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