

BACTERIURIA IN ENTERIC FEVER.

A Thesis

PRESENTED TO THE UNIVERSITY OF GLASGOW

BY

John James Buchan, SCOTLAND.

M.B., Ch.B. 1898.

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P R E F A C E .

The work upon which this study is based has for the most part been carried out in St. Helens, Lancashire; the material has been drawn from the St. Helens Isolation Hospital of 130 beds and the experimental work, done in the public health laboratory of the same County Borough.

The results differ somewhat from those of previous observers and are still to be confirmed, but special care has been taken to ensure their accuracy, and it is hoped that the investigation may prove useful in calling further attention to the subject.

It was found convenient to divide the thesis into two parts. In Part I Typhoid Bacteriuria is considered generally, and in Part II a record of the cases under observation is given.

Medical Officer's Department,
Town Hall,
St. Helens. Lancs.

I N D E X .

	Page.
Preface	2.
 <u>Part I.</u>	
Introduction	4.
General Description	5.
Methods of Examination	9.
General Results	10.
Appearance and Duration of Bacteriuria	13.
Bacteriuria in relation to General Symptoms	14.
Cause of the Bacteriuria	16.
Growth of Bacillus Typhosus in Urine	21.
Reaction of the Urine in Typhoid Fever	29.
Method of infection of urine	35.
General Conclusions	38.
 <u>Part II.</u>	
Introduction	39.
Positive Cases	41.
Summary	42.
Cases I - XVII.	43 to 59.
Negative Cases	60.
Summary	61.
Cases XVIII - XXX.	62 to 74.

4

BACTERIURIA IN ENTERIC FEVER.

P A R T I .

DESCRIPTIVE AND EXPERIMENTAL.

INTRODUCTION.

It is now 25 years ago since Roberts and Bouchard, independently of one another, first described a condition of the urine which is recognised as Bacteriuria. This term is only applied to urine containing bacteria when passed, as urine in healthy conditions, though sterile at first, rapidly becomes contaminated on standing.

Two kinds of bacteriuria have been described, — a simple idiopathic bacteriuria, in which no lesion of the urinary tract is discoverable, and a bacteriuria secondary to some pathological condition of the kidneys, ureters, bladder or urethra. The distinction between these two

varieties cannot always be made out, as a simple bacteriuria frequently becomes complicated with pathological changes in the urinary tract, while the factors which maintain simple bacteriuria are also frequently operative in cases of bacteriuria due in the first instance to local pathological changes.

The bacteriuria of enteric fever was among the first recognised, but it is only within the last few years that attention has been directed to its importance, especially in the etiology of the disease. This bacteriuria is almost invariably due to the typhoid bacillus alone, but on rare occasions other organisms may be present.

The typhoid bacillus **nearly** always occurs in the urine in immense numbers, giving rise to a peculiar and distinctive appearance, and when the bacillus is not so abundantly present, it is usually extremely difficult to demonstrate, as only stray organisms can then be found.

GENERAL DESCRIPTION.

The urine presents a whitish opalescence, which gives on shaking a wavy sheen like appearance — "a shimmer" — due to the light being glanced off the innumerable microscopic

6

solid bodies suspended in it. This shimmer disappears as the movement set up in the urine ceases. The contrast in the appearances of urine loaded with bacilli and urine free from them, is shown to some extent in the accompanying photographs, but the shimmer cannot be depicted by this means. The bacteria do not subside readily on standing, and they are not carried down by the mucus, although exceptionally with a slight excess of mucus they may to some extent be deposited. I have never seen, however, the supernatant urine wholly cleared by this means, although some observers have described the bacteria as forming a thin white layer at the bottom of the containing vessel, leaving the urine perfectly clear. After ordinary filtration through paper the shimmer is still present, as the bacteria cannot be separated by this means. The colour of the urine is usually light straw, the specific gravity somewhat low, and the reaction acid. Albumen cannot be found present in most cases by ordinary clinical methods, but, as is readily understood, compounds-proteids-are usually discovered in small quantities where bacteriuria is present.

URINE IN ENTERIC FEVER.

Normal Urine and Urine in Bacteriuria.



The photograph shows two specimens of about the same depth of colour, both taken from patients suffering from enteric fever; the one on the left was quite normal while that on the right contained immense numbers of typhoid bacilli. The specimens are in 50 c.c. Nessler glasses.

URINE IN ENTERIC FEVER.

Normal Urine and Urine in Bacteriuria.



The specimens are similar to those in the preceding photograph, but the illumination is more diffuse.

METHODS OF EXAMINATION.

In observing a case of enteric fever for the development of bacteriuria, as far as possible every specimen of urine passed should be examined at once for the physical appearances of the condition, and when these are observed, microscopic and cultivation experiments can be done to identify the typhoid bacillus. The physical appearances are almost characteristic and with a little experience are readily recognised, but it is necessary, especially when they are first seen in any case, to confirm the result by proper bacteriological investigation.

As the bacilli are so numerous, it is not usually necessary to centrifugalise the urine, in a loopful of which, examined as a hanging drop, immense numbers of motile typhoid organisms can be seen. By drying a drop of the urine on a coverglass, fixing and staining, the bacilli can be examined direct; the fixing must be done very carefully, as one is apt to wash off the bacilli in staining. In all cases coming under my observation, when the physical characters of bacteriuria were first observed, the following further tests were done.

An agar tube was inoculated, and at the end of 20 - 24 hours an emulsion was made of the growth, and this was tested

against the serum from a typhoid patient, whose agglutinating power with respect to the laboratory typhoid culture was known. Only sera with very high agglutinating powers were used, and reliance was placed only on results got in very high dilutions - at least 1:500, varying according to the serum. The bacillus was grown in peptone solution for three days, and the absence of indol formation was noted. Finally in a shake culture in litmus-lactose-gelatine, neither acid production nor gas formation was seen. If the organism responded satisfactorily to all these tests, it was thought to be the bacillus typhosus, as the margin of error in such circumstances must be extremely low.

GENERAL RESULTS.

Thirty cases of typhoid fever were specially under observation for bacteriuria. These cases were in no way selected, and they are set out in further detail in two classes in Part II of this thesis. Of the thirty cases, 17 showed at one time or other during the disease a well marked

and characteristic bacteriuria due to the typhoid bacillus.^o

I have collected and tabulated on the following page, a number of observations of this condition in enteric fever, and it will be noted that the proportion of positive results (56%) among my cases, is higher than that usually described. Of the 874 cases collected, in 209, or 24%, bacilluria was found, but this percentage varies from 5.5 and 6% in Huppe's and Karlinski's cases, to 45, 58, and 85% in Lesieur's, Enriquez's, and Wright and Semple's cases respectively. In a similar analysis by Munch* of 724 recorded cases, 233, or 32%, showed typhoidal bacteriuria.

^o In one of the negative cases, a bacteriuria was found present on one occasion in which the organism was believed to be the bacillus coli communis. Horton-Smith records cases of bacteriuria in typhoid fever due to the streptococcus pyogenes, and also to the staphylococcus pyogenes aureus.

* La Semaine Médicale, 20th April 1904, p. 121.

No.	Name.	Date.	No. of cases examined.	No. showing Bacteriuria.
1.	Bouchard.	1881.	65	21
2.	Huppe.	1886.	18	1
3.	Seitz.	1886.	7	2
4.	Chantemesse & Widal.	1887.	-	2
5.	Berlioz.	1887.	14	2
6.	Koniaiev.	1888.	20	3
7.	Neumann.	1888.	23	6
8.	Neumann.	1890.	48	11
9.	Karlinski.	1890.	44	21
10.	Enriquez.	1892.	12	7
11.	Baart de la Faille.	1895.	27	4
12.	Blumer.	1895.	60	10
13.	Wright & Semple.	1895.	7	6
14.	Max Melchior.	1895.	4	1
15.	Horton-Smith.	1897.	61	8
16.	Besson.	1897.	33	6
17.	Levy and Gissler.	1897.	22	10
18.	Petruschky.	1898.	50	3
19.	Richardson.	1898.	104	23
20.	Horton-Smith.	1899-1900.	45	17
21.	Gwyn.	1899.	-	8
22.	Schichhold.	1899.	17	5
23.	Neufield.	1900.	12	3
24.	Vincent.	1901.	46	9
25.	Schuder.	1901.	22	5
26.	Lesieur.	1903.	15	7
27.	Herbert.	1904.	98	18
	Total		874	219

Bacteriuria found in 24% of the cases.

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2. Fortschritte der Med. July 1886. p. 446. *
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17. Munch. med. Woch., December 1897, p.1475 & 1476. *
18. Centr.-Bl. f. Bakt., April 1898.
19. Journ. of Experim. Med., May 1898.
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21. Johns Hopkins Hospital Bull., June 1899.
22. Deutsch. Arch. f. klin. Med., 1899, LXIV, p.505.
23. Deutsche. med. Woch., December 1900.
24. Semaine Médicale, 1901, p.85.
25. Deutsche. med. Woch., October 1901.
26. Bull. de la Soc. Med. des Hopit. de Lyon, December 1901.
27. Munch. med. Woch., March 1904. *

* quoted from Munch ibid.

APPEARANCE AND DURATION OF BACTERIURIA.

This condition in my cases did not occur before the 14th day from the onset of the illness, nor was it first noted in any case after the 59th day of the disease; it generally occurred at the end of the third, or the beginning of the fourth, week of illness, frequently during the lysis of the fever. Horton-Smith has found bacilluria present in a case as early as the 13th day, stating at the same time that it had undoubtedly been present in this case at a much earlier period; but Lesieur has recorded cases where this condition occurred as early as on the 10th day of disease. On the other hand, Horton-Smith has known bacilluria to occur for the first time on the 14th day of convalescence. All observers agree, however, that the most frequent time for this condition to occur is during the third and fourth weeks.

In the 17 cases coming under my observation, the duration of bacilluria varied greatly. It was present in one case on only one occasion, and in another for two days, the duration varying from this short period up to nearly four weeks, when it only disappeared under treatment; in other cases, it was present, though not continuously, for a still longer period.

My observations here differ somewhat from those of other writers, notably Horton-Smith, who has not seen this condition last for a shorter period than eight days. The duration of untreated bacilluria may extend to years; Houston* records the persistence of the condition for three years after an attack of typhoid fever, and Gwyn for five years, but it would seem probable that in such cases some organic lesion must be set up, as both of the aforementioned cases showed cystitis.

BACTERIURIA IN RELATION TO GENERAL SYMPTOMS.

One of the 17 cases presenting this complication proved fatal, whereas three of the remaining cases under observation died. It would at first sight appear that bacteriuria is met with much less frequently among severe cases of enteric fever than among those running a milder course, but this is not so. Bacteriuria is a complication which occurs late in the disease, often indeed in convalescence, so that in most of the fatal cases it has not had an opportunity to develop before death takes place. Horton-Smith's results show that 17.6% of his cases with bacteriuria died, while only 14.2% of his negative

Reference.

* **British Medical Journal, 14th January 1899.**

cases proved fatal. In my own cases, if the deaths be excluded in each class, it will be seen that bacteriuria was more apt to develop in those cases which were more severe; — thus, the average duration of the illness of the 16 recovered cases showing bacteriuria was 33.4 days, while the average in the 10 recovered cases which did not show bacteriuria was 28.3 days, a difference of 5.1 days in the duration of the illness. But while bacteriuria is more likely to appear in severe cases, in some very mild cases it is also present, and in some very severe cases it cannot be found.

The typhoid eruption was noted in 14 of the 17 cases with bacilluria, and in 10 of the remaining 13 cases. In only two of the cases could the eruption of rose red spots be called profuse, and one of these cases showed bacilluria while the other did not.

Diarrhoea was noted in hospital in only 5 of the 17 cases with bacilluria, while it was present in 8 of the other 13. I will subsequently show that this result is probably not accidental, and that when a severe diarrhoea occurs in enteric fever, the case is less likely to develop bacilluria.

Albuminuria was present at one time or other in six of

the 17 cases showing bacilluria, and in 5 of the remaining 13 cases. Nephritis arose in only one of my cases, and a bacilluria of very short duration was subsequently observed. Haematuria was present only in the case with nephritis.

Cystitis appeared in one case after bacilluria had been present for more than three weeks. Short of cystitis being set up, a slight pyuria occurred in one case, which disappeared almost immediately under treatment; bacilluria had been more or less present in this case for 10 days. Horton-Smith found in his cases of bacilluria that a very large proportion (over 50 per cent) showed pyuria.

CAUSE OF THE BACTERIURIA.

From the above study, few conclusions can be drawn as to the actual cause of this condition. We are now well aware that typhoid bacilli are found in considerable numbers in the blood in enteric fever, but the organisms are not merely finding their way from the blood into the urine.

The following are the principal reasons against such a theory :-

(a). The number of bacilli in the urine is enormous,

while the number of bacilli in the blood is comparatively very small. Petruschky gives the number of organisms present in the urine in one case of bacilluria as 175 millions per c.c., and Gwyn in another as 500 millions. The difficulty of finding typhoid bacilli in the blood exists mainly on account of the very small number of organisms present.

Horton-Smith on four occasions examined the blood bacteriologically when the urine was swarming with bacilli, and on each failed to find typhoid organisms, while other observers have recorded similar experiences.

(b) When the organisms are most numerous in the blood, bacilluria is not present, and the organisms continue present in abundance in the urine after the typhoid bacillus has disappeared from the blood. Rolly*, in an examination of the blood in 50 cases of typhoid fever, found that the number of organisms present in 20 c.c. varied from 0 up to 480, and that the bacilli were more numerous at the onset and at the height of the fever than later. Bacilluria, on the other hand, is not usually present at the height of the fever, and tends to develop later. The disappearance of bacilli from the blood, and their appearance in the urine, might be at first sight

Reference.

* Munch. med. Wech. June 14th 1904.

thought to indicate their elimination by filtration through the kidney, but this cannot be so, as a well-marked bacilluria continues present long after the disappearance of the organisms from the blood.

(c) Between such enormous numbers of typhoid bacilli in the urine as those just recorded, and stray organisms found only after laborious search, cases are ^{not} found presenting intermediate varieties, and if a mere filtration from the blood were the cause of bacilluria, such intermediate varieties ought to occur. One finds a characteristic bacilluria set up and disappearing with an abruptness that makes it unreasonable to suppose that all the organisms came directly from the blood.

It would also seem unlikely that a local infection of the kidney gives rise to bacteriuria. Several observers, notably Seitz and Besson, have laid considerable stress on the occurrence of albuminuria, considering it a potent factor in determining bacilluria, but other workers, including Horton-Smith, Neumann and Blumer, do not so regard the presence of albuminuria in the urine. We have already seen that albuminuria is by no means the rule in these cases, and though my figures are not perfectly conclusive, I cannot believe from

them that the relationship between albuminuria and bacteriuria is close, or of much importance. It is difficult to understand how a severe infection of the kidney, throwing millions of bacilli each hour into the urine, could exist for any time without at least in the majority of cases giving some evidence of its presence as an albuminuria or a definite nephritis. Affections of the kidney fail to account for two of the peculiar features of bacilluria, ^{viz-} (1) its sudden appearance and equally sudden disappearance, (2) its frequent presence alone without any other clinical sign.

Horton-Smith discusses the possibility of bacilluria arising from a suppuration set up in the kidney by the typhoid bacillus, accompanied by the secondary passage of bacilli into the urine, and instances the case recorded by Flexner. But in such cases pus would always be found present in the urine also, and such a suppuration, although it would account perhaps for the rapid onset, would not account for the equal continuance and sudden disappearance of the bacilli from the urine. In any case, such typhoid suppurations of the kidneys are very rare indeed, only one being found in 289 post mortem examinations of cases of typhoid fever at St. Bartholomew's

Hospital.* The rarity of kidney complications generally, and the comparative frequency of bacilluria in typhoid fever, would of itself tend to negative the idea that bacilluria arises from such a local condition.

Cystitis is an effect rather than a cause of bacteriuria. It is not frequent among the cases presenting bacilli in the urine, and it usually occurs after this latter condition has been in existence some time. From the recorded cases, especially those of Gwyn and Houston already referred to, there can be no doubt that cystitis is a potent factor in the maintenance of bacilluria once set up, but it can hardly be considered a ^{substantial} cause of the latter.

Following then my argument, if my conclusions are correct, typhoid bacilluria cannot be accounted for by a simple escape of organisms, either from the blood, or from a lesion of the kidneys or bladder. A primary infection of the urine must necessarily have taken place, and this may have been followed by a multiplication of bacilli in the urine itself while it is retained in the bladder, but the conditions under which typhoid bacilli can grow in the urine are not ascertained. The chief points of difficulty that arise before this explanation can be accepted are :-

The information for membership status was

based on the most recent data available

as of the date of the report.

It is noted that the membership figures

are based on the information provided

by the member organizations.

Reference.

* quoted by Horton-Smith, *ibid.*

- (1) Under what conditions does the urine afford a satisfactory medium for the growth of the typhoid bacillus ?
- (2) Do those conditions exist in enteric fever ?
- (3) Does the urine frequently become infected in enteric fever without bacilluria developing when the conditions of growth are unfavourable ?

These points will be taken up in the order mentioned.

GROWTH OF BACILLUS TYPHOSUS IN URINE.

Little or no exact work has been done on this subject, but it is one of great importance, not only in this question of bacilluria, but also in the general etiology of typhoid fever. I examined many specimens of urine by inoculating them with the bacillus typhosus, and it became apparent that certain unknown conditions determined the suitability of the urine as a medium for the typhoid bacillus.

The presence or absence of albumen did not have any influence in promoting growth, as the organisms grew almost equally well in some urines containing albumen and in some which did not; while in many containing albumen the organisms would not grow at all.

The reaction of the urine in typhoid bacilluria is almost invariably acid, and in some acid urines the bacillus typhosus will grow, while in others it will not. But the bacillus typhosus, like other micro-organisms, is exceedingly sensitive within certain limits to changes in the reaction of the medium on which it grows, and it becomes therefore necessary to estimate this more accurately. The exact estimation of the acidity of the urine is held to be a matter of some difficulty, as the acidity is not due to a simple acid, but to acid salts, notably acid sodium phosphates. Various and complex methods have been devised to determine the degree of acidity of this excretion, but these methods on trial are not found to possess any advantages over the simpler means of direct titration with a standard alkali solution, using phenol-phthalein as the indicator. This has been the experience of most observers and Dixon-Mann* has stated that the complicated methods of Lieblein and others are of little value, as "in avoiding one source of error they encounter others, so that the best results are obtained by the ordinary titration method which is resorted to in the case of simple acid liquids, although on account of the imperfect saturation of the phosphates, the estimation is usually too low." My experience has been that for the present

Reference.

*Physiology and Pathology of the Urine, p.8.

(Griffin & Co., 1904)

purpose at all events the ordinary titration method is eminently satisfactory, but it must be remembered in doing it that the time reaction between the acid sodium phosphate and the alkali is a little long, and the process must not therefore be done hurriedly.

The technique is as follows :-

(1) 50 c.c. of the urine are taken and placed in a white evaporating basin, but if the urine be high coloured it is much better to take only 25 c.c. and dilute with distilled water to 50 c.c., making corresponding corrections on the result.

(2) A few drops of phenol-phthalein solution ^{are} (is) added as an indicator.

(3) A decinormal caustic soda solution is slowly added, stirring the urine well with a glass rod between each addition.

(4) When, after stirring, a slight but distinct pink colour is got, which is permanent for at least 15 minutes, the number of c.c. of decinormal soda added is read off.

If the acidity of the urine be exactly decinormal ($\frac{N}{10}$), then 50 c.c. of the standard soda solution would be required; if it be twentieth normal ($\frac{N}{20}$) only 25 c.c. would be required etc., so that the acidity of the urine may be arrived at thus :-

$$\frac{\text{Number of c.c. used}}{50} \times \frac{N}{10}$$

and the result is expressed as a proportion of normal, thus :-

$\frac{N}{20}$ (normal twentieth), $\frac{N}{36}$ (normal thirty-sixth) and so on.*

I first determined the point of acidity beyond which the bacillus typhosus would not grow. Four sets of experiments were done :-

- (1) Ordinary bouillon was used, the acidity of which was changed by standard solutions of caustic soda and lactic acid.
- (2) Bouillon and standard soda were used as in (1), but a standard solution of phosphoric acid replaced the lactic acid.
- (3) Fresh acid urine was used and sufficient standard soda solution was added to make it quite neutral. The urine was then filtered to remove the precipitate of phosphates which formed, and ^{was} put up in a series of tubes with the acidity graduated by means of standard phosphoric acid solution. The tubes were afterwards submitted to steam sterilisation on three successive days.
- (4) Normal urine of different degrees of acidity was

* It is much better to express the acidity in those terms, as no assumption is made what it is due to, and it is therefore chemically more accurate, and quite as convenient.

used. Each urine was allowed to stand for a time, filtered and then put up in tubes which were sterilised by steam on three successive days as before. In this series, and in the preceding, the acidity was always checked in tubes similarly prepared immediately before inoculation, so as to be quite certain of the reaction.

After a few preliminary tests, it became apparent that the zone which required most careful investigation, lay between $\frac{N}{25}$ and $\frac{N}{50}$ acid, and by having a series of tubes carefully graduated in acidity, it was determined that the bacillus typhosus ceased to grow at a fairly definite point.

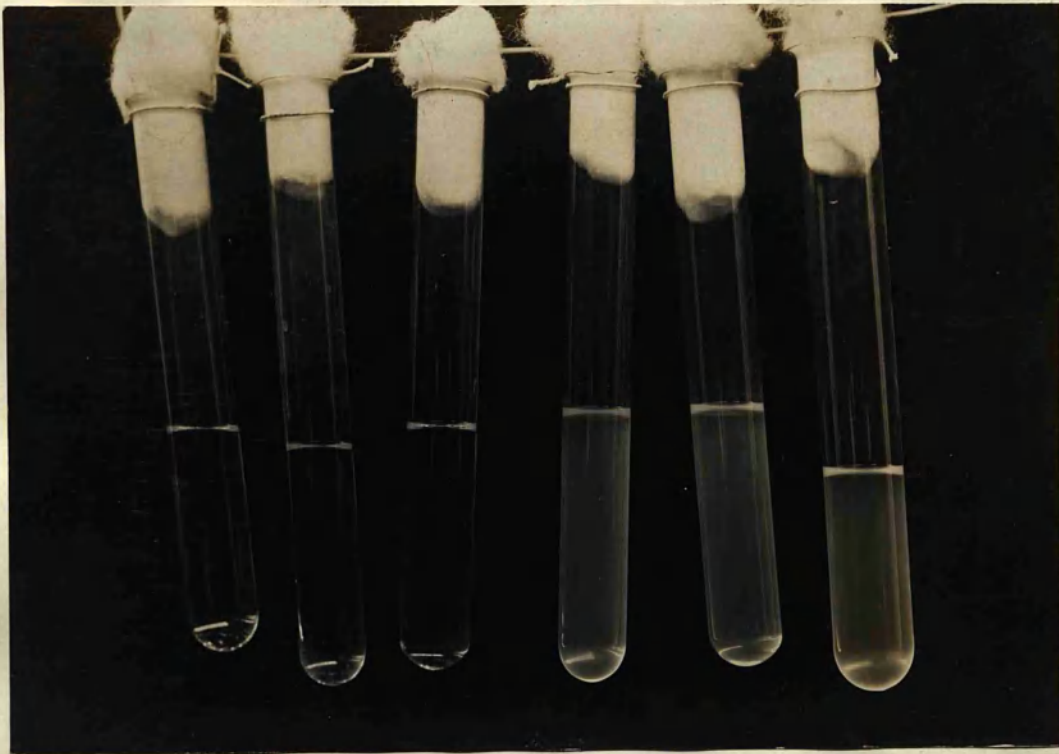
As the acidity rises above $\frac{N}{35}$ no growth of bacilli can be obtained, whereas slightly below $\frac{N}{35}$ a profuse growth can be got. This can easily be seen in the accompanying photographs, which show well how definite is the point of acidity above which growth will not take place. They also show that the result is the same whether the medium be bouillon or urine, or whether the acid be lactic or phosphoric.

GROWTH OF BACILLUS TYPHOSUS IN BOUILLON.

Photograph showing Growth at Different Degrees of Acidity.

EXPERIMENT No. 1.

Acidity changed by standard solution of Lactic Acid.



The Acidities of the tubes are :-

$\frac{N}{25}$ $\frac{N}{30}$ $\frac{N}{35}$ $\frac{N}{40}$ $\frac{N}{45}$ $\frac{N}{50}$.

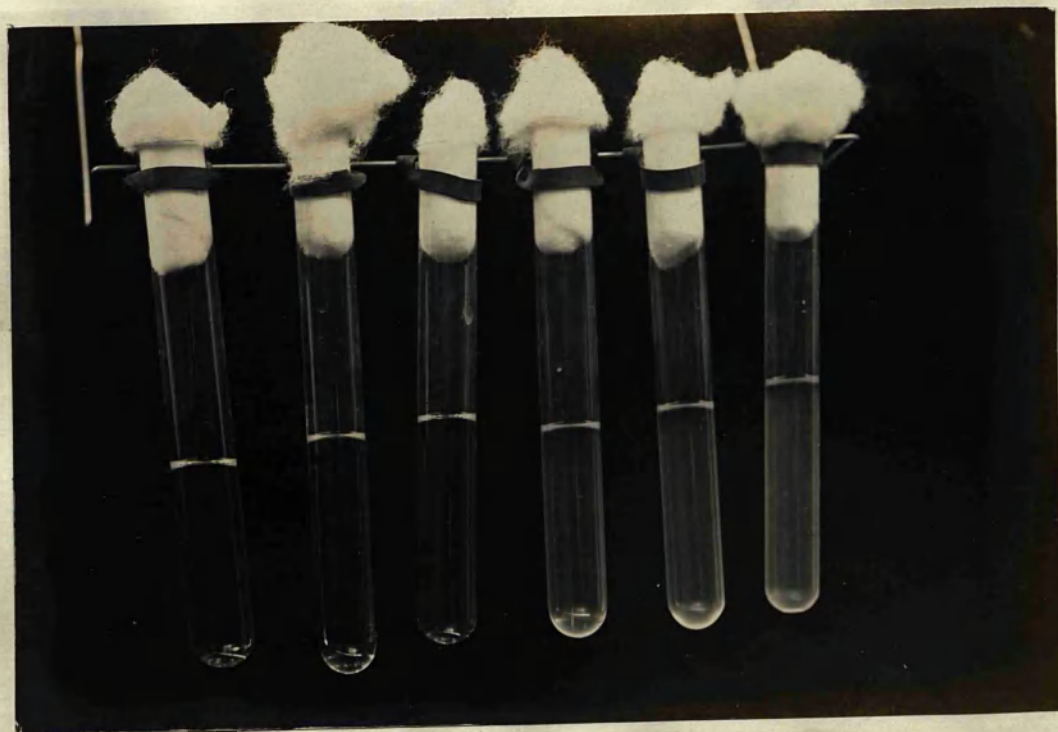
Each tube has been inoculated with the bacillus typhosus and incubated for 48 hours.

GROWTH OF BACILLUS TYPHOSUS IN THE URINE.

Photograph showing Growth at Different Degrees of Acidity.

EXPERIMENT No. 3.

Acidity changed by standard solution of Phosphoric Acid.



The acidities of the tubes are :-

$\frac{N}{25}$ $\frac{N}{30}$ $\frac{N}{35}$ $\frac{N}{40}$ $\frac{N}{45}$ $\frac{N}{50}$.

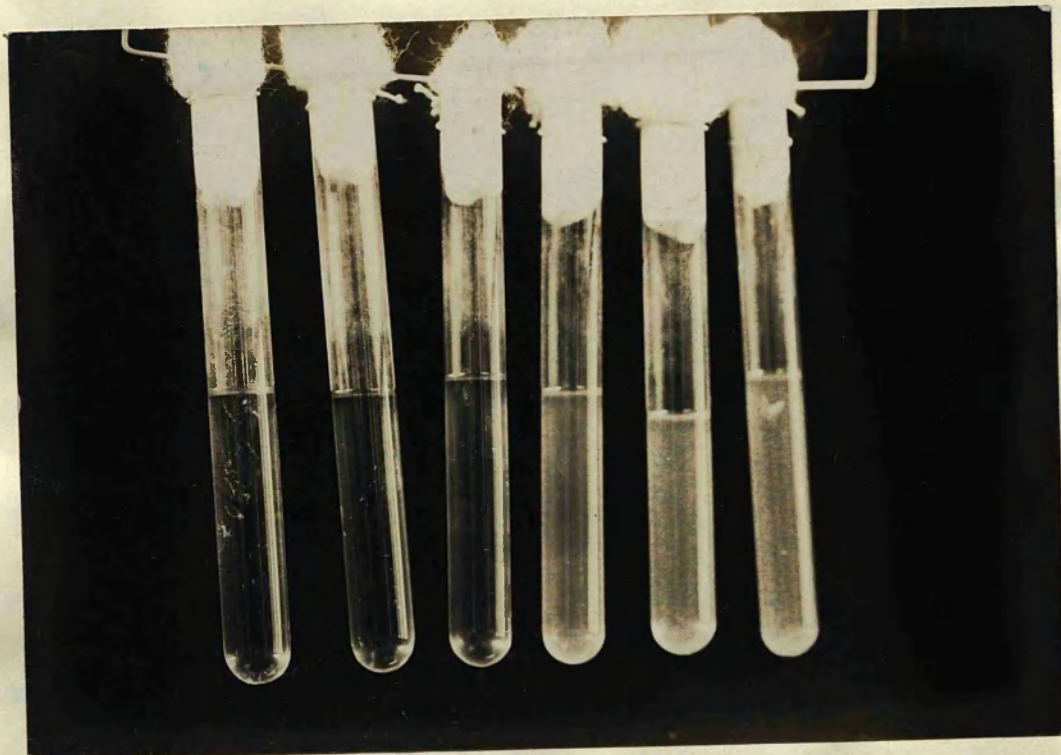
Each tube has been inoculated with the bacillus typhosus and incubated for 24 hours.

GROWTH OF BACILLUS TYPHOSUS IN THE URINE.

Photograph showing Growth at Different Degrees of Acidity.

EXPERIMENT No. 4.

Normal Urines of Different Acidity.



The acidities of the tubes are :-

$\frac{N}{24}$ $\frac{N}{30}$ $\frac{N}{34}$ $\frac{N}{40}$ $\frac{N}{46}$ $\frac{N}{60}$.

Each tube has been inoculated with the bacillus typhosus and incubated for 48 hours.

REACTION OF THE URINE IN TYPHOID FEVER.

When the reaction of the urine in typhoid fever is examined, it is found that no urine showing bacilluria has a higher acidity than $\frac{N}{35}$. The details of these examinations are shown in the cases recorded in Part II, and from these results it would seem almost certain that bacilluria can only occur when the acidity of the urine is below this point. In one or two cases, bacilluria will be seen to have occurred at $\frac{N}{35}$ acid, but never higher. This may be explained on the supposition that the urine first excreted and infected had a lower acidity than $\frac{N}{35}$, thereby allowing the bacilli to develop in it, while the reaction of the later urine was a little higher, giving rise to a $\frac{N}{35}$ acid reaction of the whole urine expelled.

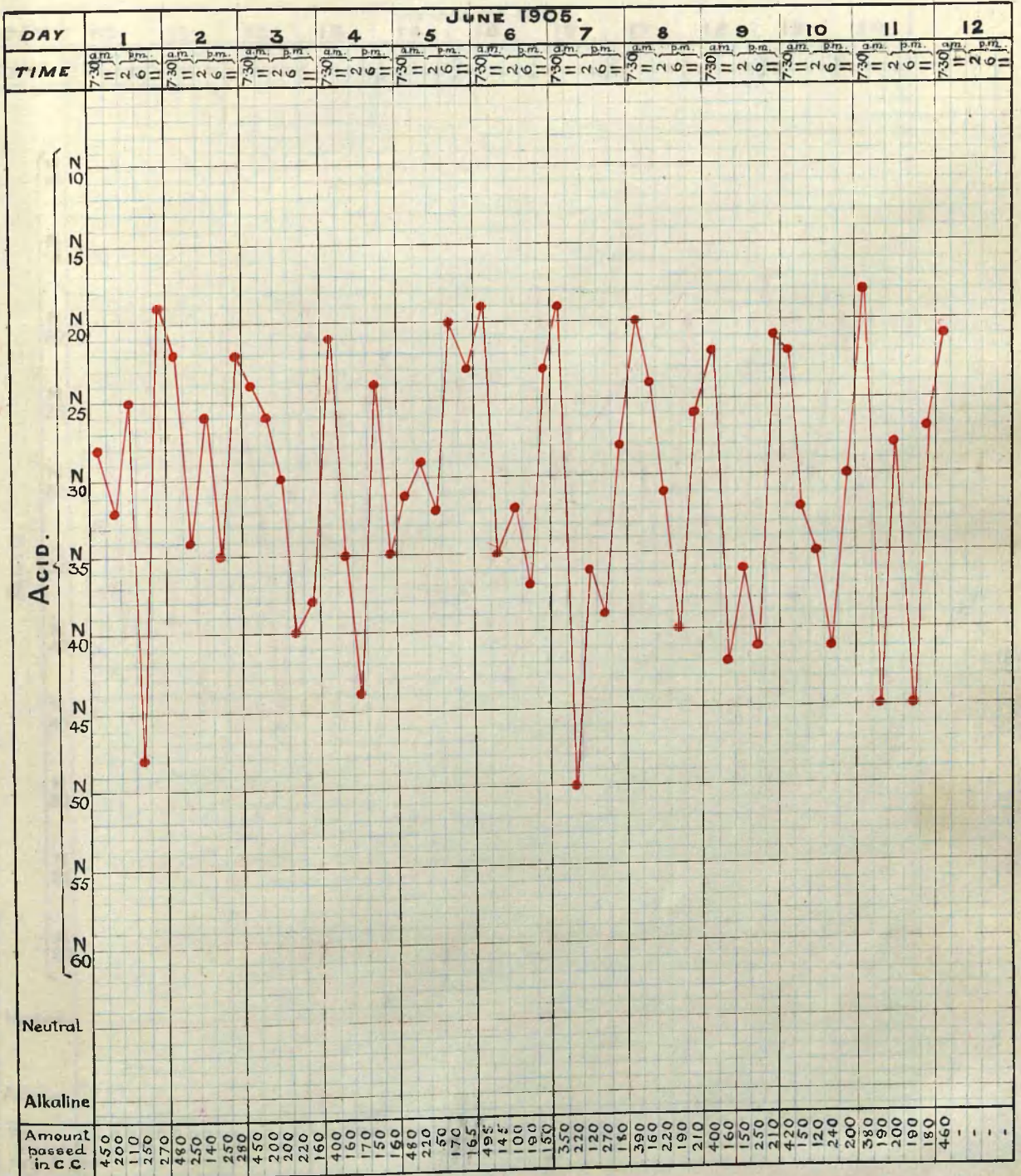
If then the bacillus typhosus grows in the urine before it leaves the bladder, when the urine has a reaction of less acidity than $\frac{N}{35}$, it becomes important to regard the variations in the reaction of the urine during the course of the fever. But before this can be done with advantage, the change in the reactions in normal conditions must be understood. It is known that the urine normally becomes less acid after meals,

sometimes indeed becoming alkaline, so that what has been called an "alkaline tide" is set up. The explanation usually given for this is, that the secretion of hydrochloric acid in the stomach sets free the bases with which it is combined in the blood, so that an increased proportion of the alkaline monohydric sodium phosphate (Na_2HPO_4) is excreted in the urine. Whatever be the explanation of the alkaline tide, it seems certain that the acidity of the urine tends fairly regularly to fall in the afternoon. I have examined the reactions of practically all the specimens of urine passed by some normal persons, and find that the acidity is highest in the specimen passed in the morning, and that it tends to fall more or less regularly towards five o'clock in the evening, when it rises again. The reaction charts of two normal males are here given, where it will be seen that the morning specimen of urine varies from about $\frac{\text{N}}{27}$ to $\frac{\text{N}}{17}$ acid, while the late afternoon specimen varies from $\frac{\text{N}}{45}$ to $\frac{\text{N}}{35}$ acid.

The influence of the time and nature of meals is admitted to be important, but even where the dietary is arranged, as in enteric fever, the morning elevation and afternoon fall

NORMAL URINE.

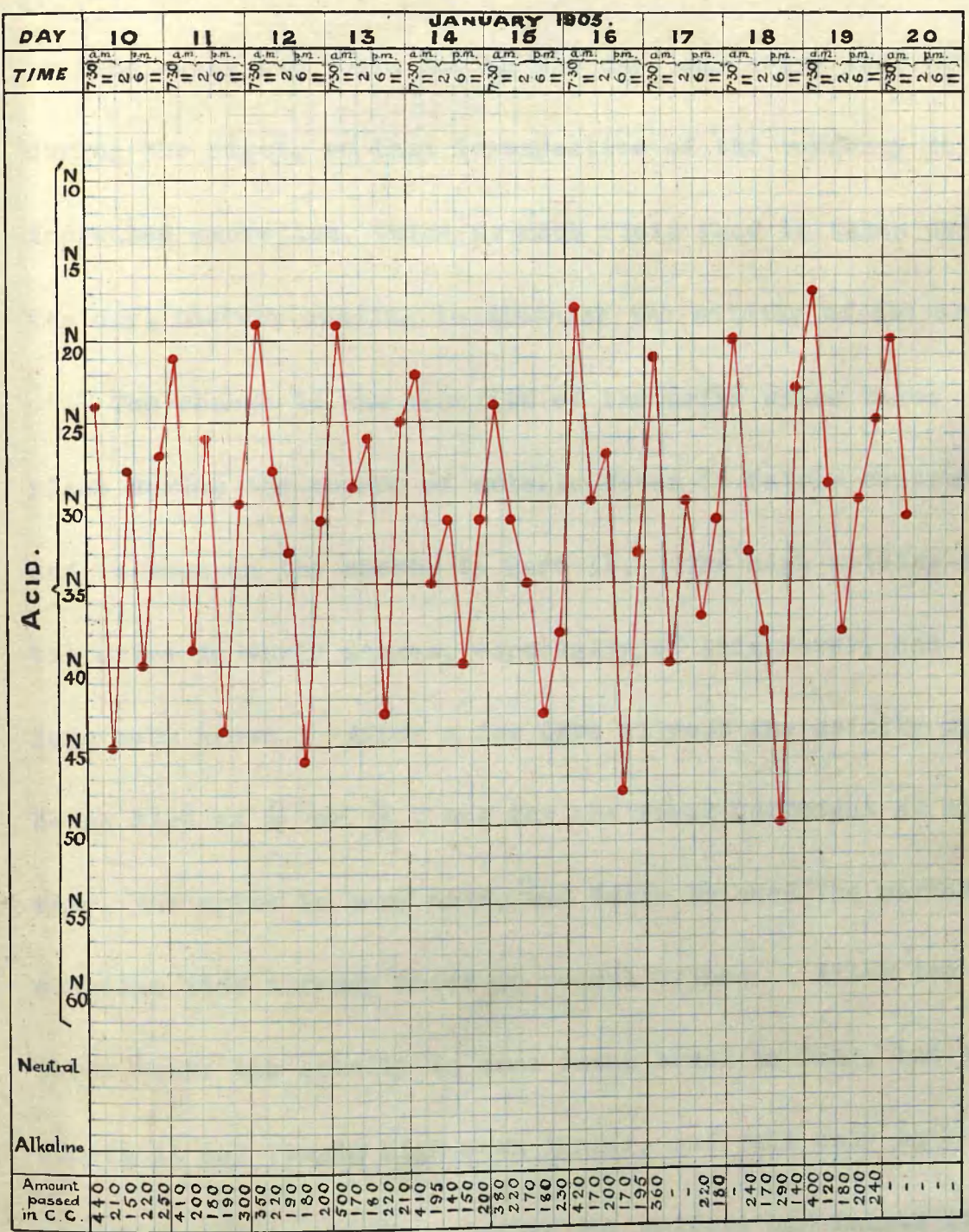
Chart showing daily variations in the Reaction.



MALE AGED 28 YEARS.

NORMAL URINE.

Chart showing daily variations in acidity.



MALE AGED 26 YEARS.

in the acidity tends to remain. This may be explained by the fact that there is always an increased excretion of fluid during the day, and that in enteric fever it is the practice to feed every two hours during the day, and every four hours during the night, so that irrespective of the tendency to increased excretion, twice as much fluid food is taken during the day, thereby tending to diminish the acidity of the urine.

The change in the reaction of the urine which takes place during the course of enteric fever is fairly constant, and is seen in the charts in Part II. The high acidity of the urine in early stages, especially, of this fever, has long been known. After a few days illness the acidity may be as high as $\frac{N}{15}$ or $\frac{N}{10}$, and for the first fortnight at any rate, the urine is very acid, and fails to show the marked alkaline tide already noted in normal urines. After two or three weeks the acidity in some cases tends to fall, but in others it may remain high much longer, and fall only as convalescence is set up. After the acidity has fallen, it usually remains low for a period varying from a few days up to several weeks. The fall in the acidity is sometimes very much delayed, and may be even then of very small amount.

Shortly after the patient becomes convalescent, the normal variations in the reaction of the urine seem slowly to become re-established. These results agree pretty closely with what is already known of the period of the disease in which bacilluria occurs, and it is only during the period of low acidity that bacilluria is noted.

Too little is known of the chemistry of the urine to enable us to explain these various changes, but the fall in the acidity later must be correlated with the previous rise in the early stage of the disease, when the increased excretion of acid salts due to the increased waste is compensated by their diminished excretion as the patient is recovering. An accidental compensation however is sometimes set up by the occurrence of diarrhoea during the disease, when as is well known, highly alkaline stools are passed. In these cases one finds the acidity usually better maintained later in the disease, and as a result bacilluria appearing less frequently. This fact is of some interest, as it indicates that contrary to the generally accepted view cases with diarrhoea are probably less infectious. *from the urine*

METHOD OF INFECTION OF THE URINE.

From what has been said, it would seem that the reaction of the urine is the most powerful factor in the causation of bacteriuria. It only remains now to enquire whether the urine becomes infected in cases, where by reason of its high acidity, it does not afford a satisfactory medium for the growth of the typhoid bacillus; and such an infection of the urine by stray organisms might quite well take place from the blood without damaging the kidney to any appreciable extent.

In the investigation of urines of high acidity, I found great difficulty at first, as I depended for my results on ordinary methods of detecting few organisms in a large volume of fluid. I collected the urine with aseptic precautions, and allowed it to stand for 12 to 24 hours in a tall sterilised glass vessel, with an accurately ground glass cover; 20 c.c. were then drawn off from the bottom with a sterile pipette and centrifugalised. One c.c. was drawn off from the bottom of the centrifugalised urine, and inoculations were made on agar tubes. My results by this method were not satisfactory, as out of eight such examinations, only a streptococcus was got apparently from

contamination, but they served to show me how few in number the bacilli in the urine usually are, where naked eye bacteriuria is not present.

Taking advantage of the fact, however, that the bacillus typhosus can be made to develop in urine, I adopted the following method, which has given better results. The parts round the meatus were carefully cleansed, and the patient was directed to ^amicturate into two flasks, both sterile and plugged with cotton wool. The first flask ^{had a capacity of} (contained) about 100 c.c., and the second 500 c.c. After the first flask was about half full, the second was used for all the remaining urine, and was immediately stoppered with the cotton wool after use. The reaction of the urine in the smaller flask was carefully estimated, and the amount of urine in the larger flask was roughly measured by comparing it with another exactly similar flask, filled to the same level with water. Sufficient $\frac{N}{10}$ soda solution, to bring the acidity below $\frac{N}{40}$, was sterilised and cooled, and then added to the larger flask, and the whole was placed in the incubator. Only urines of high acidity were examined, and in all cases the patients were males. The number of experiments of this kind done

was 10, and in no less than 6 cases the bacillus typhosus was isolated from the urine. The results are shown in the following table :-

Bacteriological examinations of urine with high acidity.

Case No.	Day of examination.	Acidity of urine.	Result.
IV	38 th	$\frac{N}{21}$	B. typh. absent
VIII	25 th	$\frac{N}{18}$	B. typh. absent.
IX	29 th	$\frac{N}{17}$	B. typh. present
IX	52 nd	$\frac{N}{21}$	B. typh. present
X	21 st	$\frac{N}{16}$	B. typh. present
X	40 th	$\frac{N}{22}$	B. typh. present
XXI	26 th	$\frac{N}{19}$	B. typh. absent
XXII	22 nd	$\frac{N}{16}$	B. typh. present
XXII	28 th	$\frac{N}{18}$	B. typh. absent
XXIX	18 th	$\frac{N}{19}$	B. typh. present

These results are much too few in number ^{in which} to base any general conclusions (on), but they show that the bacillus typhosus finds its way into the urine frequently enough, when the latter does not form a medium in which it might develop. In the etiology of the disease, it is easy to understand the importance of bacteriuria, but without bacteriuria, if the multiplication of bacilli in the urine is dependent on the reaction of the latter, then as urine

rapidly becomes more alkaline on standing, through decomposition, a point is soon reached, when, if it be infected at all, the typhoid bacillus itself will begin to grow. Such a result at any rate would seem probable, but the matter has to be worked out.

GENERAL CONCLUSIONS.

- (1) Typhoid bacteriuria is found in a large number of cases of enteric fever, probably about half.
- (2) It occurs almost always after the first fortnight of illness.
- (3) It occurs more frequently in severe cases, and in cases which have not had diarrhoea.
- (4) It is unassociated with renal mischief; cystitis may arise as its result.
- (5) It is caused by the multiplication of the typhoid organism in the urine while it is retained in the bladder.
- (6) The typhoid bacillus grows and multiplies in the bladder, when the reaction of the urine is below $\frac{N}{35}$ acid.
- (7) Such a reaction is usually got in the later stages of typhoid fever.
- (8) The urine in typhoid fever probably becomes infected in a large number of cases, even when the bacillus cannot grow in it.

BACTERIURIA IN ENTERIC FEVER.

PART II .

RECORD OF CASES.

INTRODUCTION.

In this Part the cases under observation are shortly described, reference being particularly made in each case to the diagnostic features, the appearance and duration of bacilluria, and the condition of the urine especially with regard to the reaction.

The charts attached show, in black, the temperature and other clinical facts usually noted, and, in red, the reaction of the morning and evening specimen of urine. The morning specimen chosen is that passed before 8 a.m., and the evening specimen that passed between 3 and 6 p.m.; in this manner the maximum and minimum degrees of acidity for the day are usually recorded.

On the charts, also, the occurrence of bacilluria is noted, but the results of the special examination, by the addition of an alkali, as described in Part I, in cases IV, VIII, IX, X, XXI, XXII, and XXIX, are not included. The letters A., B., C., and D., refer to the amount of albumen present in the urine, thus :- A. = trace, B. = little, C. = considerable, D. = much.

The cases have been divided into two classes, positive and negative, according as they have shown at one time or other bacilluria or not; they are set out in each class in the order in which they were admitted to hospital. A tabular summary precedes the description of the cases in each class.

No post mortem examinations were able to be obtained.

POSITIVE CASES.

Note on Treatment.

The means adopted for the treatment of Bacilluria are two in number.

(1) Washing out the bladder on two or three occasions with a mild antiseptic, such as boric acid solution. In none of the cases hereafter described, has this method been adopted alone, but in other cases I have had experience of its good results.

(2) The administration of urotropin - 10 grains, three times a day, for an adult. This has a rapid and surprising effect in clearing the urine. As will be seen in the cases, it does not act by raising the acidity of the urine; it seems to attain its result by the excretion of minute quantities of formaldehyde.

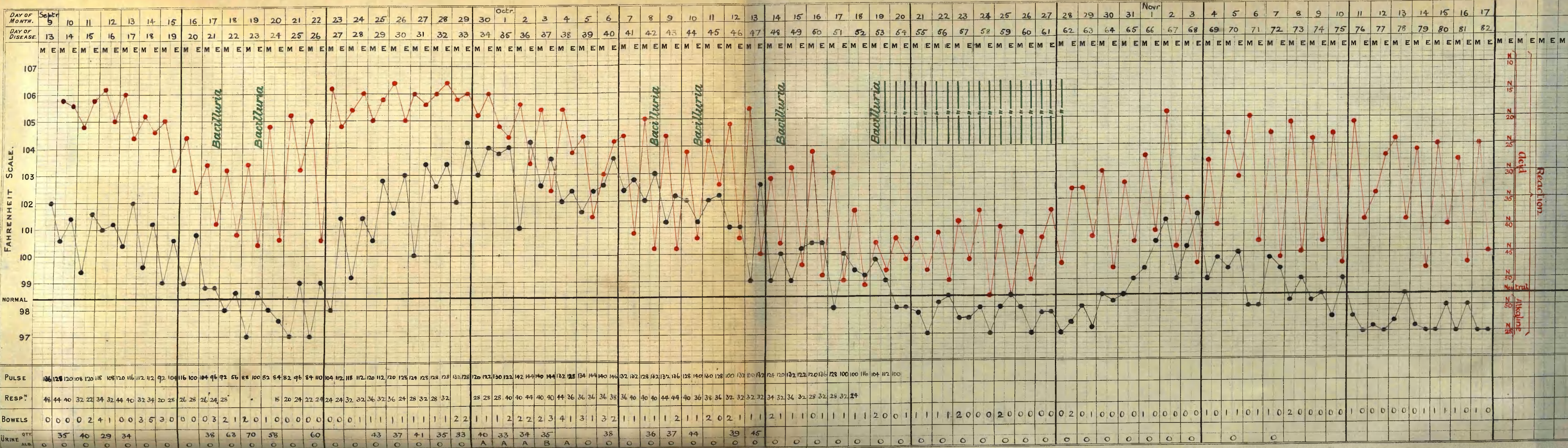
When cystitis or pyuria is set up, it is easily treated by the above methods, singly or in combination.

SUMMARY OF POSITIVE RESULTS.

Case No.	Age	Sex	Duration of illness in days.	Days on which Bacilluria was noted.	Albuminuria	Diarrhoea	Remarks
I	29	F	53	21, 23, 42, 44, 48, 53 - 62	present	present	
II	18	F	53	30, 61 - 63	present	absent	
III	12	M	24	24 - 29	absent	present	
IV	18	M	24	20 - 22, 24 - 31.	absent	absent	
V	34	M	33	28 - 53.*	present	absent	Cystitis
VI	25	F	59	59, 60.	present	present	Nephritis
VII	16	F	19	28 - 31.	absent	absent	
VIII	18	M	20	23, 24, 36, 37, 39, 40.	absent	absent	
IX	19	M	66	17, 18, 23, 25-27, 34-41, 57-61.*	absent	absent	
X	28	M	50	32, 41-45.	absent	absent	
XI	23	M	22	23, 25, 26.	absent	absent	
XII	18	M	23	20, 21, 25-29.*	present	absent	Pyuria
XIII	17	M	32	24-26, 29-35.*	absent	absent	
XIV	46	M	26	24-27, 33, 34.	absent	present	
XV	7	F	(24)	20 - 22.	present	absent	Fatal case
XVI	20	M	15	14 - 19.*	absent	present	
XVII	23	M	19	31.	absent	absent	

* The bacilluria in these cases was cut short by treatment.

Case I.



107
 106
 105
 104
 103
 102
 101
 100
 99
 NORMAL
 98
 97

10
 15
 20
 25
 30
 35
 40
 45
 50
 55
 60
 65
 70
 75
 80
 85
 90

Acid
 Neutral
 Alkaline
 Reaction

Case I.

M. A. B., Female. Aged 29 years.

Admitted 9th September 1904.

Discharged well 10th December 1904.

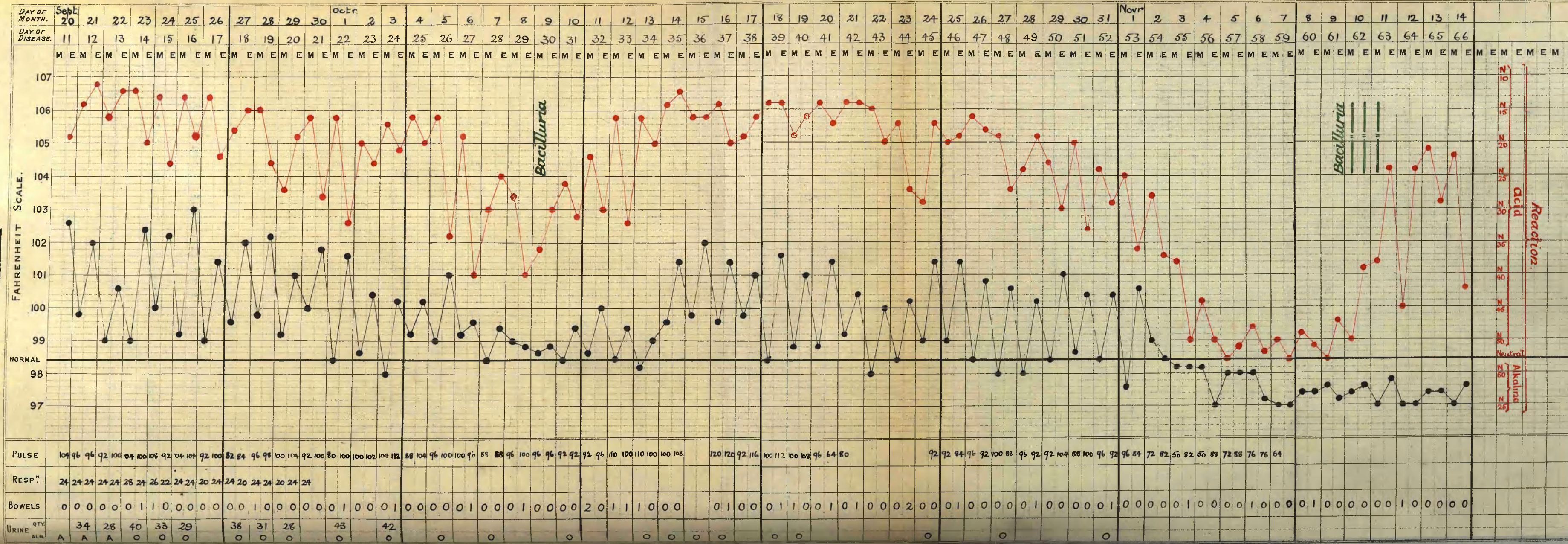
The patient was admitted on the 13th day of illness, and had a severe attack of typhoid fever, followed by a relapse.

The whole illness was of 53 days duration, the primary attack lasting 21 days, the apyrexial period 5 days, and the relapse 27 days. Diarrhoea was present during the primary attack and in the relapse; the typhoid eruption and a splenic enlargement were noted. Widal's test gave a positive result on the day after admission, and on several occasions afterwards.

Albuminuria was present from the 34th to the 38th day of the disease.

Typhoid bacilluria was noted on the following days of illness :- 21st, 23rd, 42nd, 44th, 48th, and 53rd - 62nd, — at the end of the primary attack, towards the end of the relapse, and in the first ten days of convalescence; it disappeared without treatment. The reaction of the urine fell slightly between the primary attack and the relapse, and markedly as convalescence was set up, regaining its usual variation about a fortnight after the temperature became normal.

Case II



Case II.

J. F., Female. Aged 18 years.

Admitted 20th September 1904.

Discharged well 5th December 1904.

The patient was admitted on the 11th day of the disease, and suffered from a moderately severe attack of typhoid fever lasting 53 days. The case was prolonged on account of the disease apparently relapsing just as the temperature was about to settle to normal. Diarrhoea was not present, but the typhoid eruption and a splenic enlargement were noted. Widal's test gave an unsatisfactory result on the day after admission, but on the 16th day of the disease gave a sharp positive result, in a dilution of 1-50. Albuminuria was present in small amount on admission, but continued only for a few days.

Bacilluria was noted only on the following days of illness :- 30th, 61st, 62nd and 63rd, when it disappeared without treatment. The reaction kept at a fairly high acidity throughout, but fell the first week of convalescence.

Case III.

J. T., Male. Aged 12 years.

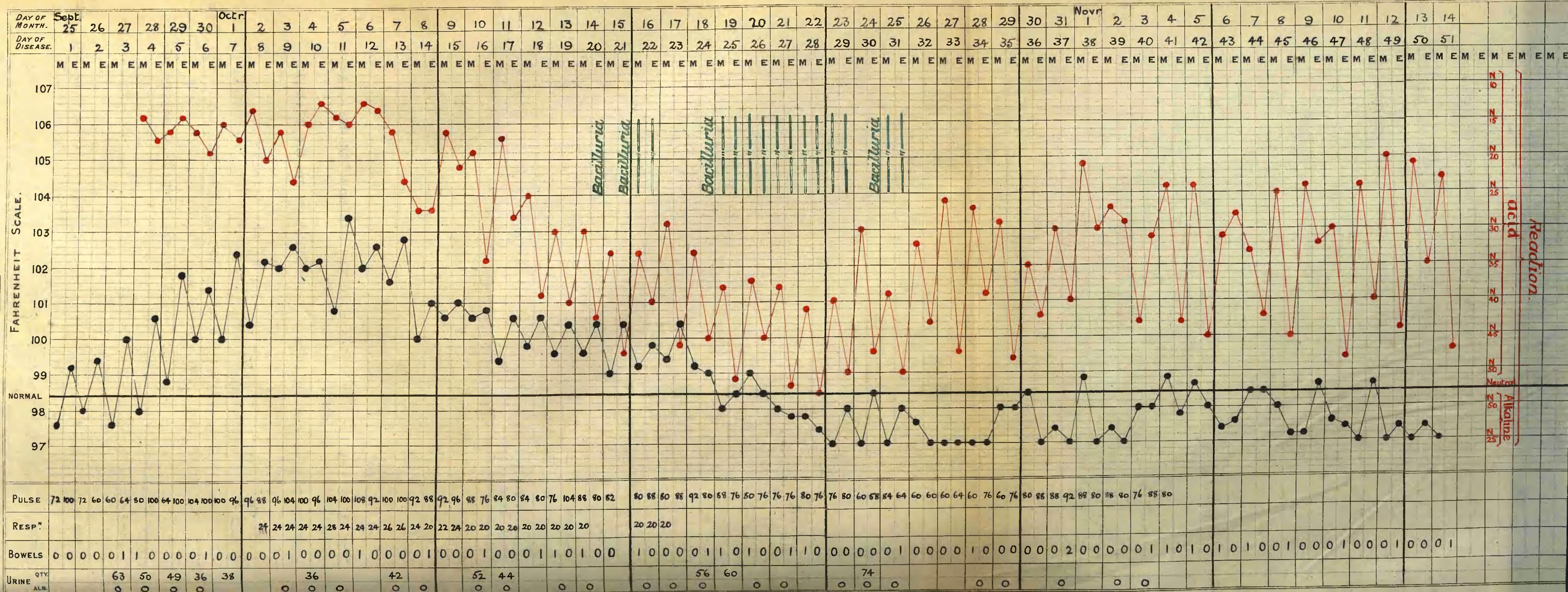
Admitted 22nd September 1904.

Discharged well 23rd November 1904.

The patient was admitted on the 15th day of the disease, and suffered from a mild attack of typhoid fever, lasting 24 days. Diarrhoea was present during the first week after admission, and a profuse typhoid eruption and a splenic enlargement were noted. Widal's test gave a positive result on the day after admission. Albuminuria was not present during the illness.

Typhoid bacilluria was noted from the 24th to the 29th day of the disease, and disappeared without treatment. The reaction of the urine showed a distinct but irregular fall in acidity during the first fortnight of convalescence.

base IV.



N 60
N 55
N 50
N 45
N 40
N 35
N 30
N 25
N 20
N 15
N 10
Neutral
N 50
Alkaline
N 45
N 40
N 35
N 30
N 25
N 20
N 15
N 10

acid
Reaction
alkaline

Case IV.

J. W., Male. Aged 18 years.

Admitted 25th September 1904.

Discharged well 4th December 1904.

This patient was under observation from the first day of the disease. He suffered from a mild attack of typhoid fever lasting 24 days. Diarrhoea was not present during the illness; the typhoid eruption was first seen on the ninth day, but no splenic enlargement could be made out at any time. Widal's reaction indefinite on the 5th and 7th days, gave a sharp positive result in a 1-50 dilution on the 11th day. Albuminuria was not present during the illness.

Bacilluria was noted on the 20th, 21st and 22nd, and from the 24th to the 31st days of illness, when it disappeared without treatment. The acidity of the urine rose much more quickly than the temperature, and showed a well marked fall at the beginning of convalescence.

Case V.

J. T. B., Male. Aged 34 years.

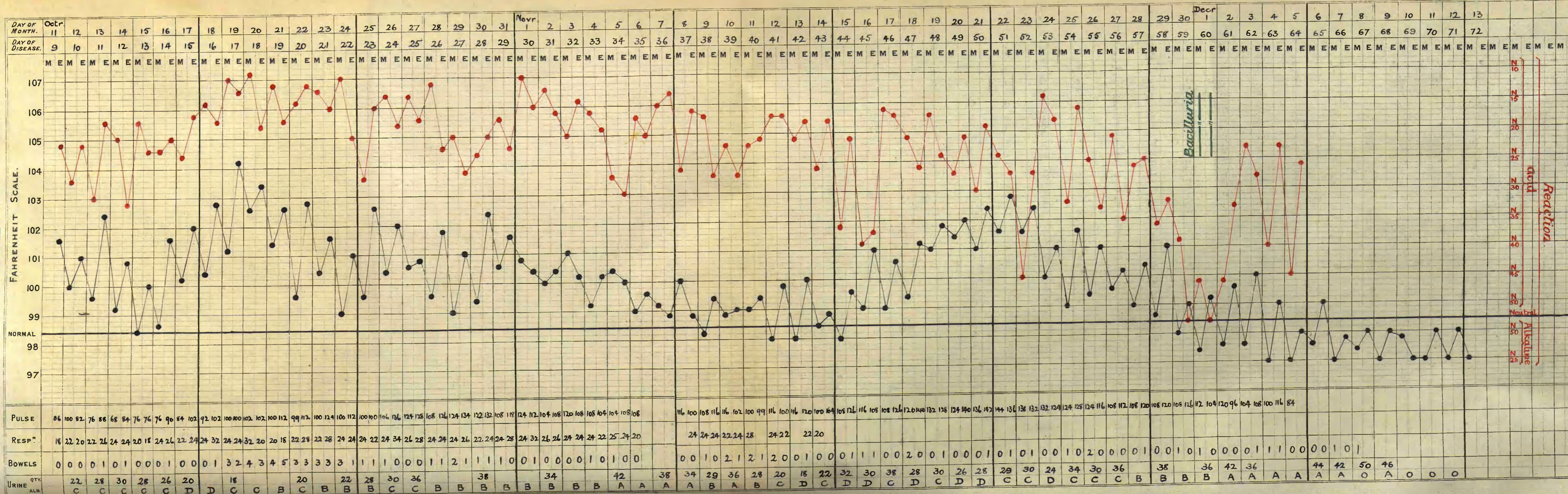
Admitted 30th September 1904.

Discharged well 22nd November 1904.

The patient was admitted on the 22nd day of illness, and had a severe attack of typhoid fever of 33 days duration. Diarrhoea was not present, but the typhoid eruption and a considerable splenic enlargement were noted. Widal's test gave a positive result on admission. Albuminuria was only noted from the 48th to 53rd day of the disease when cystitis had been set up.

Bacilluria was noted when the temperature was coming down on the 28th day, and remained present for 25 days afterwards. On the 48th day the patient had pain and difficulty in micturition, and pus was noted in the urine. Urotropin (10 grains three times a day) was given on the 51st day, the bladder was washed out with boric acid solution, and the cystitis rapidly disappeared. The reaction here presented fairly typical variations during the disease, but it did not tend to regain the normal variation after convalescence had been well established; this fact probably accounted for the development of cystitis.

Case VI



Case VI.

L. F., Female. Aged 25 years.

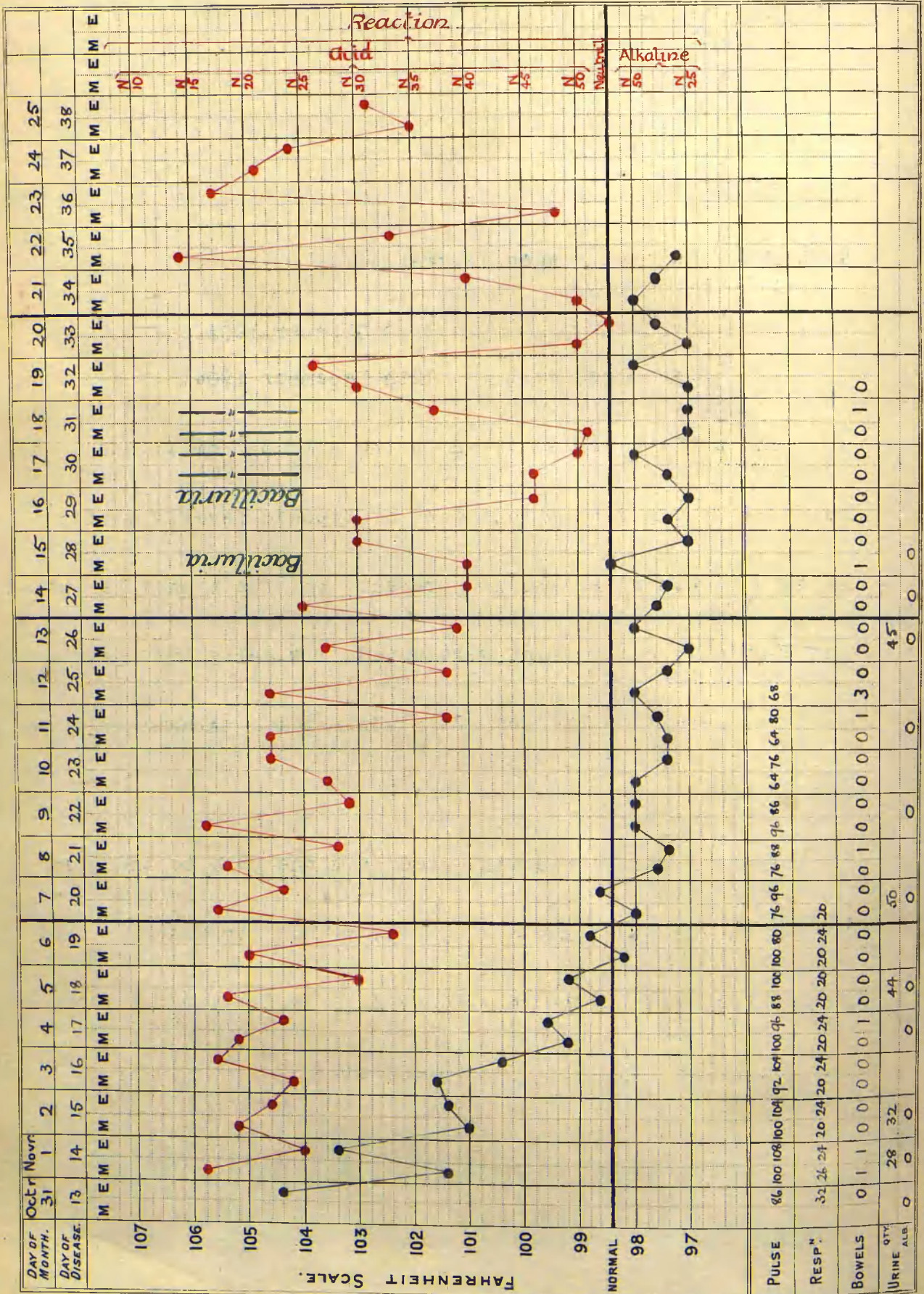
Admitted 11th October 1904.

Discharged well 5th January 1905.

The patient was admitted on the ninth day of the disease, and suffered from a very severe attack of typhoid fever, followed by a relapse. The total duration of the illness was 59 days, the primary attack lasting 37 days, the apyrexial period 6 days, and the relapse 16 days. Diarrhoea was present and the typhoid eruption and a splenic enlargement were noted. Widal's reaction was strongly positive from the day after admission. The patient suffered from Nephritis, which had apparently begun almost simultaneously with the disease; she stated that she had previously had an attack of inflammation of the kidneys, from which she had recovered. Albumen and blood were present in the urine up to the 34th day of the disease, and albumen remained present until a few days before being discharged, the blood having disappeared.

Bacilluria was noted only on the 59th and 60th day of the disease, and it disappeared without treatment. The reaction was of high acidity throughout, only falling for a few days at the end of the relapse.

Case VII



Case VII.

K. McM., Female. Aged 16 years.

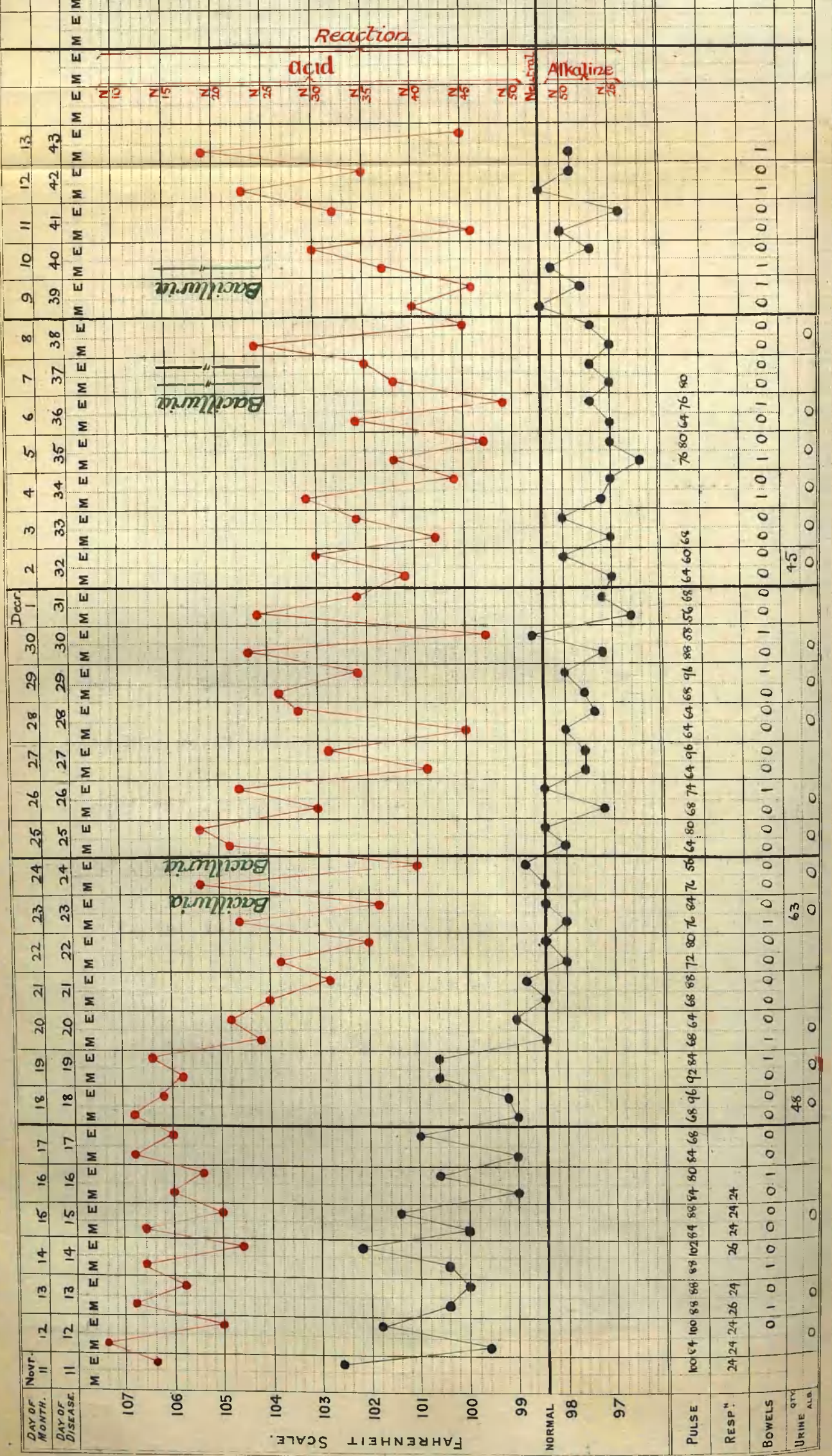
Admitted 31st October 1904.

Discharged well 12th December 1904.

The patient was admitted on the 13th day of illness, and suffered from a very mild attack of typhoid fever, lasting 19 days. Diarrhoea was not present, but the typhoid eruption and a splenic enlargement were noted. Widal's test gave a positive result on the day after admission. Albuminuria was not present.

Typhoid bacilluria was noted from the 28th to the 31st day of the disease, and disappeared without treatment. The reaction showed a late fall in acidity, which did not occur until the 10th day after convalescence.

Case VIII



FARENHEIT SCALE.

NORMAL

PULSE

RESPⁿ

BOWELS

URINE QTY ALB

Case VIII.

P. F., Male. Aged 18 years.

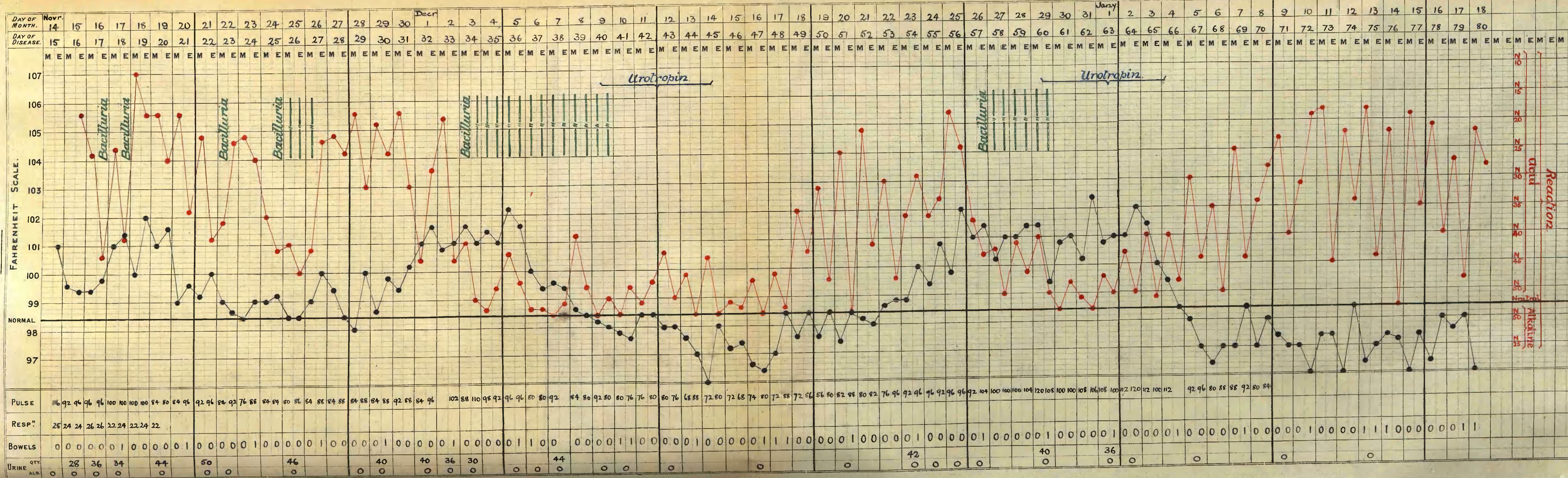
Admitted 11th November 1904.

Discharged well 11th January 1905.

This patient was admitted on the 11th day of illness, and suffered from a mild attack of typhoid fever, lasting 20 days. Diarrhoea was not present in hospital, the typhoid eruption was noted, but no splenic enlargement could be made out. Widal's test gave a positive result the day after admission. Albuminuria was not present.

Bacilluria appeared on the 23rd, 24th, 36th, 37th, 39th and 40th days of the disease, when it disappeared without treatment. The reaction showed normal variations, but the acidity tended to fall rather late in the illness.

Case IX



Case IX.

T. L., Male. Aged 19 years.

Admitted 14th November 1904.

Discharged well 15th February 1905.

The patient was admitted on the 15th day of the disease, and had a prolonged but not severe attack of typhoid fever, followed by a relapse. The duration of the illness was 66 days, the primary attack lasting 38 days (a recrudescence simulating a relapse having prolonged it), the apyrexial period 14 days, and the relapse 14 days. Diarrhoea was not present during the illness, but the typhoid eruption and a splenic enlargement were noted. Widal's test gave a rather slow positive result in a 1-50 dilution on the 15th day of the disease, but on the 20th the result was quick and satisfactory. Albuminuria was not present during the disease.

Bacilluria was present on the 17th, 18th, 23rd, 25th, 27th, and from the 34th to the 41st day of the disease, when it disappeared under treatment by urotropin, and again on the 57th to the 61st day, when it finally disappeared under urotropin. The reaction showed considerable variations, and did not follow at all a regular course.

Case X.

F. H., Male. Aged 28 years.

Admitted 14th November 1904.

Discharged well 1st February 1905.

The patient was admitted on the 15th day of illness, and had a severe attack of typhoid fever, followed by a relapse. The total duration of the illness was 50 days, the primary attack lasting 27 days, the apyrexial period 9 days, and the relapse 14 days. Diarrhoea was not present during the illness, but the typhoid eruption and splenic enlargement were noted. Widal's test gave a positive result the day after admission. Albuminuria was absent.

Bacilluria was noted on the 32nd and from the 41st to the 45th day of the disease — between the primary attack and the relapse, and early in the relapse; it disappeared without treatment. The reaction showed fairly typical variations, but the acidity fell only slightly after the primary attack, although it fell early in the relapse; in the first ten days of convalescence, the acidity was continuously very low, but bacilluria did not develop.

Case XI.

W. P., Male. Aged 23 years.

Admitted 14th November 1904.

Discharged well 4th January 1905.

The patient was admitted on the 14th day of illness, and had a mild attack of typhoid fever, lasting 22 days.

Diarrhoea was not present, nor was the typhoid eruption

or a splenic enlargement noted in hospital. Widal's test

gave a strong positive result on admission. Albuminuria

was absent during the illness.

Bacilluria was present on the 23rd, 25th and 26th days.

The reaction showed only a slight and temporary fall in

acidity on the 25th and 26th days of illness.

Case XII.

I. M., Male. Aged 18 years.

Admitted 23rd November 1904.

Discharged well 11th January 1905.

The patient was admitted on the ninth day of the disease and suffered from a mild attack of typhoid fever of 23 days duration. Diarrhoea was not present, but the typhoid eruption and a splenic enlargement were noted. Widal's test gave a positive result the day after admission. Albuminuria was present on the 29th day of illness in traces, and microscopic examination of the urine showed pus corpuscles.

Bacilluria was noted on the 20th and 21st and from the 25th to the 29th days of the disease, when it appeared that a pyuria was about to develop, but urotropin was administered and the bacilluria and pyuria disappeared at once. The reaction showed typical variations, and rose after the bacilluria had disappeared. It will be noted that the administration of urotropin, though clearing the urine, did not raise it in acidity.

Case XIII.

J. C., Male. Aged 17 years.

Admitted 24th November 1904.

Discharged well 15th February 1905.

The patient was admitted on the 15th day of the disease, and suffered from a severe attack of typhoid fever, lasting 32 days. Diarrhoea was not present, but the typhoid eruption and a splenic enlargement were noted. Widal's test gave a sharp positive result on the day after admission. Albuminuria was not present during the illness.

Bacilluria was noted on the 24th, 25th, and 26th, and from the 29th to the 35th day of the disease, when it disappeared under treatment by urotropin. The reaction showed fairly typical variations, showing a marked fall in acidity as convalescence was set up. The chart shows that urotropin does not raise the acidity of the urine.

Case XIV.

W. P., Male. Aged 46 years.

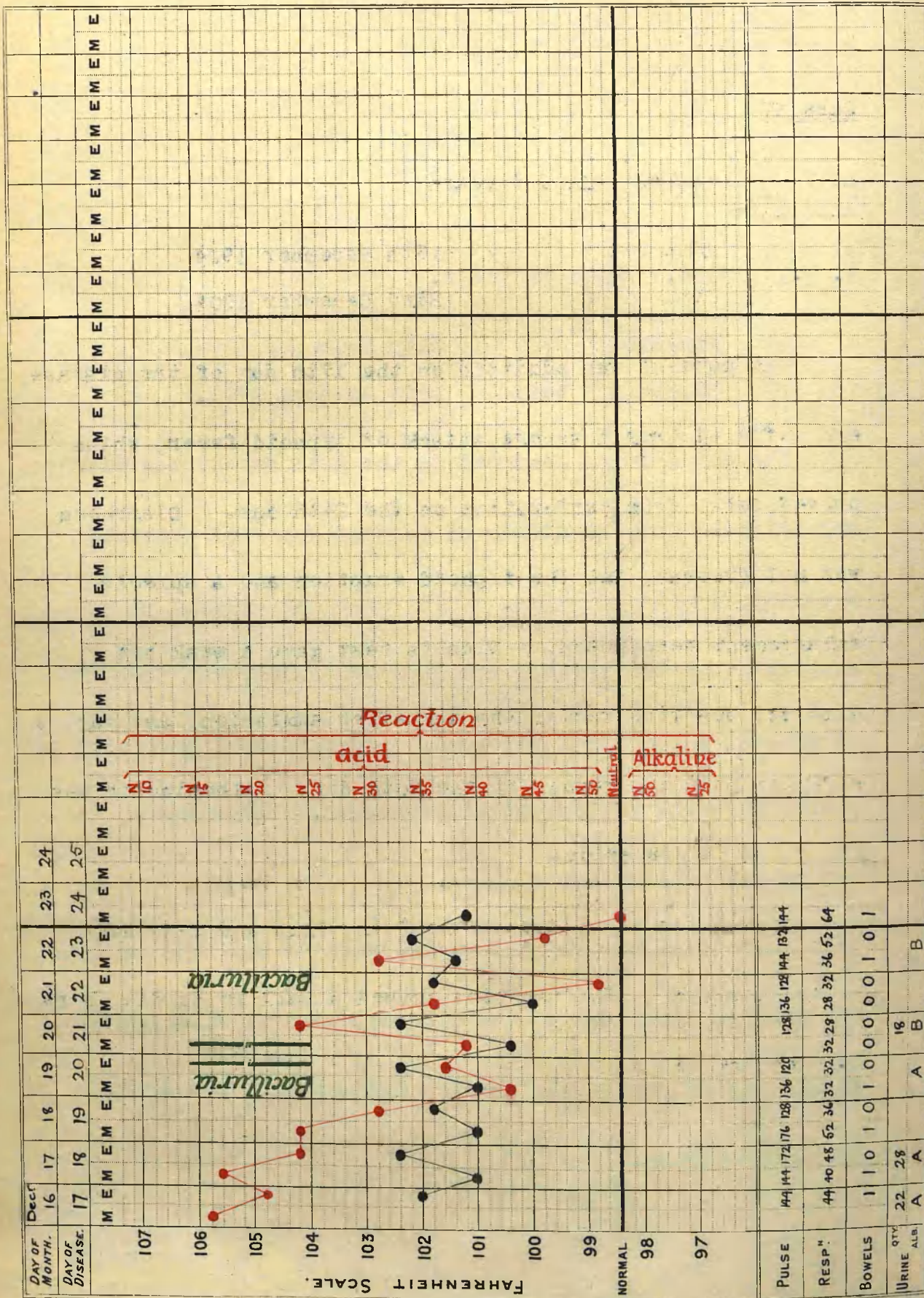
Admitted 30th November 1904.

Discharged well 15th January 1905.

The patient was admitted on the 14th day of the disease, and suffered from an attack of typhoid fever of moderate severity, lasting 26 days. Diarrhoea was present in Hospital, and the typhoid eruption was noted, but there was no splenic enlargement made out. Widal's test gave a positive result the day after admission. Albuminuria was not present during the illness.

Bacilluria was present on the 24th to the 27th, and on the 33rd and 34th day of the disease, when it disappeared without treatment. The acidity did not fall for any prolonged period.

Case XV



Case XV.

A. T., Female. Aged 7 years.

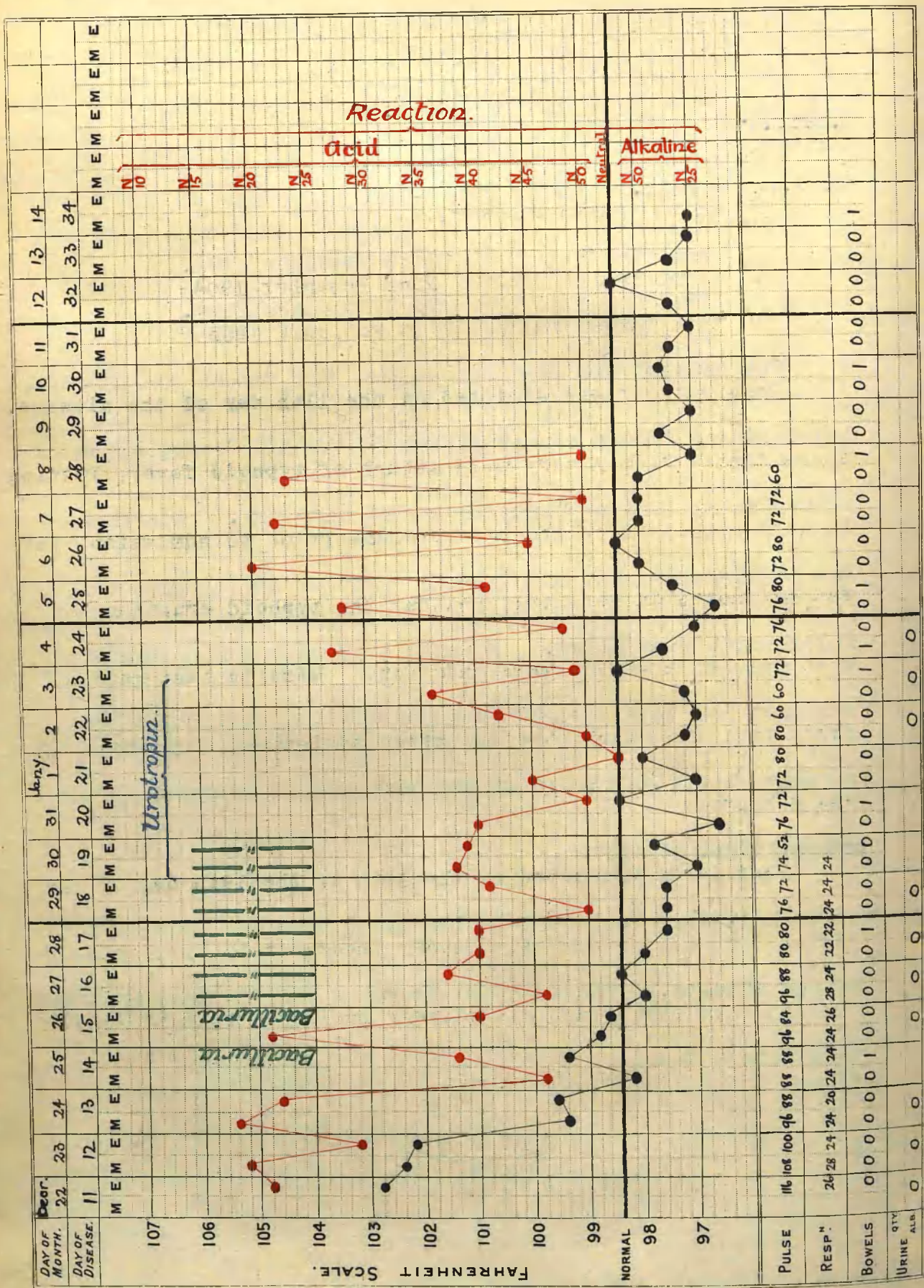
Admitted 16th December 1904.

Died 23rd December 1904.

The patient was admitted on the 17th day of the disease, and suffered from a severe attack of typhoid fever, which proved fatal from perforation on the 24th day. Diarrhoea was not present, but the typhoid eruption and a splenic enlargement were noted. Widal's test gave a weak but distinct^{ly} positive result the day after admission, and gave a stronger positive result on the 20th day. Albuminuria was present from admission.

Bacilluria was noted on the 20th, 21st, and 22nd days of the disease. The reaction showed a fall in acidity a few days before death.

Case XVI



Case XVI.

J. G., Male. Aged 20 years.

Admitted	22nd December 1904.
Discharged well	1st February 1905.

This patient was admitted on the 11th day of the disease, and suffered from a very mild attack of typhoid fever, lasting 15 days. Diarrhoea had been present prior to admission, but was not noted in hospital; neither the typhoid eruption nor a splenic enlargement were made out. Widal's test gave a sharp positive result the day after admission. Albuminuria was not present.

Bacilluria was noted on the 14th to the 19th day of the disease, when it disappeared under treatment by urotropin. The reaction showed a comparatively prolonged fall in acidity at the beginning of convalescence.

Case XVII.

J. W., Male. Aged 23 years.

Admitted 6th May 1905.

Discharged well 2nd June 1905.

The patient was admitted on the 15th day of the disease and suffered from a mild attack of typhoid fever, lasting 19 days. No diarrhoea was present, nor was the typhoid eruption seen in hospital, although a considerable splenic enlargement was made out on admission. Widal's test gave a positive result on the day after admission. Albuminuria was not noted during the illness.

Bacilluria was noted on only one occasion, on the 31st day of the disease. The reaction did not show any well marked fall in acidity.

NEGATIVE CASES.

The cases of enteric fever in which bacilluria does not develop, seem to fall into three classes.

(1) Cases in which the acidity of the urine is continuously high throughout the disease, and in which the normal variation of the reaction is set up without a preliminary fall. Cases XVIII, XIX, and XX.

(2) Cases in which the acidity of the urine falls at a time when stray organisms have ceased to find their way into the urine. This time seems to vary in different cases. Cases XXI, XXII, XXIII, XXVI, XXVII, XXVIII, and XXX.

(3) Fatal cases terminating before the acidity might reasonably be expected to fall. Cases XXIV, XXV, and XXIX.

SUMMARY OF NEGATIVE CASES.

Case No.	Age	Sex	Duration of illness in days.	Albuminuria	Diarrhoea	Result
XVIII	26	M	52	present	present	Recovered
XIX	3	F	35	present	present	Recovered
XX	23	F	19	absent	present	Recovered
XXI	24	M	35	absent	present	Recovered
XXII	11	M	23	absent	absent	Recovered
XXIII	11	M	18	absent	absent	Recovered
XXIV	29	M	(14)	absent	present	Died
XXV	26	M	(29)	present	present	Died
XXVI	34	F	19	absent	absent	Recovered
XXVII	3	M	28	absent	present	Recovered
XXVIII	12	F	32	absent	absent	Recovered
XXIX	23	M	(27)	present	present	Died
XXX	24	F	21	present	absent	Recovered

Case XVIII.

J. D., Male. Aged 26 years.

Admitted 16th August 1904.

Discharged well 22nd November 1904.

This patient was admitted on the 18th day of the disease and suffered from a very severe and prolonged attack of typhoid fever, lasting 52 days. Diarrhoea was present, and the motions passed from the 21st to 23rd day of the disease contained blood; no further haemorrhage was noted after the latter date. A profuse typhoid eruption, and a palpable splenic enlargement were made out. Widal's reaction was positive on admission. Albuminuria was noted from the 18th to the 23rd day, and from the 41st to the 45th day of the disease.

The acidity of the urine was continuously high throughout the illness, and did not show any marked fall in convalescence, before the usual variation in the reaction became established again.

Case XIX.

M. A. J., Female. Aged 3 years.

Admitted 15th September 1904.

Discharged well 13th November 1904.

The patient was admitted on the 8th day of illness, and had a severe attack of typhoid fever, lasting 35 days.

Diarrhoea was present in hospital, and the typhoid eruption and a splenic enlargement were noted. Widal's reaction was positive on the day of admission. Albuminuria was present in traces on the 10th day of the disease, but was absent on all other occasions.

The reaction of the urine was highly acid throughout the disease, and resumed, on recovery, normal variations without any preliminary fall in acidity. Diarrhoea occurred at the two periods of the disease when the acidity might have been expected to fall.

Case XX.

E. B., Female. Aged 23 years.

Admitted 16th September 1904.

Discharged well 21st October 1904.

The patient was admitted on the 11th day of the disease, and suffered from a moderately severe but short attack of typhoid fever, lasting 19 days. Diarrhoea was present in hospital. The typhoid eruption was not noted, but a splenic enlargement was made out. Widal's test gave a positive result the day after admission. Albuminuria was not present during the illness.

The acidity of the urine remained high during the illness, and the reaction returned to a normal variation without any marked preliminary fall in the acidity.

Case XXI.

I. J., Male. Aged 24 years.

Admitted 30th September 1904.

Discharged well 24th November 1904.

The patient was admitted on the 15th day of the disease, and suffered from a prolonged but not severe attack of typhoid fever. Diarrhoea was present after admission, but an obstinate constipation was set up in the fifth week; the typhoid eruption was noted, but no splenic enlargement could be made out. Widal's test was positive on the day after admission. Albuminuria was not present during the illness.

The acidity remained high for the first four weeks of the disease, in the fifth week it showed a marked fall, regaining a normal condition in the sixth week of the illness. Bacilluria was never noted.

The case was somewhat remarkable clinically by the erratic comparatively low temperature recorded during the first four weeks, when the patient presented unmistakable symptoms of typhoid fever. The temperature in the fifth and sixth weeks was also rather erratic, probably on account of the constipation which then supervened.

Case XXII.

J. L., Male. Aged 11 years.

Admitted 17th October 1904.

Discharged well 29th January 1905.

This patient was admitted on the 15th day of the disease and suffered from a moderately severe attack of typhoid fever, lasting 23 days. In early convalescence, the patient developed an otitis media which gave rise to the erratic temperatures from the 25th to the 37th day. Diarrhoea was not present, but rose red spots and a palpable splenic enlargement were noted. Widal's reaction was positive on admission.

Albuminuria was absent.

The acidity of the urine remained high until the second week of convalescence, when it fell for a few days, and afterwards showed a normal variation. No bacilluria was noted.

Case XXIII.

N. H., Male. Aged 11 years.

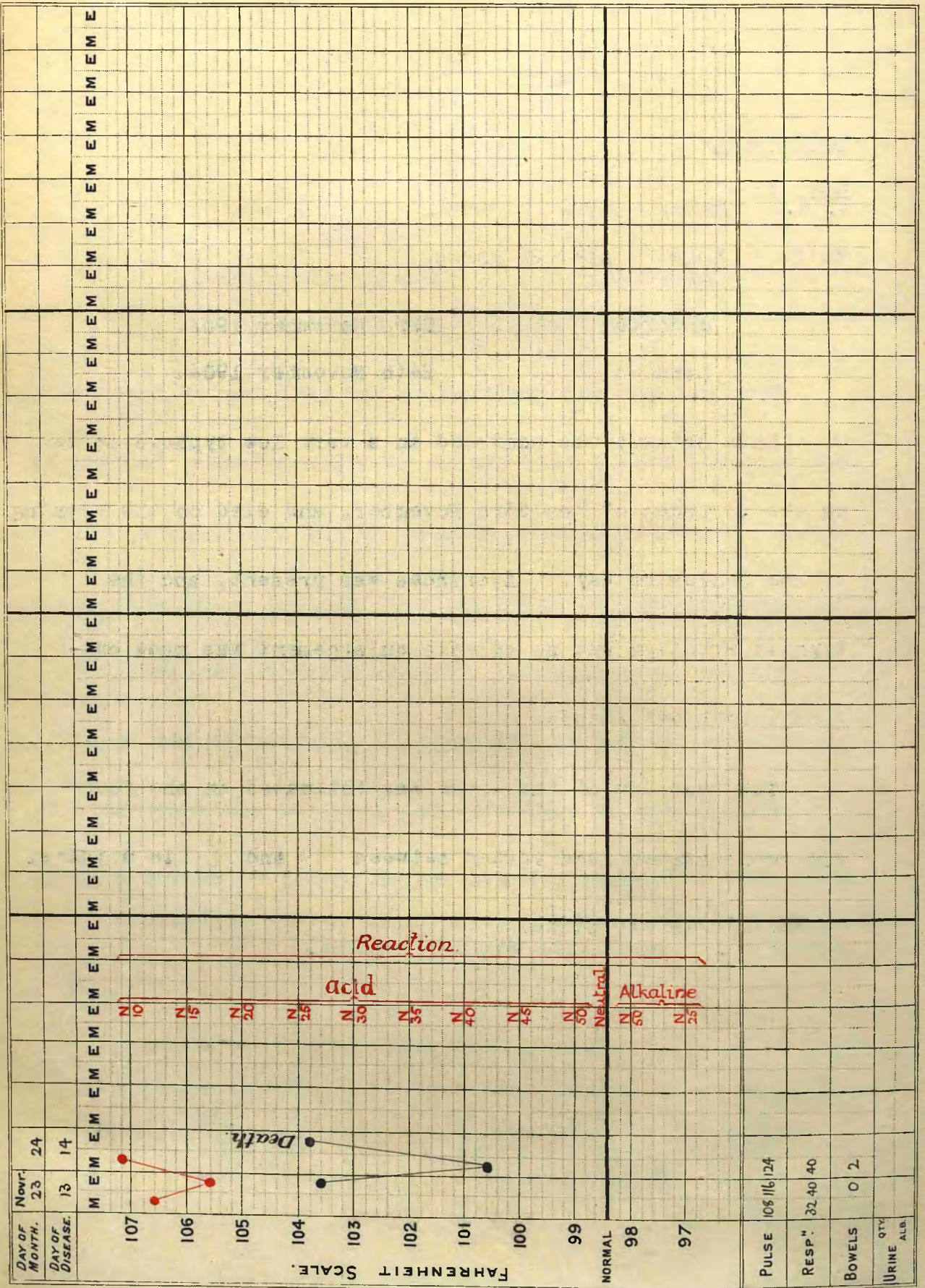
Admitted 4th November 1904.

Discharged well 1st February 1905.

This patient was admitted on the 17th day of the disease, and suffered from a mild attack of typhoid fever, lasting 18 days. Diarrhoea was not present during the illness, nor was the typhoid eruption noted in hospital, but a palpable splenic enlargement was made out. Widal's reaction was strongly positive on the day of admission. Albuminuria was absent.

The acidity on admission was low, and continued so for four days afterwards, when it began slowly to assume a normal variation. Bacilluria was not present.

Case XXIV



Case XXIV.

T. D., Male. Aged 29 years.

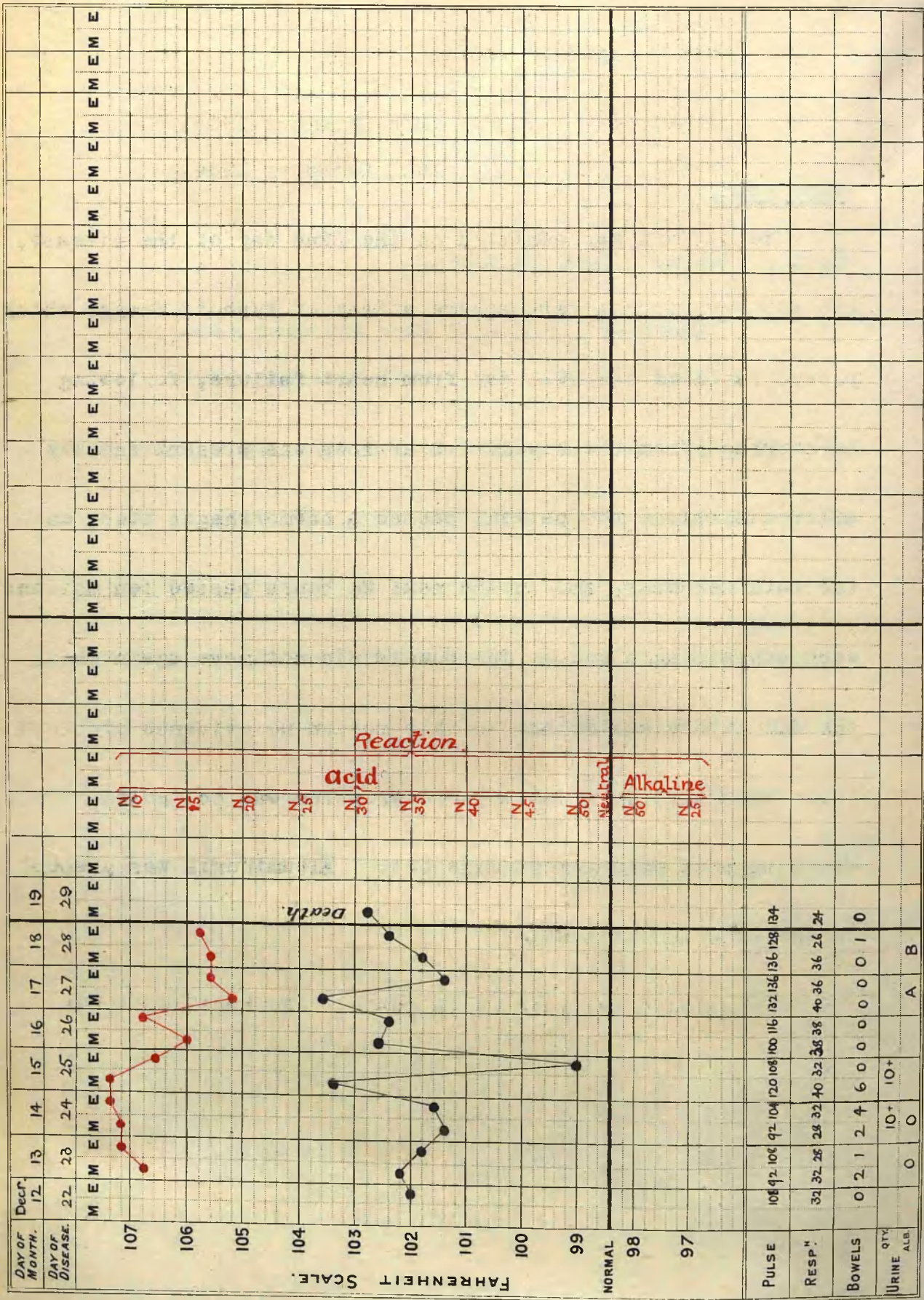
Admitted 23rd November 1904.

Died 24th November 1904.

This patient was admitted in a very low typhoid state on the forenoon of the 23rd November, and died on the evening of the following day. Diarrhoea was present, and the typhoid eruption, but no splenic enlargement, was made out. Albuminuria was absent.

The reaction of the urine was estimated in the four specimens passed, and varied between $\frac{N}{17}$ and $\frac{N}{8}$ in acidity. No bacilluria was noted.

Case XXV



Case XXV.

J. B., Male. Aged 26 years.

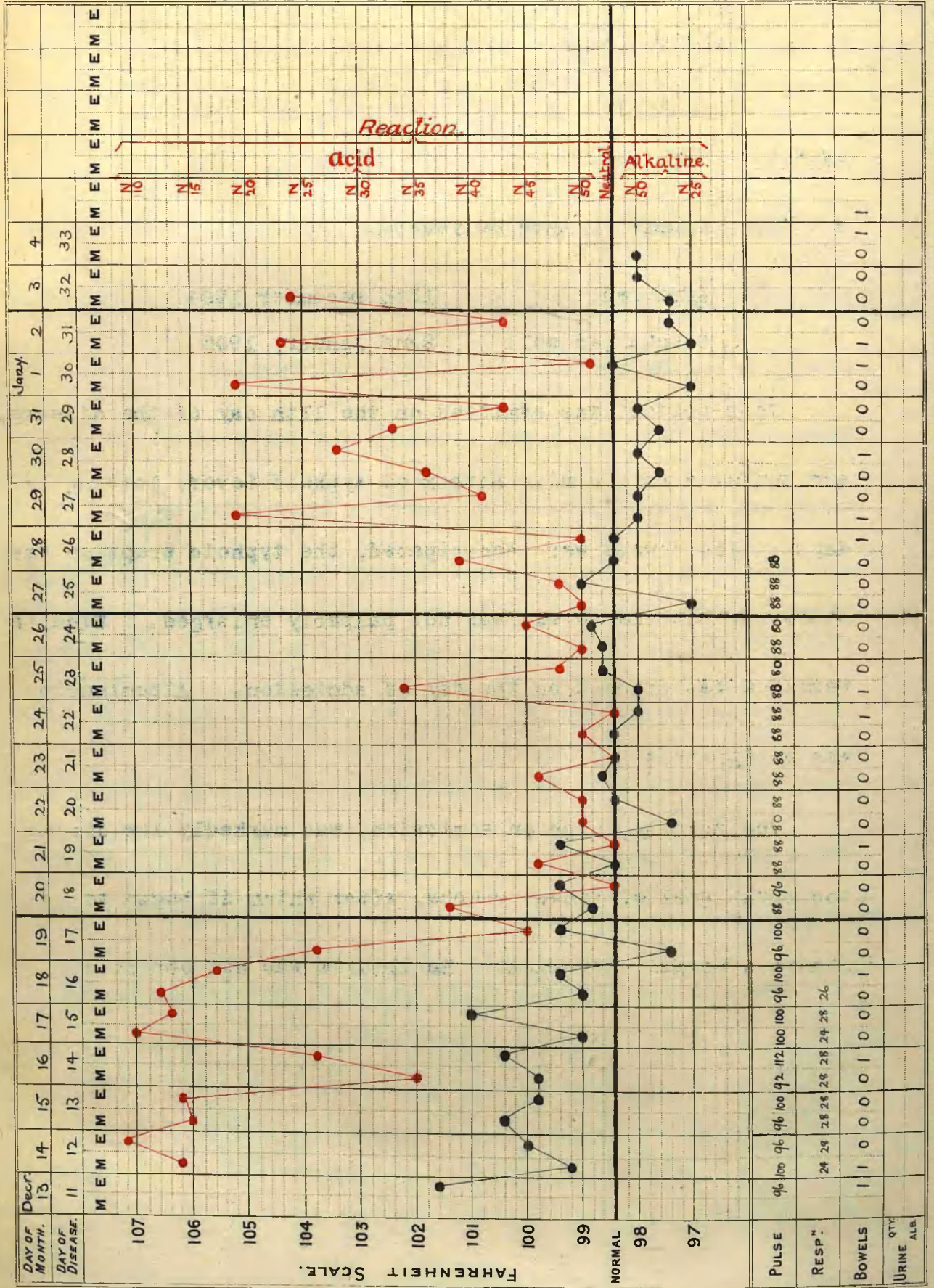
Admitted 12th December 1904.

Died 19th December 1904.

The patient was admitted on the 22nd day of the disease, and suffered from a very severe attack of typhoid fever, which proved fatal on the 29th day from heart failure, following haemorrhage from the bowel. Diarrhoea was present shortly after admission, the patient passed a haemorrhagic stool on the 14th December, and in the next 24 hours passed ten motions each containing blood. The bowels did not move again until the day before death, but in this motion no evidence of blood could be detected. The typhoid eruption was not noted, nor was a splenic enlargement made out. Albuminuria was present on the 27th and 28th day.

The acidity was high up to death. No bacilluria was noted.

Case XXVI



Case XXVI.

Mrs H., Female. Aged 34 years.

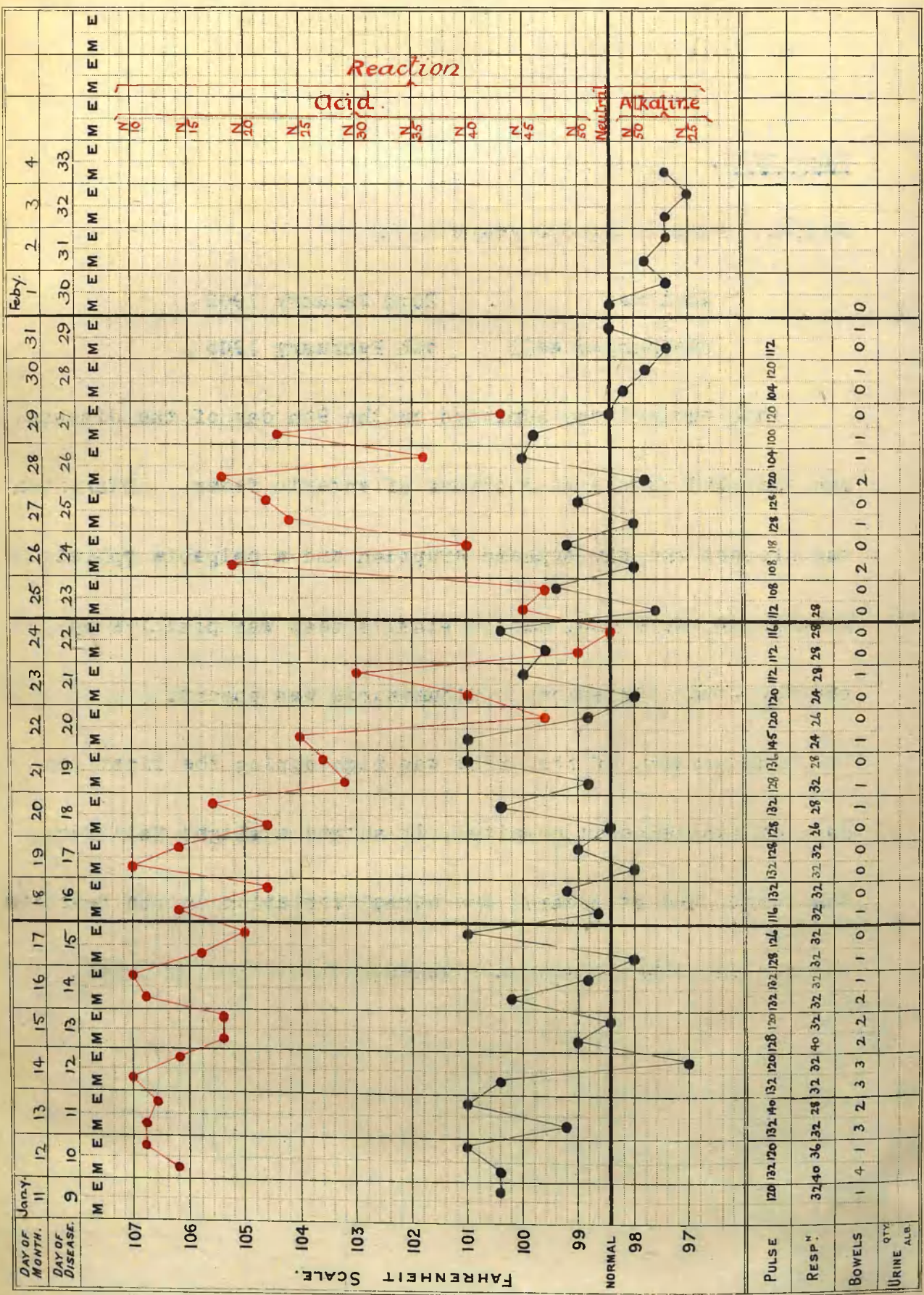
Admitted 13th December 1904.

Discharged well 22nd January 1905.

This patient was admitted on the 11th day of the disease, and suffered from a mild attack of typhoid fever, lasting 19 days. The bowels were constipated, the typhoid eruption was observed, but the spleen was not palpably enlarged. Widal's reaction was present on the day of admission. Albuminuria was not present.

The acidity, high on admission, was markedly low during the first week of convalescence, after which it began to regain a normal variation. Bacilluria was not observed.

Case XXVII



Case XXVII.

C. M., Male. Aged 3 years.

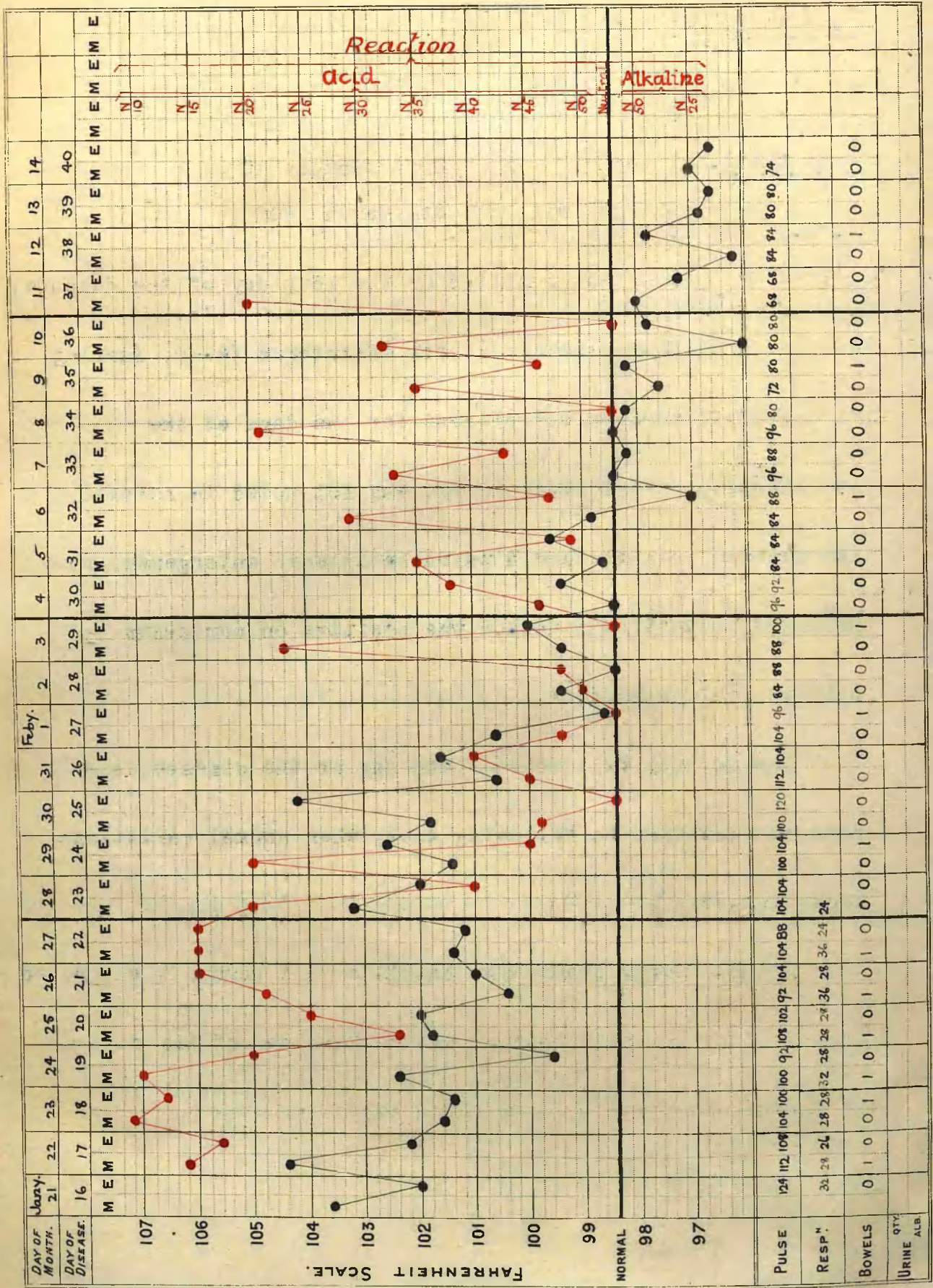
Admitted 20th January 1905.

Discharged well 5th February 1905.

This patient was admitted on the 9th day of the disease, and suffered from a mild attack of enteric fever. Diarrhoea was present, and the typhoid eruption and a palpable splenic enlargement were made out. Widal's test was positive on the day after admission. Albuminuria was absent.

The acidity of the urine was high during the first ten days of residence in hospital, it showed a slight fall for four days, and afterwards the normal variation in the reaction was set up. Bacilluria was absent.

Case XXVIII.



Reaction
 acid
 Alkaline

Case XXVIII.

F. P., Female. Aged 12 years.

Admitted 21st January 1905.

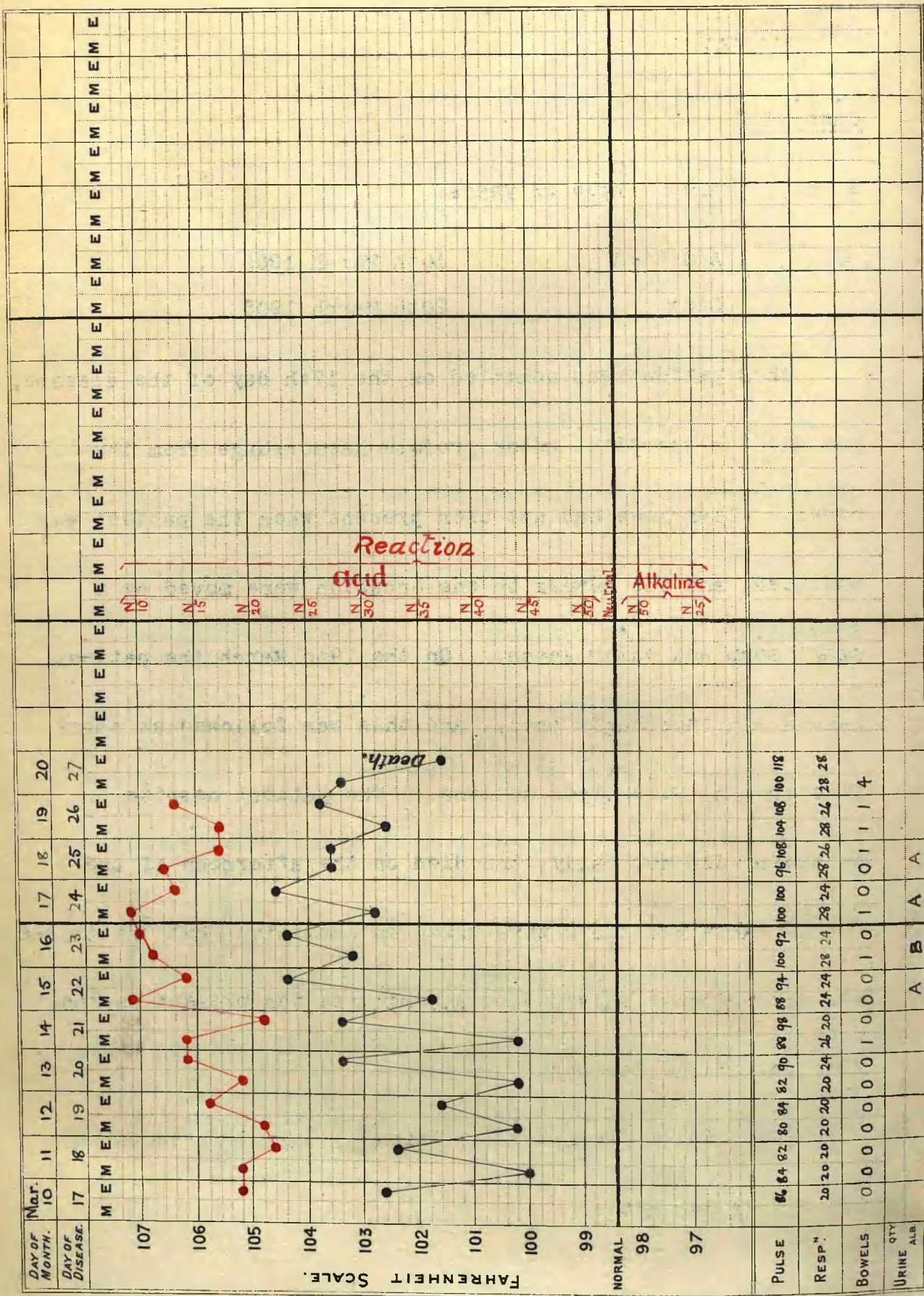
Discharged well 8th March 1905.

This patient was admitted on the 16th day of the disease, and suffered from a severe attack of enteric fever, lasting 31 days. Diarrhoea was present for two days at the commencement of the illness, but was not noted in hospital; the typhoid eruption and a palpable splenic enlargement were present. Widal's reaction was positive on admission. Albuminuria was absent.

The acidity fell on the 24th day of the disease, and remained low for the following week, when normal variations began to appear.

A bacteriuria due to the bacillus coli communis was noted in this case on one occasion, on the 28th day of the disease. No further bacilluria of any kind was noted.

Case XXIX.



Case XXIX.

W. B., Male. Aged 23 years.

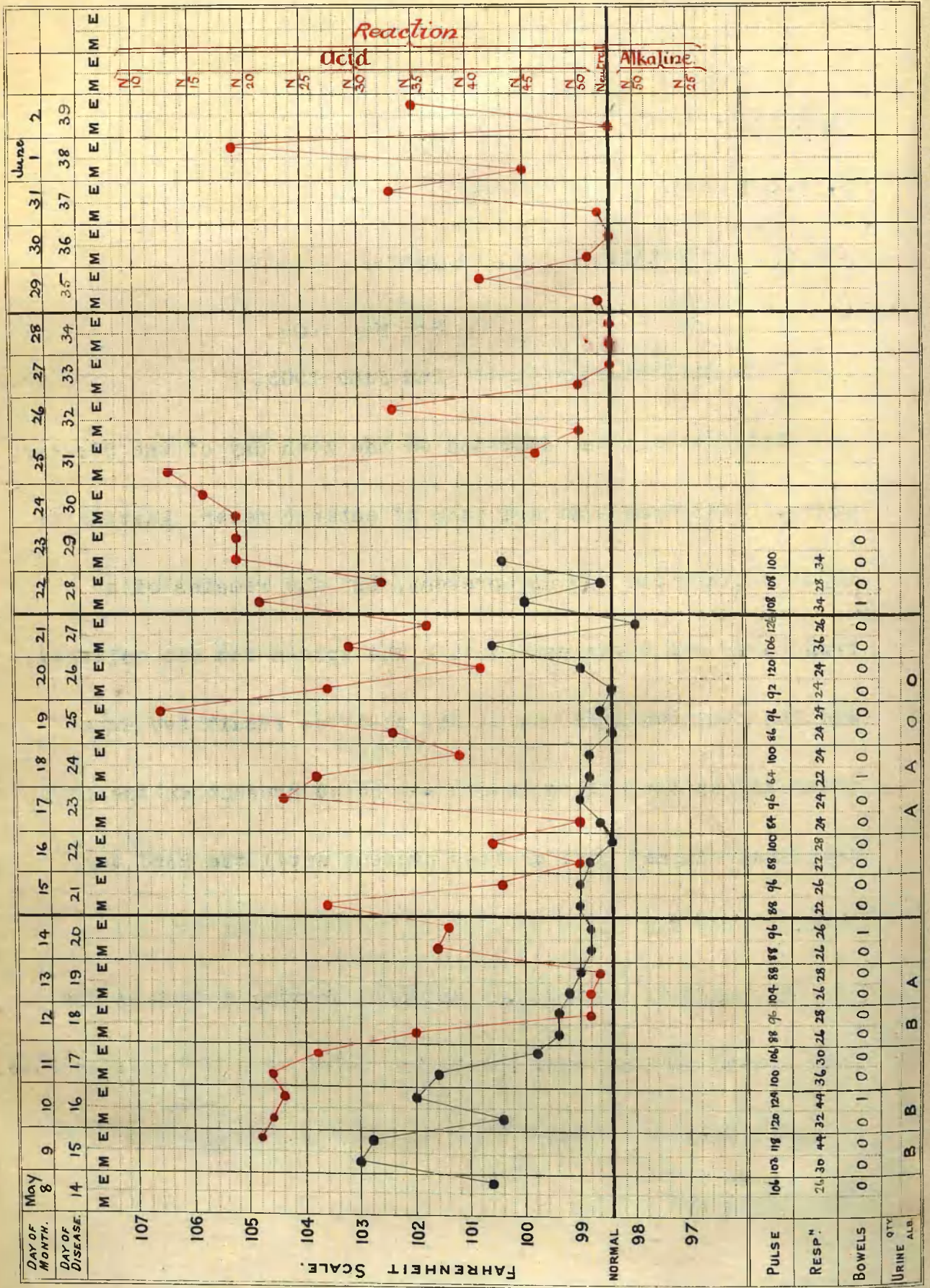
Admitted 10th March 1905.

Died 20th March 1905.

This patient was admitted on the 17th day of the disease, and died on the 27th, after profuse haemorrhage from the bowel. Diarrhoea had not been present when the patient was admitted, and the bowels on one occasion were moved by a small soap and water enema. On the 19th March the patient passed a haemorrhagic stool, and this was followed at short intervals by five other motions. The patient, despite treatment, did not rally, and died on the afternoon of the 20th. Rose red spots were noted on admission, but the spleen was not palpably enlarged. Albuminuria was present on the 22nd day of the disease.

The acidity remained high throughout the disease. No bacilluria was noted.

— Case XXX. —



Case XXX.

Mrs McL., Female. Aged 24 years.

Admitted 8th May 1905.

Discharged well 2nd June 1905.

This patient was admitted on the 14th day of the disease, and suffered from a mild attack of enteric fever, lasting 21 days. Diarrhoea was not present, but the remains of a typhoid eruption was made out. The spleen was not enlarged. Widal's reaction gave a distinct positive result two days after admission. Albuminuria was noted present on the 15th day, and remained more or less present until the 23rd day, when it disappeared.

The acidity varied considerably, showing a fall as the patient was getting well and in the third week of convalescence. No bacilluria was observed.