

ATROPINE AS A DIAGNOSTIC AGENT

IN TYPHOID INFECTIONS.

by

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INTRODUCTORY REMARKS.

Although Typhoid Fever prevails especially in temperate climates, a considerable number of cases occur in the British Isles. In 1910 there was a mortality of 46 per million of persons living in England and Wales, and this was a lower rate than in any year since 1869.

Important as the study of Typhoid Fever is to us as individuals in Britain, it is infinitely more important to us as an Empire whose Army is garrisoned in Tropical and sub-Tropical climates.

Typhoid Fever has been the scourge of armies, and before the recent war, was responsible for more deaths than powder and shot.

The history of recent wars shows how terrible has been the havoc played among troops by Typhoid.

In the Spanish American War, one-fifth of the soldiers in the National encampments had Typhoid. In 90% of the volunteer regiments the disease broke out within 8 weeks of going into camp.

In the South African War the British Army - 557,653 - had 57,654 cases of Typhoid with 8,225 deaths, while only 7,582 men died of wounds received in battle.

In/

In the Japanese Russian War, and the late war with Germany the remarkable efficiency of modern hygiene has been demonstrated, and in consequence the mortality from Typhoid Fever has been very low.

Before and during the late war, various diseases having resemblance to Typhoid Fever have been investigated, and to a great extent differentiated, but much remains to be done on the subject.

In 1911 in the Fourth Report Welcome Tropical Research Laboratories, Archibald drew attention to the presence of peculiar enteric-like fevers which are met with at times in the Soudan.

Chalmers and Macdonald have also described in the Lancet of July 22nd, 1916 - organisms, other than *B. Typhosus*, *B. Paratyphosus A* or *B*, that give rise to a fever which is clinically very much like an early Typhoid.

Frequently cases have been recorded in which a *B. Faecalis Alkaligenes Septicaemia* has at first simulated a mild Typhoid.

The importance of an early diagnosis in cases of intestinal infection is threefold.-

(1) as a guide to treatment, especially when specific therapy is available, e.g., in Amoebic and bacillary dysentery.

(2)/

- (2) to enable prophylactic measures to be taken against epidemic spread, and
- (3) as a means of determining the efficiency of prophylactic inoculation.

The introduction of the triple inoculation against typhoid and the two paratyphoid types has affected an immense reduction in the disease, but at the same time it has increased the diagnostic difficulties by masking the symptoms of disease when infection has occurred in men having only partial immunity.

The immunity conferred by inoculation is only relative, and temporary, and the diagnosis of the disease in protected men is often a matter of extreme difficulty because of the mildness or absence of the characteristic clinical symptoms.

Bacteriological studies have proved that even in un-inoculated cases, the mild and atypical cases frequently form a large proportion of the total: it is impossible to determine these on a purely clinical basis, yet they are very important because they may spread the infection at an early stage, and later a considerable number of chronic carriers results from this group of mild infections.

Absolute diagnosis can only be obtained

- (1) when proper laboratory opportunities are available for the isolation of the causal organism/

organism by blood culture, or from faeces and urine.

(2) by recourse to Agglutination tests.

Blood culture is the most reliable method of diagnosis, but it is only applicable in the first ten days of the disease, and if the case occurs within a reasonable distance of a laboratory.

Most of the cases of Typhoid that I have seen have been while on active service in German East Africa, British East Africa, Uganda, Somaliland and West Africa. In these countries when the population is scattered it is seldom possible to send a blood culture to a laboratory.

Only one or two laboratories existed in each of the countries mentioned.

The same remarks apply to South Africa where I did most of my investigations with Atropine.

In only a very limited number of cases is it possible to have a blood culture made in doubtful cases of fever.

It is equally difficult to get the Agglutination tests done, but even when this is possible the results are not so reliable.

A great deal of work has been, and is being done on the Agglutination tests, and at present there/

there is a difference of opinion as to their true value.

Martin and Upjohn in an article published in 1917 emphasise the existence of numerous difficulties in the diagnosis by Agglutination tests of the enteric fevers in typhoid-inoculated persons. After much experience they came to the conclusion that "the interpretation of observations upon the Agglutination of enteric organism will be too difficult to possess any practical value, and the isolation of the infecting organism must be resorted to for diagnosis".

Browning, Mackie and Thornton in chapters in Browning's book on Applied Bacteriology published in 1918, state that while a marked agglutination reaction in an uninoculated person is conclusive, negative results are of little significance.

On the other hand Dreyer and Inman are strongly of opinion that "accurate differential diagnosis of enteric group cases can only be obtained by routine testing of the serum of the patient against the three micro-organisms B. Typhosus and B. Paratyphosus A and B, in parallel series of observation, and by always determining the maximum dilution of the serum in which agglutination takes place". The results of/

of their work was published in a paper entitled 'The Agglutination Curve and its importance in the diagnosis of Typhoid and Paratyphoid Fevers in Inoculated Persons', which appeared in the Lancet of March 10th 1917.

In a series of 40 cases of Typhoid I attended I had Agglutination tests done and found that while positive results were reliable, negative results were not to be depended upon.

In view of the facts stated and that even if a laboratory is available, repeated and detailed tests require to be done before a definite diagnosis of Typhoid can be arrived at, and that in the several countries where I saw Typhoid cases, it was impossible to have laboratory tests done, I decided to investigate Marris' Atropine test, as it is one that can be done by every medical practitioner without special apparatus. I have applied the test in a series of about forty cases that have come under my care and propose to give the results of my observations in the present thesis.

HISTORICAL OUTLINE.

In November 1916 Captain H.F. Marris, R.A.M.C., published a preliminary report on the use of Atropine as an aid to the diagnosis of typhoid and paratyphoid A and B infections.

In October 1917 the Medical Research Committee issued a further report on Captain Marris' work.

The use of the Atropine test is simple. The patient lies horizontally, and is instructed to remain quiet throughout the test, which is not employed until at least an hour after the last meal.

The pulse rate is counted minute by minute until it is found to be steady - usually a matter of ten minutes.

Atropine Sulphate is then injected hypodermically, the dose being $1/33$ grains, preferably over the triceps region, to ensure rapid absorption.

Twenty-five minutes later the pulse is again counted minute by minute, until it is clear that any rise that may have followed the injection, has begun to pass off.

The difference between the average pulse rate before the injection, and the maximum reached after it gives the 'escape', or acceleration of the pulse rate, /

rate, brought about by the dose of Atropine.

If the escape is 14 or less the case may be regarded as one of the typhoid or paratyphoid fever.

If it is 15 or more, the reaction is said to be negative, and the test must be repeated after two or three days, and then again, if it is still negative.

Captain Marris holds that three negatives falling within the first fortnight of a febrile illness, excludes the typhoid group with a certain degree of certainty. There are exceptions but a continuation of the tests is suggested by the symptoms and remaining clinical signs.

Negative results after the 14th day, or after the fever has fallen, are unreliable.

In a series of 111 cases proved by bacterial culture to be of the enteric group, 94% gave a positive reaction to the first Atropine test applied to them.

Captain Marris used the Atropine test in over 1,000 typhoid suspects; he believes the results of its use to be trustworthy, from the fifth day of the disease to the end of the second week.

A positive reaction has been found as late as the 110th day.

A positive reaction was obtained in men aged 50 or more, who had not got Typhoid but were suffering from arterio-sclerosis.

In/

In febrile patients with a pulse of over 100, a positive reaction is to be judged with caution and the test repeated.

Similarly a negative reaction in toxæmic patients who are very ill may be regarded lightly.

Six proved typhoid cases all gave negative reactions; and contrawise prophylactic T.A.B. injections are apt to produce positive Atropine reactions in a day or two.

Particularly interesting is Captain Marris' account of the rationale of his test.

He has been led to conclude that the bacterial poisons of microbes of the enteric group, in contradistinction, from those of the other microbes, exerts a depressing effect directly upon the intrinsic rhythm centre of the heart, at the same time blocking the vagal control of the latter.

Atropine inhibits the vagal slowing of the heart; but in the typhoid fevers Atropine fails to accelerate the pulse rate much, because the heart itself is poisoned.

He finds that the normal quickening of the heart beat by the inhalation of amyl nitrite is much depressed in typhoid, and that the entire nervous injection of small doses of adrenalin solution fails to produce the transient rise in systolic blood pressure/

pressure seen in healthy men - perhaps in consequence of the action of the bacterial toxins upon the myoneural elements of the walls of the arterioles.

PERSONAL EXPERIENCE.The Value of the Atropine Test.

In estimating the value of a new test employed for diagnostic purposes that test must be subjected to critical examination.

There are few clinical tests which are absolutely reliable, for few of them yield the typical reaction with inevitable certainty in the diseases to which they are applied, and few of them fail to give the same reaction in some other diseases.

When a clinical test fulfils both these conditions it may be regarded as a perfect test.

More commonly the value of a clinical test is relative; the typical reaction is obtained in a very large percentage of cases of a given disease: the same reaction is absent in a very large percentage of all other diseases.

The numerical relation between their percentages, and the power of isolating and classifying the exceptions before the test is employed, measures the value of any given test in instances where the test may not be termed perfect.

In his work upon the Atropine reaction as a test of disease caused by organisms of the Typhoid group, Marris considered these points of view, and I have attempted to do the same in my investigations.

The normal effect of Atropine.

I have tried the test on over 100 cases, and in spite of the large dose given ($1/33$ grains) in no instance have any distressing symptoms been noticed.

The dose for children was modified, according to age, in the manner suggested by Dreyer and Walker.

The effects of $1/33$ of a grain of Atropine Sulphate hypodermically on the normal individual are as follows:-

A slight and short fall in pulse rate is usually seen, and this is followed by a steep rise within ten minutes of the injection; the rise is constant and is rarely less than 20 beats and is frequently as much as 30 beats per minute in extent.

It reaches its maximum at about 25 to 30 minutes, is maintained for varying periods, and then gradually subsides, reaching normal after an hour or more.

Dryness of the mouth occurs soon after the injection.

Dilatation of the pupils does not always appear, but usually occurs after the lapse of an hour or more.

In estimating the value of the Atropine Test I have taken as a first criterion the reactions in 30 adult cases of the Typhoid Group, in which the symptoms/

symptoms and signs, though modified, conform to the picture of Typhoid as generally recognised, and in which a Laboratory diagnosis of Typhoid had been arrived at.

The Serological and bacteriological tests were all carried out in the Bacteriological Department of the Cape Town University.

All of the Atropine Tests carried out were done by me, and the cases were under my personal supervision in Hospital.

Of the 50 cases that I am going to briefly describe, I shall only show 25 charts as these are quite sufficient to illustrate my points.

In the charts shown the numerals to the left of the temperature numerals denote Pulse Rate.

The black bands indicate the rise of Pulse Rate upon the Atropine Test (A), the lower and upper ends of the bands corresponding to pulse rate before, and after the injections, respectively.

The length of the band indicates the response.

The Red bands indicate a fall of pulse rate after the Atropine injection.

GROUP 1.

(A)

Cases with a laboratory diagnosis of Typhoid with
a Positive Atropine Test.

Case No.12.

A girl, Leah Segal, aged 18, was sent to the Out-Patient Department of the hospital with a request from her doctor for early operation, for acute appendicitis.

History.

A week previous she complained of headache, pains in the abdomen and an inclination to vomit.

No epistaxis.

Bowels constipated.

She thought she had had a temperature.

On Examination.

Face flushed; expression anxious,

Tongue furred and moist.

Pulse 120.

Temperature 100.2.

Resp. 24.

No rose spots seen, Abdomen - restricted movement with respiration.

Spleen not palpable.

On/

On palpation, the recti in the lower part of abdomen were rigid.

Tenderness in both Right and Left Iliac Fossa.

As the diagnosis of Appendicitis was doubtful, I did an Atropine Test and found that it was positive.

I persuaded the surgeon to postpone operating, at any rate, until the next day.

On the following day another Atropine Test was found to be positive, and as the case looked less like an acute abdomen, operation was not advised.

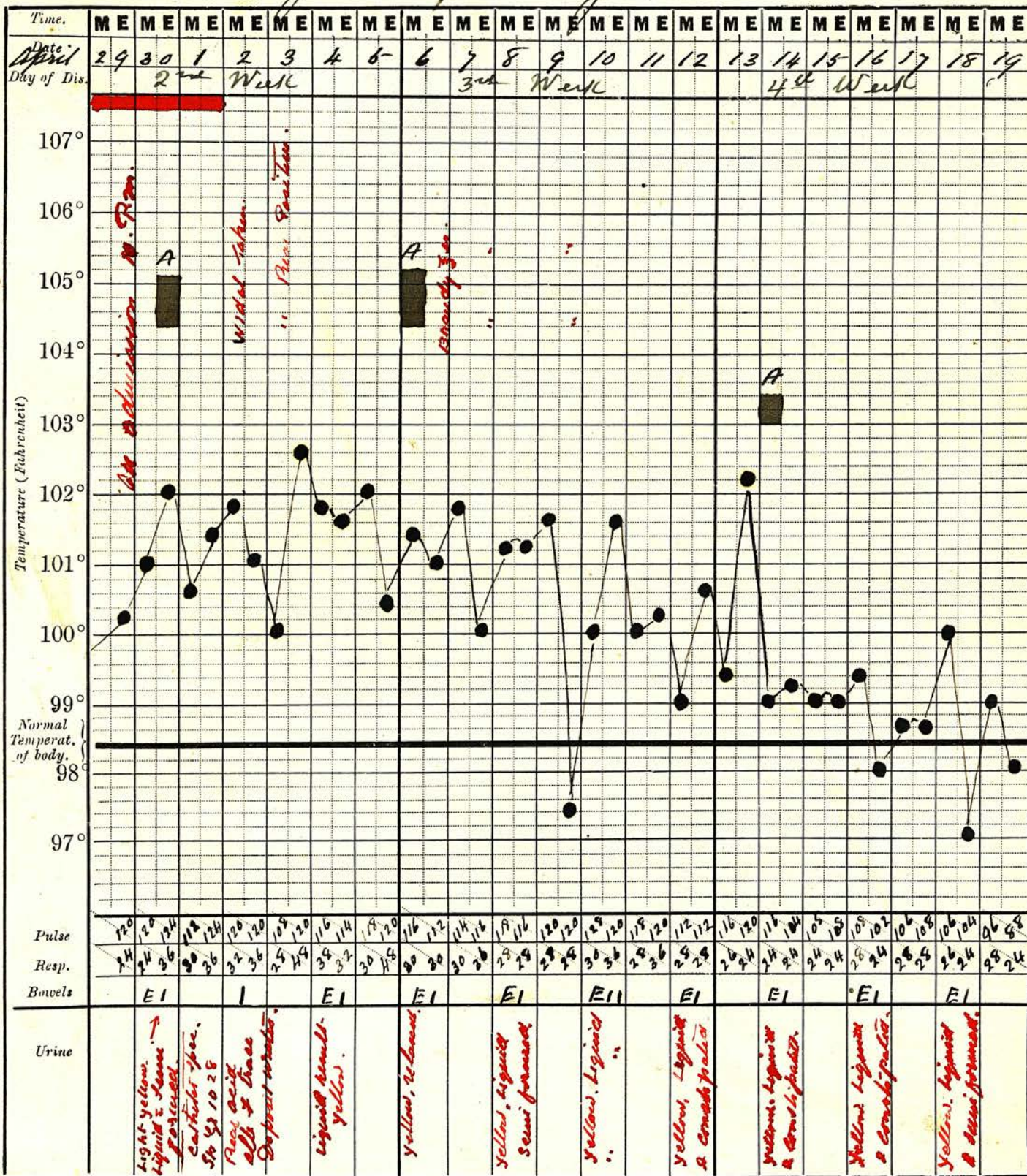
From that time onwards she ran the usual course of a Typhoid illness.

Further Atropine Tests were done in the third and fourth weeks and found to be positive.

The fever had subsided by the end of the fourth week, and in the fifth week the Atropine Test was negative.

Widal reaction was positive.

Name *Leah Segal.* April & May 1919



Parlor
140
130
120
110
100

Case No. 46.

Emily Bennett, age 28.

This patient had been in hospital for three months with Nephritis.

In the same Ward there were cases of Typhoid.

On July 14th she developed a temperature.

On the 17th July, I did an Atropine Test and this was Positive.

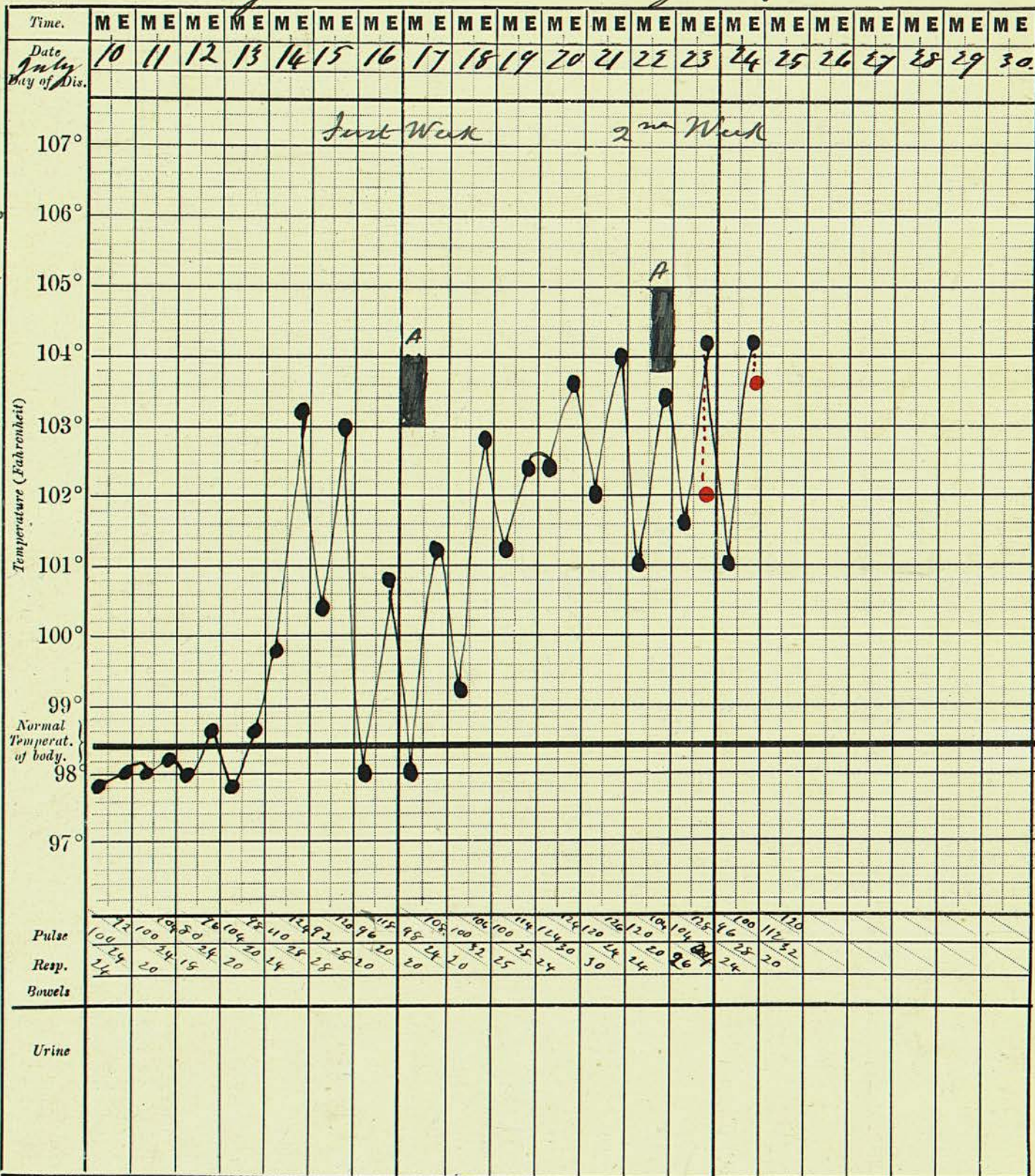
On 22nd July another Atropine Test was Positive.

In the second week she had a Positive Widal.

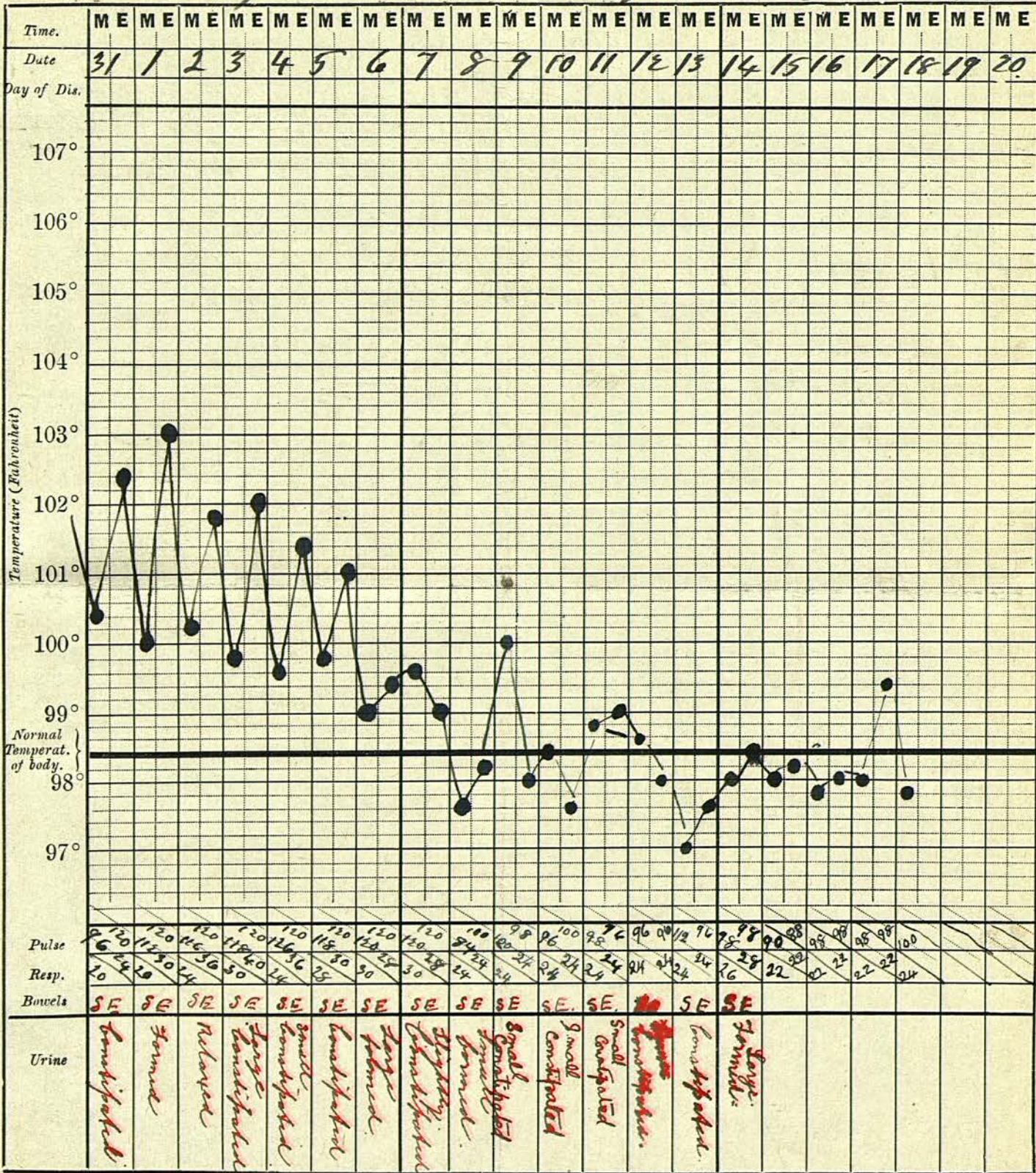
This case was particularly interesting in that it was the first opportunity I had of trying the Atropine Test on an early case of Typhoid.

It will be noticed that on the fourth day after the patient took ill, the Atropine Test was Positive.

Name Emily Bennett July Ag 28



Name *Emily Bennett* July & Aug 1919



*sp gr 1.018
Re ac Acid
also S. Trace*

Case No. 4.

Willie Williams, age 17.

Two weeks before had complained of headache and feeling hot all over.

On Admission.

Temp. 102.2.

Pulse 96.

Resp. 24.

Cheeks flushed, tongue furred and dry.

Spleen not enlarged.

No rose spots.

Bowels constipated.

Widal reaction positive.

On the third day after admission an Atropine Test was done and found to be positive.

A week later another test was done, and instead of getting a rise of pulse, the pulse dropped from 80 per minute to 72.

A week after the fever had left the patient a definite Negative Atropine was got.

Case No. 24.

Harold Ramsay, age 49.

Patient took ill ten days before admission.

On Admission.

Temp. 101.2.

Pulse 104.

Resp. 20.

Flushed cheeks, tongue furred and moist.

Spleen enlarged.

Rose spots on abdomen.

Bowels constipated - yellow result.

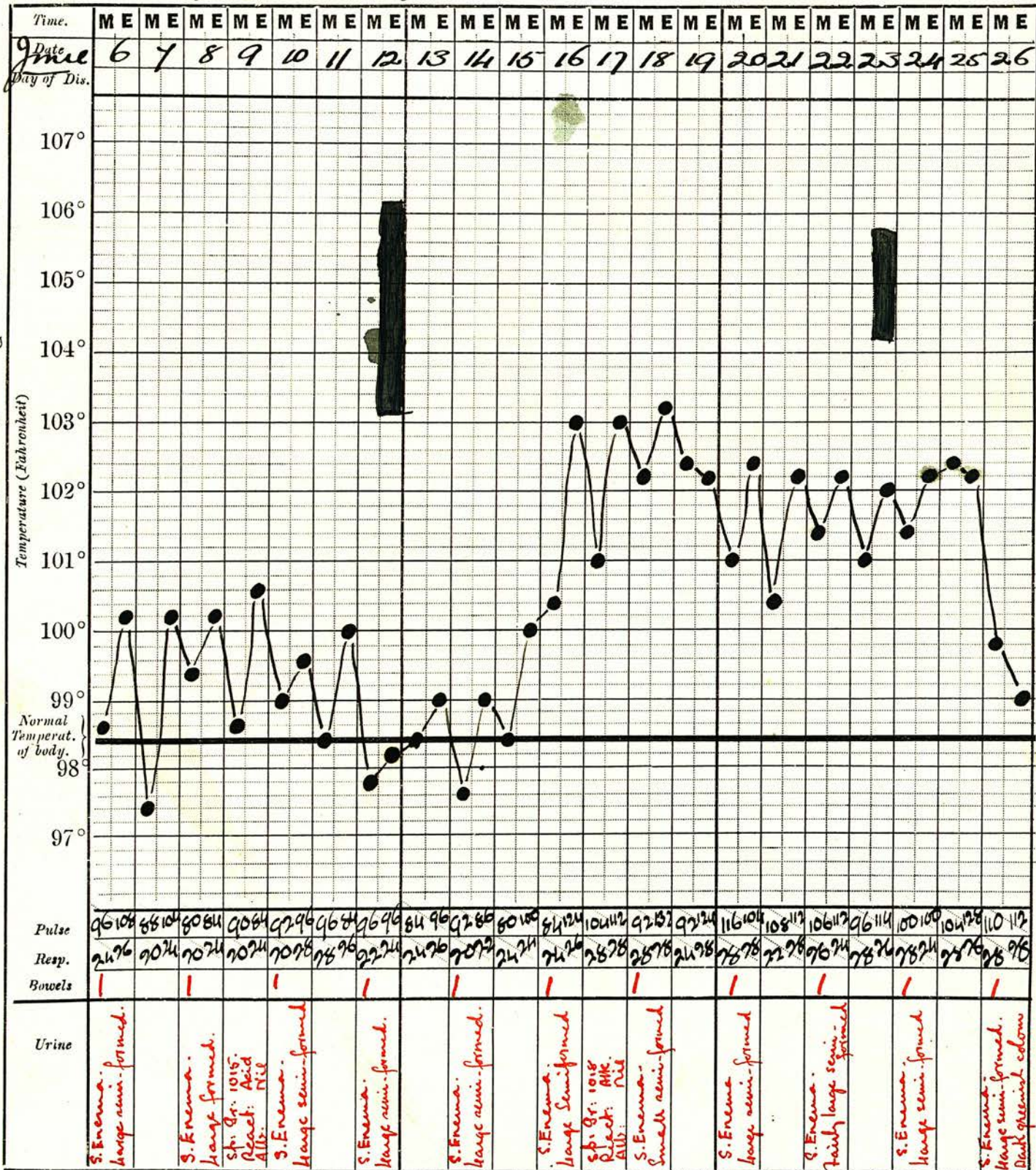
Widal reaction positive.

On the second day after admission Atropine
Test positive.

The test was again positive until the fifth
week when the temperature fell to normal, and a
Negative Atropine was got.

There was a recurrence of the fever, and the
Atropine Test was again found Positive.

Name H. J. Ramsay June. 1919.



Case No. 23.

Peter Mullen, age 20.

Had been ill for two weeks before being sent to hospital.

On Admission.

Temp. 103.2

Pulse 92.

Resp. 24.

Pale, and anxious expression.

Tongue dry and furred.

Spleen slightly enlarged.

No rose spots.

Bowels constipated - Brown result.

An Atropine was found positive two days after admission.

Ten days later, after the fever had subsided, the Atropine Test was negative.

This Chart suggests that on admission the patient was in the last stage of the disease, and illustrates the fact that as long as the toxins are present and the temperature is up, the Atropine Test is positive.

Case No. 21.

Norah Crowagon, age 24.

Was ill two weeks before admission.

On Admission.

Temp. 104.

Pulse 128.

Respr. 28.

Patient looking extremely ill.

Pale: flushed molars.

Tongue dry and furred.

Spleen palpable.

Rose spots on abdomen.

Bowels constipated - yellow result.

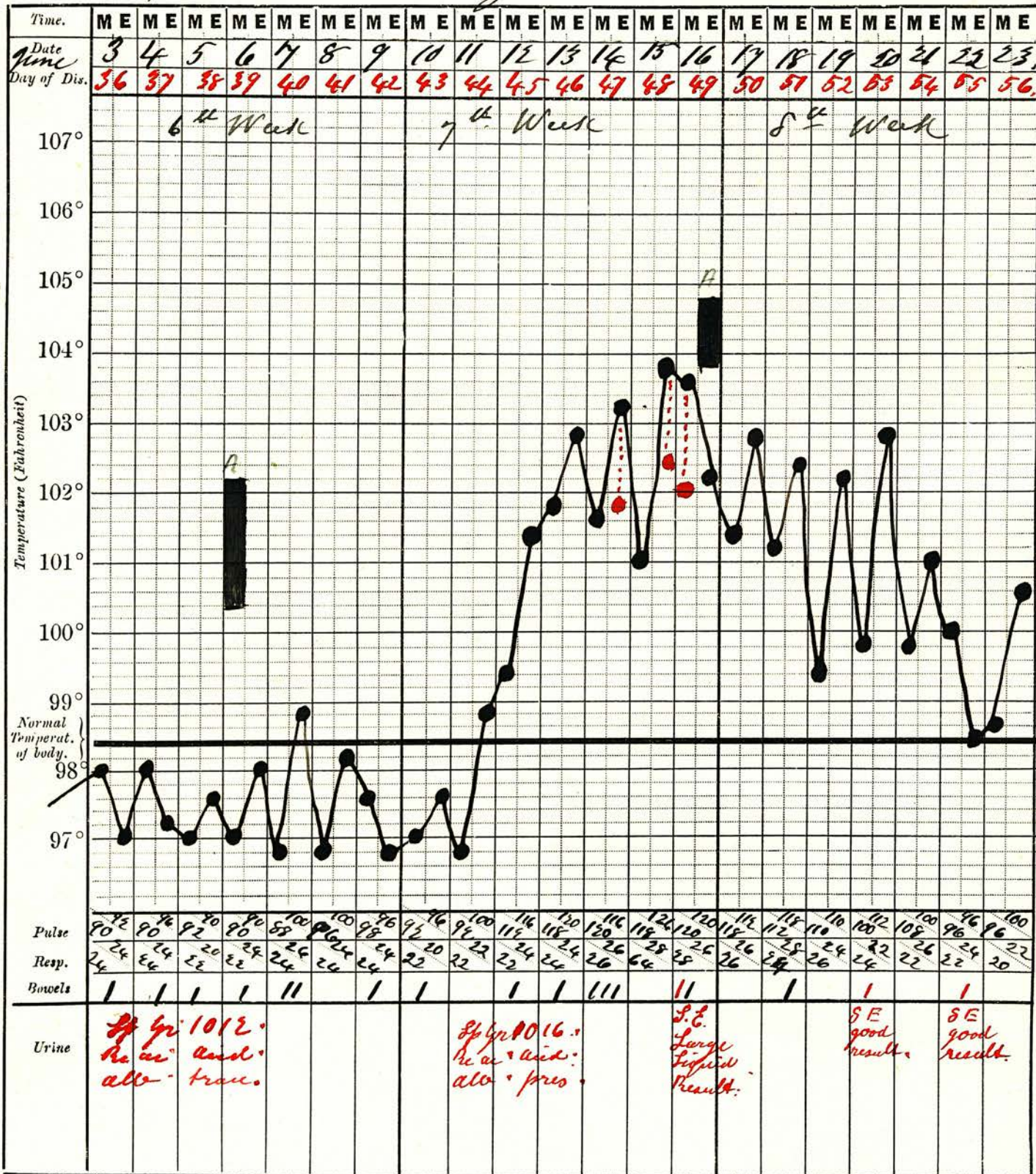
Widal reaction positive.

On the third day after admission an Atropine Test was positive.

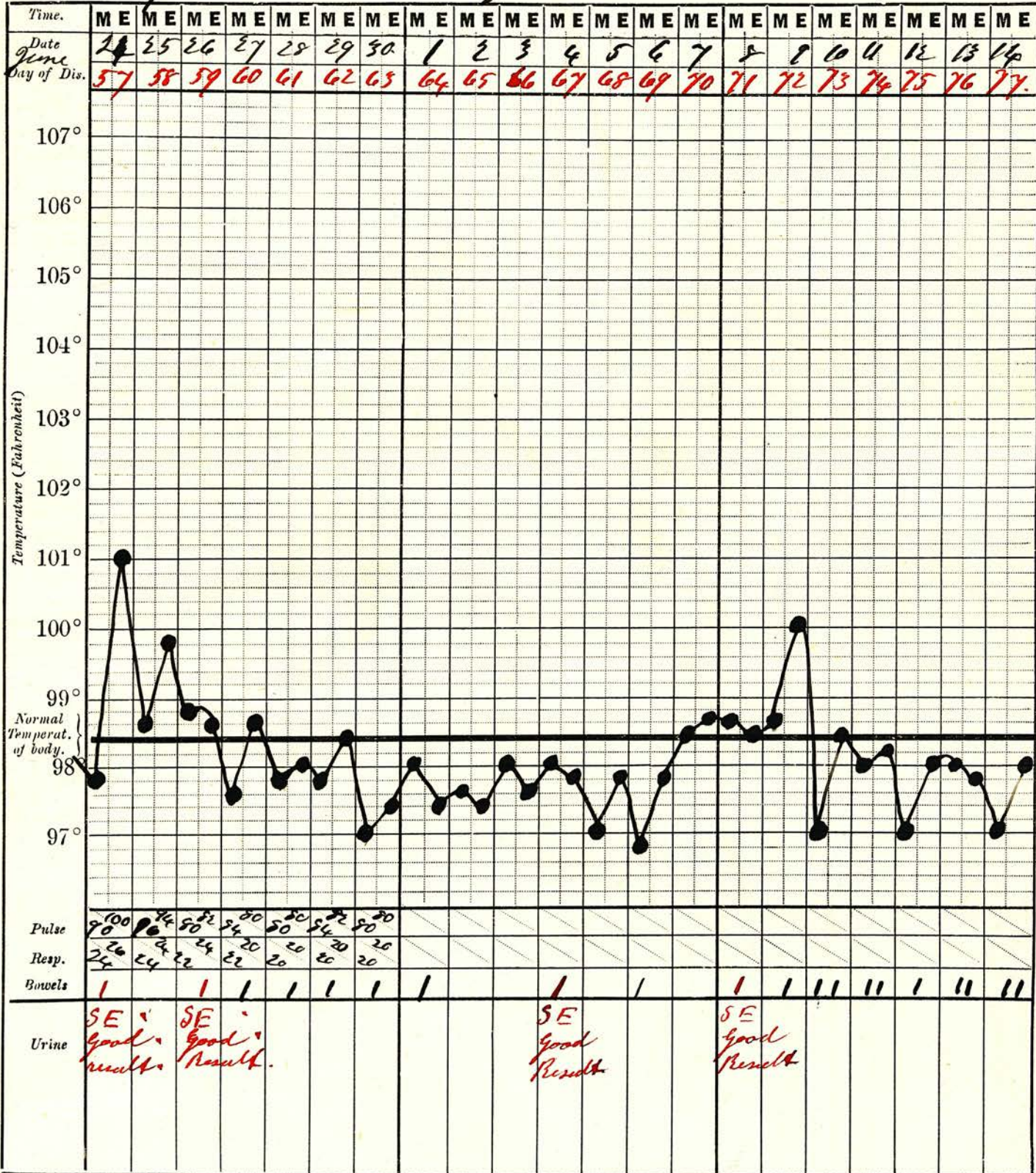
Successive tests until the temperature fell, were also positive. The temperature fell at the sixth week, and during this time the Atropine Test was negative.

The temperature went up again in the seventh week, when the Atropine Test was again positive.

Name Norah Brownayon June 1919



Name *Zorah Crowagon. June & July*



Case No. 20.

Johanna Paries, age 22.

Had been ill one week before admission.

On Admission.

Temp. 104.6

Pulse 140.

Respr. 26.

Patient had anxious expression.

Cheeks flushed; eyes sunken.

Tongue furred and dry.

Spleen palpable.

Rose spots on abdomen and chest.

Bowels constipated.

Widal reaction positive.

On the third day after admission Atropine Test positive.

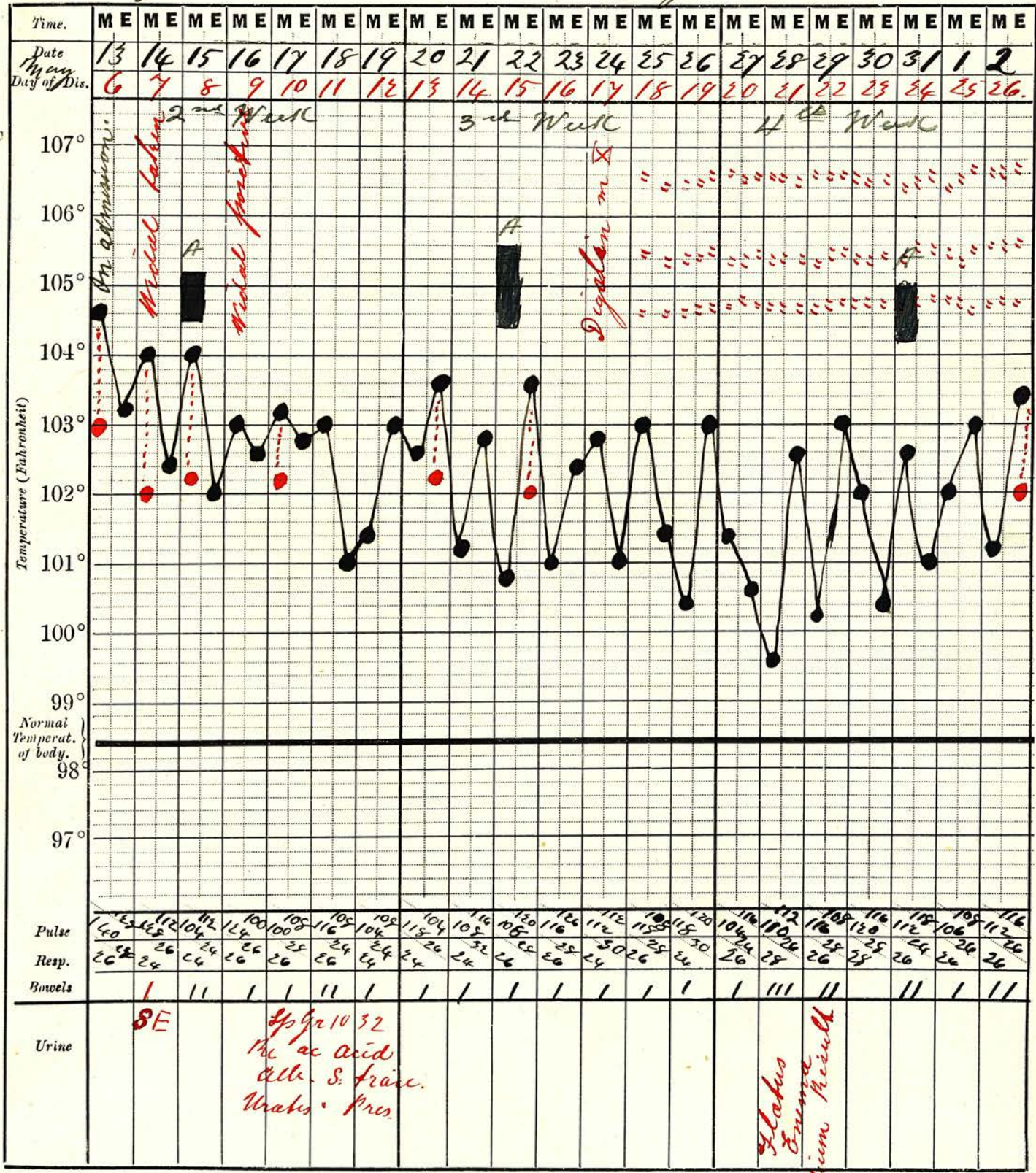
On the two following weeks Atropine Tests were again positive.

In the seventh week after the fever had subsided, the Atropine Test was Negative.

Edwin ³³ Ward

20

Name Johanna Paris. (22) May 1919 & June.



2nd Week
 Medic. Cathart.
 A
 Medic. purgans

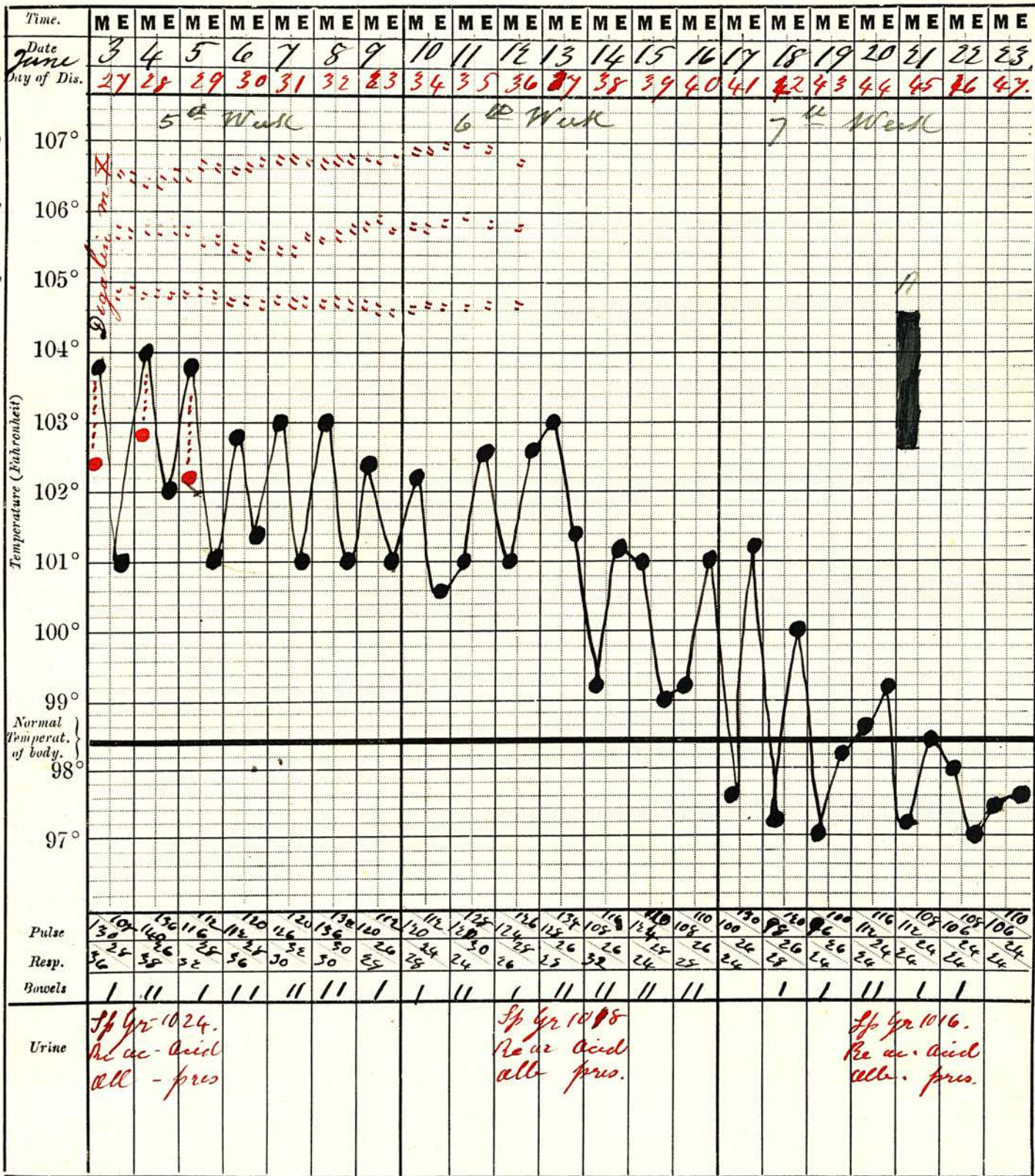
3rd Week
 A
 Digitalin

4th Week

Sp Gr 1032
 Ph. ac acid
 alk. S. franc.
 Urates Pres.

Flatus
 Eructa
 MEDIUM RIBBELL

Name *Johanna Paris June 1919*



Case No. 17.

Harold Forterin, age 16.

Had been ill for two weeks before admission.

On Admission.

Temp. 101.4.

Pulse 110.

Respr. 22.

Patient was flushed, and in collapsed state.

Tongue dry and furred.

Spleen not palpable.

No Rose spots seen.

Bowels constipated, - brown result.

Widal reaction positive.

On the fourth day after admission the Atropine Test was negative, the escape being twenty.

On the week following the test was repeated and the escape was 14. This was a query-positive.

The next week the escape was only nine. This time a definite positive.

This case demonstrates the importance of not relying too much on one test. It was not until the third test was done, that a definite positive was obtained.

Name *Arnold Polina* *Long June 1919*

Time.	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E
Date	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Day of Dis.																						
Temperature (Fahrenheit)	101.8	104.5	103.5	103.8	100.5	103.2	103.4	101.2	100.6	102.8	99.6											
Pulse	104	124	120	116	106	120	130	134	132	130	126											
Resp.	24	24	22	25	26	26	25	24	26	20	32											
Bowels	2		1	1			1															
Urine			Good Result Semi-formed yellow				Semi-formed f. Brown															

6th Week

H.L. Starch Sp. 1/100 i. Dig. Sp. 1/100

Died 9.22.19

Temperature (Fahrenheit)

Normal
Temperat.
of body.

Pulse
Resp.
Bowels

Urine

Case No. 13.

William Somerville, age 17.

Patient had been ill for two weeks before admission.

On Admission.

Temp. 103.4.

Pulse 128.

Respr. 32.

Patient looked remarkably fit in spite of his fever.

Tongue furred but moist.

Spleen not palpable.

No rose spots.

Bowels constipated.

Widal reaction positive.

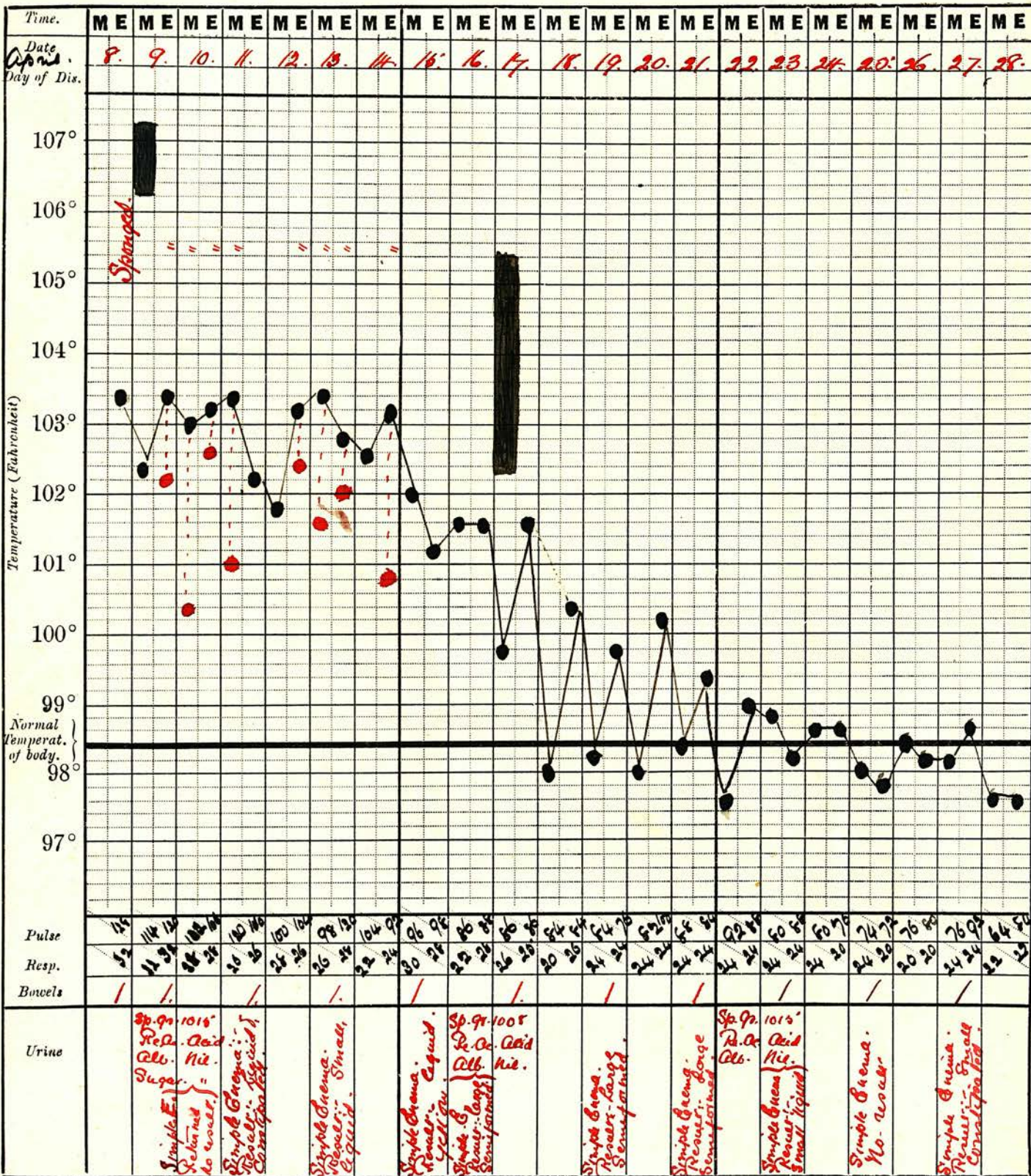
Atropine Test on the second day Positive.

Eight days later Atropine Test markedly Negative.

In this case it was noticed that while the fever was at its height - Temp. 103°: Pulse 110 - a strong positive was obtained.

The second time the test was done the temperature was below 100 and the pulse 74, the result being a strong negative.

Name *William Somerville* 1919.



Case No. 10.

Peter Rudden, age 28.

Patient had been ill for ten days before admission.

On Admission.

Temp. 102.

Pulse 104.

Respr. 28.

Patient looked extremely ill.

Face drawn and anxious expression.

Tongue dry and furred.

Spleen enlarged.

Abdomen distended.

Rose spots on abdomen and chest.

Widal reaction positive.

As the patient was extremely ill, only one Atropine Test was done. This was Positive.

The patient's temperature could not be kept down in spite of sponging and he died when his temperature reached 106.

This was the only death I had among the cases I treated for Typhoid.

Name *Reily L. Padden*

March

1918

Time.	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E
Date	9	10	11	12	13	14	15	16	17	18	19	20	21	22						
Day of Dis.																				
Temperature (Fahrenheit)	107°																			
	106°																			
90°	105°																			
	104°																			
Normal Temperat. of body.	103°																			
	102°																			
98°	101°																			
	100°																			
97°	99°																			
	98°																			
Pulse	104	98	100	106	108	110	120	112	112	120	126	128	126	134	134	140				
Resp.	28	24	32	32	24	28	28	28	36	40	36	40	36	44	40	52				
Bowels	2	1	1	1	1	2	1	1	6	2	2	6	6	1						
Urine	S. liquid yellow brown Sp. gr. 1.025 Pec. acid Album. not separated								Liquid & flatus Facies Enema. Liquid No. 1. No. Blood Facies Enema. Returned Sp. gr. 1.025 Acid. hil. Facies Enema. Returned with lot of flatus.											

Palen

130

120

110

100

90

Sponged.

*Calomet. flasser. 9 a.m.
3 x vi dr. um off.*

Ice bag applied to abdomen.

Pituitary 1/2 cc.

9 A. gr. 50.

10 a.m.

1.30

Case No. 9.

Dick Conradie, age 22.

Patient had been ill for two weeks before admission.

On Admission.

Temp. 102.4.

Pulse 120.

Respr. 28.

Tongue dry and furred.

Spleen not palpable.

No rose spots.

Widal reaction positive.

On admission the Atropine Test was Positive. Ten days later it was taken again and found still to be positive.

Seventeen other cases, with a Laboratory diagnosis of Typhoid were tried with the Atropine Test and all gave Positive results.

Name *Dirk Couzachi*
 February 19.

Time.	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
Date	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25					
Day of Dis.																										
Pulse	120	100	88	100	104	100	108	92	108	120	96	108	108	84	80	84	88	76	80	76	80	68	70	78	76	58
Temp. (Fahr.)	102.4	102.0	101.8	102.6	101.8	102.8	100.4	101.8	103.0	101.2	102.2	101.2	102.2	100.6	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.8
Resp.	28	36	40	32	36	32	36	32	32	32	28	28	25	24	24	24	24	24	24	24	20	20	26	24	20	18
Stools	1	1	1	1	2	2	2	2	2	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1
Urine	S.P. 9c. 1020 R. acid Albin pro-Sugar Nil E.S. Small Slightly Result.			E.S. Semi-formed light brown & yellow.		Relaxed yellow	Relaxed yellow.	Relaxed yellow	Slight haemorrhage	Haemorrhage 5:30 a 6:30 a.m.	Small dark haemorrhage	Small Result- darry	Small Result- dark brown	Relapsed S.P. 9c. 1015 R. acid: Albin Nil.										E.S. Consolidated & Relaxed.		E.S. Large Consolidated.
Notes									IM H gr 1/4 9:30 a.m.																	

Pulse

Temperature (Fahr.)

Normal Temperat. of body.

Pulse
Resp.
Stools

Urine

Relaxed

Relaxed

44.

(B)

The Cases in this Group had a Laboratory diagnosis of Typhoid but showed a 'Negative' Atropine Test.

Case No. 11.

Jim Banermister, age 22.

Patient took ill a week before admission.

On Admission.

Temp. 103.

Pulse 88.

Resp. 48.

Tongue furred and dry.

Rose spots on abdomen.

Spleen palpable.

Bowels constipated - yellow result.

Widal reaction positive.

On the fourth day after admission an Atropine Test was done, and found to be strongly negative, the escape being 30.

The Laboratory diagnosis was Typhoid but in spite of repeated attempts the results of the Atropine Test were always negative.

It is interesting to note that while in the fever/

fever stage the Atropine Test gave a negative result, the escape being 30.

Later, when the fever had subsided, the escape was as much as 68.

This suggests that the patient had an idiosyncrasy for Atropine and could not stand as much as the average patient.

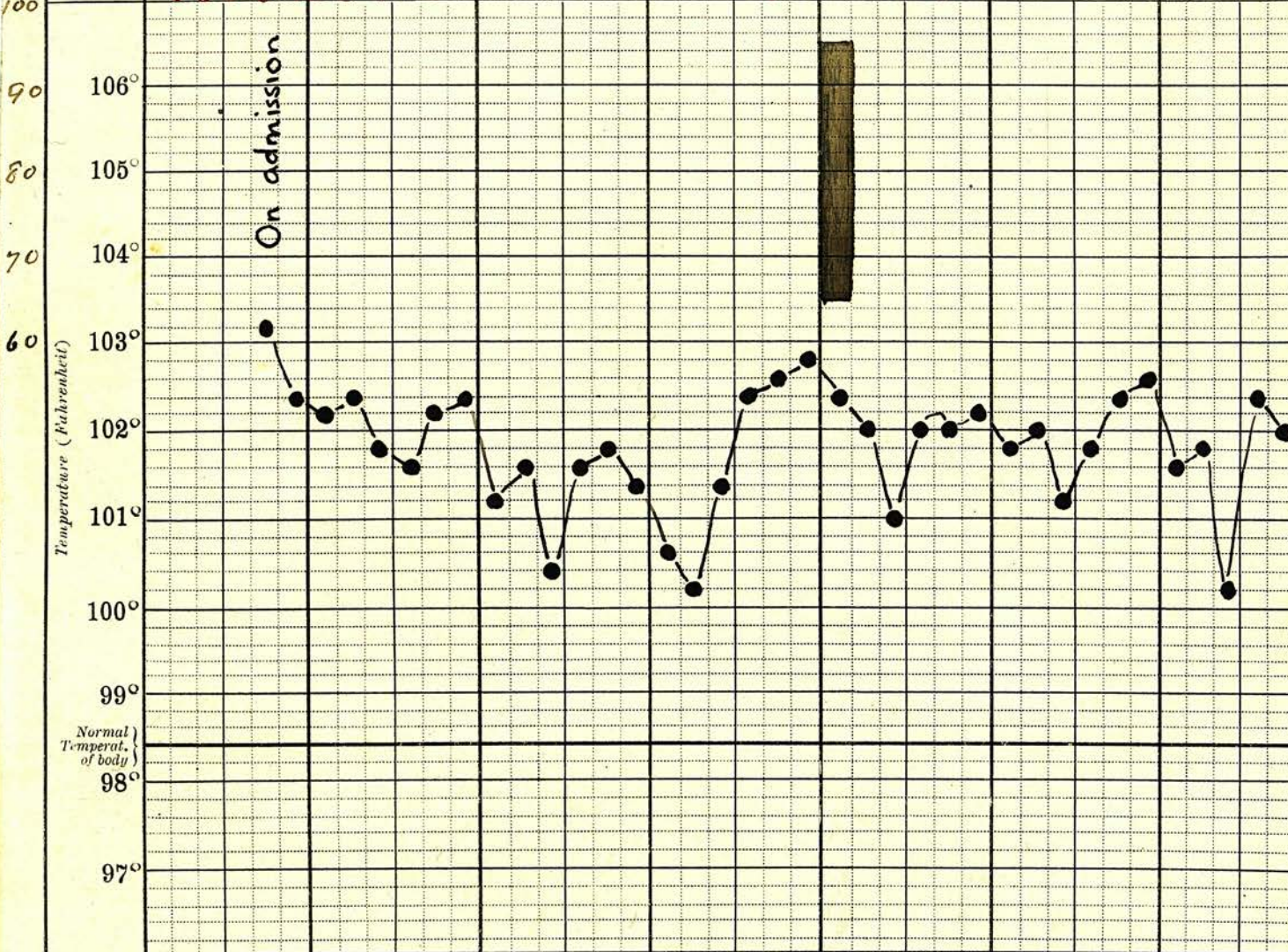
Name Jim Bauermaster. April.

Pulse

Date April
Day of Dis.

24 25 26 27 28 29 30

Time 2 A.M. 10 P.M. 2 A.M. 10 P.M. 2 A.M. 10 P.M. 2 A.M. 10 P.M. 2 A.M. 10 P.M. 2 A.M. 10 P.M. 2 A.M. 10 P.M. 2 A.M. 10 P.M.



Normal Temperat. of body

Pulse
Resp.
Bowels

88 88	80 88 76 80	76 72	76 80 64 70 72	84 84 88 88 74 64 88	80 80 74 78 76 88	76 76 68 80 66 78	80 78 62 72 76
48 40	36 32 32 28 28 32	28	32 28 28 28 24	32 36 30 28 36 28 28	28 28 36 28 28	24 28 28	24 28 24 24 24

Urine

S. Enema.
Result:
Small formed
yellowish colour
Sp. Gr. 1020
React. Alk.
Alb. Nil

S. E.
Result:
Large semi-
formed, yellow.

S. E.
Result:
Small formed.

Sp. Gr. 1020
React. Acid
Alb. Nil

Name Jim Banermaster May

Date	1	2	3	4	5	6	7
Day of Dis.							
Time	8 A M 10 P M	8 A M 10 P M	8 A M 10 P M	8 A M 10 P M	8 A M 10 P M	8 A M 10 P M	8 A M 10 P M
Pulse 100 90 80 70 60 50 Temperature (Fahrenheit)							
	Normal Temperature of body } 98°						
Pulse	76 76 80 64 80 64	80 64 68 56 60	60 88 52 60 56 60	72 74 60 64 56 58	60 60 64 64 62 58	60 64 60 64 60 56	60 56 52 60 60
Resp.	24 24 24 26 24 26	26 24 24 22 20	20 20 20 22 22 30	28 26 28 28 26 26	28 24 24 24 26 24	28 28 26 24 24 24	24 24 24 20 20
Bowels							
Urine	S.E. Result. Small constipated		S.E. Large semi-formed		S.E. Large formed	Sp. Gr: 1015 React: Acid Alb: Nil	S.E. Result. Large semi-form

Name Jim Banormaster. May.

Date	8		9		10		11		12		13		14		
Day of M's.															
Time.	2 A M	6 P M	2 A M	6 P M	2 A M	6 P M	2 A M	6 P M	2 A M	6 P M	2 A M	6 P M	2 A M	6 P M	
Temperature (Fahrenheit)	110														
	100														
	90														
	80														
	70														
	60														
	50														
	40														
	Normal Temperat. of body	98.0	98.5	97.2	97.0	97.2	97.0	97.5	97.0	97.5	97.0	97.2	97.0	97.5	97.0
	Pulse	56	50	48	60	52	48	52	44	54	48	54	46	54	44
	Resp.	24	24	22	20	20	22	22	24	20	22	20	22	22	20
	Bowels														
	Urine			S. Enema. Large semi-formed					S. Enema. Large semi-formed.		Sp. Gr: 1.012 React: Acid Alb: Nil		S. Enema. Small Constipated		

Name Jim Bauernmaster ^{49.}

Date	16	17	18	19	20	21	22
Day of Dis.							
Time.	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10
Temperature (Fahrenheit)							
	<p>Normal Temperature of body</p>						
Pulse	64 68 68 64 56	68 84 84 74 72 88	68 88 84 84 72 68	84 80 80 80 80	88 84 80 88 86	68 84 80 70 68 80	88 56 68 72 80
Resp.	20 20 20 20 24	14 12 14 24 20 96	14 14 24 14 20 20	24 20 20 20 24	24 22 22 24 24	24 24 24 20 20 20	28 26 26 24 24
Bowels							
Urine		S. Enema. Large semi-formed		S. Enema. Small. semi-formed	Sp. Gr. 1023 React: Acid Alb: Nil	S. Enema. Large semi-formed	

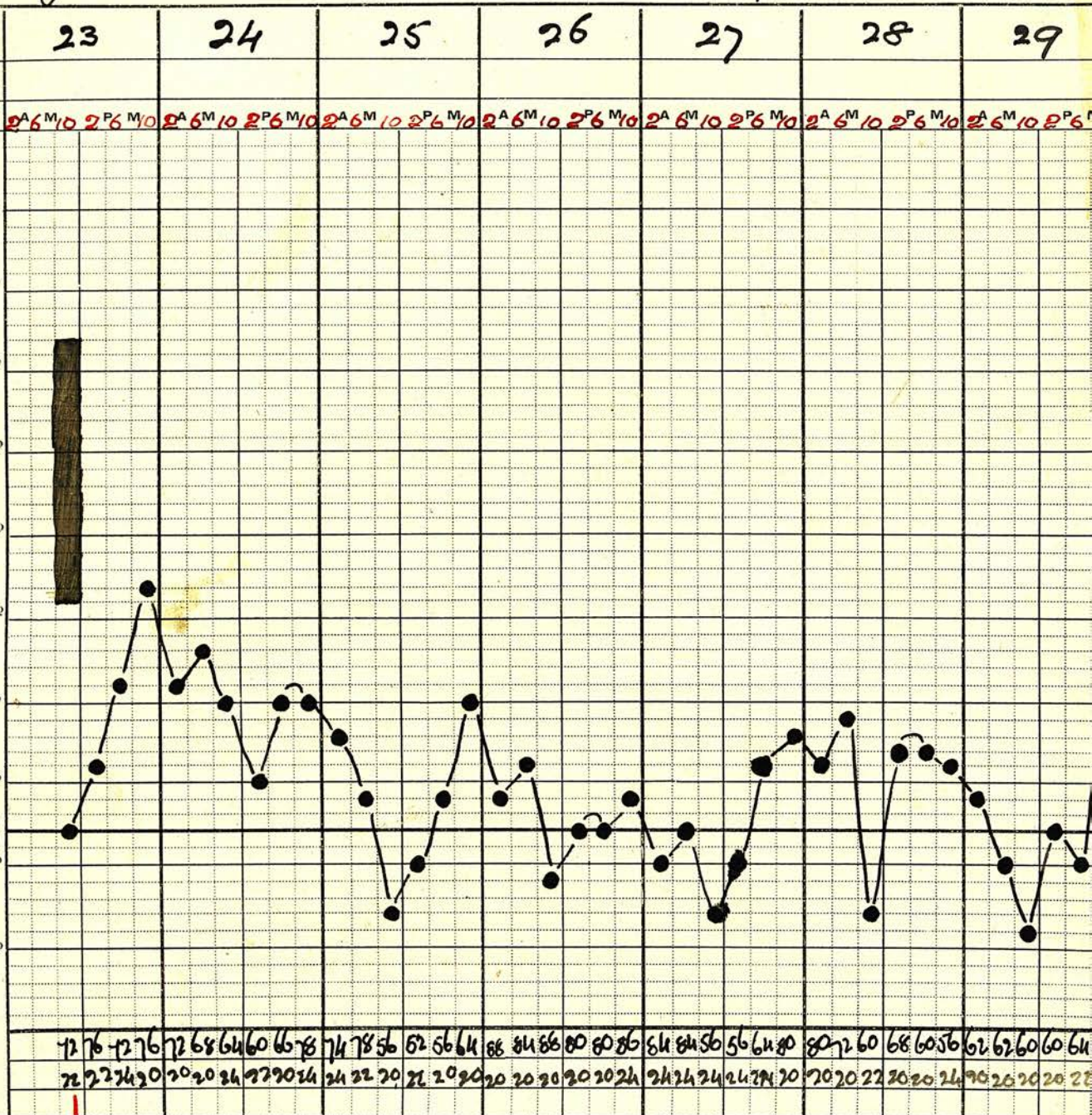
Name *James Bauermaster. May.*

Date	23		24		25		26		27		28		29	
Day of Dis.														
Time.	A	M	P	M	A	M	P	M	A	M	P	M	A	M
Temperature (Fahrenheit)														
Pulse	72	76	72	68	64	60	66	78	74	78	56	62	56	64
Resp.	22	22	24	20	20	24	22	20	21	20	20	20	20	20
Bowels														
Urine	S. Enema. Large Semi-formed		S. Enema. Large formed		Sp. Gr: 1015 React: Acid Alb: Nil		S. Enema. Large formed.		S. Enema. Large formed		S. Enema. Large formed		S. Enema. Large formed	

70
60
50

Temperature (Fahrenheit)

106°
105°
104°
103°
102°
101°
100°
99°
98°
97°



Case No. 1.

William Johnston, age 46.

Patient had been ill for two weeks before admission.

On Admission.

The patient gave one the appearance of having been ill for a long time, and suggested the third and fourth week of Typhoid.

Temp. 101.2. *

Pulse 116.

Resp. 22.

Tongue furred and dry.

The patient had numerous rose spots all over his chest, abdomen and back.

Spleen palpable.

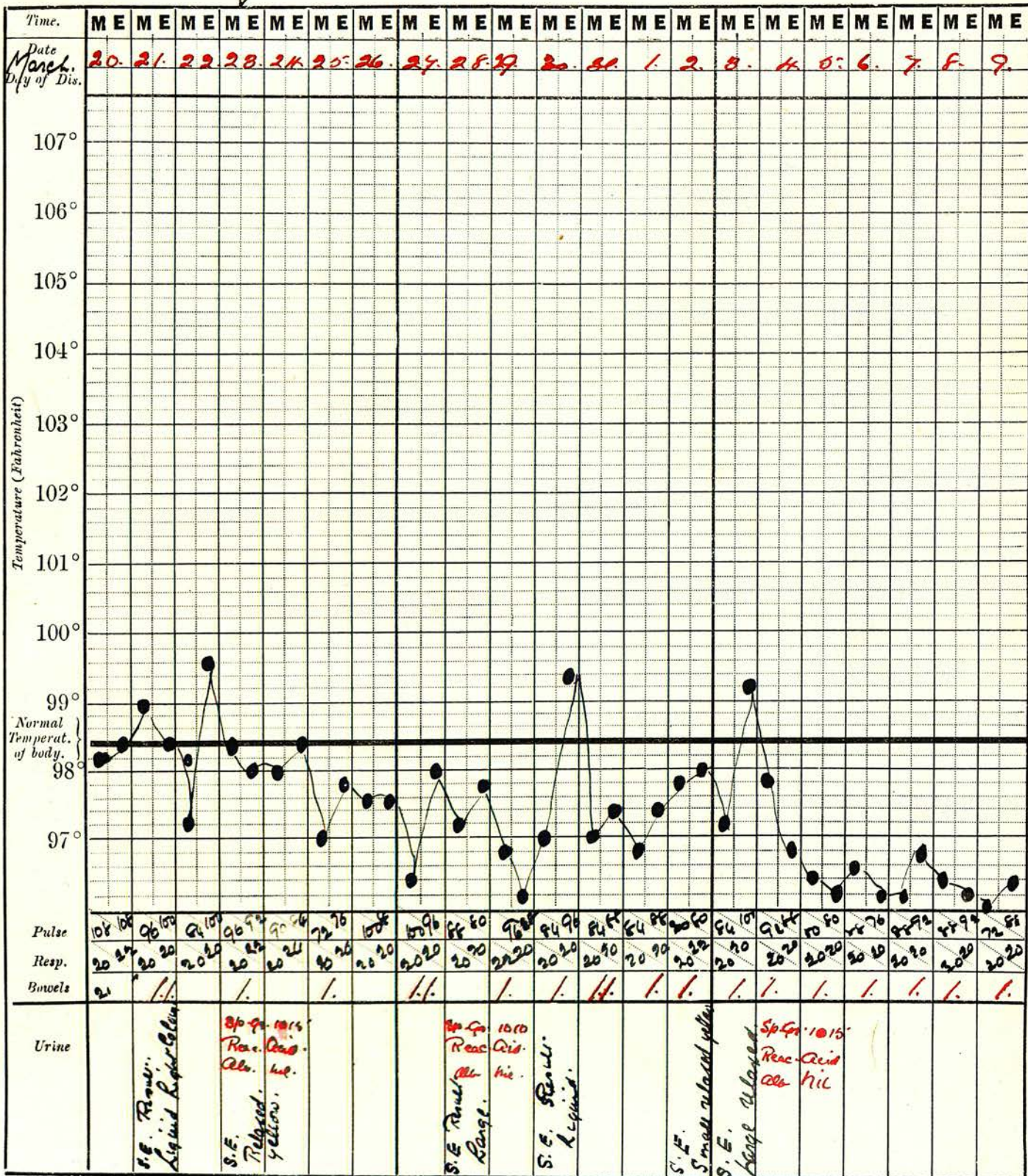
Bowels constipated.

Widal reaction positive.

Atropine Tests were done, both when the patient had fever, and after it had subsided, with Negative results.

This patient became a Typhoid Carrier, B. Typhosus being found in his urine for some time after the fever left him.

Name E. Johnston 1919.



Summary of results of Atropine Tests done on adults
with a Laboratory diagnosis of Typhoid.

Of 30 cases tested 28 gave Positive Result = 93.32.

" " " " 2 " Negative " = 6.62.

On these 30 cases over 100 tests were made and it was found that from the third day of the disease onward, the earlier that the test was done, the more likely was it to be positive.

As the fever wore off, the test became negative.

In cases of relapse, however, when the temperature was up, the test became positive over again.

In other words, that while there is evidence of the Typhoid toxins in the general circulation, the Atropine Test will probably be positive.

GROUP II.

Cases which gave a Negative Laboratory result for Typhoid, but which were positive to the Atropine Test.

Case No.2.

H. Warren, age 25.

A policemen who had been sent in by a Police Doctor as a suspected case of Typhoid.

On Admission.

Temp. 101.

Pulse 96.

Resp. 26.

Tongue furred and dry.

No rose spots.

Bowels constipated.

All of the usual Laboratory Tests for Typhoid were Negative.

The Atropine Test was strongly positive on six successive weeks.

It is interesting to note that B. Faecalis Alkaligenes was found in the blood and urine of this patient.

B. Faecalis Alkaligenes septicaemias have been frequently recorded, and may at first simulate a mild enteric infection; the organism may also occur in the blood as a secondary infection in Typhoid.

Name *L. Warren*
March

Time.	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										
Date	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24																	
Day of Dis.																																						
Temperature (Fahrenheit)																																						
Normal Temp. of body.	-----																																					
Pulse	92	84	80	92	64	112	116	96	100	80	87	80	100	84	120	88	80	84	88	100	88	100	92	90	88	84	92	100	100	96	100	96	80	100	86	108	84	88
Resp.	20	20	20	22	20	18	20	22	22	20	22	20	20	22	20	20	20	22	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	
Bowels	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Urine	<i>Spc. gr 1.005 Slightly Neutral Alba Nil.</i>								<i>E.S. Result Semi-formed.</i>				<i>Spc. gr. 1.010 Slightly Acid Alba Nil.</i>								<i>E.S. Result Semi-formed.</i>				<i>Spc. gr. 1.016 Slightly Alkaline Alba Nil.</i>													

A. Press. Opened.

120
110
100
90
80
70

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

Case No. 18.

Mrs Seymour, age 47.

Patient had been ill for some weeks before admission.

On Admission.

Patient complained of abdominal pains and headaches.

Temp. 101.

Pulse 72.

Resp. 20.

Tongue furred but moist.

No rose spots.

Spleen not enlarged.

Bowels constipated.

Two Atropine Tests were Positive, but all Laboratory Tests were negative.

It was noticed that the patient had very much thickened arteries for her age, and was probably an early arterio sclerosis.

In this case, though the temperature was over 102°, the pulse kept below 100. The case suggested to me the latter weeks of Typhoid infection. At this stage of the disease it was not worth while doing a blood culture, and experience has taught me that the agglutination test is not always to be relied upon.

Case No. 28.

Maria Petersen, age 67.

Patient had been ill for two weeks before admission.

On Admission.

Temp. 104.4.

Pulse 88.

Resp. 22.

Tongue furred and dry.

No rose spots.

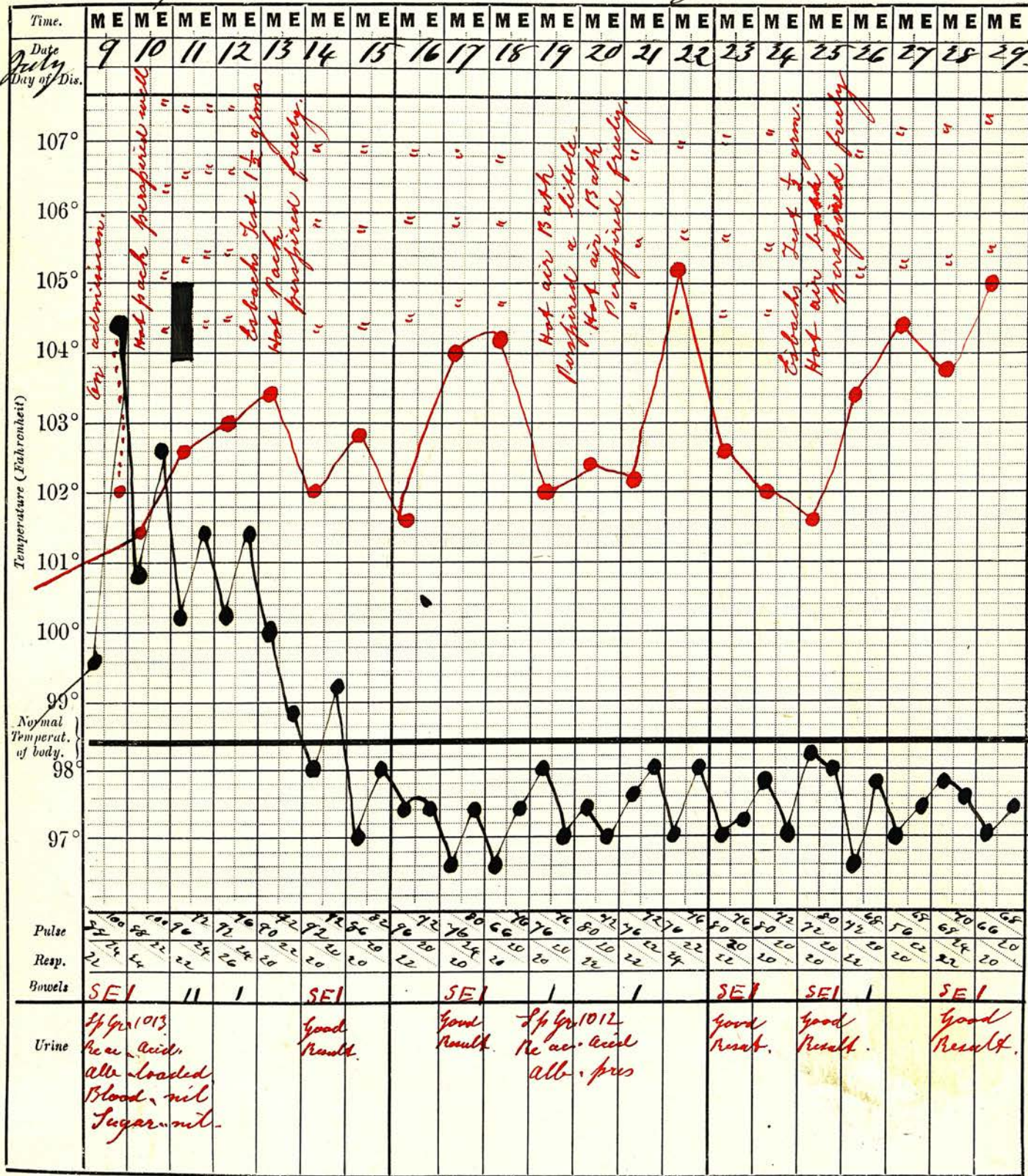
Spleen not palpable.

Bowels constipated.

Widal reaction negative.

An Atropine Test was found Positive, but the case was diagnosed as Acute Nephritis, and soon subsided.

Name *Maria Peterson* July 1919.



Case No. 43.

John Ruppig, age 24.

Patient was ill for 10 days before admission.

On Admission.

Temp. 102.4.

Pulse 78.

Respr. 26.

Although this case does not belong to this group it deserves special mention. He had been treated by his doctor for ten days and then diagnosed as Typhoid.

When he was admitted to hospital I did an Atropine Test and found it negative, the escape being 22.

The following day the result was again Negative, and as I suspected Appendix trouble, asked a surgeon to examine the case.

The same day a gangrenous appendix was removed and the patient made a good recovery.

Summary of Atropine Tests done on Adults who were
suspected cases of Typhoid.

35 Cases tested, 31 gave Positive Results and
of these 25 were proved to be Typhoid and one case
proved not to be Typhoid.

So that in 35 cases tested the Atropine Test
failed in 6 cases or had an error in 17.2% of the
total.

GROUP III.

Cases of Children with a Laboratory Diagnosis
of Typhoid.

Case No. 26.

Fred Koning, age 8.

Patient had been ill for a week before admission.

On Admission.

Temp. 102.

Pulse 104.

Respr. 28.

Tongue dry and furred.

Spleen palpable.

No rose spots.

Bowels constipated.

Successive Atropine Tests at intervals of a week were all Negative.

Four Widal Tests were made at intervals of a week, and all of these were returned as Negative.

Specimens of urine and faeces were sent for culture, with Negative Results.

As the case appeared to be clinically enterica, I sent another blood for Widal Reaction and on the/

the 34th day got the first Laboratory diagnosis of Typhoid, - B. Paratyphoid B being reported.

This case is of special interest in that for four successive weeks of an illness that was afterwards shown to be Typhoid, the Widal reaction was negative.

It has been my experience that, while positive Widal reactions are of great value, negative reactions by no means exclude the possibility of Typhoid.

Name Fred. Honing.

June & July 1919

Time.	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E
Date	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	
Day of Dis.	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	
	5 th week																					
Temperature (Fahrenheit)																						
Normal Temperature of body.																						
Pulse	74	76	74	68	70	72	62	66														
Resp.	20	24	20	20	20	20	20	20														
Bowels	E		E																			
Urine																						

140
130
120
110
100
90
80
70

Temperature (Fahrenheit)

Normal Temperature of body.

5th week

WIDAL
FAECES FOR CULTURE
NEG
NEG

WIDAL POSITIVE B. TYPHOIDICUS B.



Pulse
Resp.
Bowels
Urine

Case No. 8.

Edward Miller, age 13.

Patient had been ill for over two weeks before admission.

On Admission.

Temp. 102.6.

Pulse 120.

Respr. 28.

Tongue dry and furred.

No Rose Spots.

Spleen not palpable.

Bowels constipated.

Widal reaction positive.

Atropine Test was markedly Negative.

19

71.
1919.

Name Edward Miller,

Date	23.	24.	25.	26.	27.	28.	29.
Day of Dis.							
Time	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10	2 A M 10 2 P M 10
Temperature (Fahrenheit)	106°						
	105°						
	104°						
	103°						
	102°						
	101°						
	100°						
	99°						
	98°						
	97°						
Normal Temperature of body							
Pulse	120	114	109	98	98	94	92
Resp.	28	20	20	24	24	22	22
Binocls							
Crime							

Apr 10 20
 U₂ mixed
 alk. ind
 Sugar ind
 C. S. Result
 Large formed.
 Lys. yellow.

C. S. Result.
 semi-formed.
 yellow.

P. S.
 no result

Case No. 14.

Florence Ellis, age 14.

Patient had been ill for two weeks before admission.

On Admission.

Temp. 102.4.

Pulse 120.

Respr. 24.

Patient had the appearance of a child who had been ill for some time.

Tongue dry and furred.

Rose Spots on Abdomen.

Spleen Palpable.

Bowels constipated.

Widal reaction positive.

Atropine Tests at intervals of a week were Negative.

Name *Florence Ellis.* May & June 1914.

Time	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	
Date	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5
May Day of Dis.	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
Temperature (Fahrenheit)																					
Pulse	76	76	74	74	72	74	74	72	72	74	72	72	74	72	74	76	74	74	72	74	76
Resp.	24	24	22	22	20	20	20	20	24	22	22	24	24	24	24	20	22	22	20	20	20
Bowels		E1		E1		E1		E1		E1											
Urine	<p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p> <p>Yellow. Liguid & consist. pale.</p>																				

*High Parathyroid 37
Disinfectant 37
High Parathyroid 37
High Parathyroid 37
High Parathyroid 37*

*High Parathyroid 37
High Parathyroid 37
High Parathyroid 37
High Parathyroid 37
High Parathyroid 37*

*90 97
Pain
at
Stomach*

Case No. 15.

Oliver Ellis, age 11.

Patient had been ill for two weeks.

On Admission.

Pale, anaemic child.

Tongue dry and furred.

Rose Spots on Abdomen.

Spleen palpable.

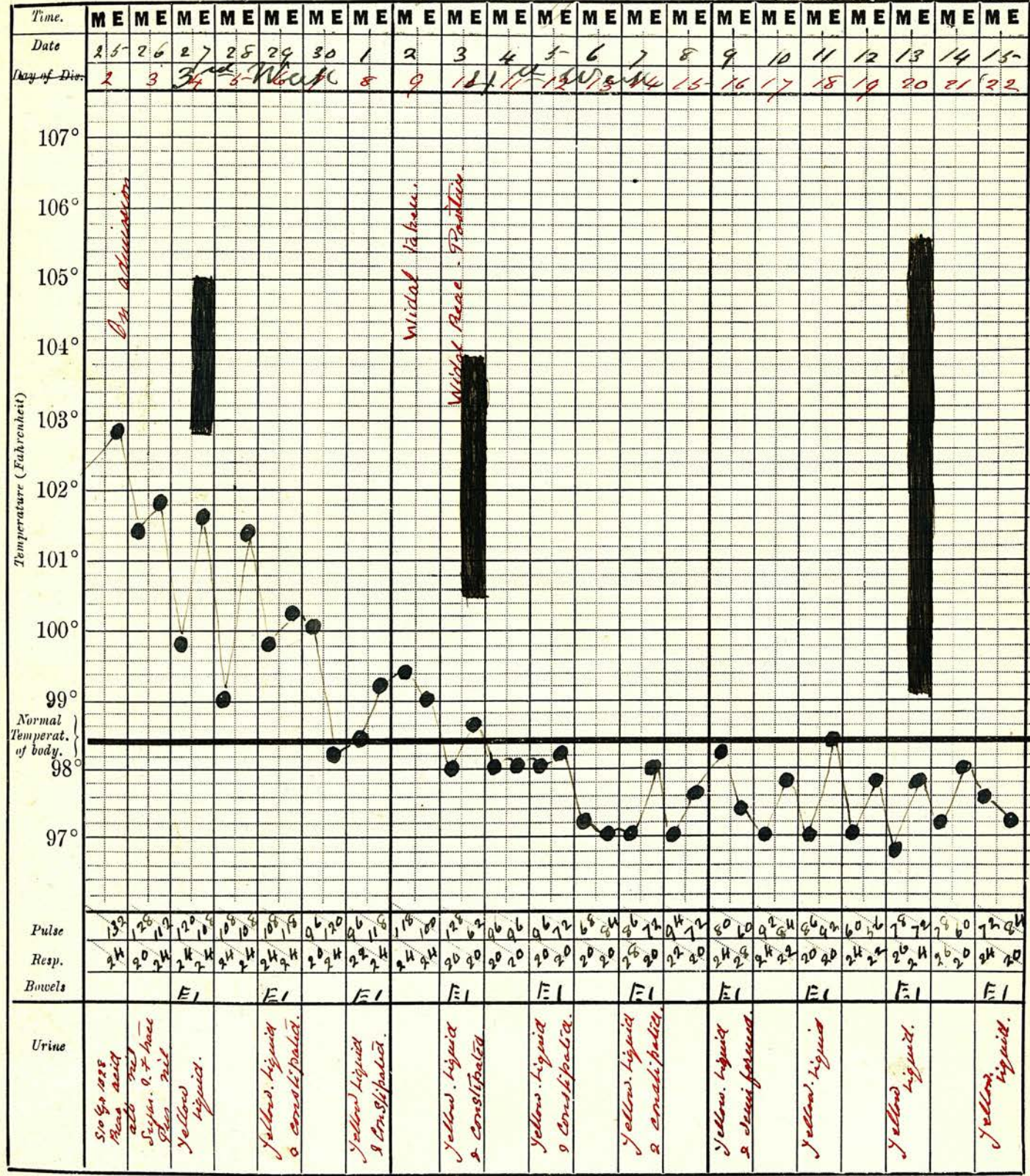
Bowels constipated.

Widal reaction positive.

This child was a sister to the child, Case No.14.

In this case successive Atropine Tests also were
Negative.

Name *Miss Ellis* April & May 1919.



On admission

Widal 1/2000.

Widal Rose 7/20000

[Blacked-out area]

Name *Oliver Ellis*. May & June 1914.

Time.	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	
Date	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5
Day of Dis.	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
Temperature (Fahrenheit)																					
Pulse	60	60	66	66	64	66	66	68	67	72	72	72	72	72	74	74	74	74	74	74	74
Resp.	26	26	26	24	24	24	24	20	20	20	24	20	20	24	24	24	20	20	20	20	20
Bowel		E1		E1		E1		E1		E1											
Urine		Returned clear liquid		Yellow. liquid & consist. part.		Yellow. liquid consist. part.		Yellow consist. part.		const. part. & liquid.											

Sp 1911078
 Rect
 All
 Sugar
 in
 Pan

Case No. 47.

Robert Somerville, age 10.

Patient had been ill for two weeks before admission.

On Admission.

Flushed cheeks.

Tongue dry and furred.

No Rose Spots.

Spleen not Palpable.

Bowels constipated.

Widal reaction positive.

Atropine Tests Negative.

Name *Robert Souverville*

Age *10 yrs.*

April

Time.	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E				
Date	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28					
Day of Dis.																										
Temperature (Fahrenheit)	103.3	100.0	101.2	99.6	100.8	100.2	101.0	99.4	100.6	100.6	99.2	99.0	97.0	100.0	97.2	97.4	97.8	97.2	97.8	97.8	98.8	98.2	97.8	97.6	98.6	
Pulse	120	102	102	120	102	102	104	100	84	76	76	76	58	76	80	78	70	76	76	80	70	84	68	76	68	80
Resp.	32	30	32	28	32	36	28	28	28	24	24	20	28	24	20	20	20	24	22	24	24	20	24	22	24	20
Bowels	4			1			1			1			1													
Urine	E. S. Resud. Semi formed large	Sp. Gr. 1015. Neutral. Albu. trace Sugar Nil	E. S. Green large liquid resud.		E. S. Resud. Small constipated.		E. S. Liquid Semi formed.	Sp. Gr. 1014. Red. Nut. Albu. Nil	E. S. Small Released.		E. S. Small. Liquid		E. S. Small. Liquid.	Sp. Gr. 1010. Red. Albu. Nil	E. S. Resud. Small. Liquid.		E. S. Resud. Small liquid yellow colorless 18 mace constip.	Large. Constip.	E. S. Resud. Small Semi formed							

Case No. 7.

Nellie Japhthi, age 11.

Patient had been ill a week before admission.

On Admission.

Temp. 103.8.

Pulse 140.

Respr. 36.

Flushed cheeks.

Tongue dry and furred.

No Rose Spots.

Spleen not palpable.

Widal reaction positive.

Pneumonia at base of right lung.

Atropine Tests Negative.

In all the Test was applied to twelve children, whose age varied from 6 to 14 years. In all of the cases a Laboratory diagnosis of Enterica had been returned.

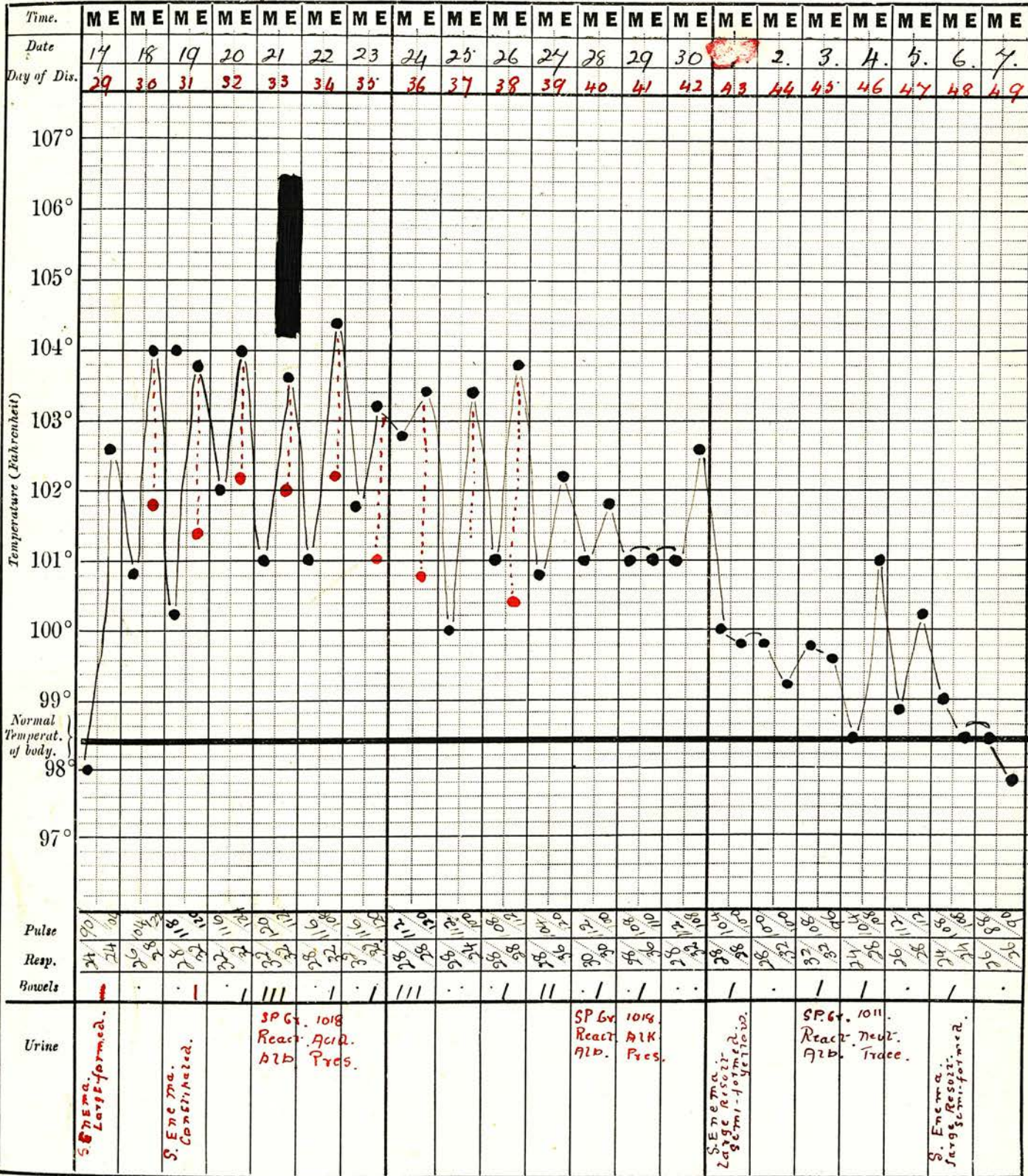
Of these, seven were in the acute stage of the disease, with high temperatures, when the test was done, but only one case of the 12 gave a Positive Result.

This Positive case was the only one of the series that had preventative inoculation against Typhoid, /

Typhoid, and this had been done a few days previously.

It was noticed that in all of the cases of Typhoid in children, the disease was of much shorter duration than that in adults. An observation was also made that the bradycardia characteristic of Typhoid in adults, was not so marked in children.

Name *Hellie Jaftha* April 1919.



GENERAL REMARKS.

At this stage I might make a few remarks about the type of cases of Typhoid that were seen.

In the majority of cases that I saw, a history of a sudden onset of the disease was given.

This sudden onset of the disease is, I think, more characteristic of Typhoid occurrence in hot climates, than it is in Europe and other colder countries.

The illness is ushered in by severe headaches, localised usually to the frontal region, by shivering or rigor and by an uneasy feeling in the abdomen.

A history of epistaxis was not uncommon.

Tenderness in the right iliac fossa was absent in most cases, though, as is shown in case No.12 it is present in some cases, and the illness may be taken for acute appendicitis.

On palpating the right iliac fossa it was often possible to feel a 'gurgling sensation'.

I have been told by those who have seen a large number of cases of Typhoid that this gurgling sensation is commonly felt in enteric cases.

The spleen was enlarged in about half of the cases/

cases seen, and more often there was a feeling of tenderness on pressure below the left costal arch.

Frequently a dull aching pain was complained of over the liver area, but this organ was not often found to be enlarged.

Diarrhoea was conspicuous by its absence, in fact most of the cases were constipated throughout the whole course of the disease.

Rose spots occurred in about one third of the cases seen. This small percentage might be explained by the fact that a number of the cases seen were black, and it was only possible to make out the rose spots in white patients.

One man had a profuse eruption all over his chest, back and abdomen.

SUMMARY OF GROUP I.

The Atropine Test was done in thirty cases of adults with a Laboratory diagnosis of Typhoid.

Of these 28 gave a positive result, or 93.3% of the total.

Two gave a negative result or an error of 6.6%.

I have already pointed out that in one of these two cases there is a suggestion of an idiosyncrasy for Atropine.

When Atropine was given in the fever stage, there was an escape of 30, but later when the fever had subsided, the escape was as much as 68.

On the 30 cases mentioned in this group, about 100 Atropine Tests were made.

It was found that from the third day of the disease onwards, the earlier that the test was done the more likely was it to be positive. As the fever wore off the test became negative.

In cases of relapse, however, where the temperature was up, the test became positive over again.

SUMMARY OF GROUP II.

This group comprises three cases returned as negative serologically, but each gave one or more positive Atropine Tests.

In case No.2 the Atropine Test was strongly positive on six successive weeks.

As I have mentioned before, *B. Faecalis Alkaligenes septicaemias* frequently simulate enteric infection.

In this case *B. Faecalis Alkaligenes* was isolated from the blood and urine. It appears to me that it is possible that the toxin given off by this organism may react to Atropine in the same way as that given off by the *B. Typhosus*.

Marris has pointed out that in patients with arterio sclerosis, and in those with high blood pressures the test shows restricted response to Atropine. This explains to some extent Cases Nos. 18 and 28, both of whom had arterio sclerosis.

SUMMARY OF GROUP III.

I have kept my observations on children apart from those on adults because, in my opinion, the whole test depends upon the vagus control of the heart. In children there is not full vagus control, and until this is developed the Atropine Test is unreliable. In the adult, stimulation of the peripheral nerve endings of the vagus inhibits the action of the heart. Atropine paralyzes the peripheral nerve endings, the vagus loses its control of the heart, and a quickened pulse results. It seems likely that the Typhoid toxin stimulates the vagus nerve endings, hence the comparative bradycardia characteristic of the illness, and it appears to me that Atropine and the Typhoid toxin are antagonistic in their action, with the result that when Atropine is given in cases of Typhoid, there is not the acceleration of the pulse that is usually experienced. Whether this theory be justifiable or not, further investigation of the antagonism of these poisons should afford most interesting and instructive problems to the Physiologist and Pharmacologist.

CONTROL CASES.

The test was also tried on many control cases, which had been diagnosed as Malaria, Pneumonia, Influenza, Amoebic and Bacillary Dysentery, Meningitis, Appendicitis, Gastric Ulcer, Puerperal fever, Acute Salpingitis, with negative results in all cases.

The value of the Atropine Test, like most other clinical tests, is relative.

As I have pointed out, the typical reaction is obtained in a large percentage of the cases (93.3%) that I have tested, and the same reaction is absent in a very large percentage of all other diseases.

As a result of the work done I have come to the conclusion that, though of value as an extra test, the test is of special use to practitioners in the county districts of Great Britain, and our colonies, where it is impossible to get a laboratory diagnosis.

It is a test which may be performed by any medical man on any patient, no matter where he be.

It is a test that, though not absolutely reliable, will, in the majority of cases, give an indication as to whether the patient is suffering from a Typhoid infection or not.

Taken/

Taken as a whole, the results of my work seem to indicate.-

1. That when done on adults in the acute stage of the disease, the Atropine Test is as reliable as any other test, except the isolation of the specific bacillus.
2. That as the disease declines, the test is more liable to be negative.
3. That until an age is reached when there is full vagus control of the heart, the test can not be relied upon.
