T H E S I S

for the

DEGREE OF DOCTOR OF MEDICINE (M.D.)

Presented To

U N I V E R S I T Y O F G L A S G O W

By

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-oOo-

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T H E S I S

"Serum Therapy in Scarlatina and Erysipelas"

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INTRODUCTORY.

The clinical investigations which form the basis of this thesis were carried out in the City of Glasgow Corporation Fever Hospital at Ruchill, between May 1926 and March 1930. A study was made first of Scarlet Fever and secondly of Erysipelas with special reference to the therapeutic value of specific serum.

Previously in this hospital, serum treatment has been confined to cases of septic Scarlet Fever which have been treated with repeated doses of Polyvalent anti-streptococcal serum. This routine measure has been found, however, to give very varying results. The method of administration consists in three injections given per rectum, each containing 30ccs. of the serum, the injections being given every eight hours until 90ccs. has been administered, this amount being repeated on alternate days.

The use of convalescent serum intramuscularly has also been tried with a degree of success, but is rather impossible on account of the large amount of serum which is necessary for a successful dose.

In connexion with Erysipelas the treatment with serum has been confined to the use of Polyvalent Anti-streptococcal serum in addition to the many varied but well recognised lines of topical therapy.

SCARLET FEVER.

The serum therapy of Scarlet Fever dates back at least a quarter of a century when Moser (1) with apparently considerable success treated cases of Scarlet Fever with serum which was prepared by immunising horses with streptococci; these organisms were derived from the throats of acute cases of the disease. Other workers, however, failed to observe beneficial results with serum obtained in this manner and this therapeutic method fell into disrepute and disuse. During the last decennium, however, a great deal of investigation has been carried out on the streptococcal group of organisms and interest has been revived in certain diseases particularly with regard to etiology and treatment. According to the work of Tunnicliff (2) and Zingher (3) and the Dicks (4), the haemolytic streptococci appear to be well defined and this work has tended to change the scientific and medical views on the control and treatment of Scarlet Fever.

Dochez (5), in his recent paper on the etiology of Scarlet Fever makes out a very strong case for the haemolytic streptococcus as the causal organism, admitting nevertheless that there are still many scientists who hold the opinion that this organism although generally present in this disease is not the main factor and is probably/

probably secondary to a filter passing micro-organism.

It is known that certain specific strains of haemolytic streptococci and their toxins produce when injected into horses an antitoxic serum which different investigators have used with varying results.

The most recent advance is the production of serum prepared from horses which have been subjected to repeated intravenous injections of streptococci and their toxins, and in addition, have had the mouth and fauces swabbed with virulent cultures of the organism until a very high stage of immunity has been reached. This serum is thus a Scarlet Fever streptococcus antitoxin and is claimed to be antibacterial.

Conflicting reports have since then been published as to the beneficial results obtained from the use of this serum in the treatment of Scarlet Fever.

The investigations of Blake (6), Park (7), Robb (8), Cushing (9) and Harries (10) are more or less in agreement that serum therapy is justifiable and of benefit when the serum is administered early.

Toomey (11) on the other hand, after an extensive survey of the literature of these investigators and many others, does not think that the antitoxin treatment justifies the expense and risk to the patient, and suggests that immunisation is preferable.

CLINICAL WORK DURING EPIDEMIC.

It is now the general opinion in the scientific world that the type of Scarlet Fever now prevalent is less severe than formerly; nevertheless, in epidemics there are still found many severe cases, and a case of Scarlatina Simplex is still liable to develop complications.

It was thought that if the most recently produced scarlet fever antitoxin was actually a specific serum it would show to advantage in the treatment of the most severe cases of Scarlatina.

An investigation as to the value of this Scarlet Fever antitoxin was undertaken at the beginning of the epidemic of Scarlet Fever in May 1926, and continued until January 1927.

During this epidemic, the general run of cases were of the mild type, but during the latter half of the year the standard of severity rose, and many severe cases were admitted to the wards. In order to test thoroughly the efficacy of the serum, only selected cases were treated. There were cases which shewed some or other manifestations of considerable toxaemia and amounted to 110 cases; eight cases of the septic type were treated, while there were two cases of malignant Scarlet Fever.

Thus/

Thus, in an epidemic in which the standard of type severity rose above the usual, 120 cases in all representing the most acutely ill scarlet fever patients admitted to hospital during the epidemic were dealt with by serum therapy.

TYPE OF SERUM.

The serum used in this investigation was concentrated Scarlet Fever Streptococcus antitoxin supplied by

(1) Messrs Burroughs, Wellcome & Co.(B.W.& Co.)... 10 cases
(2) Messrs Parke, Davis & Co.(P.D.& Co.)..... 110 cases

The potency of both types of serum is tested after preparation and the serum is put up in ampoules containing 10ccs. which represents one therapeutic dose. This dose of antitoxin is claimed to be able to neutralise 500,000 skin-test doses of Scarlet Fever toxin.

The recommended doses of both types of serum is 10ccs. for mild cases of Scarlet Fever and 20 to 40ccs. for severe cases.

METHOD.

The method of administration of the serum adopted as a routine was that of intramuscular injection into the lateral aspect of the thigh and this was found in all cases to be satisfactory in every respect.

The usual aseptic precautions were strictly adhered to, and there were no ill effects observed following administration of the serum other than slight stiffness of the muscles round the site of the injection.

In three serious cases where immediate reaction was required, attempts at intravenous injections were made, but/

but had to be abandoned on account of the existing low blood-pressures. As a rule one dose of 100cs. of serum proved effective, but some cases required a second similar dose; the latter cases were particularly severe in type. The time of administration of the serum varied considerably. Some patients were given serum on admission to hospital while some were kept under observation for 24 hours. The majority of cases received the serum on the second or third day of illness but some had been ill for as long as six days.

CLINICAL MATERIAL.

An examination of the Clinical Records of the cases of Scarlet Fever admitted to Ruchill Fever Hospital during the 1926 epidemic revealed the fact that the disease was present in different forms.

The following types of Scarlatina were observed -

(1) Scarlatina Maligna.
(2) Scarlatina Anginosa.
(3) Scarlatina Simplex.

The majority of the cases were Scarlatina Simplex but of this group many were of a severe form, while a few cases of the Adynamic type were observed.

The cases selected for serum therapy numbered 120 in all and were classified as follows -

(1)/

(1) Scarlatina Maligna, 2 cases.
(2) Scarlatina Anginosa, 8 cases.
(3) Scarlatina Simplex, (severe) 105 cases.
(4) Scarlatina Simplex, (adynamic) 5 cases.

The cases of Scarlatina Simplex (severe) all shewed to a greater or less degree some or other of the manifestations of an acute attack of Scarlet Fever accompanied by toxaemia.

Tables I to VII have been prepared shewing the sex incidence, the age incidence and the time incidence.

These tables indicate that the group of 120 cases of Scarlet Fever included both sexes and all ages between 1 and 65 years of age, the youngest child being 14 months and the oldest patient 64 years of age.

Tables III to VII indicate the variation in the time of the administration of the serum. The "Day of Admission" column indicates the length of time, in days, that the individual patient has been ill on the day of admission to hospital.

TABLE I.

SEX INCIDENCE.

MALES	70
Females	50
TOTAL NUMBER OF CASES	120

TABLE II.

AGE INCIDENCE.

AGE PERIOD IN YEARS	DAY OF ADMISSION TO HOSPITAL.					NUMBER OF CASES.
	1st.	2nd.	3rd.	4th.	over 4th.	
0 - 5	5	11	5	2	2	25
5 - 10	5	27	14	4	-	50
10 - 15	-	10	3	3	-	16
15 - 20	-	1	2	5	-	8
over 20	1	8	7	4	1	21
	11	57	31	18	3	120

TABLE III.

TIME INCIDENCE.

(Age Period 0 - 5 years)

DAY OF ADMISSION	DAY OF ADMINISTRATION OF SERUM.					NUMBER OF CASES.
	1	2	3	4	4+	
1st Day	-	4	-	1	-	5
2nd Day	-	5	6	-	-	11
3rd Day	-	-	-	5	-	5
4th Day	-	-	-	-	2	2
over 4th Day	-	-	-	-	2	2
	-	9	6	6	4	25

TABLE IV.

TIME INCIDENCE.

(Age period 5 - 10 years)

DAY OF ADMISSION.	DAY OF ADMINISTRATION OF SERUM.					NUMBER OF CASES
	1	2	3	4	4+	
1st Day	3	2	-	-	-	5
2nd Day	-	12	13	-	2	27
3rd Day	-	-	10	3	1	14
4th Day	-	-	-	3	1	4
Over 4th Day	-	-	-	-	-	-
	3	14	23	6	4	50

TABLE V.

TIME INCIDENCE.

(Age period 10 - 15 years)

DAY OF ADMISSION	DAY OF ADMINISTRATION OF SERUM					NUMBER OF CASES.
	1	2	3	4	4+	
1st Day	-	-	-	-	-	-
2nd Day	-	3	6	1	-	10
3rd Day	-	-	3	-	-	3
4th Day	-	-	-	3	-	3
Over 4th Day	-	-	-	-	-	-
	-	3	9	4	-	16

TABLE VI.

TIME INCIDENCE.

(Age period 15 - 20 years)

DAY OF ADMISSION	DAY OF ADMINISTRATION OF SERUM.					NUMBER OF CASES
	1	2	3	4	4+	
1st Day	-	-	-	-	-	-
2nd Day	-	1	-	-	-	1
3rd Day	-	-	2	-	-	2
4th Day	-	-	-	3	-	3
Over 4th Day	-	-	-	2	-	2
	-	1	2	5	-	8

TABLE VII.

TIME INCIDENCE.

(Age period over 21 years)

DAY OF ADMISSION.	DAY OF ADMINISTRATION OF SERUM					NUMBER OF CASES
	1	2	3	4	4+	
1st Day	1	-	-	-	-	1
2nd Day	-	5	2	1	-	8
3rd Day	-	-	4	2	1	7
4th Day	-	-	-	4	-	4
over 4th Day	-	-	-	-	1	1
	1	5	6	7	2	21

RESULTS.

The immediate effects of the serum were fairly constant, as observed in the cases under review. Definite effects were noted in connexion with the following points,

(1) The course of the temperature.
(2) The circulatory system.
(3) The Toxaemia.
(4) The Skin.
(5) The Mouth and Tongue.

Observations were made on the remote effects with reference to

(1) Complications.
(2) Serum Reactions.
(3) Duration of detention in hospital.
(4) Relapses.
(5) Case Mortality.

IMMEDIATE EFFECTS.

(I) The Course of the Temperature.

The most constant effect of serum when given early in the course of the disease was to produce a critical fall of temperature. In 90% of the cases an initial rise of temperature was observed within 8 hours of the administration of the serum, after which the temperature dropped steadily during the next 24 or 36 hours. This initial rise of temperature resembles that which may follow the injection of diphtheria antitoxin. In very severe cases and in cases where the serum was not administered until after the fourth day of illness, the temperature tended to fall more by lysis than by crisis, and this fall took place over 48 hours.

(II) The Circulatory System.

The effect of the administration of the serum on the circulatory system was observed to be almost as constant as on the temperature. A marked beneficial effect was produced on the condition of the heart, the pulse rate being diminished and the quality of the pulse greatly improved with a definite rise of blood-pressure.

(III) The Toxaemia.

One of the most striking effects observed was the extraordinary change in the toxaemic condition of Scarlet Fever/

Fever patients within 12 to 24 hours of administration of the serum. The disappearance of malaise, headache, delirium, pains in muscles and joints, etc., caused an intense feeling of relief and well-being; most of the patients, however ill they had been to begin with, were within 36 hours wanting to sit up and were demanding a more liberal diet.

(IV) The Skin.

The effect of the serum on the rash was to lessen its intensity and duration and subsequent desquamation was rendered less profuse. The cases of Scarlet Fever exhibiting rashes of under 48 hours duration and which were treated with serum on admission were observed to have a very quick fading of the eruption; the rash in 75% of these cases disappearing within 12 hours. It was noted particularly in six cases that there was a minimum of desquamation. In the case of children under this category, the subsequent desquamation was almost imperceptible.

(V) The Tongue and Throat.

The effect on the faucial angina, the cervical adenitis and discharges from the nose and throat was quite as striking in patients who were treated early in the course of the illness. Soon after serum treatment, marked/

marked changes in the mouth and throat took place. The disappearance of dry lips, sordes and dry tongue, was observed. The painful throat disappeared rapidly and cases where there was marked faucial congestion, palatal angina, and oedema of the uvula, showed a marked subsidence within 24 hours. An atypical peeling of the tongue was observed in most cases which were treated early by serum.

Remote Effect of Serum Therapy.

(1) The Incidence of Complications.

The question of the effect of this serum on the complications of Scarlet Fever was considered to be of prime importance. It was noted in several cases which were complicated by rhinorrhoea, otorrhoea, and cervical adenitis on admission to hospital that these complications subsided in a few days after the administration of the serum. Complications arose after serum treatment but were either transient or of a mild form. Late adenitis was observed in a few cases but was always transient; there were no cases of suppurative adenitis; otitis media complicated very few serum cases and only one case which showed hypertrophy of tonsils and adenoids to a marked degree, was detained in hospital beyond six weeks. There were no cases complicated by acute mastoiditis/

mastoiditis; rhinorrhoea occurred mainly in children but was found more amenable to treatment than in patients who had not received antitoxin; arthritis was observed in one case but it was transient and possibly in the nature of a serum arthritis; and nephritis occurred only in one serum case, the patient getting out of bed on his fourth day against regulations. Albuminuria immediately following the injection of the serum was observed in several cases but rarely lasted more than one or two days. Endocarditis occurred in two cases; one case of septic Scarlet Fever terminating fatally but the other patient made an excellent recovery.

(II) Serum Reactions.

Evidence of serum disease was confined to the appearance of a serum rash which occurred in several cases but was urticarial and of a transient nature, causing no inconvenience and requiring no treatment. The incidence in the cases treated was 14%

(III) Duration of Detention in Hospital.

Detention in hospital beyond the usual quarantine period of six weeks was confined only to two cases, and was on account of sores on the upper lip and in the nostrils although the nasal discharge had ceased.

The routine procedure with regard to the detention

of/

of patients in bed (4 weeks) and in hospital as convalescents (2 weeks) was strictly adhered to, although it was found that 60% of the patients treated with antitoxin appeared sufficiently well in all respects at the end of three weeks to warrant dismissal from hospital.

(IV) Relapses.

One serum treated case exhibited a true relapse during the fourth week of the disease. No second attacks occurred within two years so far as it was possible to ascertain.

(V) Case Mortality.

The important question of the effect on the mortality rate is very difficult to consider statistically as it is a recognised fact that the mortality rate has been decreasing along with the decrease in the severity of the type of Scarlet Fever now prevalent. In this series of cases two deaths occurred, one a septic case complicated by endocarditis and the other a case suffering from gastro-enteritis and broncho-pneumonia in addition to Scarlet Fever.

When it is taken into consideration that the cases dealt with in this series were all of a particularly severe nature and which moreover included two patients who were moribund on admission and who recovered, it is reasonable/

reasonable to conclude that without serum the number of deaths would have been greater.

EXAMPLES OF CASES.

The following brief records are given to illustrate types of Scarlatina and the effects of Serum Therapy.

(I) Scarlatina Maligna.

During the course of the epidemic two cases of Scarlatina Maligna were admitted to hospital, and although both were moribund on admission to the wards these two cases reacted in rather dramatic manner and both made excellent recoveries.

Case 45.

This boy of 10 years was admitted on the fourth day of illness; the rash had appeared after three days of headache, vomiting and sore throat; persistent diarrhoea had been present and the boy was in a low typhoid state when first seen in hospital. The Widal Reaction was persistently negative.

The clinical signs of Scarlatina Maligna were present and 20ccs. of serum administered. Improvement was noted in 24 hours and an uninterrupted recovery took place: typical desquamation was present on the 16th day of illness.

DISEASE.

SCARLATINA MALIGNA.

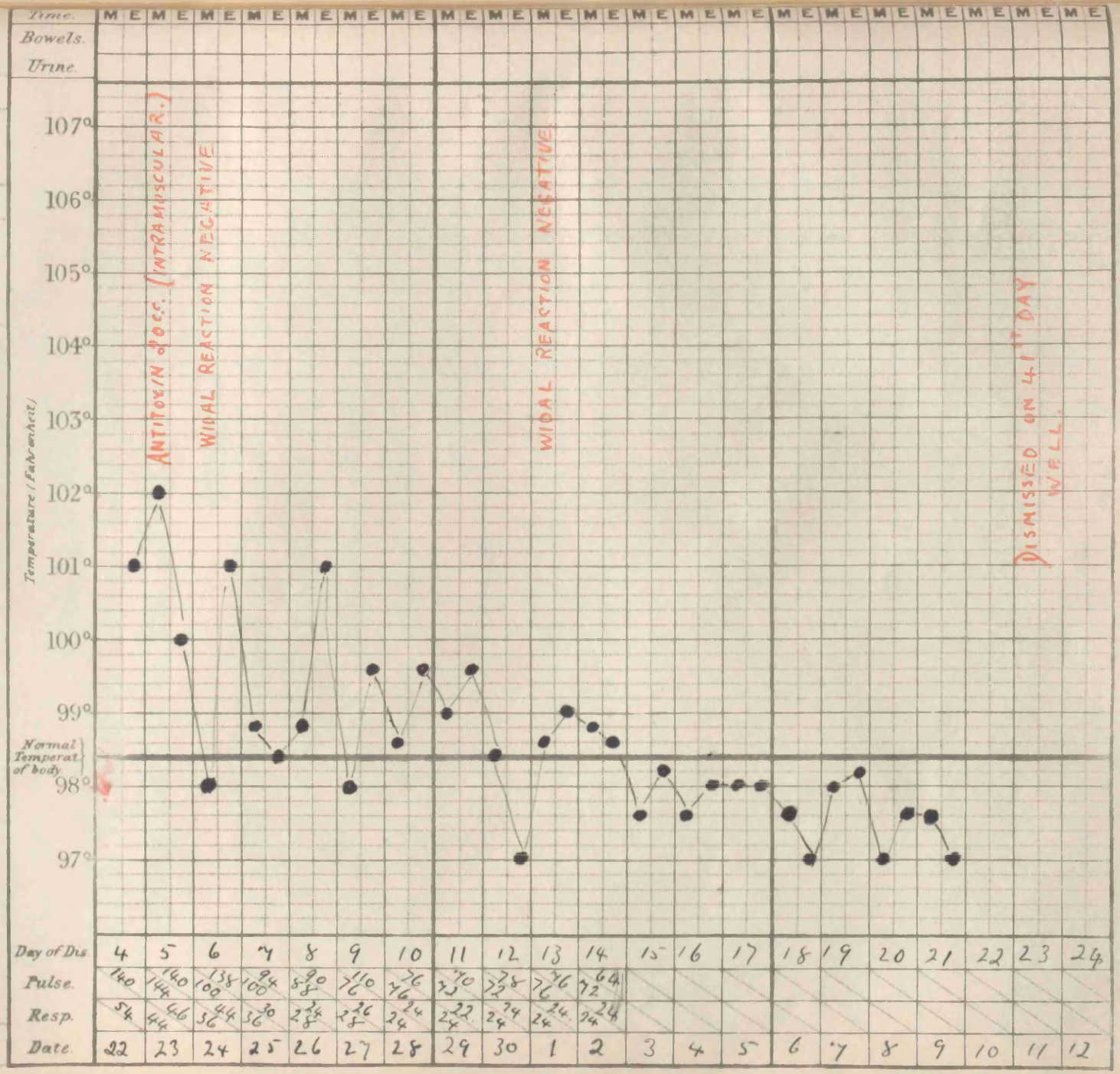
Notes of Case.

Name WILLIAM MARSHALL.

Age 10.

Diet

Case Book No. 45.



Date of admission. 22nd September 1926

Result Well.

Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co Ltd Gate Street, Kingsway W.C.2* *Gould's Clinical Chart.*

CASE No. 45.

NAME. W.M. (Male).

AGE 10 years.

TYPE. Scarlatina Maligna.

DAY OF ILLNESS ON ADMISSION 4th day.

DAY OF SERUM TREATMENT. 4th day.

CLINICAL NOTES. Moribund on admission.
Persistent vomiting; diarrhoea.
Widal Reaction negative.
T.102. P.144. R.44.
24hrs after T. 98. P.100. R.36.
Marked improvement after serum therapy.

RASH. Generalised dusky erythema; punctate rash in axillae; faded 36 hours later. Desquamation 16th day.

THROAT. Moderate faucial congestion.

TONGUE. Peeled.

TOXAEMIA. Very marked; cyanosis marked; pulse imperceptible at times; semi-conscious.

COMPLICATIONS. Enteritis (present on admission to hospital).

RESULT. Excellent recovery.

SERUM. Antitoxin 20ccs. (P.D.& Co.).

REMARKS. Immediate reaction to serum intramuscularly.
Dismissed well in 41 days.
Recovery of a case of Scarlatina Maligna.

Case 81.

This boy of 7 years was in extremis on admission to hospital on the fourth day of illness; there was a generalised dusky erythema which faded 48 hours after serum therapy; desquamation was observed on the 10th day of illness. There was marked angina of fauces and palate. Delirium was very marked; Blood Pressure 40mm. HG. Intravenous serum therapy was attempted but failed owing to low blood pressure. 10ccs. of serum was given intramuscularly, followed by slight improvement. 20ccs. of serum were given 12 hours later, followed by marked improvement. Recovery took place within 4 days.

4 HOUR CHART.

DISEASE.

SCARLATINA MALIGNA.

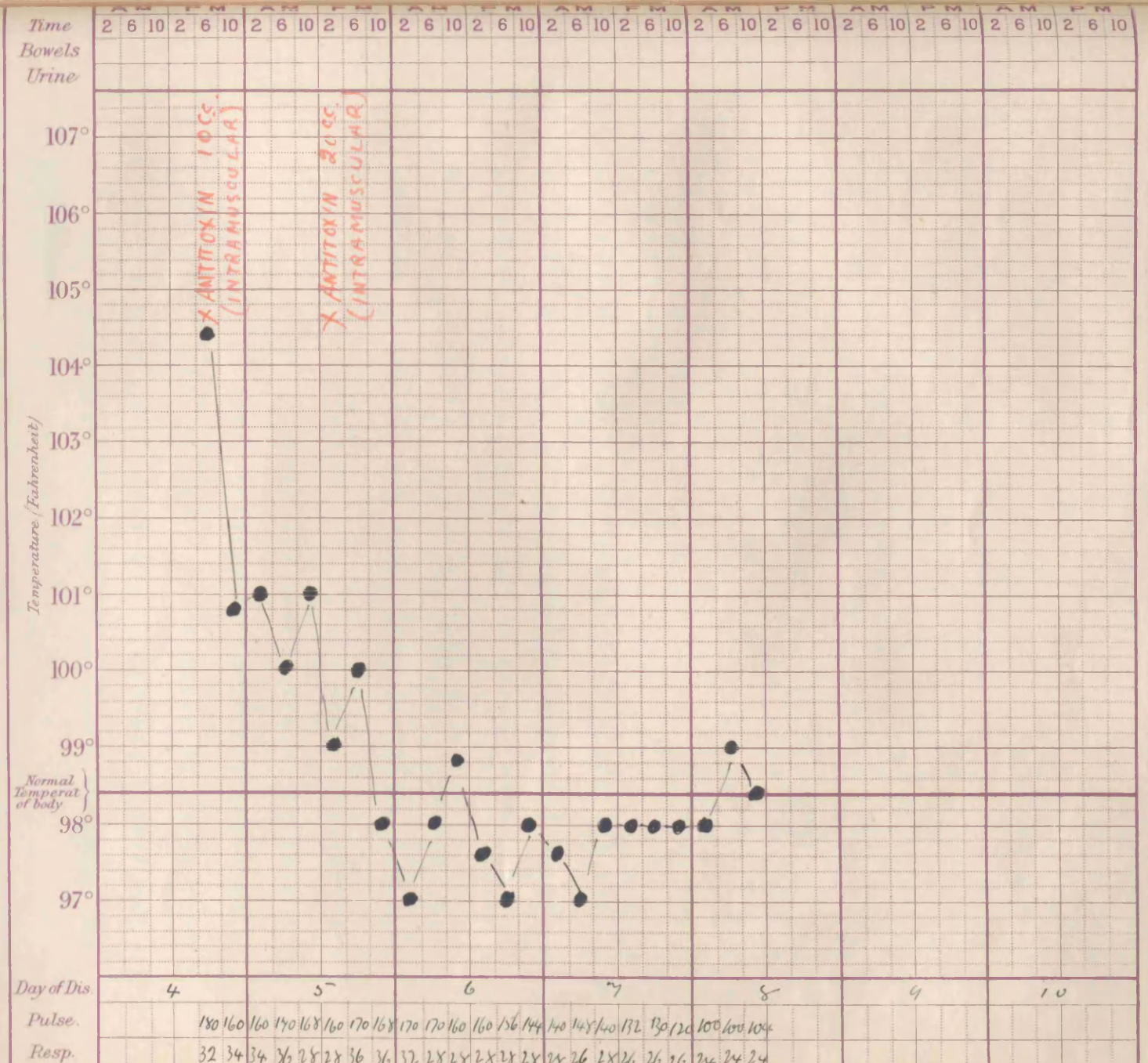
Name { WILLIAM WALKER.

Age 14 YRS.

Diet

Case Book No. 81.

Notes of Case



Date of admission

3rd Nov. 1926.

Result WELL.

Entered at Stationers Hall. Printed and Published by Wodderspoon & Co Ltd Gate Street Kingsway W.C. Goulds Clinical Chart.

CASE No. 81.

NAME. W.W. (Male).

AGE. 7 years.

TYPE. Scarlatina Maligna.

DAY OF ILLNESS ON ADMISSION. 4th day.

DAY OF SERUM TREATMENT. 4th day.

CLINICAL NOTES. Case of true toxic Scarlet Fever in extremis on admission. Greyish and cyanosed; pulse imperceptible. 10ccs. Scarlet Fever Antitoxin, followed by slight improvement. 20ccs. additional serum followed by marked improvement. Gradual recovery inside a week.

Before serum	T.104	P.180(?)	R.32.
(1) 12 hrs. after serum	T.100	P.170	R.36.
(2) 24 " " "	T. 98	P.156	R.32.

RASH. Generalised rash – dusky punctate erythema. Faded 48 hours after serum. Desquamation 10th day.

THROAT. Marked angina of palate and oedema of the uvula with ulceration of mucous membranes.

TOXAEMIA. Delirium; pulse almost imperceptible. Tongue dry and peeling. Blood pressure 40mm. Hg.

COMPLICATIONS. (1) Cervical Adenitis.
(2) Otorrhoea.
Tonsils and Adenoids removed.
(successful treatment)

RESULT. Very good.

SERUM. 30ccs. Antitoxin (P.D.& Co.).

REMARKS. Recovery of a case of Scarlatina Maligna which was admitted on 4th day of illness in extremis.

(II) SCARLATINA ANGINOSA.

The results of serum in combating the septic complications of Scarlatina Anginosa are rather unsatisfactory; of the eight cases treated by serum therapy, one case died of endocarditis, three cases were definitely not affected by the serum, and, while the results in two other cases were encouraging only two out of the eight cases appeared to derive immediate and lasting benefit.

4 HOUR CHART.

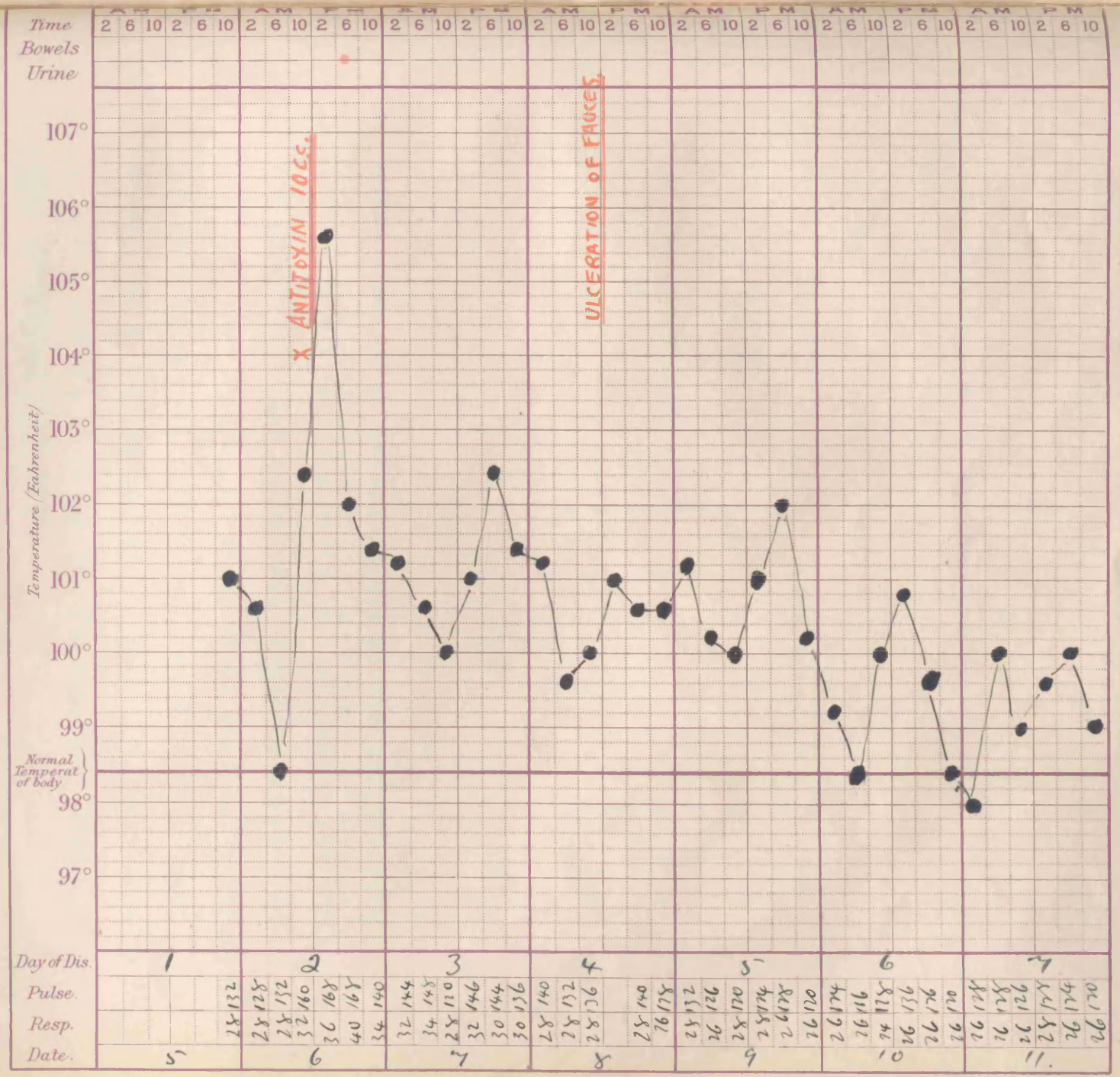
DISEASE.
SCARLATINA ANGINOSA.

Name { THOMAS KELLY.
Age 4 6/12 YRS.
Diet
Case Book No. 41.

Notes of Case

Date of admission
5th OCT. 1926.

Result DIED.



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DISEASE.

SCARLATINA ANGINOSA.

Notes of Case.

Name THOMAS KELLY

Age 4 6/12 YRS.

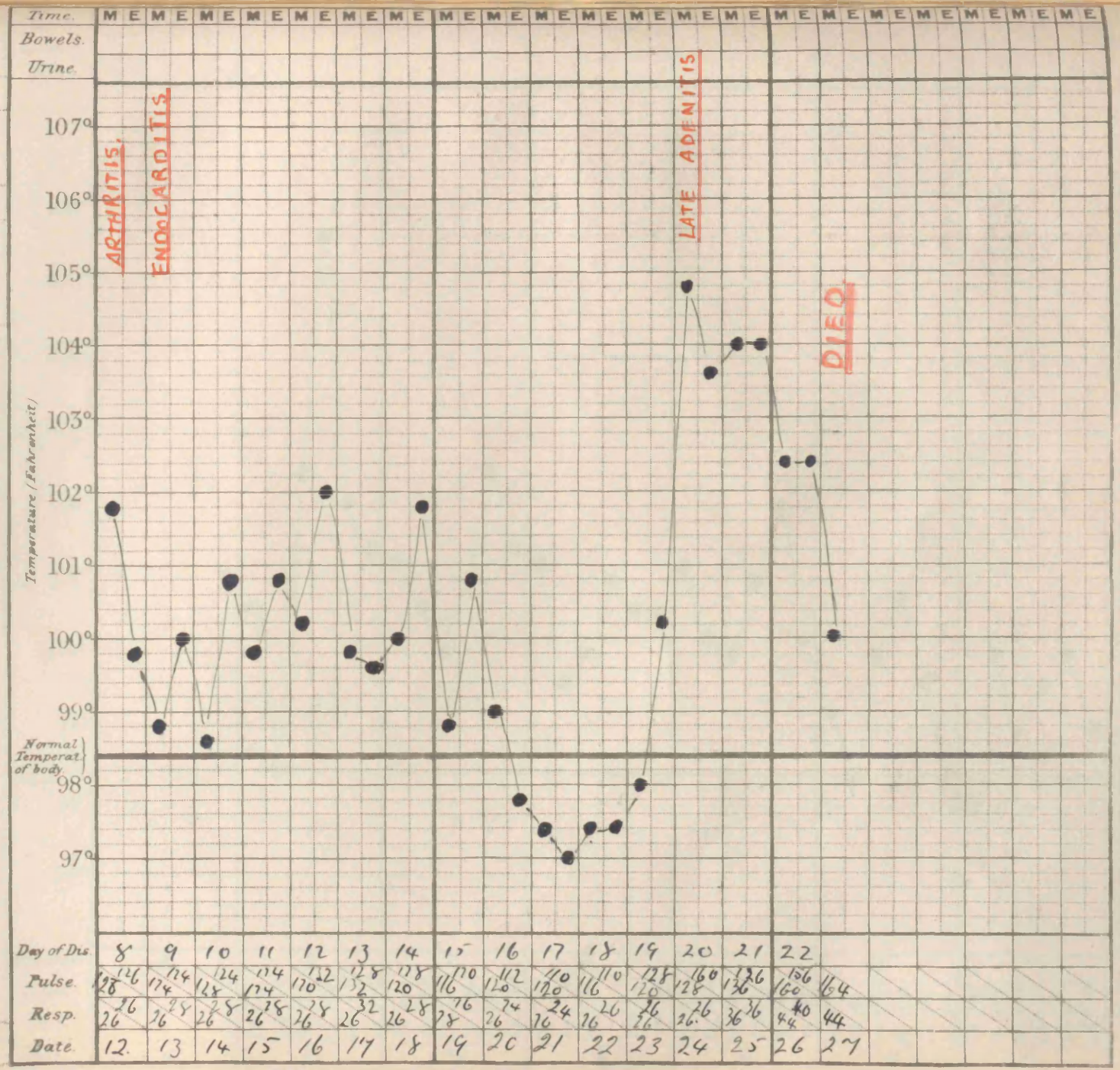
Diet

Case Book N° 41.

Date of admission.

5TH OCT. 1926.

Result DIED.



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CASE No. 41.

NAME. T.K. (Male).

AGE. 4½ years.

TYPE. Scarlatina Anginosa.

DAY OF ILLNESS ON ADMISSION. 1st day.

DAY OF SERUM TREATMENT. 2nd day.

CLINICAL NOTES. Moderately ill on admission: very ill on 2nd day. 10ccs. serum given without benefit.
Febrile course of 23 days complicated by ulceration of throat: adenitis: arthritis and endocarditis.

RASH. Moderately bright.

THROAT. Intense faucial congestion proceeding after serum therapy to oedema of uvula and palate and then to extensive ulceration of fauces.

TOXAEMIA. Considerable restlessness and irritability.

COMPLICATIONS. (1) Ulceration of fauces.
(2) Cervical adenitis.
(3) Arthritis.
(4) Endocarditis.

RESULT. Died.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Antitoxin.

REMARKS. Dosage of Serum quite inadequate.

DISEASE.

SCARLATINA ANGINOSA.

Notes of Case.

Name MARY STEPHEN.

Age 2 YRS.

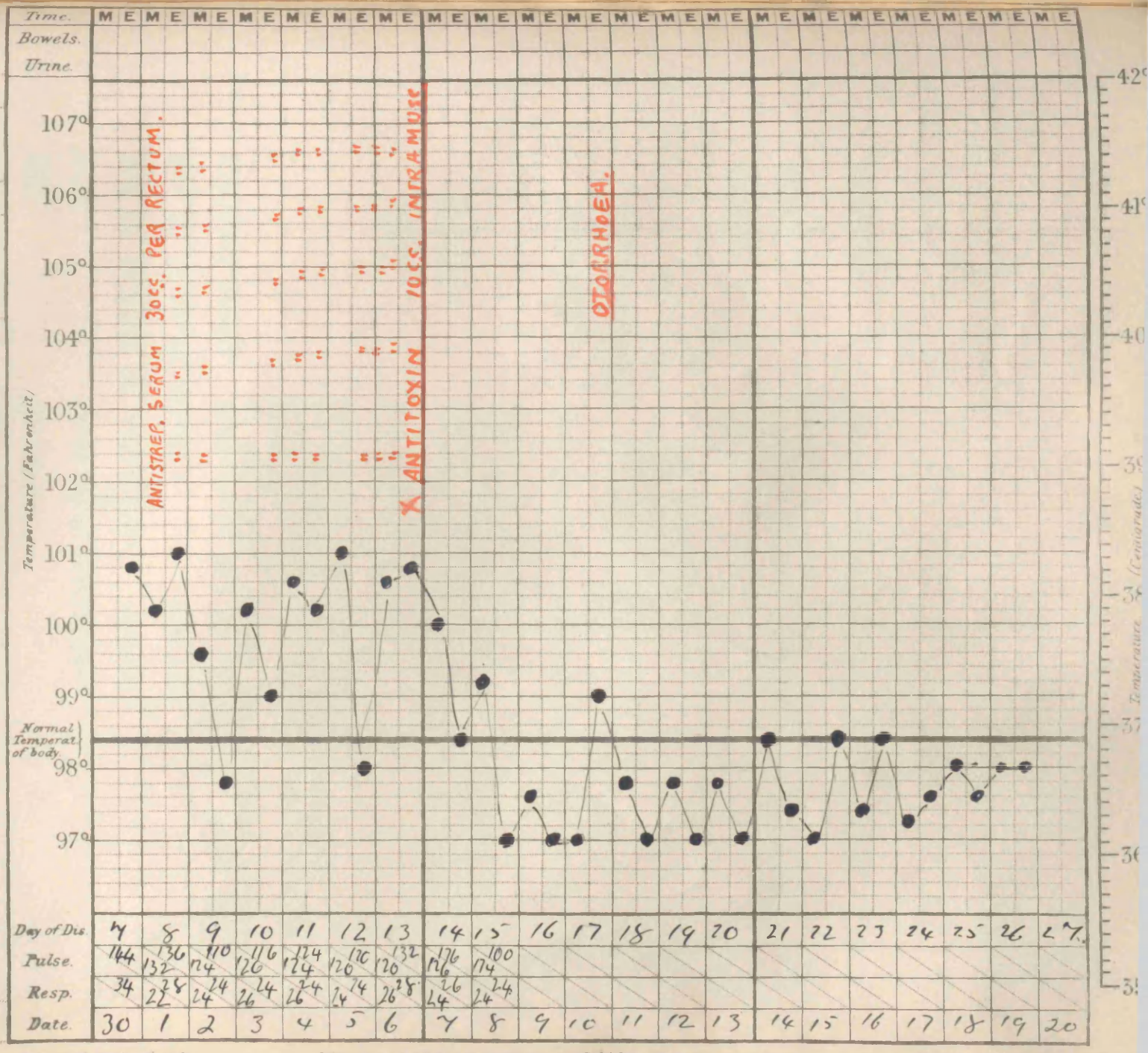
Diet

Case Book No. 43.

Date of admission.

30TH. SEPT. 1926.

Result WELL.



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CASE No. 43.

NAME. M.S. (Female).

AGE. 2 years.

TYPE. Scarlatina Anginosa.

DAY OF ILLNESS ON ADMISSION. 7th day.

DAY OF SERUM TREATMENT. 13th day.

CLINICAL NOTES. Typical case of Septic Scarlet Fever: profuse discharges, cervical adenitis: irregular fever: treated by three successive doses of Polyvalent Antistreptococcic serum (B.W.& Co.), without apparent effect. 10ccs. Antitoxin (P.D.& Co.) given intramuscularly on 13th day. T.P.R. normal within 36 hours, marked improvement.

RASH. Faded on admission to hospital.

THROAT. Intense congestion of fauces: ulceration of tonsils. Post nasal discharge profuse.

TOXAEMIA. Not marked.

COMPLICATIONS (1) Rhinorrhoea. (present on admission).
(2) Cervical adenitis (present on admission).
(3) Double otorrhoea. (after serum therapy).

RESULT. Interesting result.

SERUM. S.F.Antitoxin 10ccs. (P.D.& Co.).

REMARKS. This case was treated without benefit by Polyvalent Antistrepticoccic serum prior to (P.D.& Co.) S.F.Antitoxin.

DISEASE.

SCARLATINA ANGINOSA.

Notes of Case.

Name EDWARD HUTCHESON.

Age 3 6/12 YRS.

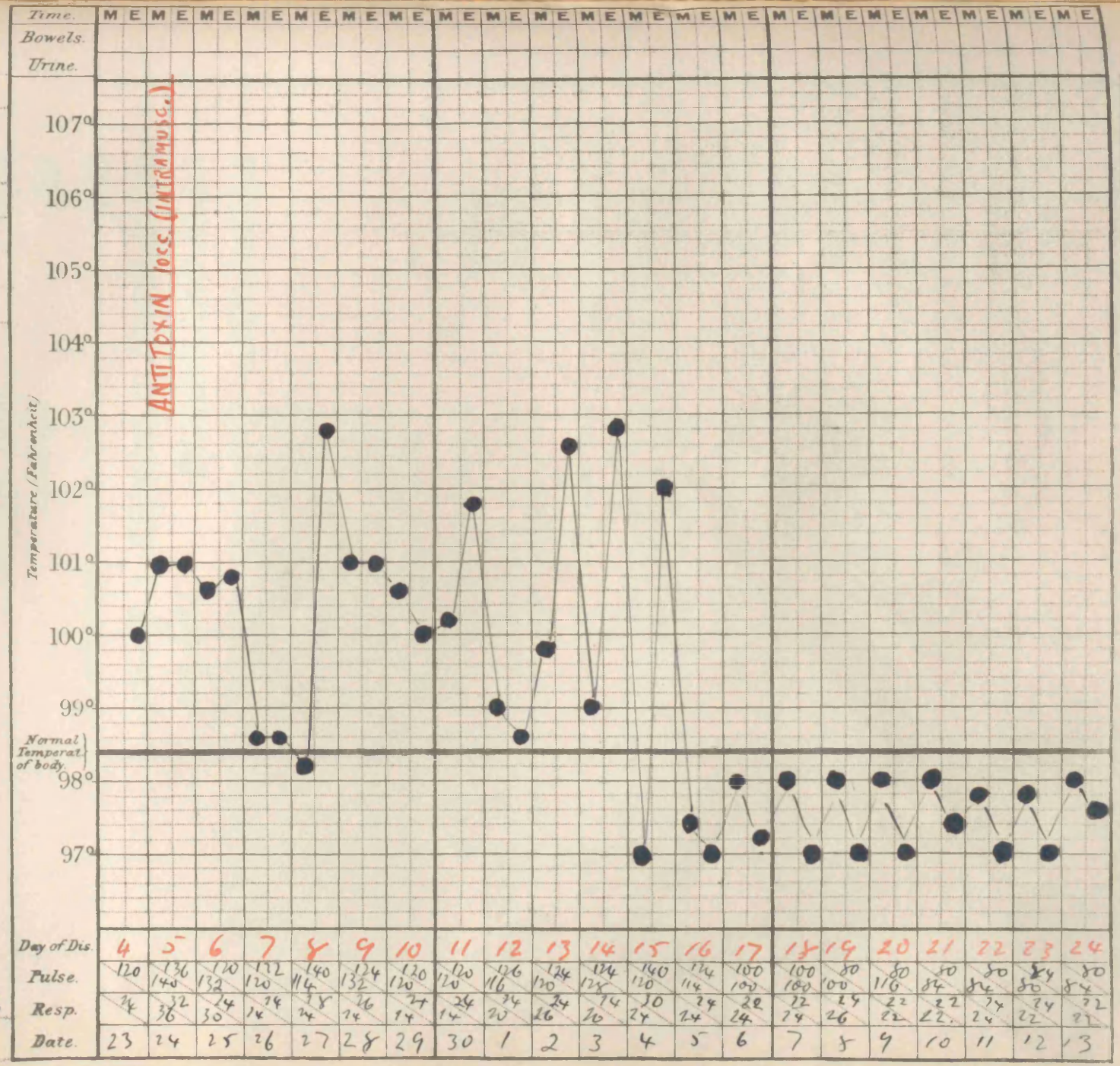
Diet

Case Book No. 35

Date of admission.

23RD SEPT. 1926

Result WELL.



Entered at Stationers Hall. Printed and Published by Wodderspoon & Co Ltd Gate Street Kingsway W.C. 2 Gould's Clinical Chart.

CASE No. 35.

NAME. E.H.

AGE. 3½ years.

TYPE. Scarlatina Anginosa.

DAY OF ILLNESS ON ADMISSION. 4th day.

DAY OF SERUM TREATMENT. 5th day.

CLINICAL NOTES. Typical septic Scarlet Fever case. Blotchy rash: profuse rhinorrhoea and cervical adenitis. T.P.R. not affected by administration of serum but rhinorrhoea and adenitis subsided in 7 days.

RASH. Moderately bright rash: blotchy on extremities.

THROAT. Intense congestion of fauces and pharynx: profuse purulent nasal and post nasal discharge. Ulceration of tonsils.

TOXAEMIA. Not marked: typical septic case.

COMPLICATIONS (1) Rhinorrhoea. (present on admission).
(2) Cervical adenitis. (present on admission).
(3) Endocarditis.
(4) Albuminuria.
(5) Serum or septic rash.

RESULT. Satisfactory in as much as complete recovery was obtained.

SERUM. 10ccs. S.F.Antitoxin (P.D.& Co.).

REMARKS. Probably quite inadequate initial dose. No polyvalent antistreptococcal serum therapy in this case.

DISEASE.

SCARLATINA ANGINOSA.

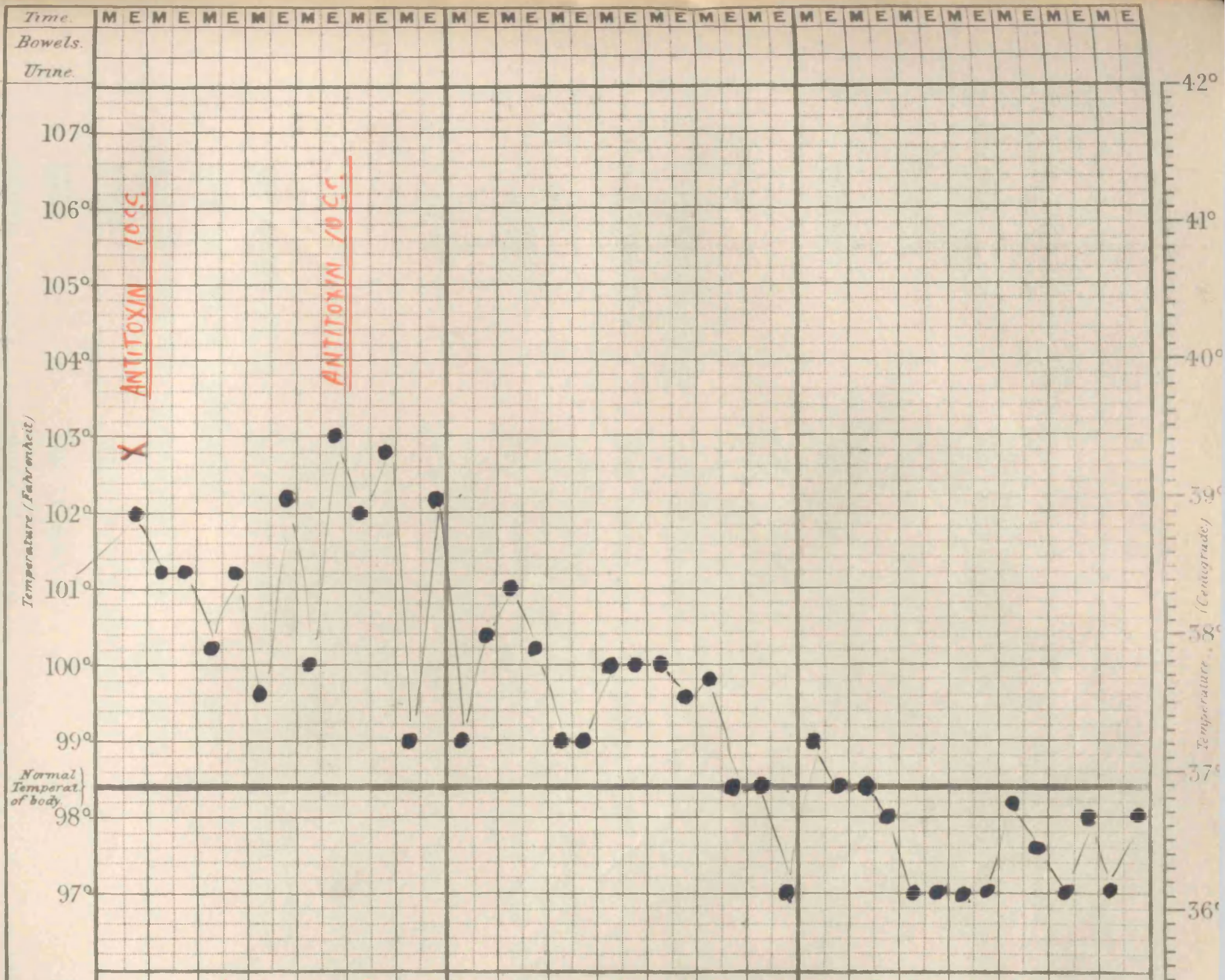
Notes of Case.

Name: MARGARET DAVIDSON (MRS)

Age: 18 YRS.

Diet:

Case Book No. 44.



Day of Dis.	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Pulse.	112	112 / 104	96 / 100	104 / 124	108 / 124	120 / 108	100 / 100	108 / 100	100 / 100	100 / 100	116 / 120	88 / 96	76 / 88	88 / 88	88 / 86	88 / 80	80 / 80	92 / 88	88 / 80	88 / 96	80 / 88
Resp.	24	24 / 24	24 / 24	22 / 26	24 / 24	24 / 28	24 / 24	24 / 24	24 / 24	24 / 24	24 / 24	20 / 24	20 / 20	20 / 20	20 / 20	20 / 20	20 / 20	20 / 20	20 / 20	20 / 22	20 / 20
Date.	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26

Date of admission. 6 OCT. 1926

Result WELL.

CASE No. 44.

NAME. M.D. (Female).

AGE. 18 years.

TYPE. Scarlatina Anginosa.

DAY OF ILLNESS ON ADMISSION. 4th day.

DAY OF SERUM TREATMENT. 4th day. (1st dose).
8th day. (2nd dose).

CLINICAL NOTES. Typical case of Septic Scarlet Fever with profuse nasal and post nasal discharges: double otorrhoea: ulceration of fauces: cervical adenitis. Cessation of all discharges by 18th day. Febrile course ended by long lysis on 18th day.

RASH. Bright generalised rash.

THROAT. Extreme degree of congestion and oedema of fauces.
Ulceration of tonsils and pillars of fauces.
Nasal and post nasal discharges very profuse.

TOXAEMIA. Not marked.

COMPLICATIONS On admission (1) Cervical adenitis (bilateral)
(2) Otorrhoea. (bilateral).
(3) Nasal and post nasal discharges.

RESULT. Excellent result to very severe case of the septic type. All discharge ceased by 18th day: allowed up 22nd day; dismissed 35th day of illness.

SERUM. S.F.Antitoxin (P.D.& Co.) 20ccs. in 2 doses.

DISEASE.

SCARLATINA ANGINOSA

Notes of Case.

Name WILLIAM BROWN.

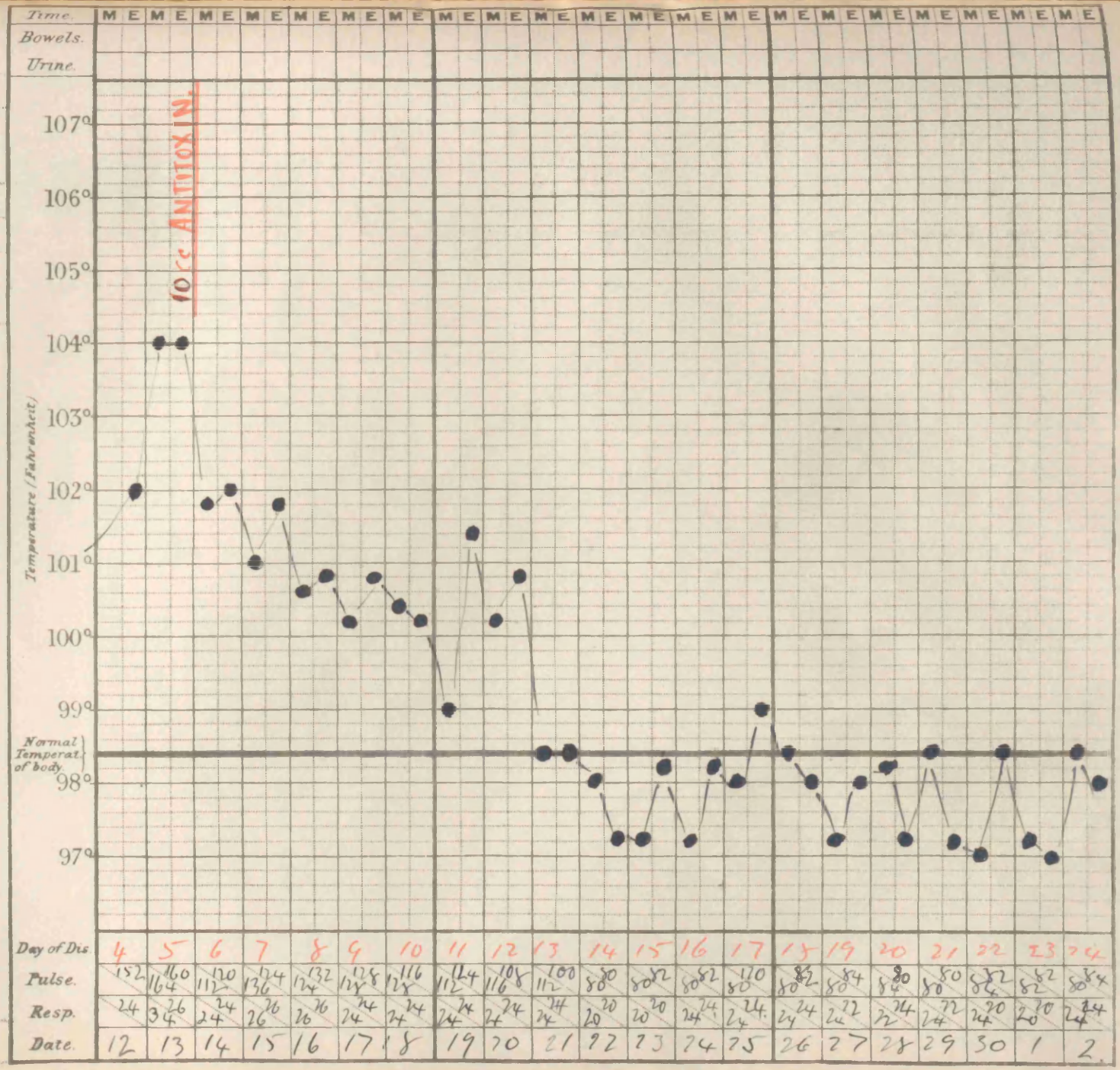
Age 4 YRS.

Diet

Case Book No. 90

Date of admission.
12TH. NOV. 1926.

Result WELL.



Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co. 1a Gate Street, Kingsway, W.C. 2.* *Goulds Clinical Chart.*

CASE No. 90.

NAME. W.B.

AGE. 7 years.

TYPE. Scarlatina Anginosa. ("Surgical Scarlet").

DAY OF ILLNESS ON ADMISSION. 4th day.

DAY OF SERUM TREATMENT. 5th day.

CLINICAL NOTES. Whitlow of finger: cellulitis of hand. Very ill on 5th day. T.104. P.160. R.28. Fall of temperature by lysis to 11th day. Pulse rate 120 per min. 12 hours after serum. Marked improvement in general condition.

RASH. Bright generalised punctate erythema.

THROAT. Congestion of fauces: tonsils swollen. Much improved after serum therapy.

TOXAEMIA. Marked delirium: absence of delirium 12 hours after serum.

SEPTICAEMIA. Irregular pyrexia (11 days): post nasal discharge: purulent discharge from whitlow.

COMPLICATIONS None.

RESULT. Good.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Anti-toxin.

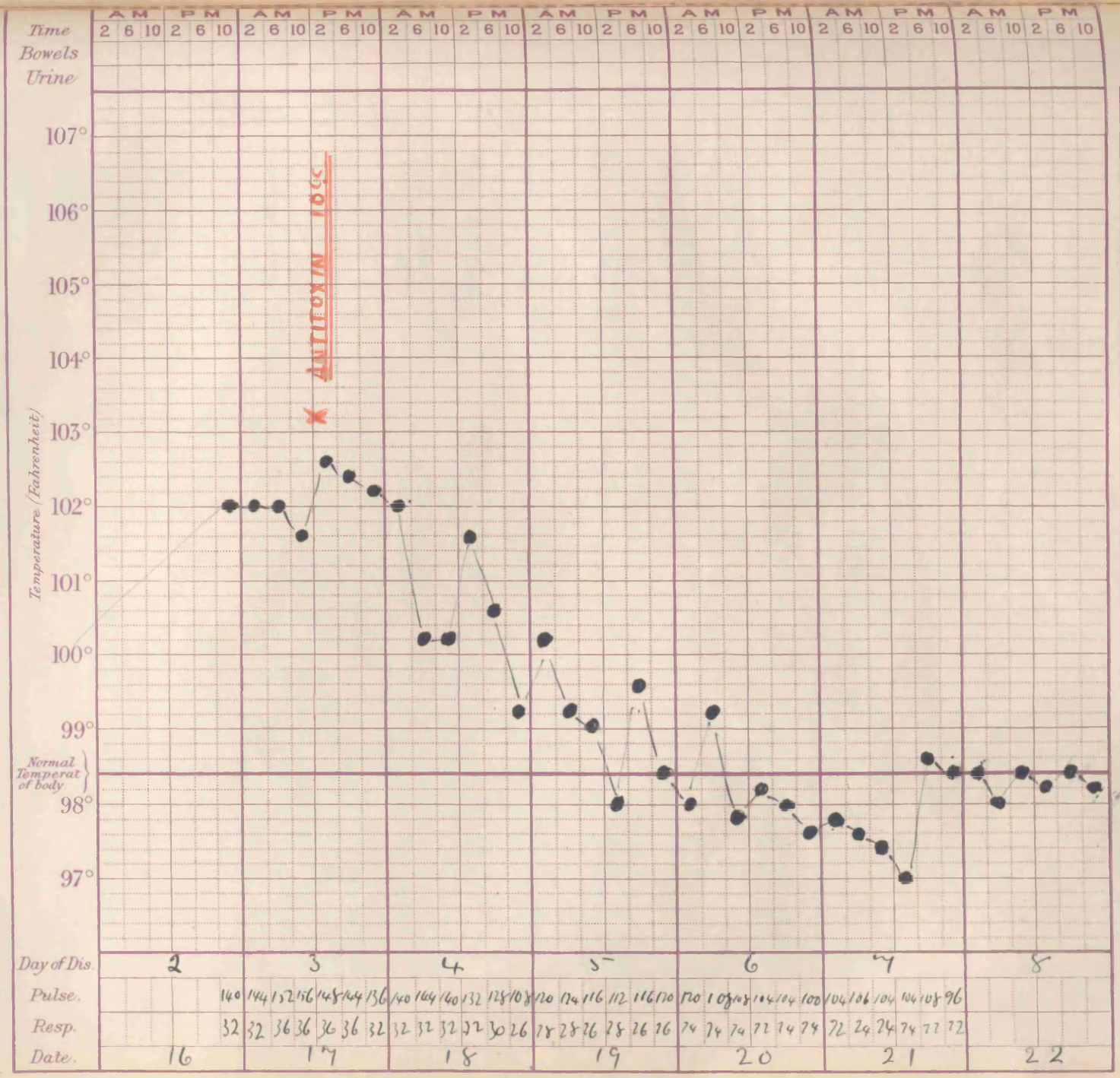
REMARKS. Marked beneficial effect in shortening acute manifestations.

4 HOUR CHART.

DISEASE.
SCARLATINA ANGINOSA.

Name THOMAS WILLIAMS.
Age 5 YRS.
Diet
Case Book Nº 57.

Notes of Case



Date of admission
OCT. 16. 1926.

Result WELL.

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CASE No. 57.

NAME. T.W. (Male).

AGE. 5 years.

TYPE. Scarlatina Anginosa.

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 3rd day.

CLINICAL NOTES. Acute Scarlet Fever developing septic type.
After 24 hours observation T.102 P.148. R.36
36 hours after serum - T. 99 P.108 R.26
Afebrile on 5th day of illness after lysis.
Marked improvement in general condition and especially of throat.

RASH. Bright generalised erythema.

THROAT. Marked faucial ulceration and oedema of uvula.
Angina of soft palate: cervical adenitis.
Purulent nasal and post nasal discharges.

TOXAEMIA. Not marked.

COMPLICATIONS. Adenitis.
Purulent Rhinitis.

RESULT. Good.

SERUM. 10ccs. (P.D.& Co.). Scarlet Fever Antitoxin.

REMARKS. Result encouraging for Septic Type.
Detention 8 weeks. Rhinitis due to Hypertrophy of Tonsils and Adenoids.
Removal satisfactory.

III. SCARLATINA SIMPLEX (Severe).

The largest group of cases treated by serum was that of the type Scarlatina Simplex. All these cases were acutely ill, and some, it must be noted, were under observation for varying periods, in view of the possibility of a spontaneous crisis and improvement early in the course of the disease.

4 HOUR CHART.

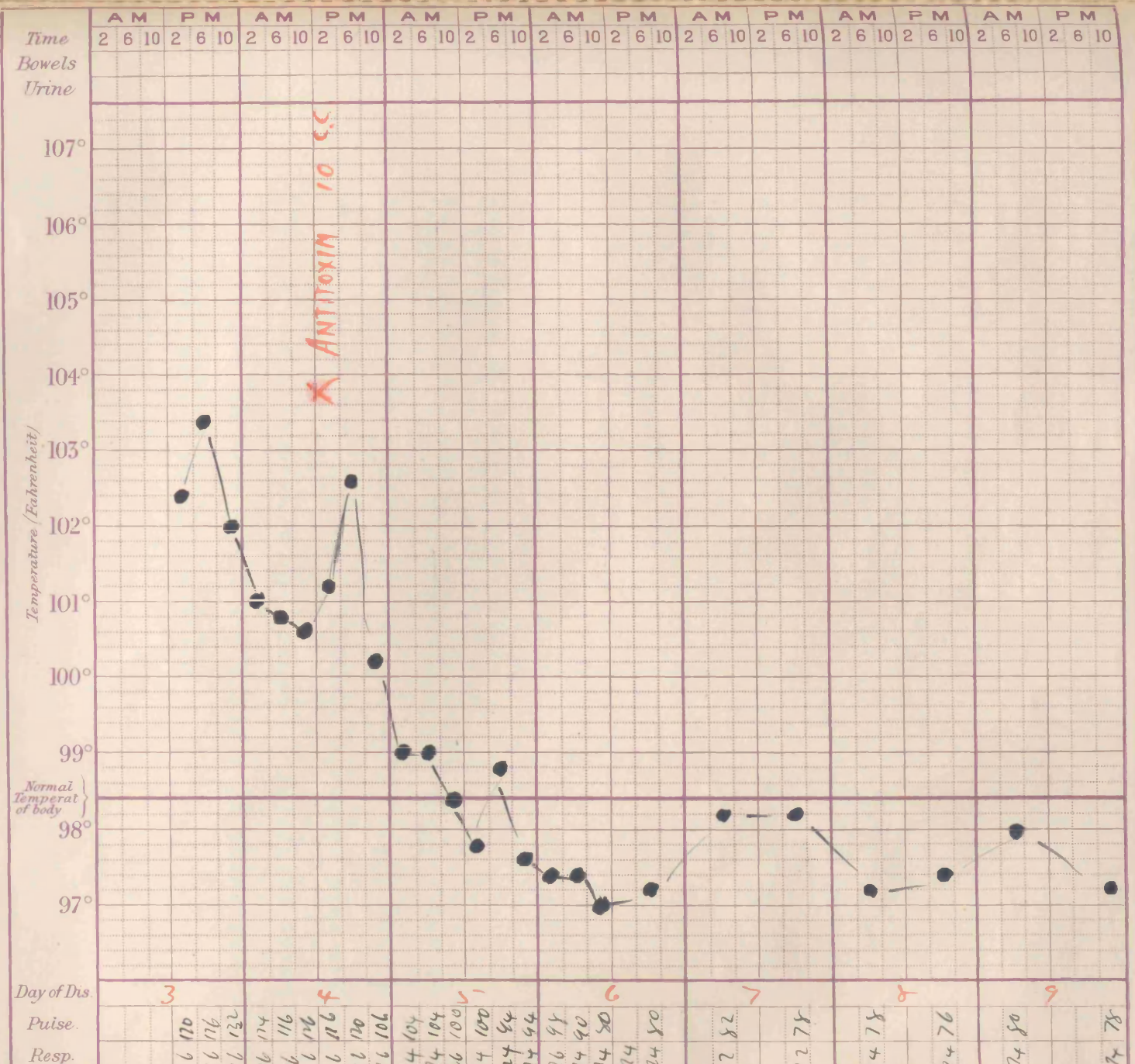
DISEASE.
SCARLATINA SIMPLEX.

Name JOHN McKENNA.
Age 9 YRS.
Diet
Case Book No. 10

Notes of Case

Date of admission
30TH JUNE 1926.

Result WELL.



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CASE No. 10.

NAME. J.McK. (Male).

AGE. 9 years.

TYPE. Scarlatina Simplex (Severe).

DAY OF ILLNESS ON ADMISSION. 3rd day.

DAY OF SERUM TREATMENT. 4th day.

CLINICAL NOTES. Acute attack of Scarlet Fever.
Before serum T.102 P.120 R.26
24 hours after serum T. 98 P.100. R.24.
Rhinorrhoea present on admission – ceased 48 hours later.

RASH. Intense rash. Petechiae marked on chest and flexures.

THROAT. Marked faucial congestion: oedema of uvula.

TOXAEMIA. Marked toxaemia. Severe headache: insomnia: restlessness: soft rapid pulse.

COMPLICATIONS None.

RESULT. Good.

SERUM. 10ccs. Scarlet Fever Antitoxin (P.D.& Co.).

REMARKS. Immediate reaction to serum.
Uninterrupted convalescence.

Note: Cessation of nasal discharge 48 hours after serum treatment.

4 HOUR CHART.

DISEASE.

SCARLATINA SIMPLEX.

Name { HELEN CARROL.

Age 14 YRS.

Diet

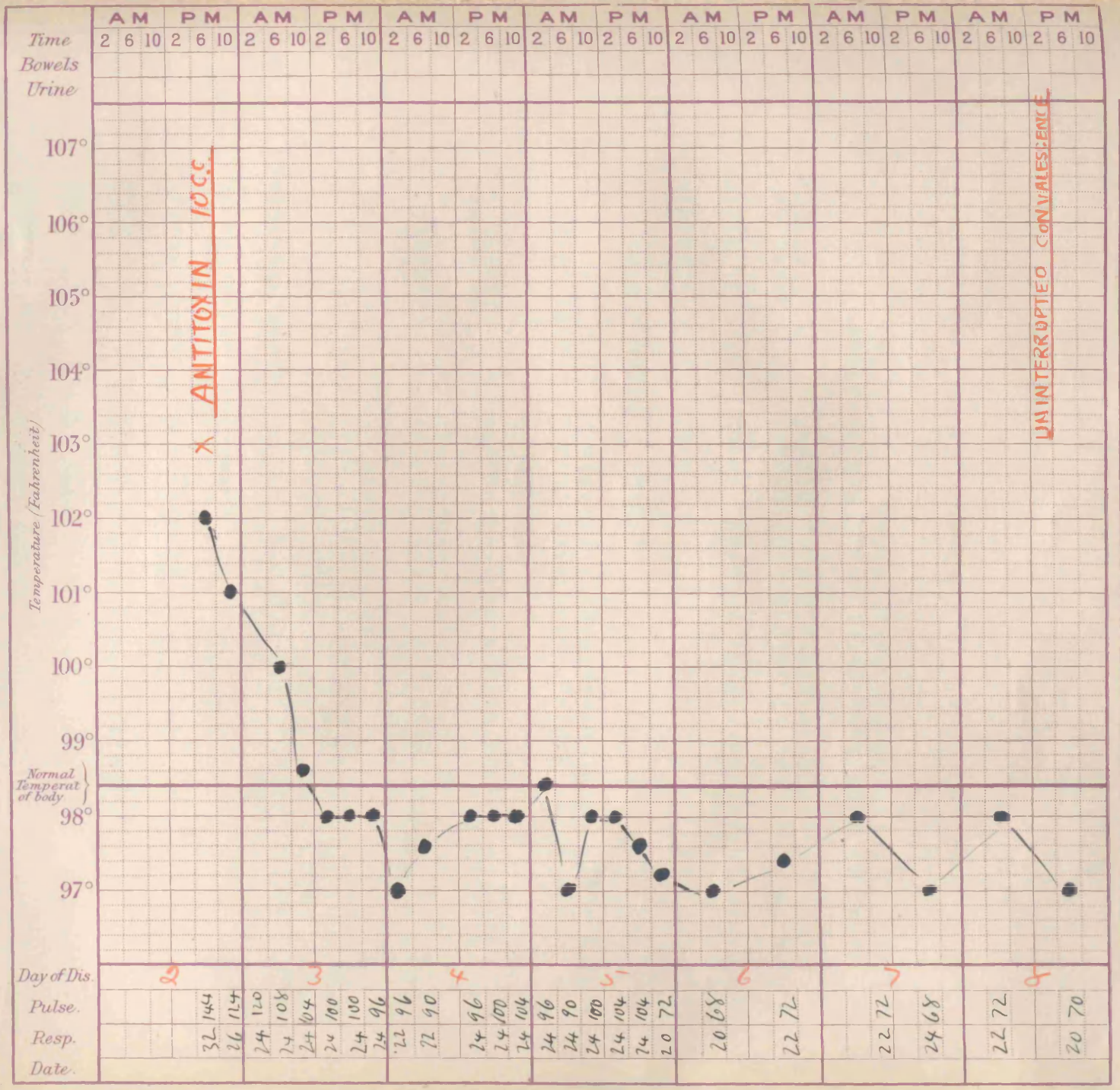
Case Book No. 32.

Notes of Case

Date of admission

13TH SEPT. 1926.

Result WELL.



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CASE No. 32.

NAME. H.C.(Female).

AGE. 14 years.

TYPE. Scarlatina Simplex (Severe).

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 2nd day.

CLINICAL NOTES. Acutely ill:
Before serum T.102 P.144. R.32.
24 hours after serum T.98 P.100. R.24.
Marked beneficial effect noted 24 hours after serum.
Uninterrupted convalescence.

RASH. Very bright generalised rash.

THROAT. Very painful. Congestion of fauces. Oedema of uvula: exudate on tonsils (swab negative.) Improvement noted 24 hours after serum.

TOXAEMIA. Well marked toxaemia: dry tongue. low tension pulse: severe headache.

COMPLICATIONS None.

RESULT. Very good.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Antitoxin.

REMARKS. Immediate reaction and beneficial response to serum.

4 HOUR CHART.

DISEASE.

SCARLATINA SIMPLEX.

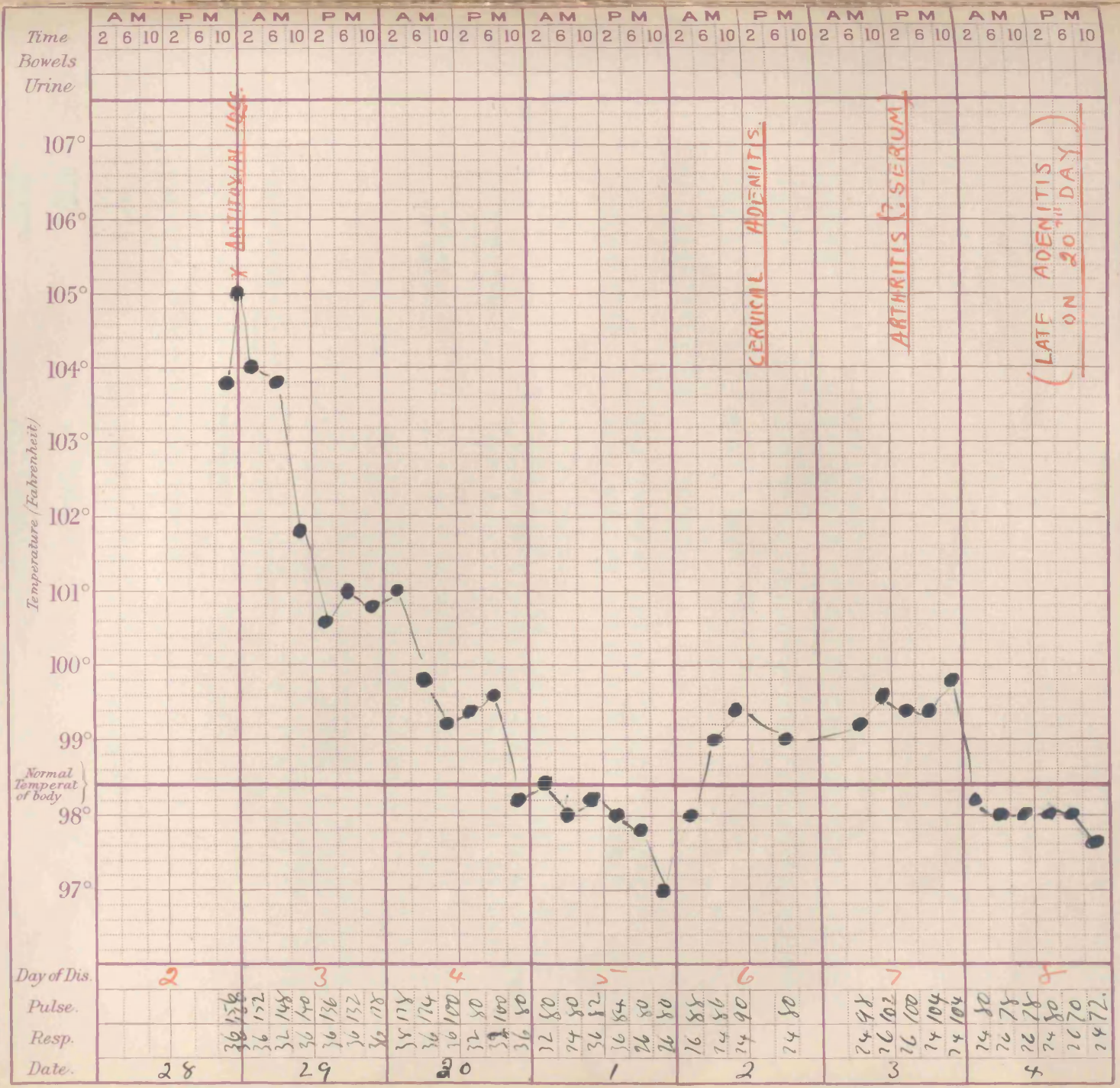
Name { AGNES DUFF.

Age 12 YRS.

Diet

Case Book No. 40.

Notes of Case



Date of admission 28TH SEPT. 1926

Result WELL.

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CASE No. 40.

NAME. A.D. (Female).

AGE. 12 years.

TYPE. Scarlatina Simplex (Severe).

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 2nd day.

CLINICAL NOTES. Acutely ill and toxic on admission.
Before serum T.105. P.160. R.36
48 hours after serum T. 98. P.88. R.26.
Marked improvement in general condition.
Rash faded: throat improved.

RASH. Moderately bright generalised rash.

THROAT. Intense congestion of fauces: oedema of uvula and soft palate: ulceration of tonsils. Improvement very marked 36 hours after serum.

TOXAEMIA. Marked by delirium: dry ulcerated tongue and sordes. Low tension rapid pulse.

COMPLICATIONS Serum arthritis (12 hours' duration).
Late cervical adenitis (24 hours' duration).

RESULT. Very dramatic result.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Anti-toxin.

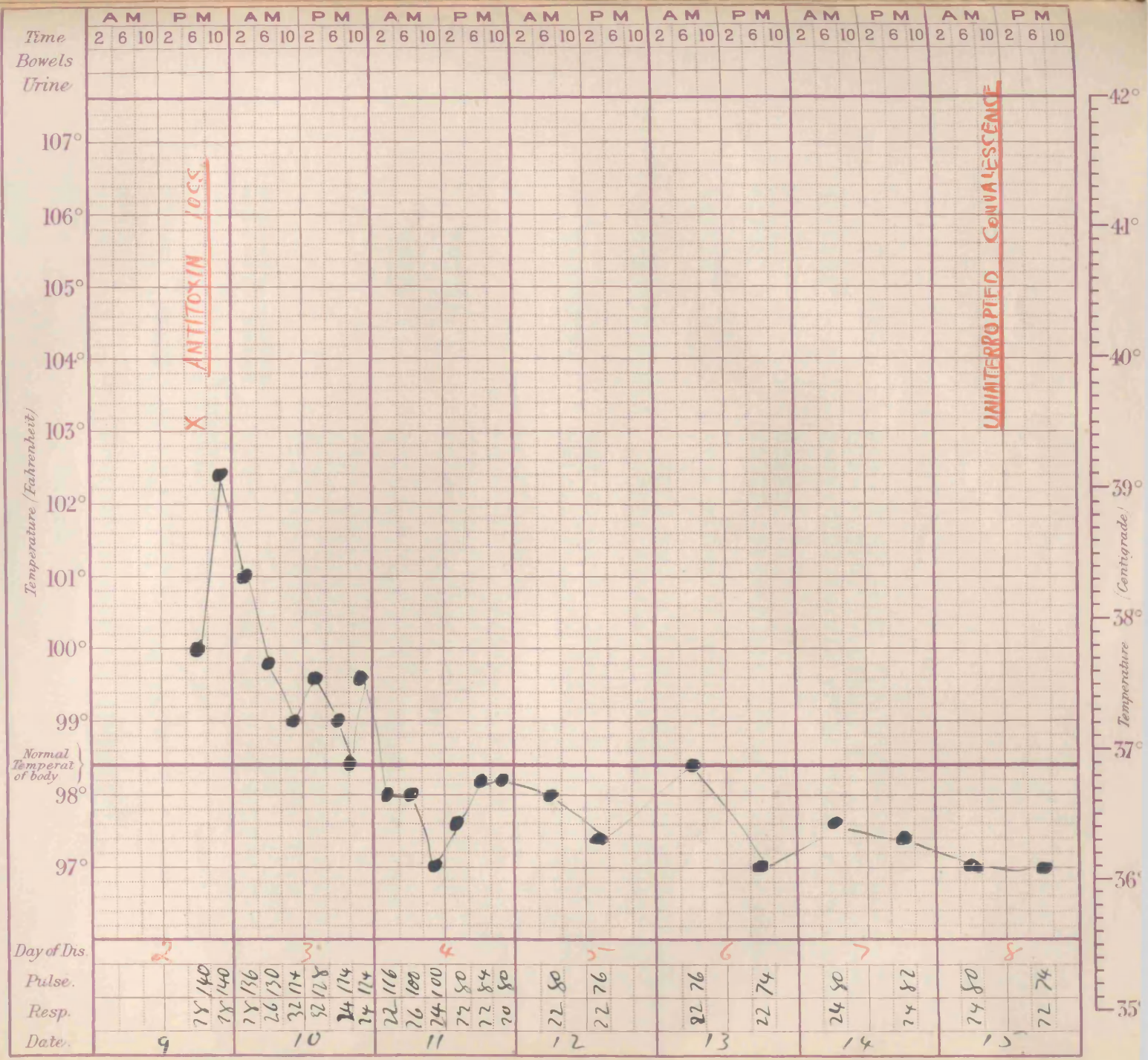
REMARKS. Immediate crisis in 36 hours after serum with marked improvement of throat condition, fading of rash, subsidence of toxaemia.

4 HOUR CHART.

DISEASE.
SCARLATINA
SIMPLEX.

Name { HUGH McDADE.
Age 11 YRS.
Diet
Case Book No° 47.

Notes of Case



Date of admission
9TH OCT. 1926.

Result WELL.

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CASE No. 47.

NAME. H.McD. (Male).

AGE. 11 years.

TYPE. Scarlatina Simplex (Severe).

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 2nd day.

CLINICAL NOTES. Acute case: very toxic on admission.
Before serum T.100. P.140. R.28.
24 hours after serum T. 98. P.124. R.24.
Marked improvement in general condition 24 hours later.
Uninterrupted convalescence.

RASH. Intense rash: petechial rash on chest and flexures.

THROAT. Congestion of fauces: oedema of uvula. Ulceration of tonsils.
Marked improvement 24 hours after serum.

TOXAEMIA. Marked by headache: dry furred tongue: sordes: low tension pulse.

COMPLICATIONS None.

RESULT. Very good.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Anti-toxin.

REMARKS. Immediate response to serum therapy.

4 HOUR CHART.

DISEASE.

SCARLATINA SIMPLEX.

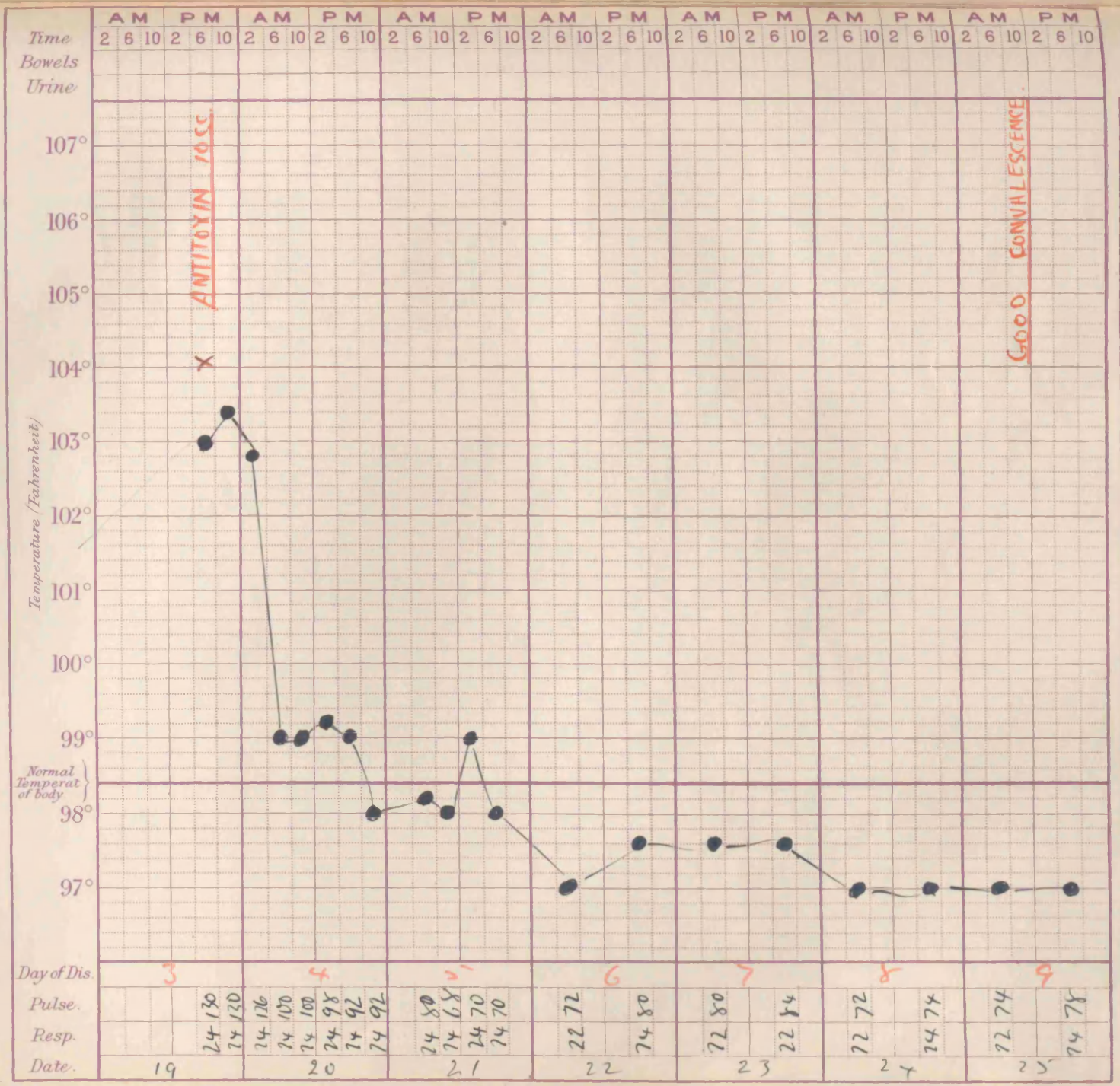
Name { WILLIAM, JACKSON.

Age 28 YRS.

Diet

Case Book No. 60.

Notes of Case



Date of admission 19th OCT. 1926.

Result WELL.

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CASE No. 60.

NAME. W.J.

AGE. 28 years.

TYPE. Scarlatina Simplex (Severe).

DAY OF ILLNESS ON ADMISSION. 3rd day.

DAY OF SERUM TREATMENT. 3rd day.

CLINICAL NOTES. Acute Scarlet Fever.
Before serum T.103 P.130 R.24
24 hours after serum T. 99 P. 92 R.22
Marked improvement after crisis.

RASH. Very bright. Faded rapidly (12 hours).

THROAT. Intense congestion of fauces: very painful: Oedema of uvula and soft palate: some ulceration of tonsils. Condition improved soon after serum therapy.

TOXAEMIA. Very marked. Dry tongue and lips. Sordes. Low tension rapid pulse. Restlessness.

COMPLICATIONS. Transient Arthritis (serum?).

RESULT. Very good.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Anti-toxin.

REMARKS. (Case No.66 W.J. a son of this patient No.60)
Serum administered to son on 5th day, result not so good.
Serum administered to father on 3rd day, result very good.

DISEASE.
SCARLATINA SIMPLEX.

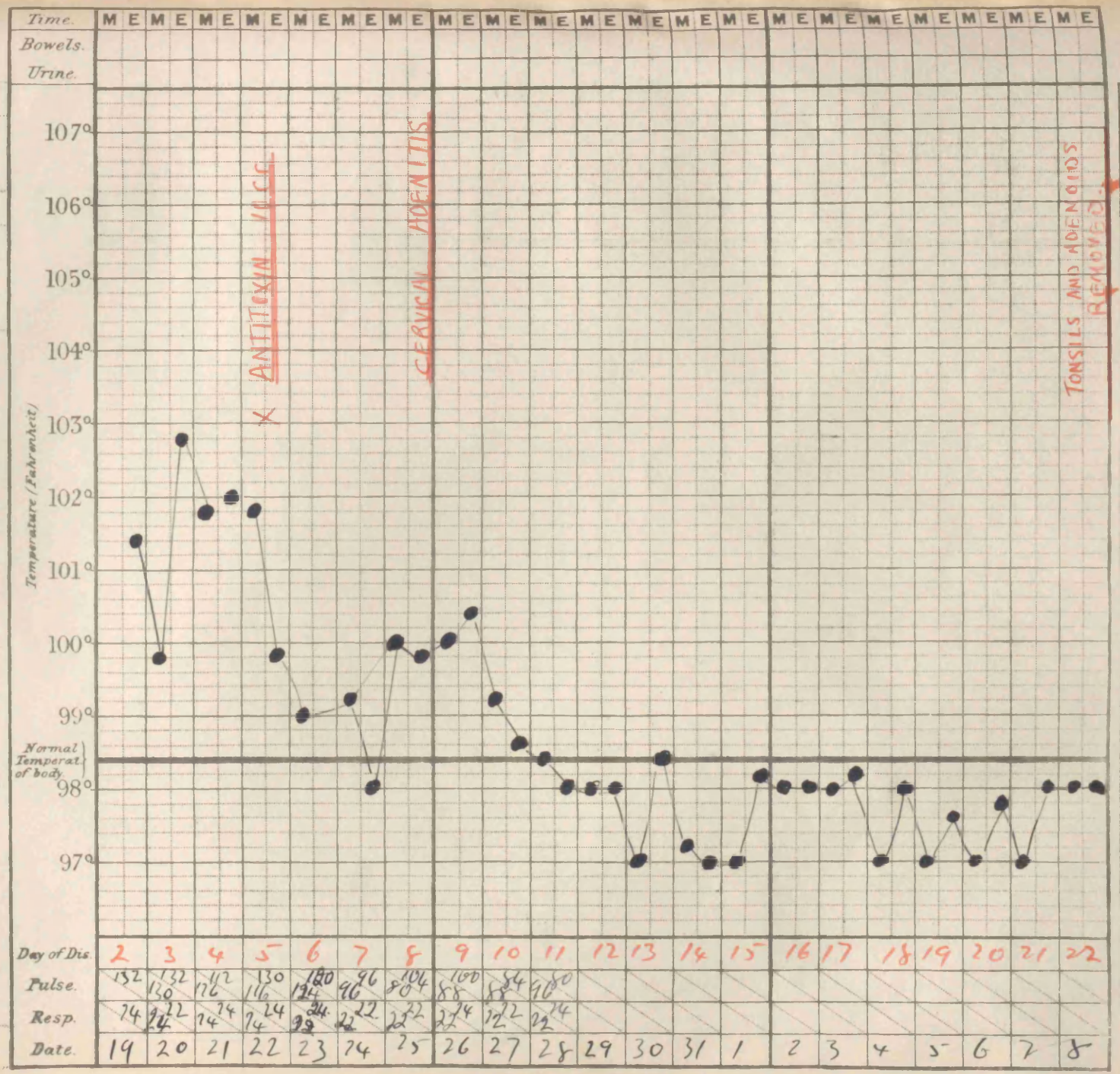
Notes of Case.

Name WILLIAM, JACKSON.

Age 9 YRS.

Diet

Case Book No. 66



Date of admission.
19TH OCT. 1926

Result WELL.

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CASE No. 66.

NAME. W.J. (Male).

AGE. 9 years.

TYPE. Scarlatina Simplex (Severe).

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 5th day.

CLINICAL NOTES. Case of Scarlet Fever under observation: moderately ill: patient on 5th day still ill: rash still bright: throat still painful.
Before serum T.100 P.130 R.24
24 hours after serum T. 99 P.120 R.22
Complete defervescence not until 11th day.

RASH. Bright until 6th day.

THROAT. Congestion of fauces: swollen tonsils. No improvement until after serum on 5th day.

TOXAEMIA. Marked by low tension pulse: varying headache. Tongue dry and furred: dry and peeled on 4th day.

COMPLICATIONS. Adenitis 8th day.
Hypertrophied tonsils. Tonsillitis 4th week.
Tonsils and adenoids removed.

RESULT. Interesting compared to Case No.60.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Antitoxin on 5th day.

REMARKS. This case indicates the necessity for early administration of serum.

IV. SCARLATINA SIMPLEX (ADYNAMIC).

The cases of the Adynamic type all responded immediately to the serum. Some examples are recorded.

4 HOUR CHART.

DISEASE.

SCARLATINA SIMPLEX. (ADYNAMIC)

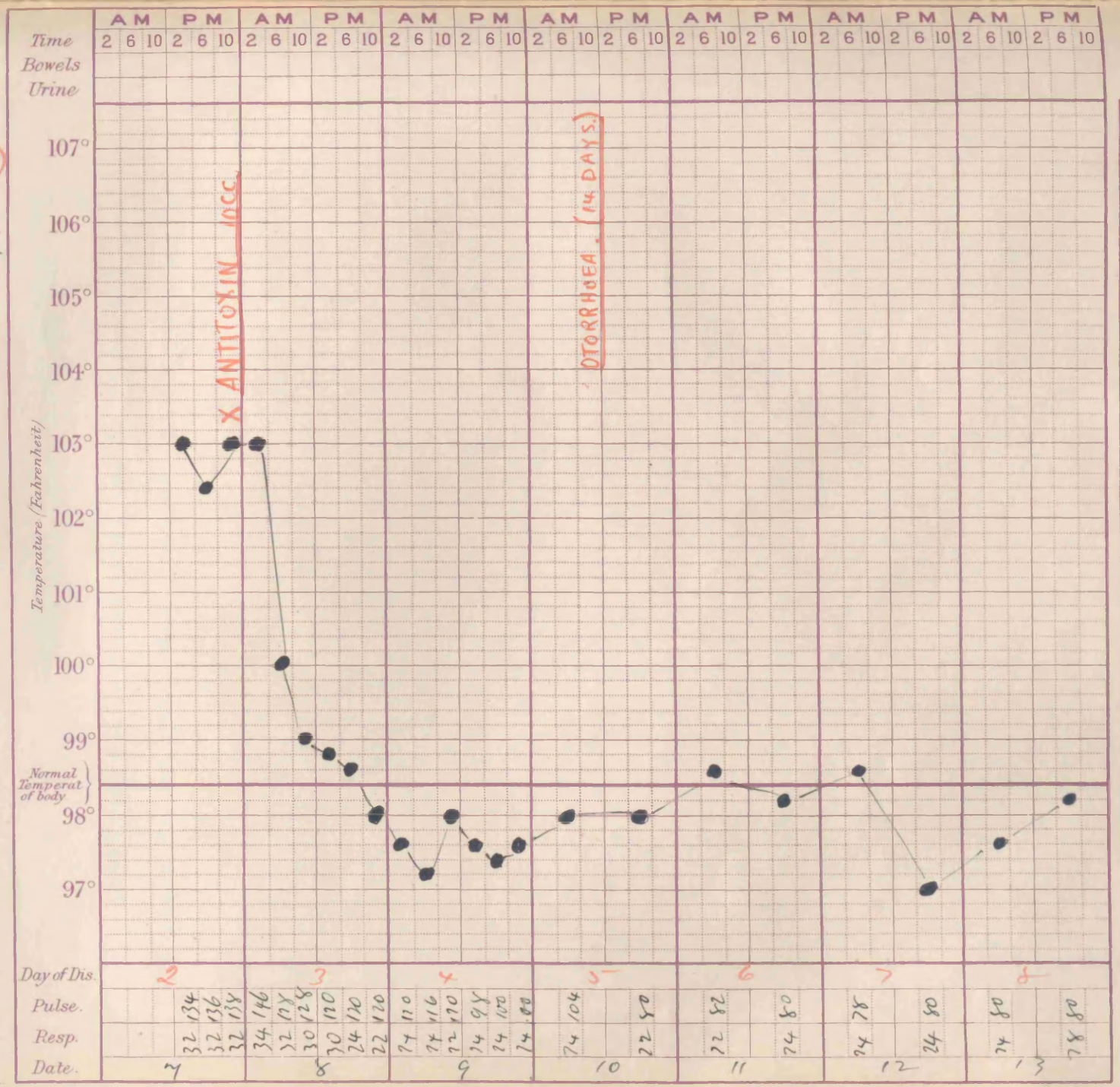
Name { THOMAS HENDRY.

Age 6 YRS.

Diet

Case Book No. 11.

Notes of Case



Date of admission

7TH JULY, 1926.

Result WELL.

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CASE No. 11.

NAME. T.H. (Male).

AGE. 6 years.

TYPE. Scarlatina Simplex (Adynamic Form).

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 2nd day.

CLINICAL NOTES. Acute attack marked by weakness: apathy: cyanosis: shallow respirations: very low tension pulse. cardiac sounds muffled.

Before serum	T.103	P.138	R.32
24 hours after serum	T. 98	P.120	R.22

RASH. Dusky punctate erythema with petechiae marked in the areas around the joints (knees, elbows and ankles).

THROAT. Moderate faucial congestion.

TOXAEMIA. Marked by weakness, sordes, circulatory disturbance.

COMPLICATIONS. Otorrhoea lasting 14 days.

RESULT. Good.

SERUM. 10ccs. Scarlet Fever Antitoxin (P.D.& Co).

REMARKS. Immediate reaction 12 hours after administering serum.

4 HOUR CHART.

DISEASE.

SCARLATINA SIMPLEX. (ADYNAMIC)

Name { RICHARD CHISHOLM.

Age 4 YRS.

Diet

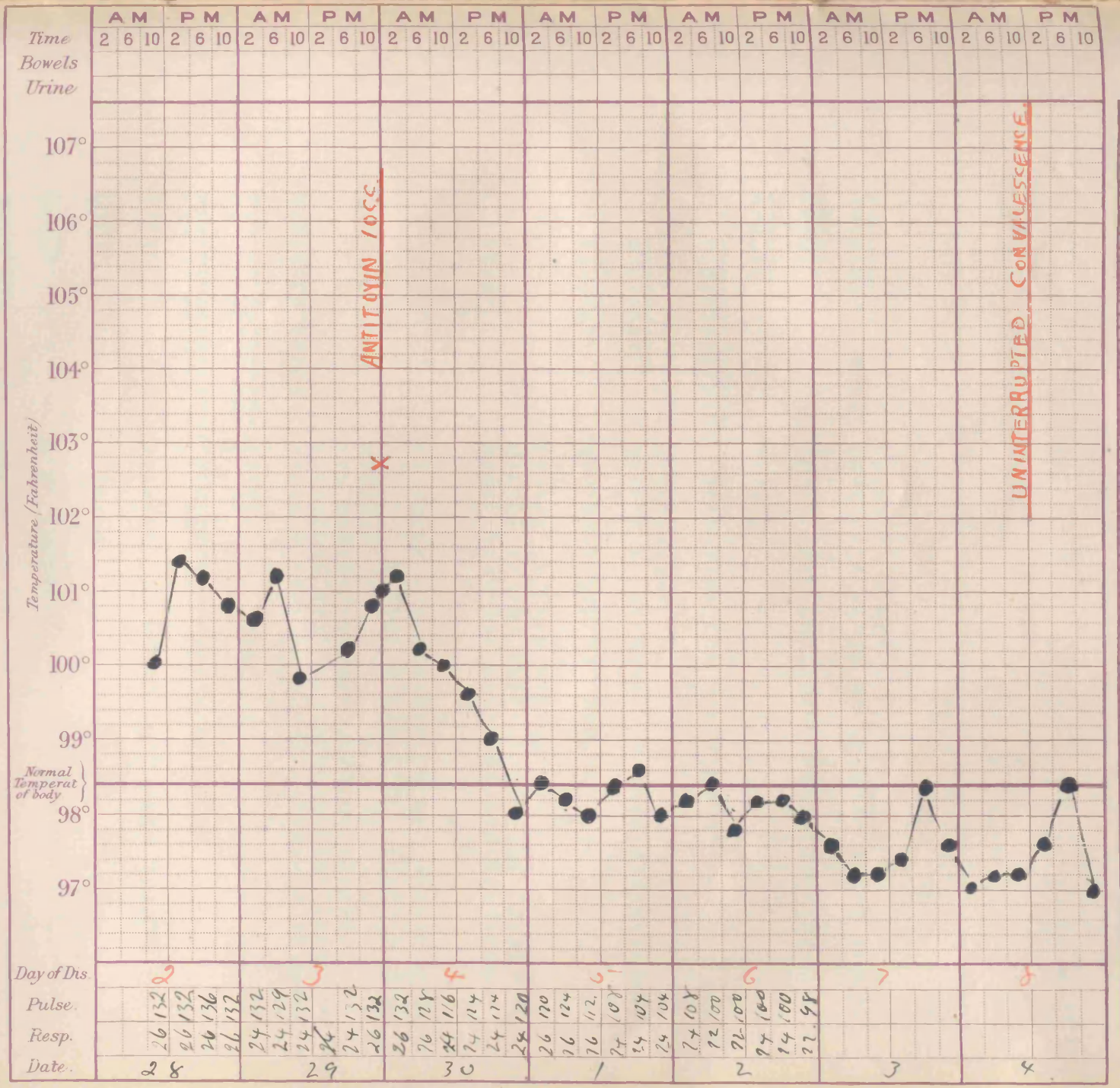
Case Book No. 14.

Notes of Case

Date of admission

28TH. JUNE 1926.

Result WELL.



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CASE No. 14.

NAME. R.C. (Male)

AGE. 4 years.

TYPE. Scarlatina Simplex (Adynamic Form).

DAY OF ILLNESS ON ADMISSION. 2nd day.

DAY OF SERUM TREATMENT. 3rd day.

CLINICAL NOTES. Acute attack marked by weakness: cyanosis: shallow respirations: very soft pulse. Dry coated tongue: sordes. Cardiac sounds soft.

Before serum	T.101	P.132	R.26
24 hours after serum	T. 98	P.120	R.24

RASH. Intense dusky erythema. (generalised).

THROAT. Faucial congestion: painful.

TOXAEMIA. Marked by circulatory disturbance chiefly.

COMPLICATIONS. None.

RESULT. Good.

SERUM. 10ccs. Scarlet Fever Antitoxin. (P.D.& Co).

REMARKS. Clinically a case of Adynamic Scarlet Fever which responded immediately to serum. Marked improvement within 12 hours.

4 HOUR CHART.

DISEASE.

SCARLATINA SIMPLEX. (ADYNAMIC.)

Name { ROSE PORTER.

Age 7 YRS.

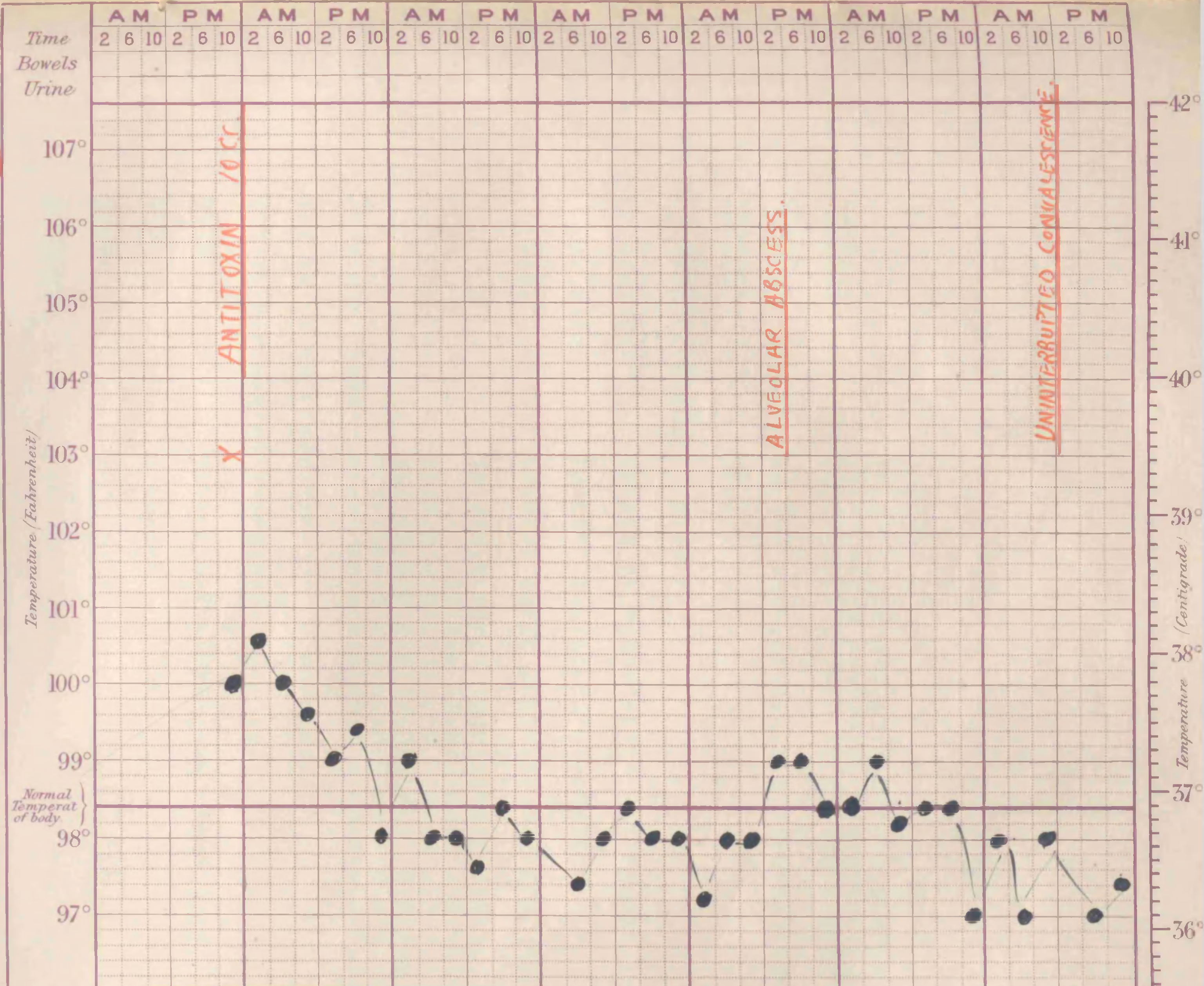
Diet

Case Book No. 38.

Notes of Case

Date of admission 26TH SEPT. 1926.

Result WELL.



Date	Day of Dis.	Time	Resp.	Pulse.
26 Sept.	3	PM 10	24	124
27	4	AM 2	26	130
		AM 6	26	130
		AM 10	24	126
		PM 2	22	124
		PM 6	24	124
		PM 10	24	120
28	5	AM 2	26	122
		AM 6	24	112
		AM 10	24	114
		PM 2	22	112
		PM 6	26	100
		PM 10	22	94
29	6	AM 2	24	90
		AM 6	22	98
		AM 10	24	96
		PM 2	24	98
		PM 6	22	98
		PM 10	20	94
30	7	AM 2	20	94
		AM 6	20	98
		AM 10	22	100
		PM 2	22	112
		PM 6	20	114
		PM 10	22	100
1 Oct.	8	AM 2	24	90
		AM 6	22	92
		AM 10	22	84
		PM 2	24	80
		PM 6	22	80
		PM 10	20	78
2	9	AM 2	22	80
		AM 6	24	78
		AM 10	20	80
		PM 2	20	80
		PM 6	20	74
		PM 10	22	80

CASE No. 38.

NAME. R.P.

AGE. 7 years.

TYPE. Scarlatina Simplex (Adynamic).

DAY OF ILLNESS ON ADMISSION. 3rd day.

DAY OF SERUM TREATMENT. 3rd day.

CLINICAL NOTES. Acutely ill: weakness and apathy marked. Pulse very soft and rapid. Heart sounds soft-gallop rythm. Cyanotic tinge present on ears and lips. Dry tongue: sordes.

Before serum T.100 P.124 R.24
24 hours after serum T. 98 P.120 R.24.

RASH. Intense dusky rash: petechiae marked in flexures and axillae.

THROAT. Fauces congested: ulceration of tonsils.

TOXAEMIA. Well marked by listlessness: dry tongue, sordes and soft rapid pulse.

COMPLICATIONS. None. Uninterrupted convalescence.

RESULT. Very good: marked improvement in cardio-vascular system within 24 hours of serum.

SERUM. 10ccs. (P.D.& Co.) Scarlet Fever Anti-toxin.

REMARKS. Excellent result in a case of Adynamic Scarlet Fever.

Summary of Results.

The following tables VIII - XII have been prepared to illustrate the number of cases of Scarlatina treated before and after the fourth day of illness, together with the percentages of cases exhibiting excellent recovery and complications in each group.

Out of a total of 120 cases of Scarlatina which were treated by serum therapy, 70% received treatment prior to the fourth day of illness. In this early group 66% made an excellent recovery, while 34% exhibited some or other well recognised complication of Scarlatina.

The number of cases treated by serum after the fourth day of illness was 37, and in this group only 48% made an excellent recovery without complications, thus indicating the advisability of early administration of serum.

TABLE VIII.

CASES TREATED BY SERUM THERAPY.	
Cases treated before 4th day of illness	83
Cases treated after 4th day of illness	37
Cases treated. TOTAL	120

TABLE IX.

RESULTS OF SERUM THERAPY BEFORE 4th DAY of ILLNESS.		
Cases treated (70% of whole).		83
Cases with excellent recovery	(66%)	55
Cases with complications	(34%)	28

TABLE X.

CASES TREATED BEFORE 4th Day.

COMPLICATIONS.	NUMBER OF CASES.
Adenitis .	9
Adenitis + Serum Rash.	4
Adenitis + Serum Rash + Rhinitis + Otitis.	1
Adenitis + Arthritis.	1
Adenitis + Rhinitis.	1
Adenitis + Otitis Media.	1
Arthritis (Serum?)	2
Rhinitis (Transient)	3
Nephritis.	1
Otitis Media.	4
Endocarditis.	1
Total Number of Cases	28
(Serum Rash 11.7%	14).

TABLE XI.

RESULTS OF SERUM THERAPY AFTER 4th DAY OF ILLNESS.	
Cases treated.	37
Cases with excellent recovery. (48%)	18
Cases with complications.	19

TABLE XII.

Cases treated after 4th Day.	
COMPLICATIONS.	Number of Cases.
Adenitis.	3
Adenitis + Otitis.	2
Adenitis + Arthritis.	1
Arthritis.	3
Albuminuria.	1
Enteritis + Broncho Pneumonia. + Endocarditis	1
Otitis Media.	2
Otitis Media + Rhinitis.	1
Otitis * Rhinitis + Conjunctivitis.	1
Rhinitis.	1
Endocarditis + Serum Rash.	1
Sub-Conjunctival Haemorrhage.	1
Tonsillitis.	1
Total Number of Cases.	19.
(Serum Rash 8.1%	3).

OTHER FEATURES OF THE INVESTIGATION.

(1) Effect on Ward Routine.

The extraordinary abatement of the acute manifestations of Scarlet Fever which followed the crisis precipitated by the antitoxin naturally reduced the actual nursing of the cases of Scarlatina considerably. In fact, the appearance of a scarlet fever ward has completely changed since the routine adoption of serum therapy, as the majority of patients are comfortable convalescents within a day or two of admission, exceptions of course being cases of Scarlatina Anginosa. Even these cases, however, respond in varying degrees to serum therapy.

(2) Cost of Treatment.

The estimation of the cost of any new line of treatment should always be borne in mind, together with the value of the effects obtained.

Serum therapy is undoubtedly costly, but apart altogether from repayment in the saving of human life, particularly in cases of Scarlatina Maligna, the actual cost of serum therapy per patient so treated is amply repaid by the saving which is produced by the beneficial effects of the serum treatment.

The/

The cutting short of the acute illness and the lessening of the detention period has definitely effected an economy of the time of the nursing staff and of the cost of hospitalisation of the patients.

(3) Diagnostic Value of Scarlet Fever Antitoxin.

During the epidemic of 1926 the use of the Schultz Charlton or blanching test on the scarlet fever rash was made in many cases. (12).

A series of 50 cases with bright rashes all under 48 hours duration were subjected to intradermal injections of scarlet fever antitoxin into the abdominal wall. The injections were made in 4 places and were of 4 strengths of serum, viz:

(1) undiluted, (2) $\frac{1}{10}$. (3) $\frac{1}{100}$. (4) $\frac{1}{1000}$.

Both types of Commercial Serum, i.e. Parke, Davis & Co., and Burroughs, Wellcome & Co. were used, and each injection consisted of 0.2cc of the serum diluted or otherwise.

The results were uniformly impressive.

Within from 4 hours to 38 hours there appeared the blanched area of about 2 centimeters in diameter around the site of the injection.

The undiluted serum resulted in the most definite extinction phenomenon, while the results of the first two dilutions were difficult to differentiate.

The/

The blanching reactions of $\frac{1}{1000}$ dilutions of serum were quite definitely less distinct than the first two dilutions.

The Schultz Charlton reaction was tried also in seven patients exhibiting enema rashes. In all cases the reaction was negative.

In two cases of chickenpox, prodromal scarlatinform eruptions were tested and proved negative.

Eleven cases of measles were also tested by the Schultz Charlton method and the blanching reaction failed in all cases.

(4) Prophylactic Value of Scarlet Fever Antitoxin.

During the years 1926-1930 the value of the Dick (13) test and the prophylactic use of scarlet fever antitoxin has been proved on 6 different occasions when scarlet fever has appeared in a ward of diphtheria patients.

The routine procedure consisted in performing the Dick test on all contacts and in administering an intramuscular injection of 2.5cc of Scarlet Fever Antitoxin to all Dick positive contacts.

This procedure has proved effective on these 6 occasions but it must be remembered that the scarlet fever patient was on each occasion immediately isolated so that too much reliance may not be placed on the efficacy

of/

of the serum. Nevertheless there are many instances on record of ward epidemics of scaflet fever on other occasions when the serum was withheld.

The value of this serum used by the method of Schultz and Charlton appears of great value from a diagnostic point of view, and particularly so in conjunction with the Dick test which indicates the individual susceptibility to the toxin of scarlet fever by a skin reaction similar to the Schick test.

CONCLUSIONS.

A careful study from the clinical point of view of Scarlatina in epidemic form in 1926 was made. During the period the use of specific serum was introduced for the first time in Ruchill Fever Hospital.

The results appear to justify the following opinion:

(1) Marked beneficial effects follow the use of Scarlet Fever Streptococcus Antitoxin when used as a therapeutic measure, in Scarlatina.

In this connexion it is important to note that these observations show (see Tables 8–12) that the earlier the serum was administered in the course of the disease the more marked were the beneficial results.

(2) Specific serum in Scarlatina while not preventing complications tends to make them more amenable to treatment when already present and to make them transient in nature and of diminished severity, should they arise, thus lessening the period of detention in hospital.

(3) Specific serum is a valuable addition to the armamentarium of medical science not only from the point of view of therapy but also of hospital administration.

(4) The maximum benefit is obtained in the treatment by specific serum of cases of Scarlatina Maligna where benefit cannot be overestimated.

(5)/

(5) The serum should be used as a routine therapeutic measure in all cases of Scarlatina Simplex other than very mild cases.

(6) The value of serum is doubtful in Scarlatina Anginosa except combined with treatment by Polyvalent Anti-streptococcic Serum.

(7) Scarlet Fever Antitoxin has a considerable diagnostic and Prophylactic value.

ERYSIPELAS.

INTRODUCTORY.

In consequence of the work of the Dicks on Scarlet Fever and of the production of an antitoxin which has, in the hands of clinical investigators, proved of marked benefit as a therapeutic measure, it only appears reasonable for investigators to renew their interest and efforts in connection with other streptococcal diseases.

A study of the literature reveals the name of Fehleisen (1) as probably one of the earliest workers in the etiological investigation of erysipelas: this was in 1883.

More recently Ruediger (2), Schorer (3), Tunnicliff (4), and Boughton (5) have contributed to this same work and their results seem to justify the opinion that cultures isolated from Cellulitis, Erysipelas, Septicaemia and Scarlatina differ antigenically and that by means of agglutination and absorption tests 91% of haemolytic streptococci from erysipelas cases could be differentiated into one typical group.

In 1895 Charrin & Rogers (6) produced an antistreptococcic serum for treatment in erysipelas and Marmorek (7) Aronson (8) and Moser (9) also reported favourably. The results of treatment have however been very variable.

In February 1924 Rivers (10) produced with a haemolytic/

lytic streptococcus isolated from a case of erysipelas a skin infection in rabbits and described also a method for demonstrating the protective properties of immune sera against this streptococcus.

In August 1924 Birkhaug (11) was able to demonstrate by intradermal protection tests in the rabbit the antigenic relationship of strains of streptococcus Erysipelatis.

Birkhaug in February of 1926, as a result of further experimental work was able to produce a soluble toxin from the streptococcus erysipelatis and established the fact that with this toxin a skin test may be of use to indicate susceptible individuals.

This Birkhaug test is thus similar to the Schick and Dick reactions.

Finally he demonstrated that this soluble toxin stimulated the production in animals of an antitoxin which neutralised the toxin.

This antitoxin (streptococcus erysipelatis) is claimed to be as specific in Erysipelas as the Strepto-coccus Scarlatina Antitoxin is in Scarlet Fever.

THE CLINICAL INVESTIGATIONS.

The clinical study was carried out in Ruchill Fever Hospital between March 1926 and March 1930, during which time an attempt was made to ascertain the value of serum therapy. A few cases which exhibited mild lesions without toxaemia were noted during the investigations but all cases dealt with by serum therapy were acutely ill with pyrexia ranging from 100°F. to 106^{2}F: the lesions were all well marked and the toxaemia was manifested by headache, often by delirium, furred tongue and sordes and a pulse of variable quality but seldom increased in rate in proportion to the elevation of temperature.

The patients were of both sexes and of all ages but young children were not included in the groups dealt with by serum therapy.

These cases were essentially of the lowest grade of hospital patient and many were unemployed and ill nourished. It is interesting to note that three patients of the middle class of society all responded in quick and rather dramatic fashion to serum therapy. These three patients were (1) a nurse, (2) a medical student, (3) a commercial traveller.

CLASSIFICATION OF CASES.

The cases resolved themselves into the following groups -

(1) Idiopathic Erysipelas (Primary).
(2) Idiopathic Erysipelas (Recurrent).
(3) Traumatic Erysipelas.
(4) Post Operative Erysipelas.
(5) Complicated Erysipelas.
i.e. cases in which erysipelas was essentialy an intercurrent infection in a patient already suffering from some disease.

TOPICAL THERAPY.

A preliminary study of topical therapy including many of the well known and well recommended lotions and ointments was made but it was very soon evident that these variations of local treatment were of no therapeutic value in a disease which was associated with some or other degree of toxaemia.

It was then decided to assume that if the disease was associated with a streptococcal toxaemia some benefit might be obtained by serum therapy.

SERUM.

During the investigations five types of serum were used.

(1) Polyvalent Antistreptococcic Serum.
(2) Scarlet Fever Streptococcus Antitoxin (P.D. & Co.)
(3)/

(3) Scarlet Fever Streptococcus Antitoxin (B.W. & Co.)
(4) Erysipelas Streptococcus Antitoxin. (P.D. & Co.)
(5) Anti-diphtheritic Serum. (B.W.& Co.)

N.B. (1) These sera are all concentrated and refined.
(2) As the day of illness appeared doubtful according to the history (many patients being delirious on admission to hospital) serum therapy was carried out as early as possible.

DOSAGE.

Variation in dosage was tried with a view to finding an adequate dose.

METHODS.

The administration of the serum was

(1) Intradermal along the spreading margin of the lesion.
(2) Intramuscular, into the lateral aspect of the thigh.
(3) Intravenous, into the median basilic vein.

GENERAL TREATMENT.

In addition to any serum therapy all patients were treated on the general lines of an infectious fever. Topical therapy was confined to the application to the lesion of one of the following sedative ointments both of which were found of equal value.

(1) Oil of Cloves - 1 part.
Oil of Eucalyptus - 5 parts.
Vaseline to 100 parts.

(2) Carbolic Acid - 2 parts.
Menthol - 3 parts.
Camphor - 3 parts.
Lanolin)equal parts
Vaseline)to 100.

TECHNICAL METHODS
AND
RESULTS OF CLINICAL INVESTIGATIONS.

(1) INTRADERMAL METHOD.

Attempts to prevent the spread of the lesion of erysipelas were made in several cases where a suitable actively spreading lesion was present.

The method adopted was that of intradermal injection of different types of sera (a) in different patients, (b) in the same patient. In all cases part of the spreading margin was left untreated as control.

The results in 10 cases were all the same - unsatisfactory. The spreading lesions continued to wander ignoring all barricades of defence.

Although the number of cases is relatively small, the treatment appeared too painful to warrant any further number of patients being subjected to this line of investigation.

(2) INTRAMUSCULAR SERUM THERAPY.

A number of cases were treated by intramuscular injection of serum into the lateral aspect of the thigh with variation of -

(1) Type of Serum.
(2) Dosage of Serum.

The/

The Sera used were -

(1) Polyvalent Antistreptococcic.
(2) Anti-diphtheritic Serum.
(3) Erysipelas Antitoxin.
(4) Scarlet Fever Antitoxin. (P.D. & Co.)
(5) " " " (B.W. & Co.)

(1) The use of polyvalent antistreptococcic serum was employed in twelve cases of erysipelas - 7 facial, 5 corporal.

In only one case was any apparent benefit derived from the treatment.

(2) Three cases of facial erysipelas with severe facial congestion were treated by Anti-diphtheritic Serum. No benefit except in the throat was observed: the erysipelas running courses varied from 10 - 15 days before spontaneous cure.

(3) Five cases of Erysipelas of the face were treated by Erysipelas Antitoxin, the dose in each instance being 20 ccs. of serum.

The results were most disappointing. The fever was maintained from 9 to 22 days and the serum did not shorten the time of toxaemia or have any apparent effect on the lesion.

(4) The treatment of erysipelas by intramuscular injection of Scarlet Fever Antitoxin (P.D. & Co.) was studied in ten cases. The doses of serum were 10 c.c (one case): 15 c.c/

15 c.c (one case): 20 c.c. (two cases) and 30 c.c. (six cases).

Three patients died, while only one case appeared to derive immediate benefit.

(5) A more extensive study was made of the use of the other type of Scarlet Fever Antitoxin, that of (B.W.& Co.) as the results were distinctly promising from the outset.

In all 41 patients were treated by intramuscular injection of Scarlet Fever Antitoxin (B.W. & Co.) There were 8 patients who received 20 c.c. of serum while 33 patients received 30 c.c. of serum.

All cases responded by a critical fall of temperature with subsidence of toxaemia within 36 hours and although in 30% of cases the lesion was found to spread after the treatment its intensity was very definitely lessened.

The lessening of the toxaemia was not marked quite so soon in those patients receiving the smaller dose of serum.

INTRAVENOUS SERUM THERAPY.

An extensive study was made of the use and value of serum given by the intravenous route in cases of severe erysipelas of the face (90 cases) and body (7 cases).

The following varieties of serum were used -

(1) Polyvalent Antistreptococcic Serum.
(2) Erysipelas Antitoxin.
(3) Scarlet Fever Antitoxin (P. D. & Co.)
(4) " " " (B. W. & Co.)

(1) In three cases of erysipelas and cellutitis occurring together the value of Polyvalent Antistreptococcic Serum was tried. The injections were followed by no rigors and by no crisis and there was little evidence of any therapeutic value, the lesion spreading for several days after treatment with continuation of toxaemia.

(2) Fifteen cases of severe facial erysipelas were treated by the intravenous injection of 20 c.c. of Erysipelas Antitoxin.

Thirteen patients had a rigor within one hour of the injection but this was followed by improvement in only two cases: Four other patients appeared to respond during the next few days, while seven cases showed no benefit at all. Two patients of this group died/

died after 3 - 7 days toxaemia from

(a) Bronchopneumonia.
(b) Cardiac failure.

Recurrence of the erysipelas occurred in three of these cases while 7 patients developed complications, such as Scalp Abscess, Suppurative Adenitis, Tonsillitis, Bronchopneumonia and Otorrhoea.

(3) Six cases of very severe facial erysipelas were treated by intravenous injections of 30 c.c. (P.D. & Co.) Scarlet Fever Antitoxin. Only one patient appeared to have a crisis with decided beneficial results: while another patient died from (1) senility, (2) myocarditis, (3) toxaemia on 5th day. The other four cases did not show any sign of response to treatment until after the 10th day in each case, while three of these cases developed complications (residual abscesses).

(4) 73 cases of erysipelas (69 facial and 4 corporal) were treated by intravenous injection of Scarlet Fever Antitoxin (B.W. & Co.)

All these cases were acutely ill and manifested signs of extreme toxaemia: all exhibited well marked erysipelas.

Ten patients died of whom seven suffered from chronic alcoholism and senility: five patients dying from terminal pneumonia and three from toxaemia and cardiac/

cardiac failure: one patient developed pneumonia during convalescence which proved fatal, while another died from specific mesaortitis.

Three of the cases which ended fatally were in extremis on admission to hospital.

The results of the treatment except in two instances were uniformly impressive. Generally a rigor followed within one hour accompanied by slight respiratory distress and often a slight cyanosis. In a small number of cases the delirium when present became more marked. This rigor appeared to be controlled in some instances by the use of adrenalin m.X by hypodermic injection but this result was not constant.

The patients were, however, generally quite comfortable two hours after the serum injection: from 12 hours to 48 hours thereafter a crisis took place in all cases accompanied by a fall in the pulse and respiration rates. Within 24 hours the signs of toxaemia subsided.

In 40% of cases the lesion continued to spread after the crisis but always appeared to be less intense and less active.

In 60% of cases the lesion commenced to subside soon after the crisis and heavy desquamation commenced within 48 hours of the crisis. Many patients expressed the/

the desire to be allowed up within two days of the treatment but the routine procedure was confinement to bed for 7 days followed by 4 days convalescence before dismissal from hospital.

Recurrence of the erysipelas without toxaemia developed in eight patients who had received intravenous serum therapy of Scarlet Fever Antitoxin (B.W. & Co.) five of whom had a long history of recurrent attacks.

In this group complications developed in only five cases: adenitis (one case), tonsillitis (one case), residual abscess of eyelid (2 cases), of scalp (one case).

THE RESULTS OF SERUM THERAPY IN ERYSIPELAS.

In the estimation of the results of serum therapy in Erysipelas, irrespective of the type of case, of the type of serum or of the method of administration, the observations were particularly noted first in connection with immediate effects and secondly in the remote effects.

The immediate effects of serum therapy were noted in connection with the following points:-

(1) The Course of the Temperature.
(2) The Circulatory System.
(3) The Toxaemia.
(4) The Erysipelas Lesion.
(5) Serum Reactions.

Observations were made on the remote effects of serum therapy with reference to -

(1) Complications.
(2) Serum Reactions.
(3) Detention in Hospital.
(4) Relapses.
(5) Case Mortality.

IMMEDIATE EFFECTS.

(1) The Course of the Temperature.

In erysipelas the temperature is generally held to be high and to run a variable course from five to fifteen days or longer. In a small series of control cases observed in the preliminary investigation on topical therapy in Erysipelas this was found to be so, the lowest temperature recorded being 100°F. and the highest temperature 105°F., while the average duration of the pyrexia was 10 days.

The results of serum therapy in the cases under review show that only one type of serum has any semblance to a constant effect on the course of the temperature. The group of cases of erysipelas treated by Scarlet Fever Antitoxin (B.W. & Co.) all showed within from twelve hours to forty-eight hours a critical fall in the temperature. In a small percentage of cases a post critical elevation of temperature was observed and might be due to recrudescence of toxaemia as no other causes could be found.

This post critical elevation of temperature rarely lasted longer than 12 - 24 hours.

In the cases treated by the intravenous method many

cases/

cases exhibited a rigor associated with hyperpyrexia and a dramatic crisis.

It is interesting to note that relapses were associated with little febrile disturbance.

(2) The Circulatory System.

It was noted in all cases that the condition of this system was directly dependent on the intensity of the intoxication.

The group of cases treated by Scarlet Fever Antitoxin (B.W. & Co.) all manifested an immediate improvement in the circulatory system after serum therapy.

All cases treated by serum intravenously who exhibited a rigor manifested also signs of a definite increase in the rate and the force of the action of the heart, but within a few hours there was noted a very definite improvement in the rate and quality of the pulse.

(3) THE TOXAEMIA.

In all the cases treated by serum therapy the toxaemia was definitely and markedly established being frequently manifested by a low tension pulse, a dry furred tongue and sordes, restlessness, irritability, marked insomnia and frequently by delirium.

It was found difficult to differentiate, in some cases, toxic delirium and alcoholic delirium as many of the male cases/

cases and a smaller percentage of the female cases were found to have a definite history of alcoholism.

The elimination of the toxaemia was found to be early and constant only in cases of erysipelas treated by Scarlet Fever Antitoxin (B.W. & Co.) and the maximum effects were obtained by large doses of serum given by intramuscular injection or in the more acutely ill cases by the intravenous route.

(4) The Erysipelas Lesion.

All the cases of erysipelas under review, whether corporal or facial, exhibited well marked lesions frequently with vesiculation.

No serum therapy was found to have a constant effect on the lesion but Scarlet Fever Antitoxin (B.W. & Co.) had apparently some effect in many of the cases.

In the group treated by this type of serum the lesion continued to spread in 40% of cases but appeared on critical and careful observation and examination to be less intense and less active.

In 60% of cases, however, the erysipelas lesion commenced to subside within 24 hours of the crisis, apparently brought about by serum therapy, and the typical heavy desquamation began to manifest itself within 48 hours of the crisis.

(5)/

(5) Serum Reactions.

No untoward effects in serum reactions were observed after intradermal serum therapy or after intramuscular serum therapy.

The intravenous route, however, when adopted, produced frequently a rigor within one hour; this was accompanied by increase in pulse rate and respiration rate and sometimes by slight cyanosis: occasionally the delirium appeared to be more marked: profuse sweating followed a rise in temperature (sometimes 107°F.) but within from five minutes to 20 minutes the patient returned to a normal state of things. This reaction was not constantly but often controlled by adrenalin injection and was looked on as possibly in the nature of a bronchial spasm or hypersensitiveness to some foreign protein in the serum.

The serum reactions were latterly eliminated almost entirely by the perfection through practice of the technique of serum therapy by the intravenous route, the features which were latterly stressed being -

(1) the previous skin testing for supersensitiveness of patients prior to intravenous serum therapy.
(2) The heat of the serum was approximated to blood heat.
(3) The rate of administration.

No untoward results were observed in the cases under review.

REMOTE EFFECTS.

(1) Complications.

The complications of erysipelas may be either of a serious nature, e.g. nephritis, pneumonia and endocarditis or what is more common, residual abscess formation.

In a series of 50 cases observed as control cases without serum therapy, complications developed as follows:-

Nephritis	2%
Pneumonia	4%
Endocarditis	2%
Abscess	30%

These complications were found to be present in almost the same percentages of all the cases of erysipelas under review, except in those cases treated by Scarlet Fever Antitoxin (B.W. & Co.), which groups exhibited complications only in five out of a total of 73 cases treated by the intravenous method, and no complications in 41 cases treated by intramuscular serum.

These complications were (1) Tonsillitis (one case), (2) Adenitis (one case), and (3) Abscess formation (4.1%).

This figure 4.1% for abscess formation is very striking/

striking compared to 30% - the figure of abscess formation found in a series of 50 control cases.

The absence of complications in the group treated by the intramuscular route is difficult to interpret except that all the most severe cases were treated by intravenous serum therapy in the hope of a more immediate beneficial reaction.

(2) Serum Reactions.

There were no cases of delayed serum sickness but 2 cases exhibited on the 11th and 14th day of the serum therapy by the intravenous route well marked serum rashes.

These rashes were both urticarial and quite transient in nature.

(3) Detention in Hospital.

Detention in hospital was definitely lessened in the group treated by Scarlet Fever Antitoxin (B.W. & Co.)

Average durations in hospital:-

(1) Cases treated by Scarlet Fever Antitoxin (B. W. & Co.) 15 days.
(2) Cases not treated by serum (50 Control Cases)...28 days.
(3) Cases treated by other varieties of serum.....26 days.

(4) Relapses.

If a relapse is taken to mean a recrudescence of erysipelas within a few days then all groups of cases with various sera exhibited relapses with the exception of/

of Scarlet Fever Antitoxin (B. W. & Co.)

In the latter group, however, a recurrence of the disease was observed in eight cases occurring from three days to six months after dismissal from hospital. All these recurrences were remarkable for the absence of toxaemia and the presence of the lesion in the same site as that of the previous attack.

(5) Case Mortality.

In this series of 178 cases treated by serum therapy 18 deaths occurred giving a figure of a fraction over 10% for the mortality rate.

It is worthy of note, however, that this figure is inclusive of all patients receiving serum therapy and that among these cases of this series under review were 5 patients moribund on admission to hospital and 12 patients suffering from some additional disease of a serious nature which might well be estimated as the cause of death rather than the erysipelas toxaemia.

EXAMPLES OF CASES.

The following brief records of cases are given to illustrate the clinical course of erysipelas treated without serum and with the different types of serum.

Cases No. 2, 4 and 6 represent control cases untreated by serum and illustrating the possibility of any erysipelas lesion assuming the wandering type with a prolonged pyrexia and toxaemia and the possibility also of residual abscess formation, thus causing a long illness and heavy cost of hospitalisation of the patient.

DISEASE.

ERYSIPELAS (WANDERING)

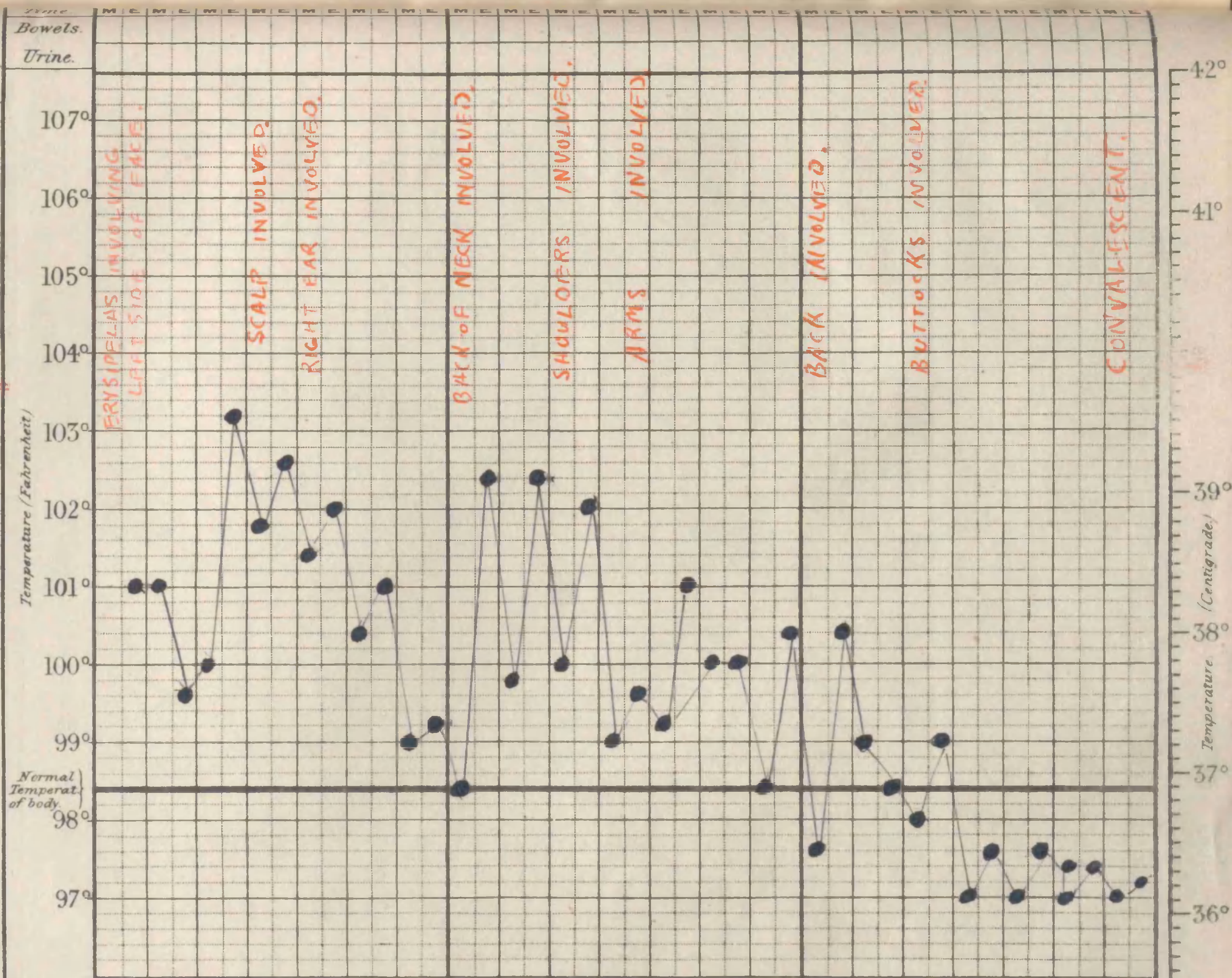
Notes of Case.

Name: JOHN EDWARDS.

Age: 38 YRS.

Diet:

Case Book No. 2 (CONTROL CASE)



Day of Dis.	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Pulse.	100	104 / 112	112 / 136	128 / 128	128 / 128	126 / 124	104 / 116	100 / 108	108 / 112	104 / 112	100 / 108	96 / 96	80 / 104	104 / 104	100 / 96	100 / 100	80 / 88	88 / 88	80 / 88	80 / 82	88 / 80
Resp.	26	28 / 26	26 / 32	32 / 36	32 / 36	32 / 26	24 / 26	26 / 24	24 / 24	24 / 24	26 / 28	24	20 / 24	24 / 24	22 / 24	24 / 24	22 / 24	22 / 20	22 / 22	22 / 20	20 / 24
Date.	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9

Date of admission. 20TH MARCH 1929

Result WELL.

Entered at Stationer's Hall   Printed and Published by Wodderspoon & Co. Ltd. Gate Street Kingsway W.C. 2   Gould's Clinical Chart

CASE NO. 2. (Control Case).

NAME. J.E.

AGE. 38 years.

TYPE. Idiopathic (Primary).

CLINICAL NOTES. Acutely ill: apparently ordinary type of facial erysipelas which progressed into the wandering type with 20 days pyrexia, 10 days toxaemia: lesion subsided after 24 days.

LESION. Bilateral facial spreading over scalp, neck, shoulders, chest, arms, trunk and buttocks.

TOXAEMIA. Well marked by sordes, by headache and later delirium especially at night.

COMPLICATIONS. Bronchitis.

SERUM. Contra-indicated on account of pulmonary condition.

RESULT. Prolonged illness: wandering erysipelas. Protracted convalescence.

REMARKS. Case untreated by serum, studied as a control case.

DISEASE.

ERYSIPELAS.
(IDIOPATHIC.)

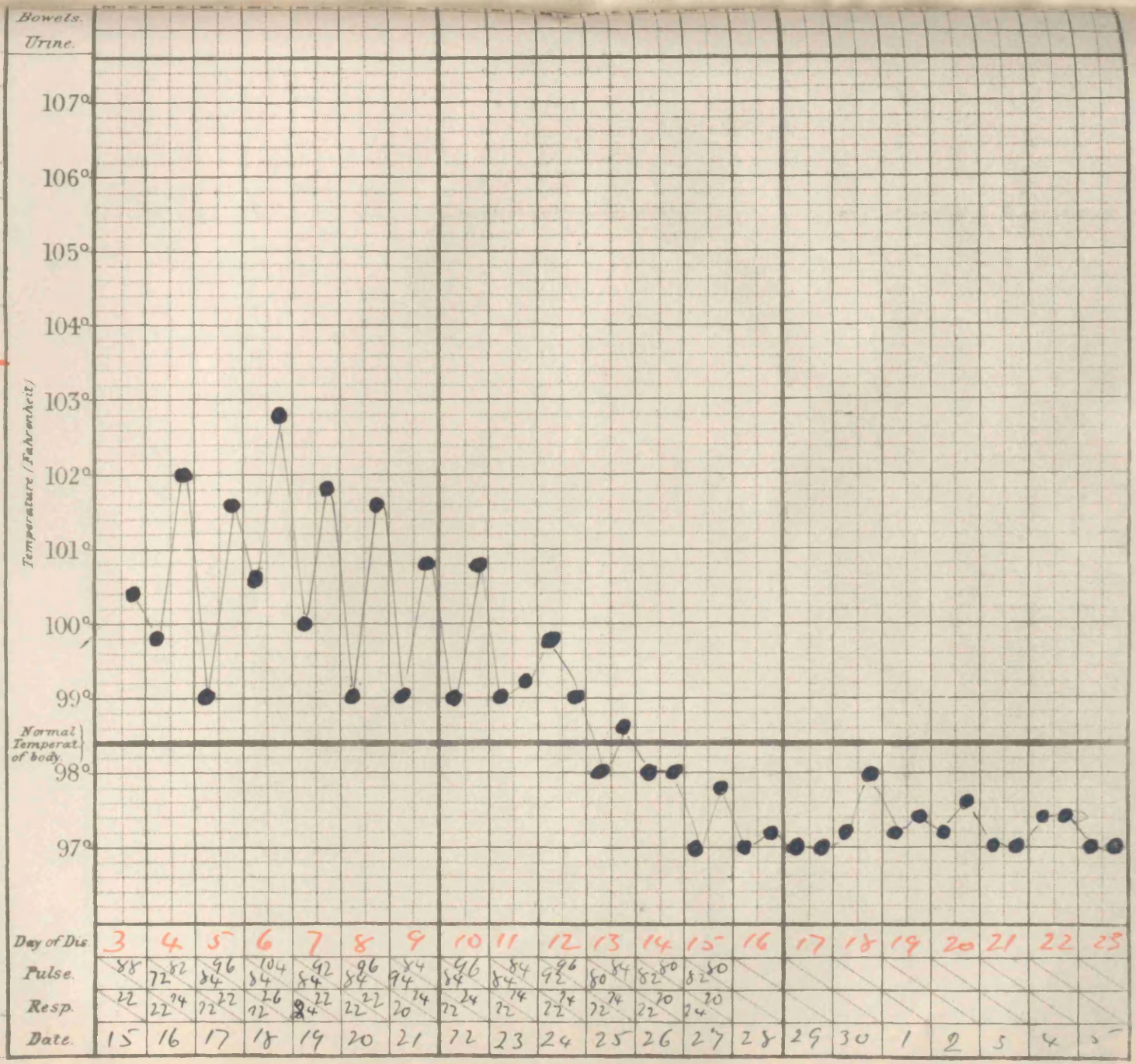
Notes of Case.

Name AMBROSE SWEENEY.

Age 58 YRS.

Diet

Case Book No. 4
(CONTROL CASE)



Day of Dis.	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Pulse.	88	72 82	84 96	84 104	84 92	84 96	94 84	84 96	84 84	92 96	80 84	82 80	82 80								
Resp.	22	22 24	22 22	22 26	24 22	22 22	20 24	22 24	22 24	22 24	22 24	22 20	24 20								
Date.	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5

Date of admission.
15TH SEPT. 1924

Result WELL.

Entered at Stationer's Hall. *Printed and Published by Wodderspoon & Co Ltd Gate Street, Kingsway W.C.2* *Gould's Clinical Chart.*

CASE NO. 4. (Control Case).

NAME. A.S.

AGE. 58 years.

TYPE. Idiopathic.

CLINICAL NOTES. Acutely ill: (3rd day of illness on admission.) Irregular pyrexia. 99o - 103°F. for 12 days, settling by lysis.

LESION. Bilateral facial erysipelas spreading over the forehead and scalp.

TOXAEMIA. Well marked by headache and vomiting (4 days): mental confusion (5 days): dry tongue and sordes (6 days.)

COMPLICATIONS. Abscess of eyelid: falling hair.

SERUM. No serum.

RESULT. Not very satisfactory.

REMARKS. Control case illustrating 12 days pyrexia with continuance of toxaemia and spread of lesion: abscess of eyelid as a complication.

DISEASE.

ERYSIPELAS.
(WANDERING)

Notes of Case.

Name JAMES SMITH.

Age 45 YRS.

Diet

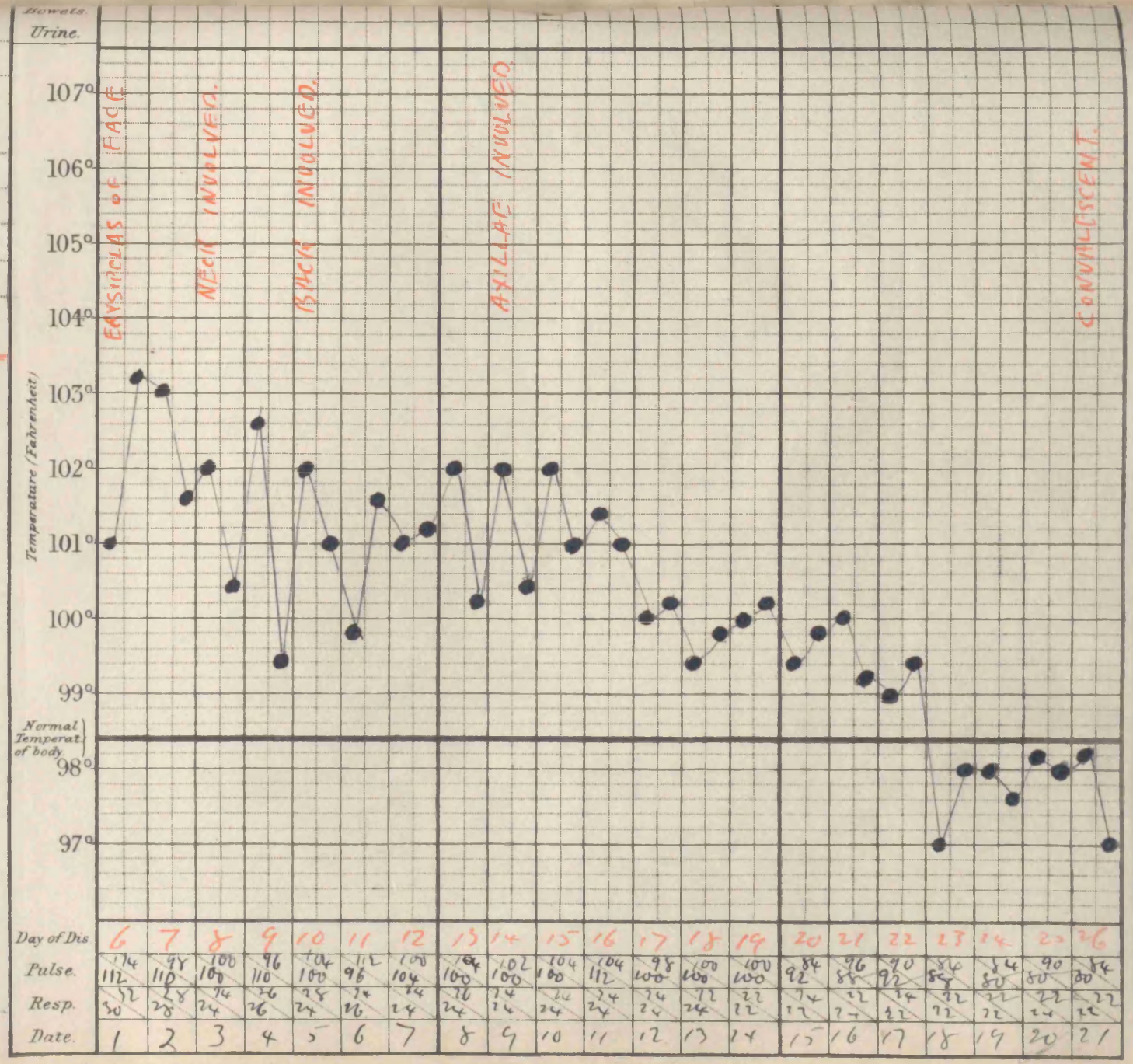
Case Book N° 6

(CONTROL CASE)

Date of admission.

1ST JUNE 1929

Result WELL



Entered at Stationer's Hall. Printed and Published by Wodderspoon & Co Ltd Gate Street Kingsway W.C. 2 Gould's Clinical Chart

CASE NO. 6 - (Control Case)

NAME. J.S.

AGE. 45 years.

TYPE. Idiopathic (Primary).

DAY OF ILLNESS. 6th day on admission to hospital.

DAY OF SERUM TREATMENT. No serum therapy.

CLINICAL NOTES. Acutely ill with irregular pyrexia 100°F. - 104°F. lasting for 20 days accompanied by spread of lesion.

LESION. Facial erysipelas, bilateral, involving both ears and finally assuming wandering type.

TOXAEMIA. Increased until delirium on 8th day: dry tongue and sordes present for 14 days.

COMPLICATIONS. Bronchitis.

RESULT. End result satisfactory.

REMARKS. As an apparent facial erysipelas which assumed the wandering type - untreated by serum - illness running a course of 20 days, with protracted convalescence.

Case No. 91. illustrates the non success of polvalent antistreptococcal serum therapy in a case of cellulitis of the hand with erysipelas of the arm, shoulder and trunk.

This serum has frequently been used in the past few years but the results have in general been unsatisfactory and unreliable and the results in cases treated by this serum in the present investigation have tended to prove that there are no apparent specific antitoxic effects obtained by its use.

DISEASE.

ERYSIPELAS.
(TRAUMATIC.)

Notes of Case.

Name { WILLIAM CAMERON.

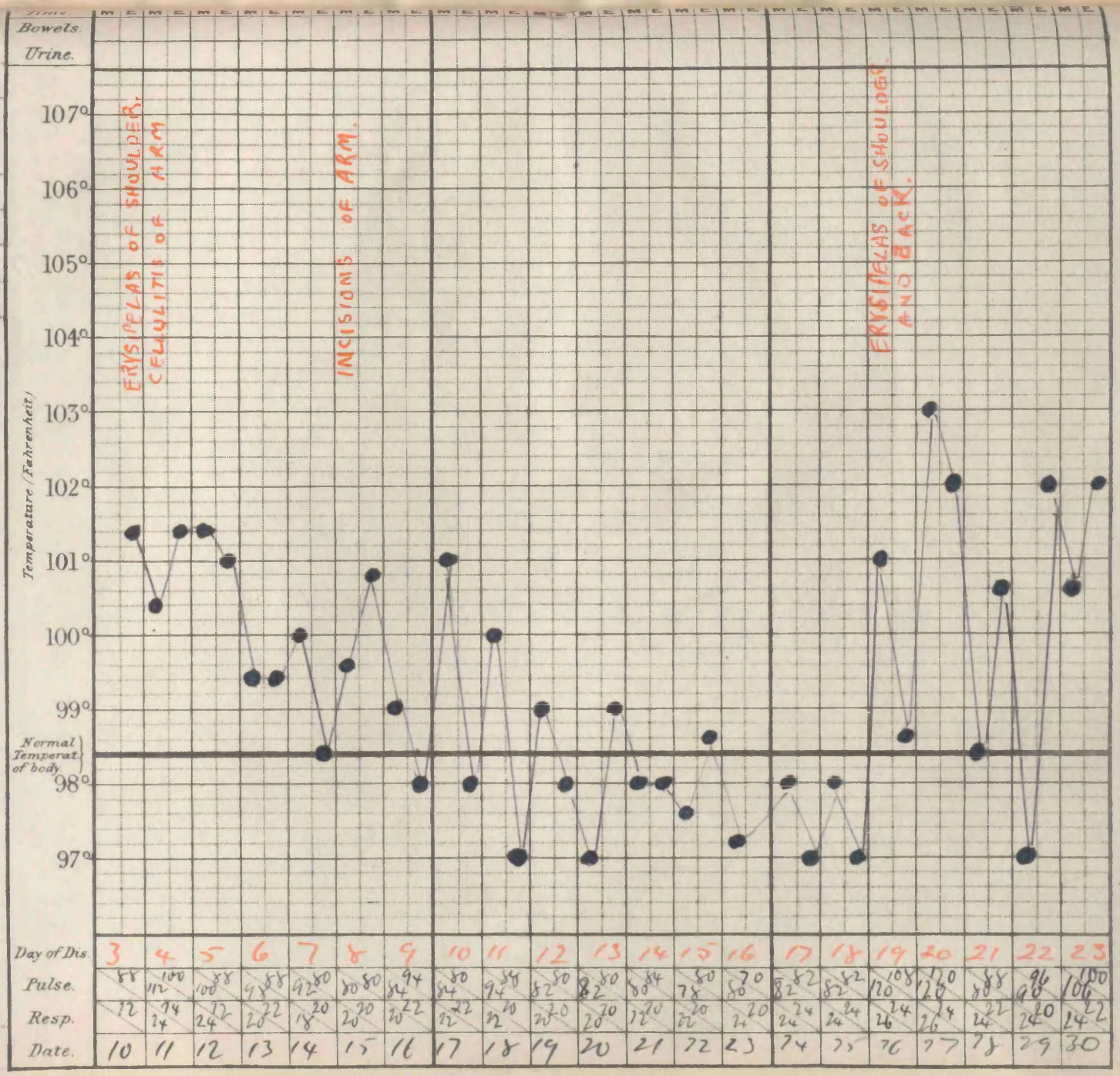
Age 49 YRS.

Diet

Case Book No. 91.

Date of admission.
10TH JAN. 1929

Result WELL.



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CASE NO. 91.

NAME. W.C.

AGE. 49 years.

TYPE. Traumatic.

DAY OF ILLNESS. 3rd Day.

DAY OF SERUM TREATMENT. 3rd Day.

CLINICAL NOTES. Injury to finger resulting in cellutitis of hand and arm with erysipelas of shoulder. No reponse apparent to serum therapy: 4 weeks acute illness.

LESION. Cellutitis of hand and arm. Erysipelas of shoulder.

TOXAEMIA. Persistent headache and vomiting: dry furred tongue, slow soft pulse, cyanosis, delirium at nights. No apparent improvement after serum therapy.

COMPLICATIONS. Abscess formation of cellular tissues of arm requiring multiple incisions. Recurrence of erysipelas in 3rd week.

RESULT. Unsatisfactory from the point of view of serum therapy.

REMARKS. Case of Cellutitis of hand and arm with erysipelas of upper arm and shoulder/

shoulder treated by Polyvalent
Antistreptococcal serum
intravenously (40 c.c.) no
beneficial results.

Cases No. 3, 4 and 5 are records of erysipelas treated by a so-called specific erysipelas streptococcus antitoxin.

These records are quite typical of the results obtained by the frequent use of this serum during the investigation. The results were very disappointing, and there was no evidence at all to indicate that the serum was possessed of any specific antitoxin.

DISEASE.

ERYSIPELAS. (IDIOPATHIC.)

Name { HENRY GREET.

Age 42 YRS.

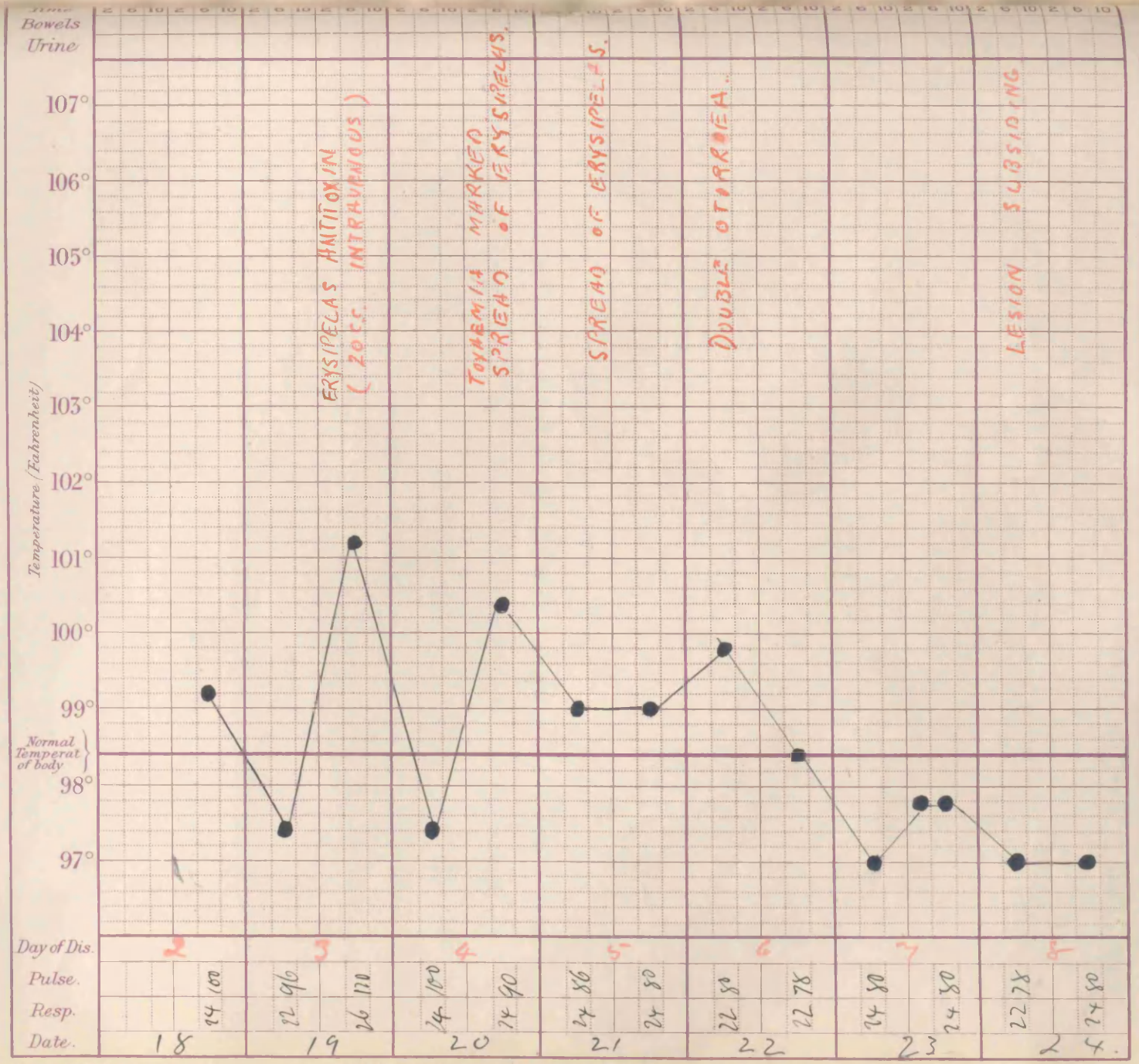
Diet

Case Book No. 3

Notes of Case

Date of admission 18TH DEC. 1928.

Result WELL.



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CASE NO. 3

NAME H.G.

AGE. 42 years.

TYPE. Idiopathic.

CLINICAL NOTES Acutely ill: Faucial congestion; irregular pyrexia for 3 days after serum.

LESION. Bilateral facial.

TOXAEMIA. Headache severe: tongue furred and dry. Toxaemia present for 6 days.

COMPLICATIONS Double Otorrhoea.

SERUM. Erysipelas Antitoxin. 20 c.c. Intravenously.

RESULT. Rather unsatisfactory: Irregular pyrexia for 7 days with continuance of toxaemia and spread of lesion.

REMARKS. No apparent specific reaction from erysipelas Antitoxin.

DISEASE.

ERYSIPELAS (RECURRENT)

Notes of Case.

Name: WILLIAM FORBES.

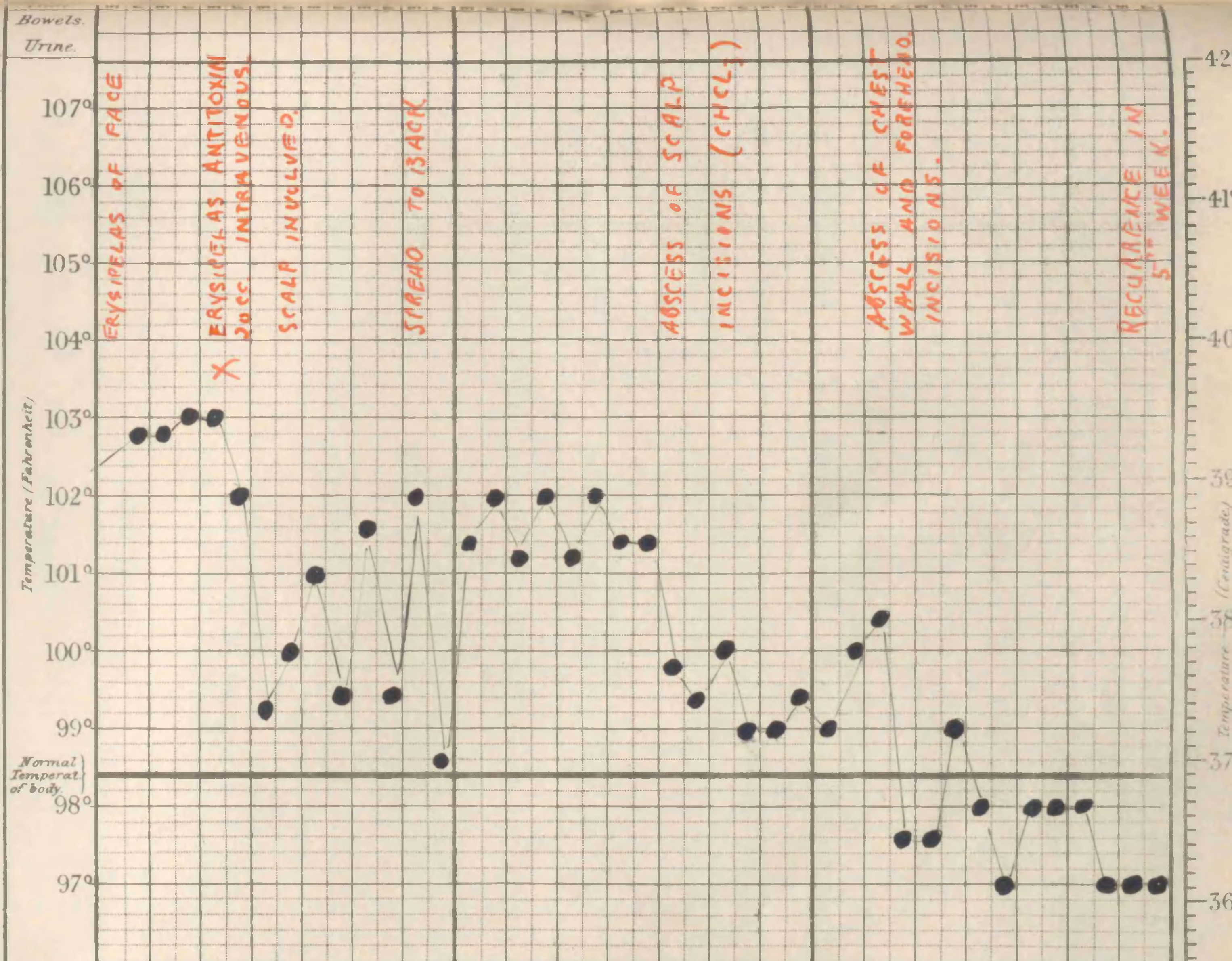
Age: 40 YRS.

Diet

Case Book No. 4.

Date of admission. 22nd DEC. 1928

Result: WELL.



Day of Dis.	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Pulse.	124	104 / 120	120 / 104	104 / 86	100 / 116	96 / 92	80 / 96	72 / 88	112 / 88	104 / 96	104 / 108	88 / 100	88 / 88	100 / 80	96 / 94	80 / 102	88 / 98	88 / 88	96 / 88	88 / 96	80 / 80
Resp.	24	14 / 14	14 / 14	14 / 14	24 / 24	22 / 24	22 / 26	26 / 22	24 / 24	24 / 24	24 / 24	24 / 14	24 / 24	26 / 26	22 / 22	22 / 22	24 / 14	24 / 22	24 / 22	22 / 22	22 / 22
Date.	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11.

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CASE NO.	4.
NAME	W.F.
AGE.	40 Years
TYPE.	Idiopathic (Recurrent)
CLINICAL NOTES	Acutely ill 4th day. T. 102.8 P. 128 R. 24. after serum therapy irregular pyrexia until the 23rd. day.
LESION	Bilateral facial erysiplas including nose and forehead.
TOXAEMIA.	Well marked by severe headache, furred dry tongue, mental confusion, low tension pulse
COMPLICATIONS.	Multiple abscess formation of scalp, chest wall, and cervical glands. Recurrence 5th week.
SERUM.	Erysipelas Antitoxin 20 c.c. intravenously.
RESULT.	Definitely unsatisfactory.
REMARKS.	Irregular pyrexia for 23 days after serum with toxaemia maintained for 8 days. Spread of lesion over scalp, neck and chest wall followed by abscess formation. Recurrence 5th week. No apparent specific reaction from Erysipelas Antitoxin.

DISEASE.

ERYSIPELAS. (IDIOPATHIC.)

Notes of Case.

Name EDWARD McKILLOP.

Age 56 YRS.

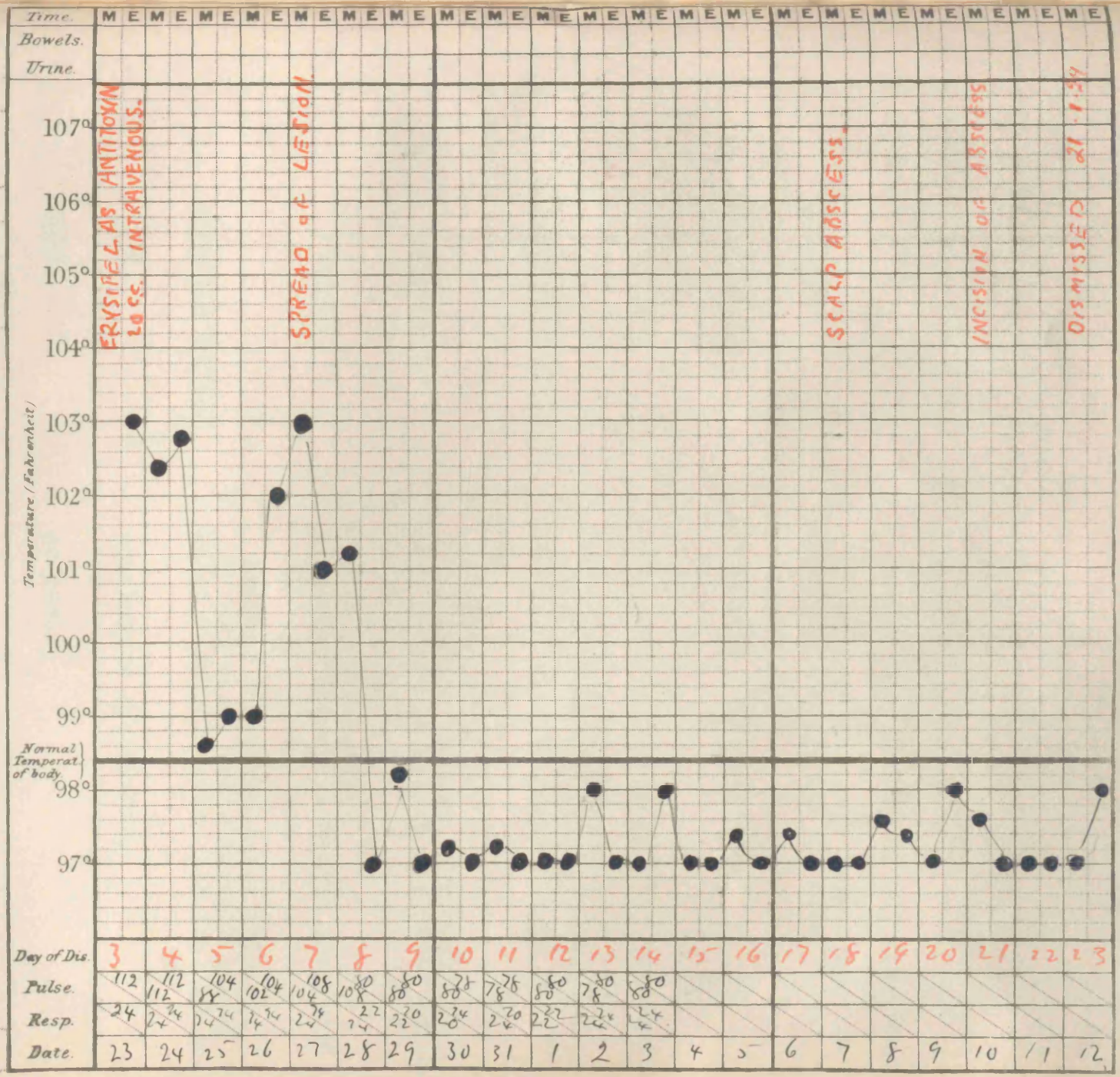
Diet

Case Book No. 5.

Date of admission.

23rd DEC. 1928.

Result WELL.



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CASE NO. 5.

NAME. E. McK.

AGE. 56 years.

TYPE. Idiopathic.

CLINICAL NOTES. Acutely ill. Before serum T.103, P.112, R.24. Irregular pyrexia after serum for 4 days. T.P.R. normal on 9th day of illness.

LESION. Bilateral facial erysipelas: scalp also involved.

TOXAEMIA. Well marked by headache and delirium: furred tongue and sordes lasting 3 days after serum therapy.

COMPLICATIONS. Scalp abscess.

SERUM. 20 c.c. Erysipelas Antitoxin intravenously.

RESULT. Definitely unsatisfactory.

REMARKS. No specific reaction from Erysipelas Antitoxin.

Cases Nos. 6, 7, 21, 26, 41 and 68 are recorded illustrating typical results of serum therapy in erysipelas by the use of Scarlet Fever Streptococcus Antitoxin. (B.W. & Co.)

4 HOUR CHART.

DISEASE.

ERYSIPELAS.
(IDIOPATHIC.)

Name { CLIFFORD DREWETT.

Age 33 YRS.

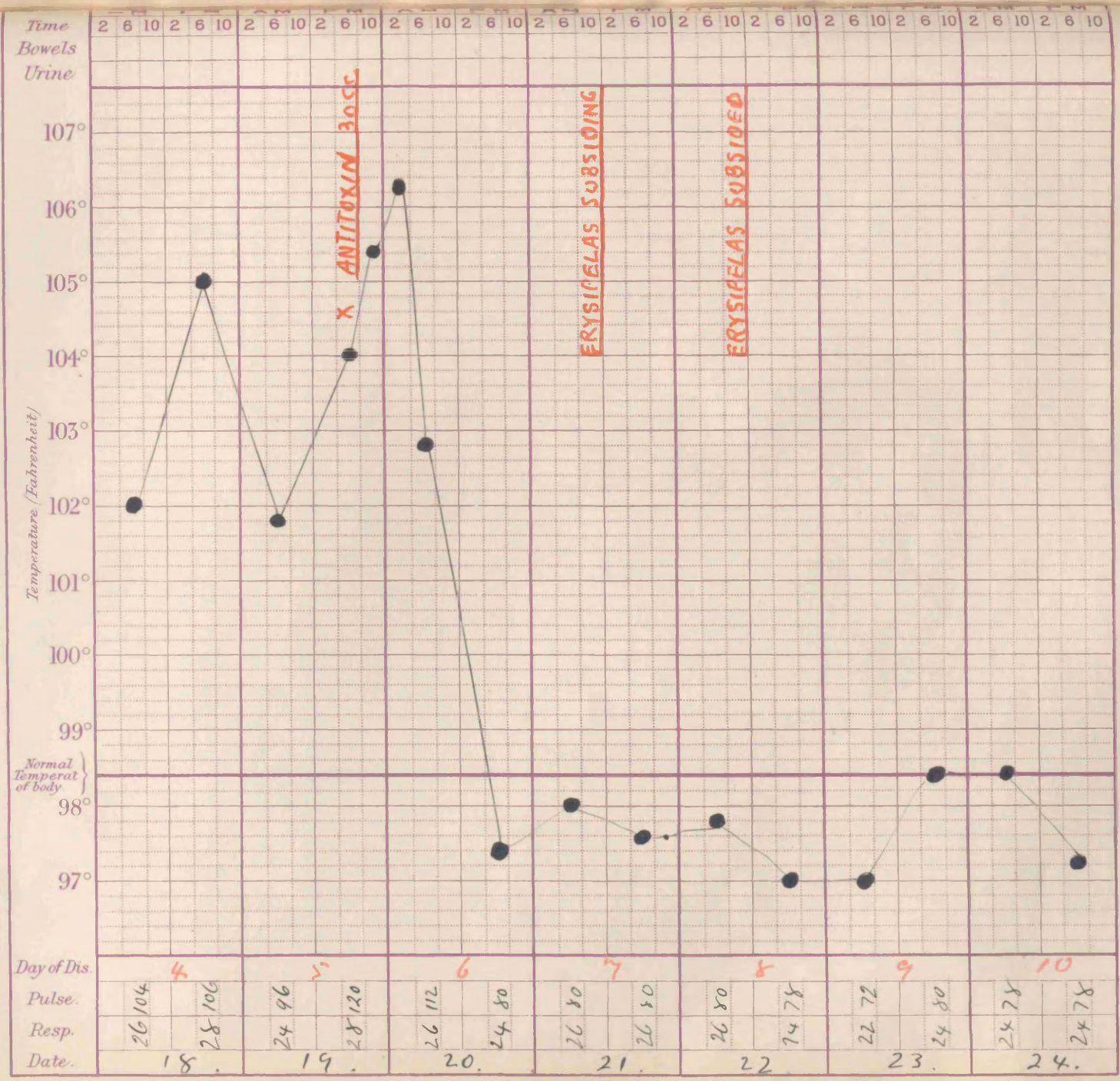
Diet

Case Book No. 6

Notes of Case

Date of admission
18TH APRIL 1928

Result WELL



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CASE NO.	6.
NAME.	C.D. (Male)
AGE.	33 years.
TYPE.	Idiopathic.
CLINICAL NOTES.	First attack of acute facial bilateral erysipelas. Acutely ill. T.104. P.120. R.28. Before serum. T. 97⁴.P.80. R.24. 24 hours after serum.
LESION.	Bilateral facial erysipelas with oedema of eyelids.
TOXAEMIA.	Marked by headache, furred dry tongue, rapid low tension pulse.
COMPLICATIONS.	Nil.
SERUM.	Scarlet Fever Antitoxin (B.W. & Co,) 30 c.c. intramuscularly.
RESULT.	Excellent: Immediate crisis with elimination of toxaemia and subsidence of the lesion: uninterrupted convalscence.
REMARKS.	The patient, a commercial traveller, was a strongly built and apparently good living type and although very ill and toxic on admisson made a dramatic recovery after serum therapy.

4 HOUR CHART.

DISEASE.

ERYSIPELAS. (TRAUMATIC.)

Name { CHARLES SMITH.

Age 31 YRS.

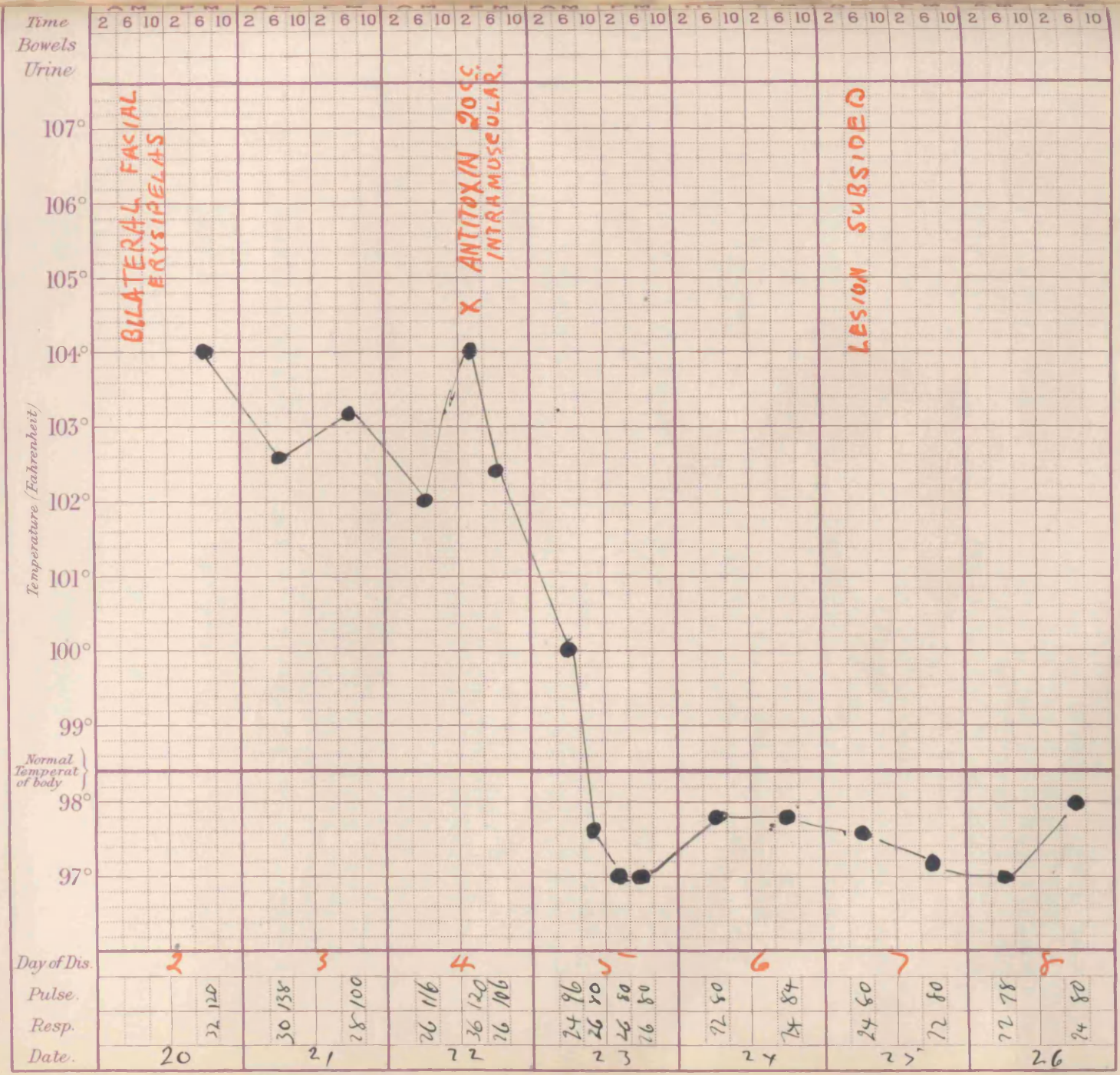
Diet

Case Book No. 4

Notes of Case

Date of admission 20th APRIL 1928.

Result WELL.



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CASE NO.	7.
NAME.	G.S.
AGE.	31 years.
TYPE.	Traumatic.
DAY OF ILLNESS.	2nd day.
DAY OF SERUM TREATMENT.	4th day.
CLINICAL NOTES.	Injury to nose - abrasion followed by acute illness. Before serum T.104. P.120 R.36. 24 hours after serum. T.97. P.80. R.26.
LESION.	Bilateral facial erysipelas, nose and forehead also involved.
TOXAEMIA.	Well marked by headache, vomiting, delirium, dry tongue and low tension pulse.
COMPLICATIONS.	Nil.
RESULT.	Excellent.
REMARKS.	Dramatic crisis after 20 c.c. Scarlet Fever Antitoxin (B.W. & Co) intramuscularly followed by elimination of toxaemia in 24 hours and subsidence of lesion within 48 hours after serum therapy.

4 HOUR CHART.

DISEASE.

ERYSIPELAS. (IDIOPATHIC.)

Name { JOHN GRAHAM.

Age 60 YRS.

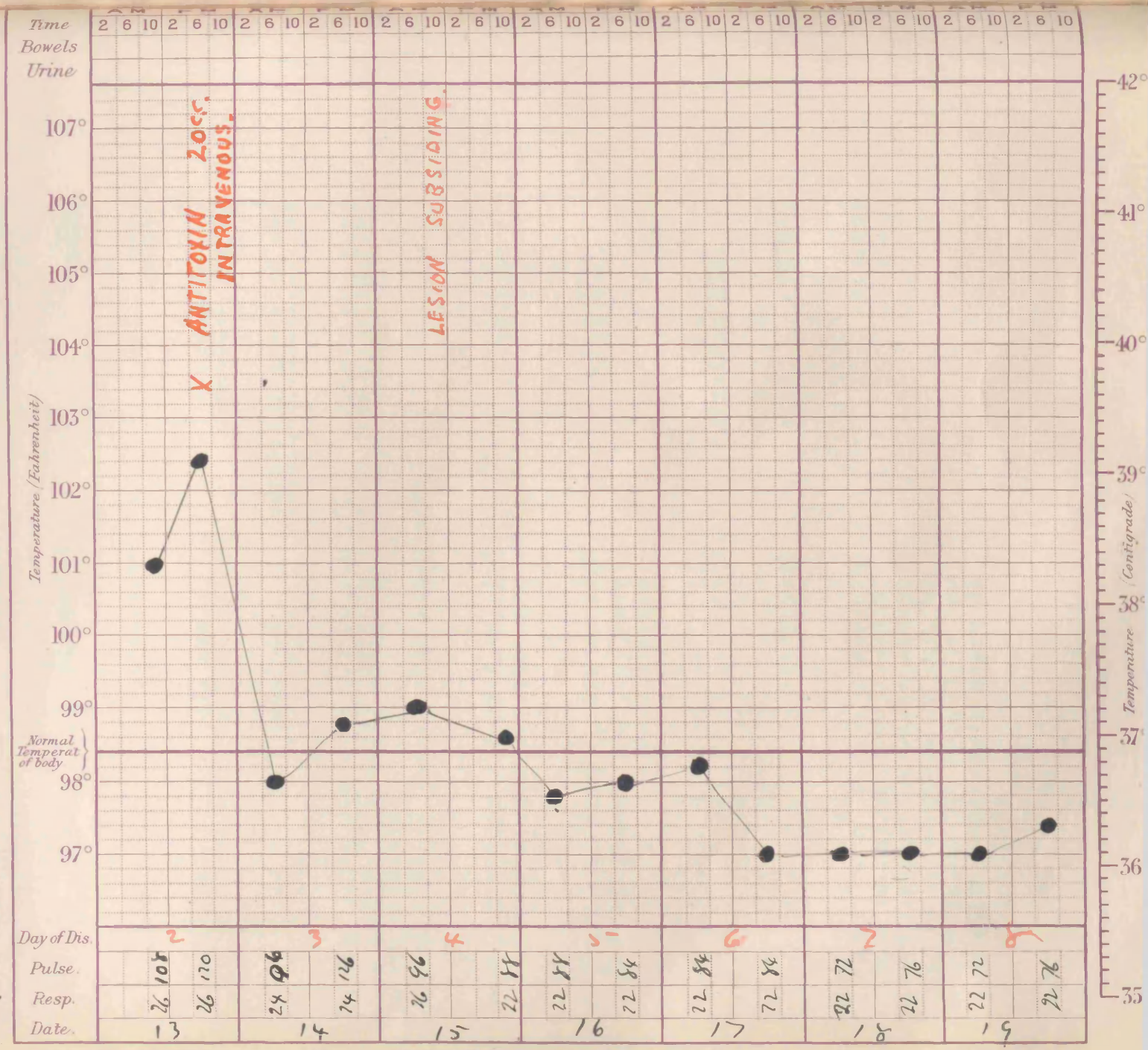
Diet

Case Book N° 21.

Notes of Case

Date of admission 13TH SEPT. 1928.

Result WELL.



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CASE NO.	21.
NAME.	J.G.
AGE.	60 years.
TYPE.	Idiopathic.
CLINICAL NOTES.	Acutely ill and rather toxic. T.102^4. P.120. R.26. Before serum. T. 98. P. 96. R.24. 12 hours after serum.
LESION.	Bilateral facial erysipelas involving also the forehead.
TOXAEMIA.	Headache very severe: tongue dry and very dirty. Slightly mentally confused.
COMPLICATIONS.	Nil.
SERUM.	Scarlet Fever Antitoxin (B.W. & Co.) 2o c.c. intravenously.
RESULT.	Excellent: immediate crisis with elimination of toxaemia and subsidence of lesion within 36 hours. uninterrupted convalescence.
REMARKS.	Slight rigor 1 hour after serum.

4 HOUR CHART.

DISEASE.

ERYSIPELAS.
(IDIOPATHIC.)

Name { JAMES FALKNER.

Age 31 YRS.

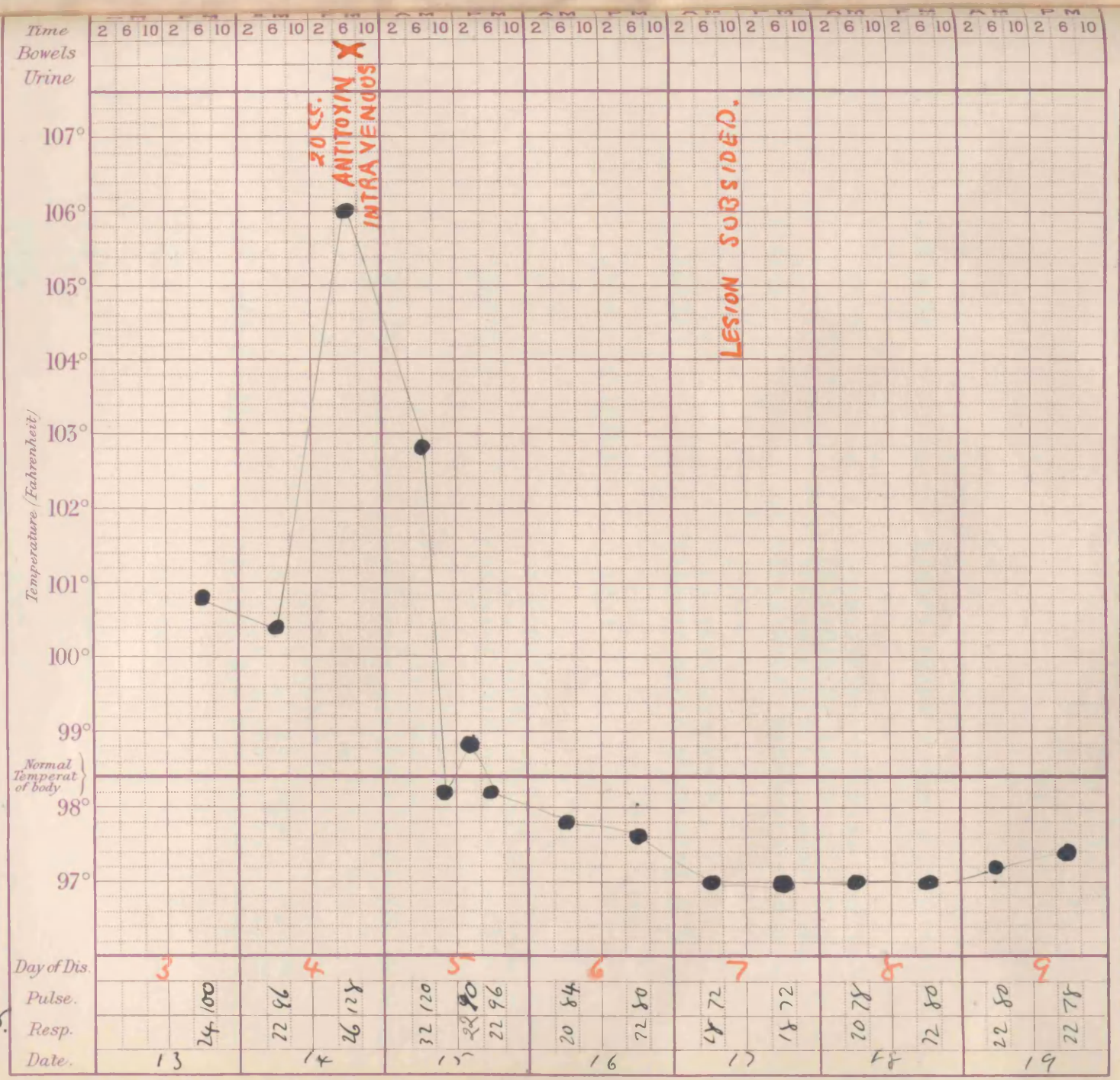
Diet

Case Book No. 26.

Notes of Case

Date of admission 13TH OCTOBER 1928.

Result WELL.



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CASE NO. 26.

NAME. J.F.

AGE. 31 years.

TYPE. Idiopathic.

CLINICAL NOTES. Acute actively spreading erysipelas of face.
Before serum T.106. P.130. R.22.
12 hours after serum T. 98⁷. P. 90¹. R.22.

LESION. Bilateral facial erysipelas spreading rapidly: subsidence within 24 hours of serum therapy.

TOXAEMIA. Headache severe: tongue very furred and dry: pulse of low tension.

COMPLICATIONS. Nil.

SERUM. Scarlet Fever Antitoxin (B.W. & Co.) 20 c.c. intravenously.

RESULT. Excellent result. Immediate crisis and post critical disappearance of fever, toxaemia and of lesion.

REMARKS. Excellent result of serum therapy in very ill patient with Scarlet Fever Antitoxin (B.W. & CO.) serum.

4 HOUR CHART.

DISEASE.

ERYSIPELAS.
(POST OPERATIVE)

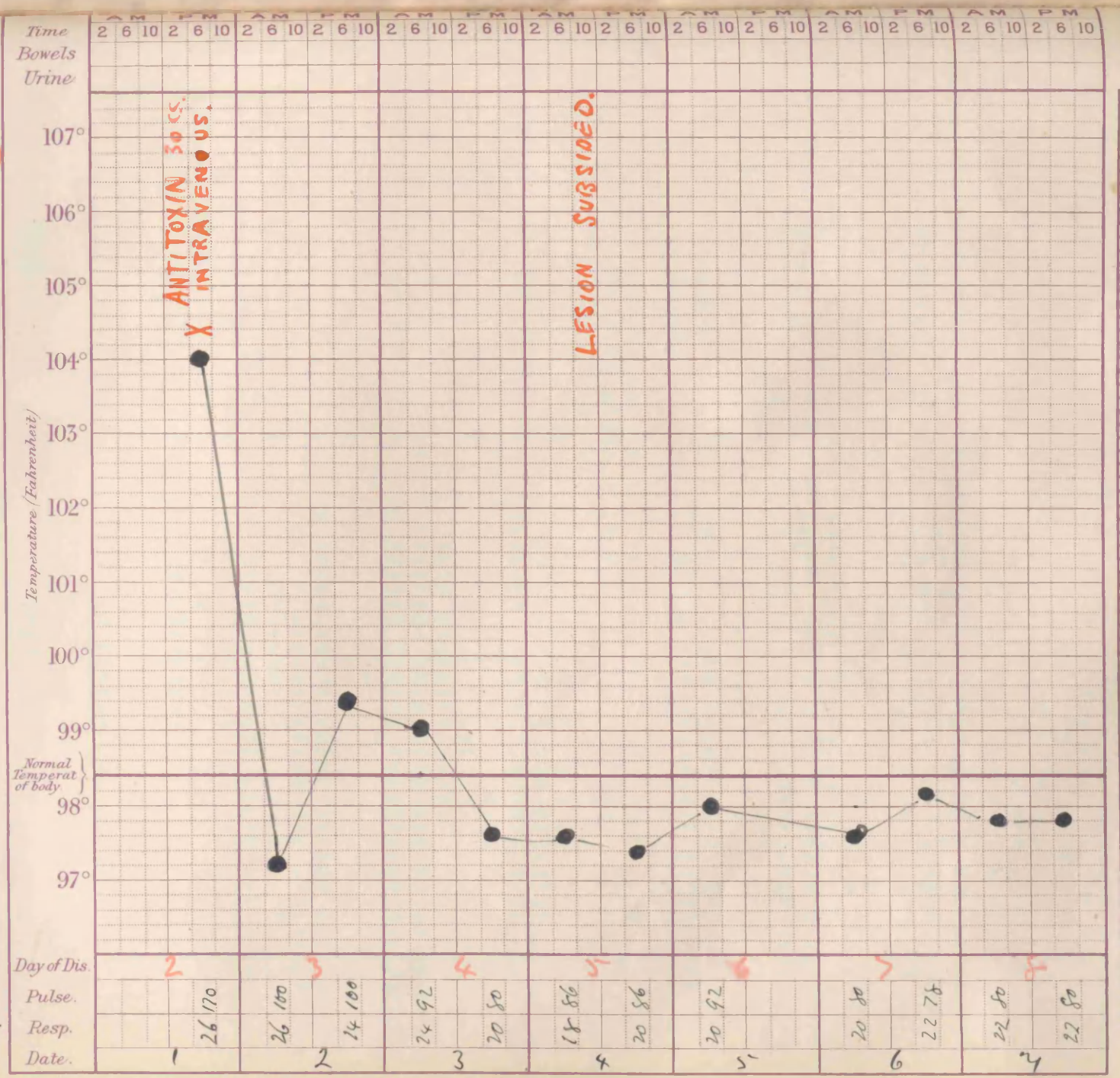
Name { STEWART ROGER.

Age 23 YRS.

Diet

Case Book No. 41.

Notes of Case



Date of admission 1ST JANUARY 1929.

Result WELL.

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CASE NO. 41.

NAME. S.R.

AGE. 23.

TYPE. Post Operative.

CLINICAL NOTES. Incised wound of neck followed by acute facial erysipelas bilateral lesion.
2nd day of illness T.104. P. 120. R.26.
12 hours after serum T.97^2. P.100. R.26.
Uninterrupted convalescence.

LESION. Bilateral facial erysipelas: subsided 36 hours after serum.

TOXAEMIA. Well marked by headache: dry, furred tongue: these toxic signs and symtoms were not present 24 hours after serum therapy.

COMPLICATIONS. Nil.

SERUM. Scarlet Fever Antitoxin (B.W. & Co.) intravenously.

RESULT. Excellent.

REMARKS. Immediate crisis after serum with elimination of toxaemia and subsidence of lesion.

4 HOUR CHART.

DISEASE.

ERYSIPELAS
(IDIOPATHIC.)

Name { JAMES HAMILTON.

Age 50 YRS.

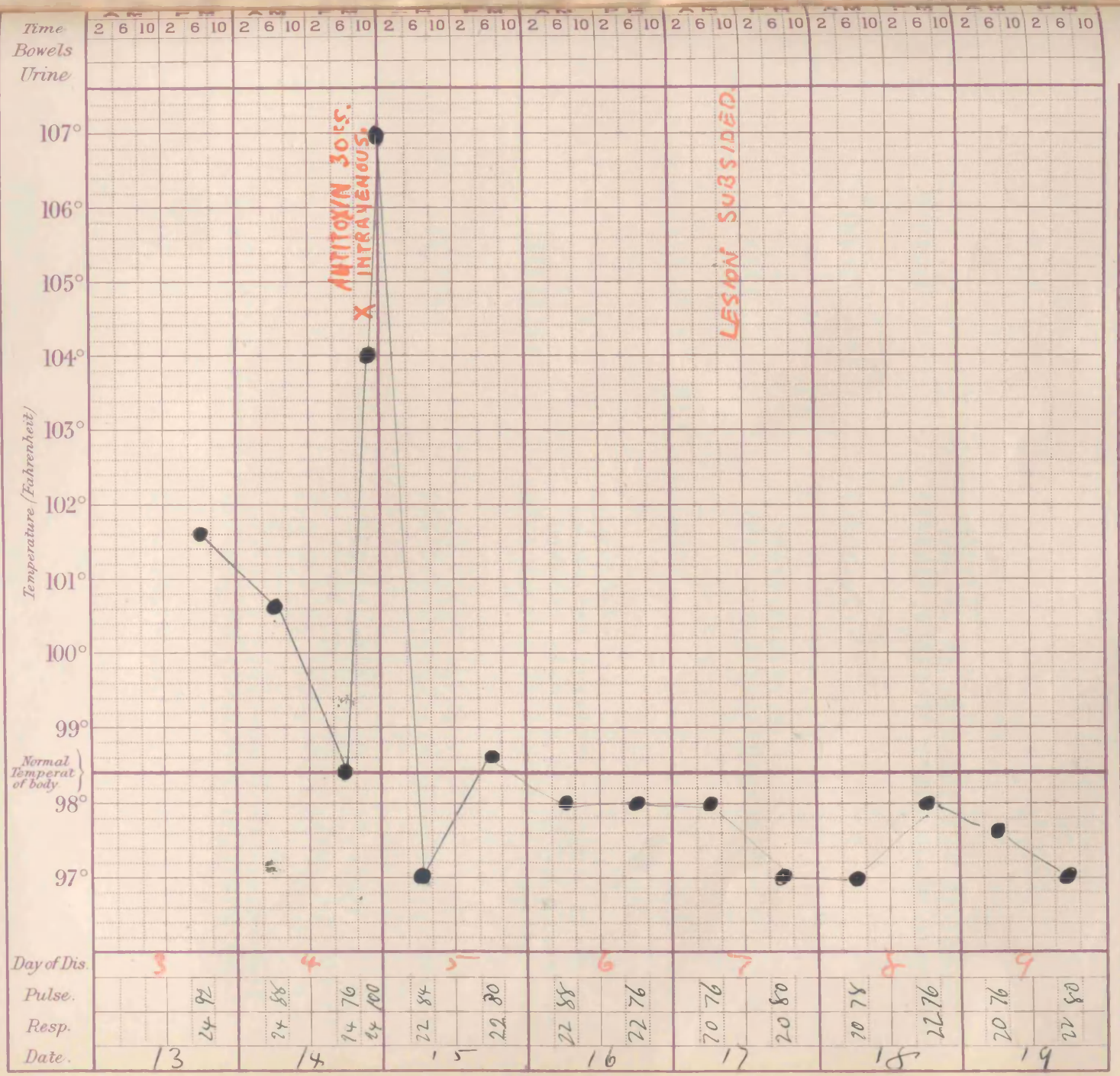
Diet

Case Book No. 68.

Notes of Case

Date of admission
13TH MAY 1929

Result WELL.



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CASE NO. 68.

NAME. J.H.

AGE. 50 years.

TYPE. Idiopathic (Primary).

CLINICAL NOTES. Acutely ill: T.104. P.100. R.24.
12 hours after serum. T. 97. P.80. R.22.

LESION. Bilateral facial erysipelas which subsided 24 hours later.

TOXAEMIA. Headache severe: slight delirium: tongue very dry: sordes present.

COMPLICATIONS. Nil.

SERUM. Scarlet Fever Antitoxin (B.W. & Co.) 30 c.c. intravenously.

RESULT. Excellent.

REMARKS. Immediate crisis with elimination of toxaemia and post critical subsidence of lesion.

Cases No. 22, 64 and 168 illustrate serum therapy in erysipelas using Scarlet Fever Streptococcus Antitoxin (P.D. & Co.)

This type of serum was apparently less reliable and of less value than the other (B.W. & Co.) Scarlet Fever Antitoxin.

4 HOUR CHART.

DISEASE.

ERYSIPELAS.
(IDIOPATHIC.)

Name: ROBERT HILL.

Age: 52 YRS.

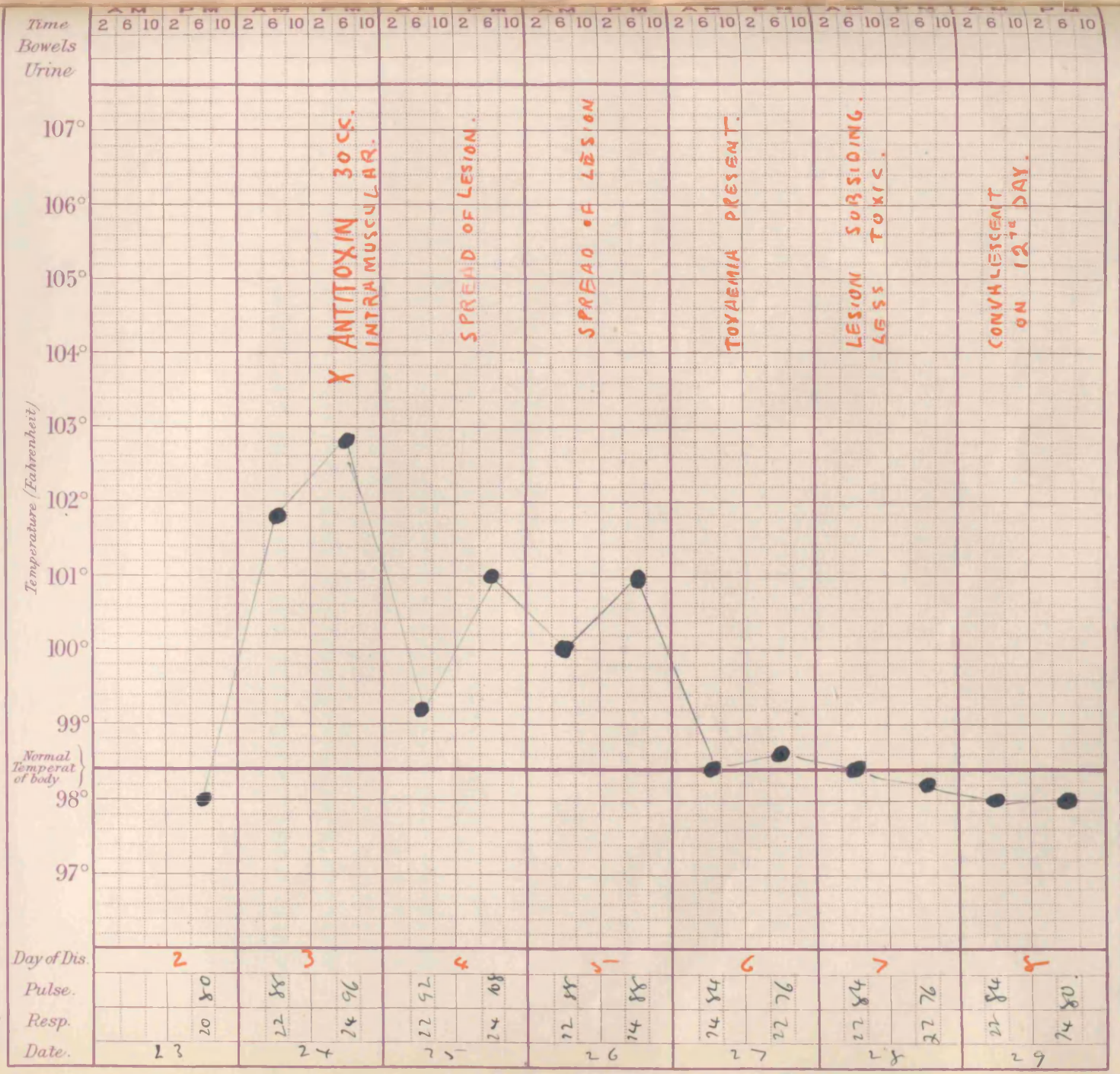
Diet:

Case Book No. 22.

Notes of Case

Date of admission
23RD SEPT. 1928.

Result WELL.



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CASE NO. 22.

NAME. R.H.

AGE. 52 years.

TYPE. Idiopathic.

CLINICAL NOTES. Moderately ill: T.102^{8}. P.96. R.24. (3rd day)
24 hours after serum. T.101. P.108. R.26. (4th day)
48 hours after serum T.101. P.88. R.24. (5th day)
72 hours after serum T.98^{7}. P.88. R.24. (6th day)

LESION. Bilateral facial erysipelas (intense.)

TOXAEMIA. Well marked by headache (severe) and by dry tongue and sordes: still toxic on 6th day.

COMPLICATIONS. Nil.

SERUM. Scarlet Fever Antitoxin (P.D. & Co.) 30 c.c. intramuscularly.

RESULT. Not very satisfactory.

REMARKS. Illustrating the lessened value of the (P.D. & Co.) brand of serum.

4 HOUR CHART.

DISEASE.

ERYSIPELAS (TRAUMATIC.)

Name JOHN CONNELLY

Age 38 YRS.

Diet

Case Book No. 64

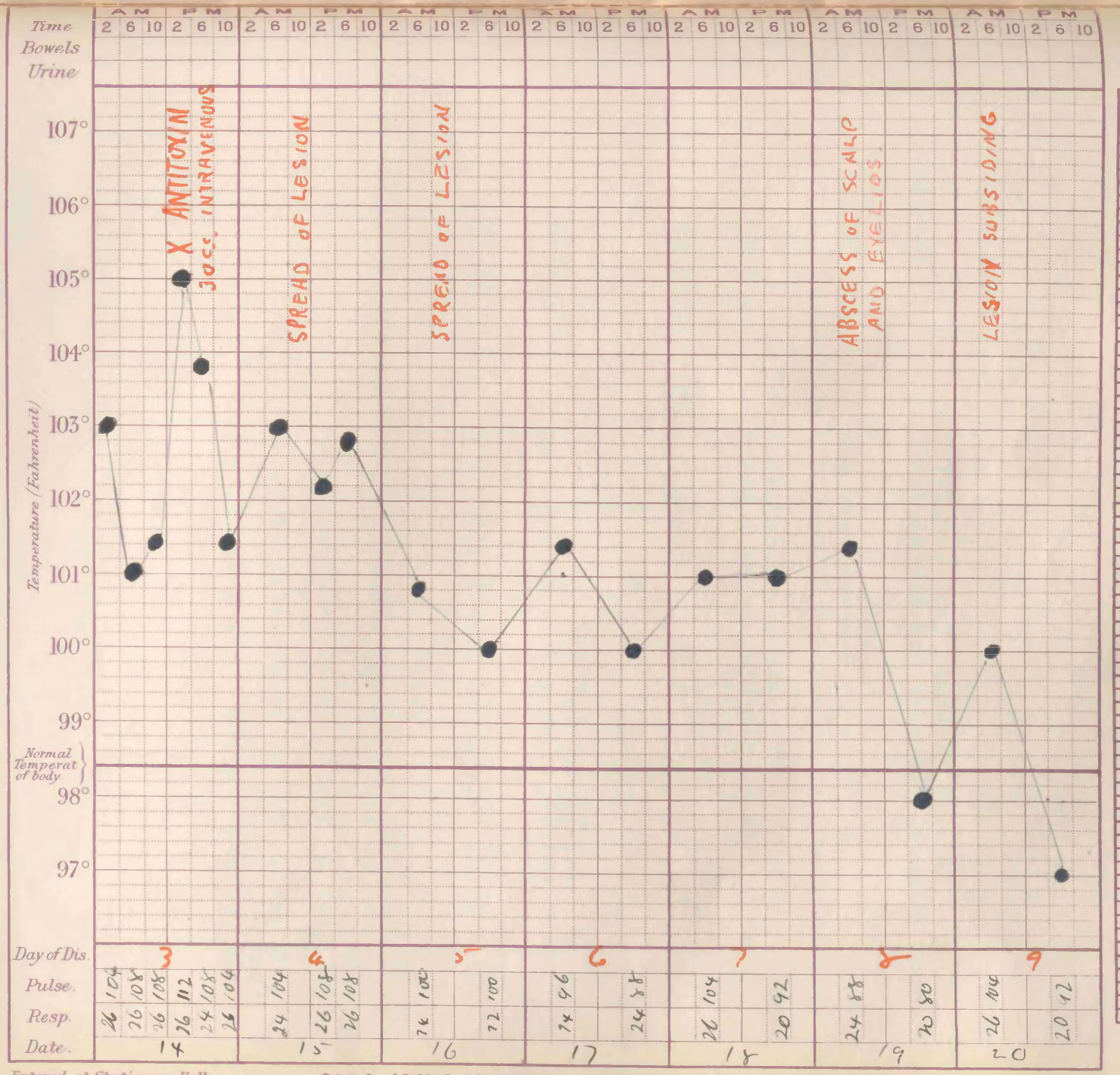
Notes of Case

ADRENALIN MI BEFORE SERUM.

NO RIGOR

Date of admission 14TH APRIL 1929

Result WELL.



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CASE NO. 64.

NAME. J.C.

AGE. 38 years.

TYPE. Traumatic.

CLINICAL NOTES. Acutely ill. Scalp wound septic.

Before serum T.105. P.112. R.26.
24 hours after serum T.102^{2}. P.108. R.26.
Irregular pyrexia until 12th day of illness.

LESION. Bilateral facial and scalp erysipelas not influenced by serum therapy.

TOXAEMIA. Headache severe: tongue very dry and furred. Delirium marked: toxaemia present 6 days.

COMPLICATIONS. Abscesses of scalp and eyelids.

SERUM. 30 c.c. Scarlet Fever Antitoxin (P.D. & Co.) intravenously.

RESULT. Definitely unsatisfactory.

REMARKS. Case of acute erysipelas of face treated by (P.D. & Co.) type of serum without beneficial effects.

DISEASE.

ERYSIPELAS (IDIOPATHIC.)

Notes of Case.

Name MRS ESTHER BOLSON.

Age 50 YRS.

Diet

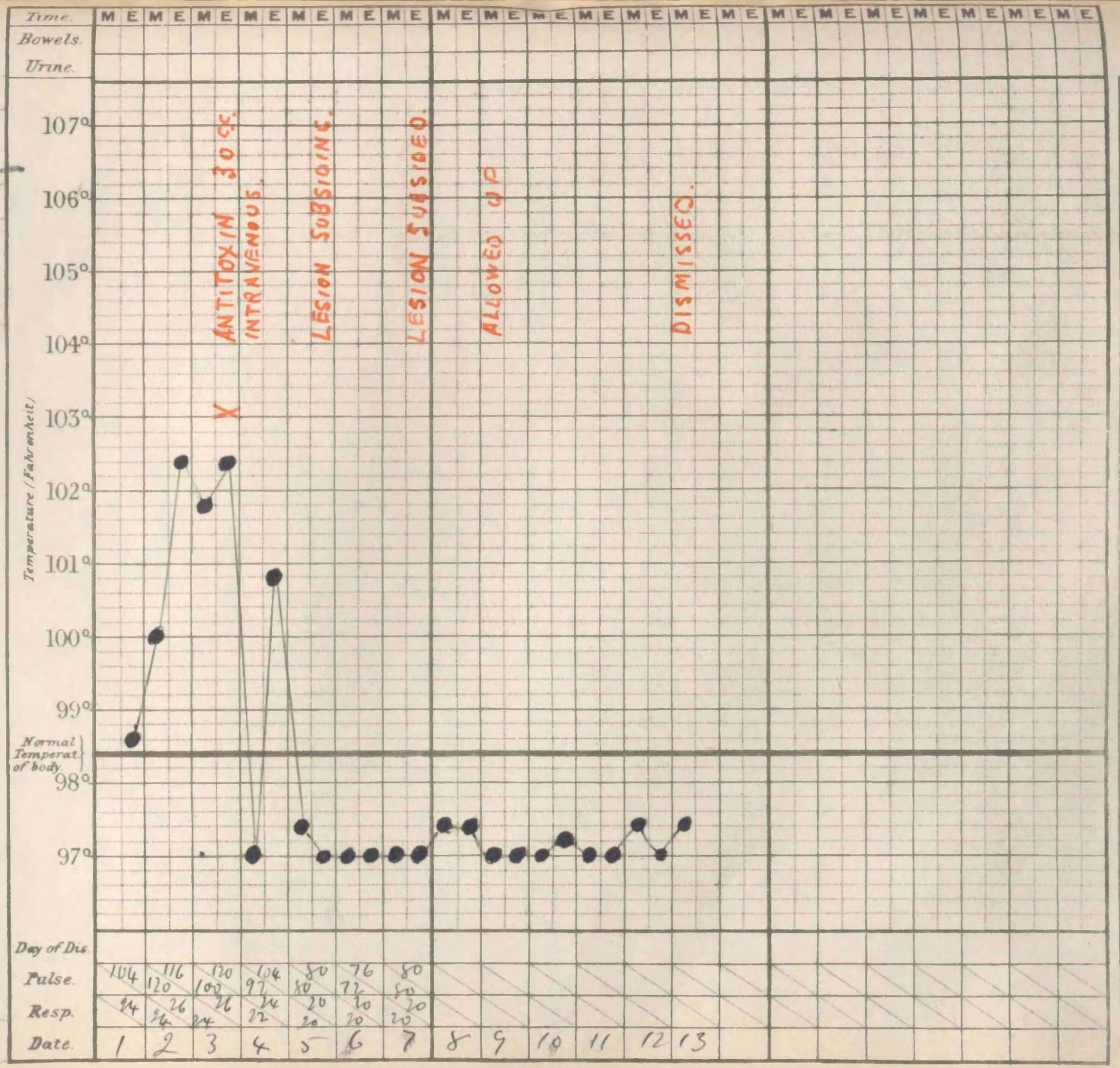
Case Book No. 168

ADRENALIN MV BEFORE SERUM.

RIGOR 45 MINS. AFTER SERUM.

Date of admission. 1ST MAY 1929

Result WELL.



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CASE NO. 168.

NAME. E.B.

AGE. 50 years.

TYPE. Idiopathic. (Primary)

CLINICAL NOTES. Acutely ill: T.102^4. P.116. R.26. before serum.
36 hours after serum T. 97. P. 92. R.22.

LESION. Extensive lesion affecting both cheeks, nose and forehead: slight spread after serum therapy.

TOXAEMIA. Moderate on admission on 2nd day of illness: very much increased by 3rd day of illness.

COMPLICATIONS. Nil.

SERUM. 30 c.c. Scarlet Fever Antitoxin (P.D. & Co.) intravenously.

RESULT. Rigor $\frac{3}{4}$ hour after serum. Crisis within 36 hours. Post critical elevation of temperature 5th day. Lessening of toxaemia and partial subsidence of lesion within 48 hours.

REMARKS. Case of acute erysipelas of face with toxaemia which responded satisfactorily to Scarlet Fever Antitoxin (P.D. & Co.) intravenously.
(Exception to the rule with this type of serum.

SUMMARY OF RESULTS.

Two tables have been prepared to summarise the results of the clinical investigations on serum therapy in erysipelas. The total number of cases treated was 178 which included 5 cases moribund on admission to hospital and 12 cases in which the erysipelas was essentially an intercurrent infection or superimposed on some other pathological condition.

Table A. shows the Age Groups, the number of cases and of deaths in each group.

The mortality figure of 10.1% is thus not corrected in any way but is inclusive of all deaths of patients receiving serum therapy even when admitted to hospital in a moribund condition.

Table B. has been prepared to summarise the results of the serum therapy investigation and shows the apparent outstanding value of Scarlet Fever Antitoxin (B.W. & Co.) as a therapeutic measure.

In estimating the beneficial results obtained, due consideration has been given to the effects of the serum on the pyrexia, the circulation, the toxaemia and the lesion; also on complications and recurrences.

TABLE A.

RESULTS OF SERUM THERAPY IN ERYSIPELAS.

MORTALITY RATE 10.1%

AGE GROUPS IN YEARS	NUMBER OF CASES	NUMBER OF DEATHS.
0 - 10	4	-
10 - 20	13	-
20 - 30	29	2
30 - 40	22	1
40 - 50	52	3
50 - 60	39	6
60 - 70	15	5
70 - 80	4	1
over 80	-	-
TOTAL	178	18

TABLE B.

RESULTS OF SERUM THERAPY IN ERYSIPELAS.

METHOD	SERUM	NUMBER OF CASES	RESULTS.					
			Ex.	V.G.	G.	F.G.	N.G.	DIED.
Intradermal	Various	10	-	-	-	-	10	-
Intramuscular	P.A.S.	12	-	-	1	-	11	-
"	A.D.S.	3	-	-	-	-	3	-
"	S.F.A.(P.D.)	10	-	1	-	-	6	3
"	S.F.A.(B.W.)	41	-	26	9	4	-	2
"	E.A.	5	-	-	-	-	5	-
Intravenous	P.A.S.	3	-	-	-	-	3	-
"	E.A.	15	-	-	2	4	7	2
"	S.F.A.(P.D.)	6	-	1	-	-	4	1
"	S.F.A.(B.W.)	73	34	16	9	4	-	10
		178	34	44	21	12	49	18

Key to above Table.

Serum.
- P.A.S. = Polyvalent Antistreptococcic Serum.
- A.D.S. = Antidiphtheritic Serum.
- S.F.A.(P.D.) = Scarlet Fever Antitoxin (Parke Davis & Co.)
- S.F.A.(B.W.) = " " " (Burroughs Wellcome & Co.)
- E.A. = Erysipelas Antitoxin (Parke Davis & Co.)

Results.
- Ex. = Excellent beneficial results.
- V.G. = Very Good. " "
- G. = Good " "
- F.G. = Fairly Good " "
- N.G. = No Good " "

OTHER FEATURES OF THE INVESTIGATION.

I. BACTERIOLOGY.

During the clinical investigations on serum therapy some of the bacteriological aspects were studied. The work consisted of the isolation of the organism of erysipelas, the preparation of the erysipelas toxin and the experimental use of the toxin as a skin test of susceptibility to the disease. This latter test is now known as the Birkhaug skin test in Erysipelas.

(A) THE ISOLATION OF THE CAUSAL ORGANISM OF ERYSIPELAS.

It was decided to make attempts to obtain cultures from various sources possibly containing the organism of Erysipelas. These sources were as follows:-

(1) The spreading margin of the erysipelas lesion.
(2) The pus of a residual erysipelas abscess.
(3) The blood of patient with active erysipelas.
(4) The desquamated skin of the erysipelas lesion.
(5) The fluid from the vesicles or bullae of erysipelas.

TECHNIQUE AND METHODS.

All technique and methods were adapted from

(1) Mannual of Bacteriology (Muir & Ritchie).
(2) Introduction to Practical Bacteriology (Mackie & McCartney).

During the bacteriological investigations the following media were used and were prepared fresh as required.

(1) Tryptic digest broth (21 days)
(2) Tryptic digest Agar.
(3) Hartley's broth.
(4) Blood Agar.

The fluid media were prepared for all primary inoculations and the solid media were used for subcultures.

PREPARATION OF MEDIA.

(1) Tryptic Digest (21 days).

(1) Fresh horse heart..... 1 lb meat.
(2) Add 1,000c.c. water.
(3) Render alkaline with 4% Na O H.
(4) Heat in Koch steriliser at 80°C. for 30 mins.
(5) Add 20 c.c. trypsin.
(6) Add 40 c.c. chloroform.
(7) Incubate at 37°C for 10 days.
(8) Add 20 c.c. trypsin.
(9) After 10th day of incubation, test reaction of medium daily with litmus paper and add 4% NaO.H. as required to keep the mixture alkaline.

(2) Digest Agar (21 days).

(1) Tryptic digest (21 days) ..... 800 c.c.
(2) Add Na.Cl. 0.25% ..... 4 gm.
(3) Add Agar fibre 3% ..... 24 gm.
(4) Dissolve at 115°C for 20 minutes.
(5) Render slightly alkaline while hot with $\frac{N}{1}$ Na.O.H.
(6) Cool medium to 40°C under tap water.
(7) Add white of an egg to 1 litre of medium, to clarify same.
(8) Put medium in Koch steriliser for 2 hours.
(9) Filter in steamer through Chardin paper.
(10) Tube the medium and sterilise same repeatedly as required.

(3) Hartley's Broth.

(1) Horse heart muscle (minced and fat free) ..... 150 gm.
(2) Tap water ..... 250 c.c.
(3) Heat in steamer to 80°C.
(4) Add 0.8% sodium carbonate (Anhydrous) ..... 250 c.c.
(5) Cool down to 45°C.
(6) Add chloroform ..... 5 c.c.
(7) Add pancreatic extract ..... 5 c.c.
(8) Incubate mixture at 37°C for 6 hours.
(9) Add 40 c.c. normal H.Cl. and heat in the steamer for 30 minutes.
(10) Cool medium and filter.
(11) Adjust reaction to pH. 7.6.
(12) Sterilise finally in Autoclave.

N.B. In step (7) the Pancreative Extract used was prepared from fresh pig pancreas.

(4) Blood Agar.

This medium was prepared according to method described by Muir & Ritchie, the blood being obtained by vein puncture from convalescent pneumonia patients.

CULTURAL METHODS.

The primary inoculations were made into both Tryptic digest and Hartley's broth and the cultures were incubated at 37°C. These were examined after 24 hours and again after 48 hours incubation.

Subcultures were made on Tryptic digest Agar and on Blood Agar plates.

STAINING METHODS.

Smears were prepared from the cultures and were stained by Gram's method prior to microscopical examination.

SPECIAL TECHNICAL METHODS.

(1) In the case of the experimental isolation of the erysipelas organism from the acute lesion, the method adopted was that of cleansing the skin with pure ether and scarification of the spreading margin of the lesion. This scarification was performed with a small sterilised scarifier at right angles to the spreading margin thus including the area of skin just beyond the actual margin. Inoculation of fluid medium was then made from the exuding blood serum which would contain some exudation from the ruptured lymphatic channels of the skin.

(2) The isolation of organisms from pus of residual abscesses/

abscesses of erysipelas was carried out according to the technique of Muir & Ritchie.

(3) Blood cultures were made from patients suffering from acute and active erysipelas lesions. The technique employed was that of Muir & Ritchie.

(4) Isolation of organisms from the desquamated skin of an erysipelas lesion was performed by transferring the skin direct to fluid medium.

(5) The inoculation of fluid medium with fluid from the vesicles and bullae of an active erysipelas lesion was performed by cleansing the surface with pure ether and then by careful puncture by means of a fine skin testing needle fitted to a small hypodermic syringe which had been carefully sterilised.

RESULTS.

After some preliminary attempts accompanied by many failures the various methods of technique were finally perfected and the isolation of organisms from the various sources was attempted from time to time as suitable cases presented themselves for admission to the wards of the hospital.

(1) Haemolytic streptococci were isolated from the spreading margin of the erysipelas lesion in 38 cases of Primary Idiopathic or Traumatic erysipelas. The result-

resulting growth in 2 other cases was staphylococcus aureus while 10 cases of Recurrent Facial Erysipelas exhibited no growth after 72 hours incubation of cultures.

(2) In twenty cases the pus from residual abscess formation was examined and found to contain the streptococci. On culture, the organisms were obtained in pure culture in 18 cases, but in 2 cases the predominating organism proved to be staphylococcus aureus, although a few colonies of streptococci were observed on subculture but died out rapidly.

(3) Blood cultures were made by vein puncture from 12 patients suffering from erysipelas: prolonged incubation resulted in 10 negative results while 2 cultures were found to be contaminated.

(4) All attempts to isolate organisms of the streptococcal group from squama proved quite unsuccessful.

(5) The isolation of organisms from the fluid of the vesicles or bullae in active erysipelas lesions was attempted in 20 cases of facial or corporal erysipelas. Haemolytic streptococci were obtained in culture only on 3 occasions.

TABLE C.

RESULTS OF CULTURES IN ERYSIPELAS.

NUMBER OF CASES.	MEDIUM.	ORIGIN	RESULT.
25.	Tryptic Digest Broth.	Spreading Margin.	Haemolytic streptococci.
13.	Hartley's Broth.	do. do.	do. do.
2.	Tryptic Digest Broth.	do. do.	Staphylococcus Aureus.
6.	do. do. do.	do. do.	No Growth.
4.	Hartley's Broth.	do. do.	No Growth.
15.	Tryptic Digest Broth.	Residual Abscess	Haemolytic Streptococci.
3.	Hartley's Broth.	do. do.	do. do.
2.	do. do.	do. do.	Staphylococcus Aureus.
10.	Bouillon.	Blood.	No Growth.
2.	do.	do.	Contamination.
15.	Tryptic Digest Broth.	Desquamation.	Staphylococci.
5.	Hartley's Broth.	do.	do.
10.	Tryptic Digest Broth.	Vesicular Fluid.	Haemolytic Streptococci. (3 Cultures).
10.	Hartley's Broth.	do. do.	No Growth.

B. PREPARATION OF TOXIN.

The preparation of erysipelas streptococcal toxin was undertaken for the subsequent experimental skin tests.

This was done by isolating the organism in pure culture from the spreading margin of the lesion exhibited by a young male adult with acute facial idiopathic erysipelas. The primary inoculation was made in Hartley's broth and resulted in a pure growth of short chained cocci which on subculture on blood agar plates exhibited well marked haemolytic reaction.

This organism proved to be highly virulent for mice which are accepted as somewhat insusceptible to the streptococci; the intraperitoneal injection of 1 c.c. of the primary fluid culture after 24 hours incubation at 37°C resulted in the death of a white mouse (No. 11). After 48 hours incubation at 37°C the culture was tested again; a series of 5 mice were each given by intraperitoneal injection 1 c.c. of the 48 hours old streptococcal culture while a control series of 5 mice each were injected intraperitoneally with 1 c.c. of sterile Hartley's broth.

The control series remained healthy while the mice died as follows:-

Mouse/

Mouse No. 12
" " 13

Mouse No.	12.	Died 2nd Day.
" "	13.	Died 4th Day.
" "	14.	Died 2nd Day.
" "	15.	Died 5th Day.
" "	5.	Died 6th Day.

The cause of death of Mouse No. 11. appeared to be from a rapidly fatal septicaemia while the virulence of the organism was high.

This virulence appeared to be lost quite definitely after the organism was incubated in fluid culture medium for the further period of 24 hours as the series of mice subsequently tested died of a sub acute septicaemia mainly characterised by prostration and diarrhoea.

Examination of the organisms of the 48 hours incubation proved them culturally and morphologically to be haemolytic streptococci and a subculture was then made into a flask of Hartley's broth (p.H 7:6.) This flask was frequently agitated and the culture incubated for 72 hours. This broth culture was subsequently passed through a Berkefeld filter and the toxin filtrate used for skin testing experiments.

The toxin was preserved by the addition of 0.5% phenol.

This toxin will be referred to as Toxin (R).

As a means of control half the toxin was boiled for 1 hour (Toxin C) while all the experiments were repeated using Erysipelas. Streptococcus Toxin prepared in Parke Davis/

Davis Research Laboratory in Detroit. This toxin will be referred to as Toxin (D).

(2) SKIN TESTING EXPERIMENTS.

Birkhaug has described the skin reaction to Erysipelas streptococcal injection intradermally and his name has been assigned to the erysipelas susceptibility test similar to the Dick and Schick tests in Scarlet Fever and Diphtheria.

Prior to performing the Birkhaug tests on patients the potency of Toxin (R) and of Toxin (D) was tested by animal inoculation. A series of mice were injected intraperitoneally with varying quantities of Toxin but all mice were unaffected. (Table D).

RESULTS OF EXPERIMENTAL INOCULATION OF MICE FOR POTENCY OF TOXIN OF STREPTOCOCCUS ERYSIPELAS.

TABLE D.

MOUSE NUMBER.	AMOUNT OF TOXIN.	TYPE OF TOXIN	RESULT AFTER 7 DAYS.
21.	0.001 c.c.	Toxin (D)	Alive.
22.	0.005 c.c.	Toxin (D)	Alive.
23.	0. 05 c.c.	Toxin (D)	Alive.
24.	0. 5 c.c.	Toxin (D)	Alive.
25.	5. c.c.	Toxin (D)	Alive.
26.	0.001 c.c.	Toxin (R)	Alive.
27.	0.005 c.c.	Toxin (R)	Alive.
28.	0. 05 c.c.	Toxin (R)	Alive.
29.	0. 5 c.c.	Toxin (R)	Alive.
30.	5. c.c.	Toxin (R)	Alive.

Two rabbits, however, receiving 0.5 c.c. of toxin intravenously both suffered from temporary malaise lasting two and three days respectively . (Table E).

As a control a third rabbit was injected with a similar amount of Toxin (c) and exhibited no abnormal signs of disturbance as a result of the experiment.

RESULTS OF EXPERIMENTAL INOCULATION OF RABBITS FOR POTENCY OF TOXIN OF STREPTOCOCCUS ERYSIPELAS.

TABLE E.

RABBIT NUMBER.	AMOUNT OF TOXIN.	TYPE OF TOXIN.	RESULT.
3.	0.5 c.c.	Toxin (D)	Malaise (2 DAYS.)
4.	0.5 c.c.	Toxin (R)	Malaise (3 DAYS.)
5.	0.5 c.c.	Toxin (C)	No effect.

The potency of the toxins was next tested by intradermal injection in a rabbit. A young rabbit was shaved over the abdomen and flanks and the skin cleansed thoroughly with ether. The injections of both Toxin (D) and Toxin (R) were made intradermally, the amounts being 0.01 c.c. of each toxin, while a similar quantity of toxin (C) was injected as a control. Both Toxin (R) and Toxin (D) produced in 24 hours a faint but quite definite circular area of erythema measuring about 1 cm. in diameter. After 48 hours these skin reactions were more clearly defined and faded thereafter leaving no observable staining and no desquamation.

The first experiment with erysipelas patients was conducted on a series of 50 cases of erysipelas of various types and at different stages of the illness. These patients were first subjected to the Dick test and subsequently to the Birkhaug test, both (R) and (D) toxins being used and the heated toxins used as a control, toxin (C).

Technique.

The streptococcus erysipelatis toxins were made up in dilutions of $\frac{1}{1000}$ and the amount injected in each case was 0.1 c.c. This amount was injected intradermally into the skin of the left forearm by means of a fine skin testing needle and syringe. The control injection was made into/

into the skin of the right forearm and the results were examined 12 hours, 24 hours, 48 hours and 72 hours later. The reaction of an erythematous area with a minimum diameter of one centimeter was considered positive. The following table shows the results with a faint positive reaction being indicated by a plus mark (+) definite positive by double plus (++), a marked positive reaction by three plus marks (+++) and a fading reaction by the positive mark followed by a minus sign e.g. (+ -).

All Dick tests were performed by using Dick Toxins supplied by Borroughs, Wellcome & Co. and the same technique as for Birkhaug Tests.

Results of Birkhaug Tests,

Using Toxin (D) , in Erysipelas.

TABLE F.

Patient.	Day of Illness of Erysipelas.	Dick Test Result.	Birkhaug Test.			
			12 Hrs.	24 Hrs.	48 Hrs.	72 Hrs.
No. 1.	2	-	+	+ + +	+ + -	+ -
2.	6	-	-	+	+	+
3.	4.	-	-	+ +	+ +	+ -
4.	14	-	-	+	+ -	-
5.	11	-	-	-	-	-
6.	10	-	-	-	-	-
7.	4	-	-	+ +	+ +	+ -
8.	2	-	+	+ + +	+ + -	+ -
9.	3	-	+	+ + +	+ + -	+ -
10.	12	-	-	-	-	-
11.	6	-	-	+ +	+ -	-
12.	4	-	-	+ +	+ -	+ -
13.	18	-	-	+	+	+ -
14.	15	-	-	+	+	+
15.	9	-	-	-	-	-
16.	12	-	-	-	-	-
17.	5	-	-	+ +	+ +	+ -
18.	14	-	-	+	+	+ -
19.	4	-	-	+ + +	+ + -	+ -
20.	11	-	-	-	-	-
21.	12	-	-	-	-	-
22.	21	-	-	+	+	+ -
23.	10	-	-	-	-	-
24.	7	-	-	+ +	+ -	-
25.	2	-	+	+ + +	+ + -	+ -

RESULTS OF BIRKHAUG TESTS USING TOXIN (R) IN ERYSIPELAS.

TABLE G.

PATIENT	DAY OF ILLNESS OF ERYSIPELAS.	DICK TEST RESULT.	BIRKHAUG TEST			
			12 Hrs.	24 Hrs.	48 Hrs.	72 Hrs.
No. 26.	3	-	-	+ +	+ +	+ -
27.	14	-	-	+	+	+ -
28.	11	-	-	-	-	-
29.	4	-	-	+ +	+ -	+ -
30.	13	-	-	+	+ -	-
31.	14	-	-	+	+ -	+ -
32.	5	-	-	+ +	+ -	+ -
33.	13	-	-	+	+	+ -
34.	4	-	-	+ +	+ -	+ -
35.	5	-	-	+	+	+ -
36.	10	-	-	-	-	-
37.	14	-	-	+	+	+ -
38.	11	-	-	-	-	-
39.	7	-	-	+	+	+ -
40.	2	-	+	+ + +	+ + +	
41.	13	-	-	+	+	+ -
42.	7	-	-	+	+	+ -
43.	3	-	-	+ +	+ +	+ -
44.	9	-	-	-	-	-
45.	6	-	-	+	+ -	+ -
46.	6	-	-	-	+	+ -
47.	10	-	-	-	-	-
48.	2	-	+ +	+ + +	+ + +	+ + -
49.	7	-	-	+	+	+ -
50.	11	-	-	-	-	-

With the same toxins the Birkhaug test was performed on a number of male pneumonia patients including 7 boys; some of the cases were ill, some were convalescent.

RESULTS OF BIRKHAUG TEST AND DICK TESTS IN PNEUMONIA PATIENTS USING TOXIN (D)

TABLE H.

NUMBER OF PATIENTS.	HISTORY OF SCARLETINA.	RESULT OF DICK TEST.	HISTORY OF ERYSIPELAS.	RESULT OF BIRKHAUG TEST.
3.	+	-	-	-
20.	-	-	-	-
2.	-	+	-	+
2.	-	-	+	+

A series of cases of Scarlet Fever at different stages of the illness were treated with the same erysipelas Toxin using Toxin (R) and in all cases the Birkhaug Test proved positive.

RESULTS OF BIRKHAUG TEST AND DICK TESTS IN SCARLET FEVER PATIENTS USING TOXIN (R)

TABLE K.

NUMBER OF PATIENTS.	HISTORY OF ERYSIPELAS	BIRKHAUG TEST.	DICK RESULT.
15.	-	+	+
7.	-	+	-

SKIN TESTS IN ERYSIPELAS USING TOXIN AND ANTITOXIN MIXTURES.

A series of skin tests was subsequently performed on erysipelas patients at all stages of the illness using mixtures of (1) Erysipelas Streptococcus Toxin (D) and Concentrated Scarlet Fever Antitoxin (P.D. & Co.)

(2) Erysipelas Streptococcus Toxin (D)

and

Concentrated Scarlet Fever Antitoxin (B.W. & Co.)

(3) Erysipelas Streptococcus Toxin (D)

and

Concentrated Erysipelas Antitoxin (P.D. & CO.)

(4) Erysipelas Streptococcus Toxin (D)

and

Convalescent Erysipelas Serum.

TECHNIQUE.

The mixture of Toxin (D) $\frac{1}{1000}$ and equal quantities of the various sera were prepared in sterile ampoules just immediately before use. The three types of antitoxin are those prepared on a commercial basis by well known drug firms.

The convalescent erysipelas serum was prepared by vein puncture of a case of erysipelas on the 10th day of the/

the illness, the patient being a male adult suffering from primary idiopathic erysipelas. The technique of the intradermal injections was similar to all preceding skin tests

RESULTS OF SKIN TESTS IN ERYSIPELAS USING TOXIN ANTITOXIN MIXTURES.

A. Mixture: Erysipelas Toxin and Scarlet Fever Antitoxin (P.D.&.Co.)

TABLE L.

NUMBER OF PATIENTS.	RESULT OF BIRKHAUG TEST	RESULT OF DICK TEST.	RESULT OF SKIN TEST USING MIXTURE.
10.	+	-	+

B. Mixture: Erysipelas Toxin and Scarlet Fever Antitoxin (B.W.&.Co.)

TABLE M.

NUMBER OF PATIENTS.	RESULT OF BIRKHAUG TEST	RESULT OF DICK TEST	RESULT OF SKIN TEST USING MIXTURE.
5.	+	-	-
8.	+	-	+ (Faint)
7.	+	-	+ (Moderate)

C. Mixture: Erysipelas Toxin and Erysipelas Streptococcus Antitoxin (prepared by Parke, Davis & Co.)

TABLE N.

NUMBER OF PATIENTS	RESULT OF BIRKHAUG TEST	RESULT OF DICK TEST	RESULT OF SKIN TEST USING MIXTURE.
2.	+	+	+
18.	+	-	+

D. Mixture: Erysipelas Toxin and convalescent Erysipelas serum.

TABLE O.

NUMBER OF PATIENTS.	RESULT OF BIRKHAUG TEST	RESULT OF DICK TEST	RESULT OF SKIN TEST USING MIXTURE.
1.	+	+	-
19.	+	-	-

INTERPRETATION OF RESULTS OF SKIN TESTING EXPERIMENTS.

The few experiments performed and the few cases tested in each experiment are perhaps inadequate on which to make definite conclusions but it would appear from the results obtained in this investigation that the toxin of erysipelas streptococcus causes a skin reaction in patients who are susceptible to erysipelas quite similar to the Dick reaction in Scarlet Fever and Schick reaction in Diphtheria. It would appear from table F and G that the Birkhaug test is strongly positive during the first few days of erysipelas and becomes negative from the 9th to the 12th day after which the reaction again becomes positive. From Table H. it appears that most adults are insusceptible to erysipelas but it is interesting to observe the positive reaction in two boys susceptible to Scarlet Fever (Dick+) and also two adults with a previous history of erysipelas. The results shown in Table K appear to indicate the susceptibility of Scarlet Fever patients to Erysipelas.

The results of skin tests in erysipelas patients using toxin antitoxin mixtures is interesting from the therapeutic point of view as additional evidence to the clinical investigations on serum therapy.

It is somewhat unexpected to find that the supposed specific erysipelas streptococcus antitoxin will not

not (Table N) neutralise an erysipelas toxin as shown by skin reactions.

There is some evidence to show that the Scarlet Fever Antitoxin does not neutralise the erysipelas toxin although the Antitoxin (B.W. & Co.) appears to have (See Table M.) some neutralising power.

The convalescent serum however is the most potent serum available as evidenced by the results of skin tests. (See Table O)

III. TRANSMISSION OF ERYSIPELAS TO ANIMALS.

During the studies of the bacteriology of erysipelas it was decided to endeavour to transmit to animals the erysipelatous skin infection from an active lesion in man.

The strain of virulent streptococci from which Toxin (R) was prepared was used as the infecting agent and three rabbits were used. The animals were shaved and the skin over the flanks cleaned thoroughly. From a subculture on Blood Agar a fine streptococcal suspension was prepared with sterile saline (0.9%). Three intradermal injections were made into the flank of each rabbit, the doses being 0.001 c.c., 0.01 c.c., 0.1. c.c., respectively. Into the opposite flanks was injected sterile saline intradermally in similar amounts.

The results of these experiments are reasonably interesting/

Rabbit No. 1. was unfortunately not properly controlled during the skin . injection and it appeared rather doubtful as to the actual injection being intradermal.

This rabbit showed three red areas of inflammation 24 hours later which rapidly became the size of sixpenny pieces and became coalescent in 48 hours. This was accompanied by malaise and latterly a phlegmonous condition became apparent but quietened down in about 6 days time leaving only a small scar.

Rabbit No.2 however developed three typical erysipelatous areas measuring 1. cm. in diameter after 24 hours. The lesion caused by the largest injection of infective material however rapidly became very acute and actively spread over the flank towards the back and across the abdomen of the rabbit.

In 48 hours the two other small lesions were submerged in the general erysipelatous lesion of the abdomen. The lesion was quite typical of ordinary erysipelas as seen in man, having an angry red appearance, hot to touch, and having quite an appreciable raised margin at the spreading edge. This lesion did not appear to cause much general constitutional disturbance after the first two days and began to subside on the fifth day. Quite appreciable desquamation was observed from the 11th. day onwards and the hair/

hair over the flanks took over 6 weeks to grow in again.

Rabbit No. 3 developed (as No. 1.) small phlegmonous lesions which rapidly coalesced.

CONCLUSIONS.

The results of the investigations on serum therapy in Erysipelas appear to justify the following conclusions:-

(1) Serum therapy as an efficacious measure in Erysipelas is confined to the use of Scarlet Fever Antitoxin (B.W.& Co) which administered early in the course of Erysipelas has a definite effect on the subsequent course of the illness.

(2) Scarlet Fever Antitoxin (B.W.& Co), when used as a therapeutic measure in Erysipelas precipitates an early crisis, within from 24-48 hours generally, accompanied by a definite elimination of toxaemia and a varying degree of subsidence of the Erysipelatous lesion.

(3) The time of the administration of antitoxin and the amount of serum used, together with the method of administration are the factors which have a definite relationship to the immediate and remote effects of serum therapy in Erysipelas.

(4) Scarlet Fever Antitoxin (B.W.& Co), when used as a therapeutic agent in Erysipelas minimises complications of the disease but does not prevent relapses or recurrences.

(5) There appears to be no specific antitoxic properties in the so-called Erysipelas Antitoxin (P.D.& Co), while the value of Diphtheria Antitoxin and of Polyvalent antistreptococcal Serum appears to be negligible.

From/

From the clinical results of the investigations the value of Scarlet Fever Antitoxin (B.W.& Co) is very much greater than Scarlet Fever Antitoxin (P.D.& Co).

(6) The Streptococcus of Erysipelas can readily be isolated from many cases of the disease by the use of special medium and technical methods.

(7) The toxin of the Streptococcus of Erysipelas can be used by intradermal methods to indicate susceptibility of the individual to Erysipelas.

(8) Transmission of the Erysipelas lesion from man to rabbits is possible but requires very careful technical methods.

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DISCUSSION.

Prior to the epidemic of Scarlet Fever in 1926, the serum treatment of Scarlatinal patients in the City of Glasgow Corporation Fever Hospital at Ruchill was confined to the use of Polyvalent Antistreptococcal Serum and to Convalescent Serum (Human).

The treatment by polyvalent antistreptococcic serum was used mainly in cases of Scarlatina Anginosa in an endeavour to neutralise the effects of the septic complications present in such cases.

Human serum removed from convalescent patients on the 10th day of the disease by vein puncture of the arm had been used prior to 1926 occasionally but only proved really efficacious when the dosage was large: in consequence of the obvious difficulties of obtaining the necessary large amount of convalescent serum for one therapeutic dose, the application of human convalescent serum therapy on a large scale is definitely out of the question. The investigations, therefore, in the light of previous serum therapy in Scarlatina, were in the nature of clinical research on the value of Scarlet Fever Streptococcus Antitoxin as a therapeutic measure in Scarlatina.

It is admitted, in the first place, that the rationale of the use of this serum presupposes a definite aetiological factor/

factor, namely the Haemolytic Streptococcus of Scarlet Fever. The modern views of the American School and of our own workers in this country appear to support the streptococcal theory rather than the Italian theory of a filterable virus as the causal organism.

Finally, the publication in 1929 of the results of four years of experimental researches on the Etiology of Scarlet Fever by Toyoda, Moriwaki and Futagi (1) in Dairen, Manchuria has brought to light many hitherto doubtful and unexplained points and difficulties in the streptococcal theory and on critical examination leaves little doubt now on the subject.

During the investigations the routine treatment of patients suffering from Scarlet Fever was not altered in any way and the technical difficulties of serum administration were not great. Criticism may be made on the selection of cases as all the really ill patients during the epidemic were treated by serum therapy thus leaving no control cases.

From the statistical point of view this selection of cases must necessarily be ill-judged, but the extraordinary value of the new serum became very obvious from the early days of the investigation and as a result the serum was not withheld from patients who were sufficiently ill to indicate that benefit would accrue from serum therapy. Thus the easy and often accepted method of obtaining control cases was not used in this investigation.

However/

However, the general control of the investigation was obtained from a clinical comparison of the lengths of the pyrexial periods, of the lengths of time of actual discomfort of the patients, of the amounts of actual nursing and of the response to such, of scarlet fever patients, before and after the introduction of serum therapy.

Moreover the fact that the use of the serum has been generally adopted in the treatment of Scarlatina since this initial investigation is of more importance from the clinician's point of view than the presentation of statistics of control cases.

Since 1926 the Scarlet Fever Streptococcus Antitoxin has been consistently relied on in many epidemics and the type of serum which tends to be especially useful in Glasgow is made by one particular firm (P.D.& Co). It is possible that the strain of organism used by the manufacturers of the serum in its preparation is the fundamental reason for this tendency. The use of the serum is attended with no untoward results under ordinary circumstances and judging by the results obtained, the Scarlet Fever Streptococcus Antitoxin is an exceptionally fine addition to the armamentarium of modern science. Particularly is this so if one considers the use of this serum also in Erysipelas which manifests many clinical signs indicative of toxaemia which is assumed, and generally accepted

to/

to be due to a haemolytic streptococcus of the same group as the streptococcus of Scarlatina.

The fact that success in the local treatment of Erysipelas is seldom met with can be estimated, and easily proved by trial, if one considers the legions of much advertised and well recommended ointments, lotions and other preparations.

A preliminary investigation on topical therapy in Erysipelas has borne out this fact and there is nothing to be gained from Vaccine therapy according to Peters (2) and also recently to Benson (3).

The investigation on the value of serum therapy in Erysipelas assumes the haemolytic streptococcus to be the causal organism, and the severity of the illness due to the general absorption of toxins produced in the local erysipelatou lesion.

The results of this investigation are, if not altogether convincing, nevertheless exceedingly interesting, and indicate that at least one serum is worthy of trial in the treatment of Erysipelas. The use of Scarlet Fever Antitoxin (B.W.& Co) in Erysipelas appears to have a definite action which it must be admitted may be partly a non-specific protein reaction and partly an antitoxic effect. The other sera used during the investigation, according to observed results, did not appear to cause specific reactions or protein reactions. The

absence/

absence of any specific reaction from the use of so-called Erysipelas Streptococcus Antitoxin prepared by a reliable firm of manufacturers is rather unexpected but the results show that there appears to be a greater proportion of antitoxin in Scarlet Fever Antitoxin (B.W.& Co) which is capable of neutralising some at least of the Erysipelas toxins, than in the so-called Erysipelas Streptococcus Antitoxin. This appears to be relatively so even with Scarlet Fever Antitoxin (P.D.& Co) which, although highly satisfactory when used in Scarlatina, yet is undoubtedly according to the observed results of the investigation, of less value than Scarlet Fever Antitoxin (B.W.& Co) in the treatment of Erysipelas.

Thus the clinical findings point to the fact that the most potent antitoxin capable of neutralising toxins from the haemolytic group is the antitoxin prepared from scarlet fever streptococci. These clinical findings bear out the results of experimental work on this subject by Parish and Okell (4) and seem sufficient to warrant the use of Scarlet Fever Antitoxin (B.W.& Co) in the treatment of Erysipelas.

The incidental work on the bacteriology, serology, skin tests and animal experimental work is open to many criticisms and the work is admittedly rather on the small scale to be particularly convincing.

All the work, however, was performed under many clinical and/

and laboratory difficulties without the help of any laboratory attendant, which necessitated much valuable time being spent on certain matters reasonably included under the heading of "spade work". Under other circumstances this time might have been devoted to a more extensive and useful collateral investigation.

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