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THE THERAPEUTIC VALUE

OF

FORMIC ACID

IN

DIPHTHERIA

IN

- (I.) CARDIAC FAILURE
- (II.) PARALYSIS.
- (III.) ALBUMINURIA.

IN THREE PARTS.



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INTRODUCTION.

If, by the term Diphtheria, the derivation *διφθερα* were to be strictly adhered to, the diagnosis of the condition and its treatment would be simple, and the results relatively bad. The local condition and its treatment is, indeed, that part of the disease which, at the present time, gives rise to least anxiety and from which the death-rate is, in comparison, relatively low.

Trousseau.
Clinique
Médicale,
1861.

To Trousseau indeed, we owe much, who, first, gave to the term Diphtheria the meaning which we now attach to it, namely, a general constitutional affection and one causing death, not only mechanically, but by a general systemic toxaemia.

While the local condition - thanks to anti-toxine serum and the gradual perfection of Intubation and Tracheotomy - is not now regarded so gravely, far otherwise is it with the general condition - the result of the toxine.

Although the introduction of the serum treatment has been followed by results little short of extraordinary, the death-rate directly due to toxic absorption and the other minor results from the same cause, namely, degeneration of muscle and nerve causing paralysis or the toxic effects, as seen on the kidney with its consequent production of albuminuria, have by no means diminished in a corresponding degree.

Such is the truth of the above statement, namely, so low is the death-rate directly traceable to obstruction, that it would seem that, except for the introduction of a more powerful and more readily absorbed antitoxin serum, little more can be done in attacking that particular complication of the disease.

If the "obstruction treatment" appears perfect or nearly so, the Therapeutics at our command - apart from the administration of antitoxin serum - for dealing with the toxaemia must so far seem inadequate.

It would appear that, broadly speaking, a sufficiently powerful dose of antitoxine administered at a time so early in the course of the disease that the toxins are annulled before they can devitalise and cause degeneration in the tissues, is perfect treatment. Such probably is the case, but, so different is the resistant power in each individual that the correct antitoxic gauge is as yet indefinable and hence methods have yet to be perfected to aid the antitoxine by increasing otherwise the resistant power of the individual.

To do so has been the object of the present investigation.

DIPHTHERIA AS UNDERSTOOD IN THESIS.

By the term Diphtheria used in the diagnosis of the following recorded cases the definition accepted by Northup has been strictly adhered to, namely: "an infectious and communicable disease characterised by the production of false membrane on a mucous or abraded skin surface and due to the presence and proliferation of the Klebo-Löffler bacillus and the toxins elaborated in its growth. The importance of the latter part of the definition, namely, the bacteriological diagnosis, has been emphasised as much as the former or clinical.

So much so is this the case that cases of purely clinical diphtheria have not been included in the following statistics, so that in every case the diagnosis of diphtheria made clinically has been supplemented and proved by the usual bacteriological investigation.

Inversely, no cases have been considered which gave a positive bacteriological result without any clinical phenomena; and again, therefore, every observation may be regarded as clinically and bacteriologically positive.

PATHOLOGY.

Heart, Nervous System, Kidneys.

Heart.

The pathological study of the Heart in Diphtheria is of comparatively recent date, namely, 1870, but, from the first carefully recorded report - that of Hagen (Archive de Physiologie 1870) - until the present time, the one constant feature is that of Fatty Degeneration of the Myocardium.

The degeneration appears in the form of fine granules or in large globules involving the greater part of the muscle cell (Northup).

It appears to be found as the first sign of change in structure of the muscle and to be an accompaniment of the later destruction in more advanced cases.

Northup also notes that simple fatty degeneration is invariably found in the severe cases of short duration, and the more destructive and degenerative changes in the prolonged cases, where there is complete breaking down of the sarcous elements and destruction of the muscle substance.

In the later stages also, there is a marked proliferation of cellular elements in the tissues

Hagen.
Archive
de Physiologie,
1870.

which, however, rarely leads to fibrous change.

Schamschin
"Ziegler's
Beiträge"
1895.

An important point bearing on the aetiology of the condition has been noted by Schamschin (Ziegler's Beiträge 1895) who states that, no matter how early in the disease, one of the first features is fatty degeneration in the walls of the small blood vessels of the Heart.

Baginsky.
"Diphther-
ia and
Diphther-
itic
Croup."
1898.

Baginsky (Diphtheria and Diphtheritic Croup 1898) sums up the main changes (i) Fatty Degeneration of the muscle elements, (ii) Fragmentation of the nuclei, and (iii) Haemorrhages from the small diseased blood vessels.

Mollet and
Regaud.
"Annales
de l'In-
stitute
Pasteur."
1897.

Experimentally, Mollet and Regaud (Annales de l'Institute Pasteur 1897) have summarised the following changes:-

(a) In the muscle fibres: granular and fatty changes with occasional vacuolisation: striation often lost.

(b) In the nuclei: nuclei distorted, swollen and stain with difficulty.

(c) in the interstitial tissues: Increase of the cellular elements between the fibres.

Macroscopically there is little to note save dilatations - especially of the right side of the heart - slight paleness of the muscle: the pericardium is as a rule healthy.

It is as yet undetermined if the microscopic changes noted above are primary, namely, due to the direct action of the toxine on the muscle, or secondary, due to lack of stimulation from an already toxic nervous system.

In support of the latter theory is the fact that Lentino found similar lesions after unilateral division of the Vagus nerve.

Against this, again, is the fact of the early degeneration of the walls of the small vessels of the Heart (Schamschin) which would equally lead to impaired nutrition and fatty degeneration of the muscle supplied.

Bolton (Lancet 1906) advances the following theory: In the acute stage of diphtheritic toxæmia, acute degenerative changes occur in certain cells of the central nervous system, and amongst these cells the nucleus of the Vagus nerve is affected and, therefore, extensive Fatty degeneration occurs in the muscular fibres of the Heart. It is thus, he says, that acute diphtheritic poisoning proves fatal, the patient dying from a primary progressive failure of the heart as the result of acute degenerative changes in the neuro-muscular mechanism of that organ. At a later stage of the disease, if the patient survives, the poison attacks the

Bolton.
"Lancet."
1906.

peripheral nerves and voluntary muscles; a primary parenchymatous degeneration occurs in the nerves and a fatty degeneration of the muscle.

Hesse.
Jahrb. F.
Kinder-
heilk.
1894.

One other view has been advanced by Hesse, (Jahrb. F. Kinderheilk. 1894) a somewhat vague one, namely, that the changes and consequent heart failure result from the effects of the poison upon the Heart but not as a result directly either of the muscle or of the nerve degeneration.

To summarise; the various theories appear to be:

- (i) Primary Degeneration of Muscle - Schamschin
- (ii) " " " Nerve - Vincent -
- (iii) A combination of both according to the stage of the disease - Bolton.
- (iv) Toxaemia of Heart directly traceable to neither - Hesse.

It would appear that Bolton's theory - an idea shared by many other authorities - has much weight, and that the fact that death from Heart Failure may be accurately classified into at least 4 classes, viz., (a) Early, (b) Late, (α) Progressive (β) Sudden, much strengthens this view.

Whatever the true cause or causes may be, the liability to Cardiac Failure is much increased by the increased coagulability of the Blood in Diphtheria, due to reduced blood pressure and weakened

action of the Heart. With this additional liability to the formation of Thrombi the danger is much increased, but can hardly as Jacobi suggests (Med. News 1898) be regarded as a cause but rather as a result.

Jacobi.
Medical
News.
1898.

Nervous System.

Although the pathological features of the Nervous system vary, in minor points, with each individual case; in the main they are very constant and may be summarised as follows:

(i) Cord.

Here, according to Rainy (Journ. of Path. and Bact., 1900), the changes are mostly cellular. There is marked chromatolysis and vacuolation of cell protoplasm.

Rainy.
Journ. of
Path. and
Bact.
1900.

In the gray matter of the anterior cornu Nissl's bodies are markedly disintegrated and generally many cells are found shrunken.

Bickele and Kalishs in 1894 described also a degeneration of the posterior roots where they enter the gray matter of the posterior cornu.

(ii) Brain.

Here the changes are generally circulatory, namely, hyperaemia, infiltration or haemorrhagic.

(iii) Peripheral Nerves.

Thomas (Boston Med. and S. Journ. 1898)

Thomas.
Boston
Med. and S.
Journal"
1898.

describes marked parenchymatous degeneration of the peripheral nerves, hyperaemia and haemorrhages, also fatty degeneration of the nerve fibres of the peripheral nerves.

(iv) Cardiac Plexus.

Vincent (Archive de Med. Exper., 1894) has described a parenchymatous and atrophic neuritis. Degeneration of the Myelin sheath, changes in the Axis cylinder and marked absence of multiplication of the nucleus were always present which as Northup points out, show a degeneration, and not changes due to an irritant.

Kidneys.

By far the most common changes found in the kidneys are those of degeneration. The epithelial cells are enlarged and irregular and in advanced cases are completely destroyed and desquamated. The degeneration is not fatty, although a slight degree of fatty degeneration is generally present, but according to Northup, some degree of hyaline degeneration is invariably present.

He also states that lesions of the kidneys of greater or less extent are found in practically all cases of fatal diphtheria.

In most cases the amount of albumen corresponds

Vincent.
"Archive
de Med.
Exper."
1894.

to the degree of degeneration present.

Welch and Flexner. "John Hopkins Bulletin". 1892.

Welch and Flexner (John Hopkins Bulletin, 1892) state that, experimentally, the epithelium of the tubules is rendered very granular and much swollen but not fatty. They also report a slight fragmentation of the nuclei in the epithelium of the tubules. Acute interstitial changes appear generally in conjunction with complications of the disease and are accompanied by marked increase in size of the kidney. Here the changes are most marked at the base of the cortex just beneath the capsule and around the glomeruli, and degeneration of the epithelium to a varying degree is always present.

The glomerular changes are of a chronic type and probably to be referred to an acute antecedent attack of endocarditis (Northup).

CAUSE OF ALBUMEN.

The exact cause of albumen in Diphtheria is as yet uncertain.

Rolleston "Practitioner." 1905.

Rolleston (Practitioner 1905) has shown that the quantity of albumen varies with the severity of the case.

As the amount of degeneration varies with the severity of the case, and in the same proportion, it is reasonable to suppose that there is a distinct analogy.

That the degeneration is produced by the direct action of the toxine of the Klebs-Löffler bacillus, although the most likely hypothesis, is by no means certain for the septic and anginous cases - produced by other organisms, Streptococci, etc., - are those in which it is found in largest amount.

That it is due to the presence of antitoxine has been practically disproved by Variot (La Diph-
Variot. "La Diph-
térie et
la Séri-
umthé-
rapie) who has also shown that
the presence of Chronic Bright's disease is no con-
tra-indication for antitoxine.

The balance of evidence then appears to prove that the presence of albumin in the urine is an indication of the severity of the toxine of Diphtheria or the presence in large numbers of accompanying organisms. Its almost invariable presence in fatal cases would also seem to show that the resistant power of the individual is an important factor.

The relationship of albumen to paralysis has been discussed since the times of Trousseau - who, in one case noted an increase of albumen coincident with the onset of paralysis - but Trevelyan (Lancet
Trevelyan. "Lancet".
1900. 1900) appears to state the matter clearly when he says that diphtheritic albuminuria has no other relationship to diphtheritic paralysis than that both complications are more prone to occur, where the diphtheritic intoxication is most intense.

CARDIAC FAILURE.

Whatever the exact cause of cardiac failure in each individual case, viz., myocardial, neural or a combination of both, the condition is an easy one to recognise.

The main features are:

Vomiting, which, as a rule, is irrespective of food. It may be a simple regurgitation or accompanied by retching.

Blueness of the skin and mucous membranes and, towards the last stage, coldness of the extremities.

These symptoms are, as a rule, accompanied by obvious signs of weakening of the heart, such as: - dilatation, irregular and intermittant pulse, 1st sound faint, short, with perhaps a systolic murmur or reduplicated at the Mitral area. There may be bradycardia or a galloping rythmic contraction; the latter, as a rule, only when the patient is in extremis.

The patient frequently complains of praecordial pain which may be very severe and may be referred, generally, to the abdomen.

As a rule, the patient lies absolutely quiet but may, towards the end, be very restless and excitable..

The temperature may be at first slightly

elevated but quickly becomes subnormal.

The patient dies on an average from 3-5 days after the first appearance is noted.

Such a type as the above is the progressive type but in other cases - usually late in the disease - the patient may die suddenly without warning.

Myers (Lancet 1900) gives the seventh day as the average number of days after the beginning of an attack of diphtheria that the symptoms and signs of cardiac paralysis are noted. He also gives the 2nd and 35th days as the two extremes.

Although so profoundly toxæmic the mental faculties of such patients are, as a rule, quite unimpaired to the end, and with this fact and symptoms and signs such as are noted above, a diagnosis is obvious and a clear division can be made between the two types, namely, progressive and sudden. The earlier symptoms of cardiac failure occur, as a rule, when the patient is and has been absolutely quiet, and are no doubt caused by the intensity of the toxæmia causing an acute degeneration. The later ones, however, frequently result from a strain - as when at stool - and this fact would appear to show that the degeneration has been present and in the myocardium, and, that the weakened muscle has been unable to respond to the additional call made on it and that the cause is not a secondary or late degeneration.

Myers.
"Lancet".
1900.

PARALYSIS.

Although in discussing the pathological changes in the nervous system it was stated that the lesions were, as a rule, constant, it by no means follows that each case of paralysis presents all features. From this fact and from the fact that some present no nervous features but muscular changes only, the aetiology of paralysis is rendered somewhat difficult.

The great varieties of paralysis and the different lesions found, all tend to render the cause obscure.

Manicatide
"Rev. mal
de l'enf"
1896.

Manicatide in 1896, for instance, reports the examination of a series of paralyzes which may be divided into at least 4 groups:

(i) Where the lesions were purely muscular with no nerve complications.

(ii) Cases of polyneuritis.

(iii) Lesions of the spinal cord which were either localised in the gray substance leading to atrophy of the muscle or involved the white matter of the cord in a manner such as is found in locomotor ataxy.

(iv) Central paralysis, chiefly resulting from changes in the circulation.

Although the ataxic symptoms often seen in diphtheritic paralysis would seem to point clearly to destruction of the muscular sense, it is mostly of a reeling or cerebellar character and the most likely hypothesis would seem to be that a degeneration has spread to the muscles of the trunk and started elsewhere.

Although conflicting, the evidence in all would seem to be, that while many cases of paralysis are due to muscular degeneration and in this class the benign or localised forms have their place, most are due to a primary central disturbance - for the central lesions are not strictly speaking degenerative - followed by a Wallerian degeneration and failure of the peripheral nerves.

The paralyzes may be classified as follows:

- (i) Localised or Benign Paralysis.
- (ii) General Paralysis.
- (iii) Cardio-pulmonary - which has been considered.

In the first group may be placed paralyzes of palate and pharynx. This is much the most common variety and Myers and others have stated it to represent from 35%-40% of the total varieties of paralyzes.

The second series includes the remaining forms of paralyzes, viz., oculo-motor, extremities,

Myers.
"Lancet".
1900.

intercostals, etc.

As regards the frequency of paralyses: on an average taken from a large number of statistics it may be stated at 12%-14%, thus; the Metropolitan Asylums Board out of 8,238 cases gave 18.50% of paralyses, Sanné reports in 2,400 cases 11%.

Woolacott.
"Lancet."
1900.

Woolacott gives an interesting table divided into Cases Serious and Moderate,

Nature of Case.	Total.	Paralysis.	Percentage.
Serious	223	64	28.6
Moderate	536	75	13.2

and this would seem to prove conclusively that the paralyses is dependent on the amount of toxins.

METHODS CLINICAL AND BACTERIOLOGICAL ADOPTED.

The methods adopted in arriving at a correct diagnosis of the condition in the following recorded cases were as follows:

(1) Clinical.

Each patient was examined with lamp and spatula for, either signs of definite membrane or signs of the implantation of recent membrane.

Again, symptoms were carefully considered, namely, either the characteristic toxaemic appearance or the equally diagnostic odour, although these

symptoms were considered as merely confirmatory and on them alone no diagnosis was made.

Diagnostic importance was, in the case of suspected Nasal Diphtheria, especially attached to such symptoms as the foregoing in conjunction with a nasal discharge. The only possible exception was in the Laryngeal case where even in the absence of apparent membrane, symptoms plus croup were considered sufficient to warrant a diagnosis.

No cases apart from such as these are included in the following series and none without the accompaniment of a positive.

(ii) Bacteriological Examination.

A swab was at once taken from the throat or nose and stained for 3 minutes with Löffler's Methylene Blue solution and examined for rods and cocci.

At the same time a culture on Blood Serum was made and left for 16 hours at a temperature of 34°C-35°C. At the end of that time it was stained with a variation of Neisser's Stain, namely, Acetic Acid, Methylene Blue and Picro-Eythrocine solution, half a minute each. X

None of the recorded cases have failed to show rods in the swab and polar staining or clumping of the Bacilli in the Culture, and both swab and culture may therefor be said to have been positive.

SKETCH OF PREVIOUS TREATMENT.

In the history of the earlier treatment of diphtheria the importance given to local at the expense of general treatment is, perhaps, the most noteworthy fact.

Until the 16th century no means were considered too harsh, thus, burning, scarification and forcible removal with pincers were the invariable rule.

In the 16th century authors on the subject began to reprobate these harsher methods, but, in lieu of better, were forced in a large number of cases to continue.

In the beginning of the 18th century, the use of drugs which destroyed the membrane by their caustic action began to be much favoured, such as Nitrate of Silver, etc.

Bretonneau (the first to clearly differentiate Diphtheria) in 1827, advocated strongly the use of alum and later, Uytterhoeven, Acetic Acid. Martin, 1858, speaks well of Hydrochloric Acid and Jenner supported this but recommended only one prolonged application. Up to this time the internal treatment was confined to stimulation by alcohol, when required, and aperients.

In 1861, Rey recommended the use of Perchloride of ^{Iron}~~Iron~~ both locally and internally, and this was for

long widely adopted.

Mercury was much used from 1880-1890 as a disinfectant either as calomel or biniode of Mercury in the shape of fumigations and internally. The general treatment consisted in alcohol and latterly strychnine.

The treatment of Diphtheria was, however, revolutionised in 1893 by Behring with Antitoxin Serum and resolved from that time until the present into treatment by serum, stimulants, as whisky, strychnine, strophanthus, digitalis and an antiseptic local treatment of the condition.

As showing more fully the treatment adopted during the past 3 years, the following detailed account has been given of the accompanying 300 control cases.

PREVIOUS TREATMENT 1904-1905 IN HOSPITAL.

- TREATMENT OF ACCOMPANYING CONTROL CASES -

The main lines of treatment were:

(i) To prevent degenerative changes in the acute stage by rest and adequate doses of antitoxine.

(ii) To prevent strain and consequent heart failure in the secondary stage by rest.

(iii) By stimulation, to assist the individual to resist the toxine until the toxine was neutralised.

(iv) In Cardiac Failure to obtain rest by preventing vomiting and to stimulate the heart.

(A) UNCOMPLICATED CASES.

(a) FAUCIAL AND NASAL.

I. General Treatment.

(i) Rest.

The patient was kept in the recumbent posture with one low pillow for at least 12 days and complete mental rest was also enjoyed - no reading, etc. If at the end of that time there were no symptoms, viz., pulse irregularity, etc. the patient was given one more pillow. At the end of 3-4 days, conditions again being favourable, the patient was permitted to sit up in bed and was allowed out of bed in blankets about 6 days later.

The patient was kept in Hospital for at least 3 weeks and was not in any case permitted to leave until two consecutive bacteriological examinations had proved negative, and until clinical symptoms had disappeared.

(ii) Stimulants.

From the day of admission the patient was prescribed small doses of Whisky and Liquor Strychninae every four hours in doses varying with the age of the patient and the severity of the case. This

treatment was continued for 10 days when, with no symptoms Syrup Easton $\zeta i - \zeta ii$ was prescribed three times daily.

Occasionally for extraneous symptoms, Non, etc. was also given.

II. Local Treatment.

In cases where the membrane was very obvious a throat paint

Px Toluol . . .	36	Parts.
Sp. Vin. Rect. . .	60	" was
Tinct. Ferri Perch. . .	4	"

applied frequently. It was found very useful both as an antiseptic and of assistance in destroying the membrane.

This was always accompanied by a swab of Boro-glyceride which was continued during residence.

In cases where the fauces were apparently septic and foul-smelling, a spray of peroxide of hydrogen was given for 24-48 hours at varying intervals.

(b) LARYNGEAL CASES WITH CROUP.

On admission the patient was placed in a cot between two steam pipes. A full dose of Vin. ~~Specae.~~ ~~mxv-mxx~~ - to assist in loosening the membrane was at once given and this was followed by small doses - ~~mii-mv~~ - every 4 hours so long as the patient remained croupy.

Tinct. Belladon. in small doses - mii-miv - every 2 hours until dilatation of the pupils was obtained, was also prescribed, to dilate the passages and act as a stimulant by paralysing the terminations of the Vagus nerve in the Heart and therefore to destroy the inhibitory action of the nerve - this result, viz. acceleration of the Heart, systolic increase, etc., was found to have excellent results.

In addition to these two drugs the patient was given small doses of Whisky and Liquor Strychninae in doses again varying with the age of the patient.

Should operative interference not be necessary, these measures were continued until the croup symptoms disappeared, when treatment on ordinary lines was continued.

(β) COMPLICATED CASES.

(i) Operative Cases.

In cases where the above treatment did not ameliorate the condition, viz., where the dyspnoea, cyanosis and signs of CO_2 toxaemia manifested themselves, Intubation was performed and the tube left in position for 2-3 days and not removed until croup symptoms had disappeared. In cases where the tube could not be retained or where it proved unsatisfactory, Tracheotomy was performed.

(ii) Cases of Cardiac Failure.

At the first sign of cardiac failure the patient's pillow was removed and he was kept flat in bed or even with the head lowered.

If vomiting had occurred Liquor Strychninae was at once stopped and Brandy alone given while an effort later was made to feed the patient with peptonised milk.

Should there again be a tendency to vomit, the patient was stimulated and fed per rectum and in cases of extreme thirst and with no contra-indications, small quantities of ice were given to suck.

On signs of further cardiac failure, Hypodermic injections of Strychnine or Strophanthin were given, generally in conjunction with Adrenalin Chloride (1-1,000).

In a few cases where the patient became extremely irritable and restless, very small doses of Morphia and Atropine were given.

(iii) Cases of Paralysees.

At the onset of paralysees the patient was kept recumbent and given increased doses of Liquor Strychninae, ~~ma~~ Massage etc., was adopted and in the case of the spinal muscles the spine was painted with Iodine Tincture and Potassium Iodide.

In the case of the palatal and pharyngeal paralysees, all ordinary precautions were adopted as regards feeding, etc.

ANTI-TOXINE TREATMENT.

As all the accompanying cases (both 100 treated with Formic Acid and the 300 control cases) were given antitoxine doses based on the same broad lines, it may be well to shortly state the views which prompted the doses.

The two main factors under consideration were:

(i) The severity of the disease

- (a) Local Condition
- (b) General Toxaemia.

(ii) The age of the disease.

(a) Faucial uncomplicated cases.

Here the dose given was, in the main, 1,000 units (P. D. & Co.) for each day of the disease, but, in cases with definite membrane, not less than 3,000 units.

If the palate or uvula was involved, the dose was not less than 4,000-5,000.

This was repeated in 12 hours if there was a further spread of membrane.

(b) Nasal Cases.

Here, as, owing to the large lymphatic area affected, the toxaemia is, as a rule, intense, the dose was seldom less than 6,000 units repeated in

24 hours if the toxæmia appeared more intense, up to a total of 24,000-30,000 units.

(c) Laryngeal Cases with Croup.

A dose of, as a rule, not less than 6,000 units in an ordinary case was given on admission and repeated every 8-12 hours until the membrane appeared to loosen.

In early Cardiac Failure, a large dose was occasionally given, repeated if the condition appeared to benefit.

CRITICISM OF PRECEDING TREATMENT.

Apart from the local treatment, and the large question of antitoxin, the treatment hitherto adopted has, as shown by this resumé, been one of stimulation, mainly by strychnine and also digitalis and strophanthus with the occasional use of hypodermic injections of strychnine or strophanthin or adrenalin chloride.

As stimulants, the one feature common to all these drugs is that they achieve their end mainly by raising blood pressure: digitalis does so partly by increasing the cardiac force and mainly by contracting the arterioles by direct action on their muscular coat and again, in a lesser degree, by

stimulation of the medullary and spinal vaso-motor centres. Strophanthus also raises blood pressure although the action on the arterioles is not present as in digitalis. Adrenalin chloride does so almost solely by contraction of peripheral vessels.

Strychnine: raises blood pressure by direct stimulation of the vaso-motor centre, which, as a result, leads to constriction of the peripheral arterioles.

In mammals while the heart is not directly affected by strychnine, stimulation of the inhibitory centre leads to a slightly slower rhythm.

It would seem therefor that, from this point of view, these drugs are not ideal in that they tend to increase the amount of work done by a heart which has a tendency to degeneration.

There are other points also in their action which appear doubtful.

Strychnine. As a nervous stimulant acts mainly on the central nervous system and it has been found that the symptoms of the drug are unaltered when the drug is prevented from reaching the peripheral nerves and muscles.

It has also been shown that almost certainly the motor cells are unaffected and that any changes - such as enlargement - found in them are due to hyper-activity and not to the direct influence of the drug.

As has been shown, however:

(i) The main changes in the diphtheritic cord are in the motor cells.

(ii) Many of the paralyses in Diphtheria are not central but peripheral or muscular.

It would appear therefor that the therapeutic value of strychnine in such a condition must theoretically, be very limited, for, in addition, it is a known fact that, while small doses of strychnine increase the tone of the muscles - namely render them more tense so that they are prepared for immediate contraction - that this is due to the action on the cord and not on the muscle fibres.

One other doubtful feature in the treatment by strychnine is the reaction and depression which follows its use and which Cushny suggests is due to the hyper-activity of the lower parts lessening the activity of the pain.

In the treatment of a disease in which paralyses is such a marked feature, it would seem that here again there is a contra-indication and that while expecting in severe cases by pushing strychnine to obtain a temporary benefit, the final result would only be exaggerated.

One other negative point in the treatment by drugs such as those mentioned, is that they make no claim to influence the third important complication

of Diphtheria, viz. Albuminuria, and would appear again by raising blood pressure to aggravate the kidney condition.

The following is an account of a drug which would appear more nearly to meet the requirements in Diphtheria:

FORMIC ACID. H. C O O H.

History, Chemistry, Properties and Therapeutics.

It occurs in the concentrated state in the bodies of ants, in the hairs and other parts of certain caterpillars and in stinging nettles. Its stimulant properties have been known for centuries, and Arabs for long have realised this and, before commencing a long and arduous ride, were accustomed to give their horses with their ordinary diet a decoction made from Ants' eggs, the result being a marked increase for the time in their powers of endurance.

The internal administration of preparations containing Formic Acid has also for centuries figured among household remedies where they were much valued for their tonic and diuretic properties.

It was not, however, until 1903 that serious scientific experiments with it were made and in that

lement.
Société
Nationale
de Médi-
cine de
Lyons.
1903.

year Clement in a paper read before the Société Nationale de Médecine de Lyons reported a series of interesting experiments which placed it in a new and important light.

Chemistry.

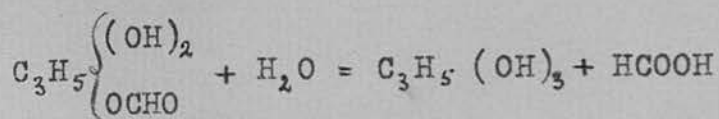
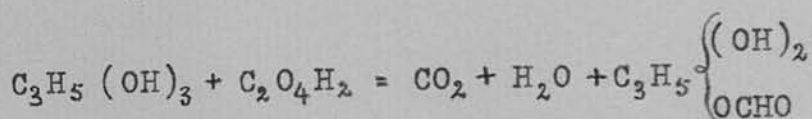
It is obtained by heating equal parts of anhydrous glycerin (or mannite) and crystallised oxalic acid in a retort to 75% until carbonic acid is no longer evolved. A fresh portion of oxalic acid is then added and the distillation is continued. This process may be repeated several times.

The distillate finally contains 55% of the acid and is redistilled over anhydrous oxalic acid when a 75% acid is obtained. This is neutralised with sodium Carbonate, the dry sodium salt distilled with anhydrous oxalic acid when a 99% acid is obtained - Lorin -.

The last trace of water is removed by distillation over boric anhydride and the acid is subjected several times to a freezing mixture, the crystals separated from the liquor and then allowed to melt; or the dry lead or copper salt is heated at 130° in a current of dry hydrogen sulphide; in the latter case the product is apt to be contaminated with sulphur products.

In the above process the crystallised oxalic acid decomposes into water, carbonic acid and Formic acid, the last of which combines with the glycerin to form monoformine, which is subsequently decomposed by water into Glycerin and Formic Acid.

The equation is:



Properties.

The acid solidifies below 0° and exhibits the phenomenon of superfusion. The liquid acid is colourless, transparent and mobile. It has a pungent sour taste and odour, and when concentrated blisters the skin - Lubig -.

Therapeutics.

Formic acid is officially used in the form of a colourless fluid of a concentration of 25%, Sp. Gr. 1060-1063.

In 1903 Clement, in a lengthy paper, stated that he had found Formic Acid to be a powerful stimulant of striped muscle and in its toxic action closely allied to Cola, Coca and Caffeine. He stated also

that the internal administration dispelled any sensations of lassitude as seen in nervous individuals, and that, experiments controlled by dynamometer and ergographs, showed a marked elevation of muscular power within two days of administration. At the same time he noted a marked improvement in muscular capacity manifesting itself in an exhibition of active and rapid movements.

Krull.
München.
1903.

In the same year, Krull - Munich - noted marked improvement in Chronic Kidney disease with Albuminuria after the subcutaneous injection of Formic Acid. He injected the preparation in the form of an aqueous solution (1:10,000 - 1:100,000) according to the age of the patient and the stage of the disease in doses of $\text{mii} - \text{mxi}$. As a result he was able to report (i) Improved nutrition, (ii) Decrease of Albuminuria, and (iii) Diuresis.

These results he obtained as a rule when there existed no advanced cardiac complications.

Clement.
Tribune
Médicale)

In 1904 Clement reported the following results:

After the administration of Formic Acid the subject performed 10 periods of work instead of 5 as before administration. In the 10 periods of work he realised with the Mosso Ergograph 479 of the weight of 5 Kgrms. instead of 132. The total work done was 106 kilogrammètres, while, before the administration of Formic Acid the subject was only

able to do 21 kilogrammètres.

The amount of work done then after the administration of Formic Acid was increased almost five-fold.

He found also that the effect on the muscular system was very lasting and persisted for 8-10 days after the administration, and that, under the influence of the drug, the painful sensation of the muscle submitted to the repeated contraction was noticeably diminished.

Another important point was that the muscles so treated recovered their energy very rapidly.

He also in the same year reported two cases of tremor due to muscular atony in which marked improvement followed the administration of Formic Acid, although the disease had existed in both cases for 10 years.

Huchard, one year later, reported the following observations:

		<i>What?</i>		
I.	Patient before administration	= 5 Kgrms.	.90	
"	one day after	" = 9 "	.60	
"	two days "	" = 9 "	.35	
"	three " "	" = 9 "	.05	
"	four " "	" = 10 "	.70	
"	five " "	" = 11 "	.50	
II.	Patient before administration	= 9 "	.900	
"	one day after	" (grms. i) = 8 "	.75	

Huchard.
(Bulletin
de l'Académie de
Médecine)

Patient	Two	days	after	administration	(grms. ii)=20	Kgrms	.625
"	Three	"	"	"	(grms. iv)=20	"	.975
"	Four	"	"	"	(grms. iv)=20	"	.200
"	Five	"	"	"	(grms. iii)=30	"	.650

He also in a large series of experiments proved that the toxicity of Formic Acid was practically nil: thus grms. 60 in a single dose were required to kill a small dog, while a dose of 11 Kilogrammes, intravenously injected into another dog, produced no symptoms other than slight vomiting.

In the same communication Huchard makes important statements on the diuretic action of Formic Acid and the Formates.

He proves, in the first place, conclusively that it is eliminated by the kidneys, thus: he injected into the Jugular vein of a dog 20 c.c. of Aqua Distillata containing in solution grms. 4 of Formate of Soda. After 48 hours there was excreted 453 c.c. corresponding to 2 grms .22 of the Formate and further series of experiments confirmed these observations.

He also, as did Krull, noted its diuretic action and the rapidity with which it was produced.

In a case of sclerosis of the kidney in which the quantity excreted was 1,000 c.c., he noted that

in 4 days it rose to 2,700 after the absorption of 3 grammes of Formate of Soda.

A further series of experiments were:

Amount of urine in 24 hours	2,500 c.c.
After grammes 3 of Formate of Soda	3,750 c.c.
Drug stopped	2,550 c.c.
After Grammes 3 of Formate of Potash	4,000 c.c.
3 days after stoppage of Drug	2,400 c.c.

He further noted that in every case the quantity of albumen was diminished, and in most cases to a very marked degree. Again, that the acidity of the urine is much diminished and that the urine, at first, is always alkaline.

Garrigue.
Annales
des Prac-
iciens)
1904.

L. Garrigue recorded similar results obtained with Formate of Soda, viz. an increase in the excretion of urine from 20 grms - 50 grms per day.

The injection of Formic Acid in a concentrated form has been found to raise blood pressure (Garrigue, Clement, etc.), but later experiments with the dilute acid have proved that there is no increase of blood pressure either in artero sclérosis or advanced cardiac lesions. The Formates do so to a slight degree, and of them, Formate of Soda is the most pronounced.

SUMMARY OF CONCLUSIONS, PART I.Pathology.

1. That the main changes observed are degenerative.
2. (a) That degenerative changes occur in the nerve cells as a result of the Diphtheria toxine, and that, while they may recover, they may atrophy and that the nerves, of which they are the trophic centres, undergo Wallerian degeneration and lose their conductivity.
(b) That degeneration occurs in muscle fibres as a direct result of the toxine.
3. That Cardiac Failure is dependant on both forms or both combined, according as it is Progressive, Sudden, Early, Late.
4. That Paralysis depends on both forms or both forms combined, according as it is Benign or General.
5. That changes in the Kidney in Diphtheria are those of degeneration.
6. That Albuminuria is not caused by antitoxin but is due to toxaemia, and that the amount of albumen is an indication of the severity of the disease and the amount of general toxaemia.

Treatment.

7. That treatment, apart from antitoxine and local treatment, has hitherto depended mainly on the following drugs: Digitalis, Strophanthus, Adrenalin Chloride, and above all, Strychnine.
8. That all these drugs raise blood pressure and therefor, theoretically, add strain to the Heart.
9. That none have any effect on albuminuria and would be expected to increase degenerative changes in the kidney by raising blood pressure.
10. That Strychnine acts mainly on the Central Nervous System.
11. That many forms of paralysis are not central.
12. That Strychnine does not affect Motor Cells.
13. That it is the Motor Cells which are affected in Diphtheria when the Central Nervous System is affected.
14. That treatment by Strychnine is followed by reaction and depression and cannot with safety be pushed.

Formic Acid.

15. That Formic Acid ²⁵55% does not raise Blood Pressure.
16. That Formic Acid is a powerful stimulant of all striped muscle and gives a marked increased capacity for work.
17. That Formic Acid improves the appetite and general nutrition.
18. That Formic Acid is a diuretic with an influence in reducing albuminuria.
19. That its stimulant effect on the muscular system is lasting.
20. That so far as is known it is not toxic.
21. That in its action it is allied to Caffeine or Coca.

Diagnosis of Recorded Cases.

22. That from the fact that only those cases have been recorded which were positive both clinically and bacteriologically, the following cases are those of True Diphtheria.

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Part II.

Details of
100 Cases

on

Formic Acid.

The accompanying cases were under
my observation as House Physician
to the Edinburgh City Fever Hospital.

Index of Cases.

Deaths from Cardiac Failure =

N^{os} 53 + 61.

Paralysis =

N^{os} 59, 73, 85.

Albumen =

N^{os} 2, 3, 17, 42, 47, 57, 76, 85, 90, 99.

Cases complicated with measles: —

N^{os} 21, 29, 43, 59, 73.

Cases complicated with Scarlatina: —

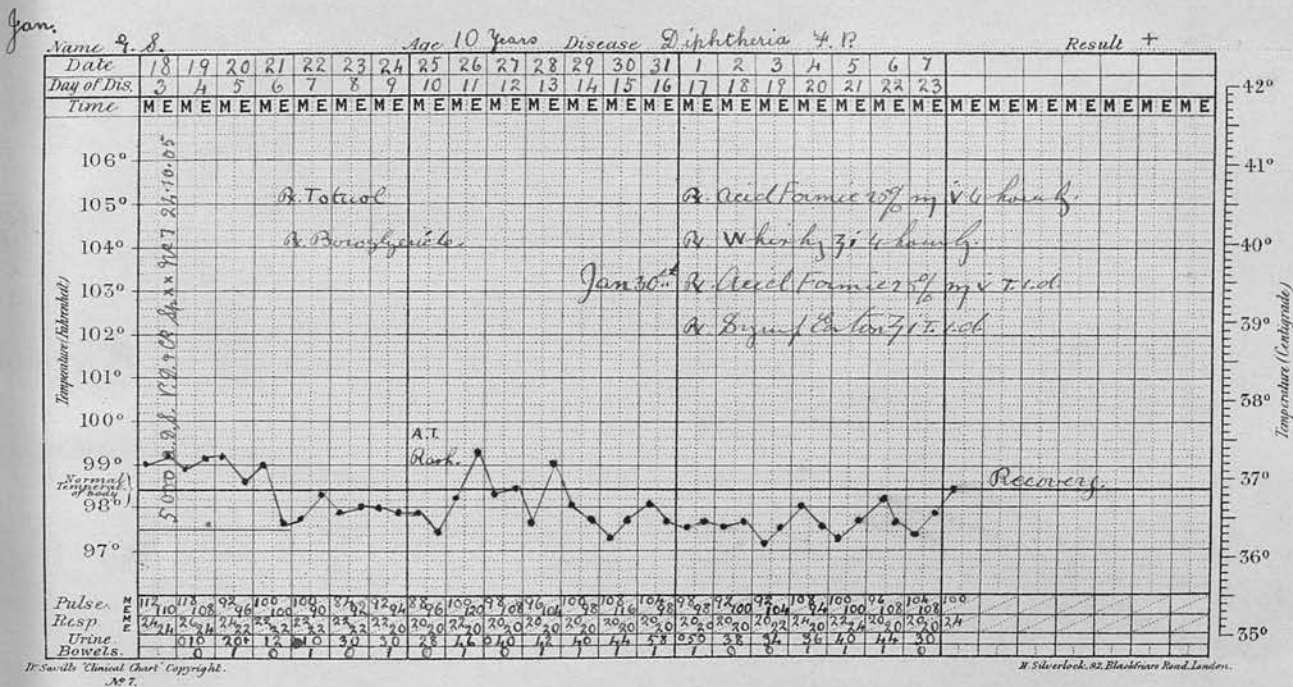
N^{os} 89, 47, 46.

Cases with symptoms of impending Cardiac Failure =

N^{os} 10, 19, 39, 45, 57, 59, 76, 81, 89.

with
Explanatory Chart.

Case I.



Description of Case.

Both tonsils enlarged. Right tonsil almost completely covered with thick tough white membrane. Palate also slightly involved. Left tonsils covered at base only with similar membrane.

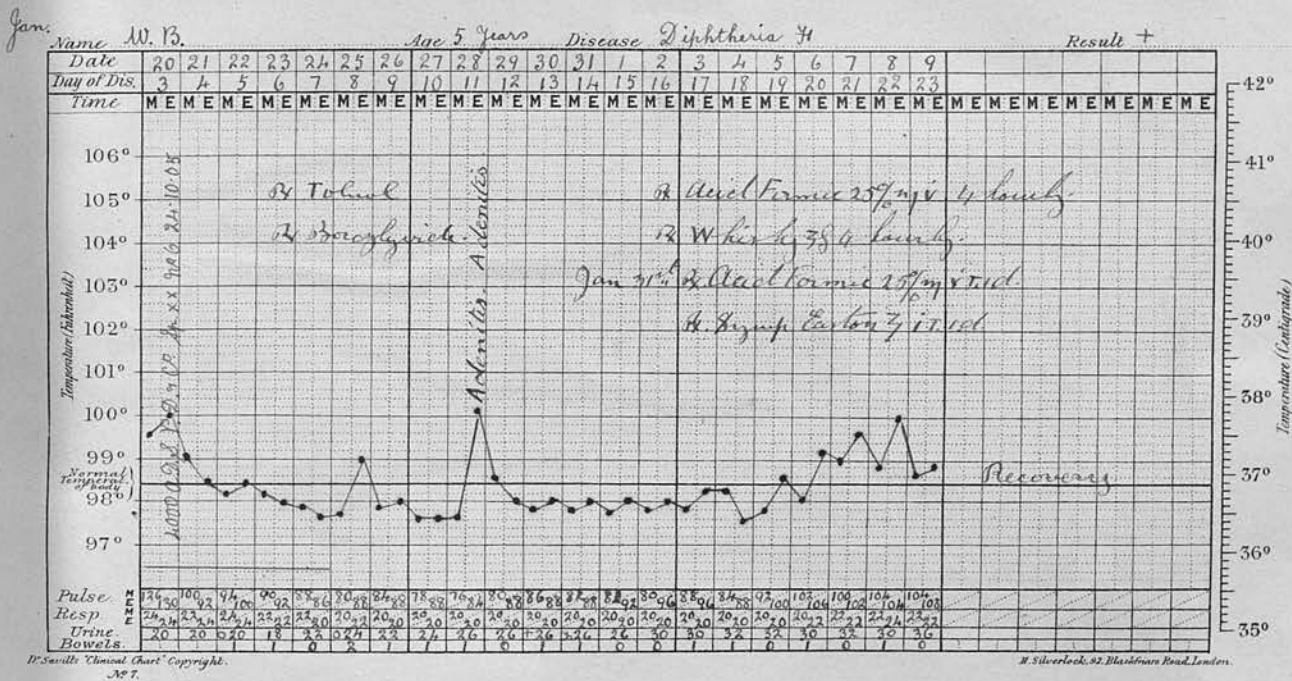
Swab = A few short and medium rods & short streptococci many diplococci.

Culture = Negative.

History

made an uneventful recovery.

Case II



Description of Case.

Back tonsils congested & enlarged. Right tonsil completely covered with white, tenacious, thick membrane. Left tonsil only at base. Pulse very soft but regular. Heart = Mitral area a soft blowing systolic murmur with occasional reduplication of 1st sound.

Swab = Good short rods. Pauci & diplococci.

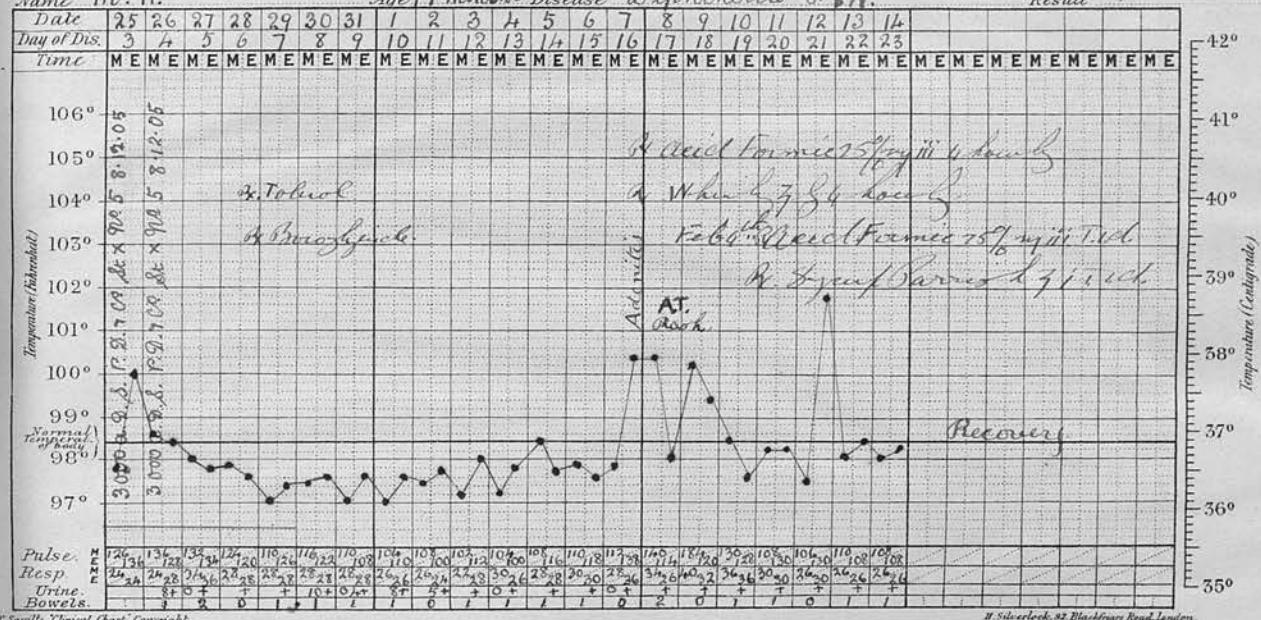
Culture = Negative Positive.

History.

Pulse gradually improved & heart condition also. Adenitis on Jan. 28th. Left hospital in good health.

Case IV.

Name M. H. Age 17 months Disease Diphtheria H.N. Result +



Description of Case.

Slight enlargement & congestion of tonsils. There is a patch of dark gray membrane at base of right tonsil, and a smaller patch at the base of the left tonsil. Patient is very toxicæmic looking. Pulse soft but regular.

Exalts = very good clusters & polar & terminal rods.
a few cocci.

Culture = Neisser Positive

Next Day

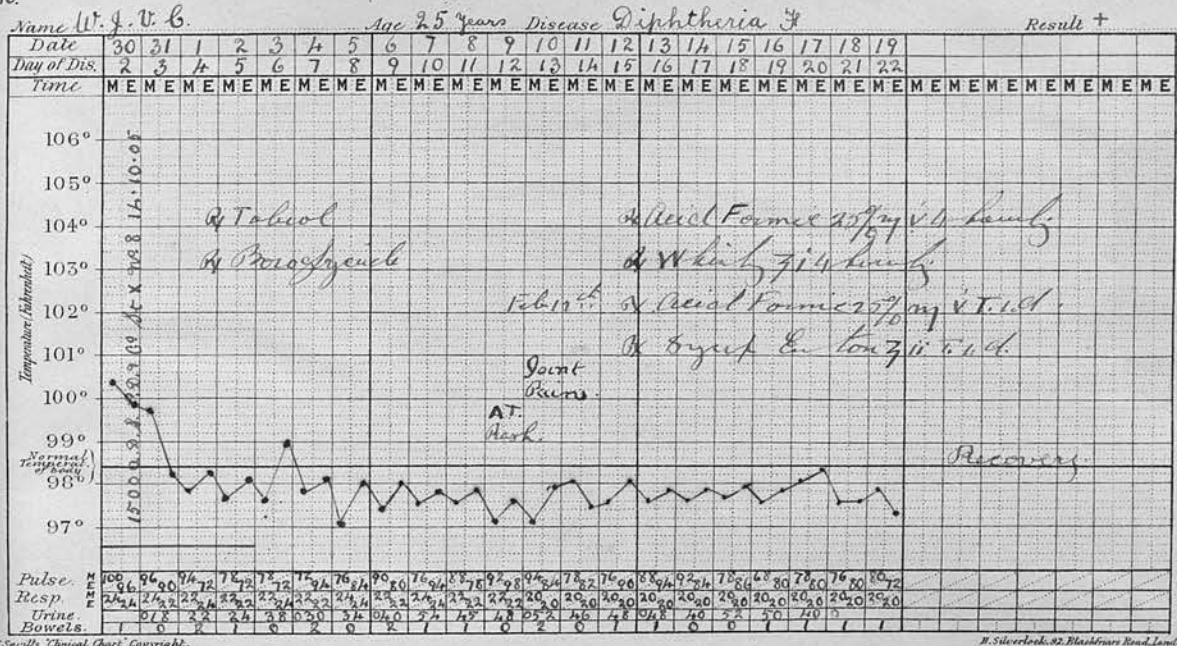
Jan. 26th Well marked discharge from both nostrils

Culture = Neisser Positive.

Feb. 8th Antitoxin rec'd - morbilliform & slight adenitis. Left hospital in good health.

Case VII.

Jan.



Description of Case.

Fauces slightly congested. Left tonsil is enlarged & covered with discrete patches of grayish-white thick membrane. Pulse is low tension but regular. Colon is good.

Cultures = Good short rods. Some long, thin rods
Staphylococci & Diplococci.

Culture = Negative.

History

Feb 9th Antitoxin rash - morbilliform on face & extremities.

Feb 10th Slight joint pains. Slight stiffness in knee joint. Tendon reflexes unaffected.

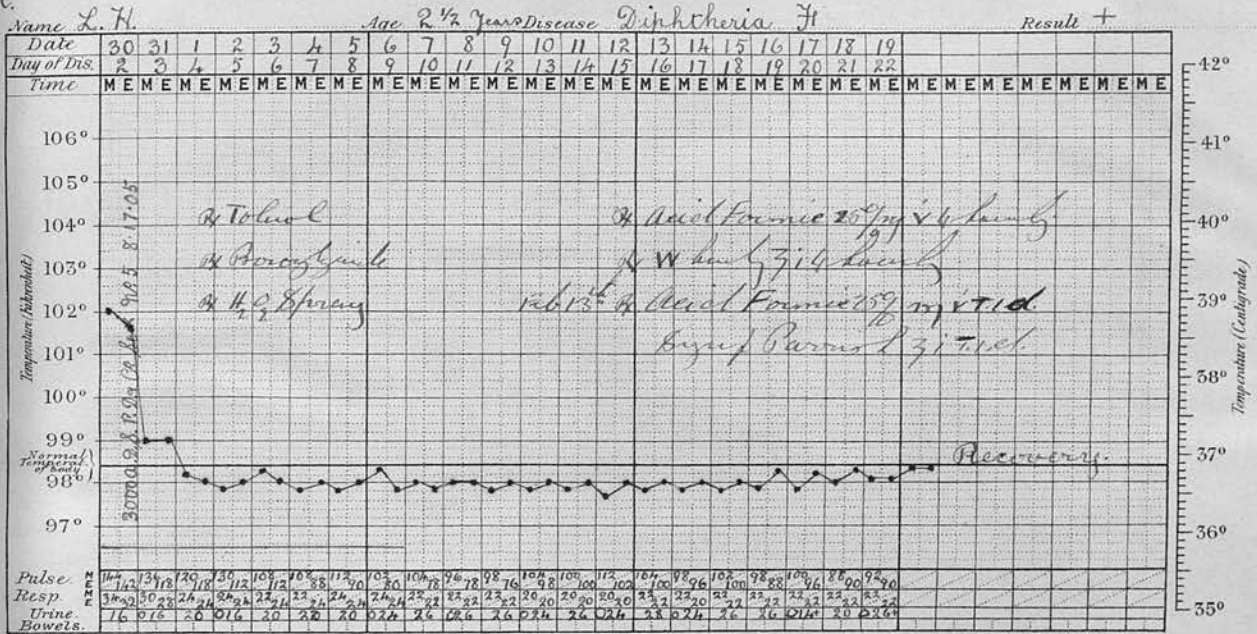
Feb 12. 2 well & returned made good recovery.

W. Saville 'Clinical Chart' Copyright, 1907.

H. Silverlock, 82, Blakelane Road, London.

Case VIII

Jan.



Description of Case.

Marked enlargement of tonsils. Both are covered at base with thick gray tenacious membrane and covered anteriorly with similar disintegrated membrane. Uvula & palate unaffected. Face is very pale & patient has poisonous appearance. Pulse is regular but rather rapid.

Swabs = Good rods. mostly short rods. Some long thin rods. Staphylococci & Diplococci.

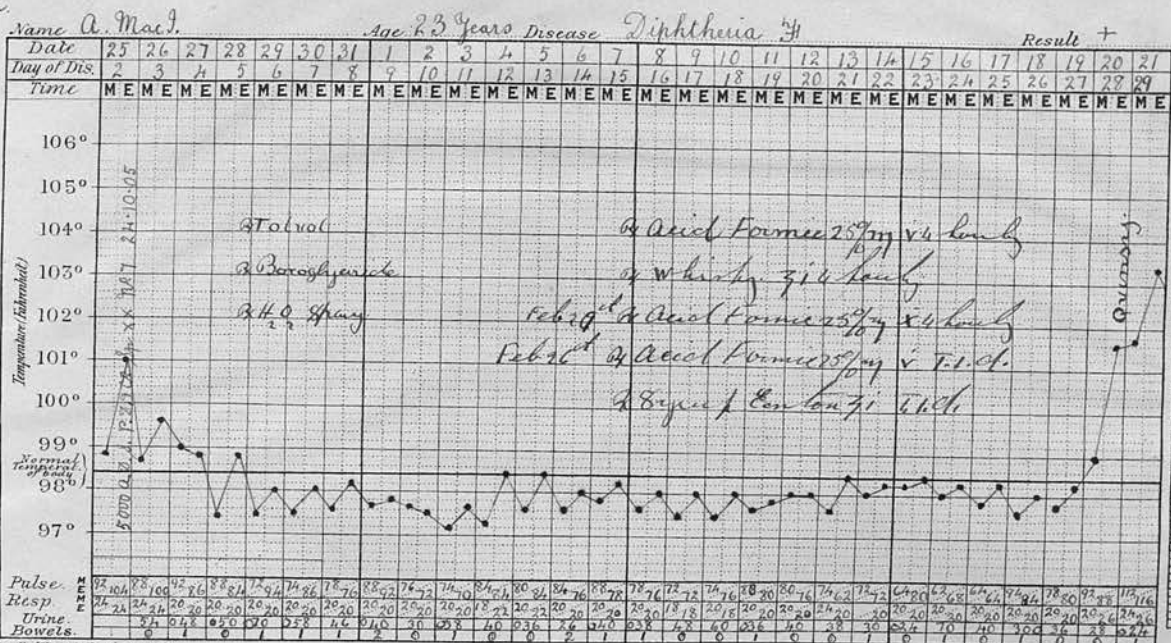
Culture = Murrey Positive.

Hinting

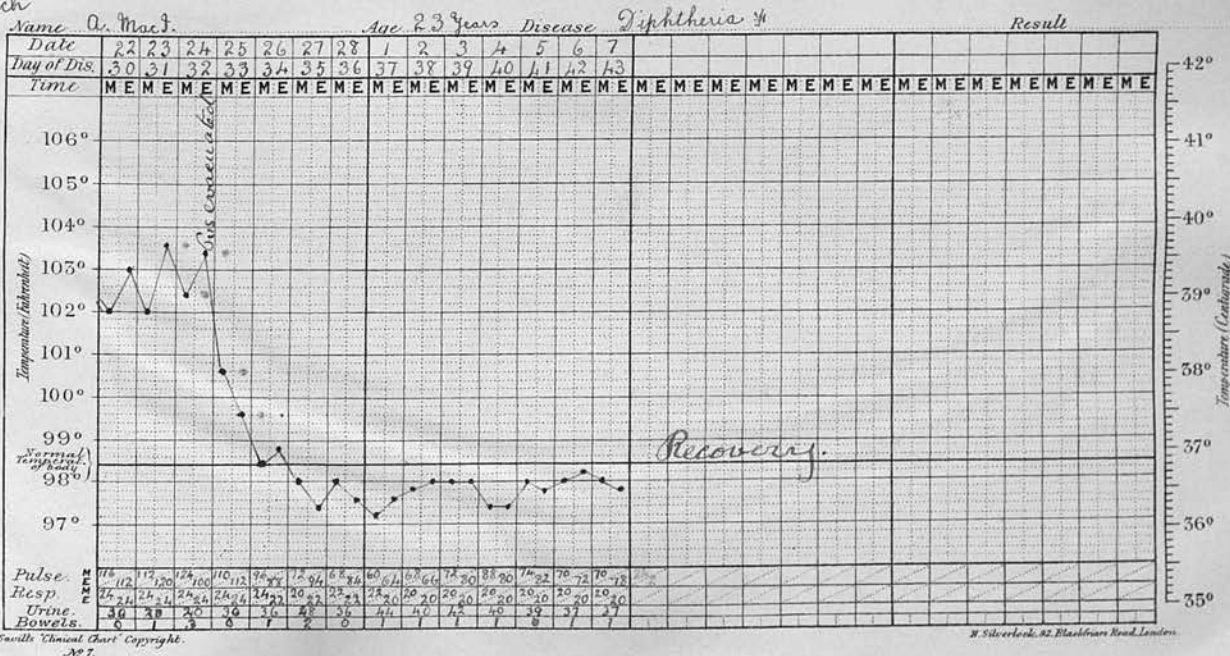
Feb 5th Pulse is irregular & volume is poor. Some of Fomies acid doublet = my v 1/4 hourly. Feb 7th Good colour Pulse regular. After this patient made uninterrupted recovery.

Case X

Jan.



March



Description Case X

On admission: Fauces were very congested. Slight enlargement of right tonsil. Left much more enlarged. Base of right tonsil completely covered with dark gray thick membrane which spread far back posteriorly. Left tonsil covered at base with similar membrane. Uvula and palate free. Patient pale & very poisonous looking. Pulse slightly irregular and volume and force poor.

Swab = Short polar stained rods. Many short streptococci & a few Staphylococci.

Culture = Negative.

History

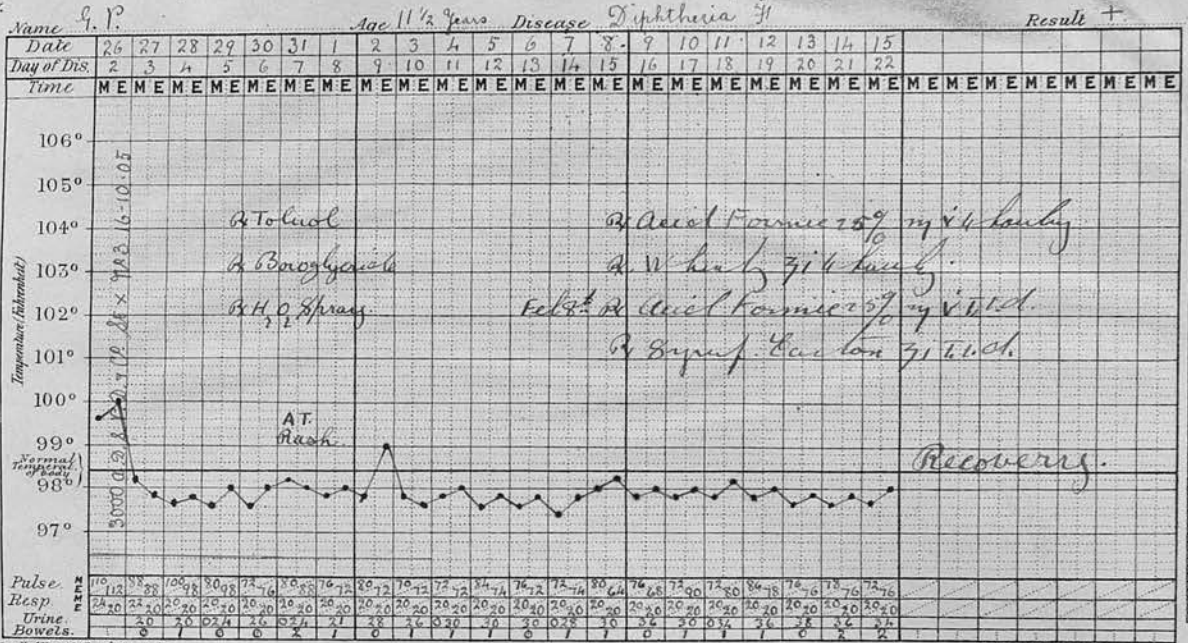
Jan. 26th To come complaining of feeling of pressure & slight proceroidal pain near mitral area. There is a slight blowing systolic mitral murmur. Pulse is slightly thready & force & volume poor.

Jan 30th Pulse & general condition much improved. Pulse is regular. Pain is gone.

Feb 8th Pulse excellent. Pulse regular & good. Mitral systolic murmur almost imperceptible.

Feb 20th Throat painful. Left tonsil enlarged. Right tonsil slightly so. Feb 25th Pus evacuated from both tonsils. Patient afterwards made good recovery and left for home well.

Case XI



Description of Case.

Fauces congested. Marked enlargement of right tonsil - almost to mid-line - Right tonsil connect at base with dark gray membrane. Anterior surfaces membrane shiny & glistening. Pulse is regular. Palms very pale.

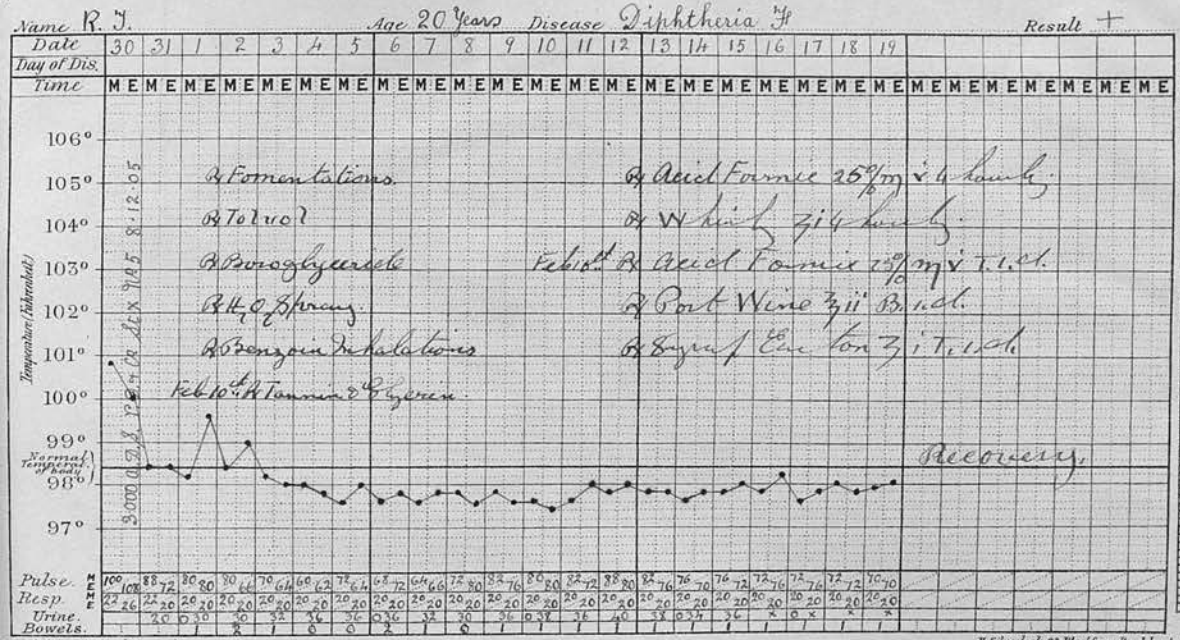
Swabs = Good short thick rods, good clusters
 Cocci anal diplo-cocci.

Culture = Neisseria positive.

History.

Jan 31st. Antiseptic antitoxin rash.
 Patient made an uninterrupted recovery. Pulse always regular & good.

Case XIII



Description of Case.

Post tonsils covered at base with thick grayish-white membrane which is somewhat shagreened & at centre dark gray in colour. Maximal enlargement of cervical glands. Heart: slight enlargement of left side. Heart & aortic mitral murmur not pronounced. Pulse regular & volume good.

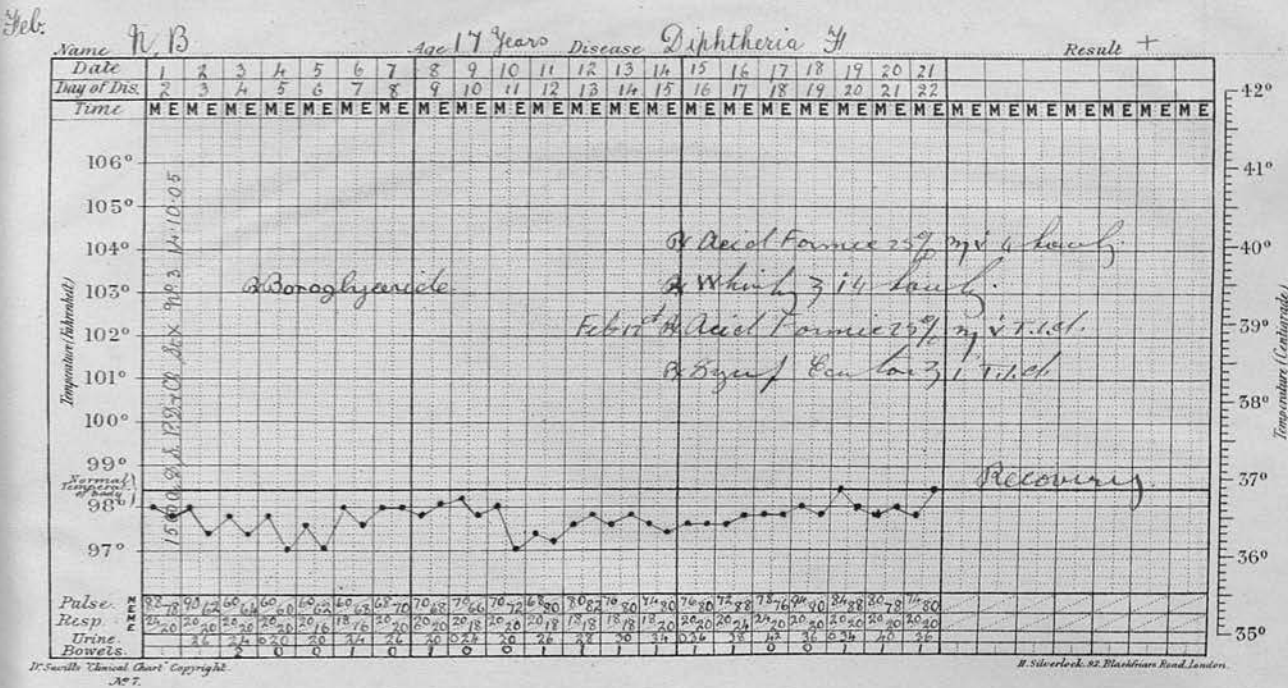
Exudate = Thick & hot wabs. Difflod St. ph. cocci.

Culture = Mixed Positive.

History.

Patient made good recovery. Heart & aortic murmur was still enlarged left side but murmur not so obvious. Pulse excellent.

Case XIV



Description of Case.

Fauces are a little injected. No tonsillar enlargement. No definite membrane but patches of filmy membrane base of soft palate. Pulse is slightly irregular with poor volume.

Swab = Short rods. Thick rods.

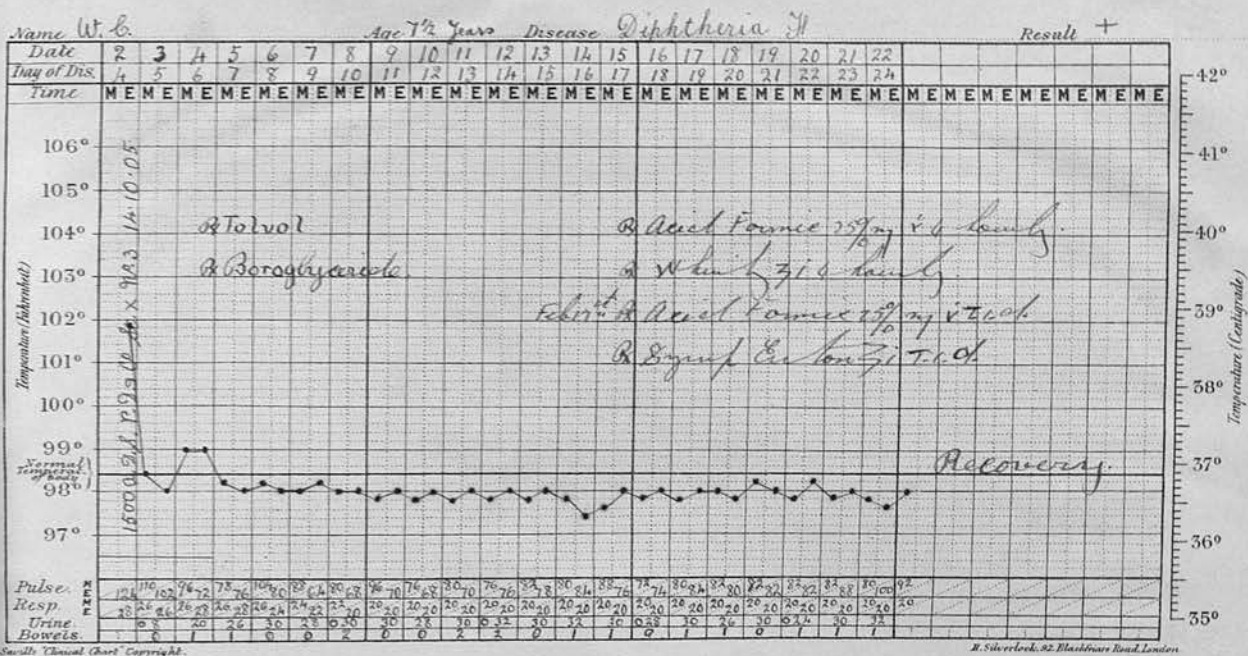
Staphylococci and Diplococci.

Culture = Mixed Positive.

History.

Feb. 9th Got up in bed & felt faint. Pulse irregular.
 Feb 18. Has vertigo since 9th Is a good colour with regular good pulse. Nocturnal cough.
 Left for home in good health.

Case XV



Description of Case.

Right tonsil at base is completely covered with granular membrane which is very tough & thick. The left tonsil has a small patch of similar membrane at base. Throat & palate free. Child is very pale & pinched looking. Pulse is slightly shrunken & irregular.

Swab = Medium rods. Good clusters & polar staining.

Short streptococci. Diphlo- & Staphylococci.

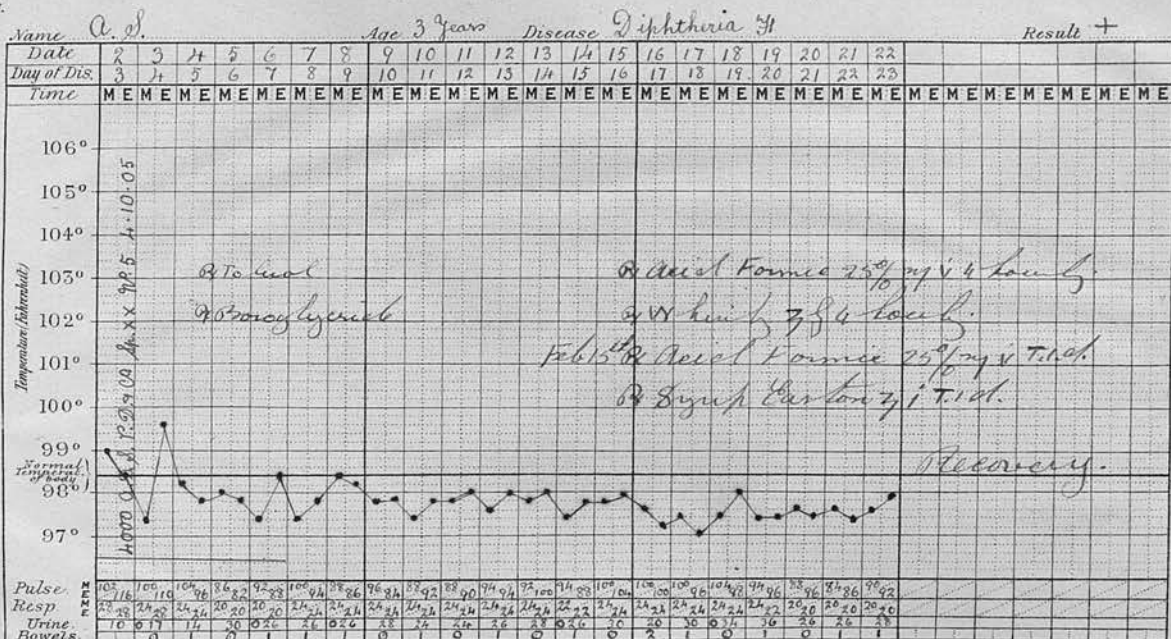
Cultures = Neisseria Positive.

History.

Pulse regular & good by Feb 11th. Made good recovery.

Case XVI

Feb.



Description of Case.

Fauces congested. Right tonsil enlarged. Left slightly. Right tonsil is completely covered with gray loose membrane. Membrane is exceedingly thick. Left tonsil is covered at base with similar tenacious membrane. Patient is very pale. Pulse irregular. Volume poor.

Swab = Good Polar stained rods. Good clusters. *Staphylococci* & *Diplococci*.

Culture = *Mucos Ponticus*.

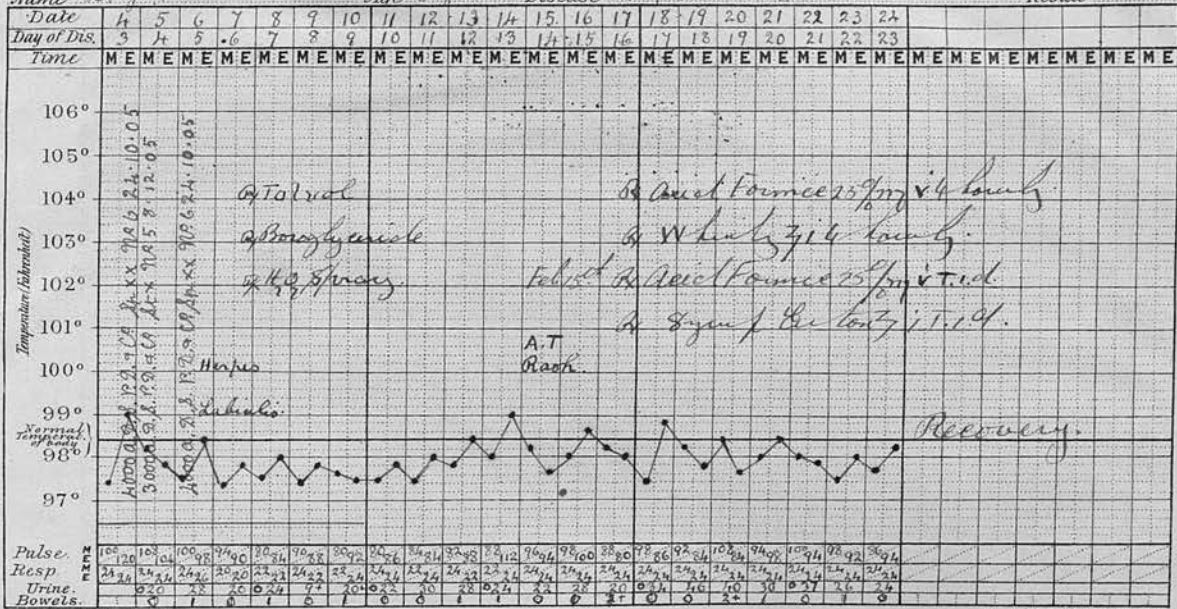
History.

Feb 7th Slight bellyache. Pulse not so marked by irregular. Feb 15th Pulse regular volume & taught better. & a good colour. Left home eventually in good health.

Case XVIII

Feb.

Name L. J. Age 8 Years Disease Diphtheria Result +



Description of Case.

Fauces congested. Both tonsils slightly enlarged & both are completely covered with whitest-grey membrane. Membrane on left side & tip covered with similar membrane. Pulse is regular but poor volume.

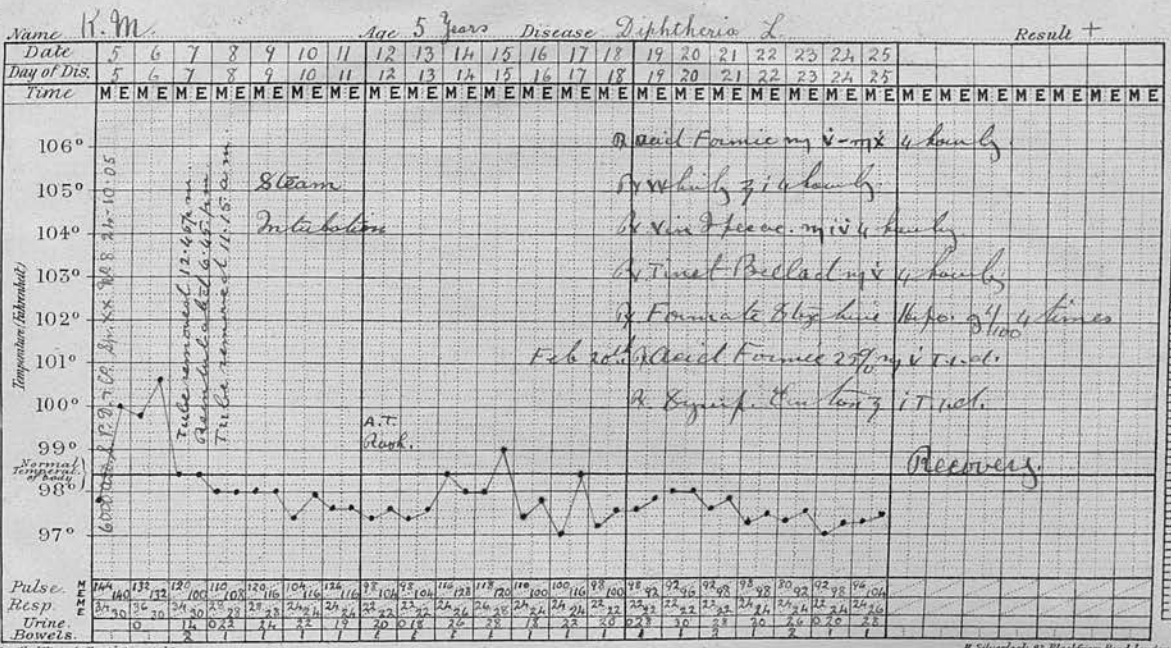
Swab = Medium & short polar sterical rods. Oval clusters. Staphylococci & Diplococci.

Culture = Neisseria Pointing.

History

Feb 5th Membrane spread to right side of mouth & partially
 Feb 6th Membrane spread slightly on to palate right side.
 Feb 10th Slightly morbilliform antheroin ex. on face.
 Feb 16th Good colour. Pulse regular. Heart normal.
 Patient made a number of urine interrupted recovery.

Case XIX



Description of Case.

Patient on admission very pale and collapsed. A frequent harsh strident cough. Voice very husky. Induration of intercostal spaces very marked & all external & internal muscles of respiration. Pulse irregular & thin. Is very restless and anxious looking. Fauces injected but free from membrane.

Swab = Short polar stained rods

Staphylococci & Diplococci.

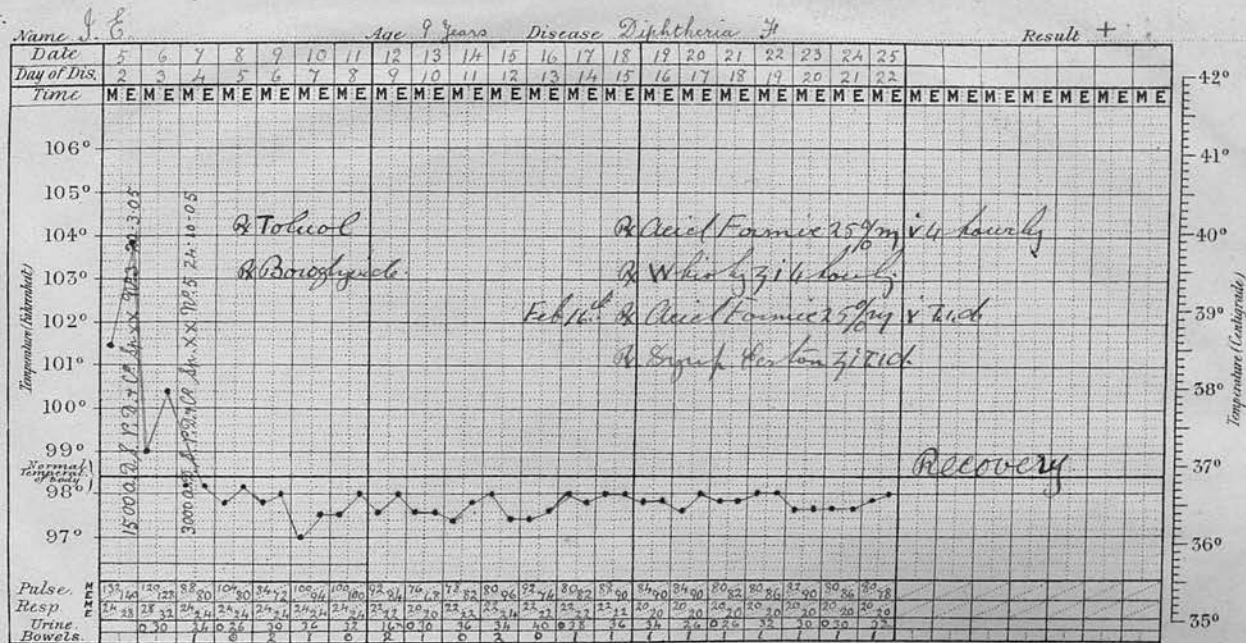
Culture = Positive Neisser.

History.

Was at once given 8 team & stimulated oil. see chart.

Description of case XIX - con -
After half hour of a time as there was no
improvement was intubated with No 4 rubber tube
After two unsuccessful attempts with an
ordinary tube. At 12.30 p.m. child collapsed
& was given hypodermic of Erythrae Formate $\frac{g}{100}$
There was within 5 minutes a distinct improvement.
2 a.m. Pulse improved but still very pale.
4.45. Patient became cyanosed & pulse very feeble
& irregular. Was again given Formate Erythrae $\frac{g}{100}$
Pulse & colour improved within 10 minutes
Feb 6th Pulse regular. Colour improved. Was
breathing easily. Heart dilated right side
slightly. 12.30 p.m. Breaths dilated & collapsed.
stopped. Feb 7th Pulse & colour still good
Tube removed 12.30 p.m. 6.45 p.m. Patient
had severe paroxysm of coughing & collapsed.
Given Formate Erythrae $\frac{g}{100}$ & rein-tubated.
8.45 p.m. Pulse regular but colour not good.
9.30 p.m. Again given Formate Erythrae $\frac{g}{100}$
12 p.m. Pulse regular & good volume & force
Colour much improved Feb 8th 12 a.m. Has left well
Breathing easily. Good pulse & colour. Tube removed
via. Throat. stopped & Acid Formic 25% $\frac{mg}{\text{inj}}$ & increased to $\frac{mg}{\text{inj}}$
Feb. 9th Breathing well. Good colour & pulse. sore diminished.
Patient made good recovery & left perfectly well.

Case XX



Description of Case.

Slight congestion of Fauces. Left tonsil covered at base with tough, tenacious gray membrane. There is a smaller patch of similar membrane on the anterior surface of right tonsil. Mucosa free.

Patient is good colour with good regular pulse.

Swabs = Mucicet roach, long thin & short rods.

Bacilli good. Loci & Diplococci.

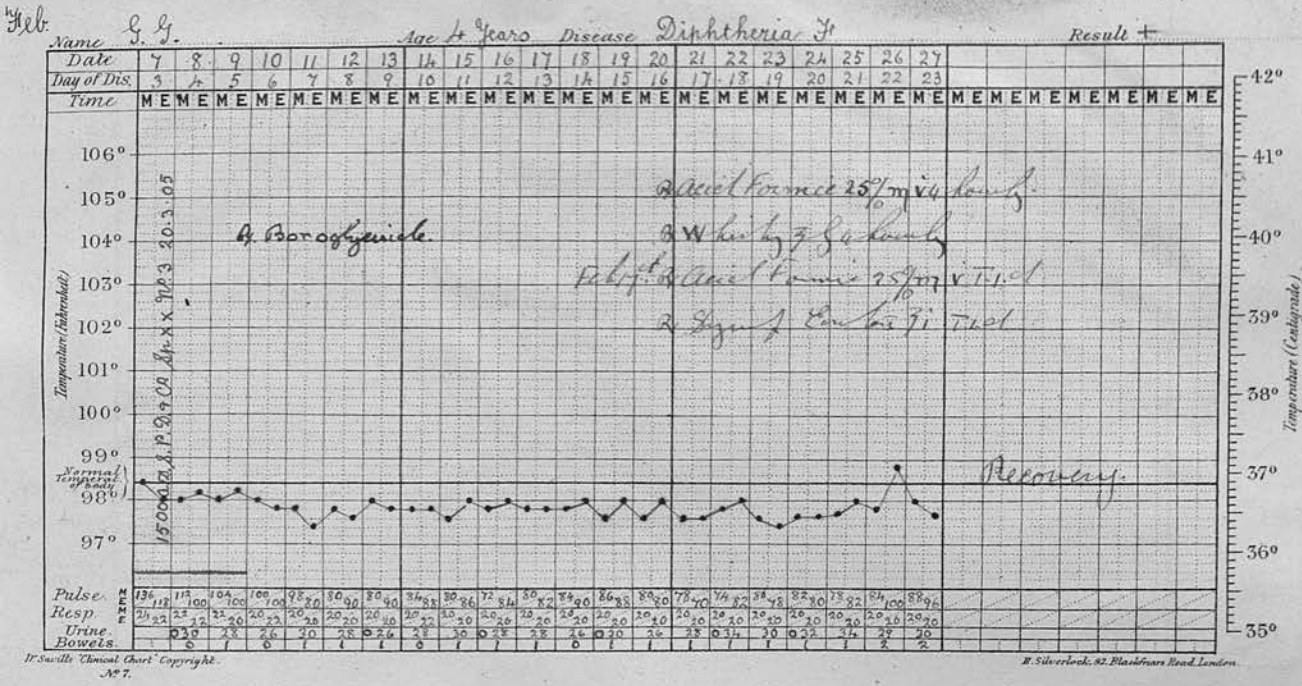
Culture = Neisser Pointing

History

Feb 7th Membrane spread slightly on the left tonsil. Colour good. Pulse good.

Patient afterwards made an uninterrupted recovery.

Case XXIII



Description of Case.

Fauces not congested. Tonsils not enlarged. Patch of filmy white membrane base of right tonsil & tip of uvula. Pulse regular & good.

Swabs = medium sized polar stained rods.

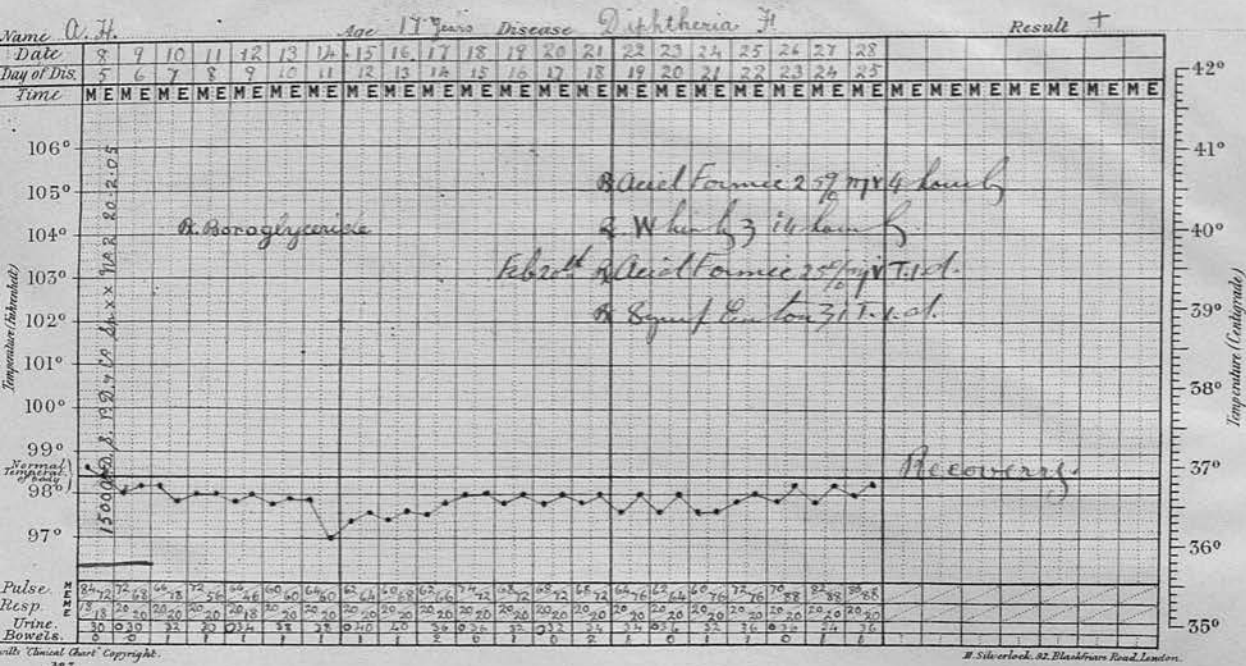
Long thin rods cocci & diplococci

Cultures = Newer Positive

History

Pulse remained regular & good. Patient also and patient made an uninterrupted recovery.

Case XXIV



Description of Case.

Coast tonsils are slightly enlarged and covered with thin greyish yellowish membrane. Throat & palate free. Pulse is slow but regular with good volume.

Swab = Short Polar stained warts? Loesi

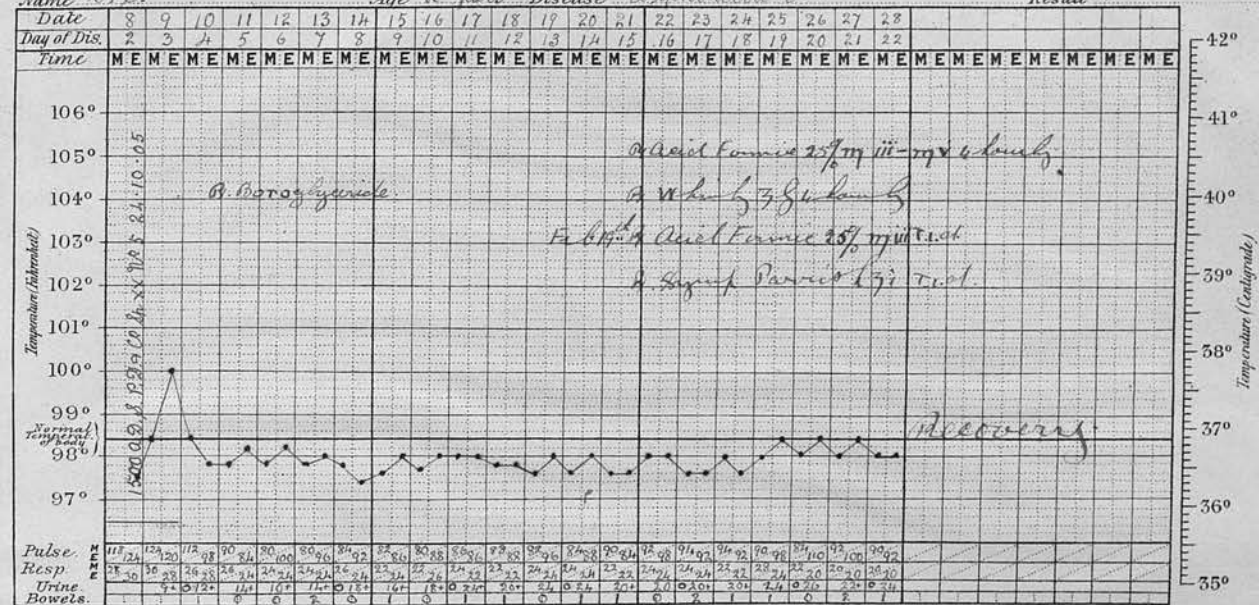
Culture = Nesser Positive

History

Patient made uncomplicated recovery.

Case XXVI

Name G. S. Age 2 Years Disease Diphtheria Result +



Description of Case.

A small patch of grayish membrane which becomes blanching on removal at base of left tonsil. Throat & right tonsil free. Pulse soft but regular.

Swab = a few short thick rods & spores.

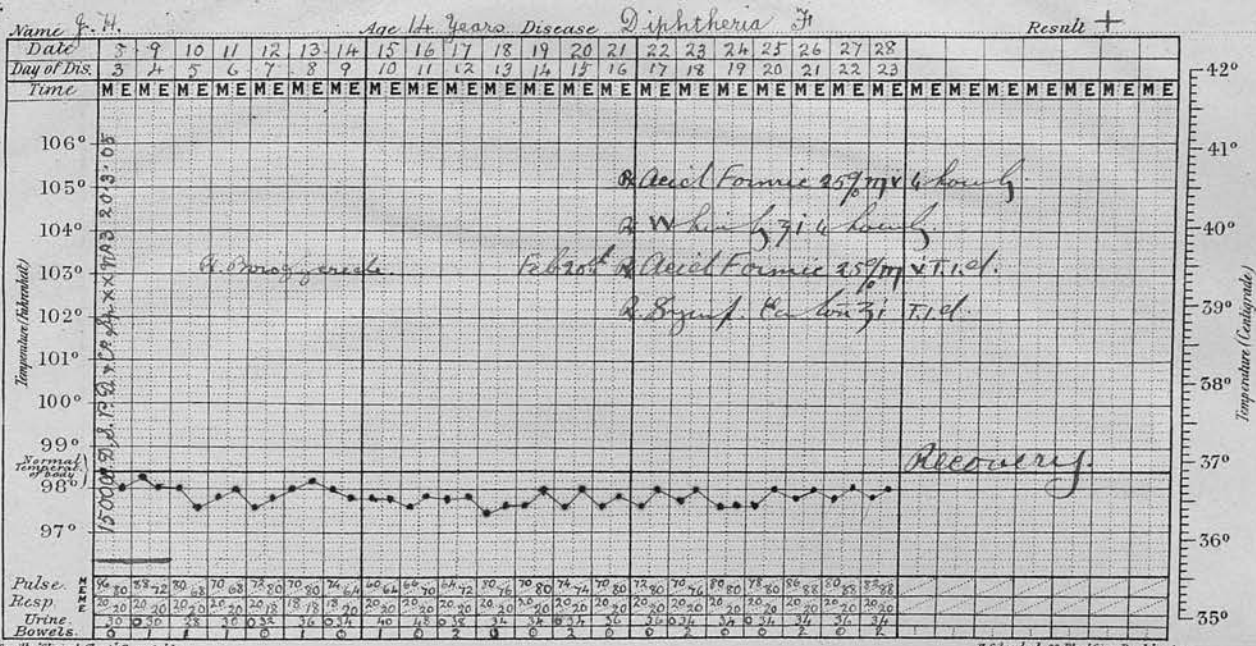
Culture = Negative

History

Pulse improved in volume and force by Feb 16th. Was always regular. Marked improvement in colour. Patient made uncomplicated recovery.

Case XXVIII

Feb.



Description of Case.

Patch of grayish looking membrane base of right tonsil. No tonsillar enlargement. Fauces are slightly injected. Pulse & color good.

Exurb = Good short rods & diplococci.

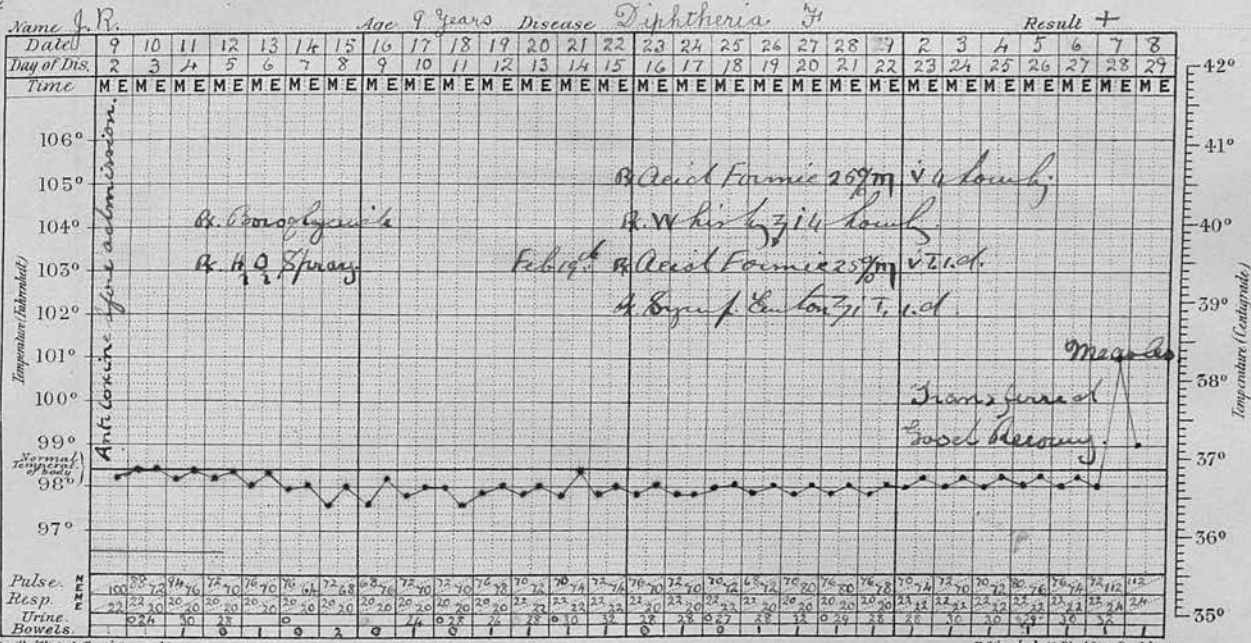
Culture = Mixed Bacteria

History

Patient made an uncomplicated recovery.

Case XXXIX

Feb.



Description of Case.

Fauces congested. Post tonsils enlarged. Both tonsils covered with grayish white membrane which appears to be loosening.

Mouth & palate not involved. Pulse regular & good. Sa good colour.

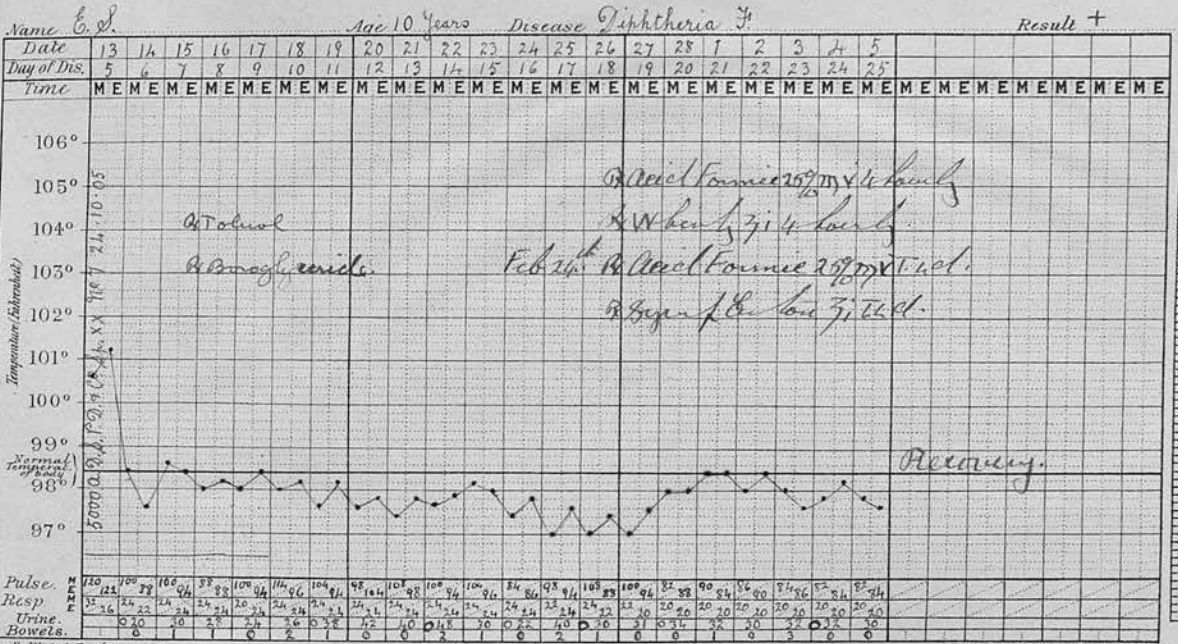
Swabs = Very good mixed results. Polar staining. Good cultures. Diplococci.

Culture = Newer positive.

History.

Made good recovery but contracted measles on Feb 29th. Recovered & left for home in good health.

Case XXXVIII



Description of Case.

Both tonsils are completely covered with very thick dark gray tenacious membrane. Uvula right side & tip is also covered with similar membrane. Pulse is regular and good in time & force.

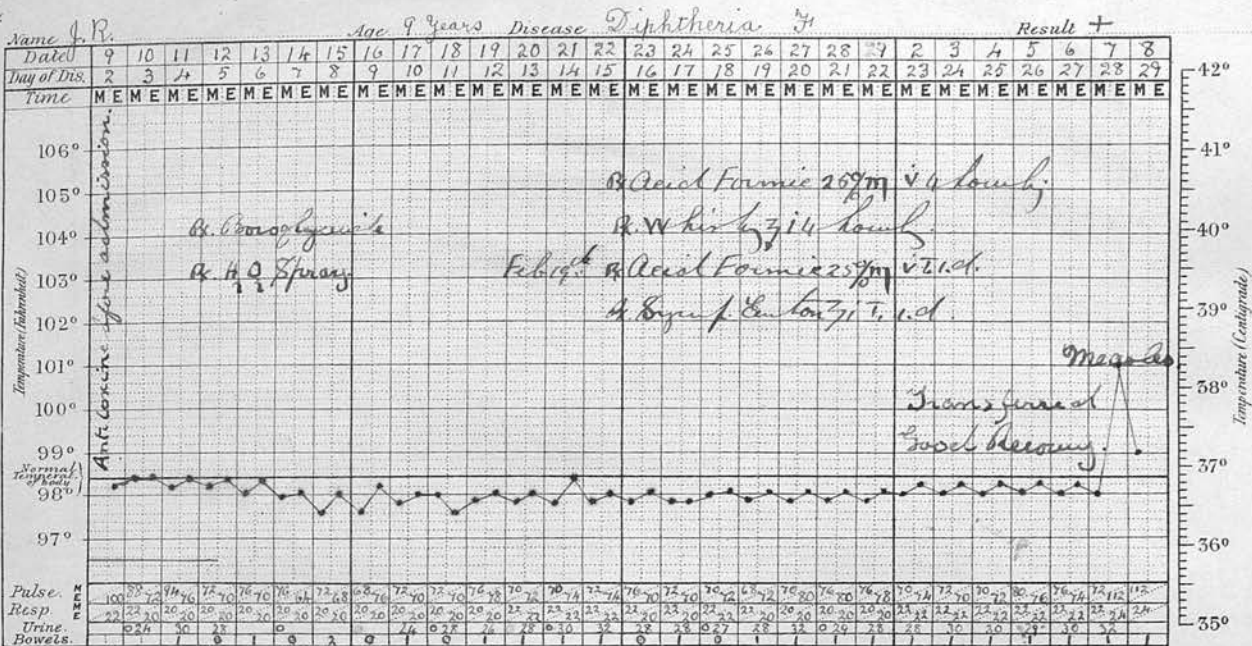
Growth = Good pale stained roots. Good clusters of staphylococci.

Culture = mixed bacteria.

History

Case slightly soft on 14th & 15th. Appetite improved and patient made an uncomplicated recovery.

Case XXIX



Description of Case.

Fauces congested. Both tonsils enlarged. Both tonsils covered with grayish white membrane which appears to be loosening.

Mucosa of palate not involved. Pulse regular & good. Good colour.

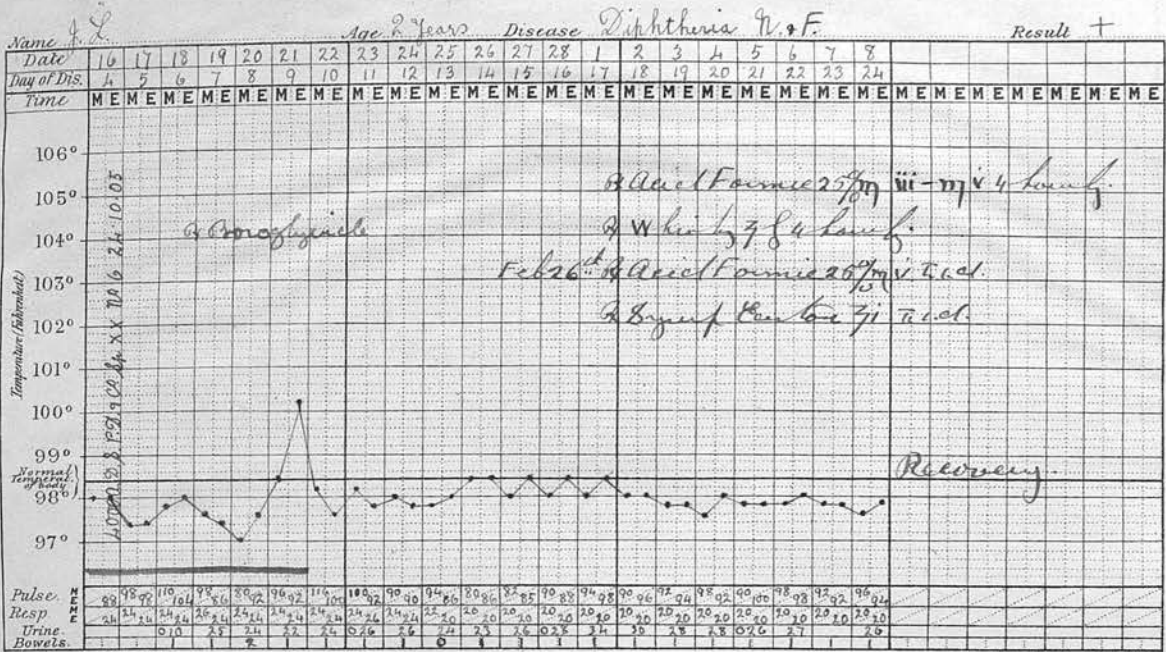
Swabs = Very good mixed results. Polar staining. Good cultures. Diplococci.

Culture = Negative Result.

History.

Made good recovery but contracted measles on Feb 29th. Recovered & left for home in good health.

Case XXXIV



Description of Case.

Fluor discharge from left nostril. Fauces are not congested. Suspicious film on gray patch of membrane have left nostril. Voice clear. No cough. Pulse is regular. Good volume & force. Patient is very pale & lethargic.

Swab = Bone joint rods many large diplococci. Staphylococci.

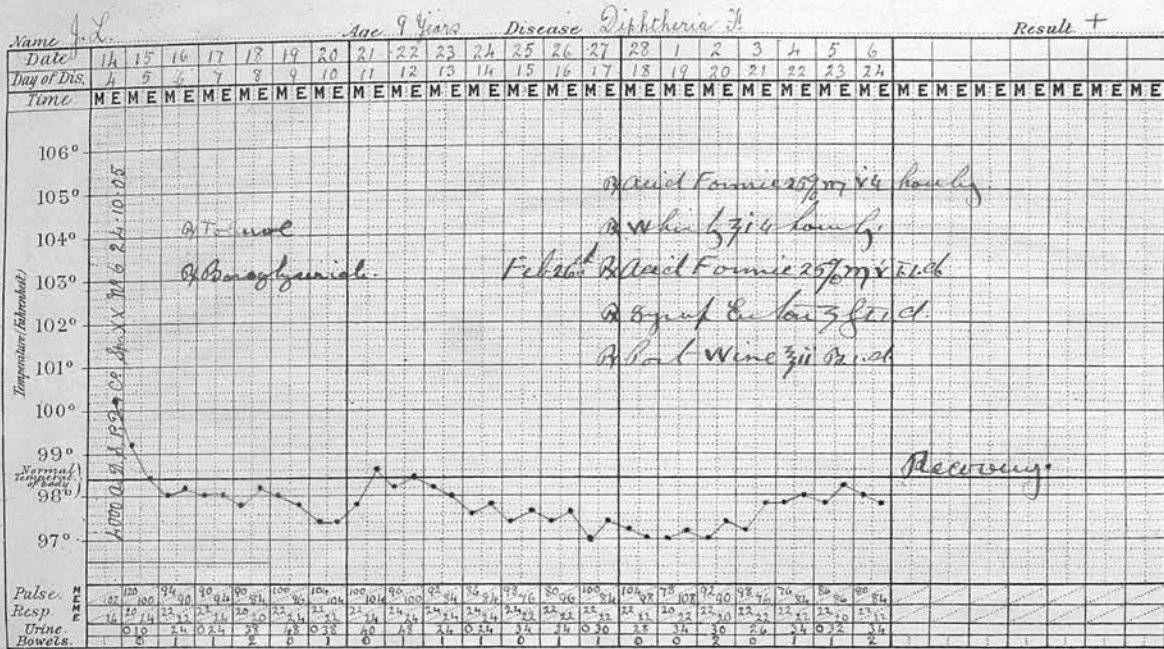
Swab = Throat = Good short rods. Diplococci.

Cultures = Negative Positive.

History

Patch on left nostril was present for 7 days. Patient made an uncomplicated recovery.

Case XXXVII



Description of Case.

Back teeth connect at base with thick tenacious patch of slant grey membrane. Fauces congested. Pulse is very soft & compressible but regular.

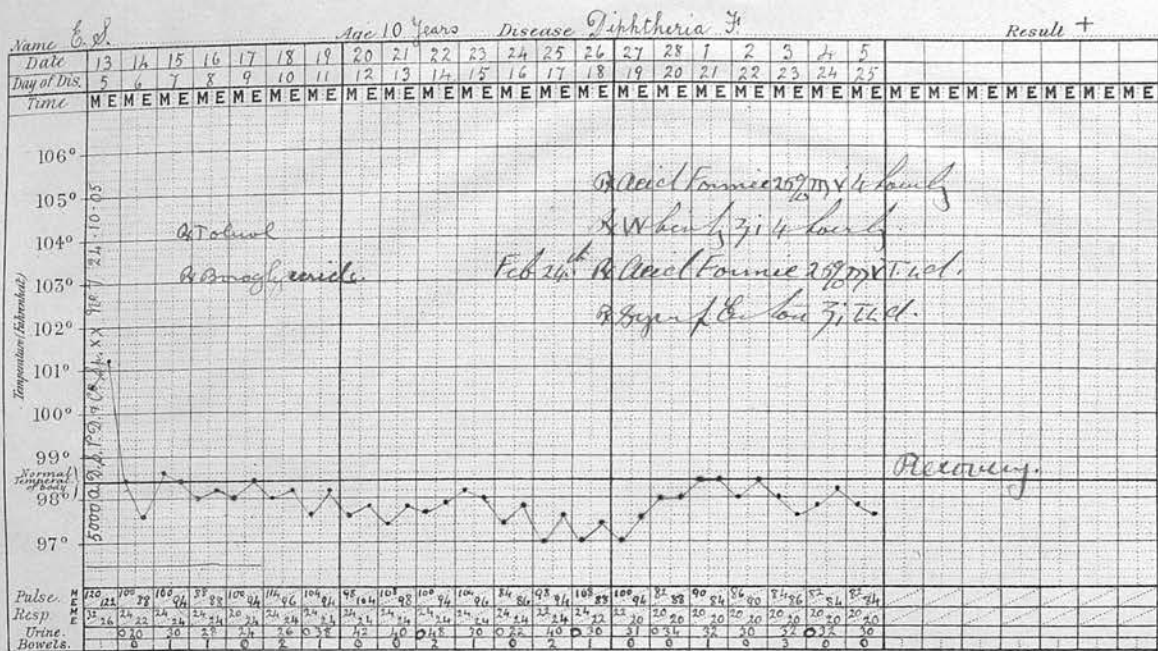
Swab = Many good medium rods. Some pale staining. Diphtheria and Loeffler.

Culture = Negative

History

Pulse gradually improved & patient who on admission had been very pale and toxic, became good colour and made an uncomplicated recovery.

Case XXXVIII



Description of Case.

Both tonsils are completely covered with very thick dark gray tenacious membrane. Tonsilla right side & tip is also covered with similar membrane. Pulse is regular and good nature & force.

Growth = Good pale stained roset. Good

culture. *Staphylococci*.

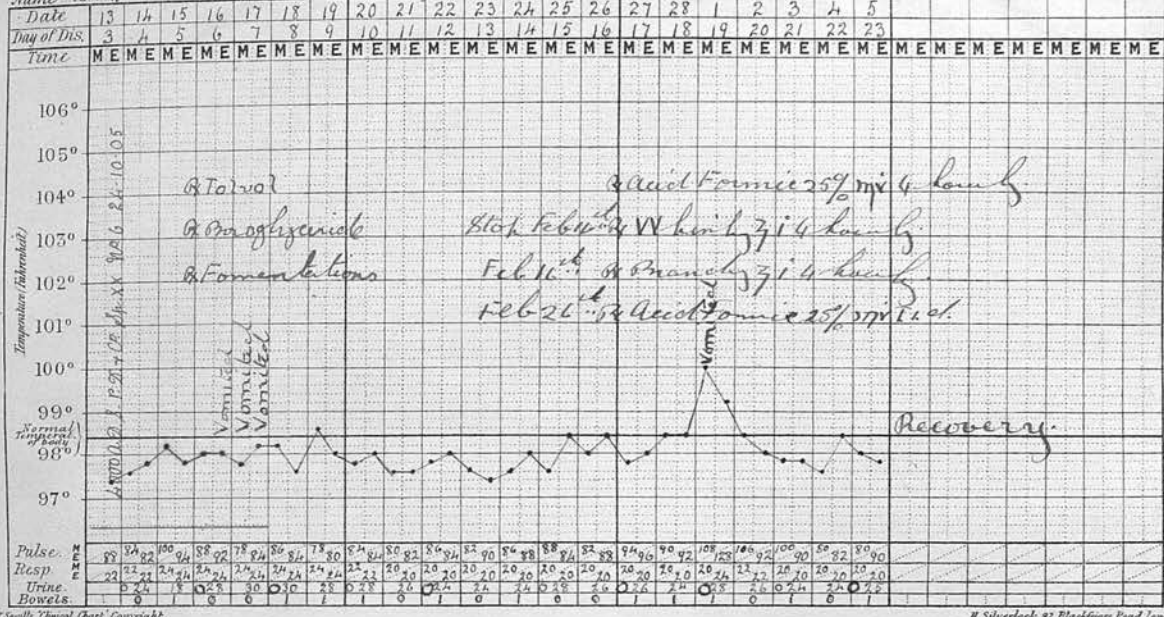
Culture = *Neisseria* positive.

History

Case still soft on 14th & 15th. A patient improved and patient made an uncomplicated recovery.

Case XXXIX

Name B. M. Age 5 years Disease Diphtheria Result +



Dr. Swell's 'Clinical Chart' Copyright 1907

H. Silverlock, 92, Blackfriars Road, London.

Description of Case.

Both tonsils are covered at base with thick tough dark-gray membrane. The membrane on the right tonsil is thicker than that on left. Fauces are congested. Throat and palate are free from membrane. Patient is very pale and poisoned looking. Pulse is regular but soft.

Swabs = Short rods with diplococci and Staphylococci.

Cultures = Neisser's positive.

History

Feb 15th. Patient vomited this morning one

Description of case XXXIX - con -
and a half hours after food. Slightly
cold extremities but pulse regular
and colour good. Heart not enlarged.
Aortic area. ^{1st} sound faint. Other
sounds clear. Complaints of slight
pain just above costal margin in
middle line. Pulse 112

stomach & given Fomies Acid by 190 Bunsen by
by the mouth & hourly. Milk perforated.
Feb 17th Again vomited 1 hour after food
Feel per rectum. Pulse remains regular
& good. Is a good colour & warm.
No pain.

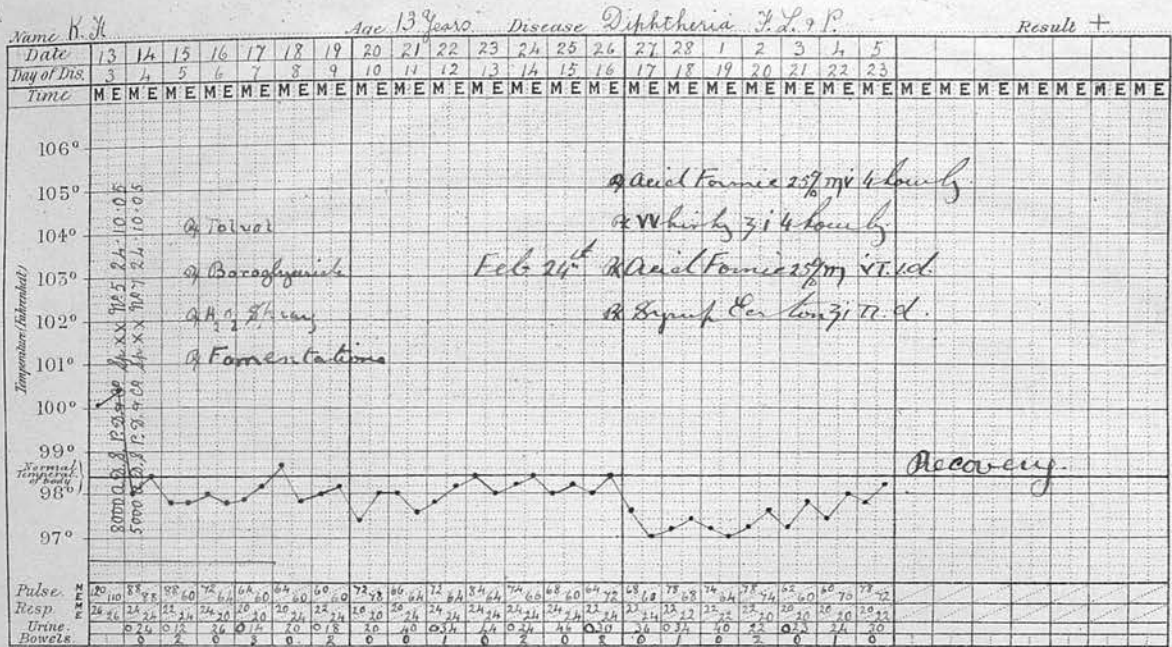
Feb 18th Has not again vomited.

March 1st Vomited this morning after
food. No pain. Good Pulse & regular
Good colour. Heart not enlarged.
Sounds all over clear

Patient subsequently made an
uninterrupted recovery.

Case XL

Feb.



Description of Case.

Left tonsil is enlarged & completely covered with very thick & tenacious grayish-white membrane. Palate is involved on the same side. Stomach on left side and at tip is covered with a similar membrane. The voice is very hoarse and there is an occasional short harsh cough. There is very marked enlargement of the cervical glands on the left side of the neck. Patient is pale and pulse is soft and rapid.

Swabs = Mucous coats, mostly & heat coats
 Palate stained coats. Plaster.

W. Smith's Clinical Chart Copyright No. 7.

H. Silverlock, 52, Blackfriars Road, London.

Description of Case XL - con-

Staphylococci and diplococci anal cocci.

Culture = Mermer Contine

History

At night patient was very restless.

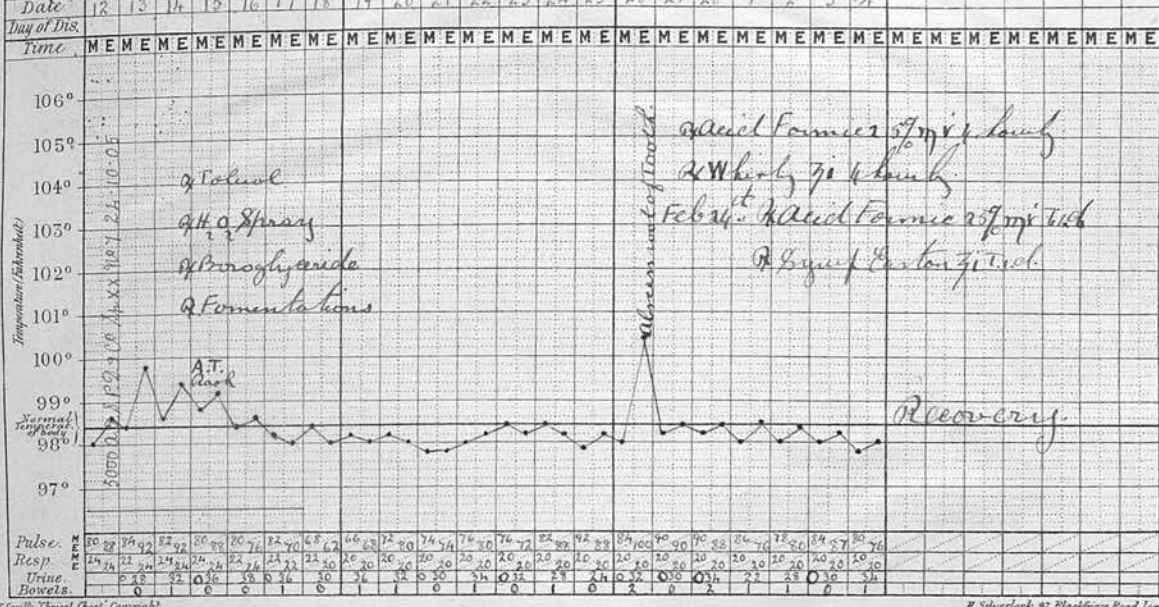
Feb 14th Process still present on palate anal
is very thick. Patient's colour is better and
the pulse is regular and good. Heart not
enlarged. Mitral area slightly soft
showing systolic murmur.

Feb 18th Patient has lost her poisonous
appearance. Good colour. Pulse regular
and good volume and force.

Patient's symptoms made an uncomplicated
recovery.

Case XLI

Name: D. W. Age: 16 Years Disease: Diphtheria Result: +



Dr. Swell's Clinical Chart. Copyright, 1917. Silverlock, 92, Blackfriars Road, London.

Description of Case.

Oral tonsils are completely covered with gray membrane which is very thick & tenacious. Soft tonsillar enlargement. Uvula unaffected. Face is slightly flushed & pulse is full and regular.

Smears = mixed rods. Short and long thin spint rods. Cocci and Staphylococci.

Culture = Dreyer Positive

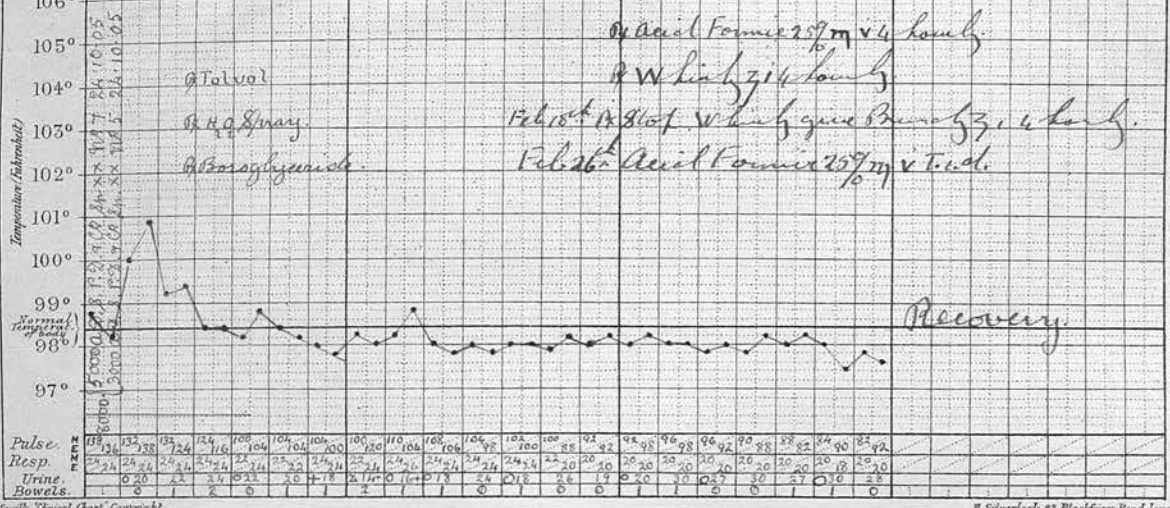
History

Feb 14th Polarity erythema antitoxin with some escharitis on buccal form on trunk. Had slight fever not of right premaxilla on 25th & 26th. After this had an uncomplicated recovery.

Case XVII

Feb.

Name	Age 4 Years. Disease Diphtheria																							Result
Date	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	1	2	3	4			
Day of Dis.	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23			
Time	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E		
Temperature (Fahrenheit)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0		
Pulse	118	132	138	124	116	104	104	100	100	110	106	106	104	102	100	98	92	94	98	98	96	92		
Resp.	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24		
Urine	0.20	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2		
Bowels	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		



Description of Case

Back tonsils and uvula completely covered with very thick dark gray membrane. Palate not affected. Voice is clear but there is an occasional short explosive cough. Child is very pale and poisoned looking. Pulse is soft and somewhat irregular both in time and force. Beat. Slight enlargement left side. 1st sound in aortic area is faint other sounds clear.

Swab = Good short rods anal Coeci
Culture = Negative

History

Feb. 18th Patient vomited one and a half hours

H. Swill "Clinical Chart" Copyright. '16 7.

J. Silverlock, 92, Blackfriars Road, London.

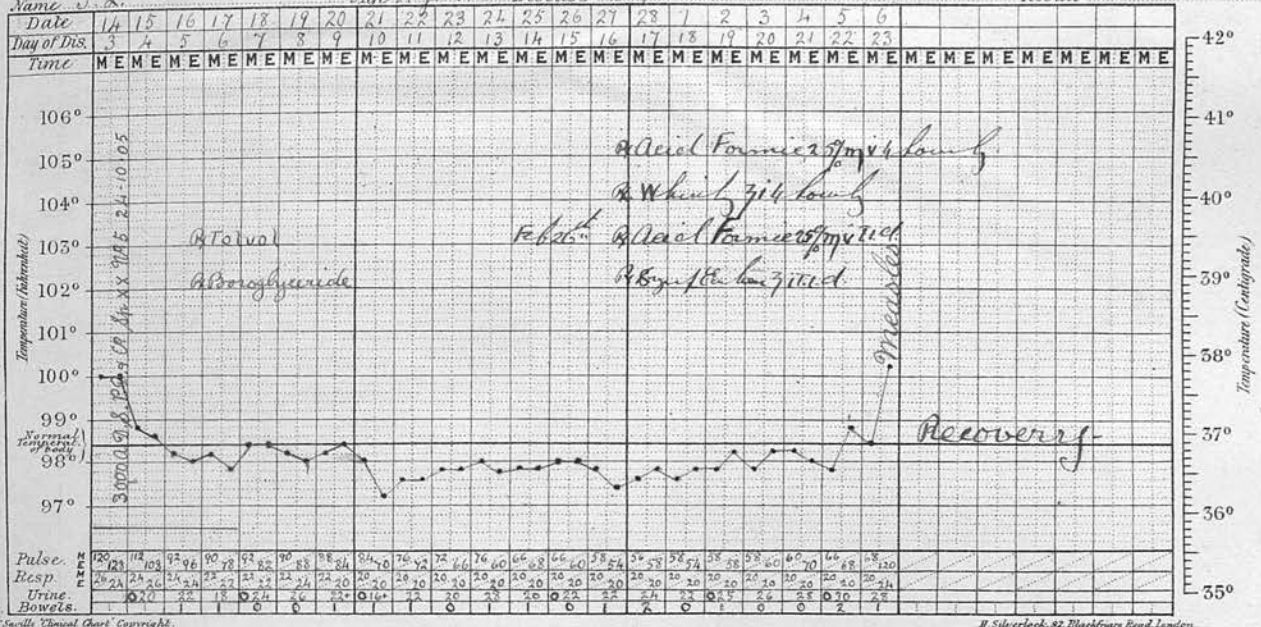
Description of case ~~XIII~~ - con -

after food. Is very pale and pulse
soft but regular. Given Bismuth
instead of Whisky, peptonized milk etc.
Feb 19th vomited last night 1 pint. No
pain. No murmur. Pulse is still soft
but regular. A trace of albumen in urine.
Feb 21st Pulse much improved. Pain
is also much better. No further sickness.
Patient afterwards made an
uncomplicated recovery.

Case XLIII

Feb.

Name J. L. Age 4 Years Disease Diphtheria II Result +



Description of Case.

Large patch of very adherent dark gray membrane over base of right tonsil. Left tonsil has a smaller patch at base of similar membrane.

Patient is a good color & has a good, regular pulse.

Swab = Good short rods. Diplo? Staphylococci.

Culture = Negative

History

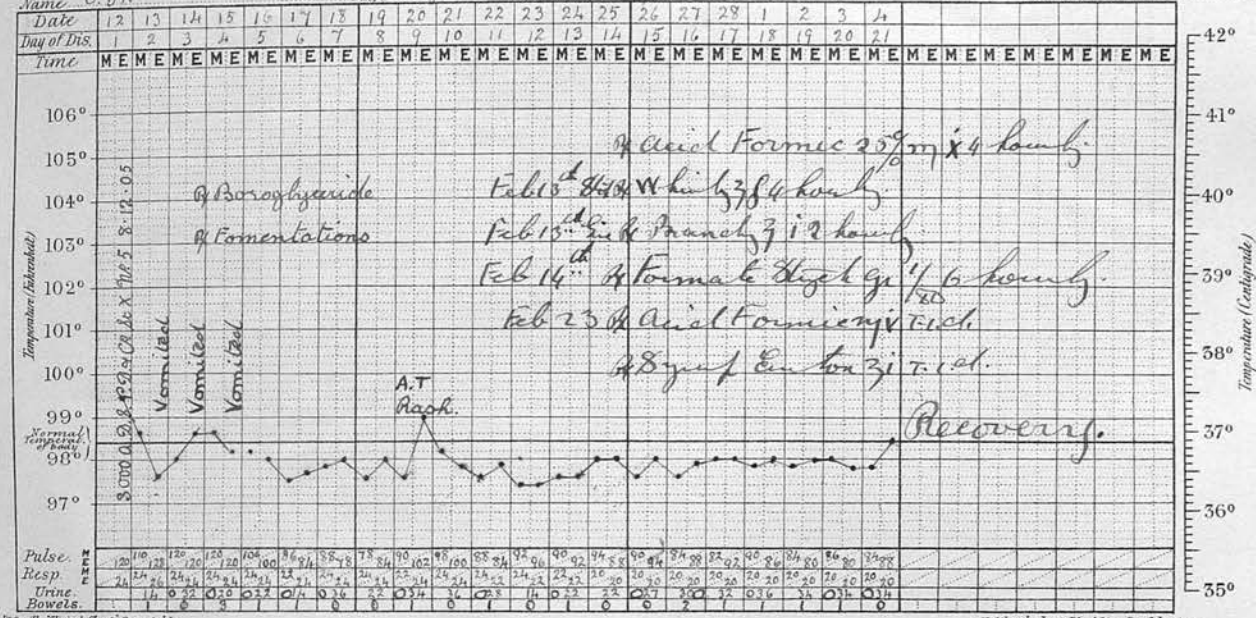
Patient eventually contracted measles & was then forced to another ward where he made uncomplicated recovery from both diseases.

W. Saville 'Clinical Chart' Copyright No. 7.

H. Silverlock, 82, Blakmore Road, London.

Case XLV

Name G. H. Age 8 Years Disease Diphtheria ? Result +



Description of Case.

Fauces are congested right tonsil very slightly enlarged with a filmy gray patch at base. Uvula & palate free. Left tonsil free. Marked enlargement of right submaxillary gland. Patient is very pale and toxicemic looking. Pulse is regular but poor in volume & strength.

Swabs = Good cultures of faintly staining rods. Some good rods diplococci and Staphylococci.

Culture = Negative.

It. Swell's Clinical Chart Copyright 1917.

H. Silverlock, 92, Blenheim Road, London.

History Case XLV

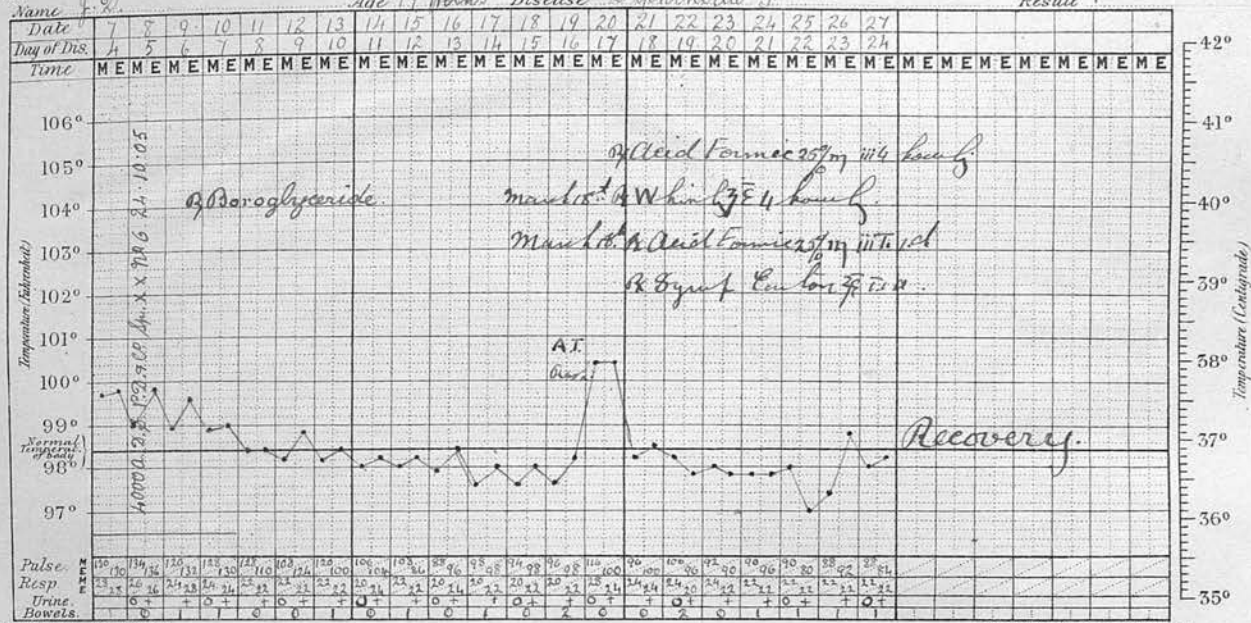
Feb 13th 12. noon. Has vomited 3 times during part 12 hours irrespective of food. Pulse is very soft & somewhat irregular. Patient is very pale. Given Salines, Brandy & Acid Fomix per rectum. At 5 p.m. given Peptonized milk, vomited. No pain but pulse very irregular. 6 p.m. Given Formula & Sydenham q'100 hypodermically. 8 p.m. Pulse has much improved. Is regular & volume & force better. No further sickness. 12 p.m. Has again vomited. Pulse is still regular. Heart not enlarged. Aortic 1st sound faint. Nutrition & salines continued. Feb 15th Has not again vomited. Retains Peptonized milk Brandy & Acid Fomix by mouth. Feb 17th No further sickness. Pulse is good. Pulse regular & good. Feb 20th Diffuse erythematous eruption on trunk. Patient afterwards made an uninterrupted recovery.

Case XLVIII

March

Age 19 Males Disease Diphtheria 71

Result +



Dr. Smith's "Normal Chart" Copyright 1917 No. 7.

Silverlock, 82, Blackheath Road, London.

Description of Case.

Right tonsil completely covered with thick white membrane which is very tenacious. Left tonsil slightly congested. Patient is pale and poisoned looking. Pulse is regular and good volume etc.

Swab = Faint rods *Staphylococcus* Ovoids

Culture = Negative.

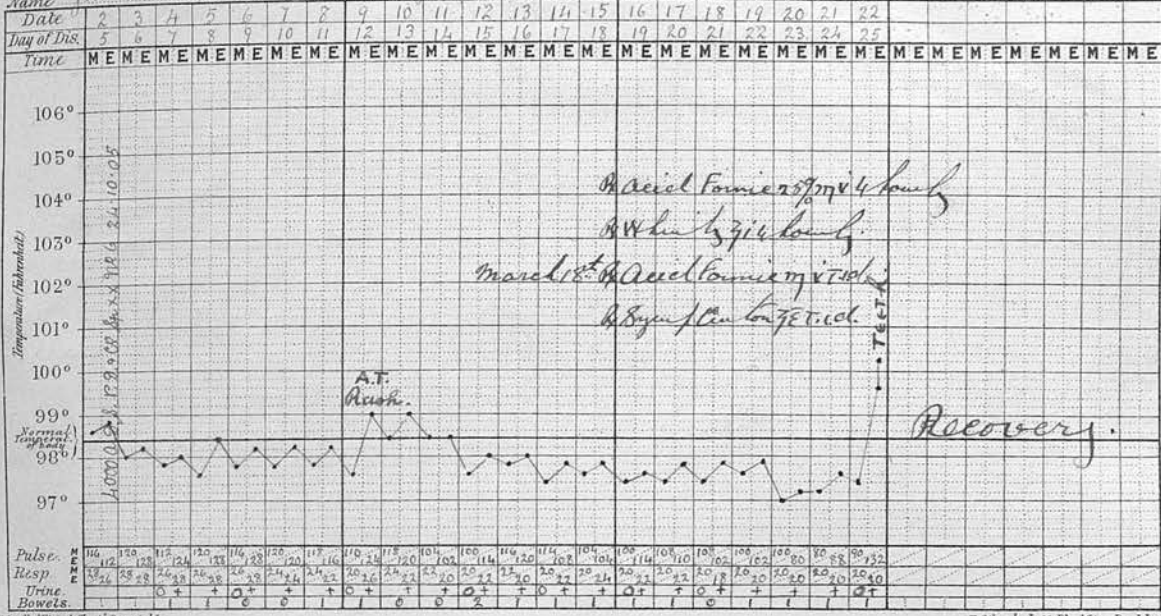
History

Patient's colour much improved by the 13th. Pulse remained regular & good. Slight antitoxin rash - morbilliform - on trunk on the 17th. Patient afterwards made an uninterrupted recovery.

Case II

March

Name J.D.G. Age 2 Years Disease Diphtheria N. Result +



Description of Case.

Slight congestion of fauces. Nasal discharge marked from both nostrils. Slight excoriations at nostrils. Patient is very pale - waxy looking - appears very toxicemic. Stools is regular but very soft.

Swab = Nose = Very good short polar staminal rods. *S. floccacei*.

Throat = Short thick rods. *Staphylococci*.

Cultures = Negative

History

Patient improved in colour & per se by March 7th. Had a tertiary temperature for 3 days on 25th. Made otherwise an uncomplicated recovery.

D. Scott's "Clinical Chart" Copyright 1917.

H. Silverlock, 92, Blenheim Road, London.

Description of Case LIII - con -

soft and irregular.

Swab = Good rods, thick short rods.

Polar stained rods. Diplococci
and Staphylococci.

Culture = Neisseria Conjunctiva

History

Patient on 25th still looked very toxicemic
and pulse was very soft and irregular.
Membrane spread slightly on right side.
March 1st Pulse is stronger and more regular.
Heart Aortic 1st sound replaced by faint systolic
murmur. March 4th Patient vomited twice

irrespective of food. Pulse very irregular
& very soft. At times almost imperceptible.

Is very pale & listless. Hypochromic etc.

March 5th No change but no further

vomiting. March 6th Became restless at

4 p. m. and returned to bed by 10 p. m. Died

at 4 a. m. March 7th

A case apparently hopeless from the
start. Although the case is charted
as being admitted on 4th day of disease
a subsequent examination of parents proved

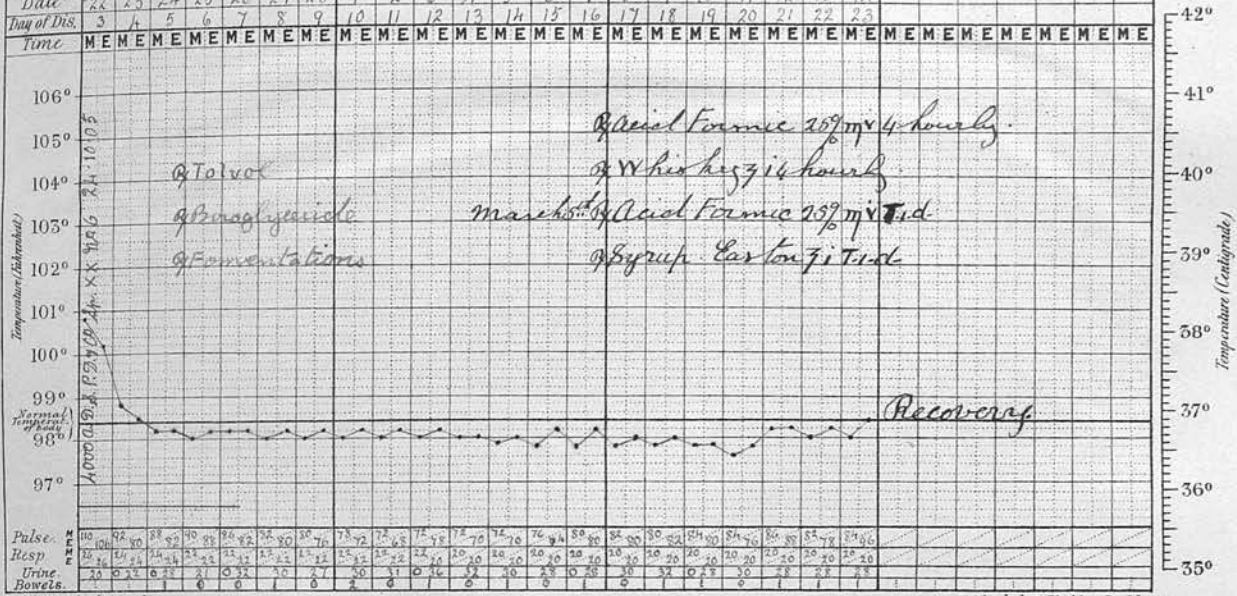
child to have been ill for at least 7 days

Facts which were borne out by appearance on admission

Case IV

Name: J. J. Age: 14 Years Disease: Diphtheria Result: +

Date	Day of Dis.	Time	Temp. (Fahrenheit)	Pulse	Resp.	Urine	Bowels
22	3	10:05	100.0	92	20	0.2	0
23	4	10:05	99.5	90	18	0.3	0
24	5	10:05	99.0	88	16	0.4	0
25	6	10:05	98.5	86	14	0.5	0
26	7	10:05	98.0	84	12	0.6	0
27	8	10:05	98.0	82	10	0.7	0
28	9	10:05	98.0	80	8	0.8	0
29	10	10:05	98.0	78	6	0.9	0
30	11	10:05	98.0	76	4	1.0	0
31	12	10:05	98.0	74	2	1.1	0
1	13	10:05	98.0	72	0	1.2	0
2	14	10:05	98.0	70	0	1.3	0
3	15	10:05	98.0	68	0	1.4	0
4	16	10:05	98.0	66	0	1.5	0
5	17	10:05	98.0	64	0	1.6	0
6	18	10:05	98.0	62	0	1.7	0
7	19	10:05	98.0	60	0	1.8	0
8	20	10:05	98.0	58	0	1.9	0
9	21	10:05	98.0	56	0	2.0	0
10	22	10:05	98.0	54	0	2.1	0
11	23	10:05	98.0	52	0	2.2	0
12	24	10:05	98.0	50	0	2.3	0
13	25	10:05	98.0	48	0	2.4	0
14	26	10:05	98.0	46	0	2.5	0
15	27	10:05	98.0	44	0	2.6	0
16	28	10:05	98.0	42	0	2.7	0
17	29	10:05	98.0	40	0	2.8	0
18	30	10:05	98.0	38	0	2.9	0
19	31	10:05	98.0	36	0	3.0	0
20	1	10:05	98.0	34	0	3.1	0
21	2	10:05	98.0	32	0	3.2	0
22	3	10:05	98.0	30	0	3.3	0
23	4	10:05	98.0	28	0	3.4	0



Description of Case.

Both tonsils a little enlarged and covered with white-gray thick membrane which on right tonsil appears to be disintegrating. Marked enlargement of cervical glands. Patient is pale & listless but pulse regular & good.

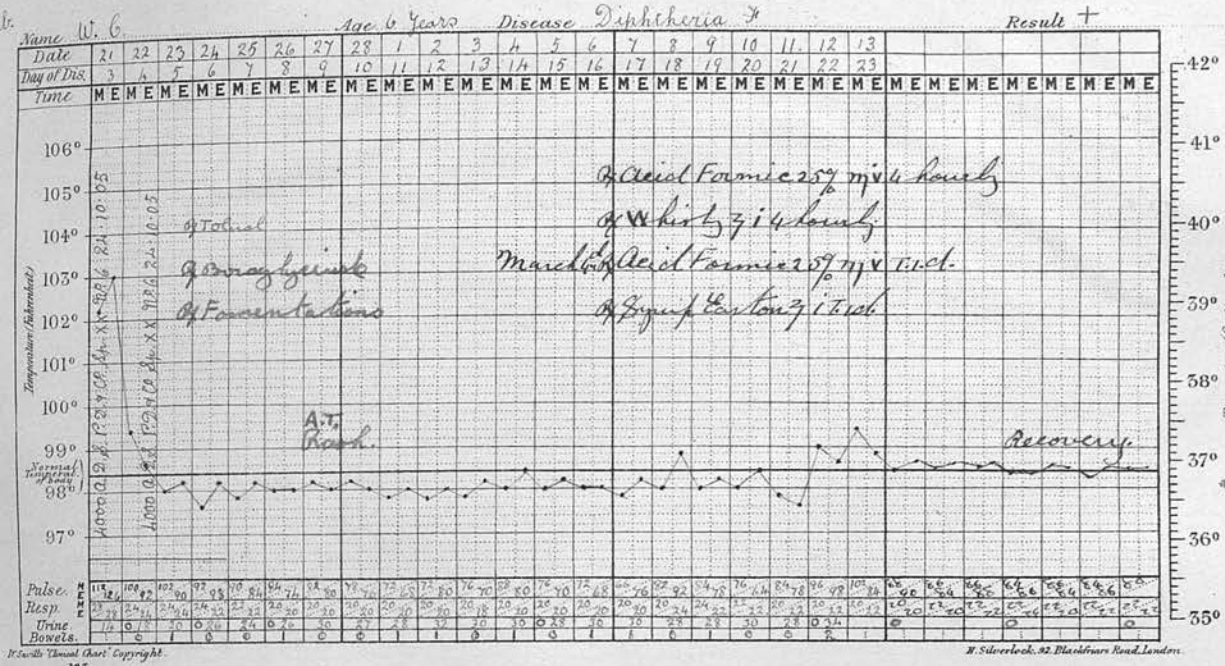
Swab = Some good short rods. Long thin rods. Short streptococci and diphtheriae & Staphylococci.

Culture = Neisser Positive

History

Patient improved in color by 20th and afterwards made an uncomplicated recovery.

Case LVI



Description of Case.

Back tonsils completely covered with thick white membrane which has a slightly spongy to palate on right side. Mucosa free. Patient is pale and lethargic. Pulse regular and good volume. Heart nothing to note.

Sputa = Good polar stained rods.

Diplococci and Staphylococci.

Culture = Newnes Positive

History

Feb 22nd Pulse is soft & slightly irregular. Feb 25th

Irregularity gone. Is better volume & force.

Feb 25th Multifum erythematous antibiotic red trunk.

Patient after 6 days made uncomplicated recovery.

Case LVII

Name	No.	Age	Disease	Result																			
		7 years	Diphtheria	+																			
Date	18	19	20	21	22	23	24	25	26	27	28	1	2	3	4	5	6	7	8	9	10		
Day of Dis.	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23		
Time	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M	E	M



Pulse, Resp., Urine, Bowels. © 1917, "Blood Count" Copyright. #5 Moorlock, 92, Blackfriars Road, London.

Description of Case.

Right tonsil completely covered with thick dark gray membrane. There is a small patch of similar membrane just posterior to left tonsil. Throat & palate free. Marked enlargement of cervical glands. Pulse is slightly irregular. Good volume. Patient is sweating and is very pale and poisoned looking.

Swab = Good medium. Polar stained and in clusters Staphylococci and Diplococci.

Culture = Negative

History

Description of Case **LVII** - con. -

History

Feb 20th Still very pale & prostrated looking
vomited twice. Pulse still slightly
irregular. 8 p.m. Patient vomited once
more after peptonized milk. Feel per
rectum for night Feb 21st Again
vomited. Is looking pinched. Pulse
is soft but is now regular. 2 p.m.
Again feel Peptonized milk & medicine
by mouth. Feb 22nd Has not again
vomited. Pulse is regular.

Feb 24th Patient is a better colour. Pulse
is regular & not so soft. Heart not
enlarged. No murmur. Aortic 1st sound
is faint. A trace of albumen in urine.

Feb 25th Much improved. Colour good.
Pulse regular & volume much better
& bright, & takes food well. Heart
not enlarged. Both sounds equal
No murmur.

Patient's progress made an
uncomplicated recovery. She had
on one day only a trace of albumen.

Description of Case LVIII - con. -

History - con. -

and poor in volume and force. Membrane appears to be disintegrating.

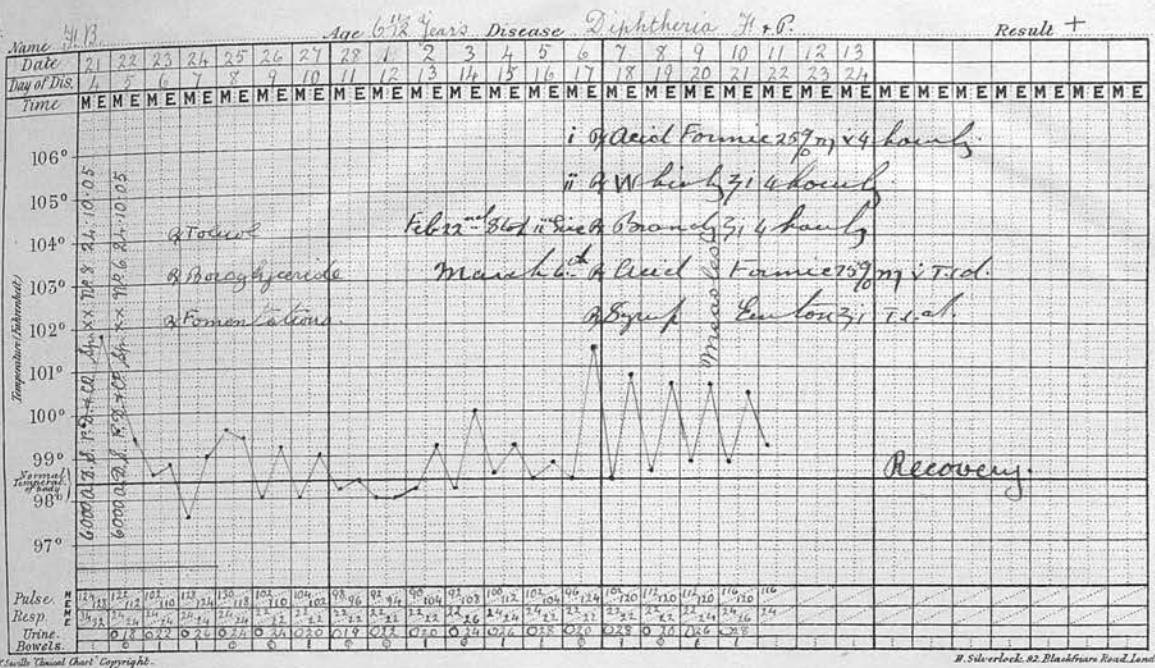
Feb 19th Patient's colour has improved. Is not so listless and prostrated looking. Pulse is now regular although still soft. Local condition has improved.

Feb 21st General condition much improved. Pulse regular. Is better volume and force.

Feb 27th Improvement continues. Heart not enlarged. No murmur.

Patient subsequently made an uncomplicated recovery.

Case LIX



i Acid Fomice 25% 4 hourly
 ii B.W. 1/2 4 hourly
 Fibra-blet 2 6 hourly 3/4 hourly
 Marsh's Acid Fomice 25% 4 hourly
 Syrup Eucalypti 4 hourly
 Marsh's

2 Tonic
 2 Boroglyceride
 2 Formen Lactans

6000 2 1/2 4 hourly
 6000 2 1/2 4 hourly

Description of Case

Both tonsils are enlarged. Left tonsil is completely covered with thick white membrane. Palate also involved. Right tonsil is covered with similar membrane at base. Uvula covered with similar membrane. Great enlargement of cervical glands. Patient is pale and exhausted looking. Appears very toxicæmic. Pulse is soft. Irregular.

Swab = Good for the stained rods
 Staphylococci & Diplococci.

Culture = Mucor Ponticus.

Description of Case LIX - con -

History.

Feb 22nd Membrane & praecium on palate
to my throat and tenacious. Heart
not enlarged. Slight soft flaccid
mitral systolic murmur. Other sounds
clear. Pulse still irregular & soft.

Feb 23rd Vomited after food. Colour
is bad. Patient is slightly cold in
extremities. Pulse is irregular.

Feb 24. Pulse rather improved & is
more regular & better volume.

Feb 25th marked change. A better
colour. Pulse regular. Slight &
better generally.

Patient continued to improve until
March 6th when he contracted Measles.

Treatment - Ferric Acetate - was stopped
and 16 days after the stopping
of the drug he developed a slight
palatal paralysis. He subsequently
made a good recovery.

Description of Case LXI - con-
History

Feb 21st Very pale & obviously severely poisoned
Pulse is slightly irregular every 80.

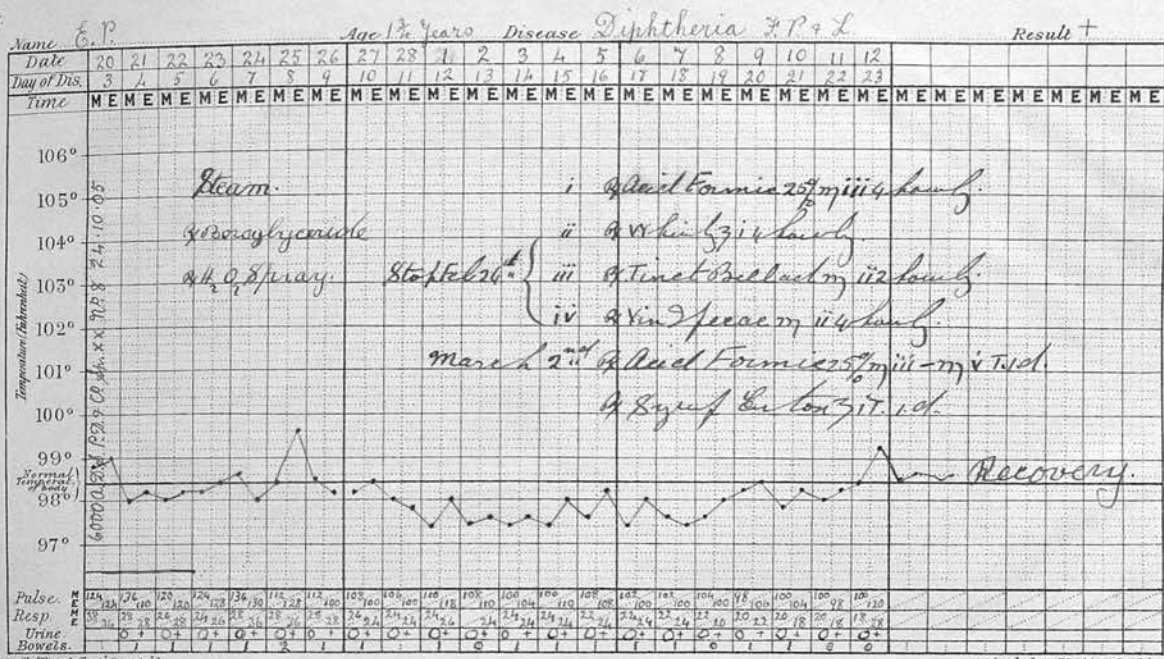
Feb 23rd Vomited twice. Aortic 1st sound
almost imperceptible. Pulse very irregular.

Feb 24th Same as 23rd. Given Formula of 8th Feb
9/80. Marked improvement in pulse &
color but only temporary.

Feb 25th Given stimulants (with chest.)
Nutrient & Salines. No improvement.

Feb 26th Died at 9.15 p. m. The end
in this case was almost identical as
patient had shown slight improvement
in heart, pulse & color for 12 hours
previously. It is interesting also to note
the absence of albumen which at no
time was present although frequently
looked for with care. The child
was extremely toxicemic from admission.

Case LXII



Description of Case.

Voice is hoarse - whispering - Frequent short
 cough. Distinct indrawing of
 intercostal spaces. Both tonsils covered
 with thick dark-grey membrane. Palate
 involved with similar membrane above
 right tonsil. Uvula free. Enlargement
 of cervical glands. Patient's colour is
 good and pulse soft but regular.

Swab = a few short rods. Staphylococci
 and diplococci

Culture = Negative
History

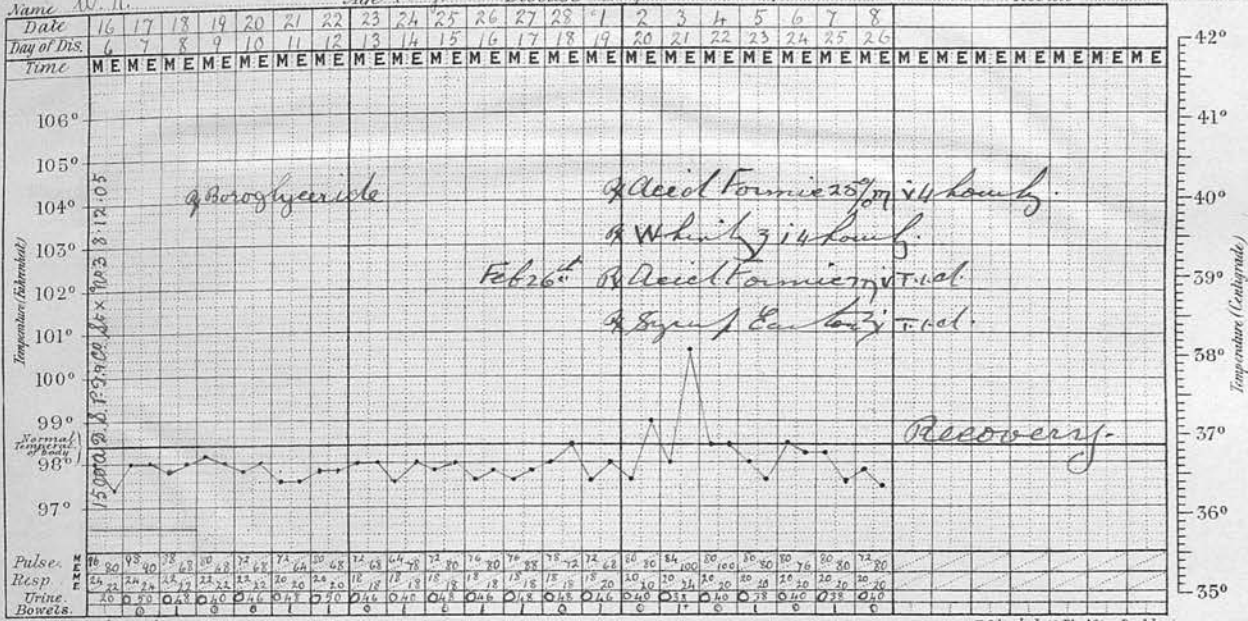
Description of Case **LXXI** - con-
History

Feb 20th 8. p.m. Bowditch has much
improvement. No marked induration of
intercostal spaces. Lung has diminished
Colour good. No abnormal cardiac
condition Pulse regular.

Feb 21st Bowditch has still further
improvement Good colour and Pulse
is regular with good volume and force
Patient subsequently made an
uncomplicated recovery.

Case LXIV

Feb. Name W. R. Age 18 Years Disease Diphtheria II Result +



Description of Case.

Small patch of dark bluish-gray thick membrane at base of left tonsil. Color is good. Pulse is regular and good.

Swab = Good short, thick rods.

Diplococci and Staphylococci

Pulture = Murrel's Culture

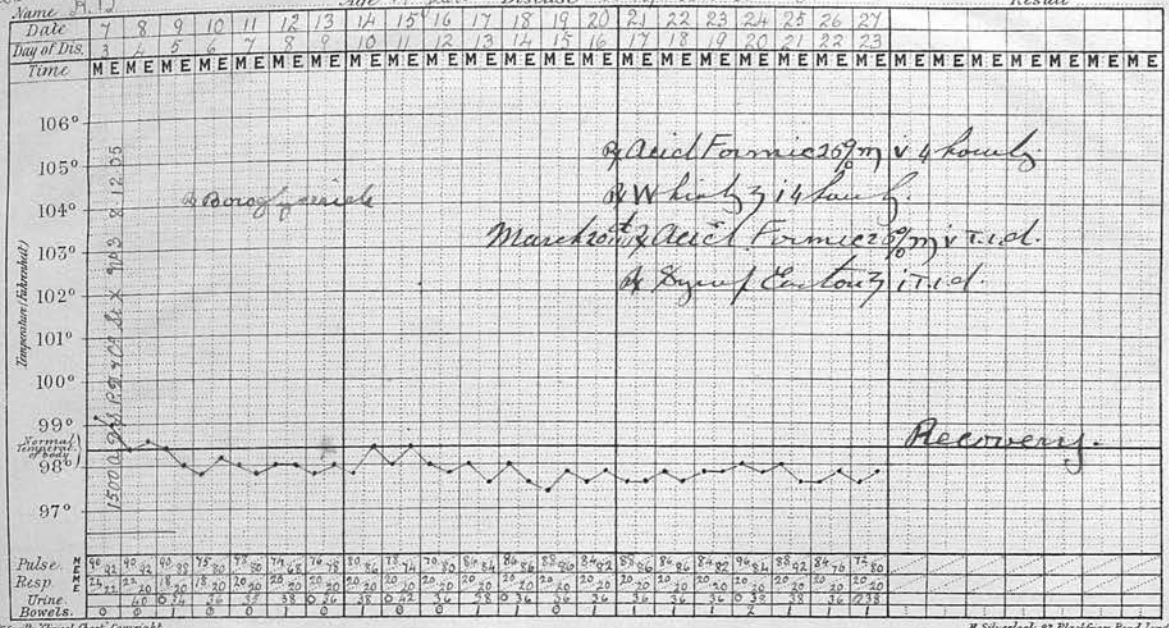
History

The temperature rose slightly on March 2nd but there was nothing obvious to account for it. Except for this patient made an uncomplicated recovery.

Case LXVII

March 11 B

Age 19 Years Disease Diphtheria Result +



100cc of formalin
 100cc of 1% formalin
 100cc of 1% formalin
 100cc of 1% formalin

Recovery

Description of Case.

Both tonsils covered with thin transparent
 yellowish-white thick, tenacious membrane
 Uvula and palate unaffected. Pulse
 regular slow and fair volume.

Swabs = Mixed rods in clumps. Stains
 Diplococci and Staphylococci.

Culture = Neisser Bouctus
Identities

Slight fever on 5th day subsequent to
 patient made uncomplicated
 recovery.

Description of Case LXVIII - con -

Swab = Good short rots. Polar stained
rots in clusters. Some long, thin
rots. Difloccus and Staphylococci.

Culture = Neisseria

History

March 4th 1. a.m. Respiration has been gradually
getting more laboured. Intermittent spasms are
now being increasing. Very severe & paroxysmal
cough. Intubated with black rubber tube

tube No 2. 11. a.m. Has had good night. Is
sleeping quietly. Pulm is good. Pulse is
regular & good volume & force. March 5th

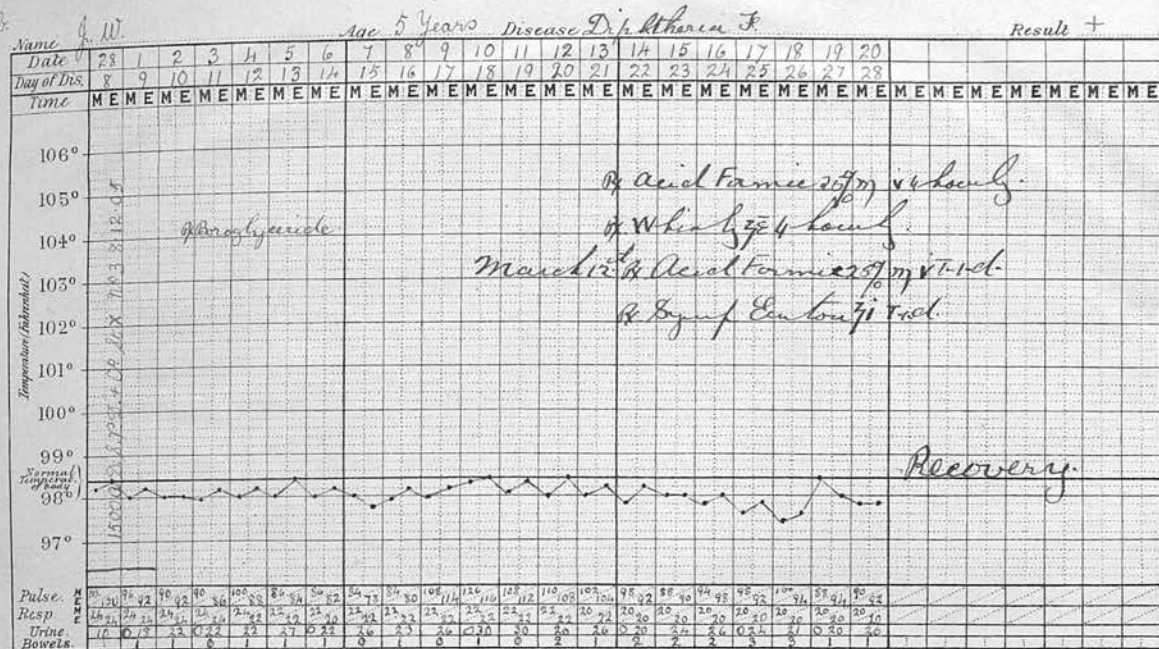
Respiration easy. Pulm good. Pulse good.

2. p.m. Collapsed while struggling with a
nasal fist. Given Formulae Styr. of $\frac{1}{100}$ and
given rectal feeding for 8 hours. Tube
removed at 10 p.m.

March 7th Pulm good. Pulse regular
and good volume & force. No cyanosis
abnormality.

March 11th Temperature rose. Given 4000 ADS units.
Patient's strength made an uncomplicated
recovery.

Case LXIX



Description of Case.

Rostr. tonsils are covered at base with white filmy patch of alab. membrane. Patient is good colour. Pulse is regular and good.

Swabs = Coval short rods with Diplococci and Staphylococci.

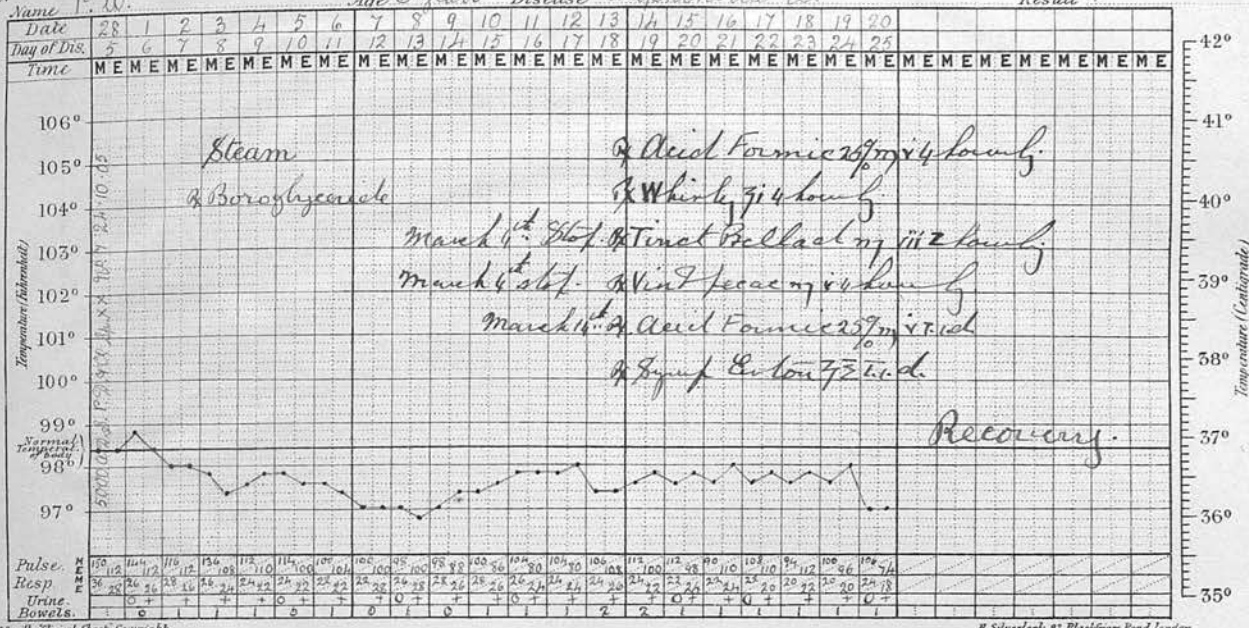
Culture = Negative.

History.

Patient made an uncomplicated recovery.

Case LXX

Feb. Name P. W. Age 3 Years Disease Diphtheria L. Result +



H. S. Gault's Clinical Chart Copyright No. 7.

H. Silverlock, 82, Blackhorse Road, London.

Description of Case.

Stint slightly cyanosed. Fauces congested. No membrane. Voice is very husky and there is a frequent short croupy cough. Respirations are laboured and indrawing of intercostal spaces obvious although not very severe. Pulse is irregular and very soft. Slight enlargement of right side of heart. No murmur.

Swab = Short rods and long thin rods Streptococci and Diplo & Staphylococci

Culture = Neisseria Pontine

Description of Case LXX - con. -

History

March 1st Marked improvement in character of respirations. No cyanosis. Pulse still irregular and soft.

March 2nd Pulse slightly improved. Irregularity not so marked. Heart in a better groove.

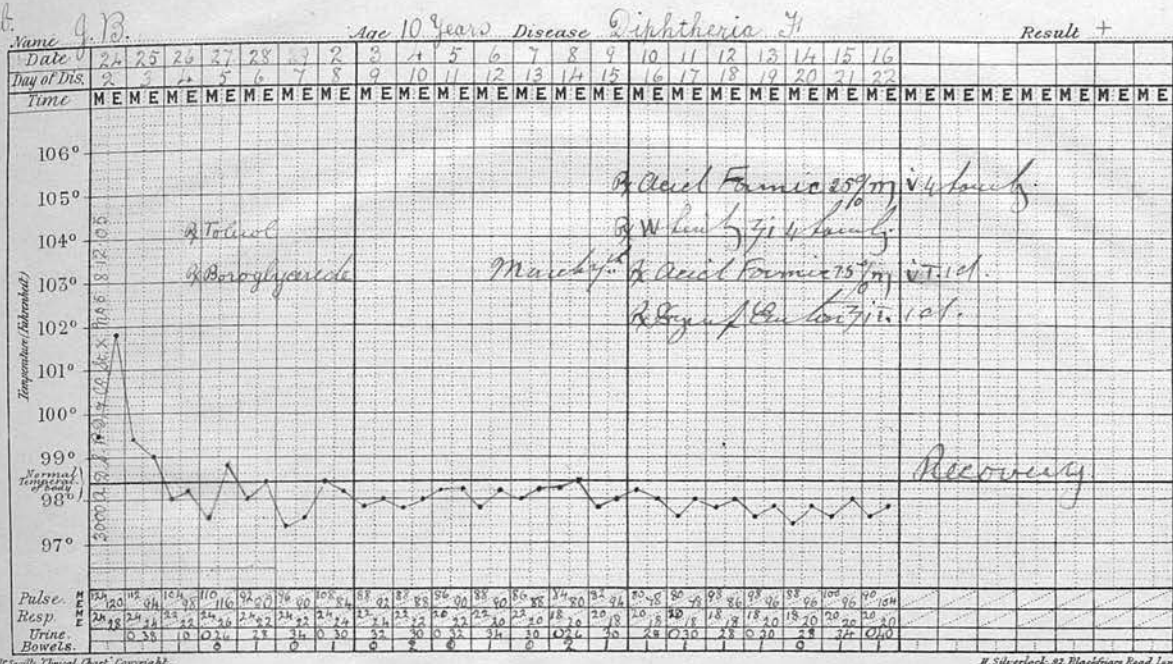
March 4th Steam removed. No cough. Respirations easy. Pupils slightly dilated.

March 5th Pulse is now regular but is soft. Pulse is good.

March 14th Pulse is good. Pulse is regular with good volume. Heart not dilated. No murmur. Respirations easy. Food slowly medicine stopped. Patient subsequently made an uninterrupted recovery.

Case LXXIII

Feb.



Description of Case.

Both tonsils are enlarged. The left tonsil is completely covered at base with thick dark grey membrane. Uvula free. Patient is a good colour and pulse is regular and strong.

Swab = mixed rods. Good polar stained rods. Short thick rods & long faint rods. Staphylococci & Diplococci & Cocci.

Culture = Newer Positive
Hinton

Patient made an uncomplicated recovery

St. S. Clinical Chart. Copyright 1917.

H. Silverlock, 82, Blenheim Road, London.

Case XXXIII - con -

for three weeks when measles symptoms appeared & he was transported to another ward. Aril Formie at the same time unfortunately was discontinued. 18 days after the stopping of the drug there was an impairment of the tendon reflexes & by it difficulty in walking. The paralytic symptoms however passed off in about 14-18 days & patient made a good recovery.

Description of Case LXXVI - con-
enlargement of the cervical glands.

Swab - throat - = very good short polar
stained rods in clusters diplo and
Staphylococci.

- Nose - = Good short rods and
large diplococci.

Cultures = Misses Positive
History

Feb. 27th Breathing still labored. Patient
restless. Pulse irregular. Heart. Left
side slightly enlarged. 1st sound
faint. Mitral soft systolic murmur.
Membrane has increased. 2000 A.D.S.

4:30 p. m. In evening of in two talo-fusses
marked. Cough is "looser" Pulse softer
and more irregular.

11 p. m. Attempted intubation to
relieve heart and for some paroxysm
of coughing. Large piece of thick
white membrane $2\frac{1}{2}$ inches in length
expelled after attempted
introduction of tube which failed.
Breathing very much improved.

12:30 p. m. 6000 A.D.S.

Feb 28th Had one severe fit of coughing at 1 p. m.

Description of Case LXXVI - con-

Patient still very pale. No cyanosis. Pulse is irregular and very soft. Occasional short cough. Indrawing of intercostal spaces is marked.

March 1st 12. p.m. Pulse is very bad irregular very soft and rapid.

Given Hypodermic Formate & Sydnine at 3 after Hypodermic Sydnine Hydro at 12

had no effect. Slight pulse markedly improved. At 8 a.m.

given again Hypodermic Formate of Sydnine $\frac{1}{100}$. Pulse improved. Pulse

became slow & fuller and Breathing also improved much. 5 p.m. Symptoms

of Broncho pneumonia. Respiration very rapid. No symptoms of high obstruction.

Pulse is more regular & in volume better but still rapid. 8 p.m. Given 10000

units. A.D.S. March 2nd 10. a.m. Slight improvement. Pulse better. Pulse is regular.

Has had Formate & Sydnine $\frac{1}{100}$ at 4 a.m. and 9. a.m. Given 8000

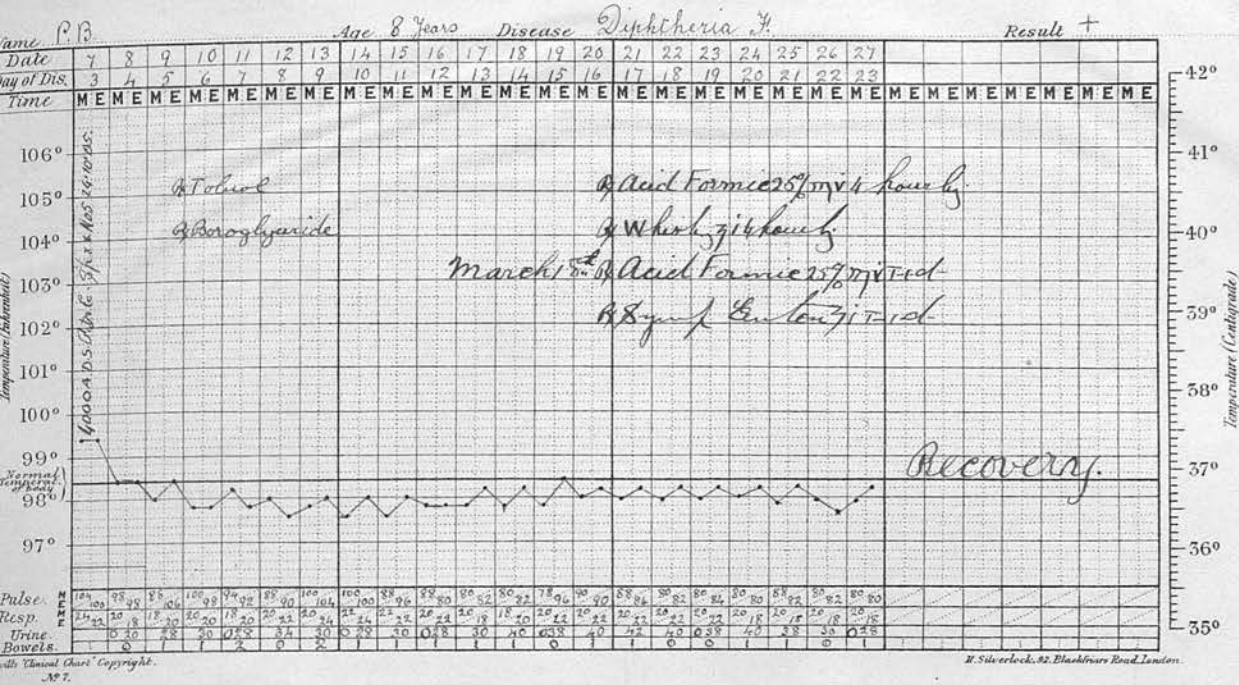
units A.D.S. 8 p.m. Has slept well at intervals. Pulse is regular. No

further cardiac dilatation.

Description of Case LXXVI - con-

March 3rd. Has had good night. 8 left.
respirations reduced and not laboured
but regular and good volume and
force. Pulse has much improved.
March 4th. Respirations are rapid (48)
From March 4th the patient gradually
improved and made an uncomplicated
and complete recovery. Respirations
were normal by March 10th. The
cardiac enlargement markedly decreased.
An interesting point apart from the
great severity of the case is the
fact of the ordinary injection of
8 cc's his failing to react on March
3rd and the great success of the
Formate injections each of which
was followed by marked
improvement.

Case LXXVIII



Description of Case.

Left tonsil covered with grayish white thick membrane. Slight congestion of Fauces.

Pulse is somewhat rapid & regular but volume poor.

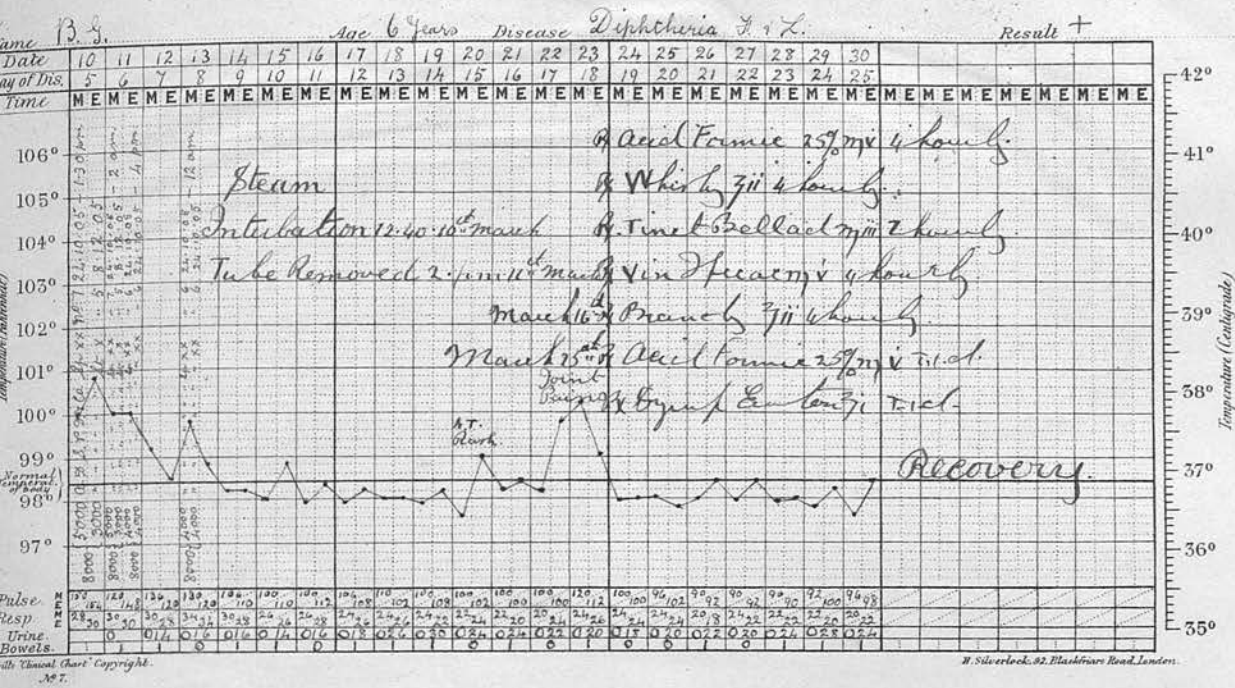
Swab = Local polar stained rods in clumps. P. occi.

Culture = Neisseria Portia.

History

Patient made a rapid and uncomplicated recovery.

Case LXXXI



Description of Case.

Patient on admission very agitated. Vomited twice within 30 minutes of arrival. Induration of intercostal spaces marked. Voice extremely hoarse. Short cough rough which is frequent. Fauces congested, with much mucous. Right tonsil completely covered with very thick membrane. Left tonsil covered at base. Pulse is very soft & irregular. Heart. Slight enlargement of right-ventricle. 1st sound very faint - almost inaudible. Soft blowing mitral regurgitation.

Description of Case LXXXI - con -

Swab = Short Colon stained rods in clumps

Staphylococci.

Culture = Neisseria Conjunctiva

History

12:40. p.m. March 10th Breathing very laboured. Cyanosis marked. Intubated. Marked relief and expulsion of much thick mucus. Child is very quiet and listless. March 11th Pulse is more regular but still very soft.

2 p.m. Tube removed. 1:30. p.m. Child became very cyanosed and pulse almost imperceptible

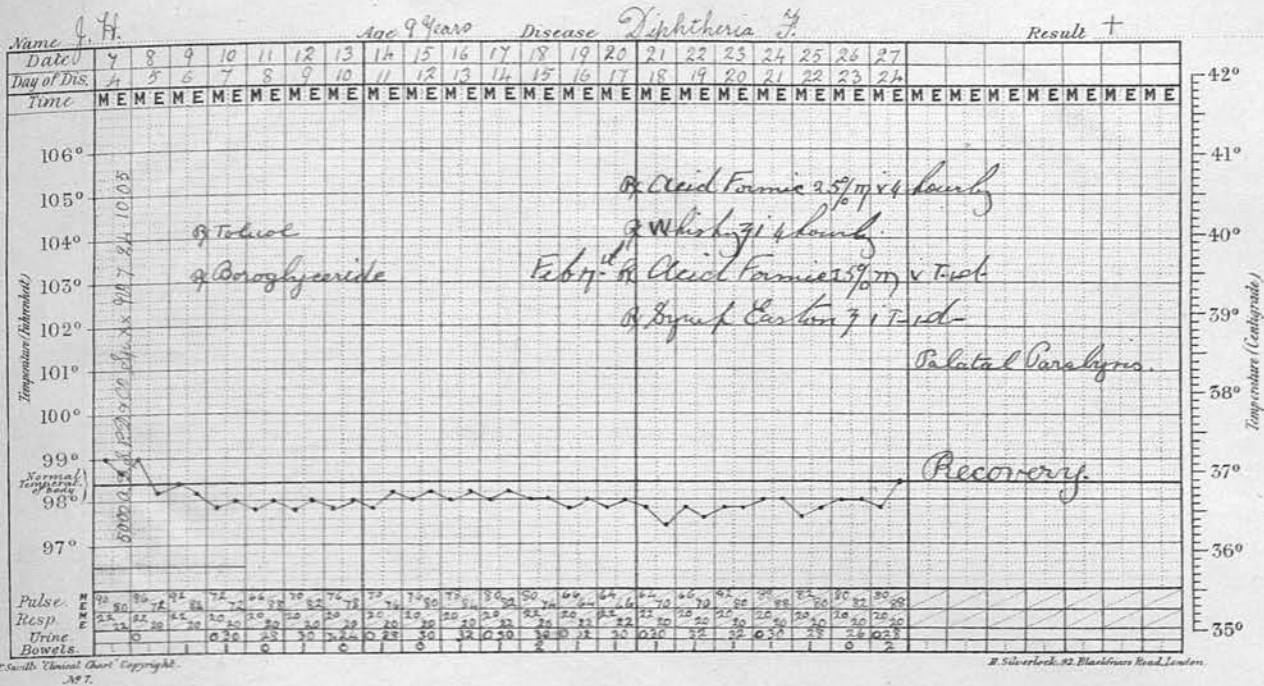
Given Hypoclemic Formulae of Styrsky $\frac{1}{80}$ Colours and pulse improved markedly in 30 minutes. Breathing also improved

March 13th Pulse is regular. Still soft. Colour is good. March 15th Vomited 10" after food. Colour bad. Pulse regular but soft.

March 20th Right side of heart diminished. Colour is good. Pulse is regular with fair volume and force. No further sickness.

After this except for joint pains which lasted for 2 days patient made an uncomplicated recovery and left for home apparently quite well.

Case LXXXV



Description of Case.

Fauces congested. Right tonsil enlarged and covered completely with thick dark gray membrane. Uvula covered with similar membrane. Patch a hot base of left tonsil. Patient is pale and poisoned looking. Pulse is slightly irregular and volume is poor.

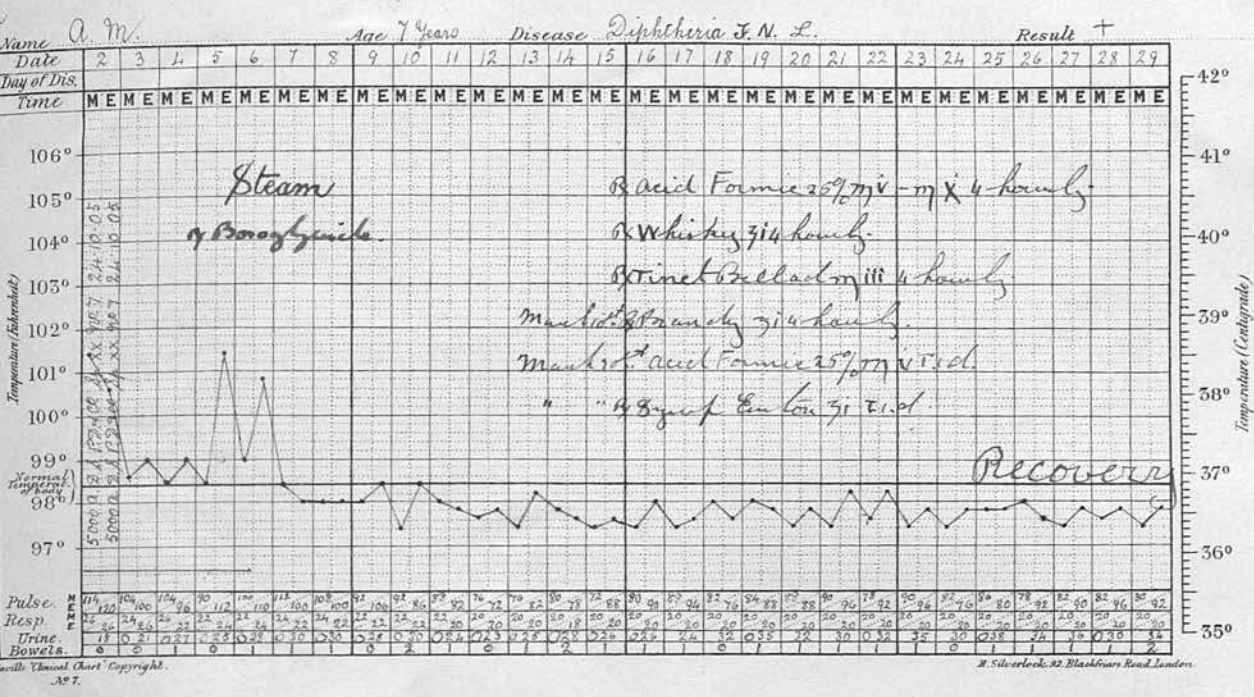
Swab = Pus from base of tonsil membrane. rods. Staphylococci & Diplococci.

Culture = mixed. *Corynebacterium*

History

March 8th. Left palatal paralysis in which eventually passed off. Otherwise patient made good recovery, other reflexes normal.

Case LXXXIX



Description of Case.

Patient had at time of onset of diphtheria been suffering for 5 weeks from Scarlatina. Both tonsils completely covered with thin dark gray membranes. Stomach frequent crampy cough. Breathing slightly obstructed. Nasal discharge from right nostril. Palate slightly involved on right side. Pulse regular.

Swabs = mixed wabs. Polar stained wabs. Staphylococci & Diplococci.
Nose = Polar stained wabs and cocci

Description of Case LXXXIX - con.-

Pulvis = Nerve Contin.

History

March 3rd. Bowstring which became worse
in proect with steam. No cardiac
enlargement. Slight blowing Mital
up to the mmm. 1st round faint.

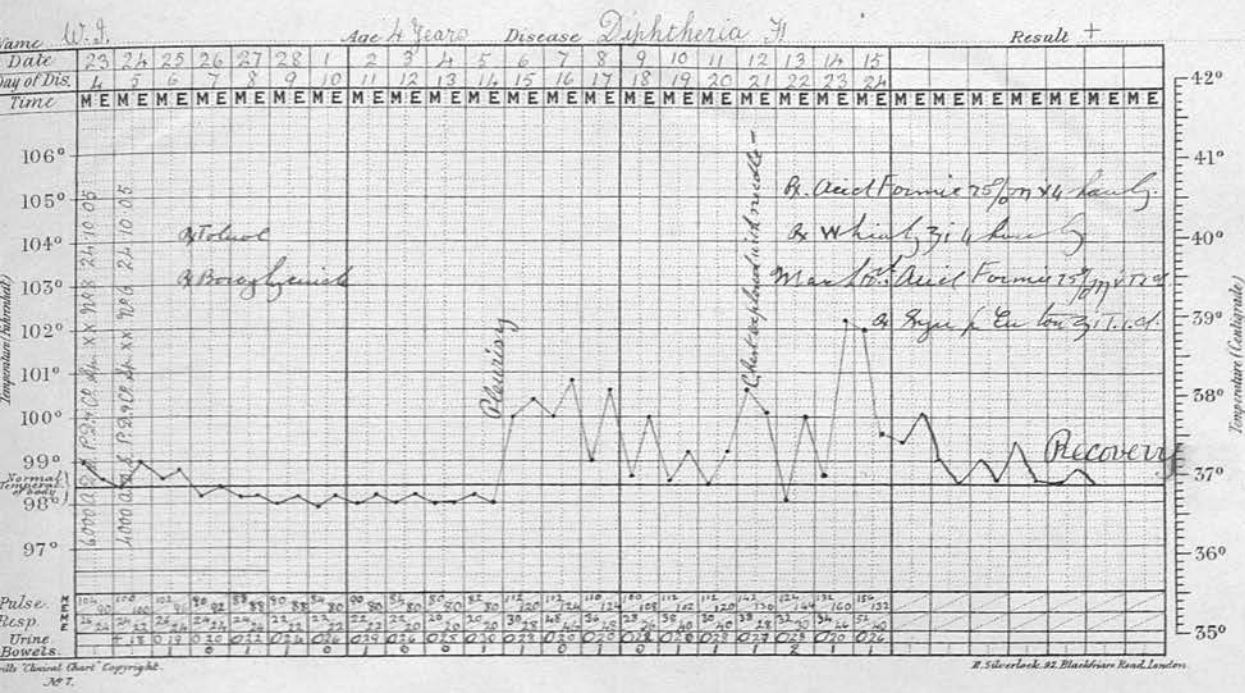
Pulse regular & soft. Slight pain Mital Region

March 9th. Pulse progressively softer and
is slightly irregular. Vomited once
1 1/2 hours after food. Color very pale.
Acid Formic increased to mg x 4 hours.

March 10th 9 p.m. Color improved slightly
Pulse is slightly irregular but not
so soft. March 10th - 14th Patient
remained much the same. Color
gradually improved. Was not again
sick. Pulse varied. Was always
slightly irregular & always stayed
in the evening

After this date pulse gradually
improved & became quite regular
Color was good. No further vomiting.
Cardiac condition improved & finally
patient made an uncomplicated
recovery

Case XC



Description of Case.

Fauces congested. Left tonsil completely covered with thick, white, tenacious membrane. Palate also largely involved on same side. Right tonsil is covered at base with similar membrane. Uvula also completely covered. Patient is fair colour with soft but regular pulse.

Swabs = Mixed rods. Good number of short pleomorphic rods. Staphylococci & Cocci.

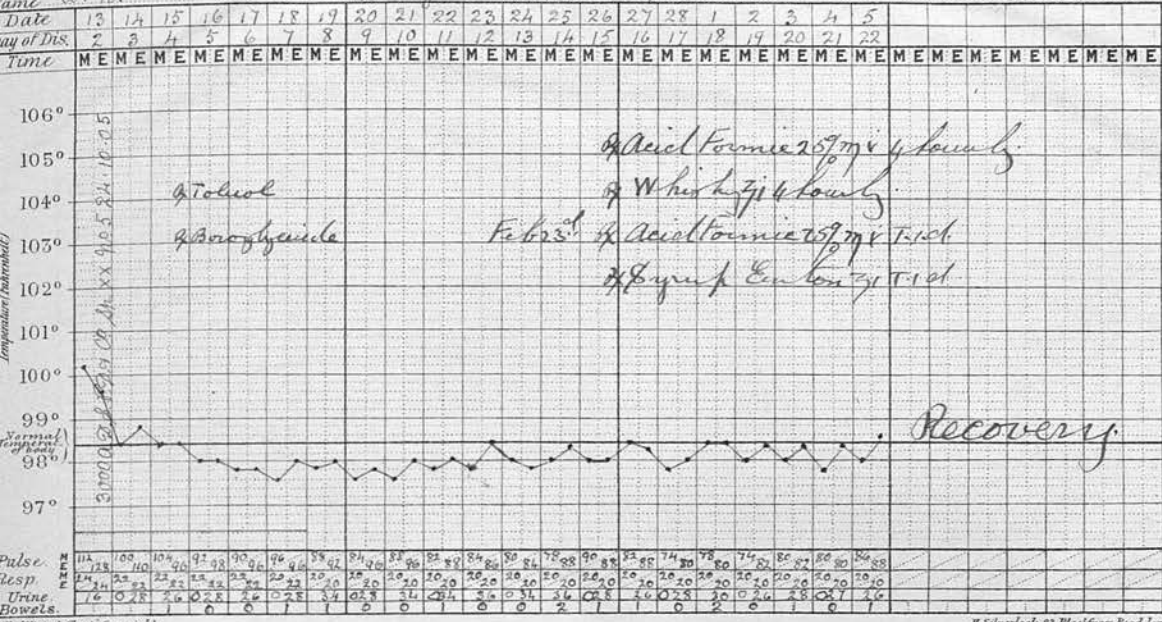
Culture = Negative
Whitney

Patient developed on March 5th Pleurisy with

Description of case XC - con-
eventually effusion. Chest was explored
with needle but only clear fluid found
eventually fluid disappeared but right
apex of lung was suspicious of pt.
Patient given open air treatment
and subsequently made good
recovery. He had albumen but no
paralysis and pulse and colour were
good during illness. Left hospital
apparently in good health.

Case XCII

Name W. G. Age 8 Years Disease Diphtheria I. Result +



Description of Case.

Both tonsils are covered at base with thick, dark, gray membrane. Uvula has a patch of similar membrane at tip. Patient is good colour. Pulse is regular and of good volume.

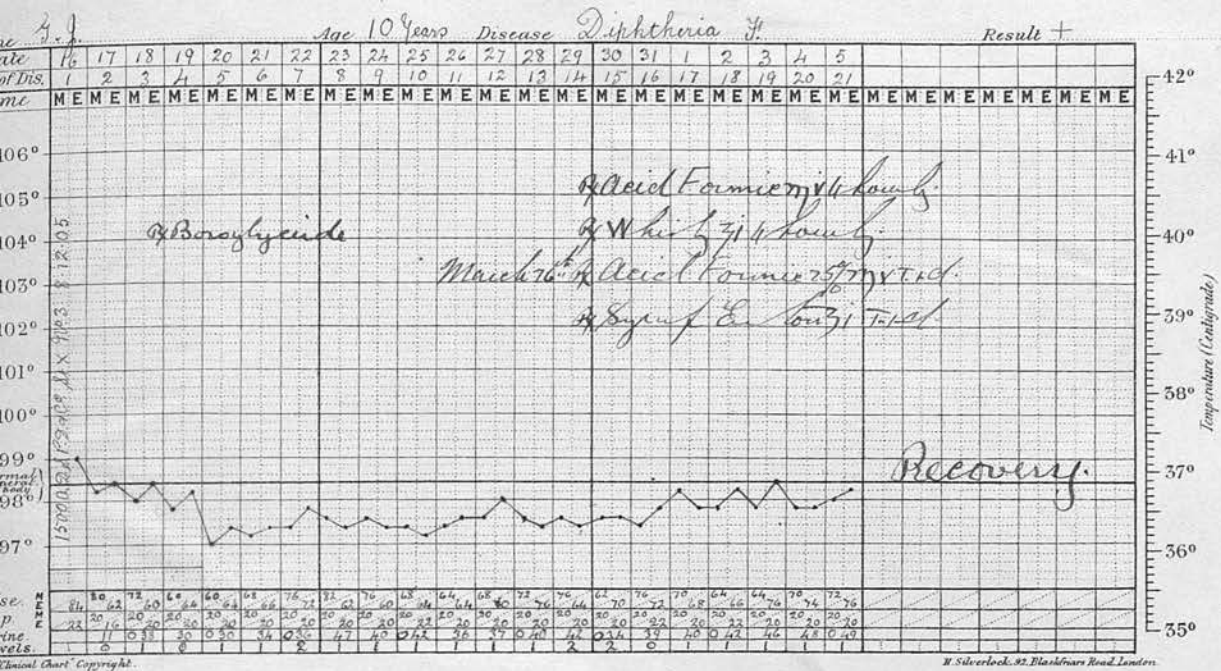
Swab = Good cultures of both polar stainer rods. Streptococci
Staphylococci & Diplococci.

Culture = Negative Positive

History

Patient subsequently made an uncomplicated recovery.

Case XCV



Description of Case.

Both tonsils have small patch of thin membrane at base. Pulse is slightly irregular but volume is good.

Patient is good colour.

Swab = Short rods Staphylococci.

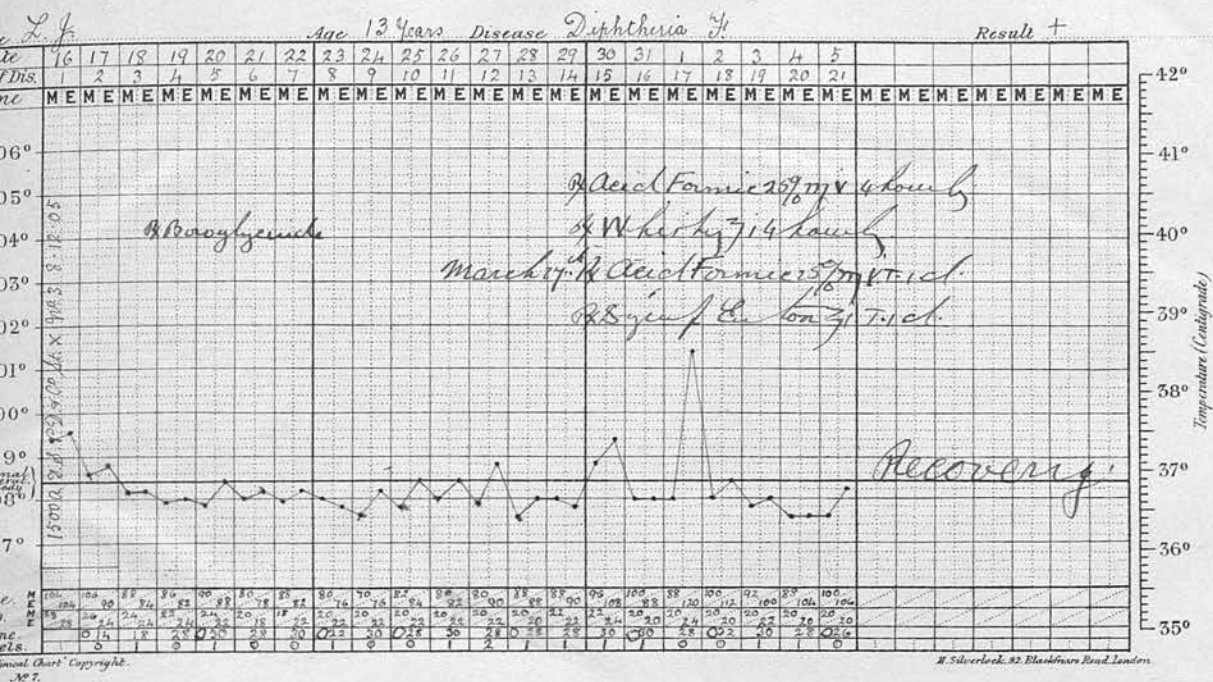
Culture = Neisseria Positive

History

March 18th Pulse is regular. Heart not enlarged. Aortic 1st sound faint. No murmur. Patient is healthy

make good and uncomplicated recovery.

Case XCV



Description of Case

Patient's colour is good. Both tonsils are covered with thick white membrane which is loose and abortive granular.

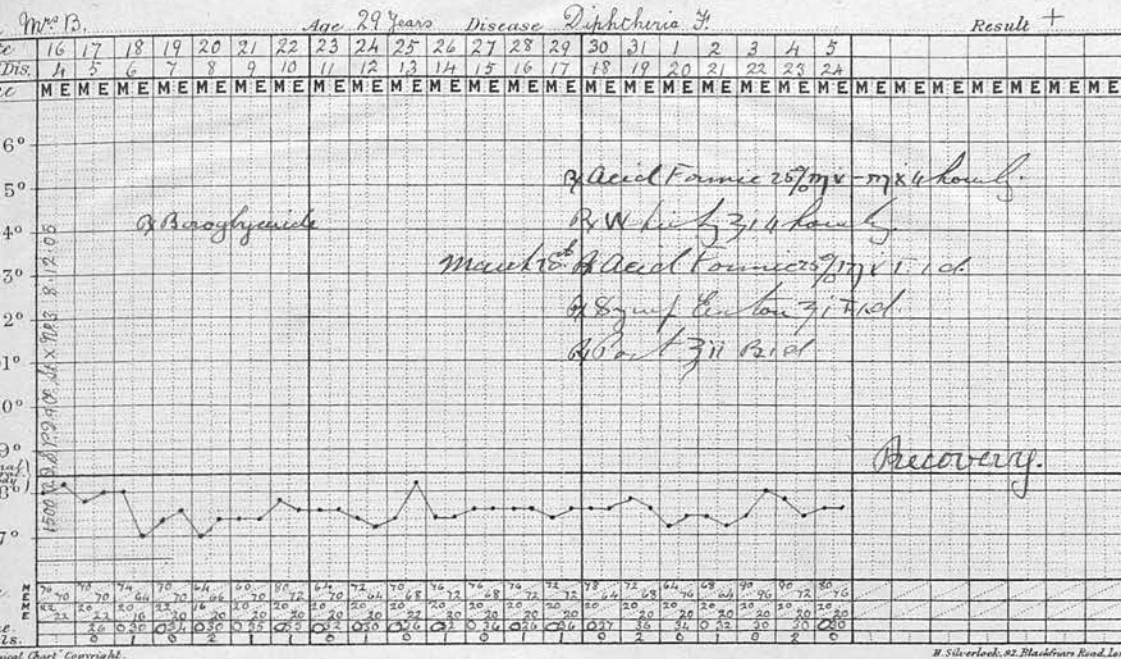
Pulse is good and regular.

Swab = Short polar stained rods and cocci.

Culture = M. diphtheriae
History

Patient subsequently made an uncomplicated recovery.

Case XCVI



Description of Case.

Fauces injected. Patch of grey membrane at base of left tonsil. Pulse is dicrotic but regular.

Swabs = Good clusters of short rods with polar staining. Staffs & Diplococci.

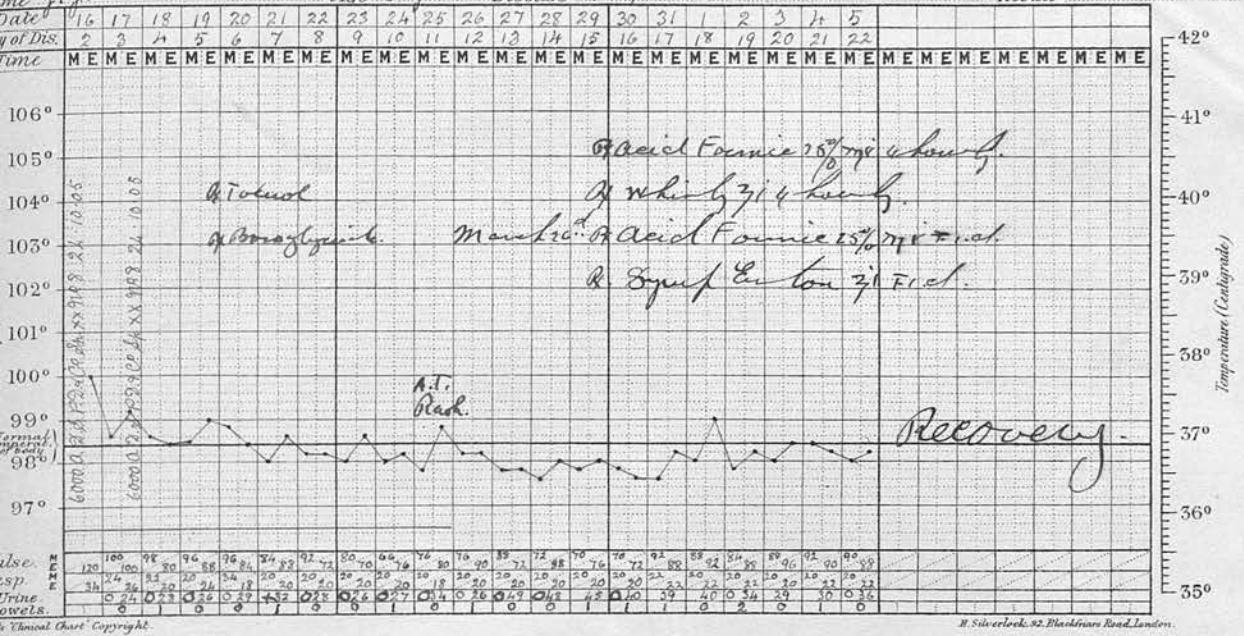
Culture = Negative

History

Pulse was always regular and patient eventually made an uncomplicated recovery.

Case XCIX

Age 8 Years Disease Diphtheria $\frac{1}{2}$ & $\frac{1}{2}$ Result +



Description of Case.

Both tonsils are completely covered with very thick white membrane. Uvula also quite covered. Pulse regular but not always quite the same volume. Bowel things hours slight obstruction but there is no induration.

Swabs = Good short Bacilli stained rods. Diff. spec.

Culture = Never positive.

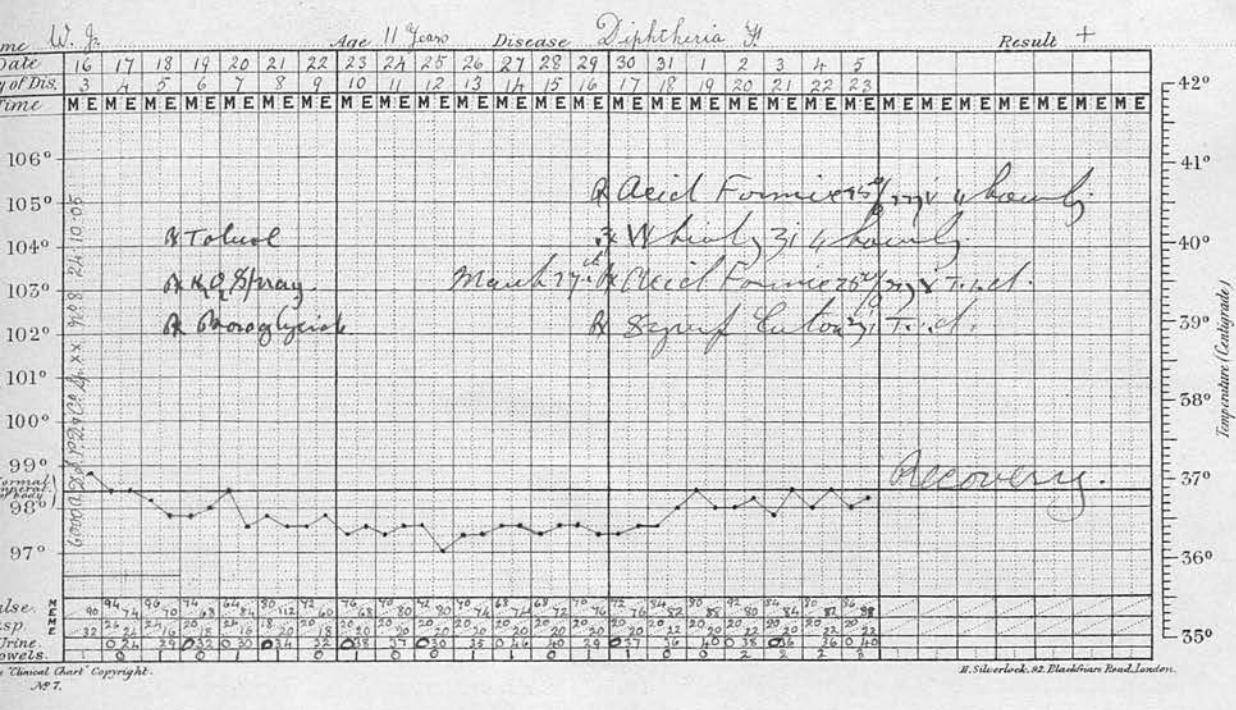
History

Membrane removed by March 18th Linn 6000 units A.D.S. After which patient made an uncomplicated recovery.

Throat Chart Copyright 1917

H. Silverlock, 92, Blackfriars Road, London.

Case C



Description of Case.

Back teeth covered at base with thick black grey membrane. Mucosa also affected on right side. Pulse not quite regular in time or force.

Swab = Good culture of short, thick polar stained rods. Spirilla & Staphylococci and Diplococci

Culture = Neisseria Pontis

History

March 18th Pulse regular. No cardiac abnormality. Subsequently patient made uncomplicated recovery.

Part III.

- I. Statistics of Foregoing Cases . . .
- II. The Degree of Severity of Foregoing Cases
- III. Influences in Selection of Control Cases
- IV. The Relative Severity of Formic Acid with
Control Cases
- V. Statistics of Control Cases . . .
- VI. Comparison of Statistics . . .
- VII. Analysis of Results in:-
 - (i) Cardiac Failure . . .
 - (ii) Paralysis . . .
 - (iii) Albuminuria. . .
- VIII. Conclusions.

STATISTICS OF ACCOMPANYING CASES.

The accompanying statistics of the cases have been compiled with reference to the three main diphtheritic lesions, namely, Cardiac Failure, Paralysis, Albuminuria.

The deaths from Cardiac Failure - and in the case of the cases treated with Formic Acid this was the only cause of death - have been divided into 2 groups, each with 2 subdivisions, namely, (I.a) Progressive, (I.b) Sudden; (II.a) Early, (II.b) Late.

In the first group of cases the definition and dividing line is comparatively simple in most cases, but in the two cases referred to has been somewhat difficult.

In most cases the symptoms of progressive heart failure may be summed up as a gradually increasing intensity of the cardinal signs and symptoms of Cardiac Failure, namely, - Cardiac pain, vomiting, irregularity of pulse, etc., culminating in death. In the case recorded this was well exemplified. In the other case, No. 61, which has been classified as Sudden, there was also a series of progressive symptoms, but owing to the fact that the patient was apparently recovering, it has been classified

as sudden, in that it was not expected to occur when it did, if at all.

The second classification has been made on strictly orthodox lines, namely, the occurrence before or after seven days from the onset of disease - a view held by Myers, Trevelyan, and many others.

In the case of the Paralysis they are, both here, and in the control cases, minutely differentiated, but no attempt has been made to identify them with the date of onset of the disease.

The results of the statistics will be dealt with fully, later.

Formic Acid.

1906.

Analyses of Cases. January 18th - March 18th.

<u>N^o. of Cases.</u>	<u>Died.</u>	<u>Paralyses.</u>	<u>Albumen.</u>
	<u>Cardiac Failure.</u>	<u>all varieties.</u>	
<u>100.</u>	<u>2.</u>	<u>3.</u>	<u>10.</u>

Analyses of Paralyses. January 18th - March 18th.

<u>Paralyses.</u>	<u>Palate.</u>	<u>Extremities.</u>	<u>Other varieties.</u>
<u>3.</u>	<u>2.</u>	<u>1.</u>	<u>0.</u>

Average age for 1906 = 11.3 years.

Analyses of Deaths from Cardiac Failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
<u>1.</u>	<u>1.</u>	<u>1.</u>	<u>1.</u>

(each case comprised two varieties.)

Average dose of Antitoxin = 62.65 units.

THE DEGREE OF SEVERITY OF FOREGOING CASES.

From the details of the foregoing cases it is evident that there are at least one or two cases of each variety of diphtheria shown among them. The cases are in no way selected, cases being taken strictly in rotation on their arrival at hospital. As before stated, the only cases rejected were those in which the clinical diagnosis was not fully borne out by the bacteriological examination.

An even more important point has been to attempt to determine the severity of the epidemic which, if mild, would modify the value of the results.

Two main factors have been investigated to determine this:-

1. The average amount of Antitoxin.
2. The average age of the patient.

The average dose of Antitoxin.

As shown before (page 24), the doses of antitoxin have been given more or less on a fixed scale in relative proportion to the severity of the cases and the complications arriving in them. This applies strictly for the preceding four years, as, before that date, the theories of the amount of

antitoxin were not so fixed as they at present are. As the doses of antitoxin in the hospital have been prescribed for the past four years and also for the 100 cases treated by Formic Acid by the same individual acting on the same fixed principles, it is possible, accordingly, to judge by the average dose the average severity of the case.

The average dose of Antitoxin for the past three years is 6,300 units, thus:- for 100 consecutive cases considered in 1904 it is 6,400 units, for 100 consecutive cases considered in 1905 it is 4,760 units, for 100 consecutive cases considered in 1905-06 it is 4,820 units, and for the 100 cases treated by Formic Acid it is 6,265 units; so that from this standpoint the cases may be judged to be of at least average severity.

The age of the patient has been the second factor observed.

Varying as the mortality does in diphtheria with the age of the patient, this must necessarily be of great importance, and Myers (Lancet 1900) has shown in a large number of cases how definitely true this is; thus in 275 cases of paralysis and paresis taken from 1,316 cases of diphtheria, the following results were obtained:-

The 275 cases taken in Five yearly periods.

Age periods.	Males.	Females.	Total.
Under 5 years	59	45	104
5 to 10 years	66	72	138
Over 10 years	22	11	33
Totals	147	128	275

Thus out of the 275 cases there were 174 cases occurring between the ages of three and eight, equalling 63.2 per cent. of the total number; again there were 40 cases between the fifth and sixth years of age, equalling 14.5 per cent; while in the cases of cardiac paralysis the great proportion of cases occurred between the ages of two and nine, the majority occurring in the sixth and seventh years' age-period.

The average age of the successive groups of one hundred cases has been 12.2, thus:- for 100 consecutive cases considered in 1904 it is 9.7 years, for 100 consecutive cases considered in 1905 it is 12.5 years, for 100 consecutive cases considered in 1905-06 it is 10.5 years, and for the 100 cases treated by Formic Acid it is 11.3 years; so that in this respect they compare more than favourably with preceding epidemics, and the fact that in the 100 cases treated by Formic Acid, twelve patients

were between five and six years of age, while fifty-five were between the ages of two and nine, would appear to prove that the ordinary percentages of paralysis and cardiac failure might have been expected.

It would seem, therefore, with such a positive result in both the factors taken into consideration, that it is safe to assume that the severity of the cases considered was at least an average one.

INFLUENCES IN SELECTION OF CONTROL CASES.

In order to analyse more thoroughly the results of treatment in the foregoing cases, a careful analysis has been made of three series of cases, each series numbering one hundred cases. Each series has been composed, as in the cases under consideration, of consecutive cases save that, as before, none have been considered which were not also bacteriologically positive.

In order that the type of the disease might be as similar as possible in the control cases as in those treated by Formic Acid, two series, each of one hundred cases, have been considered in 1904 and 1905, each as nearly as possible in the same months, viz:- January, February and March. The remaining

one hundred cases are those immediately preceding the cases treated by Formic Acid so as, if possible, to ensure that the particular epidemic did not vary to any degree with those of others.

There are then 200 cases taken from the corresponding season of the year for the past two years and 100 cases which may fairly be said to be of the same epidemic as that considered.

It may be well to state once more that by 'control cases' is meant the 300 cases dated 1904, 1905, 1905-06, and that the treatment adopted in all these cases was exactly similar, while that, as has also been stated before, the treatment by Antitoxin is the only connecting link between those cases and those treated by Formic Acid.

RELATIVE SEVERITY OF CASES TREATED BY FORMIC ACID AND CONTROL CASES.

On the same principle but with more minuteness the relative severity of the two groups of cases may be adjudged as follows:-

1. The control cases - namely, cases treated as detailed in Part I., page/9, are (a) either of the same months in the years, or (b) the same epidemic.

2. The average dose of Antitoxin for the control cases, namely:- for 1904 = 6,400 units, for 1905 = 4,760, for 1905-06 = 4,820, while that for 1906 = (the cases treated by Formic Acid) 6,265. It would appear, therefore, that from this standpoint the cases were of quite as great if not greater severity.
3. The average age of the patients in the control cases was:- for 1904 = 9.7, for 1905 = 12.5, years, for 1905-06 = 10.5, while that for 1906 was 11.3, and that again from this standpoint the cases are at least as severe as the preceding ones.
4. The two groups of cases are composed of cases both clinically and bacteriologically positive.
5. That the cases under treatment by Formic Acid were kept under observation even longer than the preceding ones (page 20) and that, therefore, paralysis occurring later in the disease was even less likely to have escaped notice.

STATISTICS OF 300 CONTROL CASES

The statistics of the accompanying control cases have been arranged in the same manner as those of the cases treated with Formic Acid.

The cases are in each series consecutive cases, nor, as has been said, are they in any way selected cases, except that no cases have been included which were not both bacteriologically and clinically positive.

As will be observed the statistics are much the same, but rather better than a wide series of statistics taken from other hospitals, namely about 11.3% for cases treated on the third and fourth day from the onset of the disease. Although the different series of cases are given separately, an average result of the three groups of cases is also appended, that a broader basis may be given for the results of comparison. The results of comparison will be discussed in detail later.

1904.

Analyses of Cases January 12th 1904 - March 18th 1904.

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralyses.</u>	<u>Albumen.</u>
<u>Jan: 12th 1904.</u>	<u>Cardiac failures.</u>		
<u>100.</u>	<u>10.</u>	<u>17.</u>	<u>45.</u>
<u>March 18th 1904.</u>	<u>Bronchopneumonia.</u>		
	<u>1.</u>		

Analyses of Paralysis January 12th 1904 - March 18th 1904.

<u>Paralyses.</u>	<u>Palate.</u>	<u>Accom. & Recti.</u>	<u>Extremities.</u>	<u>Jules costals.</u>
<u>17.</u>	<u>7.</u>	<u>6.</u>	<u>6.</u>	<u>0.</u>
<u>Mixed Paralysis.</u>	<u>Palate + legs = 5.</u>	<u>Accom + Recti + legs = 4.</u>	<u>legs + Accom. st. = 4.</u>	
<u>8.</u>	<u>" + Recti = 3.</u>	<u>" + " + Palate = 3.</u>	<u>" + Palate = 5.</u>	
	<u>- + Accom. = 3.</u>			

Average age for 1904 = 9.7 years.

Analyses of Deaths from Cardiac Failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
<u>7.</u>	<u>3.</u>	<u>within 7 days.</u> <u>4.</u>	<u>6.</u>

Average dose of Antitoxin 1904 = 6400 units.

1905.

Analyses of Cases - January 16th 1905 - March 20th 1905.

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralyses.</u>	<u>Albumen.</u>
<u>January 16th 1905.</u>	<u>(Cardiac failure)</u>	<u>(all varieties)</u>	
<u>100.</u>	<u>7.</u>	<u>17.</u>	<u>35.</u>
<u>March 20th 1905.</u>			

Analyses of Paralyses. January 16th 1905 - March 20th 1905.

<u>Paralyses.</u>	<u>Palate</u>	<u>Accom. + Recti.</u>	<u>Inler costals.</u>	<u>Extremities.</u>
<u>17.</u>	<u>8.</u>	<u>8.</u>	<u>1.</u>	<u>4.</u>
<u>Neurological Paralyses</u>	<u>Palate + legs = 4.</u>	<u>Accom. + recti + legs = 2.</u>	<u>Inler cost + accom. + recti = 1.</u>	<u>Extremities + Palate = 1.</u>
<u>7.</u>	<u>" + Accom. = 3.</u>	<u>" " + Inler cost = 1.</u>		<u>" + Accom. = 2.</u>
	<u>- "Recti = 1.</u>	<u>" " + Palate = 4.</u>		<u>" + Recti = 3.</u>

Average age for 1905 = 12.5 years.

Analyses of Deaths from Cardiac Failure.

<u>Progressive</u>	<u>Sudden</u>	<u>Early</u>	<u>Late</u>
		<u>within 7 days.</u>	
<u>4.</u>	<u>3.</u>	<u>3.</u>	<u>4.</u>

Average dose of Antitoxin 1905 = 4760. units.

1905 - 1906.

Analyses of Cases. November 9th 1905 - January 20th 1906

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralyses.</u>	<u>Albumen.</u>
<u>November 9th 1905.</u>	<u>Cardiac failure</u>	<u>All varieties.</u>	
<u>100.</u>	<u>9.</u>	<u>8.</u>	<u>34.</u>
<u>January 20th 1906.</u>			

Analyses of Paralysis. November 9th 1905 - January 20th 1906.

<u>Paralyses.</u>	<u>Palate.</u>	<u>Recti.</u>	<u>Extremities.</u>	<u>Spinal muscles.</u>
<u>8.</u>	<u>5.</u>	<u>1.</u>	<u>3.</u>	<u>1.</u>
	<u>Palate+legs = 2.</u>		<u>legs+Palate = 2.</u>	

Average age for 1905 - 1906 = 10.5 years.

Analyses of deaths from Cardiac failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
<u>5.</u>	<u>4.</u>	<u>2.</u>	<u>7.</u>
		(within 7 days)	

Average Dose of Antitoxin = 4820 units.

Total Averages of Control Cases.

Cardiac Failure.

1904. = 10%. 1905. = 7%. 1905-06 = 9%.

Total Average = 8.6 %.

Paralysis.

1904 = 17%. 1905 = 17%. 1905-06 = 8%.

Total Average = 14 %.

Albumen -

1904 = 45%. 1905 = 35%. 1905-06 = 34%.

Total Average = 38 %.

Cardiac Failure.

Paralysis.

Albumen.

8.6.

14.

38.

COMPARISON OF STATISTICS

The remaining statistics show a comparison between those cases already described treated by Formic Acid and the control cases treated as described on page . The results, when described together, appear more than good and the necessity of proving that the types of epidemic were equally severe the more apparent.

As will be shown later, also when dealing fully with the more severe cases in the series treated by Formic Acid, nine of the cases there described had the cardinal signs and symptoms of impending cardiac failure and yet recovered, it is therefore not too much to expect that with different treatment the statistics might have been similar. Thus the death-rate in the Formic Acid cases is 2%, while nine cases during the first five days had vomiting, irregularity of pulse, pain, etc. - and yet recovered. This would have given a percentage of 11% which is practically the percentage of the control cases and for most hospitals. It is also interesting to note, as will also be shown later, that in the cases of paralysis, two occurred in cases complicated with measles and not until 16-18 days after the accidental stoppage of the drug.

The results in Albuminuria are again more than good and are even proportionately better than those of Cardiac Failure and Paralysis.

It will be best to discuss these points under "Analysis of Results" after the statistics themselves have been considered.

Strychnine.

1904. January - March. Analyses of deaths from Cardiac Failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
<u>7.</u>	<u>3.</u>	within 7 days. <u>4.</u>	<u>6.</u>

Strychnine.

1905. January - March. Analyses of deaths from Cardiac Failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
<u>4.</u>	<u>3.</u>	within 7 days. <u>3.</u>	<u>4.</u>

Strychnine.

1905-06. November - January. Analyses of deaths from Cardiac Failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
<u>5.</u>	<u>4.</u>	within 7 days. <u>2.</u>	<u>7.</u>

Formic Acid.

1906. January - March. Analyses of deaths from Cardiac Failure.

<u>Progressive.</u>	<u>Sudden.</u>	<u>Early.</u>	<u>Late.</u>
1	1	within 7 days. 1	1

Strychnine.

1904. Analyses of Cases. January 12th 1904. - March 18th 1904.

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralysis.</u>	<u>Albumen.</u>
<u>January 12th 1904.</u>	<u>Cardiac failure</u>		
<u>100.</u>	<u>10.</u>	<u>17.</u>	<u>45.</u>
<u>March 18th 1904.</u>	<u>Bronchopneumonia</u>		
	<u>1.</u>		

Strychnine.

1905. Analyses of Cases. January 16th 1905. - March 20th 1905.

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralysis.</u>	<u>Albumen.</u>
<u>January 16th 1905.</u>	<u>Cardiac failure.</u>	<u>all varieties.</u>	
<u>100.</u>	<u>7.</u>	<u>17.</u>	<u>35.</u>
<u>March 20th 1905.</u>			

Strychnine.

1905-06. Analyses of Cases. November 9th 1905. - January 20th 1906.

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralysis.</u>	<u>Albumen.</u>
<u>November 9th 1905.</u>	<u>Cardiac failure</u>	<u>all varieties.</u>	
<u>100.</u>	<u>9.</u>	<u>8.</u>	<u>34.</u>
<u>January 20th 1906.</u>			

Tannic Acid.

1906. Analyses of Cases.

<u>No. of Cases.</u>	<u>Died.</u>	<u>Paralysis.</u>	<u>Albumen.</u>
	<u>Cardiac failure</u>	<u>all varieties</u>	
<u>100.</u>	<u>2.</u>	<u>3.</u>	<u>10.</u>

Strychnine.

1904. Analyses of Paralysis. January 13th 1904 - March 18th 1904.

Paralysis. - Palate. - Accou + recti. - Extremities. - Inter costals

<u>17.</u>	<u>7.</u>	<u>6.</u>	<u>6.</u>	<u>0.</u>
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Strychnine.

1905. Analyses of Paralysis. January 16th 1905 - March 20th 1905.

Paralysis. - Palate. - Accou + recti. - Inter costals. - Extremities

<u>17.</u>	<u>8.</u>	<u>8.</u>	<u>1.</u>	<u>4.</u>
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Strychnine.

1905-06. Analyses of Paralysis. November 9th 1905 - January 20th 1906.

Paralysis. - Palate. - Recti. - Extremities - Spinal muscles.

<u>8.</u>	<u>5.</u>	<u>1.</u>	<u>3.</u>	<u>1.</u>
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Tornic Acid.

1906. Analyses of Paralysis.

Paralysis. - Palate. - Recti. - Extremities. - Other varieties

<u>3.</u>	<u>2.</u>	<u>0.</u>	<u>1.</u>	<u>0.</u>
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ANALYSIS OF RESULTS

Although the broad results of treatment are well seen in the tables of statistics, it will be best to more minutely examine each complication in detail and to attempt to give an explanation of the results.

Cardiac Failure

With an improvement in the death-rate from 8.6% to 2% it must seem as though Formic Acid has a distinct and definite effect in this - the most serious diphtheritic complication.

Cases 10, 19, 39, 45, 57, 59, 76, 81 and 89 are all types of cases which may fairly be said to have shown symptoms and signs of heart failure sufficiently severe as to have warranted a very bad prognosis in the ordinary course of the disease. In case 89, cardiac pain, vomiting, obvious toxæmia, irregularity of pulse, pallor, occasional coldness of limbs, systolic mitral murmurs and weakness of the first sound of the heart are signs and symptoms which, in the ordinary course of the disease would warrant a prognosis of the worst type and more especially when occurring late in the course of a severe attack of scarlatina.

Still more striking is Case 76, where, with symptoms of impending heart failure and toxæmia to

a more than marked degree there was present broncho-pneumonia and, as in Case 89, complete recovery.

A specially interesting feature in Case 76, is the fact that a hypodermic injection of Strychnine Hydrochlor, given as a control experiment had no effect on the pulse or general condition, while with an equal dose of the Formate a marked improvement was visible within forty minutes, improvement which was increased and maintained with two similar doses. It may also be pointed out that at the time of administration, the pulse was running and almost imperceptible.

In the two cases which died, although one was progressive and the other - as has been shown "doubtfully" sudden - the degree of toxaemia before the first administration was extremely profound and it would seem impossible to overcome a toxaemia which had already poisoned every system and organ.

One other interesting point is that there were no threatenings of Cardiac Failure in any of the cases in the very late stages of the disease, a fact which would seem to prove how thoroughly the toxaemic element had been eliminated and how thoroughly the stimulant effect had persisted.

The main features in all the cases are:+

1. The remarkable regularity of the pulse even after irregularity has been present in

most pronounced degree. With the exception of some four cases, the pulse has been regular within five days of administration and in the great majority of cases within three days of administration.

2. The marked improvement in the general nutrition of the patients, as shown by their colour, appetite, lack of depression, etc., which has been, as is noted in the details of the cases, as a rule, within four days of administration and which would point to a successful combating of the toxaemia.

So far, then, the results appear to show that Formic Acid and the Formates have a distinct stimulant effect on the heart and that, given a not too profound toxaemia before administration, the general nutrition and vitality of the muscles is so improved as to combat with success the toxaemia of this particular disease and to prevent a subsequent degeneration.

To what may this be due?

As has been shown, the line of treatment carried out in these cases - namely by Formic Acid and by the occasional use of Belladonna - was one of stimulation by non-blood pressure raising drugs. The former treatment, on the other hand, - namely treatment by Strychnine, strophanthus, digitalis

and adrenalin chloride,- was entirely by drugs which raised blood pressure, in different ways but with the same result. If, however, as in diphtheria, the heart is weakened by toxæmia and the inhibitory apparatus is also affected, as shown by the condition of the pulse, and if degeneration is the almost constant accompaniment, as is the case, it would seem that by raising blood pressure and so increasing the amount of work which the heart has to perform, that a contrary result to what is hoped for, must ensue - namely an increase of degeneration and a further strain to the heart.

The addition, in occasional laryngeal cases, of Belladonna which, in small doses, modifies the inhibitory action of the Vagus nerve and so increases the output of the heart per minute, has been therefore strictly in accordance with views such as these.

It is possible, therefore, that the astonishing difference in the results obtained from the two courses of treatment has been due to the broad fact that, whereas the 300 control cases were treated by strychnine, strophanthus, adrenalin chloride, etc. - namely, blood-pressure raising drugs - the 100 cases treated by Formic Acid and occasionally Belladonna, were treated by non-blood-pressure raising drugs, and that, therefore, the heart was not so severely

taxed as regards the amount of work imposed upon it in the latter cases.

It seems more probable, however, that the results are due to a combination of this fact with the actual stimulant properties of Formic Acid, and that with a gradual stimulation of striped muscles all over the body and direct stimulation of the heart, the resistive power of the individual must be enormously increased unless, as has been shown in the two cases referred to, degeneration has already occurred in an advanced degree. If this is the case, the nervous system must be indirectly benefited, for the exact selective influence of diphtheritic toxine is as yet uncertain, and it is, therefore, by the combination of these two factors that results, so good as these, have been obtained.

It may be urged, that, for this complication of the disease, 100 cases does not leave a sufficient margin as to warrant the obtaining of a definite result. While this, no doubt, is true, so large a percentage of recovery among cases with undoubted signs and symptoms of impending Cardiac Failure would seem to negative this assertion and, in any case, to prove the necessity of a prolonged and exhaustive trial of the drug in the disease.

but Streptomycin
stimulates the
heart & also
the peripheral
circulation.



+
↓

Paralysis.

While the percentage of paralysis of all varieties - namely three, is not far different from that of the deaths from Cardiac Failure, the improvement in results is much more marked.

A fall in the Paralysis rate of 11%, namely, from 14% to 3% is more satisfactory even than the results of the former complication.

While the results of the total numbers of paralysis appear more than good, the mild type of the paralysis is also satisfactory. Thus, of the three cases of paralysis recorded two were benign, namely palatal, and the third a very slight paresis of the lower extremities with only slight alteration in reflexes, and a subsequent complete recovery. In the two palatal cases there was in both cases an alteration in speech, but no difficulty in swallowing.

A third interesting feature of these cases of paralysis is the fact that two out of the three recorded cases occurred during a subsequent attack of measles, and that in both cases the drug had been discontinued from 16 to 18 days before the symptoms appeared.

Thus, cases 59 and 73,- the first, a case of palatal paralysis and the second, one of paresis of the lower extremities, were both treated for diphtheria for two and a half weeks with Formic Acid;

both developed measles, and were transferred to another ward, where for sixteen to eighteen days, the drug was unfortunately discontinued and the paralysis appeared.

It is possible that the paralysis in both cases was the result of the Measles Toxaemia, following on the Diphtheritic, or again that it was due to a too early discontinuance of the drug. It would seem impossible to differentiate on account of the similarity of both cases, and it would seem safer to assume that a combination of both circumstances was the cause. This in fact must almost of necessity be so, for, with an increase in the degree of Toxaemia, the necessity for the continuance of treatment must be more apparent.

Here again as in the results of Cardiac Failure doubt might be expressed as to the severity of the epidemic, but proof as to this would seem to have been proved positive, and out of the hundred cases, at least twenty-five cases were so extremely tox-aemic as to warrant a doubtful prognosis of paralysis, and, under ordinary circumstances, a percentage at least average in number and type with the cases cited as control.

The multiplicity of lesions described in this complication of Diphtheria, render it the more

difficult to give an adequate explanation of the results of this treatment. As has been shown by Manicamide, many of these lesions are purely muscular, and with the use in frequent small doses of such a drug as Formic Acid, results similar to these might be expected. In those cases where the lesion is primarily central with a Wallerian degeneration of the peripheral nerves, it would seem as though two objects might be obtained: (i) To give complete rest, and by using Formic Acid to keep the muscular system in tone and the general nutrition good, until the nervous system - if not too severely poisoned - recovered; or (ii) to attempt to prevent this occurring in a severe form by successfully combating as soon as possible the toxæmia by early large doses of Formic Acid and the Formates.

With such statistics from treatment such as this, it may be considered if hitherto the muscular element in diphtheritic paralysis has not been underestimated, and that many of the early, and less severe forms of paralysis are not muscular, with a less severe degree of nervous element than is generally supposed.

A theory such as this would appear to suit well the results obtained with Formic Acid in these cases, and might explain the diminished number of deaths from Cardiac Failure as well as the lack of paralysis of other varieties.

Albuminuria.

Although the diuretic effect of Formic Acid and the Formates in the disease has not been pronounced, the great reduction in the percentage of albumen - namely from 38% to 10% - is noteworthy.

While in one case (No. 90) the amount was great and prolonged, it may be noted that the patient was suffering from pleurisy with effusion and a high swinging temperature. In the remaining case, the appearance of albumen was within two days of admission and was only present, at the most, on two occasions. There were, apart from the absence of albumen, no noteworthy features in the urine.

That the Formic Acid exercises any direct effect on the kidney is difficult to suppose and it would seem as though the result was obtained chiefly by the general condition of the patient being so good as to be highly resistant to the toxine, while that in the percentage and doses given the blood-pressure was not raised and no diuresis ensued.

It is interesting to note that in the two cases in which antitoxine was given in largest amount - namely 76 and 81 - albumen appeared on the second day in one only and not again, and this would, in a slight degree bear out the observations of Variot that the two are in no way connected.

There can be little doubt that the amount of albumen is, as a rule, in proportion to the severity of the toxaemia and the explanation of the results obtained would seem to be as stated above, rather than any direct action of the drug on the kidneys.

CONCLUSIONS.

It is difficult not to conclude that results, such as these, are sufficiently successful as to at least warrant a thorough and prolonged trial.

It may be urged that the influence of antitoxin has not been given the prominence due to it, but has purposely been disregarded as being in the same proportion for the Control Cases.

Treatment would, therefore, appear to resolve itself into:-

1. Adequate and early doses of Antitoxin;
 2. Rest in proportion to the severity of the case;
 3. Gradual and proportionate stimulation by Non-blood-pressure raising drugs;
 4. The use of Formic Acid and the Formates;
- and until proof positive negatives it, that, with such results, a thorough trial of such lines of treatment must be made at the expense of the older treatment which relied for stimulation solely on an increase of blood pressure, while it would seem to be the case that Formic Acid and the Formates, by their influence on every complication of importance in diphtheria, render them, in that disease, drugs of the greatest importance.