A Thesis on the History, Aetiology and the Antitoxic Treatment of Diphtheria.

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A Digest of the History, Aetiology and the Antitoxic Treatment of Diphtheria with some original observations made as Medical Officer of Health for twelve years in fourteen rural parishes in Wales.

Introduction. I have chosen this subject because of the extensive experience I have had in the disease and the great interest which I have taken in its treatment by Antitoxin.
Diphtheria is a disease the importance of which from the point of view of a Medical Officer of Health can scarcely be over-rated and it is an excellent example of the application of bacteriological methods to the treatment of an infectious disease and its study opens up a wide field for researches into the bacteriology of other affections.

History. The term Diphtheria is derived from the Greek διφθέρα a skin or membrane.

The disease has been known from remote times and was described by Aretaeus of Cappodocia about 50 A.D. as Syriac and Egyptian ulcer and Aetius of Armidea noted symptoms of paralysis of the palate in connexion with this affection.
In the 16th Century the disease was epidemic all over Europe and was termed Morbus Strangulatorius, Gangrenous ulcer &c. but at this time the relations between the faucial and laryngeal lesions were not recognised and, indeed, it was not until the 19th Century that this relationship was pointed out by French observers and to Bretonneau is not be given the credit of distinguishing between Diphtheria and other laryngeal affections all having previously been called "Croup".
Bretonneau was the first to use the term Diphtheria and he rightly regarded it as a contagious disease though he was unable to reproduce the affection in animals and he included under the name all pellicular inflammations of the throat.

Trousseau pointed out that Diphtheria caused death not only mechanically but also by Systemic poisoning and he looked upon the membrane as a result of infection and not as the primary lesion.
In the latter half of the 19th Century Virchow, Cohnheim and Peterson made many investigations as to the nature of the membrane but it was not till 1883 that Klebs described a bacillus as existing in the false membrane and this was first cultivated by Löffler in the following year. It was however, left for Roux and Yersin by a series of researches to shew that the most important features of the disease could be produced by using the separated toxines of the disease and these researches have been further amplified by the various chemico-pathological experiments of Dr. Sydney Martin..
It may now be taken as a logically established fact that the so-called Klebs-Löffler bacillus is the direct "cause" of the disease known as Diphtheria and this fact goes a long way towards explaining the various aetiological factors of this affection.

Many Physicians hold that this particular bacillus should always be detected before one makes a diagnosis of Diphtheria but in general practice it is not well to adhere too closely to this postulate and although we know that the presence of false membranes is not absolutely peculiar to Diphtheria, nevertheless, to an experienced eye the existence of a membrane on certain mucous surfaces is not unfrequently sufficiently diagnostic of this affection. It is impossible to exaggerate the great importance of recent researches both bacteriological and chemical on the nature of Diphtheria as they have thrown a great deal of light not only on this disease but on allied infectious disorders and in this connexion it may be stated that the researches of Dr. Sidney Martin have been of peculiar interest.

Epidemics. That Diphtheria is an epidemic disease has long been known and indeed Bertel considers it as one of the oldest of all epidemic affections.

In this Country Diphtheria occurred in a sporadic form during the earlier half of the 19th Century and it assumed an epidemic form when the so-called "Boulogne sore-throat" was so rife on the neighbouring French coast.
From 1855 to the present time this disease has been continuously present in this Country.

Geographical Distribution. According to Nothnagel Diphtheria is a disease of world-wide distribution.
Until recent years available statistics even in the most advanced countries were very incomplete and were limited to fatal cases.

Seasons. Most authorities state that the greatest prevalence of the disease is in the months of October and November.
My own statistics in 70 cases shew that two-thirds of the cases occurred from the beginning of October to the

end of March or in other words that the disease was twice as prevalent in the six months October to March as in the six months from April to September. Alternately fine and wet weather seems to predispose to attacks of Diphtheria but Continuous wet weather as in 1903 militates against the occurrence of epidemics as the poisonous effluvia are washed away and do not therefore accumulate. In 1903 I observed that towards the end of October and in the earlier part of November, during which time there was a spell of fairly fine weather, the disease again shewed a markedly increased prevalence.
It appears to me that when a recedence of water after heavy rains occurs the soil gradually attains a peculiar moist state favourable to the growth of the germ of Diphtheria and when the soil becomes really dry the bacillus is unable to thrive.
In Thorne's "Diphtheria" p. 18 it is stated that Hirsch declares that neither soil

nor altitude have any influence upon the development of Diphtheria or on its epidemic diffusion but I must say that I cannot from my own personal observations agree with that Authority. And I may state that Thorne's researches in North Wales (a district with geological and physical features allied to those of the district which I have under my supervision) are in agreement with mine. One of the most fatal epidemics I have ever seen occurred in a village called Llangybi in Cardiganshire. There was a shallow stream running through this village and the flow during the time of this epidemic (June 1894) was practically stagnant and the adjoining soil was marshy and of a dark clayey consistence. After this epidemic the bed of the river was made deeper and the land well-drained with the result that no cases have since been notified from that village.

In February 1899 an extensive though

mild epidemic of what I considered to be Diphtheria occurred at Llanfair about two miles from Llangybi above mentioned. In this case about 40 School children exhibited enlarged tonsils covered with a thin white film. As there was no evidence of Scarlatina and as a few of the children afterwards shewed signs of faucial palsy I concluded that I had to deal with a mild epidemic of Diphtheria. On visiting the School I found that it was much exposed to the South-Westerly winds and that the soil consisted of yellow clay with here and there pools of water. I found the School-room itself in a satisfactory sanitary condition and I ordered thorough drainage of the play-ground with an excellent result. I think these observations tend to shew that exposed clayey retentive soils at least predispose to Diphtheria. The number of cases of this disease occurring in newly-built cottages in rural districts is, I think, worthy of notice.

These cottages are usually inhabited before they are completed, and the most striking defect in their sanitation is the absence of a trough to drain away the rain water dropping from the eaves which consequently tends to accumulate at the back and front of the house, and as evaporation occurs when the weather becomes finer a certain moist-state of the soil is left which in my opinion predisposes to Diphtheria. In general it may be stated that the Diphtheria bacillus requires in order to thrive a certain temperature and moisture and this is often provided by the ebb and flow, so to speak, caused by the alternation of dry and of wet weather.

Age. From the age of 3 to 12 is usually considered to be the most common period for the occurrence of Diphtheria. The number of cases during the first year of life is very

small although it is stated by Dr. Greswell (Thorne p. 40-41) that infants may suffer from Diphtheritic deposits on the fauces without any evident inconvenience and that the absence of symptoms may be due to the rudimentary character of the tonsils at that age.

I have on several occasions noted the whole of one family affected with Diphtheria except the infants whom I have especially and carefully examined and out of the 70 cases which have come under my especial observation I have not seen one case in infancy.

It is to be noted that the greatest prevalence of the disease in children between the ages of 3 and 12 corresponds more or less to the end of the first dentition. Children's teeth begin to decay about the 3rd year and from that time up to the 12th year the mouth is in a more or less septic condition and is thereby, I considered, rendered more liable to

diphtheritic infection. Although I can find no reference to this particular predisposing Cause in the numerous writings on Diphtheria I would venture to offer this as one of the factors predisposing to the liability to the disease at this time of life.

Sex. The published statistics in regard to the incidence of Diphtheria in Males and females are somewhat contradictory.
My own experience seems to shew that after the age of 5 girls are more liable than boys to Diphtheria in the proportion of 4 to 3 and I think that this may be attributed to two factors, viz:-
firstly, the prevalence of the habit of kissing among females and secondly their spending more time indoors.

Constitution. The presence of Adenoids and of enlarged tonsils, the Scrofulous habit and of certain exanthemata especially Measles seem

to predispose to the development of Diphtheria and in such cases the explanation is probable that the Löeffler bacillus finds a suitable medium for its growth. On the other hand certain individuals exhibit a more or less marked immunity and it is interesting to note that Lubowski has shewn that the blood of such persons possesses a decided antitoxic property.

Diphtheria in the lower Animals.

Clifford Allbut states that cats are liable to Diphtheria. Dr. Ridley (B. M. J. April 14th. 1900) quotes cases of septic throats communicable to man from poultry suffering from "gapes" though he did not conclude that the affection was diphtheritic in nature.

In March 1900 I came across what appeared to me to be a very direct communication of Diphtheria from fowls. I was asked to see three children whom I found suffering

from undoubted Diphtheria and indeed two of the cases afterwards exhibited ocular palsy and paresis of the legs. The father of these children kept a large number of poultry and some of his fowls died while his children were down with the disease and I found that the cause of death was what could only be called Diphtheria. I do not think there can be much doubt as to the genuiness of these cases which I investigated with much care having in my mind the possibility of such an occurrence. I may be allowed to mention that these observations of mine were made before the appearance of Dr. Ridley's communication and, indeed, I went a step further in coming definitely to the conclusion that my patients were suffering from undoubted Diphtheria.

The Influence of Sanitary Circumstances on the prevalence of Diphtheria. The fact that

the mortality from Diphtheria has increased 63% in England and Wales since 1870 (Allbutt p. 711) whereas the mortality from zymotic diseases in general including Diphtheria has fallen from 4.8 to 2.5 per cent (due to improved sanitation) tends to shew that insanitary conditions have but little influence in causing Diphtheria and many skilled observers have failed to satisfy themselves that the rise of polluted waters is one of the causes of a Diphtheria outbreak. It is quite possible that polluted air by lowering the general vitality may in that way predispose to Diphtheria.

The rise of the subsoil water may predispose to Diphtheria by forcing upwards the germ charged air and also a fall of the barometer causes an effusion of polluted air.

The specialities of the Maidstone epidemic were attributed to conditions affecting the barometer, the rainfall and the subsoil water level.

Since most cases of Diphtheria can be attributed to antecedent cases the balance which can be put down to purely insanitary conditions is very small and since the demonstration of the Löeffler-bacillus and its relation to Diphtheria it can, I think, be fairly said that Diphtheria is a specific disease and cannot arise de novo though, of course, we cannot deny that certain circumstances will predispose to the growth of this germ while other circumstances may actually bring the germ into the air which is breathed and in this connexion it is to be especially remembered that emanations, damp and cold readily produce sore-throats in some people and this condition is peculiarly favourable to the growth of the diphtheritic bacillus and cases may be instanced in which a throat affection which was of a simple inflammatory nature to commence with has ended in a severe infective Diphtheria.

Schools and Diphtheria. It has been already mentioned that Diphtheria is most prevalent in children between the ages of 3 and 12 years and it may be especially noted that the disease is five or six times commoner in those attending School.

School attendance acts in the following ways-

(1) By the assembling together of children at an age when they are most susceptible to Diphtheria.

(2) The children are, of necessity, placed for several hours in the day in exceptionally close relation to each other.

(3) The closer the aggregation and the greater the lack of ventilation the greater is the risk of infection.

(4) The faulty sanitation in Schools and in playgrounds by inducing sore-throats favours the reception of Diphtheria.

(5) The practice of kissing, of transferring sweets from mouth to mouth and of the joint use of drinking cups is favourable to the spread of the disease.

(6) In country districts it is common to

carry milk to School in tin-cans and for different children to drink it from the same cup.

Modes of Infection. The modes of infection in Diphtheria are numerous. The disease may be conveyed from one person to another by the inspiration of air from infected persons, by coughing or by Kissing.
It may be stated here that mild cases of catarrhal Diphtheria and chronic cases (especially Diphtheritic rhinitis) are more responsible for the general spread of the disease than are the severer cases where proper precautions are taken early.
In connexion with the spread of infection it can, I think, be taken as generally granted that Diphtheria is at first a local affection.
Dr. Havilland Hall (B. M. J. Oct 31st 1903) has pointed out that the localisation of the disease to the naso-pharynx is more frequent than is generally recognised. In primary laryngeal Diphtheria clinical

evidence favours the view that the Klebs-Loeffler bacilli enter the system through the laryngeal mucous membrane but we are still in the dark as to the special factors that determine the point of ingress. The usual course, however, is for the larynx to be affected by extension from the pharynx.

When we consider that many cases of Diphtheria are determined by the infection from an overlooked case of nasal Diphtheria and that no definite period can be fixed for quarantine we should be sure that both the nasal and buccal secretions are free from the Diphtheritic bacillus before the patient be allowed to intermix.

Beside direct infection it is necessary to bear in mind that indirect infection may occur from clothes, wall-papers, toys &c.

In September 1899 I was able to trace the conveyance of the disease seven miles in two directions across a moor. In this case three families lived at distances of seven miles from one another and I found that the mothers of two of the families

visited the one infected house and conveyed the disease to their own homes. No other cases occurred in the whole district around and neither of the mothers suffered from the disease and, moreover, I was able to absolutely exclude infection by means of milk and I think the only conclusion that could be arrived at was that the infection was conveyed by the clothes.

Milk and Diphtheria. It has been contended that Diphtheritic infection may in some cases be explained by causes operating through the cow which cause her to produce milk capable of inducing the disease.

A ropiness of the milk was brought under the notice of Dr. Cameron as a sign of infection by Diphtheria.

Sewage contamination of the utensils used in the dairy has also been suggested as a cause. Instances have been quoted of houses supplied by a certain Dairy in which the inmates have been infected with diphtheria whilst others

in the neighbourhood not supplied from the same source have been unaffected. According to Thorne it was noticed at York Town and Canterbury that the better class people as compared to the Cottager were attacked in the proportion of 84 per cent of the former to 22 of the latter. The explanation may have been that the one class was supplied with a different milk or, perhaps, that they consumed more milk, richer milk or kept it longer on the premises.

In connexion with the relation of milk to the spread of Diphtheria the following question must naturally crop up, viz:- How does the milk acquire an infective properly? It has been pointed out- by Power that no theory of infection by human agency or by unwholesome conditions at the farm affords any solution of the difficulty. It has been held that the cow herself may suffer from Diphtheria and though it is generally held that the Klebs-Löeffler bacillus is the cause of Diphtheria Klein

asserts that a smaller bacillus is really the true bacillus Diphtheriæ and he found that milch cows after infection may develop vesicles followed by crusts on the udders and teats which he considered to be local manifestations of the constitutional affection induced by the Diphtheria inoculation.
In my experience Diphtheria from milk infection is uncommon and I believe that the milk must be contaminated in some way after it leaves the cow or else I should expect the disease to be more prevalent in rural districts since a large number of the children are brought up on farms and the disease instead of being so rare in infants would if the above theory be correct be far from uncommon since the infants are chiefly reared on cow's milk which is not only non-sterilised but is often kept warm over night by being placed under the pillow in order to save the parents the trouble of getting up. Moreover the sanitation of

of farms is as a rule bad in Wales.
I believe human beings infect milk oftener than vice versa.
In the B. M. J. Oct 17th 1903 (p. 1002 & 1003) Dr. Spotiswoode Cameron points out an instance where the infection of milk was traced to the throats of those handling the milk before its transmission to the dealers or retailers. On changing the personnel of the farm the cases of Diphtheria ceased.
Sir Henry Littlejohn in B. M. J. June 16th 1900 (p. 1512) also quotes a somewhat similar mode of infection of milk by human beings.

The village of Slaney by ther with 600 to 700 inhabitants has for several years been almost entirely supplied with milk from two farms both of which are kept in an indifferent sanitary state but, nevertheless, I have had no reason to suspect that Diphtheria has been communicated through the milk (except on one occasion noted later on which was not proven.)

Although it has been held by high authorities that the most common cause of Diphtheria is milk directly infected by the cow yet I have always felt very sceptical on this point and have been on the look out for a case.
In November 1903 a dairy-maid was notified to me as suffering from Diphtheria and afterwards in the same house a child and an elderly woman were attacked. The house and dairy are situated about 20 yards from the river Leify on a flat, sandy porous soil and between this homestead and the river are cottage gardens saturated with pig and human manure.
In another house about 50 yards off on the same side of the river another case occurred and two cases were noted in different houses about twenty yards on the other side of the river - These three houses were all supplied with milk from the house first mentioned but many other houses lying on a higher plane away from the river

Though having the same milk supply were not in any way infected so that I had to eliminate the milk supply as the source of infection.
The only explanation I was able to give of the outbreak of the disease was that the soil being flat, porous and saturated with manure was for the greater part of the year in that moist-state which I believe is favourable to the growth of the germ of Diphtheria.
I may point out in connexion with these cases that in the house first-affected there is a staired tunnel which is close and stuffy. During the Summer months there is rarely much fire in the kitchen but towards October a big fire always burns in the grate with the result that the foul air forced from the soil by the subsoil water is drawn through the tunnel into the kitchen which room the inmates mostly inhabit and the particular person first infected was one who was peculiarly liable to "Sore-Throats".
Most of my observations on Diphtheria

have tended to convince me that a certain humidity of soil is an important factor as a starting point of Diphtheria especially when associated with foul emanations and this point is, I think, less clearly recognised in Urban than in rural districts as in the former other factors are more liable to come into operation and to attract attention.

Some General Conclusions in Regard to the Aetiology of Diphtheria.

I think I am justified in making some general conclusions from data already given.

(1) Diphtheria first appears as a local membranous deposit the general infection being of a secondary nature.

(2.) The Klebs-Löeffler bacillus, a vegetable germ, is the essential cause of the local disease and the general Symptoms are due to the absorption into the System of toxins (the result of the life processes of the bacillus.)

(3). Diphtheria or a disease resembling it is found in certain animals and can be communicated to man from them or vice versa.

(4) In my opinion "direct" infection by milk from the cow is not so definitely proven as some Authorities would have us believe.

(5.) The rise and fall of the subsoil water appears to have an important relation to the development of Diphtheria

(6) The diphtheria bacillus being a vegetable germ requires, like other vegetable fungi, a favourable moisture in which to thrive.
Clayey retentive soils and a porous soil saturated with albuminous matters are almost always associated with Diphtheria when this Disease does not arise from direct infection.

(7) Schools are undoubtedly important factors in determining the spread of the disease especially in rural districts.
The check of the disease after closure

of the School is not so readily observed in towns as in the country for in the former there are more numerous factors for its extension.

The Antitoxic Treatment of Diphtheria.

Until the introduction of Antitoxin by Behring the Treatment of Diphtheria was in an unsatisfactory state. In certain diseases the blood serum of artificially protected animals if injected into others still susceptible has a protective power and Behring conceived the idea that a similar Treatment might be adopted in Diphtheria in man. To Aronson we owe the immunisation of horses from which the serum now in use is obtained. Antitoxic serum is now almost universally considered as the true specific for this disease. Baginsky who made a most searching investigation into this subject states that the mortality has been reduced by Antitoxin

from 48·4 to 15·6 per cent.
The earlier it is used the better the prognosis. The statistics being as follows:-

1st day of disease the mortality is 3·5 %
2nd " " " " " " 8 %
3rd " " " " " " 12 %
4th " " " " " " 23 %
5th " " " " " " 35 %.

Laryngeal cases give a worse prognosis even with antitoxin than other forms. Rothnagel states that the number of cases coming under operation after antitoxic treatment has been reduced to the half. When operative interference is deemed necessary intubation seems to give better results than tracheotomy, viz:- 42 to 30·8 %. The mortality previous to the introduction of antitoxin was according to Monti 73·3% and to Macnaughton 69·5%. The death-rate afterwards fell from 70% to 16·6 %. Nasal cases involving the choanae are very fatal especially in infants.

Infants are rarely affected but when so the mortality is 80 to 90 per cent.

According to Nothnagel (p. 151) Antitoxin produces the following effect on the membrane of Diphtheria - In a few hours it becomes blanched and appears swollen, presenting more or less a granular appearance with congestion of the thicker mucous membrane around. Later the membrane loosens at the edges, becomes rolled up and afterwards detaches itself. He further states that the temperature rises one or two degrees in four or five hours after injection.

My own experience is that in a few hours a general reddening of the cutaneous surfaces appears but the thermometer does not indicate any rise of temperature.

Indications for the use of Antitoxin

(1) In all children over twelve months residing in a house where diphtheria is

Suspected, 2000 units should be injected even when there are no symptoms. Infants need not be immunized unless symptoms appear. All children's throats should be examined as Diphtheria can be easily overlooked.

(2) In croup inject without delay at any age and a culture should be taken at the same time.

(3) Even in pseudo-diphtheria one is on the safe side in giving Antitoxin though Hothnagel (p. 165. Vol iii) states that in cases in which bacteriological examination does not shew the presence of Diphtheria bacillus, Antitoxin cannot be expected to be of use.

(4) When Tuberculosis is associated with Diphtheria it is perhaps advisable to with-hold it and depend on other treatment unless the case is very severe.

In children under five especially, alcohol and antitoxin are my sheet anchor in the treatment of Diphtheria

As the struggle accompanying local remedies to the throat in young children do more harm than good. The disease except in its initial stage becomes constitutional and has to be treated on those grounds. The Diphtheritic poison is neutralized by the Antitoxin.

Bordet in B. M. I. (p 76. Nov. 14. 1903) states that the fact that antitoxin counteracts toxin in virtue of a direct combination is settled, but the exact nature of the re-action remains to be defined. The absorption of the active principle of the serum by the cells is compared to the absorption of colours.

Ehrlich seems to consider that the combination of toxin and antitoxin is in variable proportions.

According as one adopts the view of the combination of toxin and antitoxin in fixed proportions or in variable proportions one will be led to attribute to the mixture of toxin

and antitoxin distinct compositions.
In the first case we should have to consider that the mixture contains two substances - toxin free and active and toxin saturated and harmless - in the second case we should have to suppose that the mixture contains only one substance - toxin incompletely saturated and simply attenuated.
Ewing (p 163 Rothnagel) believes that hypoleucocytosis is due to antitoxin injection and when it does not occur a fatal outcome is to be expected.
These results are confirmed by Schlesinger.
Roger has noticed a diminution in red cells and haemoglobin following injection of antitoxin, which, he believes to account for anaemia in children, following immunizing doses of serum.
The anaemia in my opinion is due to the toxine of the disease itself as Anaemia and renal disease were frequent sequelae of Diphtheria before antitoxin was ever introduced.
Antitoxin has a beneficial influence on

the disease in from 12 to 36 hours after its administration. It seems to me to act as a diaphoretic and especially as a diuretic, as well as by neutralizing and attenuating the toxin. I have repeatedly noticed that a large quantity of urine is voided within 12 hours of its being injected. In severe cases 6000 units or more should be used and even in the last extremis it can do no harm. I have seen three cases of what were considered fatal croup cured by it. The first time I used it was in a case of extreme prostration, another child having died in the same house a few hours previous, and improvement could be seen in 24 hours. If one can get the case when the patches on the throat are of a creamy or condensed milk colour the chances of recovery are very favourable.

Five fatal cases occurred with me out of 41 undisputable cases of

Diphtheria.

The 1st was not seen till 4th day, epistaxis, purpuric haemorrhages all over body, died whilst being raised on to bed-pan from Cardiac paralysis.

2nd died suddenly on the 10th day in trying to get out of bed after being ordered to keep quiet. probably Cardiac paralysis.

3rd. Complicated with broncho-pneumonia.

4th. Cardiac failure. not resting as directed.

5th. Not seen till the 6th day when toxaemia was extreme.

After the first dose of 2000 to 6000 units according to the severity of the case another 2000 units should be injected at least every 24 hours until the improvement is decided.

This is obtained usually in 24 to 36 hours, the white patch commencing to fade assuming the appearance of

a withered or blighted flower. In another 48 hours or sometimes sooner the patch separates and leaves a clean, raw surface, but sometimes small specks of a somewhat darker hue may reappear in another 24 hours when it is advisable to give another 2000 units. Usually we have then a marked improvement in the pulse which may approach its normal rate, sometimes a little lower, and the skin is bathed in perspiration not unlike the crisis in pneumonia. I used to inject the Antitoxin into the back, but now I find it easier to do so into the subcutaneous tissue of the thigh, as one can hold the little patients limb oneself and not depend on others.

The strictest antiseptic precautions should be taken. After injection a lump the size of a pigeon's egg is formed under the skin and this must not be rubbed but allowed to disappear by absorption, a

small pad of antiseptic wool being bandaged loosely over the seat of puncture.
It is sometimes advisable before injecting to give a little brandy as the prick of the needle causes faintness in some patients.
No regard to the age of the patient need be paid in regulating the dose.
It has been asserted that erythema and abscesses have occurred at the seat of puncture but this must be due to sepsis of needle or serum. Marked joint pains are also being attributed by some to antitoxin but one gets those in tonsilitis when patient is of a rheumatic diathesis. Anuria, Convulsions, tetanus, cardiac and other paralysis are stated to be caused by antitoxin but it is more likely that it acts as a preventive against the above alleged symptoms.

It is an interesting fact that the temperature in Diphtheria may be practically normal or comparatively high. When it is raised it appears to me that the streptococcus pyogenes acts in combination with the bacillus Diphtheriae.
I was called to a case of Diphtheria in a young Minister about 10. a.m on Nov. 14th. 1903. There was a dirty greyish membrane on the left tonsil and a spot on the uvula - pulse 105. temperature 102.2. Chlorine water was given as gargle, but in the evening the temperature and pulse were about the same as in the morning. Quinine in 5 grain doses was then administered. The following morning the pulse was 85 and temperature normal. Medicine was discontinued. About 4 p.m. temperature went up to 101.2 and pulse to 95. The membrane spread to the right tonsil and was more extensive even when pulse and

temperature were down during the day of the 15th. About 4. p. m the Quinine mixture was resumed and 2000 units of Antitoxin given. About 10 p. m. temperature was 99 and pulse 82, altering really before the antitoxin had time to have any effect. On the morning of the 16th. in about 16 hours after injection of antitoxin both temperature and pulse were normal with only insular spots of membrane on tonsils and healthy or rather clean spaces between. From which time uninterrupted recovery ensued.

In puerperal fever one often has a similar lowering of temperature with fairly large doses of Quinine. It is stated by Nothnagel in his Encyclopedia (p. 114) that the temperature is lower in Diphtheria than in pseudo-diphtheria, but I think we may have the streptococcus of pseudo-diphtheria and the bacillus diphtheriae acting in

Conjunction causing an unusual rise of temperature. In these cases Quinine will lower the temperature but will not affect the diphtheritic membrane. After the injection of Antitoxin I have noticed that the temperature may not diminish for perhaps 12 hours or more after signs of blighting of the membrane, if Quinine or some other antipyretic is not given, which appears to shew that Antitoxin has no effect in pseudo-diphtheria. Antitoxin consequently acts as a diagnostic remedy as well as having a prophylactic and curative effect on Diphtheria. If the membrane is not modified in 24 to 36 hours after antitoxin administration in a suspected moderately severe case of Diphtheria, the probability is that true Diphtheria does not exist.
