**Micro-organism of diphtheria with experimental results in animals / by Albert Wilson.**

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# *Micro-organism of diphtheria with experimental results in animals.*

By Albert Wilson, M.D., Leytonstone.

Diphtheria, according to Dr. Thorne, is increasing, and is the universal enemy of mankind. It attacks the rich and noble as freely as the poor and humble, and it draws no distinction between the strong and the weak. The high mortality caused by diphtheria demands the closest study as to treatment.

The scientific treatment must have as basis a clear and accurate knowledge of the pathology. The first stumbling-block in the pathology of diphtheria is *absence of definition.* There are many cases in which it is difficult to prove, but impossible to deny, that they are diphtheria. To overcome this difficulty we resort to the term "diphtheritic," using it in a self-contradictory sense to mean "not diphtheria," but something like it. The word diphtheritic so commonly used, as, for instance, in scarlet fever throat, corresponds to a counterfeit coin. If a throat is diphtheritic it is true diphtheria, even if in a mild form. If it be not true diphtheria, it is not diphtheritic.

Instead of suggesting a strict definition of diphtheria, I will confine myself strictly to my subject.

Loeffler, Klebs, and others have isolated a bacillus which they consider the cause of this disease. But their inoculation experiments have, so far as I know, not produced definite results. Oertel considered the specific organism as cocci, for he found them in sections of the internal organs.

Klein has, however, superseded all other observers with a series of elaborate experiments, and proves another bacillus than that one of Loeffler and Klebs to be the true diphtheria bacillus. I will call this the *Klein bacillus.* Klein has furnished the Government with a full report of his investigations.

As my results are different, I must briefly recapitulate his research with slight criticism.

In Section A, Klein describes *cover-glass* specimens of diphtheritic membrane, obtaining thereby abundantly his special germ. My

experience has been that such membrane contains an uncertain variety of germ, being attached as dead tissue for hours or days in the mouth, with swarms of organisms continually in contact with it. It thus becomes a pabulum for any germs.

Klein washes his membranes in *sterilized salt solution*, which, he says, removes "most of the microbes." I think most bacteriologists will regard this as open to error in isolating pure cultures. Yet by these means Klein states that he has obtained his bacillus "in almost pure cultivation." Klein also states that the foreign organisms "occupy the most superficial layer of the membrane." Surely one must admit that with their rapidity of growth, superficial organisms would penetrate throughout the membrane. *Klein's bacillus* is "constant in the membrane," while Klebs-Lœffler bacillus is inconstant.

In *sections* of membrane and tissue Klein found, with some exceptions, his bacillus "present only in the membrane itself," "chiefly in the superficial layer." This might almost be taken indirectly as *evidence against his bacillus* being the cause of diphtheria. He then made many inoculations in various animals of pure culture of the Klein bacillus. The *general result* was local phlegmon, going on to form a *necrotic tumour* at the seat of inoculation. This "tumour, due to necrosis of the tissue,"—"looking remarkably like the human diphtheritic membrane." But the same might he said of the dead tissue of a carbuncle, and I feel the assumption and the comparison to be wrong.

In many of his fatal cases, he found "fatty degeneration of the cortex of the kidney," and as many of the cats which died of naturally acquired diphtheria had similar kidneys, Klein assumes this as proof of his bacillus being the specific organism. But it is not so, for fatty degeneration of the cortex of the kidney occur in many forms of poisoning, in septicæmia, and in several acute febrile disorders, and is most certainly *not pathognomonic of diphtheria*.

Next Klein produces *corneal ulcer* in the cat by rubbing membrane on an injured cornea, and finds his bacilli in the ulcer. But this is only a case of reaping what he sows, and bears no relation to the main question, for corneal ulcer is not diphtheria. He also inoculated *cows* and gets vesicles on the teats containing his bacilli. But this cannot be considered diphtheria.

Cats supposed to be fed on these cows' milk became ill, and out

of fourteen, five died, of which two had membrane in the trachea, containing his bacilli. But it was not proved that there was any connection. The symptoms were coryza, sneezing, coughing, pulmonary trouble, and emaciation.

Klein then experimented on cats and produced pneumonia in them by injecting *his cultures into the trachea*, and finally assumes that in the cat "the probable seat of the local disease is in the lungs and not the fauces." Yet he states that when cats naturally acquire the disease they cough, and get husky, and claw at the throat. I must therefore differ from Klein, that diphtheria in man corresponds to a lung disease in the cat or an udder disease in the cow. As a rule, Klein did not get the common symptoms of diphtheria either in the pharynx or in paralysis. His results, fatty parenchymatous kidney, pneumonia, inflammation or hæmorrhages of the internal organs, and serous membranes, correspond to *blood-poisoning by germs.*

*Résumé of objections to Klein's Bacillus diphtheriæ.*

1. Because diphtheritic membrane from its situation and exposure is contaminated with a variety of foreign organisms.
2. Because Klein's mode of purifying the membrane is inefficient.
3. Because as a rule the bacillus is not found in the tissues, but confined to the membrane only. "The diphtheritic bacilli do not extend further than the diphtheritic membrane."
4. Because in not one of his inoculation experiments did he produce the symptoms of diphtheria. Either inflammation or membrane in the fauces or paralysis.
5. Because all the symptoms from the inoculation of his bacillus, corresponded with those of ordinary septicæmia, or blood poisoning from germs, namely, pneumonia and hæmorrhages in the internal organs, and serous membranes and, in the latter stages, fatty degeneration of the cortex of the kidney.
6. Because the last symptom he counts as pathognomonic of diphtheria, whereas it occurs in septicæmia as here, also in many acute febrile disorders, and some forms of poisoning.
7. Because his comparison of the necrotic tumour at the seat of inoculation to diphtheritic membrane is far-fetched.

8. Because he assumes without any foundation that human diphtheria becomes pneumonia in the cat, and udder disease in the cow.

My own research, during the last few years, in cases of diphtheria, lead me to regard *micrococci* as the prevailing organisms in severe cases.

My cases were all treated *antiseptically*, thus, to a large extent, excluding foreign organism. I always examined membrane on the first day of its formation, at a later date there was a great variety of organisms.

In progressive cases also, one sees in the surrounding mucous membrane the following changes:

(1) Redness, swelling, and even œdema.

(2) A thin grey or milky-white exudation.

(3) Membrane formation.

It is to this *thin grey exudation*, preceding the membrane, that I wish to call very special attention; it is specially evident in the malignant cases, requiring the closest watching and treatment. It is not alluded to in books or writings.

The reason of this is probably that, for want of antiseptics, the mucous membrane is not clean, and therefore this condition cannot be seen.

With a view to discover and prove the organism of diphtheria, I performed the following experiments and inoculations.

Dr. Enraght, who is associated with me in practice, assisted me conjointly throughout, watching every detail, and corroborating every observation.

I selected a severe case of diphtheria in a boy aged 10, and removed some *membrane* on the third day. With this I inoculated *six tubes* of sterilized gelatine.

The results were two tubes remained clear and free from germs, due to the antiseptic action on the membrane of the drug employed. Four tubes yielded a mixed growth of cocci, baccilli, and threads.

From a *plate cultivation*, I got three kinds of organism. Two forms of micrococci, different sizes and growths. One bacillus, which rapidly *liquefies gelatine*, evolving a chrome green colour. Doubtless these microbes dissolve the membrane; I have not found a description of it, and will call it, *pro tem.*, the *Liquefying Bacillus*.

Grown in parsnip infusion, it forms a brown scum, with bubbles of gas underneath, with an absence of green coloration.

I both fed pigeons and *inoculated* them with each of the following four cultures:

(1) The liquefying bacillus.

(2) The larger micrococci.

(3) The smaller micrococci.

(4) The mixed culture of bacilli, thready and cocci.

No visible effect resulted with the first three, and therefore I concluded that the above organisms are innocuous.

The pigeon injected with the mixed culture died emaciated on the ninth day, but with no paresis or throat symptoms. Therefore its death was not associated with diphtheria.

Having failed to obtain a specific organism in the membrane, I next examined the *thin grey exudation* already described.

At the bedside, with delicate forceps, sterilized by heat, I pinched the thin grey layer without removing a visible portion, and inoculated a tube of sterilized gelatine.

(The following day this area was *covered with membrane*).

The throat was cleaned with lactic acid and boracic acid hourly previous to my inoculation.

Kept at 60° F. for six days, *the forceps track* showed turbidity, with small colonies like the ova of pediculi, but smaller. The surface of the gelatine was funnel-shaped at the puncture, the upper part turbid and liquid, with a small orange-coloured deposit.

Microscopic examination showed an absolutely *pure culture of very small cocci* (about $\frac{1}{25000}$th of an inch diameter). They were mostly in pairs, but also in beads and gloca masses.

Incubated for thirty-six hours at 90° F. the gelatine became turbid throughout.

From this tube I made subcultures. With the original culture I inoculated two pigeons.

(All pigeons used were strong, healthy birds, mostly cocks. I selected pigeons knowing that they were prone to diphtheria).

*Exp.* 5.—Inoculated a pigeon with 20 minims of the *original culture.* It was paralysed in the legs and semi-paralysed in the wings in eight or nine hours, supporting itself on the beak and wings. But it slowly improved after a day.

On the third day a yellow membrane was attached to the right pharynx, which bled on attempting to remove it.

On the fifth day the membrane nearly disappeared. Nine days after it was killed because there remained loss of co-ordinating power.

*Exp.* 6.—Another pigeon *similarly treated* became ill the same day.

In two days the pharynx was covered with membrane which extended to the larynx, and the animal died of dyspnœa between the third and fourth day. Paralysis set in on the second day.

The cocci were found in the blood, and also in the membrane of the throat, together with bacilli and other microbes.

*Exp.* 7.—A pigeon was inoculated with a mixed culture of No. 6 membrane. The bird was poorly some days, but no membrane in the throat. It had, however, a putrid affection of the gullet.

*The inference* from the experiments where throat disease and paralysis occurred is that the cocci injected are the real diphtheritic germs. Hence I would call them, *pro tem.*, the *Diphthero-cocci.*

At first I thought the rapid paralysis was due entirely to the absorption of the effete product of the cocci in the gelatine, what might conveniently be called the diphtherin. This I afterwards disproved.

Experiments with the *subcultures* incubated at 90° F. showed *attenuation of the cocci.*

*Exp.* 8.—A pigeon was inoculated with 20 minims of the secondary culture. In two to three days there were ulcers on the pharynx, with a yellow deposit or membrane.

There was also leg weakness, so that it could not perch. It was well in a week.

*Exp.* 9.—A pigeon was inoculated with the same quantity of a parsnip infusion, containing a similar secondary culture. The effect was *nil.*

The vegetable infusion was not proper pabulum for the diphthero-cocci.

Experiments were made with a subculture grown for thirty days, at 60° F., with a view to testing *diphtheria as a constitutional or a local disease.*

*Exp.* 10.—A pigeon was inoculated with 20 minims of the subculture. In two to three days the throat became red, with small white patches. There was leg weakness. In a week it was well.

*Exp.* 11.—A pigeon was *scratched in the pharynx* and the subculture rubbed on. Slight yellow membrane found on the scratches on

the second day but disappeared in a day or two. There was no leg weakness, *and no constitutional effect.* (To be referred to later.)

*Exp.* 12.—A pigeon was *both scratched and inoculated* as in the last two. On the second day there were distinct small patches of membrane with ulceration. There was also inability to perch. It was well in a week.

The *inference* of the last five experiments is:

(1) Diphthero-cocci in subcultures may become *attenuated* producing only slight sore throat and general weakness.

(2) Diphtheria is more probably *a constitutional* disease than a local.

I made a second series of experiments from a very *malignant case of diphtheria.*

On the *first day* of the little girl's illness, when the membrane was forming in small patches on one tonsil, I inoculated a tube of gelatine by means of a sterilized wire, with which I punctured a small patch.

In eight days at 60° F. *the characteristic appearance occurred in the gelatine.* The minute colonies, the funnel-shaped depression in the gelatine, the slow and turbid liquefaction, with an orange coloured deposit.

It was a *pure cultivation* of the same small cocci. After two days in the incubator at 90° F. I made the following inoculations.

*Exp.* 13.—A pigeon, injected 20 minims of the culture. Death in eight or nine hours.

*Exp.* 14.—A pigeon, injection 6 to 7 minims. In ten hours it was paralysed, could not stand or fly. Died in about twenty hours. Diphthero-cocci in the blood. No reliable throat symptoms as died in the night.

*Exp.* 15.—A pigeon was inoculated with *the washings of the syringe,* less than one minim.

Next day ill, will not feed. Helpless in twenty-four hours, lying on one side.

Whitish *membrane* all over the pharynx, which extended to the larynx. Died in about thirty-six hours.

*Exp.* 16, was performed to see if the rapid death and paralysis were due to the effete poison of the cocci, *the diphtherin.* Therefore 12 minims of the original culture sterilized by heat were injected. The bird never had any apparent ill effects.

The *inference* must be that the *large dose of virulent cocci* in the

blood killed before local throat symptoms could manifest themselves, as in the case of "suppressed scarlet fever." Yet we know that the poison of diphtheria is very depressing, affecting powerfully the spinal cord and medulla. Apparently nature has the power of *eliminating the diphtherin without the cocci.* But when cocci are also present manufacturing fresh supplies of diphtherin in the blood, then the animal dies of the poison.

A third series of inoculations were made with a *pure culture of diphthero-cocci,* obtained from exudation and ulceration of the soft palate on the *ninth day* of the disease in the last case.

*Exp.* 17.—A pigeon, 20 minims of the above culture injected. In ten hours the animal was quite paralysed, and died in eighteen to twenty hours. The throat was dubious.

*Exp.* 18.—A pigeon, *half a minim injected.* In two days, red ulceration with *yellow deposit* on the surface occurred round the glottis and on the pharynx. On the third day a thin white membrane came off the palate, leaving an ulcer behind. The bird was ill, but not paralysed. It got well in a few days.

*Inference.*—As the case progressed the *diphthero-cocci* got *slightly attenuated.* I made a *subculture* of these active germs, but unfortunately it got *impure;* bacilli resembling the *Bacillus subtilis* appeared, yet I *inoculated two pigeons.*

*Exp.* 19.—The pigeon used in Experiment 11, where local throat inoculation of the diphthero-cocci had been ineffectual five days before, was inoculated with 20 minims. The next day there was paralysis of the legs and paresis of the wings and yellow membrane in the pharynx. On the second day it died.

This was a *complicated experiment.* Was the virus in the subculture of cocci, or in the foreign bacillus, or was it the double dose of cocci in the same bird, calling the local throat inoculation into renewed vigour?

To test the impure subculture, I similarly inoculated another pigeon.

*Exp.* 20.—The following day it was semi-paralysed. The throat was dubious. On the second day it began to recover, and was quite well in four or five days.

Time forbids that I should describe *a further series* in which five mild cases occurred in one family, and in three of which I got the *typical cocci,* and choosing the most abundant crop, obtained by inoculation, throat ulcers with yellow exudation in a pigeon.

*Exp.* 21.—Having *proved the coccus* to cause both membranous and ulcerated sore-throat, and also paralysis, I next studied the influence of chemicals on its growth. It grows best in neutral, or slightly alkaline gelatine. Acids are injurious to its growth.

The following substances *prevented the growth of the diphthero-cocci* in sterilised gelatine:

| | |
|---|---|
| Boracic acid | 2 per cent. |
| Salicylate of soda (useless if weaker) | 5 „ |
| Hydrargyri Perchloridum | 1 to 5000 |
| Carbolic acid | 1 to 400 |
| Creolin (Jeyes) | 1 in 400 |
| Tinctura Eucalypticus | 2 per cent. |
| Hydrogen peroxide (20 vols.) | 2 „ |
| Sodæ Bicarb. | 10 „ |
| Benzoic acid | 1 „ |
| Antipyrin | 5 „ |
| Quinine | 10 „ |
| Resorcin | 1 to 400 |
| Iodine | 1 to 500 |
| Liq. Ferri Perchlor. fort. | 2 per cent. |
| Hydrochloric acid (sp. gr. 1·16) | 5 „ |
| Lactic acid (sp. gr. 1·21) | 1 „ |
| Zinc chlor. | ½ „ 1 to 200 |
| Nitric acid, B.P. | 2 „ |

The following substances were *useless* in arresting the growth of the diphthero-cocci:

| | |
|---|---|
| Chlorate of potash (saturated aqueous solution) | 10 per cent. |
| Liquor Potass. permanganate | 20 „ |
| Salicylate of soda | 2 „ |
| Jeyes | 1 in 2000 |
| Chloride of lime | 2 per cent. |
| Sulphurous acid | 5 „ |
| Hydrochloric acid (1·16) | 1 „ |
| Liq. Ferri dial. | 10 „ |
| Quinine | 5 „ |
| Sulphite of soda | 10 „ |
| Hyposulphite of soda | 5 „ |
| Sulphocarbolate of soda | 20 „ |
| Pot. Iodid. | 15 „ |
| Iodine | 1 in 1000 |
| Acid. Phosph. dil. | 10 per cent. |
| Sodæ Bicarb. | 5 „ |

From this, one sees the *absolute inefficiency of chlorate of potash* and *permanganate of potash*, so much used at present; also the uncertainty of sulphurous acid from its volatility. Also *sulphocarbolate of soda very inefficient.*

From the fact that dialysed iron is inert, and that 5 per cent. of hydrochloric acid is fatal to the cocci, one must infer that the *benefit of tinct. ferri perchlor.* in diphtheria arises *from the hydrochloric* acid by its local action.

On the other hand, there are *many non-irritating, yet potent antiseptics*, proved by experiment, and also I may say by the bedside; especially boracic acid, hydrochloric and lactic acids, and salicylate of soda.

My experiments were carried on in two houses. There was a cat in each house. *Both cats fell ill* with laryngitis, cough, choking and clawing at the throat, also great debility and paresis. One recovered spontaneously, the other by the use of salicylate of soda. On the other hand, most of *the dead pigeons were given to another cat*, which was unaffected. But here the acidity of the stomach might destroy the germs.

There are many *interesting questions* opened up for discussion:

Is diphtheria a *local or a constitutional* disease?

I think the experiments point to a constitutional disease, primarily, of which the local manifestation is the throat affection.

How does the poison enter the system?

Is it by sowing germs on an inflamed tonsil, or by inhalation of germs into the lungs?

Is it by infected food coming in contact with the tonsils?

Can infected food act through the stomach?

Finally, *what is diphtheria?*

Are the sympathetic sore throats and the ulcerated throats, caught from a palpably true case, also diphtheria?

Are they due to attenuated germs?

What is the relationship then of mild diphtheria to the Infectious Disease Notification Act?

I should not fulfil the purpose of my licence unless I laid stress on the *practical results* of the experiments.

First: It establishes *diphtheria as a constitutional disease.* Hence the importance of *internal remedies*, such as the salicylate early in the disease to act on the germs in the blood. Yet by experience, many, and I myself, have succeeded by local treatment only, but it

is with difficulty in severe cases. Therefore both means demand attention.

Second: As to *local treatment*, let us banish chlorate and permanganate of potash for ever.

If we use with frequency watery solutions of the acids, and stronger glycerine preparations of the non-irritating drugs, we cannot fail to succeed.

I have found the steam carbolic spray of value in laryngitis even after the formation of membrane, and lately have used small injections of pilocarpine, one twenty-fifth of a grain, with great success in loosening and bringing away membrane from the larynx.

Pilocarpine also is of value in eliminating the diphtherin from the system, and thus preventing both the cardiac depression and nerve paralysis.

*May 5th*, 1891.

*Table of Inoculation of Diphthero-cocci, &c., into Pigeons, with the Result.*

| No. of experiment. | Material for inoculation. | Early observations and progress. | Final result. | Inference of experiment. |
|---|---|---|---|---|
| 1 | 3 pigeons fed with Bacillus liquefaciens viride | In drinking water and bread soaked in cultures | No effect | The liquefying Bacillus harmless by the mouth. |
| 2 | 2 pigeons fed with Bacilli from diphtheritic membrane | Ditto | No effect | The Bacilli of diphtheritic membrane harmless by the mouth. |
| 3 | Inoculation with pure culture of Bacillus liquefaciens viride | — | No effect | The liquefying Bacillus harmless by inoculation. |
| 4 | Inoculation with large micrococci from membrane | — | No effect | The micrococci of diphtheritic membrane inert by inoculation. |
| 5 | Inoculation with small micrococci from membrane | — | No effect | Ditto. |
| 6 | Mixed cocci Bacilli (Löffler's) filaments | Very poorly in about 4 or 5 days | No throat affection; weak, emaciated; died 9th day | The Bacilli of diphtheritic membrane kill by systemic disease. |
| 7 | Diphthero-cocci from grey exudation | Paralysis and white patches of membrane on throat in 2 days | Membrane extends to larynx; dyspnœa, paralysis; death on 4th day (diphthero-cocci in the blood) | Diphthero-cocci cause death by diphtheria proper and paralysis. |
| 8 | Ditto | Paralysis in 6 hours; in 2 days yellow membrane in throat | After membrane ulceration slowly healed; loss of co-ordinating power remained; killed about 9th day | Diphthero-cocci cause diphtheria proper, paralysis, loss of co-ordination. |
| 9 | Subculture of the above diphthero-cocci | In 3 days raw ulcers on throat; weak on legs | 10 days after, snuffles and weak on legs | Attenuated diphthero-cocci produce sore throat and paresis. |
| 10 | Same subculture, but in vegetable infusion | No effect | No effect | Diphthero-cocci grown in vegetable infusion instead of gelatine absolutely inert. |
| 11 | Same subculture in gelatine inoculated | Weak on legs, and throat slightly ulcerated | Well in 3 or 4 days | Same as in Exp. 9. |
| 12 | Same subculture in gelatine not inoculated; scratched on throat | Where scratched slight patches next day; ulcerated throat for 1 day | Well in 4 or 5 days | Local infection in throat of diphthero-cocci produce no membrane nor constitutional weakness. |

| | | | | |
|---|---|---|---|---|
| 13 | Same subculture in gelatine inoculated, and also scratched on throat | In 2 days leg weakness; in 3 to 4 days yellow membrane on scratches | Well in 5 or 6 days | Attenuated diphthero-cocci act feebly if both locally and constitutionally. |
| 14 | Impure culture attenuated cocci in pigeon 12 | Next day completely paralysed; on second day membrane in throat | Died in about 48 hours | Impure or mixed culture of attenuated cocci fatal, when same pure cocci inert. |
| 15 | Impure culture from throat of bird 7 | In 2 to 3 days leg weakness; putrid throat affection | Snuffles, no true membrane; recovered in 8 or 10 days | Illustrates some connection between throat and throat. |
| 16 | Diphthero-cocci from malignant case, 20 minims | Died in 6 to 9 hours paralysed | No time for throat symptoms | Rapid poisoning of nerve centres from diphthero-cocci. |
| 17 | Diphthero-cocci from malignant case, 7 minims | Died in less than 21 hours | No time for throat symptoms | Ditto, corresponds to suppressed scarlatina malignans. |
| 18 | Diphthero-cocci from malignant case, less than 1 minim | Thick grey exudation and membrane in 24 hours | Died in 36 hours paralysed | Acute diphtheria proper and paralysis from diphthero-cocci. |
| 19 | Impure subculture same as Exp. 14, 20 minims. | Leg weakness next day; throat dubious | Well in 3 days | Attenuation of diphthero-cocci by subculture. |
| 20 | Diphthero-cocci obtained on 9th day from same case, 20 minims | In 12 hours paralysis | In 24 hours death | Diphthero-cocci become attenuated as the case progresses, and small dose not fatal. |
| 21 | The above, 1 minim only | In 2 days yellow membrane round glottis | Recovered in 4 or 5 days | |
| 22 | Diphthero-cocci same as Exp. 16, 17, and 18. Gelatine sterilized by heat, 12 minims inoculated | No effect | No effect | The diphthero-cocci being killed, the diphtherin *per se* is inert, unless decomposed by heat. |
| 23 | Diphthero-cocci from a 3rd case, milder | In 2 days membrane on throat; no leg weakness | Well in 4 days | Diphthero-cocci from mild case of diphtheria are attenuated. |
| 24 | Cat fed on all the dead pigeons and nothing else for 5 days | No effect | No effect | Though cats subject to diphtheria by inhalation, yet by the stomach probably incapable of infection. |

(When not stated otherwise, 15—20 minims of culture in neutral gelatine were inoculated over the pectoral muscles.)

## ADDENDA.

The *clinical aspect of diphtheria* is so interwoven with its pathology that I wish to make a few observations on this subject.

I would *define* a typical case of diphtheria as a specific inflammation of the tonsils and fauces, with sloughing exudation and ulceration, followed by prostration, and in severe cases by paralysis of certain nerves. The disease is due to micro-organisms.

I conclude that diphtheria must be classed as a true *constitutional fever*, having observed that cases both mild and severe begin with chilliness or rigors, and subnormal temperature; and in the second stage there is a varying rise of temperature.

In the first stage, which varies from twelve to thirty-six hours, there is usually great pain in the tonsil or submaxillary glands, but no pain in swallowing, thus differing from quinsy. There may be no alteration in the tonsil beyond increased redness. It is usually as the temperature rises that the exudation appears on the tonsil.

The temperature may vary from 100° F. to 104° F., and usually subsides from the third to seventh day; but it is no guide as to the severity of the case, not even in fatal cases.

The pulse is, however, of use to indicate the effect the disease has on the constitution. In severe cases, while the temperature remains normal, the pulse may keep up to 120 or 130, with feeble impulse and marked dicrotism.

Among the *constitutional effects* of diphtheria, the general debility, the anæmia, the weakness of cardiac muscle, and the *albuminuria*, are such as might attend any exhausting fever; whereas the paralysis of various nerves, and the loss of co-ordinating power in walking, are results *peculiar to diphtheria.*

The *local symptoms* appear in the following order:

Pain, either in one or both tonsils, and in the lymphatic glands.

Redness of the affected tonsils, spreading to the mucous membrane.

Tenderness of the neck outside.

Grey or yellow slough or membrane, commencing on the tonsil in small patches. The membrane consists of fibrine, leucocytes, epithelium. It contains micro-organisms, some of which may be associated with the disease, but most certainly more gain access from the externa world.

Swelling and œdema of the adjacent mucous membrane as the disease spreads.

A milky or *grey transparent exudation* forms on the swollen mucous membrane, and passes on to form fresh membrane or slough.

In a few cases I have watched this thin exudation on the tonsil *precede the membrane*, and I attach the highest importance to this early exudation as being *the only true hunting-ground for the organism of diphtheria.*

I have seen this primary exudation form like a veil on the swollen, but unbroken, uvula and soft palate, in a case where one tonsil only was affected, and that was healing, but local painting with boracic was refused. In this case, treated with carbolic spray, the germs could not enter from without. Clearly it was a constitutional disease, and the morbid material of the blood manifested itself locally in this exudation as much as the rash in scarlatina.

Almost as rapidly as the exudation appeared on the soft palate, it also occurred in the larynx, such being indicated by hoarseness, cough, and aphonia, &c. The child had many struggles for breath, but died comfortably in five days, due probably to the depressing action of the diphtherin. I mention this as many state that death is from asphyxia, and with a struggle.

The later stages are separation of the membrane, with or without hæmorrhage, ulceration, and granulation.

One is obliged to recognise at least three types of diphtheria.

(1) *Very mild or sympathetic throats.*—These are often contracted from severe cases. There is the febrile state, with pain and redness of the tonsil. They are *diphtheritic* in the true sense, and capable of giving a severe attack to another person. In April last I had marked proof of this:

A had well-marked diphtheria; B, attending to her, developed a "sympathetic" throat, without any apparent ulceration or exudation, but feverish (TC. 102); C had an interview with B, and was not otherwise exposed to infection, and in four days developed well-marked diphtheria.

(2) *Mild type*, with all the symptoms well marked, but recovering in some cases spontaneously, or, with treatment, in a day or two.

(3) *Severe type* of many grades: cases in which, with active and constant measures, the cases only yield in ten to fourteen days, in

some cases invading not only the nares, but also the larynx or trachea.

These cases are commonly fatal. In old times most of them were fatal. But it is the treatment of these which I wish to emphasize, believing that a fatal result ought to be only as rare as in typhoid or scarlatina.

I have noticed in epidemics, where the early cases were severe, that the later cases became mild. Similarly, I have frequently observed mild cases caught from contact with severe or very severe cases. The converse I have observed more rarely.

I was much struck in the last case quoted in my paper, where diphthero-cocci obtained on the first day were most fatal to pigeons; those obtained on the ninth day of the disease were much attenuated. This is a matter of great importance in searching for the specific organism, for observers might get *pure cultures of attenuated and inert diphthero-cocci;* hence the importance of selecting malignant cases, and examining at the onset of the disease.

I also found my *subcultures always became attenuated*, which corresponds to the usual clinical facts.

It is a strong argument against Loeffler's bacillus, that it is almost always fatal, and frequently takes two to three weeks. Such is quite different from the clinical facts of diphtheria, where the organism is either rapidly fatal, or in many cases so attenuated as to be practically harmless.

*The treatment of diphtheria.*—The *chief treatment should be local;* but in very severe cases, though local means will end successfully, I can testify that internal remedies greatly facilitate recovery.

For years I never gave a drop of medicine, and without a fatal result. But after further study of the clinical aspects, and after scientific confirmation from my experiments on the pigeons, I am bound to regard diphtheria as a *constitutional disease*, and, if so, it demands *internal remedies*, as salicylate of soda, resorcin, quinine, and so on.

In *local treatment* two things are essential. First, to select a *reliable and non-irritating antiseptic.* Second, to make sure of reaching the seat of the disease sufficiently, frequently, and efficiently.

I would recommend for all mild cases spraying frequently with 1 to 2 per cent. of lactic acid, or 5 per cent. of hydrochloric acid, or 2 per cent. of carbolic acid (?), or 1 per cent of resorcin, or 25

per cent. of sulphurous acid (?), or 1 to 3000 of perchloride of mercury, occasionally spraying out the nares.

Medicine need not be given in mild cases. The spray should be used *hourly* at first. Chlorate of potash and permanganate of potash to be carefully avoided. Perchloride of iron is useful only on account of the hydrochloric acid. In severe forms, and in children who cannot be sprayed, to paint the throat with glycerine preparation every two or three hours—10 per cent. salicylate of soda in glycerine; saturated solution of boracic acid in glycerine.

On account of its affinity for water, glycerine rapidly penetrates the mucous membrane, carrying with it the antiseptic.

The *treatment recommended by Loeffler*, in 'Deutsche medicinische Wochenschrift' for March 5th, 1891, seems to me *exceptionally harsh and irritating*. He recommends gargles of corrosive sublimate, 1 to 1000; 3 per cent. of carbolic acid, dissolved in 30 per cent. of alcohol; also alcohol and oil of turpentine, to each of which is added 2 per cent. carbolic acid. Also concentrated watery solutions of creasote. These irritating drugs savour very much of the early days of antiseptics, when pure carbolic acid, with putty, were used as surgical dressings.

Some of the above (*e.g.* turpentine) are almost caustic in their action.

As a result of using the more efficient and less irritating drugs, I have found almost every case, however severe, yield to treatment.

In my early days, especially when I have contemplated tracheotomy, but failed to obtain permission, by persevering with measures already described the cases have gradually recovered.

So impressed have I been on this subject, that I am tempted to feel that if a case can be saved it is *possible without tracheotomy*.

I attribute death in two of my cases of tracheotomy to diphtherin poisoning, as *post-mortem* showed all the membrane had been removed from the trachea, larynx, and even fauces.

I strongly urge the carbolic spray or other antiseptic inhalation, iodoform insufflation, and small doses of pilocarpine hypodermically, as soon as the disease invades the larynx.

In *searching for the specific organism*, the condition of the mouth, the fauces especially, and the membrane are of the utmost importance.

In all my cases, I have examined throats which had been *efficiently cleansed* with one or other of the above antiseptics. In

this way foreign organisms were to a large extent excluded, and the results must be very different from those obtained in the manner which past observers investigated. While different observers have obtained different results, I cannot too strongly advocate *the pure or aseptic method of investigation.* I also consider that all experiments based on the examination of dead membrane are wrong.

Among further errors of observation, I would refer to the 'Annals de la Policlinique de Paris,' May, 1891. M. H. Giblet finds the *Staphylococcus pyogenes albus* in false membrane, and adds it to "the list of micro-organisms capable of producing false membrane"!!!

Welch and Abbott (in the 'Bull. of Hospital,' ii, 11) state that "every postulate necessary to prove that the specific cause of producing diphtheria is the Klebs-Loeffler bacillus has been fulfilled." Yet in *no one case has this bacillus, on inoculation, produced diphtheria.* Take their own experiments: "Guinea-pigs inoculated with their cultures die in one to five days of *systemic* disease, the bacilli only being found at the point of inoculation," and *no throat symptoms.*

"Rabbits inoculated survive five to twenty days, developing as a rule paralysis," but *no throat symptoms.* But "streptococci were also found in most cases in the diphtheritic membrane."

Loeffler found his own bacilli would develop in eight hours on gelatine. If this be so, how can we rely on membrane which has been twenty hours or even longer in the mouth, which swarms with many varieties of germs?

Though inoculations of the Klebs-Loeffler or any other bacilli may cause death, yet death is not *diphtheria*, and up to the present these experiments with pure cultures of cocci are the only ones in which *membranous sore throat and paralysis have followed inoculation in a distant part of the body.*

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