

Original Articles.

THE IMPORTANCE OF BACTERIOLOGICAL INVESTIGATIONS IN CASES OF DIPHTHERIA.¹

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In September, 1893, a series of observations in cases of suspected diphtheria was commenced at the Bacteriological Laboratory of Harvard Medical School. From September, 1893, to October, 1894, 500 cases were examined, and of this number 133 proved to be diphtheria, or 26.6 per cent. These observations have been essentially different from any attempted, thus far, in this country; for they have been dealing not with the well-marked characteristic cases of diphtheria, but with the mild and doubtful cases in which a diagnosis is impossible without a bacteriological examination.

It is now generally conceded that the presence of the Klebs-Löffler bacillus is positive proof of the existence of diphtheria, and that persons in whose throats this organism is found are sources of danger to the community, and that they continue to be sources of danger so long as this organism continues to exist. Much has been said regarding the existence of the pseudo-diphtheria bacillus; and an attempt has been made by some observers to throw discredit upon the important discovery of Klebs and of Löffler. While it is perfectly possible that in certain rare instances a bacillus of a non-virulent type morphologically similar to the diphtheria bacillus may be found in persons with normal throats, still this occurrence is so exceptionally rare that it does not have any very important bearing on the accuracy of bacteriological diagnosis. It has also been claimed by some members of the profession that the inoculation of the tubes was extremely difficult, and that for this reason this method of diagnosis was not of practical use. In reply to this, it may be said that of the 800 tubes inoculated, there were only six cases in which there were no growths. This would seem a sufficient answer to the statement that this method of diagnosis is not of practical use. Any one who has had any experience in diphtheria knows perfectly well, that in a family of four or five children, one or two may have perfectly characteristic attacks of the disease, while the remaining children, without having any constitutional disturbance, without having any membrane in the throat, may have a slight seropurulent discharge from the nose which has nothing of itself characteristic of diphtheria, and in which a diagnosis of diphtheria could not possibly be made without a bacteriological examination. Many such cases have been examined during the past year, and in a large percentage of them diphtheria bacilli were found, the virulence of which was proved by their action on guinea-pigs. The occurrence of diphtheria during an attack of scarlet fever has been considerably overestimated by the profession. In these investigations 36 cases of scarlet fever in which there were marked throat symptoms were examined, and in nine of them diphtheria bacilli were found. The number of cases of measles, with marked throat symptoms, examined, is too small from which to form any satisfactory conclusions. In these investigations the average length of time in which the diphtheria bacillus was found present, has been 15½ days. In one instance the diphtheria bacillus was found to exist 72 days, but

in this particular case it is a question whether or not there was a re-infection.

A short history of a few of the cases examined may be of interest.

In Case 15 the physician gives the following history: A boy, five years of age, complained of slight sore throat, and had a small white spot on one tonsil. The boy was not especially ill, and this small white patch on the tonsil disappeared in three days. A culture taken on the first day of the illness, however, contained large numbers of diphtheria bacilli.

Case 23 was that of a boy who had a slight discharge from the nose. There was absolutely no constitutional disturbance, but bacilli of diphtheria were found in the culture.

Case 35 was that of a young lady with a temperature of 104°, pulse 120, having had a chill at the onset of the disease; in fact, the case presented all the clinical appearances of an attack of follicular tonsillitis, but a bacteriological investigation proved the presence of the bacillus of diphtheria. As this case occurred in a family in which there were several small children, if the patient had not been promptly isolated, the results would have been disastrous. In this particular case, it is of interest to note that the bacilli remained in the throat for about four weeks, and also that they retained their virulence, which was proved by the inoculation of guinea-pigs.

Case 38 is of interest from the fact that although there was some redness of the fauces and marked constitutional disturbance, there was no membrane to be seen, but the patient died forty-eight hours after the culture was made in which the diphtheria bacillus was found, with the symptoms of laryngeal stenosis.

In Case 48 the patient had an undoubted attack of diphtheria a month before the cultures were made. At the time of the culture, although the patient was in comparatively good health, there was a slight nasal discharge from which the culture was made. The diphtheria bacillus was found; and in order to settle the question of the virulence or non-virulence of the bacillus, a guinea-pig was inoculated with about two cubic centimetres of a bouillon culture twenty-four hours old. The guinea-pig died at the end of twenty-four hours, and the autopsy showed marked edema of the internal organs. The bacilli of diphtheria were found at the point of inoculation.

The history of Case 51 is as follows: Mrs. B., age forty-seven, had diphtheria three times, the last time about twenty-eight years ago. On November 15th, returning home from a concert, where she perspired very freely, felt chilly, and on the next day had a slight attack of acute coryza, which on the following day was quite marked and accompanied by malaise, headache of a dull character, chiefly frontal, and there was also very slight pain on swallowing. On November 17th there was no membrane to be seen, nor was there any marked congestion of the throat. There was an indistinct swelling about the size of a bean at the angle of the jaw at the left side. On the right tonsil there was a suspicious-looking thin film, covering nearly the whole of the tonsil. On the left tonsil there were several minute points about the size of a pin's head. The film upon the right tonsil, to which allusion has been made, was easily removed. Temperature was 102°, pulse 96. In short, the history of this case and the appearance of the throat would seem to justify a diagnosis of follicular tonsillitis. Cultures,

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however, made from this throat, showed the presence of the bacillus of diphtheria. In this case the bacilli continued in the throat for 19 days.

Case 64 is of interest from the fact that on the second day after exposure to diphtheria, before the appearance of any membrane and before there was any marked constitutional disturbance, bacilli of diphtheria were found. Forty-eight hours after the culture was made a membrane appeared.

Case 85 is that of a child eight years old, who had no membrane in her throat, but the culture was taken from a follicular plug. Bacilli of diphtheria were found. The child died eight days after the culture was taken, of laryngeal stenosis, intubation having been performed for the relief of this symptom three days previous.

Cases 88, 89, 90 and 91 are of interest from the fact that the local symptoms were very mild. Diphtheria bacilli were found, and the subsequent history of the cases justified the bacteriological diagnosis of diphtheria.

Case 109 is of interest from the fact that there was a very slight amount of membrane in the throat, and no constitutional disturbance. Bacilli of diphtheria were found in the culture, and disappeared at the end of two weeks.

In Case 116 a soft, yellow membrane, covering the whole of the left tonsil, friable on the surface but adherent at the base, was seen. Temperature 101° , constitutional disturbance moderate. The bacillus of diphtheria was found in the culture.

Case 119 was that of a girl four years old, who had very slight constitutional disturbance. In this case the diphtheria bacillus continued for about two weeks.

Case 128 is that of a young man who had a mild attack of sore throat, who was not ill, but who was in a situation where he must have communicated diphtheria to many people, if the disease had not been recognized by means of a bacteriological examination. The virulence of the bacillus was demonstrated, in this case, by its effect on guinea-pigs.

Case 135 is that of a child who had no throat symptoms, but did have a slight muco-purulent discharge from the nose. A culture taken from the throat was negative. A culture taken from the nose, however, was almost a pure culture of the diphtheria bacillus. In this case the child was not ill. He would have been a source of great danger if he had not been isolated.

Case 138 is worthy of mention because, although there was a slight membrane in the throat, this membrane did not present to the eye the characteristic appearance of a diphtheritic membrane. A culture, however, made from this throat revealed the presence of the diphtheria bacillus.

Case 147 is that of an extremely mild case of sore throat, in which a positive diagnosis without a bacteriological investigation was impossible. Cultures from the throat revealed the diphtheria bacillus.

Case 156. E. R., two and one-half years of age, had a slight sore throat, and also had a suspicious-looking membrane on the arm at the site of a recent vaccination. Very little constitutional disturbance. No membrane in the throat. Cultures made from the throat contained no bacilli; but the culture made from this suspicious-looking place on the arm contained the bacilli of diphtheria.

Case 171 is that of a boy four years of age, in

whose throat, twenty-four hours after removal of the tonsils, a membrane appeared; and it became a matter of great importance to decide upon the nature of this membrane. Cultures taken from it proved that it was not of a diphtheritic nature.

Case 180 is a case of purely nasal diphtheria, no membrane having been seen at any time in the throat. There was a profuse nasal discharge, from which almost a pure culture of the diphtheria bacillus was made.

The history of Case 182 has a typical clinical history of acute follicular tonsillitis. Five or six small spots were seen in the throat, but no extensive membrane was found. A culture, however, from this throat contained the diphtheria bacillus.

Cases 202 and 204 are of interest as illustrating the point that diphtheria can be diagnosed by bacteriological investigations before the appearance of any membrane or before there is much constitutional disturbance. In these two cases, as it was known that the patients, adult women, had been exposed to diphtheria, cultures were made from their throats, and the presence of the diphtheria bacillus detected forty-eight hours before the appearance of any membrane.

Case 267 illustrates the importance of a bacteriological investigation where there is a profuse nasal discharge without any constitutional disturbance.

It is unnecessary, however, to cite any more cases.

One very important and interesting point showing the value of a bacteriological examination in cases of diphtheria is the history of 18 cases of nasal diphtheria in which there was very little constitutional disturbance, and in which there was no membrane to be seen. Without a bacteriological examination these cases could not have been recognized as diphtheria. Cultures, however, made from the nasal discharge, proved the presence of the diphtheria bacillus, the virulence of which was tested by its effect upon guinea-pigs.

The following quotation from the report of Dr. W. H. Park, Inspector of Diphtheria to the New York Board of Health of New York City, illustrates the importance of cultures in all cases of a profuse nasal discharge in children. He says:

"A child was admitted into a hospital ward in an anemic condition and with a chronic coryza. Five days later four children in his neighborhood developed diphtheria. Two of these died. In seeking the cause of the diphtheria, suspicion was directed to the child by a slight nasal discharge. Bacteriological examination showed this secretion contained many diphtheria bacilli. On further examination it was found that the child came from a family in which, three weeks before, there had been a case of diphtheria.

"In a family of eight children one child sickened with diphtheria, and a second child, a baby, was sent to a neighbor. The next day cultures showed this baby, as well as two of the other children, all of whom were apparently healthy, were infected with diphtheria bacilli. The three apparently healthy but infected children, as well as the sick one, were at once quarantined, but already one of the family to which the baby had been sent had contracted diphtheria from it."

The cultures from 70 non-diphtheritic throats were examined in order to investigate as to the frequency of the, so-called, pseudo-diphtheria bacillus. Seventeen of the patients were suffering from chronic

diseases of the throat, 15 from uterine disease and the remainder from surgical and medical diseases. In no instance was an organism found that would be likely after a careful examination to be mistaken for the diphtheria bacillus. In these investigations a certain number of bacilli were found, but they were either long slender bacilli, or short stout ones, having no morphological resemblance to the diphtheria bacillus.

In a "Report of the Present State of Knowledge respecting the Etiology and Prevention of Diphtheria," presented on behalf of the English Committee to the Eighth International Congress of Hygiene and Demography at Buda-Pesth, Edward Seaton, M.D., F.R.C.P., says:

"Finally, it must be said that progress in medical preventive work generally (which must obviously include experimental research work) is retarded in a considerable degree by the popular or general conception of the scope of 'hygiene.' This in England has come to have far too narrow a signification. The term hygiene is almost always used to apply to structural works (for example, water-supply and drainage), materials, etc., which, however important they may be as necessary for the prevention of some (so-called) preventable diseases, are apparently useless for the prevention of others, which are also entitled to be called preventable. It will be impossible to combat diphtheria, influenza and other diseases which can only be properly termed preventable when the public and governments understand the necessity for the systematic encouragement of scientific observation and research bearing on the public health, and the furtherance of medical preventive work generally."

In a "Report on the Etiology and Prevention of Diphtheria," presented on behalf of the German Committee to the Eighth International Congress of Hygiene and Demography at Buda-Pesth, F. Löffler, M.D., says:

"(1) The productive agent of diphtheria is the diphtheria bacillus. Dispute as to the etiological definition of this bacillus exists no longer. We can, therefore, henceforth indicate as diphtheria such forms of disease as are infested with the bacillus.

"(2) Not infrequently cases appear in the early stages to the clinical observer as true diphtheria, which, however, are caused by other organisms, as streptococci, staphylococci, pneumococci, and in light or graver form may be mistaken for diphtheria. But the differential diagnosis can be effected through bacteriological research. Statistical compilation on the epidemic spread of diphtheria, as well as on the character of diphtheritic epidemics, cannot represent an exact definition so long as the bacteriological investigation of cases suspected of diphtheria fails to mark a division between true diphtheria bacillus and cases merely resembling diphtheria.

"(3) Diphtheria epidemics show a various character, as do many other epidemics of infectious disease. The course of the epidemics is often very light, but also much more severe, indicated by the high figure of the death-rate, the rapid infection of the larynx and the nose, and by severe heart and kidney affections, and consecutive paralyzes. But also in the same epidemic instances of severe and light forms of disease frequently alternate irregularly.

"(4) The variation, of course, will be determined by several factors: (a) By difference in the number

and the virulence of the diphtheria bacilli; the causes of the latter are not yet absolutely known. (b) By concomitant bacteria, and indeed as much by pathogenic as saprophytic. The processes of infection with regard to the diseased mucous membranes in the passages and in the nose appear to influence the course of the disease unfavorably, in part by increasing the virulence of the bacilli, in part by weakening the body through absorption of decomposition product. (c) By individual tendencies not yet thoroughly recognized.

"(5) The diphtheria bacilli can appear in the passages, especially of the nose, of separate individuals without causing indications of sickness, which it first induces when it has actually established itself. Lesions of the mucous membranes, small eruptions, catarrhal changes, are favorable to its residence. In brief, meteorological conditions giving admission by the first approach to catarrh (especially cold, damp weather), appear to favor the sickening from this cause. But this influence has to be more closely observed.

"(6) Diphtheria is most rapidly communicated by direct contact between sick and well, through spitting, coughing, sneezing, kissing, and grasping of the hands, whereby the hands come into contact with flesh secretion; also freely through utensils which the sufferer has fouled with his secretions; by beverages, food, eating and drinking vessels, cast-off washing clothes and other articles, as pocket-handkerchiefs, playthings, even long after their actual infection.

"(7) The sick is infectious so long as he has bacilli upon the mucous membranes. The bacilli usually disappear with, or soon after the disappearance of the local signs, but they may be detected still lively and virulent in the passages or nose for weeks and even months.

"(8) On inorganic matters condensed and excluded from light the bacilli can maintain themselves for a period of months; accumulations of dirt, dark and close dwellings favor thus the preservation of bacilli and the extension of disease.

"(9) As a specially noticeable vehicle for the extension of disease is to be noted, the crowding together of susceptible individuals, especially in families of many children. But other gatherings of people, apart from children, where separate persons do not come into such proximity as the members of a family, may offer facility for the extension of infection, as schools, barracks and the like.

"(10) The diphtheria bacillus is so far not identified with certainty as the cause of other diseases similar to diphtheria or of other spontaneous disease of lower animals. The possibility of the conveyance of true diphtheria from sick animals to human beings is thus outside our present knowledge. It is desirable that the governmental investigating committee should combine with research regarding diphtheria coming under their notice the similar diseases of animals, and also the communication from animal to human beings of diseases resembling diphtheria.

"(11) As prophylactic means are to be considered: (a) Care for cleansing, keeping dry, sufficient ventilation and lighting of the dwelling; (b) careful cleansing of the mouth and nose, gargling with weak solutions of common salt and carbonate of soda, thorough brushing of the teeth, extraction of bad teeth, attention to the deeper cavities of the tonsils, and removal

of hypertrophied tonsils; (c) cold douching of the throat in times of diphtheria prevalence.

"(12) Every case suspected as diphtheria must, when possible, be bacteriologically investigated. The physicians must have easy access to the required materials for carrying on the culture, for example, in the chemists' shops. The investigation has to be carried on by specialists, as in the case or cases of suspected cholera.

"(13) All cases proved bacteriologically to be true diphtheria, as well as all cases suspected as diphtheria which have not been bacteriologically investigated, must be dealt with under police regulations.

"(14) Every diphtheria case must be isolated, either in a separate room of the dwelling or in an isolation ward. In order to restrict as much as possible the spread of the bacilli by the sick, a local anti-bacillar treatment must be employed with a view to prophylaxis against the early stages of the disease.

"(15) One of the most effective means against the spread of diphtheria is the protective inoculation, with antitoxin, of susceptible individuals in the neighborhood of the patient, especially of children.

"(16) In every case of diphtheria, disinfection is imperative. This is needed for all utensils for the sick, as well as for the sick themselves and the sick-room.

"(17) Convalescents from diphtheria must not mix freely with others, till bacteriological investigation has proved the absence of the bacilli."

Dr. William H. Welsh, in a paper entitled "Bacteriological Investigation of Diphtheria in the United States," read at the Eighth International Congress of Hygiene and Demography, held at Buda-Pesth in September, 1894, says, "In 752 cases of diphtheria in New York the diphtheria bacilli disappeared within three days after the complete disappearance of the exudate." He also says, and this is a very important point: "A bacillus in no way distinguishable in morphology or in culture, including the formation of acid in bouillon, from the usual diphtheria bacillus, but devoid of virulence, exists. The virulence was tested by injecting into half-grown guinea-pigs one-half to one per cent. of their weight of forty-eight-hour bouillon cultures. This bacillus, although it has been called by some investigators the pseudo-diphtheria bacillus, should not be so designated. It is the genuine diphtheria bacillus devoid of virulence. It was met with in a comparatively small number of cases, out of a large number examined.

"Exceptionally it may occur together with the virulent diphtheria bacillus in diphtheria, and occasionally it takes the place of the virulent bacillus during or after recovery from diphtheria. In several instances it was found in healthy throats. The name pseudo-diphtheria bacillus should be confined to bacilli which, although resembling the diphtheria bacillus, differ from it not only by absence of virulence, but also by cultural peculiarities, the most important of the latter being greater luxuriance of growth on agar and the preservation of the alkaline reaction of bouillon cultures. The pseudo-diphtheria bacillus may render bouillon cultures acid in forty-eight hours when grown anaerobically. The pseudo-diphtheria bacillus in this sense was found in a number of cases, but not frequently. It is probably of different species from the genuine diphtheria bacillus, and is without diagnostic importance."

So far, there have been no investigations to prove that this non-virulent form may not, under suitable conditions, become extremely virulent; and until this point is firmly established it is the part of wisdom to consider this non-virulent form as a probable source of danger.

From the opinion of the authors quoted, and from the results of the 500 cases of suspected diphtheria investigated at the Bacteriological Laboratory, it is evident, that, to accomplish anything in diminishing the frequency of this disease, it is of paramount importance —

First, That in suspected cases of sore throat, or in cases where there is a profuse nasal discharge, a bacteriological investigation should be made.

Second, That in any case of diphtheria the patient should not be removed from isolation until there have been two negative cultures from the throat and from the nose.

Third, That the pseudo-diphtheria bacillus, so called, is not insufficiently frequent to cause any great error in diagnosis.

REMARKS ON DIPHTHERIA.¹

BY H. C. ERNST, M.D.

BEFORE there can be had a proper appreciation of the work that is to be presented here this evening, there must be a statement of facts in regard to diphtheria that are now too well supported by experimental evidence to permit any hesitation in their acceptance. There have been certain points in regard to this disease that have been well known for some time, points that later evidence has but brought more distinctly into view. The first and most important, the one that had to be first determined in order to any further intelligent study of the disease, was its cause; and this has been known for years to be a specific bacillus, commonly given the hybrid name of Klebs-Löffler, but properly called the bacillus of diphtheria. Seen first by Klebs in diphtheritic processes in 1883, isolated and described by Löffler in 1884, this peculiar and specific micro-organism has been the subject of many painstaking researches since that time; and the results that have come from these researches have been but confirmatory of the claims first made for it — that it is the actual cause of the process with which it is associated, and that without its presence diphtheria does not exist. This much has been settled for some time; so much so, in fact, that more than two years ago, in writing an article upon diphtheria, I had no hesitation in making the statement that doubtful cases of the disease could only be determined by means of the cultural diagnosis. This opinion was held by others engaged in similar lines of work; but in the study of the subject and of the best cultural characteristics by which this bacillus might be most easily and definitely separated from others similar to it, certain elements of confusion seemed to arise that threatened to obscure the desired precision of results.

The first of these was the presence, recognized by Löffler himself, of the so-called "pseudo-diphtheritic bacillus," a bacterium possessing apparently precisely similar characteristics to the true bacillus of diphtheria, with the extremely important exception that it manifested no pathogenic properties upon inoculation into

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