lished by the writer and since confirmed by Flexner, Booker (Johns Hopkins Bulletin, March, 1895), and others. The Löffler bacilli of diphtheria, in the cases of lacunar diphtheria are found, not so much on the surface of the tonsil, but in the depths of the lacunæ, in the fibrinous plugs, which occlude the lumina of the lacunæ. The bacilli are of equal virulence, whether obtained from the first group of mild cases or the third group of fatal septic lacunar diphtherias. The bacilli retain their virulence for weeks in the depths of the lacunæ, the patient being in apparent full convalescence, or the tonsils having returned to almost the normal size and appearance. In one case virulent bacilli were obtained from a lacunar plug of the tonsil in the third week of convalescence. A lacunar plug in one case, in which virulent bacilli had been isolated early in the disease showed non-virulent bacilli fully three weeks after the outset of the disease. In other words, virulent bacilli were replaced by the non-virulent variety in this particular lacunar amygdallitis.

Enough has been cited above, of the bacteriology of these cases, to show the importance of this class of cases of diphtheria. Too much weight can not be attached to these facts. We must not be turned aside by any fallacious arguments which continue to harp upon the desirability of a membrane in order to entitle a case to the dignity of the term, *clinical diphtheria*. This term, I believe, was first introduced into medicine by Trousseau. It is a landmark in the history of modern medicine, but it is time to protest against its use as a weapon with which to cast contempt on the class of cases concerned in this paper.

If prophylaxis is the ideal of modern hygiene, then the class of cases treated of in this paper, take a rank first in importance. Innocent in appearance, they are the means of disseminating a dread affection. Serious and unremitting isolation is the only method by which we can show our appreciation of their serious nature. Their importance crops out in the operating room constantly. At the last meeting of the American Pediatric Society, the writer of this paper insisted that those cases of tonsillotomy upon enlarged tonsils which were followed by membranous diphtheria, or even croup, were undoubtedly of the nature of the cases described in this paper. It has been shown by the writer that in these large tonsils, virulent diphtheria bacilli exist long into convalescence. As long as they are left to the natural fluids in the lacunæ no harm results to the patient, and we have even reason to believe, as pointed out in my second paper, that they gradually lose their original virulence. Cut this tonsil, however, and you expose to the propagation of the bacilli in the lacunæ the most favored of growing media, a freshly cut surface bathed in lymph, and a membrane results, in some cases spreading to the fauces and larynx. One case of this kind is enough to convince the most skeptical, and yet there are many such, doubtless, who are waiting for the case to occur to them.

Diagnosis.—How can we approach the diagnosis of these cases? The old methods, such as proposed by Henoch, only apply to cases which finally develop membrane or portions of membrane. If we wish, however, to pick out the pure lacunar diphtherias in which membrane never forms, we will find that our safest method is the bacteriologic test. To test the urine to wait for specks of membrane to appear, only delays matters and does not aid us, for we have not

only albuminuria in the streptococcus tonsillitis, but also glandular swellings and prostration with low and high curves of temperature. The opponents of bacteriologic diagnosis say that the Löffler bacillus has been found on the normal mucous membrane. Would you call such a case diphtheria and isolate it? The answer to this fallacious argument is plain. The well authenticated cases in which investigators of acknowledged rank (Löffler, Roux) have found virulent bacilli on the normal mucous membrane, are exceedingly rare and exceptional. They are found in throats perhaps exposed to a diphtheria atmosphere. Since the inauguration of the simple crude methods of diagnosing a case of diphtheria by growing a culture and staining a few covers has come more and more into vogue, the bacilli in the normal throats have multiplied in frequency. We would ask that methods showing such evident flaws be not taken too seriously. They are necessary in rapid hygienic work, but must not be brought forward as an argument.

Given an angina in which Löffler bacilli have been demonstrated to exist in large numbers, such a throat is diphtheritic and must be grouped with diphtheria, membranous or otherwise. It should be unmercifully isolated, whether it isolates the patient from friends and family or sends the patient into a contagious ward where severe cases of diphtheria are treated. It has been maintained that the placing of such cases among severer cases is an injustice to the patient. Those who have studied diphtheria since the discovery of Löffler must subscribe to the views brought forward by Escherich. These mild cases of diphtheria must be explained on the ground of immunity. They do not develop membrane and can not develop severe diphtheria, because in these particular individuals there is a natural or acquired immunity which protects them against the severer manifestations of the disease. If you place them, therefore, in a ward in which there are very severe cases of diphtheria, no more injustice is done to the mild case of diphtheria than would be done to a correspondingly mild case of measles placed in a ward with very severe and complicated measles.

On the other hand, these mild cases of diphtheria or lacunar diphtheria or diphtheria "sine membrana," are capable of communicating fatal or severe diphtheria to others. If we grant the above, which is the result of years of work at the bedside and in the laboratory, the principal arguments of the alarmists fall to the ground.

CLINICAL EXPERIENCE WITH ANTITOXIN IN PRIVATE AND HOSPITAL PRACTICE IN THE TREATMENT OF DIPHTHERIA—(ALL FORMS).

Read in the Section on Diseases of Children at the Forty-sixth Annual Meeting of the American Medical Association, at Baltimore, Md., May 7-10, 1895.

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NEW YORK.

My first successful case with antitoxin was published in the *New York Medical Record*, Oct. 6, 1894, in which a child 11 years old was attended by Dr. Gerlach. In this case I injected 5 ccm. of Aronson's antitoxin between the shoulder blades. The child was discharged, cured, on the fourth day. This pa-

tient was presented before the New York Post-Graduate Clinical Society at its first meeting in the Hospital Building in October.

Since then I have published a series of papers, embodying various clinical experiences; notably, however, papers that appeared on Nov. 17, 1894, in the *New York Medical Record*. A series of thirty-six cases, which were attended by me, was published in the January number of the *American Journal of Medical Sciences*, wherein I reported a very successful list of cases.

My percentage of deaths was but 5.8 per cent. The antitoxin used was brought over by me from Berlin last summer. Some of my patients were attended in the Municipal Hospital, Philadelphia, through the extreme courtesy of Dr. Welch, the supervising physician in charge, and also through Dr. Edward Davis, the editor of the *American Journal of Medical Sciences*. It is only necessary for me, however, to refer to the paper read by me before the German Medical Society of New York on March 4, 1895, in which I reported a series of 223 cases. These were largely made up of cases attended in hospitals and private practice, but most of them were those seen in consultation. The paper has since then appeared *in extenso* in the *New York Medical Record*, April 6, 1895. The mortality among the 223 cases was 15.11 per cent. This was by me in January, and can be accounted for in various more than twice as much as the first mortality, reported ways: 1, a great many cases were seen in consultation and were cases which were moribund, in other words, hopeless cases, and cases in which antitoxin was used as a last resort; 2, a great many deaths were also in children that had been suffering from mixed infections, cases of scarlet fever and diphtheria, cases of chickenpox and diphtheria, cases of measles and diphtheria. It is here that we can not look for any benefit from the antitoxin, because in some cases, especially in those which were fatal, I found that I was rather called upon to treat cases of septicemia and not cases of toxism, caused only by one infection, the Klebs-Löffler bacillus but rather the combined septic influences of the Klebs-Löffler bacillus and the streptococcus in scarlet fever and other microorganisms with which we are not so familiar.

A very interesting case, and one which I published in detail, was a consultation case with Dr. Roberts, of New York, wherein I refused to inject antitoxin, owing to a scarlet fever complication. In this case we had both diphtheria and scarlet fever, and the child presented a typical appearance of sepsis. The child died about one or two hours after I saw it, and if I had injected this case, we might have believed the antitoxin was again inert. I had, however, injected a prophylactic dose of antitoxin in another child in the same family, in the presence of Dr. Roberts. This child had been exposed to diphtheria, remained immune and was well when I last heard from it through Dr. Roberts, the attending physician.

The constant differences in strength, presence of noxious albuminoidal bodies, and other drawbacks, have given rise to complaints of inefficacy, occurrence of secondary effects and sequelæ, and even deaths. The use of such uncertain preparations tends to create confusion, and has already given rise to personal recriminations in the medical papers. The investigations of Wernicke, Ehrlich, Behring and Aronson on the question of acquired immunity from diphtheria, which were published in the scientific journals,

have enabled some manufacturers to produce a serum which is more apt to prejudice the value of the original discovery than to supply the demand for an efficient remedy.

It may be pointed out here, that antitoxin is not made by merely inoculating an animal, drawing off the blood after a certain interval, coagulating and separating the serum. Antitoxin and serum are not synonymous terms. Aronson's antitoxin, with which the best results were obtained, and on which the first clinical reports have been based, is a highly concentrated antitoxin, from which the inert and noxious constituents of the serum are eliminated.

The antitoxin made in Schering's bacteriologic department is, since April 1, controlled by the German government. The official demands require: that the serum is clear, containing at the most only a slight sediment; that the preservative is used in the proper proportions and that the antitoxin possesses the specified degree of immunizing power. This control is carried out in the Berlin Institute for Infectious Diseases; the weighing out, the drawing of samples, and filling in the factory being conducted in the presence of a sworn State officer. Further, the State requirements include the control of the health of the animals; the keeping of a control book, in which entries are made of all the horses, the period of their treatment, the amount and frequency of the blood-drawing, etc.

Physicians will readily see the importance of this measure, giving a satisfactory guaranty that the preparation has been made, tested and put up under the direct supervision of the German government and independent scientific experts.

Another important point in connection with the preparation is its keeping qualities. Dr. Aronson's antitoxin, which is preserved with four tenths of 1 per cent. of trikresol, keeps for an unlimited period of time, and according to the latest investigations, retains its full efficacy for at least one year.

In order to illustrate a few cases which have not been hitherto published and which are some of my most recent publication cases, permit me to offer the following:

Katie K., child, 4 years old, was brought to the office of Dr. R. H. Theyson, on April 13, 1895, to be treated for vomiting. Examination found the temperature 100, pulse 100, very slightly congested. April 14, temperature remained 100, pulse 110, vomiting had ceased; congestion in the throat slightly increased. The Doctor put the child on the ordinary form of antipyretic treatment and also prescribed an astringent for the throat. April 15, the temperature was 103, pulse 120 and slight patches of dirty white membrane were visible on the left tonsil, a small patch on the uvula and the breath was fetid. The child was apparently in good health and lively. On April 16, at 9:30 a. m. the temperature was 103, pulse 140, the child very sleepy and extremely rapid increase of the membrane, which was thick and tough, covering both tonsils, pharynx, uvula, and there was an acrid discharge from both nares. The breath was extremely vile. This case was also seen on the same day by Dr. Brackes. I was called in consultation at 7:30 on the evening of April 16, with Dr. Theyson, and found the throat completely covered with large masses of pseudo membranes. Temperature 103, pulse 104. In order to corroborate the diagnosis, I made a culture on blood serum through the courtesy of the attending physician, which proved Klebs-Löffler bacilli, and I was also asked to inject antitoxin. I injected 5 ccm. of Aronson's antitoxin, using the ordinary antiseptic precautions for the skin and instruments, between the interscapular region. The morning after I injected the antitoxin the temperature was 103, the pulse 140. The child feels brighter and there seems to be no increase of the membrane. Slight amount of albumin in the urine. April 18, pulse 140, temperature 102, vomited some small pieces of membrane at 9:30 in the even-

ing. Owing to a feeble pulse, free stimulants were ordered. April 19, pulse 120, temperature 120. The child has vomited considerable pieces of membrane. Two pieces were the size of 10 cent pieces. The appearance of the membrane in the throat is somewhat thinner. April 20, temperature 100, pulse 110, child very bright. April 21, membrane has disappeared from both tonsils, seems to be very thin on the posterior nares; temperature 100, pulse 110. April 22, temperature 99, pulse 110. April 23, temperature 98.5, pulse 90. Membrane is gradually disappearing. April 24, temperature 101, pulse 100, membrane almost gone; albumin still in the urine. April 25, temperature 98, pulse 100, discharge from the nares stopped. April 26, 27 and 28, temperature 99 and pulse 100. On April 26, membrane disappeared. April 28, patient discharged cured.

Temperature: April 13, 100° F.
 " 15, 103° F.
 " 17, 103° F. Aronson's antitoxin injected.
 " 18, 102° F.
 " 19, 100° F.
 " 22, 98.6° F.
 " 24, 101° F.
 " 25, 98.6° F.

Pulse: April 13, 100.
 " 15, 140.
 " 18, 140. Antitoxin injected.
 " 18, 140, morning.
 " 18, 125, evening.
 " 19, 120.
 " 20, 100.
 " 23, 90.
 " 24, 100.
 " 25, 26 and 27, 100.

On April 16, the culture made by me proved Klebs-Löffler bacilli. This is one of my typical cases, as I have seen them and as I have been used to treating them and, although it was agreed that this was a very bad case and that under ordinary circumstances we would give a very fatal prognosis, this child is well and received no other medication, excepting nasopharyngeal irrigation and local applications of some antiseptic solution.

A second case equally interesting is the following: I was called on April 13, by Dr. A. W. Newfield, to see a case of laryngeal stenosis and membranous diphtheria, involving the complete naso-pharynx, both tonsils and uvula. The child was in such bad condition, that although I was called to inject antitoxin, I told the attending physician that it would very likely require intubation before evening. This was about 3 p. m. That evening, Dr. Emil Mayer was called in consultation to introduce a tube. The following day, by appointment, I met Dr. Newfield, Dr. Emil Mayer and Dr. N. S. Roberts. On talking this case over, we decided that there still was severe laryngeal stenosis, and it was agreed that I should be permitted to examine the case. I was surprised to find no tube. It was plain to me that the child had probably coughed up the tube and swallowed it. I was permitted to intubate the child, which was rapidly done in the presence of the three physicians. Breathing at once was easier and the stenosis relieved. I did not hear from the case until Tuesday, when Dr. A. W. Newfield, the attending physician, called on me to extubate, as the child was entirely well. I begged the doctor to permit the tube to remain *in situ* for at least two days longer; on the following Thursday I removed the tube. The child remained well.

In this case the prognosis was so bad that it was considered a hopeless case and the attending physician believed, as well as I did, that the case was a bad one, but having seen worse cases get well, I decided to give only a cautious prognosis. In this case the urine was examined by Dr. Newfield and found normal; there evidently was no irritation caused by the antitoxin. I injected only 5 ccm. of Aronson's antitoxin between the shoulder blades and ordered nasopharyngeal antiseptics, consisting of washing the nares and throat with a normal saline solution (warm).

The third case and still more interesting than the above two, was one that was referred to me by the kindness of Prof. H. J. Boldt of this city on April 7. A child, about 2 years old, in extreme dyspnea, was seen by Professor Boldt and he wrote me that it was of the utmost importance to relieve the laryngeal stenosis by intubation. I intubated and the relief was immediate. I allowed the tube to remain three days and extubated, when the membranes reappeared

and it was necessary to re-intubate. This has been done in all four times. The depth of the disease and the malignancy of this case can only be imagined, when we consider that we have an extension of the disease from the pharynx to the larynx, and from the larynx to the trachea and as far down as we can not see but only conjecture. Long shreds of membrane are to-day coughed up, exactly as they were two weeks ago. The temperature has been varying between 108 and 101.

Owing to the great risk of feeding and causing pneumonia, in all my cases I have insisted from the first in feeding per rectum, by using an emulsion, consisting of the yolk of an egg and starch water, and beef tea mixed with starch water, and also injected stimulants in the same manner when indicated. I have found that children can get along very well for a week without feeding through the mouth, nor do I give anything through the mouth to quench thirst, but rely solely upon these enemata for both thirst and nourishment.

In all my cases it has been a surprising fact, the amount of good that could be done by combining intubation and antitoxin, but we must know that we are using antitoxin and a reliable preparation of the same only. The condition of the glands, the condition of the pseudo membrane, the temperature curve, the pulse, the heart's action, the urine, the skin and the eruptions following injection of antitoxin are points on which I have already elaborated in the series of papers, which I have quoted in the beginning of this short paper and to which I would beg to refer. I can not therefore take up your valuable time and go into detail on the above subjects without encroaching on the time usually allotted to a paper of this kind. Suffice it to say, that the mortality of my cases of diphtheria, as compared with the mortality of my cases of diphtheria before the antitoxin era is at least 500 per cent. better.

When such eminent men as Professors Heubner, Baginsky, von Wiederhofer of Vienna, von Ranck of Munich, Rauchfuss of St. Petersburg, von Mehring of Halle, Vierordt, von Norden, Seitz of Munich and others, will suddenly change all hitherto known therapeutics, and as at the Thirteenth Congress of Internal Medicine, which was held in Munich in April, 1895, suddenly drop all former medication and get enthusiastic over antitoxin and what it will do in diphtheria, then there must be some real reason for it. When I was at Berlin, Professor Baginsky told me that the mortality of diphtheria had been during the last four or five years about 40 to 42 per cent, and suddenly during the introduction of antitoxin, the mortality went down to about 12 per cent. Through some accident no antitoxin could be had for a short time, and again the mortality rose to almost 50 per cent., and then when antitoxin was again to be had, went down to 10 per cent. These facts, as they are the true statistics from one of the renowned hospitals in Berlin, the Emperor and Empress Frederick Children's Hospital, will speak volumes. The same can be said about the sudden enthusiasm of Professor Heubner.

There are a great many contra-indications to the use of antitoxin and these have been pointed out by me in an elaborate paper published in the *Medical Record* on April 6, 1895. Especially must we be careful where there has been a severe form of kidney trouble prior to the attack of diphtheria and especially so where there has been a great amount of irritation in the urine. But do we not always use great

caution when putting a patient under ether and inquire whether he has had kidney trouble formerly? We all recognize there are certain drugs that would irritate the kidneys, that would interfere with the usual heart's action, some like digitalis, that have a very irritable effect upon the stomach; again other drugs in which we must use great caution, owing to their injurious effect within the body. If this be so, why should we not use great caution and judgment in prescribing antitoxin, and inquire if there are not some contra-indications for its use, but with my experience to-day, covering over 260 odd cases, we must believe that some of the brilliant results attained by me have been due and only due to antitoxin. I will only refer to the case I have reported, in consultation with Dr. Newfield and which was intubated in the presence of three colleagues. The other case of Dr. Theyson is equally illustrative. I would not be willing to attend a case of diphtheria to-day, with what I have learned and seen in hospital and private practice, without antitoxin, any more than I would be willing to attend and promise a good result in any form of intermittent fever without quinin, or promise any decent result with other drugs than mercury in syphilis.

Having directed your attention to the good results obtained by the use of antitoxin, permit me, conclusion, to say, that I have had experience with but one patient in New York with domestic serum; this was in consultation with Dr. Landes. A third physician injected the antitoxin. The patient died the following morning. I was so much disheartened by the case that I have never since—nor had I previously used or prescribed—domestic antitoxin. I believe that we are justified in prescribing a specific kind of antitoxin, just as much as we are to-day in the habit of using standard preparations to specify good drugs in other diseases.

187 2nd Avenue.

CLINICAL OBSERVATIONS IN THE TREATMENT OF DIPHTHERIA WITH ANTITOXIN.

Read in the Section on Diseases of Children, at the Forty-sixth Annual Meeting of the American Medical Association, at Baltimore, Md., May 7-10, 1895.

BY A. CAMPBELL WHITE, M.D.

NEW YORK.

The medical profession in America has now had an experience of about one year with the antitoxin treatment of diphtheria. It is true that during the first six months the source of our supply of antitoxin was from abroad, and that this supply was necessarily limited, but during the past five or six months the supply has been about equal to the demand, and not many cases of diphtheria, particularly in the larger cities, need have suffered because of an inability to obtain serum of proper quality and strength.

The desire, or ambition, on the part of the medical profession to give this remedy a trial has certainly not been lacking; for I believe I am safe in saying that nothing in the domain of medicine has so attracted the universal attention of the profession and the public the world over, as this treatment of diphtheria with antitoxin.

Our National government, some of the State governments and the leading bacteriologists and clinicians of our country have manifested an active interest in testing the efficacy of this treatment. In doing this, Americans have only been following the

example of Germany, France and England, where the treatment has been afforded a considerably longer and much more extensive trial.

It seems, therefore, as if the theory of the antitoxin treatment of diphtheria should by this time either be discarded or denounced as unsound and worthless by those who have been carefully and scientifically testing its merits all over the world, or the theory should be accepted as giving to us a remedy with which to combat one of the most fatal diseases coming under the care of the physician, and pointing the way to the successful treatment of many other dreaded diseases of bacterial origin.

Have we, then, after this universal and extensive use of antitoxin any evidence or testimony to show that it does not overcome the toxemia of diphtheria, or that it is contra-indicated in the treatment of diphtheria? If so, what is the evidence, and what is the source of this evidence?

Have we any evidence or testimony that antitoxin does overcome the toxemia of diphtheria? If so, what is this evidence, and what is its source?

1. *What has the Work in the Laboratory Shown?*—The process of the manufacturing and testing of antitoxin, I consider one of the soundest proofs of its efficacy. If we could find anywhere the testimony of a bacteriologist of experience that antitoxin does not save the life of a guinea pig or other animal, when this animal is injected with several times the fatal dose of the diphtheria toxin, we might then hesitate in our belief in its utility. But we can not find such testimony; and have we any authority for believing that the same phenomena do not occur in man as in the guinea pig, dog, horse and other animals, when the cause of the phenomena is the same in both cases? The results in the laboratory all tend to demonstrate the feasibility of the antitoxin theory.

2. *What has Clinical Study Demonstrated?*—It must have impressed every one forcibly who has followed the literature upon this subject, that nearly all the unfavorable reports have come from those whose experience has been extremely limited, that is, we see an occasional report of a case that has received antitoxin, and later died; or, sometimes a very complete report is made of an individual case, showing that after an injection of antitoxin there is a sudden development of alarming symptoms, quickly followed by death, or the patient may have lived some time after the injection, suffering all the time from symptoms which have never been seen before in the course of an attack of diphtheria. In either case we are to believe that antitoxin is the factor which has caused the fatal termination. Then, again, we read more reports to the effect that antitoxin has no influence whatever on the course of diphtheria, either good or bad.

Before accepting these reports of extremely limited numbers of cases as an evidence against the use of a remedy which, in the experience of so many, has given such great promise of good, we should carefully eliminate the possibility of there having been other factors than antitoxin in determining the unfortunate results of these cases. The entire solution at a low temperature might be injected directly into a blood vessel—the same might be true of a considerable quantity of air, for it is extremely difficult with most of the syringes used, not to have some air in the cylinder at the time of injection. Either of these accidents might cause a sudden and fatal termination.