

most of his cases the dose recommended by Marmorek. The death rate was 14.6 per cent., while the average death rate from 1890 to 1895 in this hospital was 24.9 per cent. He believes that but little importance is to be attached to these figures, owing to the great variation in the mortality in this disease, and concludes, that he is unable to draw any conclusion from his experiments, except that the disease was no worse for the treatment and that he intends to continue its trial.

In measles, as in scarlet fever, we believe that the complications are for the most part due to streptococcus infection, and the serum should be equally efficacious here.

It seems to me, although I have seen no suggestions for such application, that the greatest field for usefulness for an anti-streptococcus serum would be in tuberculosis. For some years the belief has been growing that pure, uncomplicated, non-septic tuberculosis is relatively a mild, curable and often self-limited disease. It is the complications that kill in tuberculosis. Most of us will agree that when there is any benefit from the administration of creosote and its allies, it is due to the action on the septic processes and not on the disease itself. And not a few hold that the chief, though not the whole benefit of mountain climates, is the aseptic atmosphere. Most of you are probably familiar with the work published by Prudden last year, where he conclusively showed that for rabbits, at least, cavity formation in tuberculosis was almost entirely due to secondary streptococcus infection. Now, if with this serum we can hold in check the septic processes we will have half conquered the disease. Although the work with this serum is still in the experimental stage, the outlook is very promising.

Anti-tubercle Serum.—Maragliano, Boinet, Picq, Babes, Maffucci, Paquin and others have reported work in this line. Most of them claim good clinical results. But tuberculous patients under any treatment, and without any, often improve and occasionally get well. So that, whether with justice or not, the claims of these investigators have met with but little approval. In experimental animals the best results I have seen reported are a prolongation of life in guinea pigs from an average, for untreated animals of some fifty days, to ninety in the treated ones. No treatment yet devised, be it serum or anything else, can save a guinea pig when inoculated with tuberculosis. And while our experimental animals are far more susceptible to the inoculated disease than man, the profession at large will be slow to trust any remedy that can not give demonstrable results in animal experiments.

Anti-pneumonic Serum.—The work of the Klemperer brothers on the immunization of rabbits against pneumonia has been followed up by Emmerich and Fowitzky, Redner, and Foa and Carbone. It has been possible to immunize a rabbit so that it would withstand more than three hundred thousand times the fatal dose of the germs for an untreated animal. With serum taken from such highly immunized animals it is possible to save inoculated rabbits if the serum is given five hours or earlier after the infection. In rabbits pneumonia is often fatal in twenty-four hours. The duration of the immunity produced in rabbits is long. After three months they resist fatal doses of the germs. So far as I know, the successful immunization of larger animals capable of producing serum

in quantities sufficient for the treatment of the disease in man has not yet been reported.

Anti-rabic Serum.—Following the general lines of procedure in this field, the Italian bacteriologists have produced a serum for the treatment of hydrophobia. Their experimental work seems to be convincing. They claim many advantages for this serum over the Pasteur method of vaccines. The claims are that results are more certain and the dangers of treatment lessened, and of even more importance, the serum keeps well and can be used anywhere by any practitioner.

Anti-venom.—Drs. Calamette of Paris and Fraser of Edinburgh seem to have succeeded in producing a very satisfactory serum for antagonizing snake poison. That animals could be immunized to these poisons was shown years ago by Dr. Sewell in Michigan University. It seems that the serum produced from the venom of any one of the serpents is antagonistic to the poison of the whole group.

Typhoid.—In general the statements I have made in regard to cholera are true for typhoid. Animals have been immunized and a protective action can be demonstrated, but clinically the results are not convincing. Here, as in cholera, a germicidal instead of antitoxic action is shown. But where in cholera there is a specific action against one germ, it seems that in typhoid the serum antagonizes all related germs, as the coli group. This is as we find it in the streptococci.

Syphilis.—It is well known that one attack of this disease confers an almost perfect immunity against subsequent infection. Attempts have been made to borrow this resisting power. The serum of persons who have recovered from the disease has been injected into those who have been recently infected. Again syphilitic nodules have been macerated and this material injected into animals and their serum in turn used for the treatment of the disease. Good results are claimed from the serum of animals that have been treated for some time with mercury and iodids.

Smallpox.—Practically the same experiments have been tried with smallpox, the serum of immune individuals being used. Again, the serum from vaccine heifers that have become refractory to the inoculation has been used in treatment. Thus far the results of this treatment in these two diseases have not been noteworthy.

Possibly the best thing I have to report in the line of serum-therapy is the continued growth of the belief that disease can be conquered; that knowing the cause and the methods of many disease processes, we can and will find preventative or curative measures.

THE USE OF ANTITOXIN IN THE TREATMENT OF DIPHTHERIA AND MEMBRANOUS CROUP.

WITH A COLLECTIVE REPORT OF ONE HUNDRED AND THIRTY-TWO CASES.

Read before the Indiana State Medical Society, May 29, 1896.

BY E. L. LARKINS, M.D.

TERRE HAUTE, IND.

During the year 1894, there were reported to the Board of Health at Terre Haute, Ind., 233 cases diagnosed as *diphtheria*. Of this number 102 were males and 131 females. There were 39 deaths recorded as

due to the disease. During the same period, 19 cases were reported to the Secretary of the County Board of Health, in the county outside of the city, of which number 9 were males and 10 females, with 6 deaths, making a total number of cases reported for the county 252, and the total number of deaths 45.

During the year 1895, there were reported for the city 182 cases, of which number 79 were males and 103 females, with 23 deaths. For the same period in the county outside of the city, 11 cases of which 7 were males and 4 females, with 6 deaths, making the total number for the county of 193 cases and 29 deaths. From Sept. 1, 1894 to April 1, 1895, there were reported 197 cases, of which 92 were males and 105 females. Of this number, 20 were fatal—9 males and 11 females.

From Sept. 1, 1896, to April 1, 1896, there were reported 150 cases, of which 62 were males and 88 females. In this period there were 21 deaths—12 males and 9 females.

Prior to Sept. 1, 1895, antitoxin had not been used except in a few cases. Since that time, it has been used by a majority of physicians in Terre Haute, and with a view of ascertaining as nearly as possible, the exact number of cases treated with it, with results, etc., I sent out a chart and find the total number to be 132, with 18 deaths, or 13.6 per cent., a summary of which is as follows:

SHOWING THE USE OF ANTITOXIN IN DIPHTHERIA AND MEMBRANOUS CROUP.

Number of cases reported, 132. Males, 61; females, 71.

Times used: 98 cases, one time; 25 cases, two times; 3 cases, three times; 4 cases, four times; 2 cases, six times.

Day of disease used: 21 cases, first day; 41 cases, second day; 24 cases, third day; 22 cases, fourth day; 8 cases, fifth day; 4 cases, sixth day; 10 cases, seventh day; 1 case, eighth day; 1 case, thirteenth day.

Age of each: 1 case 2 months, 1 case 5 months, 1 case 8 months, 1 case 10 months, 1 case 11 months, 7 cases 2 years, 16 cases 3 years, 13 cases 4 years, 18 cases 5 years, 14 cases 6 years, 13 cases 7 years, 16 cases 8 years, 3 cases 9 years, 10 cases 10 years, 3 cases 11 years, 3 cases 12 years, 1 case 14 years, 1 case 15 years, 2 cases 17 years, 1 case 27 years, 1 case 35 years, 1 case 50 years.

Number of cases of membranous croup, 8; times used in each case, from one to six; result, six recoveries and two deaths.

Number of immunizing injections given, twenty; result, immunity in all. In nearly every case no effort was made at isolation. No unfavorable symptoms reported.

Original location of disease and extension to other parts: Fauces in almost all cases, and tonsils principally; extension to larynx, 29 cases, 5 deaths; intubation 7 times, 3 deaths; extension to nares, 18 cases, 8 deaths; tracheotomy not reported.

Disease extended after injection in only one case, and in that the physician said he was not certain how long the child had been sick before he was called.

Death did not occur in any case where injection was used within the first forty-eight hours of the disease.

Did not notice any unfavorable effect of the injection.

Number of deaths, 18; within the first 24 hours in 14 cases, in 2 days in 2 cases, in 2 and 8 weeks in 2 cases.

Days of disease: 1 case 3 days, 4 cases 4 days, 6 cases 5 days, 3 cases 7 days, 1 case 8 days, 1 case 9 days.

Number of cases followed by sequelæ, 9; otorrhea in 1, nasopharyngeal paralysis in 6, aphonia and paralysis of right side of face and neck in 1, and paralysis of all voluntary muscles except of the head in 1. Recovery in all.

Thus we have the following table for the years:

	No. of Cases.	No. of Deaths.	Mortality Per cent.
1894	252	45	17.8
1895	193	29	15
Sept. 1, 1894 to April 1, 1895 .	197	20	10.1
Sept. 1, 1895 to April 1, 1896 .	150	21	14

Number treated with antitoxin from Sept. 1, 1895

to April 1, 1896—males 61, females 71; total 132, number of deaths 18, mortality, 13.6 per cent.

In the majority of cases only one injection was given to each patient, but in several it was repeated two or three times, and in two laryngeal cases six injections were administered, the cases being desperate and one eventually recovering.

It would appear from recent experience and a study of the literature upon the subject, that some of the deaths herein reported might possibly have been avoided had the remedy been vigorously pushed to its full therapeutic effect. It is the opinion of all observers that the earlier in an attack of diphtheria antitoxin is used, the better the results and consequently the greater the chances of recovery, and in an analysis of this collection of cases the statement is abundantly verified. In the 132 cases only one death is reported where the remedy was used within the first forty-eight hours of the disease, and in this case, there is doubt about the length of time the child had been sick before the physician was called. One physician reports a series of fifteen and another ten cases without a death, three of the latter being laryngeal, and with nearly all, the remedy was used on the first day, in four or five on the second day and in only three on the third day. In one case it is reported used on the thirteenth day, but upon inquiry the physician states the child had tonsillar diphtheria, from which it apparently recovered, but it subsequently extended to the larynx, for which latter involvement antitoxin was used with favorable results.

According to the reports read, the death rate increases *pari passu* with the length of time the disease had run before the remedy was used. In the 17 of the above 132 cases in which I used antitoxin, the result was favorable, except in two of the three cases where it was administered on the fourth day of the disease. These two proved fatal on the fifth day in twelve and eighteen hours after the injection, from sepsis consequent upon extension of the disease to the nares and laryngeal obstruction from extension to the larynx. I advised the use of antitoxin when I first saw the children on the second day of the disease, but the parents objected. I am still of the opinion that the children would have recovered had the antitoxin been used when I first saw them. On the fourth day of the disease when it became apparent that the children were sinking, request was made to have the antitoxin administered, but it was then my opinion, concurred in by the consulting physician that nothing would avail, as the little sufferers were beyond hope of recovery. In this collection of cases, the ages ranged from two months to seventeen years, but the great majority were from three to eight years of age.

Membranous croup is here classed separately from diphtheria, on account of the uncertain relation of the two diseases. There were eight cases of croup reported with two deaths, neither tracheotomy nor intubation being performed in any of them. These were reported as idiopathic or true croup—croup commencing in the larynx, in contradistinction to secondary croup, or diphtheritic laryngitis, due to extension of the diphtheritic process from the fauces. Of the latter class, twenty cases are given, with five deaths. In two of these the nasal and post-nasal cavities were extensively involved also, and it is difficult to determine which contributed most to a fatal termination—sepsis or laryngeal obstruction. In the

above twenty cases, intubation was performed seven times, with three deaths. No case of tracheotomy was reported.

In eighteen cases, the disease extended to the nares, eight of which died. The time of death in reference to the injection, was within the succeeding twenty-four hours in all but four. Two of these are given as the second day and two in two and eight weeks respectively. The last two cases were evidently due to some secondary effect of the disease.

The time of death in reference to the day of disease (except in the last two cases above mentioned) is given from the fourth to the eighth day. This taken in connection with the time in which death occurred after using the injection, clearly shows that the remedy was not used until after systemic infection had taken place, or laryngeal obstruction had so prostrated the system that the therapeutic effort of the antitoxin could not be obtained. Then, too, the remedy may not have been used as vigorously as it should have been.

There were reported twenty cases in which immunizing injections were given with no development of the disease and no unfavorable symptoms were observed to follow. In only two of the 132 cases is the disease reported to have spread after the injection was used. In one case of diphtheria, the nervous symptoms in a choreic patient, aged 12, appeared aggravated during the next 24 hours and then improved. In this series, six had post-diphtheritic paralysis; one had otorrhea. In one case the paralysis effected the lower limbs and in another case the whole voluntary muscular system, except the head. Aphonia and paralysis of the muscles of the right side of head and neck in one. All recovered.

I will only give the history of a few illustrative cases:

On the morning of Nov. 8, 1895, I was called to see Frank M., age 7 years, and found him recovering from a severe convulsion. The history obtained, was that of some error of diet on the previous day and he had had a light chill a few hours before the spasm. As convulsions were easily provoked in the child there seemed to be no special reason for alarm, but his general condition lead me to suspect some grave disease. Pulse was 110, feeble; temperature 101 degrees, and he had vomited once during the morning. The throat was not examined on account of his general nervous condition.

I prescribed calomel, quinin and bromids, hot mustard foot-bath and hot cloths to the head and over the stomach. In about an hour and a half, I was hurriedly sent for, as the child had another convulsion. I increased the bromids and ordered a general hot pack in blankets. He soon recovered from the spasm and had no more during his sickness. I advised isolation, as I thought it might be diphtheria. Calomel $\frac{1}{4}$ gr. every hour; quinin $2\frac{1}{2}$ grs. every three hours and bromids as necessary, were given during the afternoon and night, followed by castor oil the next morning.

November 9, 9 A.M., temperature 100.5, pulse 112, complains of nausea and weakness. Examination of the throat shows the whole fauces deeply congested, tonsils swollen and a gray deposit on each about the size of a split pea. Diagnosis of diphtheria was made. Quinin was continued, mercury bichlorid one-sixteenth gr. in elix. pepsin and bismuth every two hours and teaspoonful of whisky every two hours,

were given. Local applications of Loeffler's solution were made every four hours, and spray of peroxid of hydrogen 50 per cent. with saturated solution potassium chlorid every two hours; 4 P.M., the membrane has covered both tonsils and the uvula, and the child has had nasal hemorrhage.

November 10, 9 A.M., temperature 100, pulse 115. Throat emits a very fetid odor and there is a thin acrid nasal discharge. The whole fauces is completely covered by a thick leathery grayish-white membrane. The membrane is visible in the anterior nares and the child has a coarse croupy cough. I explained to the parents the serious and probably fatal condition and advised that antitoxin be immediately given. The mother dissented. The child's condition continued to grow worse and by the morning of 11th laryngeal obstruction was added to the faucial and nasal involvement. A more serious condition could not be depicted. They now consented to the use of antitoxin and I gave the child a full dose of the Behring No. 2. Now I would give the No. 3, and repeat in six or eight hours, in such a case. The laryngeal obstruction continued to grow worse during the day. In about six hours after giving the injection the child seemed much worse, but rallied some toward evening. About 8:30 P.M. I was sent for hurriedly, as the child was thought to be dying. A severe attack of dyspnea came on and the mother laid him on the lounge, thinking he was dead. When I arrived, he had rallied and was breathing better and improvement was continuous and rapid. I considered the sudden increase of dyspnea the night before, to be due to loosening of large portions of membrane thus producing complete obstruction of the larynx. I now omitted the mercury and gave small and frequently repeated doses of tincture chlorid of iron.

During the whole sickness effort was made to keep the nose and throat clear of septic matter, by the use of syringe and spray. The appetite was irregular and proper feeding was attended with difficulty. Aphonia remained several weeks after recovery.

I have given at length the history of this case in order to show by comparison the probable effect of antitoxin. About two weeks after my last visit to this patient, I was called to see two other children in the same family, one aged 5 years, and one 11 months.

The course of the disease was exactly the same, with the exception of the initial convulsion. I advised the immediate use of antitoxin, but the mother strenuously objected. I could not then conceive, that with such practical demonstration of the efficacy of the remedy in the other child, why objection should be made to its use in these two.

The children continued to grow rapidly worse until the afternoon of the fourth day of the disease, and all hope of recovery was abandoned, when request was made to have the antitoxin administered. My opinion, concurred in by the consulting physician, was that nothing would do any good, as the children were dying. Behring No. 2 was given, but both died in twelve and eighteen hours respectively.

It may be said that if antitoxin saved the first, it should have saved the other two. The inference is not justified, as the latter were profoundly septic, in addition to having laryngeal obstruction. The argument in this is, not that it saved one, but if used not later than the second day it would probably have saved all of them. Subsequent experience in the use of the remedy confirms my belief in this statement.

I will relate one other case of diphtheria, in a girl aged 8 years, who had enlarged tonsils and almost complete nasal obstruction from adenoid growths in the post-nasal cavities. The initial chill, followed by vomiting, occurred in the evening, and I was called the next morning. I found a typical case of diphtheria, the membrane covering the tonsils and extending up the edges of the palate. The characteristic acrid nasal discharge was present, showing extension to that cavity. The breath had a very fetid odor and her general condition showed profound infection. A full dose of Behring No 3 was immediately given, and a No. 2 given the next morning. We could do little with sprays and washes and no effort was made at local application. She immediately began to improve and the recovery was uneventful. I attribute her recovery entirely to the antitoxin.

A marked feature in this case was the very great reduction in size of the tonsils after recovery. An older brother of this girl had diphtheria in November, 1895, to whom two injections of Behring No. 2 were given, and his general health has been better since than ever before. Previous to this sickness, he was subject to frequent attacks of sick-headache, but now seems entirely free from them.

The effect, apparently, of antitoxin in the case of a delicate, nervous girl, 5 years of age, to whom two injections of Behring No. 2 were given, and in whom choreic movements had been frequently noticed and nystagmus was almost constantly present when the child was excited, was that since recovery both have disappeared, and she appears perfectly well.

Diarrhea did not follow the use of antitoxin in my cases, but constipation was of such frequent occurrence that I suspect some causative relation.

In the treatment of membranous croup with antitoxin, I have only one case to relate. I was called in November, 1895, to see a girl aged 5 years. I informed the mother of the serious illness of the child, prescribed the usual remedies and advised that antitoxin be used. Consent was given. Next morning I injected a full dose of Behring No 3. By this time the disease was fully developed. In twelve hours another dose of Behring No. 2 was given. Next morning the child was better. There was considerable dyspnea for two days, but the child recovered without further treatment, except some simple remedies.

In all the cases, except two, in which I used antitoxin, I called another physician to see the case, that it might not be said I used it where no diphtheria existed.

Reliance was placed in all cases upon the clinical picture of the disease for diagnosis. This is partly in accord with the recommendations of the boards of health of New York, St. Louis, Chicago and other cities, as they advise the use of antitoxin in suspicious cases, and especially in those where the physician is satisfied diphtheria exists, and not wait for a bacteriologic examination, as that can be made later. It is in the early use of antitoxin that its specific effect can be obtained.

The Klebs-Löffler bacillus develops upon the false membrane, and in most instances accompanies the local manifestations of the disease. The streptococcus, said to be the most virulent of the supposed pathogenic microorganisms, develops beneath the membrane, is a late product of diseased action, and is found in cases termed mixed infection. They are found (as the Klebs-Löffler bacillus) in the throats

of healthy persons, and even in the substance of the tonsils.

As to medical treatment of these cases, it has been claimed that it in no wise interfered with the use of antitoxin. I believe that large doses of bichlorid of mercury, in some degree at least, counteracts the effect of the antitoxin. Lately, I have confined myself to the use of small and frequently repeated doses of tincture chlorid of iron, and the moderate use of quinin and whisky. The free use of warm salt water or listerin properly diluted, for the purpose of keeping the parts clean, appears to answer every purpose.

This paper deals principally with an analysis of the reported cases.

Antitoxin in the treatment of diphtheria being of comparatively recent introduction, personal experience of the general practitioner must necessarily be limited in its use, and in many instances no opportunity has been afforded to observe its effects. It is from the experience of others that we must learn, and through collective investigation knowledge may be acquired by comparison.

The 132 cases herein given were reported by twenty-five physicians. The report is confined to Vigo County and principally to the city of Terre Haute. It will be observed that more deaths occurred in 1895 than in 1894, presumably on account of the greater severity of the disease. The report represents only the rate per cent. of deaths to the number reported and not to the actual number of cases, as physicians there seldom report more than one case in a family.

No subject could be of more profound interest to the physician, than that of the cure of diphtheria. In using the word *cure*, I refer to its literal meaning and practical application. No discovery since the days of Jenner, when he listened to the story of the milkmaid, and placed the practical banishment of that dreadful scourge, smallpox, within the power of all civilized nations, has been of such great value to mankind.

In antitoxin, I believe we have a true specific for diphtheria. In theory, and probably in fact, it is based upon the principle of vaccination, viz, *to render the human body immune to a virulent disease by introducing artificially into the system, a protective product developed through modification of its specific agent in foreign media.* After successful vaccination, a person may have varioloid, and thereafter, as a rule, be immune to the contagion of smallpox. The immunity conferred by the antidiphtheritic serum in the healthy subject appears to be practically evanescent, but what subsequent effect in this line, a curative dose of antitoxin has upon the human body suffering from a fully developed diphtheria case, has not been observed. So far as I am aware, a second attack of diphtheria has not been recorded as occurring in a patient cured of the first attack by antitoxin. It is well known that one attack of diphtheria confers immunity for a time, and it may be that the introduction of antitoxin into the system in the developed stage of the disease, may so fortify the protective elements that the body will not again become susceptible to the contagion.

The length of time in which antitoxin has been used is not sufficient for extended observation in this direction, but a second attack would be worthy of record.

The exact manner in which antitoxin cures diphtheria, is not definitely settled. According to the law

of Behring, material is developed in the blood which neutralizes the effects of the specific poison of the disease, and confers immunity to those in whom the serum of such blood is artificially introduced. The studies of Pfeiffer have, however, led him to the conclusion that substances are formed which destroy the infectious material and therefore eradicate the cause of the disease. It may be that cell action is so stimulated and the metabolic processes so changed that effectual resistance is offered, through the medium of the blood serum, to the further invasion by the infectious material. This is probable, as experimenters have found that the supposed pathogenic microorganisms may be cultivated in the blood serum of animals immunized for the disease which they produce. Moreover, antitoxins are held in solution in the blood, but do not pass through the coats of the vessels.

SERUM THERAPY IN DIPHTHERIA.

Read in the Section on Materia Medica, Pharmacy and Therapeutics at the Forty-seventh Annual Meeting of the American Medical Association, held at Atlanta, Ga., May 5-8, 1896.

BY EDWIN ROSENTHAL, M.D.

PHILADELPHIA, PA.

Since the introduction of the diphtheria antitoxin as a specific remedy in diphtheria, I have used it in 127 cases of diphtheria with a record of five deaths.

As the character of my cases were in many instances of the most dangerous variety, and in nineteen instances necessitated the operation of intubation, I may not be misjudged if I ascribe to the specific action of antitoxin the results obtained.

To briefly summarize my work they are: Tonsillar 67; pharyngeal and tonsillar 14; nasal, pharyngeal and tonsillar 1; pharyngeal 1; laryngeal 12; tonsillar and laryngeal 18; pharyngeal, tonsillar and laryngeal 8; nasal, pharyngeal, tonsillar and laryngeal 4; pharyngeal and laryngeal 2; total 127; number of deaths 5.

The ages were: Under 1 year 4 cases; between 1 and 5 years 55 cases; between 5 and 10 years 30 cases; between 10 and 20 years 13 cases; between 20 and 40 years 25 cases. Nearly 50 per cent. occurred below the age of 5 years and about 25 per cent. between the ages of 5 and 10 years.

1. The deaths occurred below the age of 8 years and were as follows: Age 1 year, 7 months; variety, laryngeal and tonsillar; operation, intubation; time of injection, about seventy-two hours after injection; time of death, forty-nine hours after injection and intubation; cause of death, sepsis.

2. Age, 2 years, 2 months; variety, laryngeal, tonsils, nasal, pharynx; operation, intubation; time of injection, about the fifth day; time of death, thirty-three hours after injection and intubation; cause of death, sepsis and nephritis.

3. Age, 1 year; variety, tonsils, nose, pharynx, lymphatics; time of injection about the fifth day; time of death, three days after injection; cause of death heart failure—a septic case.

4. Age, 8 years; variety, tonsils, nose, pharynx and larynx; time of injection, about the fifth day; time of death, nine days after injection; cause of death, heart failure.

5. Age, 1 year 1 month; variety, tonsils, nose, pharynx and larynx; time of injection, fourth day; time of death, five days after injection; cause of death, heart failure.

They were as regards sex, 51 males, 76 females.

The time in which injections were made: first day, 21 cases; second day, 52 cases; third day, 34 cases with one death; fourth day, 8 cases with one death; fifth day 6 cases with three deaths; sixth day, 3 cases; seventh day, 1 case; eleventh day, 1 case; seventeenth day, 1 case.

Many cases were immunized, using for that purpose antitoxin from several laboratories. In those cases immunized no visual traces of the disease were seen, although the bacteriologic examination frequently revealed the Löffler bacilli. In one case treated for diphtheria of the faucial variety (case 87) a re-infection took place on exposure six months afterward (case 123) the disease manifesting itself in the same way. This proves, that while antitoxin has curative and immunizing virtue, it does not confer lasting or permanent immunity; but the susceptibility to infection remains as in any other form of treatment.

The complications noted: Broncho-pneumonia five cases, only seen by me in the laryngeal variety. Nephritis one case. Albumin was found frequently both before and after injection, antitoxin not increasing the amount. Sepsis four cases. Eruptions noted in about fifteen cases, and was also noticed in several cases that received an immunizing dose.

Sequelæ: Undoubted paralysis of the lower extremities in a female suffering from diphtheria of the laryngeal variety with membranes on the tonsils, complicated broncho-pneumonia, intubated, the tube being worn twelve days, and who received 1,000 units of Behring's antitoxin. The age of this child was 1 year 10 months; the injection was made on the third day, and there was perfect recovery months afterward. Heart failure in two cases, after disappearance of the membranes; in one case three days after the visits ceased. Ozena was noticed in one case.

Method of using the diphtheria antitoxic serum: Antitoxin should be chosen of undoubted reliability. I am persuaded that my results are mainly due, not only to my method, but to the purity and efficacy of the antitoxin used. The technique pursued in the one case is that pursued in all.

Antitoxin is graded as regards strength into what is termed by its originators antitoxic normals or immunity units, which is an amount of antitoxic serum required to save a 500 gramme guinea pig from a minimum fatal dose of the diphtheritic toxin. The number of immunity units per c.cm. gives a standard strength of the serum; for instance: one one-hundredth c.cm. will protect a 500 gramme guinea pig, therefore 1 c.cm. of antitoxic serum, which protects 50,000 grammes of guinea pig, contains 100 immunity units, and would protect an individual weighing one hundred times as much as a guinea pig (about one hundred and twenty pounds, if the susceptibility were the same. The serum, of which 1 c.cm. equals 100 immunity units, is that with which most of my work was done. Serum of greater strength was used. Knowing the strength of the serum makes me have no regard for the quantity used, as I grade my dosage in immunity units and so apply it.

The technique. The antitoxin serum is used as a curative or immunizing agent by subcutaneous injection into the tissues of the body. For the purpose of making these injections any hypodermic syringe may be used if of sufficient capacity, as the Pravaz syringe, the Koch bulb syringe; I prefer a special antitoxin syringe, made for this purpose, having a capacity