FISCHER (L.)

A Plea for the more Extensive Use of Antitoxine in Diphtheria.

Résumé of One Year's Experience. Indications and Contraindications for its Use, with Some Practical Points in the Application of the Same.

BY

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When, in September of last year, I had the honor of being invited by Professor Roosa to read a paper on antitoxine before the New York Post graduate Clinical Society little was known of the therapeutic value of this drug on this side of the ocean. My experience at the time was limited to only a few cases in this city, but by far the most was learned in Europe from such authorities as had been using the remedy in the laboratory as well as at the bedside.

The history of the manufacture of this wonderful agent has been so often described in detail by myself and by others that I do not think it wise to again rehearse it, but would rather speak of the practical value gained by the use of this remedy.

Several papers have appeared by me from time to time, notably, however, the paper published in the *Medical Record*, October 6, 1894, in conjunction with a paper by Professor Baginski, from whom I learned the clinical value of this new therapeutic agent. Later, a series of papers appeared, with more experiences, in the *Medical Record*, November 17, 1895; also in the December issue of the *Post graduate;* a very elaborate paper in the *American Journal of the Medical Sciences* for January, 1895; then a very complete article, embracing in all two hundred and twenty-five cases, appeared in the *Medical Record* of April 6, 1895. This paper was read before the German Medical Society of this city on March 4, 1894.

In our country so much has been said in favor of this valuable remedy that what has been said against it would be as infinitesimal as an ordinary mortal trying to swim against the great tide of success! At the Munich Medical Congress, last April, it was the unanimous opinion that no remedy had up to the present time been used in diphtheria that, from a scientific standpoint, exerted a healing effect. In looking over the materia medica and studying what remedies can be used with success in diphtheria, there is not a single drug with which we can positively say we can cure diphtheria. Modern science has taught us that the local manifestation of the disease can be determined by making a culture from the pseudo-membrane, and in these cultures we find at times a streptococcus, at other times the streptococcus in combination with the Klebs-Loeffler bacillus, and again at other times we find the pure Klebs-Loeffler bacillus; so that there are various clinical and bacteriological manifestations which, although appearing differently under the microscope, prove to the clinician that they are probably various forms or modified forms of the same disease, and are virtually combined under that one term, diphtheria. We

are, however, dealing not only with the local manifestations of the disease, but with the complications, and it is rare to find a patient with a simple, ordinary, membranous diphtheria—proper care being taken—to die, unless some special reason exists for it. Let me illustrate: If I were called to a robust child, in good hygienic surroundings, that had a slight elevation of temperature, and found a small diphtheritic patch of membrane on one or both tonsils and the glands of the neck swollen, if there was a good, strong, regular pulse, and I had a good, common-sense mother or nurse looking after it, I should certainly expect a recovery if the ordinary rules of antisepsis (antisepsis, practically speaking, meaning only cleanliness) were carried out; whether the ordinary salt solution or boric acid or permanganate of potassium were preferred would be immaterial, for the latter merely tend to destroy the germs on the surface and do not by any means destroy the germs in the deeper structures.

In a case like the one above described I should invariably give a good prognosis, and have found that by injecting five cubic centimetres of a good standard preparation of antitoxine I could accomplish all that was desired without subjecting the body to the poisonous influences of the internal administration of bichloride of mercury. I am confident that every clinical observer can go into the wards of a diphtheria hospital and pick out the patients that had been subjected to the administration of bichloride of mercury, for there is an extreme pallor of the skin, a so-called anæmic appearance, which is usually recognized by the skilled clinician, so much so that he can recognize at once those cases that have received a bichloride treatment and those that have not. The same holds good of those cases treated with calomel, whether by fumigation or by its internal administration. So much can be said for bichloride

of mercury, that enough bichloride of mercury can never be introduced into the body to render the blood thoroughly aseptic. If this could be accomplished, then we should not only kill the germs, but at the same time kill our patient.

Some very interesting cases were reported by me at the Section in Diseases of Children of the American Medical Association held at Baltimore on May 8th. It was highly interesting to hear some very eminent gentlemen in our profession extol antitoxine, and to hear the almost unanimous verdict in favor of this new agent during the course of the discussion. Let me repeat again what I wished to impress in my paper read at Baltimore, that antitoxine and blood serum are two distinct remedies, or rather, that they are not synonymous terms. While we may have blood serum manufactured and sold and labeled as antitoxine, a great many failures that are reported are due to the fact that these specimens are blood serum pure and simple, and do not contain any antitoxine, and hence are worthless for therapeutic purposes. It is therefore of the utmost importance to have an absolutely reliable remedy before promising any success; and how disappointed do we feel if a patient, let me say, receives a dose of morphine to produce healthy refreshing sleep, and tells us the following day that he was awake all night, due at times to either the smallness of the dose or the unreliability of the drug used. If it is proper for practitioners all over the world to specify a certain chemical or a certain drug and ask for it, or if it is proper to specify a certain brand of wine when we desire to get it, then I do not see why we can not specify a certain brand of antitoxine in order to test the real merit of an article so valuable in the treatment of this disease. It is not my intention in the course of this paper to belittle the preparations of antitoxine manufactured and sold in our country; but I have had the greatest success with the

antitoxine manufactured at Berlin and tested by the German Government, and the results have been so satisfactory that I could not but continue in the present path of success.

On April 13th I was called in consultation by Dr. Newfield, of 111 East One Hundred and Sixteenth Street, to see a case with severe laryngeal, pharyngeal, tonsillar diphtheria. The case was seen between three and four in the afternoon of Saturday, and at the time that we saw it, it was evident that nothing but the gravest prognosis could be given. The child had been very ill, and although I injected five cubic centimetres of Aronson's concentrated antitoxine in the interscapular region, I told the attending physician that in my opinion it would be wise to hold ourselves in readiness to intubate the child within five or six hours if the symptoms of dyspnœa and laryngeal stenosis did not disappear. The doctor promised to meet me the following morning at eleven o'clock, provided I was not called on the Saturday evening in question, to intubate. For some reason the attending physician was very considerate, and, not wishing to trouble me, as the patient was several miles from my house, called in a laryngologist, Dr. Emil Mayer, to perform the intubatior When I saw the case on Sunday morning I had the pleasure of meeting, besides the attending physician, Dr. Newfield, Dr. Emil Mayer, and Dr. N. S. Roberts. This was about eighteen to twenty hours after my injection of antitoxine had been given. Although by midnight the child had been intubated by Dr. Mayer, the violent coughing had forced the tube out, and when we saw it on Sunday morning there was marked depression at the scrobiculus cordis and at the jugulum on inspiration, which are such prominent symptoms of laryngeal stenosis wherein we almost always require either to intubate or to perform tracheotomy. Through the courtesy of the three physicians mentioned, I was permitted to introduce a suitable tube as rapidly as possible. There was an immediate relief of the stenosis following the introduction of the tube, so much so that two days later I had the pleasure of a visit from Dr. Newfield, who told me that the child was

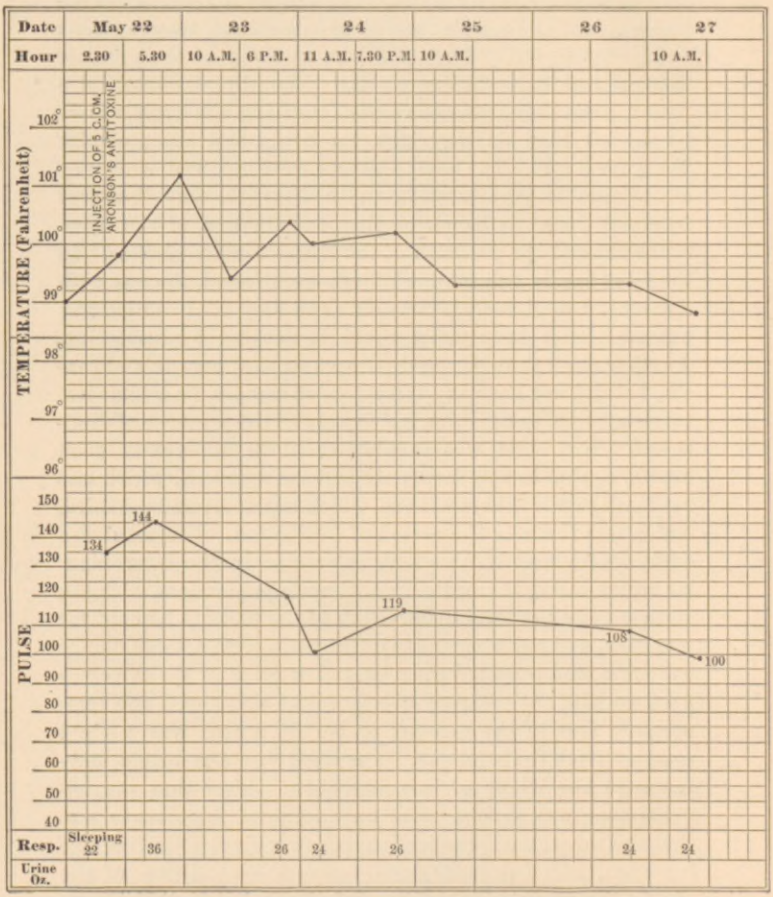
absolutely well, so far as he could see; that not only had the stenosis of the larynx remained away since the introduction of the tube, but that the pseudo-membranes, which had been so very visible on Saturday and also on Sunday, had gradually melted away and disappeared. This was in all about two days following the injection of this one bottle of Aronson's concentrated antitoxine containing five cubic centimetres.

In all my cases my experience with intubation has been uniformly good where the treatment has been combined with the use of antitoxine. I have thought it, however, safer generally to allow the tube to remain *in situ* three or four days, so that I asked the doctor to please allow the tube to remain in the child's throat until Thursday, which was in all less than four days. I removed the tube on Thursday, and the child has been well and remained well since that time. No emaciation, albuminuria, or other symptom or complication has arisen since then, and I believe that this is one of my most successful cases, or at least one of the usual successful class that I have been reporting from time to time.

In most cases, especially where we are not dealing with a very intelligent class of people, I have found that the attending physician is usually bothered to administer some medicine, so that we have almost always been forced to administer a placebo in most of our cases. If a placebo is given we can give anything that will do neither good nor harm in order to quiet the minds of the parents.

An equally instructive case is the following: W. S., three years old, was seen by me on the 23d of May. Previous history: Had had measles in March, with a sequela of otitis media of the left ear. In the same month a case of diphtheria occurred in the house. The child was well until Sunday, May 19th, when the first symptoms appeared. Languor, general malaise, vomiting on Sunday and again on Tuesday; epistaxis every night as well as during the day on

exertion and excitement. When seen on Wednesday, the 23d of May, the child was in the following condition: Temperature, 99·9° *per rectum;* pulse, 134; respiration, 22. Skin active and normal, bowels regular, appetite good, tongue clean; child very heavy-looking, peevish; swelling of the anterior mastoid and submaxillary glands. The throat contained a heavy, yellowish-gray membrane, covering the tonsils more on the left than on the right, the uvula, and the posterior pharyngeal wall. The nasal passages were involved, shown by a considerable expectoration and a dirty ichorous discharge from the nose. A bacteriological examination of the membrane showed the presence of the Klebs-Loeffler bacillus. In the same family two other children were found, the one with a severe form of acute pharyngitis and very mild septicæmia, but no visible membranes could be located by inspection. Another child showed slight patches on the pharynx and tonsils, but did not have any symptoms of malaise, or a temperature elevation, or anything which showed the presence of diphtheria. This child was running about in apparently good health, so that in this family we had the first case, which was very malignant; the second one, which was mild; and the third, which was really in the period of incubation. I injected five cubic centimetres of Aronson's antitoxine in the interscapular region, using the ordinary antiseptic precautions with the syringe as well as local disinfection of the parts to be used for injection, and covering the injected place with a small film of collodion, and irrigated the nose and as much of the throat as possible with the ordinary normal saline solution. The temperature rose in the evening to 101° F., which was a slight reaction from the injection. The child was very bright, having slept the whole of this afternoon. After that the improvement was steady. The only point of importance was that the throat was practically clean four days following the injection. An interesting point was the condition of the child's temperature, which is well illustrated in the accompanying temperature chart.


Date
May 22
23
24
25
26
27
Hour
2.30
5.30
10 A.M.
6 P.M.
11 A.M.
7.30 P.M.
10 A.M.
10 A.M.
TEMPERATURE (Fahrenheit)
INJECTION OF 5 C.CM. ARONSON'S ANTITOXINE
102°
101°
100°
99°
98°
97°
96°
PULSE
150
140
130
120
110
100
90
80
70
60
50
40
134
144
119
108
100
Resp.
Sleeping 22
36
26
24
26
24
24
Urine Oz.

For the careful report in this case, as also for the subsequent taking of temperature, I am greatly indebted to Dr. A. Levinson. This child was given the injection in the presence of Dr. Nelson, Dr. Howard B. Gates, Dr. Tinley, Dr. Selling, and Dr. Levinson. There was also a slight laryngeal stenosis with a croupous cough, so that a diagnosis of nasal, tonsillar, pharyngeal, uvular, and laryngeal diphtheria was made. This case showed such rapid improvement that nothing but the antitoxine and the warm salt water locally was used.

Such cases I could record by the dozen. An important point in conjunction with this case is the fact that a child which lived two flights above this one with diphtheria, in the same house, was attacked with a severe fever and convulsions. When I saw the child, which was a few days after I had given the injection in this case of diphtheria, it was practically moribund, and I pronounced the case a hopeless one of diphtheria. The child died before I left the house. I am confident that in the case in which I used the injection, which was of the extremest type of diphtheria that we have seen during this winter, the patient would have practically succumbed to the septic influence of diphtheria, for I believe that we all recognize that where pharyngeal, tonsillar, and uvular diphtheria exists, we can in a good, healthy child under good hygienic conditions give a fair prognosis; but that where the elements of laryngeal complication, with stenosis and croupous cough, exist, marked dyspnœa, with a tendency to cyanosis, with distinct evidence of carbonic-acid poisoning, we are justified in calling such cases very grave ones. The same is also true where we have nasal complications, for in my experience nasal diphtheria has been one of the worst to combat in all the cases that I have had.

Another equally instructive case is one which I saw

in consultation with Dr. S. H. Smyth, of No. 112 East Tenth Street, some time ago. I prefer to report the case from the pen of Dr. Smyth. He writes:

"I was sent for to see B. B., female, aged ten years, on May 13th. On the previous evening the child had a chill, followed by fever and vomiting. As she complained of sore throat, I made an examination and found both tonsils covered with a dirty gray membrane. The temperature was 103°, pulse 120. Diagnosticated diphtheria.

"*May 14th.*—Temperature, 101°; pulse, 100. Membrane had extended, covering the uvula as well as the tonsils. There was an excoriating discharge from the nose, together with a croupy cough.

"*15th.*—Symptoms much the same. Breath very fœtid.

"*16th.*—Dr. Fischer saw the child with me, and, concurring in the diagnosis, at my request he injected antitoxine. This was at 4.30 P. M.

"*17th.*—No particular change noticeable, except that the discharge from the nose had stopped. Temperature and pulse both seemed normal.

"*18th.*—Membrane began disappearing from left tonsil. No cough; temperature and pulse same.

"*19th.*—Membrane disappeared entirely from tonsils, leaving the parts very red and inflamed.

"*20th.*—Membrane entirely disappeared. The child did well, except that the throat was somewhat painful until the 26th, when there was a slight patch on either side of the uvula which disappeared entirely by the next day. After this the child made a steady recovery. There is no paralysis. There was no albumin in the urine at any time. I might say that a report from the health department verified the diagnosis."

In Dr. Smyth's case judicious treatment, consisting of hygiene, diet, and supporting treatment generally, was all that was necessary to complete the cure in that case. Dr. Smyth was very careful to use the proper local antiseptics

previously, and did not resort to antitoxine until he believed that the disease would extend either upward or downward, or until he saw that there was a nasal involvement. The patient, besides, was an extremely restless and nervous girl. In these cases so much more patience is required to apply the old forms of treatment, consisting of spraying or swabbing the throat generally. In such cases as these the rule has been to administer one injection of antitoxine and await the effect of the same in the following thirty-six to forty-eight hours, and, if no marked improvement existed, then I have resorted to a second injection of the same dose as the first.

A similar case to the one just reported I had in consultation with Dr. Bullard, which I have previously reported in a large series of cases in the *Medical Record*, April 6, 1895. In Dr. Bullard's case the child struggled against pharyngeal irrigation, and besides absolutely refused to take a mixture that the attending physician prescribed, consisting of iron and glycerin, and finally was so obstinate that it refused food, and Dr. Bullard told me he believed that nothing would be of any service as long as the child remained so obstinate. The surprising benefit following the injection of antitoxine made by me was so marked that all symptoms disappeared within a few days. We gave the antitoxine a careful trial in Dr. Bullard's case, for we discontinued all other forms of medication.

One of the worst cases that I have attended this year was sent to me through the courtesy of Professor H. J. Boldt, and I reported it at the meeting of the Pædiatric Section in Baltimore, May 8th:

This child (Dr. Boldt wrote to me asking me to intubate the child R. on Sunday, April 7th) I saw at noon and found it in a condition of extreme dyspnœa, cold extremities, cold perspiration, sunken eyes, contracted fontanelle, gasping for

breath. The examination showed a very weak heart sound, pulse feeble, little or no appetite; the bowels very loose; the child in extreme agony, panting for breath. The well-known croupous cough was occasionally heard, besides the familiar inspiratory crowing that we are used to hear in laryngeal stenosis. An inspection of the throat showed nothing abnormal. The tonsils, pharynx, and uvula were apparently clean, and but for the presence of a slight reddening I should not have pronounced it a case of diphtheria. A culture made and sent to the health department showed, however, the presence of Klebs-Loeffler bacilli. I very rapidly intubated with a No. 2 tube. The child was immediately relieved. The stenosis that existed seemed to gradually disappear after the reaction from the intubation subsided. Besides ordering a mustard bath, I gave nothing. In the evening the mother reported favorable progress. The child improved fairly well, slept all night, and, although we had quite some difficulty to encounter with feeding, the child was gaining strength. The following day I ordered rectal feeding, using the yolk of an egg beaten up with starch water and occasionally an emulsion containing beef tea and other nutrient enemata, and allowed the tube to remain undisturbed. I had found that after a few days the child suffered neither thirst nor hunger and got along very well with feeding *per rectum*, so that I advised the mother to allow the mouth to remain absolutely dry, and when the child had very severe thirst I told her to place a piece of ice, surrounded by a piece of clean linen, in the child's mouth in order to cool it.

In several of my cases I have been extremely successful in avoiding the usually fatal complication of pneumonia in the course of intubation cases by not feeding by the mouth, and I believe if more children were fed by the rectum the mortality in intubation cases would be greatly lessened. In this case, after three days, the child had improved very much, so that I removed the tube. The mother called on me an hour later, saying that the symptoms of harsh breathing and croupy cough (just as I had found them three days previous) had reappeared, and begged of me to reinsert the tube. The moment I put the

tube *in situ* the child's breathing was again apparently normal, and but for the slight shock following the introduction of the tube there was nothing unpleasant from the reaction of the second intubation. I again cautioned the mother regarding the feeding and allowed the child to progress in the natural way. Solid stools were passed once a day and sometimes even but once in two days, and it was necessary once during the course of the treatment to give an enema, cleaning the child's bowels, showing that a carefully administered enema will not only be retained but be absorbed by the rectum, and, being guided by the condition of the child's pulse and the heart's action, I am persuaded that this child received ample nourishment to give it strength.

A very bad case was reported by me in the *American Journal of the Medical Sciences* for January, 1895, which was seen by me in consultation with Dr. R. K. Valentine, of Brooklyn. Under ordinary conditions a most fatal prognosis would have been given, and it was only judicious attendance and careful attention to details of supporting diet that enabled Dr. Valentine to keep his patient for three or four days, in a hopeless case of septic diphtheria, in a tolerably fair condition. The case was reported *in extenso* in the *North American Journal of Homœopathy* for February, 1895, to which I should like to refer for the details of this instructive case. The child received one injection of antitoxine subcutaneously in the interscapular region in the evening, and the following day it was so improved that the benefiting influence of the antitoxine was visible. Two or three days following the injection the doctor agreed with me that what had been a malignant and septic case of diphtheria was changed into a mild form of diphtheria—the pulse, heart's action, and general appearance of the child, previous nose-bleeding, all changed, and the child was rapidly improving. The patient was discharged cured within a week after the injection of the antitoxine.

A very instructive case was one which I saw on July 17, 1895, in the children's department of the German Poliklinik:

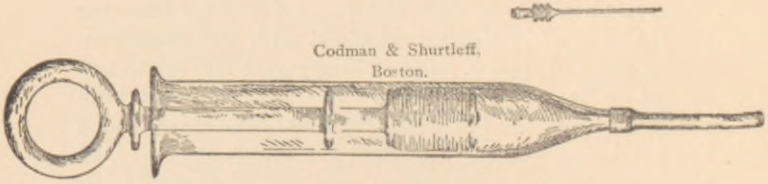
The child had been ill two days and had been attended by a physician who had diagnosticated fever (?). A careful examination of the throat made by me showed the presence of large patches of dirty membrane covering the pharynx, the tonsils, the uvula, and as much of the throat above and below as could be seen with the naked eye. A croupy, barking, hoarse cough indicated the involvement of the larynx, and a further examination of the chest wall showed extensive dyspnœa; besides the general appearance of the child indicated a rapid carbonic-acid poisoning. There were blueness of the finger nails, cyanosis, and the generally livid expression of the child indicated that it was fast succumbing to the septic influences of diphtheritic poison. The main thing when I first saw the child was to relieve the stenosis and allow a proper influx of oxygen into the lungs. I therefore rapidly intubated with the assistance of Dr. Joel. This was at 9 P. M. The stenosis was at once relieved and the child allowed to go to sleep to overcome the exhaustion following the intubation. After giving the usual precautions as to feeding by the mouth, I ordered an ice bag on the top of its head and cold sponging to the body at intervals of fifteen minutes to check the perspiration and to freshen the child up generally. The following morning the child's breathing was much easier and the stenosis entirely relieved; but, as the temperature, which had been at the time of intubation 101°, had gone up the following morning to 102°, and the pulse, which at the time of intubation had been 130, had gone up to 142, I decided that the inflammatory condition and the diphtheria generally had not been improved. I then injected five cubic centimetres of Aronson's diphtheria antitoxine in the interscapular region. On the evening following the injection of antitoxine the temperature still remained as in the morning, 102°, pulse was still 140, and there was no visible sign of improvement. The stenosis had been entirely relieved, judging by the quiet

breathing. The child, when I saw it, was asleep and appeared to rest very easily. The difficulty of feeding was manifest, and I gave instructions not to feed at all by the mouth, but to rely in this case solely on nutrient enemata. I ordered the yolk of an egg beaten up with starch water, alternating with starch water and beef tea and starch water with veal tea, made in the same manner as beef tea, giving an injection every two hours. Before administering the nutrient enema I instructed the mother of the child to wash the lower bowel (rectum), using a teacupful of ordinary Castile-soap water to cleanse away any fæces that might possibly be there. As in the case previously reported above, not only was the injection very easily retained, but it was necessary to inject a pint of water containing some glycerin in order to cause a free movement of the bowel on the second day following the commencement of the nutrient enemata. Large masses of solid fæces of a brownish-yellow color were passed with the enema, showing not only that the nourishment was well absorbed, but that it was easily retained until the injection was given. The pulse, which had before been weak, was on the second day following the injection of antitoxine, combined with this treatment, strong, full, and regular. The child appeared very bright and seemed to be gaining strength. This treatment had been continued in all for five days, when the membranes, which had previously completely covered the throat, as mentioned above, had entirely melted away. No signs of stenosis existing, I decided to remove the tube, which was done with no unpleasant symptoms following. There exists to-day, about nine days after treatment, a slight cough and also a slight hoarseness, which are possibly the effects or the results of pressure by the intubation. The temperature is normal, the pulse is between 95 and 100, the appetite is ravenous, the bowels are regular, the urine, which had been examined several times, has shown only slight traces of albumin, but enormous quantities of phosphates or urates and casts microscopically. There has been no eruption in this case following the injection of the antitoxine, or any unpleasant symptom which could be directly or indirectly attributed to the action

of the antitoxine. The specimen used was of the latest importation, which, as is well known, is tested at present by a special officer detailed from the German Government for this purpose.

Cases such as have been cited I could cite by the score, but they would only reiterate what I have already carefully detailed as the effects and proper results attended by the use of a good and reliable antitoxine.

A word about the syringe to be used. While there are at present dozens of syringes in the market, made of tin, zinc, and all sorts of metal, hard rubber, black and of other colors, I have found that the best syringe that could be used for the purpose is the one which has been made by Codman & Shurtleff, of Boston, of which the accompanying cut is an amply good illustration. In the administration of antitoxine everything depends on (1) the absolute



purity of the substance used; (2) the reliability of the same; (3) the administration of the proper quantity, after having been assured of the quality used; (4) the absolute sterility of all substances coming into contact with the antitoxine, and, first of all naturally, the syringe and its attachment; (5) the absolute sterility of the skin of the patient prior to the injection of the same; (6) and last, but not least, the strictest antisepsis or asepsis of the operator or physician giving the injection. The syringe, therefore, should be boiled and properly sterilized. I pre-

fer to use a 0·5-per-cent. solution of trikresol, or, if that is not handy, carbolic acid of 0·5-per-cent. solution will do equally well. The syringe which has been constructed by Codman & Shurtleff consists entirely of glass and has a glass piston with an asbestus packing. A small, flexible rubber-tube attachment allows of an easier method of injection, and is well appreciated by those who have any experience in the handling of children, and know how restlessly they will toss about, and how difficult it is at times to administer an injection without doing some damage to either the patient or to the needle. The rubber attachment, therefore, on this syringe is of some value, as is the small rubber attachments on our large aspirators, which are so well known in diagnosticating the presence of pus in suspected empyema cases. Another great advantage of this syringe is that the rubber can be thrown away and a fresh piece used with each injection, and that the glass syringe can be boiled in any antiseptic solution. I need not refer to the fact that all metal syringes, be they of silver or other metal, corrode in the presence of bichloride of mercury, and, as the bichloride is one of the most favored antiseptics among physicians to-day, it is well to remember that this syringe, being of glass and glass only, can be put into bichloride as well as into any other antiseptic solution and stand the boiling. A disadvantage, if I may call it such, is that it must be handled with care, as we would any other instrument made of glass, on account of its being brittle. I have been in the habit of using a glass tongue spatula for examining the throat, so that the absolute sterility of the instrument coming in contact with the patient can be assured by proper disinfection after using it.

Among the most recent publications pertaining to serum therapy, I should like to refer to that most admirable book

by Professor Adolph Baginsky, which details all his most recent experiences to date in the Kaiser and Kaiserin Friedrich Children's Hospital. In our country a most excellent book has recently appeared by Dr. George M. Sternberg, Surgeon General of the United States Army, entitled *Immunity, Protective Inoculations in Infectious Diseases, and Serum Therapy.* I have the honor of being quoted by Dr. Sternberg on pages 166 and 167. As recent experiences have altered some of the technical details there, I will first reprint from his work and then give the alteration in question. In his book he says:

"Fischer (January, 1895) reports thirty-four cases—thirty malignant and four mild—treated with a mortality of two = 5·8 per cent. He says:

"These cases were not selected, for some were poorly nourished, some in excellent vitality, with careful nursing and good hygiene. The main point was to apply the antitoxine as early as possible, and counteract the septic matter absorbed, and thereby avoid complications, besides using the local treatment of swabbing the throat with a 1-to-2,000 bichloride-of-mercury solution, using a fresh swab for each application and burning the same immediately after using it.

"The technique of injection is simple. Having properly sterilized the syringe by boiling and using 0·5-per-cent. trikresol, I commence by injecting ten cubic centimetres in mild cases and twenty cubic centimetres in malignant cases, by pinching a fold of the skin in the interscapular region and allowing the serum to be slowly injected. I believe it proper, however, to have a syringe of suitable size and inject the required amount, rather than inject in several places. The calibre of the latter must necessarily be quite large, owing to the thickness of the serum, which is at times rather mucilaginous. It is proper to note all differences and effect on the false membrane and the swelling of the glands, the behavior of the temperature, the condition of the urine, the effect on the heart, and especially the pulse.

"There should be no hesitation in injecting on the second day, and, if no effect is seen, repeating the injection on the third day, as there is absolutely no risk from the injection. It is a perfectly safe remedy, and shows no immediate reaction. It differs from tuberculin and vaccine in that it causes no reaction. A case of antitoxine treatment will show no symptoms directly attributable to the remedy, unless it be in some cases of urticaria. The temperature does not fall by crisis, but by lysis, with antitoxine treatment. Massage of the serum after the injection should not be practised, according to Heubner, Aronson, Baginsky, and others."

As the more recent specimens of antitoxine appeared, it was noted that the healing dose, or rather the dose contained in one of the small brown, glass-stoppered bottles, was five cubic centimetres according to the label. I have repeatedly measured the exact amount, and have invariably found that it was between five and six cubic centimetres. This whole quantity should be injected where the skin hangs very loosely, the most convenient place being the one in vogue in Berlin at the Kaiser and Kaiserin Friedrich Children's Hospital, the interscapular region. I also give preference to this point for the injection because the child, lying face downward, does not see the needle and is not so quickly demoralized, and can be easily held by the assistants holding the shoulders and the legs of the patient respectively. I therefore do not, as I am quoted by Sternberg, commence with an injection of ten cubic centimetres, but rather commence with one of five cubic centimetres of Aronson's concentrated antitoxine, and if then there is no immediate relief following, say within twenty-four to forty-eight hours, I repeat the same dose, giving the injection in the immediate neighborhood of the first one. I have never seen any ill effects following the injection done under proper aseptic or antiseptic precautions. Professor Baginsky, of Berlin, reports but one case of ab-

scess following the puncture. I have frequently seen patients in private practice that had suffered an abscess following the puncture of an ordinary hypodermic needle after receiving an injection of morphine, so that I believe that every careless puncture of the skin, which can by reason of septic matter on the needle carry into the body beneath the skin various micro-organisms, may in this way form the focus for an abscess, and that the accidental injection of morphine or antitoxine has absolutely nothing to do with the infected matter carried in by a dirty or sometimes rusty needle. I invariably seal the point of puncture with a drop of flexible collodion, which I always carry in a small bottle having a cork with a small camel's-hair brush fitted in its centre, so that it is constantly moist with collodion and therefore does not harden. The technics then of the injection is so simple than any one can use it.

The complications arising during the course of the antitoxine treatment of diphtheria are mainly due, as experience has taught me, to the same causes that were formerly so prevalent before antitoxine was used, so that an albuminuria or nephritis or paralysis in the various forms, resulting or coming on as a sequela to the diphtheria, should not be attributed offhand to the antitoxine. A careful study of the complications and sequelæ of the several hundred cases which I have had has convinced me that, although I have seen a certain batch of cases in which all forms of complications ensued, another batch of cases would have no complications and a smooth termination ending in recovery and no loss of flesh, perhaps a slight anæmia due to the exhaustion caused by this infection within the body. In a previous paper in the *Medical Record*, April 6th, I have distinctly stated that albuminuria was sometimes seen so soon after an injection of antitoxine and sometimes could be made to disappear when the anti-

toxine was discontinued, and again to reappear when the antitoxine was again injected, so much so that I looked upon one and the other as a matter of cause and effect. I should like to correct myself, for in a larger number of cases, with an equally careful observation by myself as well as my colleagues, I am convinced that, although there may be impurities in the antitoxine which may at times cause an irritation of the kidneys, by far my greater number of cases not only did not show any unpleasant effects after the injection, but even the kidneys behaved much better, and kidney complications, such as albuminuria, nephritis, etc., were, on the whole, greatly lessened and improved by this mode of treatment.

I am willing to again correct myself in regard to the use of antitoxine in those cases of diphtheria in which a complicating scarlet fever arises, for I have seen a very good result in a child recently in which the scarlet fever predominated and in which the latter was a complication to the diphtheria, which had commenced ten days prior to the first symptom of vomiting and twelve days prior to the first appearance of an eruption. The same holds good in a complication of measles during the course of a diphtheria. While I will not say that all cases of diphtheria with measles, as well as all cases complicated by diphtheria in conjunction with scarlet fever, must and do end well, I am willing to be placed on record as having seen in all from twenty to thirty cases of the so-called mixed infections—*i. e.*, scarlet fever complicating diphtheria, measles complicating diphtheria, and chicken pox complicating diphtheria—in which I am confident that the worst symptoms were at times modified if not benefited by an injection of antitoxine. It all depended upon the dose used and also the kind of antitoxine injected. Naturally, an important point in the treatment of this most fatal dis-

ease is the so-called symptomatic treatment; by that I mean that a sudden high fever should be looked to at once, and the cause of the same looked into, if possible. So, for example, I could cite the case of a child, which was under treatment for diphtheria of a malignant type, in which laryngeal stenosis supervened, where it was necessary to intubate, and in which, after the final removal of the tube, the child was really convalescent. On the eleventh day from the commencement of the treatment a sudden elevation of temperature gave all indications of some existing trouble. A careful examination of both tonsils and the uvula showed a slight amount of dry and moist mucous râles; no dullness could be made out on auscultation; a slight cough existed, which later I attributed to the irritation caused by the tube used for the intubation. Nothing else was found. The child, being two years old, was not expected to expectorate as older children would, consequently the question of pneumonia was rather doubtful and a further careful examination was necessary. It was then found that the child had eaten oranges and cheese and drank some beer; in other words, a mixed and faulty diet existed, resulting in an acute catarrhal gastric fever. Having corrected the gastritis, I watched the lungs for the possible appearance of pneumonia. I determined that we were dealing with one of those acute septic forms of gastritis and corrected it at once. The child remained well after two days of treatment. It required but one careful irrigation of the stomach with a quart of normal saline solution to free it as much as possible from the offending septic material, and thus it is that these grave symptoms may sometimes cause death if all possible precaution is not used, as it had been used in the course of this serious trouble.

Another equally interesting case is one which had been

seen and treated by three physicians prior to my seeing it:

I saw the case in consultation and treated it with Dr. S. Cohn, of this city. Prior to this the child had been intubated by several physicians, among them Dr. Goodman and Dr. L. Kohn, and had been seen by Dr. Weissberger. This child when I saw it had a tube within the larynx which was entirely too large, so that a great deal of trouble with dyspnœa arose directly from the tube. The first indication was to relieve the stenosis by removing the larger tube and placing a smaller one. Besides, a temperature of 105° appeared every evening, followed by a fall to 101° in the morning. This kept on for three consecutive weeks, although at the end of eight or nine days the temperature remained normal for three or four days. A careful examination of the lungs revealed a pneumonia, first on one side, and, after a resolution had set in, it was followed by the same condition of affairs on the other side. The pneumonia was evidently the result of "*Schluckpneumonie*," which is so often caused by swallowing fluids which enter the trachea and lungs through the tube instead of going to the œsophagus and stomach. In order to guard against a repetition of this in this case, and besides to give the child the very best opportunity to recover, we resorted to rectal feeding and did not give anything by the mouth for a number of days. The child's strength remained well; it did not lose flesh, and seemed, but for the anæmic condition following the diphtheria, to get well, and is well to-day, which is about three months since the commencement of the treatment. The urine in this case did not show any casts, but contained varying quantities of albumin, sometimes slight traces, at other times almost fifty per cent. of the volume, so that, although a distinct nephritis existed, it passed off without further treatment. A peculiar condition of affairs was noticed the second week of the treatment of this case. The temperature, which had remained normal for two days, suddenly rose to 105°. The stomach was in good condition; there was no other reason for a febrile con-

dition, excepting the possibility of a pulmonary complication. The question of an exanthematous eruption came up, but was dismissed, so that I decided to reinject the case with five cubic centimetres of Aronson's antitoxine. Within twelve hours after this injection, without any further treatment, the temperature went down to 101°, and the following day, thirty hours after the injection, the temperature was normal, so much so that Dr. Cohn and myself were led to believe that we were dealing with an extensive diphtheritic, membranous laryngo-tracheitis, for about thirty hours after this injection a large cast was coughed out which was about four inches long, which showed a complete extension of the disease from the larynx to the trachea and finally the bronchial tubes inot the smaller bronchi.

Where a febrile condition has existed for more than a week following the injection of antitoxine in a given case of diphtheria, where the urine is quite free from albumin, where there is no history of an exposure to an exanthematous eruption, if all further factors, such as gastritis and other diseases, are wanting, and there is no really assignable cause for the existence of the fever, it has been my rule to suspect an extension of this pseudo-membranous condition downward, especially so where the larynx had been involved primarily, and the more so when we hear on auscultation some moist râles or dry râles and other signs pointing to the existence of a bronchitis without distinct manifestations of the disease. In such cases I have given the most benefit by resorting to a second injection of antitoxine in the same dose as I commenced—namely, five cubic centimetres. In order to illustrate the fact that antitoxine can be used to advantage in all forms of diphtheritic processes, I desire to record the following case :

A child was taken down with a severe form of diphtheritic croup; was attended by a physician without antitoxine and died. In the same house another child came down with

diphtheria about a week later. I was called on the second day of the disease, and but for a slight drowsy condition and also a small membranous deposit on the pharynx I should have called this a mild case of diphtheritic pharyngitis. The temperature did not go beyond 100° and the other factors in this case were so mild as merely to mark it as an ordinary case of mild diphtheria. The child was well as far as we could determine in about a week after the commencement of the treatment, which I have heretofore detailed. It was then that the trouble in this family commenced. The mother of this child had been in puerperium since the second day after the commencement of her child's diphtheria. From that time it was noticeable that she had had fever. Her midwife used all necessary precautions, such as antiseptic irrigations and all modern dressings, but the temperature persisted, and the question of retention of placenta or other *débris* post partum came up. She finally sent for me to examine this woman. I was surprised to find a large, yellowish-white, croupous deposit covering the external genitals as far as I could see, probably in all covering three or four inches of mucous membrane. The temperature of the woman was 105°, she was constantly drowsy, complained of a burning pain in and around the genitals, of excessive thirst, and otherwise had no further symptoms. On questioning her, I found that her child, four years of age, which had suffered with diphtheria, had slept on her bed every night during his illness, as she thought she could be of some service in nursing him. It was easy, therefore, to associate her infected condition with that of her diseased child. The midwife had given her several doses of quinine on the day previous, and but for a buzzing noise in her ears it did not seem to relieve her condition. I ordered an enema of soap and warm water to clear her bowel; I used locally a hot solution of 1-to-5,000 bichloride of mercury by soaking weak iodoform gauze in this solution and changed this antiseptic every few hours, and gave her an injection of ten cubic centimetres of Aronson's antitoxine. What had been one large, solid mass on the day of injection appeared to be a shriveled, loose mass of suppurating tissue on the

following day. The temperature, which at the time of the injection had been 105°, came down the following morning to 102·4°, and two days after the injection it came down to 100·2°. Instead of the croupous deposit, there was a large amount of pus flowing constantly from the external genitals, so that it appeared as though an abscess involving the whole of the external and internal genital tract had been opened. From this time forward nothing of any importance appeared; the patient made a complete recovery in about two weeks although her temperature came down to normal on the fifth day after the injection. The further treatment of this case consisted of local antiseptic dressings of iodoform gauze, and, as I found a large ulceration involving the perinæum, I sent the case to the Post-graduate Hospital for operation. The patient was operated on and is entirely well.

The second case of this kind occurred in a patient of Dr. S. Cohn of this city. According to the doctor, he changed his clothes, bathed, and used all necessary antiseptic precautions in going from one patient's house to the other. Still, for some unexplained reason, the patient in puerperium contracted fever, and, as he was exceedingly careful of the condition, he suspected at once the possibility of an infection from an outside source. When I was called in consultation I found the patient suffering from very high fever, constant headaches, some pain in the abdomen, but no distinct evidence of any croupous or diphtheritic deposits. That it was a case of septic peritonitis we easily agreed, and it was determined to try the efficacy of antitoxine in this case. I therefore injected five cubic centimetres into the right abdominal region and gave the patient a placebo. The attending physician had previously used all necessary intrauterine irrigations and used all careful details in the treatment of this puerperal stage, so that there could have been nothing but possibly an infection through some unexplained reason. On the following day the temperature had gone down two degrees, so that we were so much encouraged by this that the doctor asked me to give a second injection of antitoxine. Following this second injection the temperature

went down to 100°, and but for slight therapeutic measures nothing required looking after. Dr. Cohn attended to all the other details of her treatment and, besides giving pills containing inspissated Warburg's tincture, employed nothing but careful dieting.

It was primarily a case in which the septic elements were destroyed by the introduction of antitoxine into the system, and if, as the two previous cases just cited show, any step toward the amelioration of the septic condition in the puerperal stage—and I think it is well worth considering—I believe that I am justified in saying that these two patients were saved directly by the introduction of this new therapeutic measure; and although I am not willing to say that all patients with puerperal fever can and will get well by the treatment just detailed, I am confident that possibly some of the patients that are left to the ordinary means of to-day, to die of septic diseases, can be cured if this treatment is tried. I repeat, however, that my experience in septic puerperal diseases is limited to two cases, both of which were successfully treated.

An equally instructive case was one similar to one that I reported last September at the meeting of the Post graduate Clinical Society:

A child, ten days old, had had extensive sloughing of the umbilical cord. A child in the same family was sick with diphtheria for a number of days. The physician in attendance was rather puzzled at the peculiar state of affairs of the navel. It was in a highly inflamed condition, the tissues surrounding the umbilical cord were covered with large membranous deposits for several inches. When I saw the child in consultation, I at once associated this factor with the child that was sick with diphtheria, and told the attending physician that I believed it to be a case of diphtheritic omphalitis. When I saw the case the child was seventeen days old. Iodol was sprinkled over the external surface, also

the ordinary lotio nigra had been used with little or no effect. The temperature of the child was 102°, and all in all the child appeared to be dying. It refused the breast, and was constantly crying; had had several movements of the bowels lately; peevish; had his legs flexed on his abdomen. We decided that as the child had probably been infected, an injection of antitoxine might do some good. I injected in this case three cubic centimetres of Aronson's antitoxine in the interscapular region and applied lead water locally. Whether the antitoxine or the lead water did the most good I am not prepared to say, but the very fact that calomel and limewater had been used for several days prior to the commencement of this treatment without any avail points to the fact that the antitoxine must have had some direct specific effect, for two days following the injection large deposits, which consisted of pseudo-membranes, sloughed away, and a culture made from a piece of this pseudo-membrane showed the presence of Klebs-Loeffler bacilli. It was then more than ever that I believed that I was dealing with this true form of diphtheritic omphalitis. In this same child, following the disappearance of the omphalitis, which lasted in all eleven days after the commencement of the injection, a severe diphtheritic conjunctivitis was set up, owing most likely to the carelessness with which the nurse handled the baby and the probability of the carrying of some of the infected material of the inflamed navel to the eyes. In fact, the nurse admitted having used the same towel to wash the eyes and the eyelids that she used to dry the umbilicus, so that we had here again the direct transmission from the umbilicus to the conjunctival mucous membrane.

I could continue to report other interesting cases, but desire to confine myself to the fact that not only necessarily must a diphtheria be located in the nose, in the throat, on the tonsils, on the larynx, or even in the trachea, but that all diphtheritic processes involving, as in the case reported above, cutaneous diphtheria, conjunctival diphtheria, omphalitis, diphtheria of the external genitals—in fact

in all processes in which I have suspected a croupous or diphtheritic foundation, I have used antitoxine with most positive results, and I believe that some of our patients with septicæmia that died from external cutaneous diphtheria could have been saved by the timely injection of a sufficient quantity of proper antitoxine.

One word more as to the strength of the antitoxine.

Strength of Antitoxine.—Heretofore antitoxine has been prepared and put up in bottles of various sizes, the one being known as antitoxine to confer immunity, and really a prophylactic antitoxine, which was a very weak therapeutic agent in comparison with the antitoxine that was put up in larger bottles for healing purposes only. A very wise plan has, however, been adopted abroad of putting up the antitoxine in phials containing five cubic centimetres only. This quantity is sufficient for an ordinary healing dose in a mild as well as in a malignant case of diphtheria; but if a case shows no alleviation of its most urgent symptoms within the first twenty-four to thirty-six hours following this injection, then a wise plan is to inject the same quantity on the day following the first injection. The most important change that has transpired within the last few months in the manufacture of the antitoxine is that the German Government will not permit this therapeutic agent to appear in the market without giving it its official seal, after having tested its strength and the quantity of normal antitoxine units. It is therefore very pleasant to know that the firm of Schering & Glatz have only one kind of antitoxine, which should be used in the dose above mentioned. In order that I may be properly understood, I should like to state that a child two years old can be infected and have as much septic matter in its system as an adult from a given patch of diphtheria. In fact, the child, being more prone to the action of this diphtheritic poison, shows more mani-

festations of the disease than an adult, and hence it is that the same dose of five cubic centimetres can be injected with impunity into an infant as we would inject into an adult within the same time and in the same locality. I should like to emphasize this point, owing to the large number of questions that have been put to me by various correspondents since the publication of various papers on antitoxine by me.

The Effects of Frost and Heat.—A series of very interesting experiments have been conducted by Dr. Hans Aronson, of Berlin, to determine the efficacy of antitoxine after having been subjected to a freezing temperature, owing to numerous inquiries following a severe spell of cold weather during last winter. Fortunately, according to Aronson, the antitoxine does not lose any of its therapeutic value by being subjected to low temperatures far below the freezing point. This is very important for us to know, especially in the smaller towns, where a supply of antitoxine is not so near at hand, and where physicians have usually taken some antitoxine and kept it as a precautionary measure. While speaking of the effect of cold, a word about the action of very warm temperature is also not amiss. Antitoxine can stand very high temperature without being decomposed; this has also been conclusively proved by experiments, so that we have neither to fear from either the extremes of heat or cold as endangering the value of this drug.

According to the statement of Dr. Hans Aronson, the antitoxine sent to this country by the Schering Chemical Works, of Berlin, manufactured in their bacteriological laboratory under his supervision, will keep at least a year, and specimens of longer time than this have been tested and found efficacious; but I believe that an antitoxine that will retain its active power for a year is all that we can desire.

It is my earnest hope that the good results attained by me in the management of some of the most malignant cases of diphtheria that I have known since I have been in practice shall be also repeated by those colleagues who have hitherto been skeptical in the use of this valuable remedy, and I believe that the large number of consultations that I have hitherto reported have been only due to the fact that most physicians still believe the antitoxine treatment to be in its experimental stage. A careful review, however, of this paper will prove the fact that my cases have not been selected, but that I have usually been called especially in those cases which have been kindly referred to me by physicians in this and the neighboring cities, and have been cases in which antitoxine was only called for as a last resort and where most frequently all the customary treatments of diphtheria hitherto in vogue had been unsuccessfully applied, so that I may candidly say that the complications arising in the course of some of my cases have been rather due to a long-continued disease which has really undermined the whole organism of the patient and saturated it with the septic elements of the diphtheria and its products, and that while we were really called to a so-called case of diphtheria it was in most cases a long-continued diphtheritic septicæmia that required skillful management. Such brilliant results as I have observed from combining antitoxine with intubation and antitoxine with tracheotomy have never hitherto been attained by me in the mildest form of epidemic and with the strongest patient before me.

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