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[Reports to the Supervising Surgeon-General M. H. S.]

The serum therapy of diphtheria.

INSTITUTE PASTEUR, PARIS, *October 20, 1894.*

SIR: While attending the eighth session of the International Congress of Hygiene and Demography, held in Budapest in September last, Prof. E. M. Roux, of the Pasteur Institute, read a paper before the section of hygiene on the serum therapy of diphtheria, in which he gave to the world the results of his labors during the past three years. No subject at any congress has, I dare say, been the cause of so much discussion as this, and, on the whole, elicited nothing but praise. The results obtained by Professor Roux in the treatment of cases of diphtheria are so astounding that at first one is almost compelled to ask oneself, "Is this possible?" But when the methods are known and the array of statistics are given, there can hardly remain a trace of doubt. A greater part of what I am going to say has, I know, been published in the daily and medical press, and the only apology I offer for the repetition is that it is well worth reading twice.

It appears that at last we have found a method which is not only good in one disease, but the principle of the method can be applied to many. It at last has opened up a new field for work in infectious diseases.

Availing myself of the kind invitation of Professor Roux to come to the institute, and there learn by practical experience the exact methods employed in the preparation of the antidiphtheritic serum, and also to observe the effects of the new treatment at the hospital for diphtheria, I arrived in Paris on September 20, and immediately commenced my work.

Every facility has been afforded me by the gentlemen connected with the institute to make my stay pleasant and profitable. My sincere thanks are due to all, and especially so to Professor Roux and Drs. Martin and Chaillu.

I have been in no hurry to report on what I have seen, nor to form an opinion of the merits of the treatment. After spending a month at the

institute and hospital, I have seen sufficient to enable me to form an intelligent estimate of its value. There is still more to be said in its favor than was claimed for it by Professor Roux at Budapest. It has passed the experimental stage, and will in the future be reckoned in value for the treatment of diphtheria as vaccine is for the prevention of smallpox.

The steps necessary in the preparation of the serum antitoxine may be divided into three: First, the preparation of the toxines of diphtheria; second, the immunization of animals; third, preparation of and conservation of the serum.

Preparation of the toxines.—The toxines are prepared from a bouillon culture of virulent bacilli of diphtheria. As the methods employed in the institute are somewhat different from those of other continental laboratories, and in many instances, as in this, are superior, I will give them in detail: A virulent culture of the *bacillus diphtheriæ* is selected—one which is fatal to a 500-gram guinea pig in from twenty-four to thirty hours. From this culture a flask of alkaline peptone bouillon is inoculated. After it has remained in the thermostat for twenty-four hours at a temperature of 36° C., it will be found rich in bacilli. This culture may be termed the stock culture for others which are destined for the toxines. For this latter a special form of culture flask is employed, in order to permit of a special method of cultivation of the bacilli, whereby the toxines formed are much stronger and, it is claimed, somewhat different in their character than when the ordinary methods are employed. The flasks used are known as the Fernbach flasks, and are large, flat-bottomed, Florentine flasks, provided with a tubulature on the side, within about an inch of the bottom. The neck and tubulature are constricted near the mouths for the reception of the proper cotton plugs. These flasks are filled to a short distance below the tubulature with an alkaline peptone bouillon and then sterilized. Soon after this the flasks are inoculated with the bouillon culture of the *bacillus diphtheriæ*, about 40 c. c. to each flask. They are then placed in the thermostat for twenty-four hours in order to "start" them, when each flask is connected with an aspirator and a current of air is slowly kept moving through the flask in the direction from the mouth and to the tubulature. The air, before entering the flask, is passed through an ordinary wash bottle, in order that it may be moist, so as to prevent the evaporation which would occur, as well as to maintain the best conditions for culture. This method, so far as I know, is practiced only in this institute. It is the discovery of Dr. Fernbach, who observed that so long as the bacterium remains in the active living state—or, in other words, maintains its integrity—little or none of those substances known as toxines or ptomaines are set free, but as soon as you present the conditions most favorable for the development of bacteria the life of the individual bacterium is shortened, and it completes its cycle, ending in proliferation and setting free the nucleins from it.

When a bacillus, such as that of diphtheria, is grown under the same conditions as cited above there is a greater quantity of the nucleins formed than would occur under the ordinary conditions of culture.

These flasks are kept at a temperature of 37° C. for from three to four weeks. At this time the bouillon is rich in flaky masses of the bacilli. If examined microscopically the masses are found to be nearly, if not all, disintegrated bacilli. Sometimes a few bacilli are encountered, but they have in a great measure lost their characteristic form.

Filtration of the cultures.—Without further preparation the cultures are filtered through a Chamberland filter tube into sterilized flasks, and kept until required for use. Each lot of the toxines is tested for vir-

ulency by standardizing it by injections into guinea pigs. The usual strength, being $\frac{1}{10}$ c. c., will kill a 500-gram guinea pig within twenty-four hours.

The filtrate will preserve its virulency for a considerable time, provided it is kept away from light and maintained at an equal temperature. Boiling the cultures or even heating them to a degree that will kill the bacilli is not practiced, for it has been found that either process impairs the strength as well as changes some of its properties. Large quantities of cultures are kept growing, a special room being employed for this purpose, as each horse will require a large amount of the toxine to immunize it and to maintain the antitoxine in the blood after immunization is completed.

Immunization of animals.—The antitoxine for the treatment of diphtheria is in solution in the blood of an animal rendered refractory to the disease. The manner of producing immunity in an animal may be performed in one of two ways—by injections of the toxines or by inoculations of the bacilli. The former method has been found to be the best, and at present is the only one in use. In the experiments of Professor Roux and Dr. Martin animals of all kinds were used, but now they use the horse, as it has been found to be the most satisfactory. It stands the process of immunization better, and gives a serum stronger than other larger animals, i. e., in the same length of time, besides furnishing a larger amount of serum. The present method of immunizing the horse is somewhat different in its details from that given in Professor Roux's paper, being much simpler.

A horse is selected which is sound, having been subjected to injections of tuberculin and mallein, the age not playing any particular part; usually it is from 6 to 8 years—a cab horse which has seen better days. At first a trial injection of the toxine is made, usually less than a cubic centimeter, carefully noting the general and local reaction. In some horses even the trial dose has a profound effect, but usually there is quite considerable local and general reaction. If the animal becomes quite ill a small quantity of Gram's solution is added to the next dose, and even the next following if the reaction is too strong. After this the horse bears the increasing dosage with little or no discomfort.

The general plan for the injections is as follows: First day, $\frac{1}{2}$ c. c. of pure toxines, of which $\frac{1}{10}$ c. c. fatal to 500 grams of guinea pig; eighth day, 1 c. c.; fourteenth day, $1\frac{1}{2}$ c. c.; twentieth day, 2 c. c.; twenty-eighth day, 3 c. c.; thirty-third day, 5 c. c.; thirty-eighth day, 8 c. c.; forty-third day, 10 c. c.; forty-seventh day, 20 c. c.; fifty-first day, 30 c. c.; fifty-sixth day, 50 c. c.; sixty-second day, 50 c. c.; sixty-eighth day, 60 c. c.; seventy-fourth day, 100 c. c.; eightieth day, 250 c. c.; eighty-eighth day, 250 c. c.

When the first injections are given there is quite a marked local and general reaction to the poison; there is an œdema at the point of the injection, which is followed by a distinct inflammatory process—hard in the center and soft and œdematous at its periphery. The general reaction is manifested by a rise in the temperature, 1°–2° C., loss of appetite, and occasionally cramps. The reaction must be taken as the guide in the future dosage, and a sufficient time must be allowed to elapse between the injections for the complete recovery from the general and local effects. As the quantity of the toxines is increased the general effects generally decrease, perhaps a rise of a degree for twenty-four hours. The local effect partakes more of an œdema, and has the character of an inflammation.

At a certain stage, usually after two months' treatment, when 50 to 60

c. c. can be injected without harm, there is no general reaction, but a large œdema at the site of the injection, which disappears within from twenty-four to forty-eight hours. Towards the last, even when 200–300 c. c. are given, there is only an enormous œdema, which disappears within from twelve to eighteen hours. When these inordinately large quantities can be given with only a local reaction being manifest, the horse has come well under the influence, and the blood will be found to be rich in the antitoxine.

There is a curious fact well worth noting: At the end of the second month of the treatment, when the horse can bear as much as 50–60 c. c. of the toxines without discomfort, the blood will be found to contain but little of the antitoxine. The antitoxine only appears after repeated stimulation of the cells (?) by the large and frequent doses of the toxines.

The subcutaneous injections do not yield a serum as rich in the antitoxines as when the toxines are injected directly into the blood current. When it is desired to do this, towards the last of the treatment, the toxines are injected directly into the jugular vein. The process is tedious and requires a longer time, and for practical purposes has not been found so satisfactory as the simple subcutaneous injection. The strength of the serum is tested by using young guinea pigs of 500 grams weight. One gram of the serum usually will protect 50,000 grams of guinea pig against a fresh virulent culture of the *baccillus diphtheriæ*. This is the strength that is used in the hospitals. By the intravenous injections a serum of the protective strength of 1 to 100,000 can be obtained. For practical purposes the 1 to 50,000 strength has been found as satisfactory as the stronger.

Withdrawal of blood—Preparation of the serum.—The abstraction of blood from the horse is a simple procedure, the blood being drawn from the jugular vein by means of a special trocar and canula. The trocar and canula are about 4 millimeters in diameter, and are somewhat larger than the ordinary form. The top of the canula is shouldered so as to receive a metal plug, which is also canulated. This metal plug is attached to a rubber tube a half meter in length; to the other end of the tube is attached a glass tube of 10 cm. length. The instruments, tubes, etc., are sterilized, and then kept in a 5 per cent solution of carbolic acid. Ordinary wide-mouthed bottles of 2,500 c. c. are used for receiving the blood. These are prepared by having pieces of paper tied over the mouths, and over this another paper in the shape of a hood is placed; the bottles are then sterilized. When all these preliminaries are finished, the horse is made ready for the bleeding; a small "twitch" is placed around the upper lip and made taut; the blindfold is thrown over the eyes. The hair is next clipped from over the place for the insertion of the trocar, and the place is then scrubbed with carbolic acid, 5 per cent solution. The skin is incised sufficiently to allow the trocar to pass through the tissues without the force that would be required to puncture the vein if the skin was intact, thus preventing accidental wounding of the vein. The jugular vein is compressed by the hand and the trocar is passed well into the vein, the point being directed downward. While this is being done, the assistant holding the bottle plunges the glass tube into it, when the trocar is withdrawn, and the canulated plug is inserted into the canula.

Six to eight liters are taken from the horse at one bleeding. When the bottles are filled to the desired height the blood is allowed to coagulate, when it is placed in the ice chest. Within twenty-four hours the cerum will be found to have separated. Usually from 2½ to 3 liters are obtained from each bleeding. The serum is withdrawn from the

bottles by means of the Pasteur filling pipettes, and transferred to the proper receptacle, for use or preservation. The manner of its preservation is exceedingly simple: A small piece of camphor is placed in each bottle or flask; this, it is claimed, tends to preserve it, should any chance micro-organism be dropped in, and exerts an inhibitive influence against its deterioration. If there is a suspicion that the serum has become contaminated in the various manipulations, it can be filtered through a Chamberland filter. This process will doubtless be applied when it is desirable to keep the serum for a long time. The serum can also be desiccated in vacuo. In this state it can be preserved for a long time without deteriorating, although it loses its strength to a considerable degree in the desiccating process. There is another objection to it in the dried state: It is the fact that it causes considerable irritation when injected subcutaneously, which does not follow the injection of the serum.

It is also noted that the serum has a tendency to deteriorate after being kept for awhile; especially is this to be observed when it is exposed to light or subjected to variations of temperature. This disadvantage they hope soon to overcome. I do not mean that it will not keep for two or three months before it begins to show deterioration. It has much the same behavior as vaccine.

Mode of administration, etc.—To illustrate the exact methods which are used here in the administration of the serum, I can do no better than to quote in extenso from a lecture given by Dr. Louis Martin to the physicians of Paris on Sunday, October —, 1894:

"A syringe containing 20 c. c. is used. It is sterilized in boiling water. It is composed of a barrel of glass and metal, the glass and metal being separated by two india-rubber washers; (2) of an india-rubber piston; (3) of an adjustment consisting of an india-rubber drainage tube 10 cm. in length; (4) of a needle 4 or 5 cm. long. This tube is placed between the syringe and the needle for the convenience of administering an injection in case the child should move.

Before sterilizing, the syringe should be ascertained to be in good working order, the permeability of the needle should be ascertained, and the two india-rubber cushions through which the piston passes should be in good condition. Having taken these precautions, and leaving the screw which is attached to the glass cylinder slightly open, immerse the syringe in water and keep the water at the boiling point for five minutes. Withdraw the syringe and allow it to cool.

Having charged the syringe with serum, take it in your right hand between the last three fingers and the palm. Between the thumb and forefinger take the needle close to its base; that is to say, at its point of junction with the india-rubbber drainage tube. With the left hand take up a fold of the skin of the side and insert the needle at the base of this fold so as not to penetrate the subcutaneous cellular tissue when you make the injection.

When the needle is inserted change the hand that holds the syringe. After this, with your right hand gently press the piston of the syringe while you impart to it a slightly rotary motion. Charge the syringe with precisely the quantity to be injected.

Before injection the skin must be thoroughly cleansed with an antiseptic solution (preferably bichloride of mercury, 1 to 1,000). The injection made, cover the spot with absorbent cotton. This cotton forms a sort of collodion with the serum which flows back through the orifice, and thus completely closes it. A slight œdema occurs during

the process of injection, but disappears within fifteen minutes or half an hour. There is no general reaction.

It has already been stated that serum may be used preventively or therapeutically. In other words, it may act as vaccine or a remedy. Under the following circumstances it may be employed as a preventive:

When a case of diphtheria occurs in a family or among a number of children, the other children belonging to the family or group should be protected by one injection of 5 c. c. of serum for children of less than 10 years and 10 c. c. for children over that age. This will generally prevent an epidemic, or, in case of some of the children having been infected from the first case, it will mitigate the attack. It is not now possible to state how long this immunization will last.

With regard to the therapeutic use of the antidiphtheritic serum, there is one general rule to be followed under all circumstances: When the physician suspects a case of diphtheria he should immediately inject under the skin of the side 20 c. c. of serum at one dose. When the patient is over 15 years of age it is preferable to inject 30 or 40 grams at the same time, but with two injections, one on the right side, the other on the left, in 15 or 20 gram doses. No serious objection can be made to these injections. The only risk incurred is that of giving rise to slight urticaria. If the case is veritable diphtheria no precious time will have been lost.

As soon as the injection is made, or, better still, before making the injection, in order not to disturb the patient after the operation, open his mouth, charge the wire spatula from the false membrane or the mucus of the posterior pillar, and without loss of time plant your two serum tubes in the manner previously described.

Twenty-four hours later, examination of the tubes will give important therapeutic indications. If there is no diphtheria, discontinue the serum. If there is diphtheria, examination of the cultures will show whether it occurs pure or in combination with other symptoms.

The indications for serum therapy depend on (1) the condition of the pulse, (2) on the temperature, (3) on respiration. The local conditions (false membrane) supply useful indications even in the absence of bacteriological examination, but the latter furnishes analogous indications and is more reliable. Neither the appearance nor quantity of the false membrane can decide the main point in prognosis and treatment, namely, whether the diphtheria is pure or complicated.

The local treatment in diphtheria.—Treatment with serum does not rule out all local treatment. Roux stated this most emphatically at the congress of Budapest. He proscribes all traumatism, and, in consequence, all caustic applications, and he forbids treatment with carbolic acid and bichloride, experience having shown the ill effects from combining serum treatment with treatment by carbolic acid or bichloride. During a period of eight days the writer treated the children in the diphtheria pavilion concurrently with serum and bichloride. He had 3 deaths from diphtheritic angina in which tracheotomy had been performed, while cases of croup, treated during the same week and in the same surroundings with serum exclusively, recovered. The writer did not feel authorized to push his experiments farther.

But while Roux discouraged the use of carbolic acid, he advised washing the throat three times a day with boric solutions or 50 grams of Labarraque's solution in a liter of water. These washings have the advantage of destroying any germs that may be present and of preventing the microbic angina, which may succeed the angina of a cured case of diphtheria. Roux is so little opposed to local treat-

ment that he advises touching the throat with compound blue, and has recently tried a mixture of equal parts of camphor and menthol reduced to a viscous state in a mortar. The writer, in all the cases treated by him with serum, touched the throat with salicylated glycerine (5 per cent of salicylic acid). In light cases the false membrane is easily detached from the throat and the mouth is cleansed so rapidly that the local treatment need not be long continued.

It is needless to add that serum treatment does not change the alimentation of the child. It must be well nourished in all cases in which serious albuminuria does not impose an exclusive milk diet.

Pure benignant diphtheritic angina.—Let us take a case of pure diphtheria and follow its clinical history:

On the first day, following the general rule, we injected 20 c. c. of serum. The pulse was then 148, temperature in the evening, 38°; no trouble in respiration; no albumen.

Twenty-four hours after injection the pulse fell to 108 and the temperature in the evening, far from increasing, had declined a little (37.8° instead of 38°). This slight diminution, occurring coincidentally with a considerable decline in the pulse, made a second dose of serum unnecessary.

Diphtheritic angina of a serious character.—On the first day the writer administered 20 c. c. of serum, but this dose was found to be insufficient, for on the following day there was an elevation of three-tenths in temperature, and the pulse was accelerated from 144 to 164. This simultaneous increase indicated that the disease was not eradicated. It was therefore necessary to repeat the dose, giving 20 c. c. at one time, or, better still, 10 c. c. in the morning and 10 c. c. in the evening.

On the third day the temperature declined one degree. The pulse kept at the same point, 160, and albumen appeared in considerable quantity. Prognosis had to be reserved, since for one favorable symptom—lower temperature—there were two unfavorable symptoms—accelerated pulse and considerable albumen. A fresh dose of 10 c. c. was therefore administered. On the following day pulse and temperature were alike lowered, the quantity of albumen was slightly diminished, and the treatment was stopped. The patient recovered.

In conclusion, pure diphtheritic angina requires from 20 to 50 c.c. of serum, administered in the course of three days. With this treatment cure is the rule. I have only to recall here the figures quoted by Roux at Budapest: 120 cases of pure diphtheritic angina, 9 deaths. In regard to these 9 deaths it should be stated that in 1 case the child succumbed to tuberculosis, in 1 to measles, and that the 7 others died less than twenty-four hours after reception into hospital.

We now reach associated diphtheritic angina.

The writer will not insist here on the cases in which the diphtheritic bacillus is found associated with the little Brison coccus. This association does not complicate prognosis.

Diphtheritic angina associated with streptococcus.—We have here selected the associations which most complicate prognosis, namely, association of the diptheritic bacillus with the streptococcus and staphylococcus.

On the first day 20 c. c. were administered. Twenty-four hours later all the lines were descending; that is to say, and this fact is of great importance, the evening temperature was lower than that of the morning. Ten c. c. only were then administered. Microbic association being granted, it was preferable to inject on the second day 20 c. c. instead of 10 c. c. The results observed on the succeeding day confirmed the advisability of thus increasing the dose.

On the third day one of those surprises occurred which often manifest themselves in cases of associated angina: All the lines went up suddenly and considerably, and, a very serious symptom, respiration was accelerated to such a degree that an attack of bronchial pneumonia was apprehended. It was therefore urgent to increase the dose and to administer 20 c. c. This was done.

On the following day the symptoms were all ameliorated. All the lines declined sensibly; the evening temperature was even lower than that of the morning, and if the microscope had not apprised us of association with the streplococcus we would have discontinued the treatment. On the fourth day a fresh dose of 10 c. c. was administered to provide against a new attack. Albumen not being present in large quantities, this dose was not exceeded.

On the fifth day pulse, temperature, and respiration offered more favorable indications. Albumen, it is true, had slightly increased, but not sufficiently to necessitate a fresh dose of serum. But if the augmentation had been more considerable we would still have injected 5 or 10 c. c.

The presence of albumen in the urine indicates the action of the diphtheritic toxine on the abdominal filter. It is, therefore, advisable to slightly increase the doses of antitoxine to neutralize as much as possible the effect of the toxine on the kidneys.

In this connection it may be well to reply to an objection that has been raised, Has antitoxine an injurious effect on the kidneys?

To answer this question it is only necessary to quote the figures cited by Roux. Before treatment with injections of antitoxine, albumen was found to be present in two-thirds of the cases of pure diphtheritic angina; after treatment it was found in scarcely half the cases.

We pass over association with staphylococcus. Its development does not differ from the preceding, and its gravity is secondary to the first.

In the three cases just presented, and which I have selected as typical, the patients recovered. When the pure diphtheritic angina ends in death, this generally occurs in less than twenty-four hours after commencement of treatment. In some cases of pure but toxic angina—that is to say, in cases of general infection—death may supervene, by cachexia, paralysis, cardiac affection, kidney troubles, etc., seven or eight days after the commencement of treatment. These cases are very rare (1 or 2 per cent at most), but the writer felt obliged to mention them. Generally, in cases of associated angina where death is delayed, it is due finally to pulmonary complications or even sometimes to generalized infection, caused by associated microbes.

It now remains to consider croup, otherwise diphtheritic laryngitis.

Nonoperated cases of croup should be treated in the same manner as angina, always taking into account the indications furnished by respiration.

As in the case of angina, pure croup should be distinguished from—

Associated croup.—Case: On the first day, the day on which tracheotomy was performed, 20 c. c. of serum were injected, according to the general rule laid down. The dose was repeated on the second day. On the third day pulse and temperature were ameliorated, respiration was increased, and no albumen was present. At the third dose 10 c. c. were administered.

On the following day the tube was taken out, the child breathed well; temperature and pulse continued good.

Croup associated with streptococcus.—Case: The case is not so simple with associated croup. In the typical case selected for illustration the

prognosis was extremely grave on the day succeeding tracheotomy. In spite of the 20 c. c. administered on the day of the operation, all the lines were shown to be ascending. Albumen was found in considerable quantity. It was found necessary to repeat the dose.

On the day following this second dose there was general amelioration. All the symptoms were improved, but in view of the fact of microbic association treatment was continued for two days in doses of 10 c. c. a day.

In spite of these repeated doses, respiration was accelerated on the fifth day. Broncho-pneumonia, so frequent and so terrible a complication in associated croup, threatened the patient. It was considered advisable to administer a new dose of serum, but the quantity was reduced to 5 c. c. on account of the fall of 1° in temperature and considerable diminution in the quantity of albumen.

On the sixth day the tube was removed. The child recovered, but a fatal result in such cases is only too frequent.

To prevent the development of broncho-pneumonia in cases of this sort, the writer always injects 1 c. c. of mentholated oil once a day into the tube. This mentholated oil consists of: Menthol, 4 grams; oil of sweet almonds, 100 grams.

THE STAGES OF SERUM THERAPY.

Summary.—In 1883 Klebs discovered the diphtheritic bacillus in the course of experiments with false membrane.

In the following year, 1884, Loeffler isolated the microbe, indicated its preferred culture medium, reproduced false membrane in animals, but failed to reproduce the paralysis. As a conscientious observer, he required fresh proofs to establish in an indisputable and absolute manner the specific nature of the Klebs-Loeffler bacillus.

Roux and Yersin, by reproducing diphtheritic paralysis (memorial of 1888), completed the proof desired by Loeffler.

Continuing their investigations, they discovered the diphtheritic toxine, and with it reproduced diphtheritic paralysis, as they had previously done with the microbe.

On the basis of these noble experiments, and confirming their results, the German bacteriologists undertook vaccination against diphtheria. In the first rank of these may be named Carl Frankel and Behring.

Behring, in conjunction with Kitasato, discovered the principle of serum therapy for tetanus and diphtheria. From that moment the attempt was commenced, in both France and Germany, to apply this principle to the treatment of diphtheria in the human subject.

In the galaxy of workers who have pursued the study of diphtheria and its treatment, two names should be associated in the first rank—the name of the German Behring and that of the Frenchman Roux.

But above all other names towers the name of Pasteur."

During my stay in Paris ample opportunities have been afforded me to witness the effects of the serum therapy in the treatment of cases of diphtheria in the hospital for sick infants. From my observations made therein—for one month—I can but corroborate the statements already published. I have been able to follow the cases from the time they entered the hospital until their discharge, noting everything which has been done. I have tried hard to find fault, to pick flaws in the statistics, but have signally failed. The work must stand for itself.

Of the whole number of cases which have come under my observation (82), 3 have died, about 4 per cent. This percentage of recoveries is greater than for the past three months. From August 1 to October 15

the mortality has been a little over 11 per cent. The statistics show that there has been a gradual diminution of the mortality since last May. This can be best explained in two ways: First, the climatic conditions; second, a better knowledge of the serum therapy.

The cases are, on their admission, classified, according to their symptoms, as anginas and croups. As soon as possible a bacteriological examination is made of each case according to Loeffler's method, and they are then given their true classification.* They are divided into three classes—diphtheria pure, diphtheria associated with streptococcus or staphylococcus, or with both, and simple anginas. The treatment of the case depends largely upon the above classification.

As a routine measure the little patient is given an injection of the serum, from 15 to 20 c. c., as soon as it is admitted. If the bacteriological examination shows the case to be one of diphtheria, and of short duration, another injection may be given, which is usually sufficient. If found to be one with diphtheria and the pus cocci, the dose is increased and given at short intervals. If a simple angina, nothing further is done. Great stress is laid upon the class of cases in which the diphtheria is complicated with the pus cocci, especially so when the streptococci are present. The prognosis in these is, from the very commencement, looked upon as grave. The treatment avails but little after the malady has existed three or four days. This class of cases, it is needless to add, furnishes the majority of the deaths.

If these cases can be taken in hand during the commencement, or even as late as the second day, the result is, as a rule, good. Cases in which tracheotomy becomes necessary are nearly, if not always, those in which there is a double infection.

The efficacy of the serum is better shown in the tracheotomies than in all the others. The mortality under the usual conditions has been from 1889 to 1894 something frightful to contemplate; fully 85 per cent of the little patients have succumbed. Since the commencement of the serum treatment the death rate has been lowered to less than 47 per cent, and the cases upon which tracheotomy must be performed are fewer and fewer. The operation is seldom if ever done on cases above 6 years—usually under 4, the majority from 1 to 3. Intubation has not been adopted in either of the diphtheria hospitals. An attempt is now being made by Drs. Martin and Chaillu to have it introduced. I am of the belief that this procedure will still further reduce the mortality.

Another fact worthy of note is that there are seldom any of the complications in diphtheria that were formerly present. Diphtheritic paralysis is rare, pneumonias are less frequent, and, although albuminuria exists in nearly every case of several days' duration, fatal cases of nephritis are gradually becoming less frequent. To better illustrate the effect of the serum, I have taken at random several cases which have been under my own observation, and have transcribed the temperature charts. I regret that the pulse and respiration curves can not be given, as they were not kept, or if so, imperfectly. The temperature is taken as the guide. Experience has shown that the pulse and respiration are synchronous with the temperature. It is now possible to immunize the reagents to the disease. Unfortunately the immunity is not of long duration. The longest time in which it is thought to be protective is

* The service of the hospital is not under the direction of Professor Roux. He has been permitted by the staff to make his experiments in the diphtheria pavilion. The classification is one of routine practice, little or no attention being paid to the true condition of the case. Hence diphtheria infection and simple anginas are treated alike, the latter constantly exposed to infection.

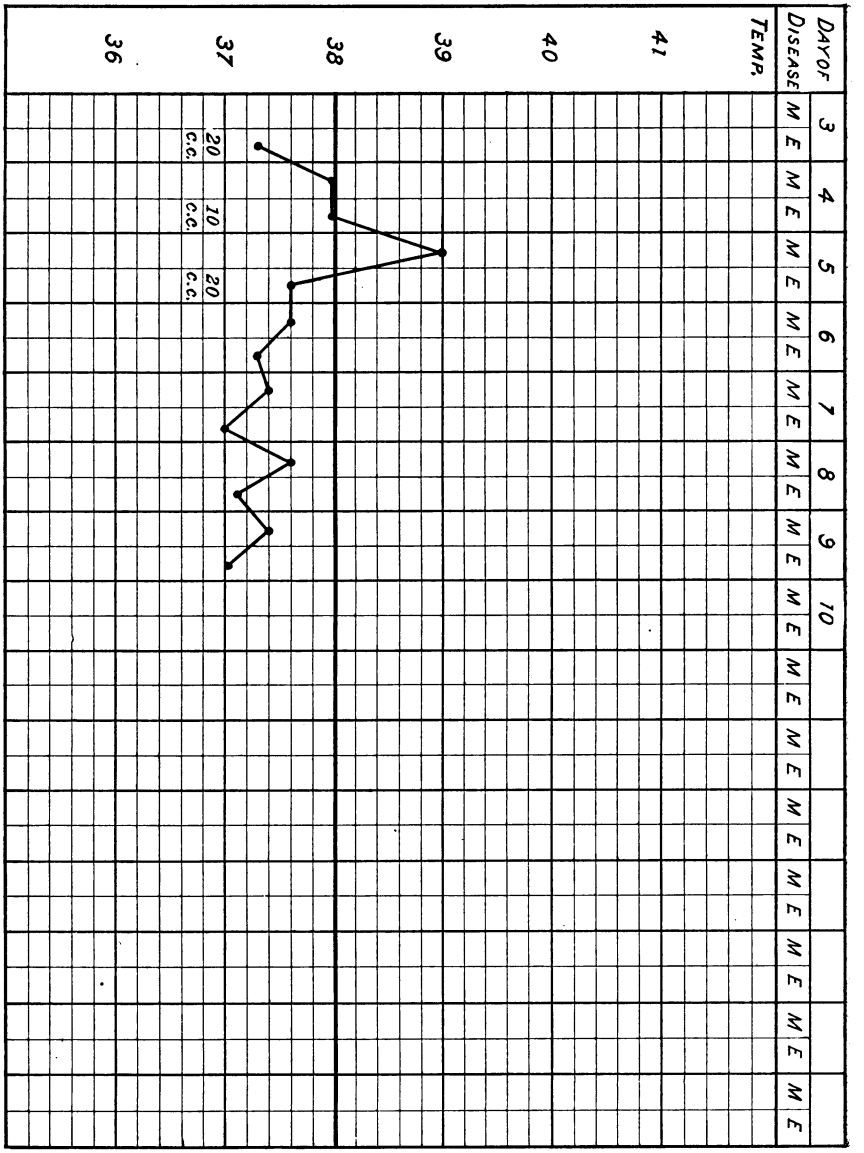
six weeks, one injection from 10 to 20 c. c. being sufficient. This has not only been practiced in the wards of the hospital, but in families of children where one has succumbed to an attack of diphtheria and others have been exposed. In some instances when the child is practically in the commencement of the disease, the bacilli have been found in the saliva, yet there is no sign of disease. In every instance, whether in hospital or in homes, there has been no record of failure to protect.

The future possibilities in this direction can not be overestimated, as we have in the serum the almost absolute preventive of epidemics of diphtheria. In closing these few observations, I must add my insignificant tribute to the magnificent work of Professor Roux and his assistants, and to Dr. von Behring on his discovery, not forgetting that all the splendid achievements of the present, those almost in reach, and even those of the far future, are founded upon the principles discovered by my compatriot, Dr. George F. Nuttall, the pioneer who was the first to make clear the rationale of the bacteriocidal properties of the blood.

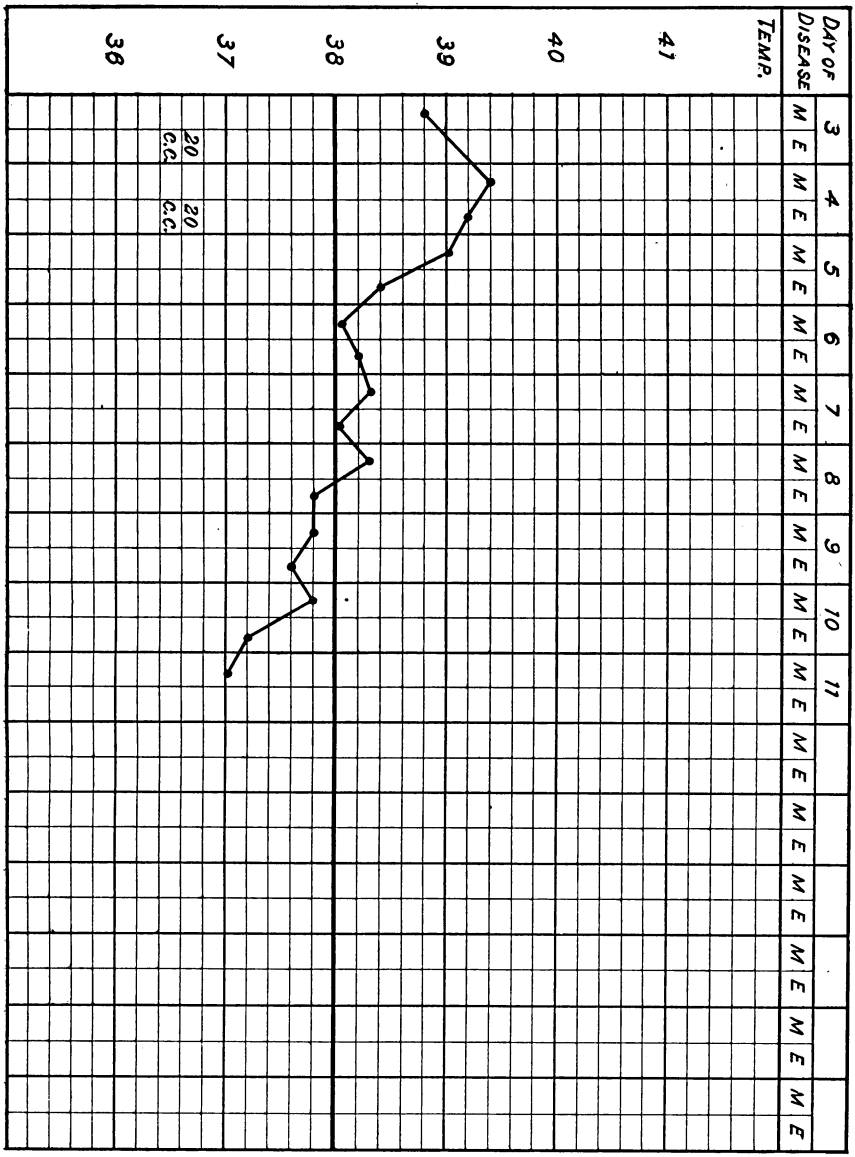
Respectfully, yours,

J. J. KINYOUN,
Passed Assistant Surgeon, M. H. S.

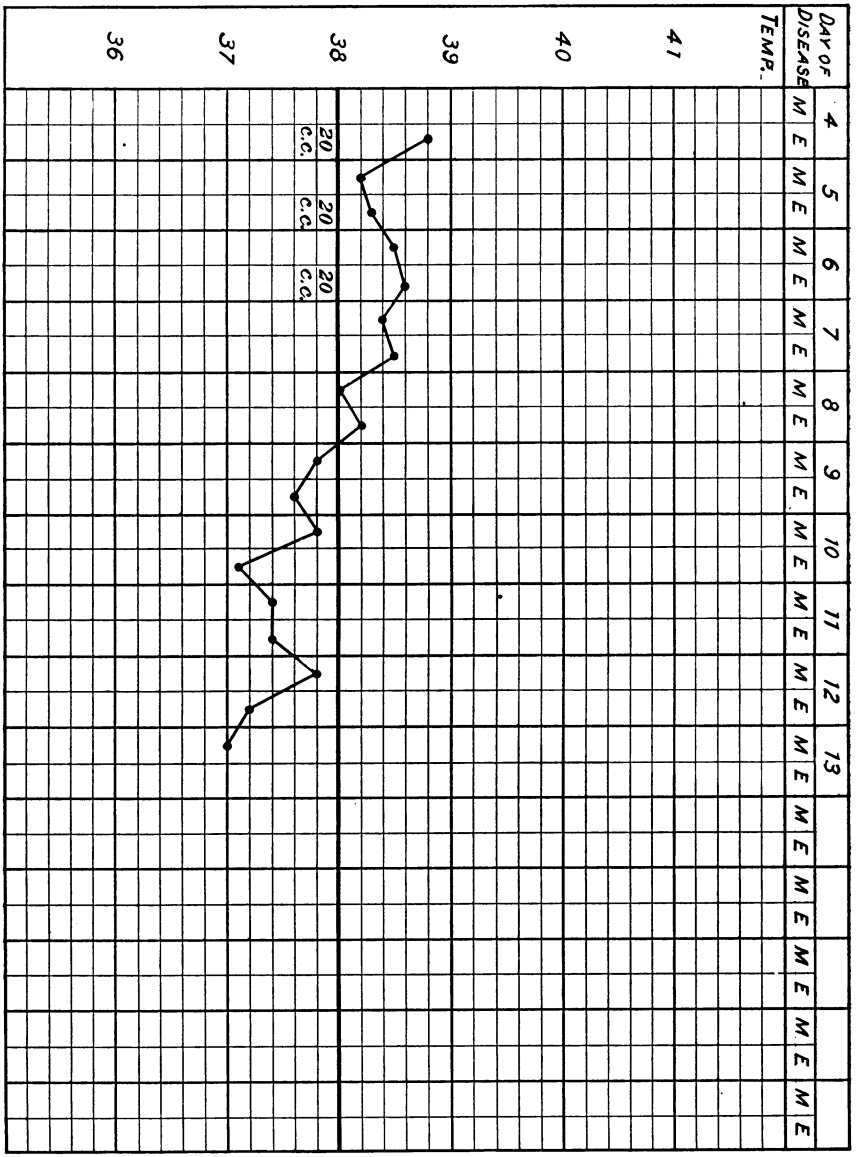
CASE I. *Age 2 years. Faucial diphtheria.*



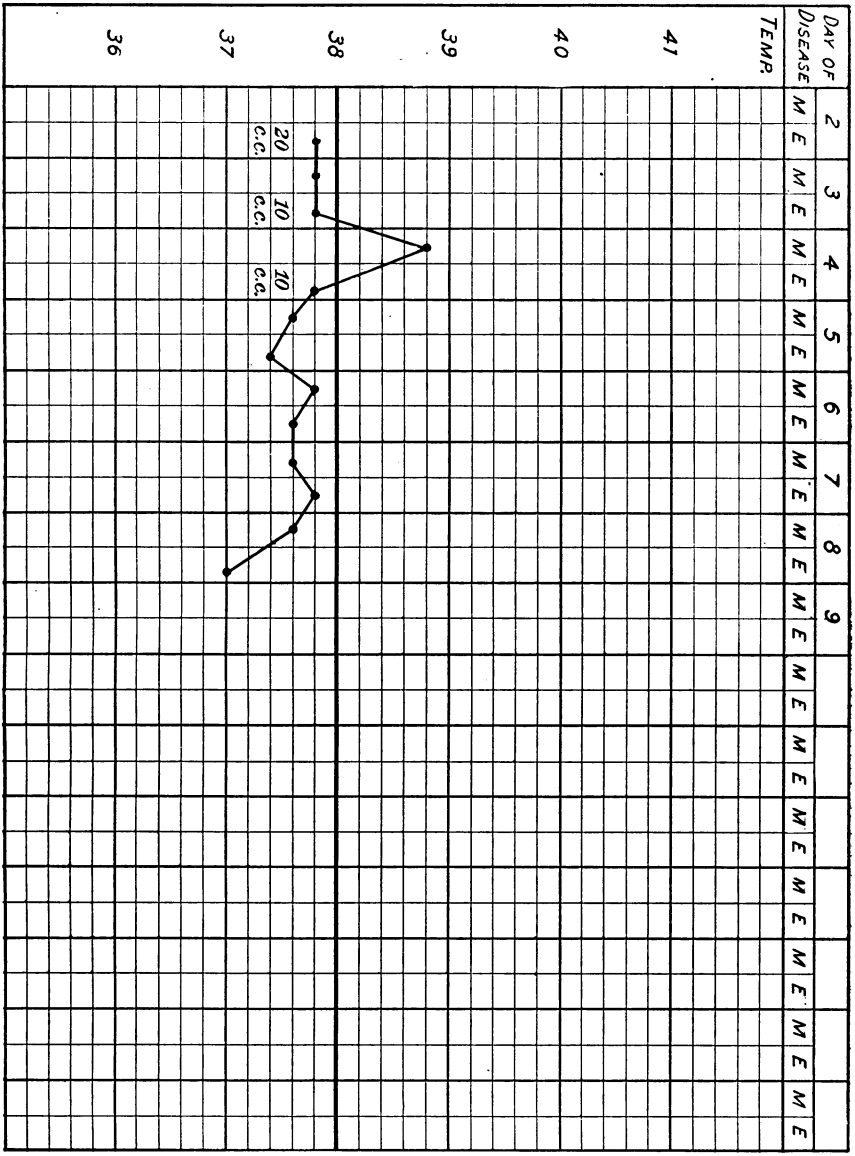
CASE II. *Age 20 months. Faucial diphtheria.*



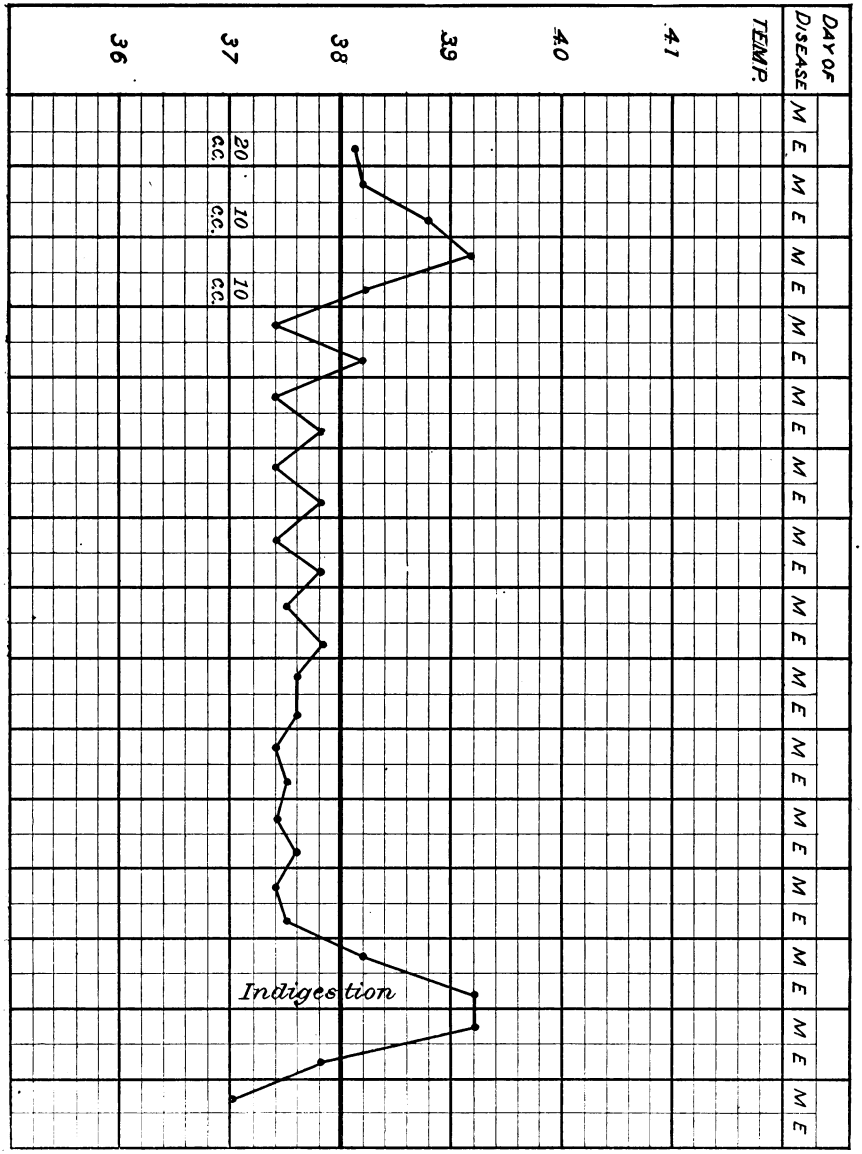
CASE III. *Age 4 years. Faucial diphtheria.*



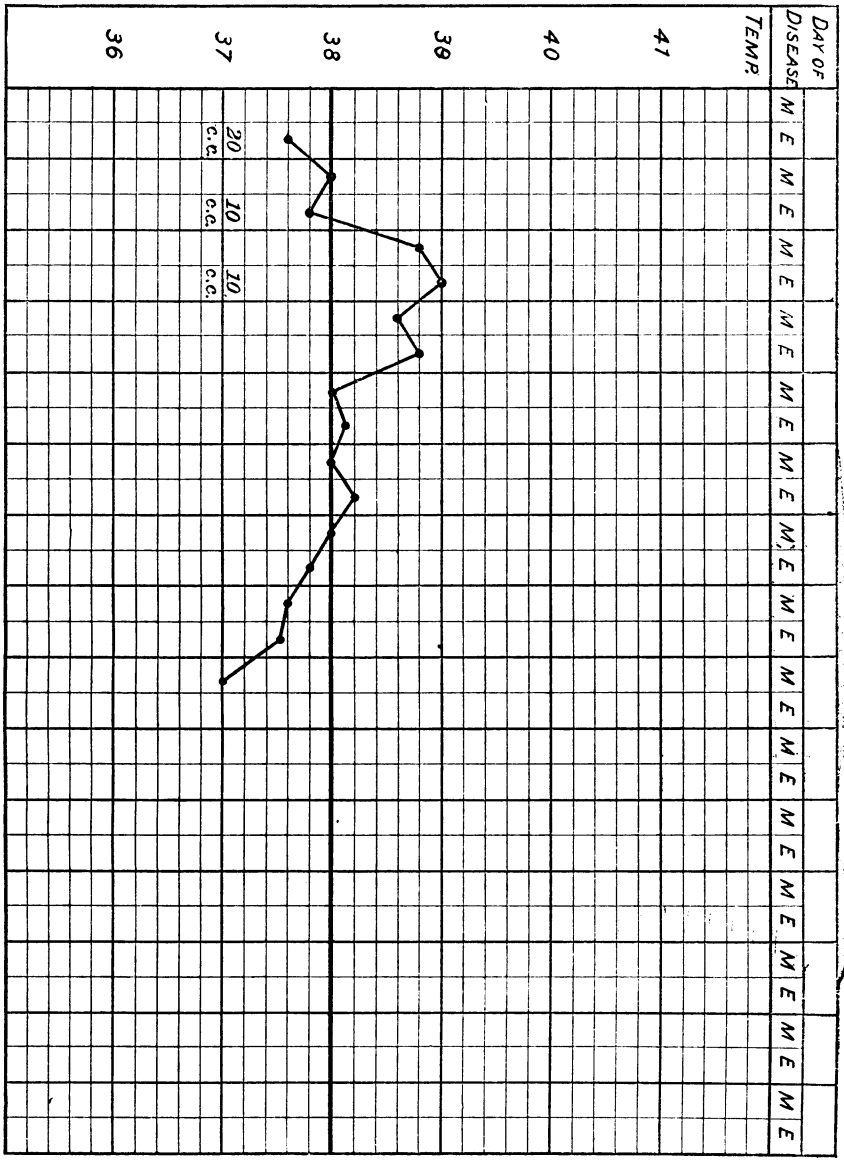
CASE IV. *Age 5 years. Faucial diphtheria.*



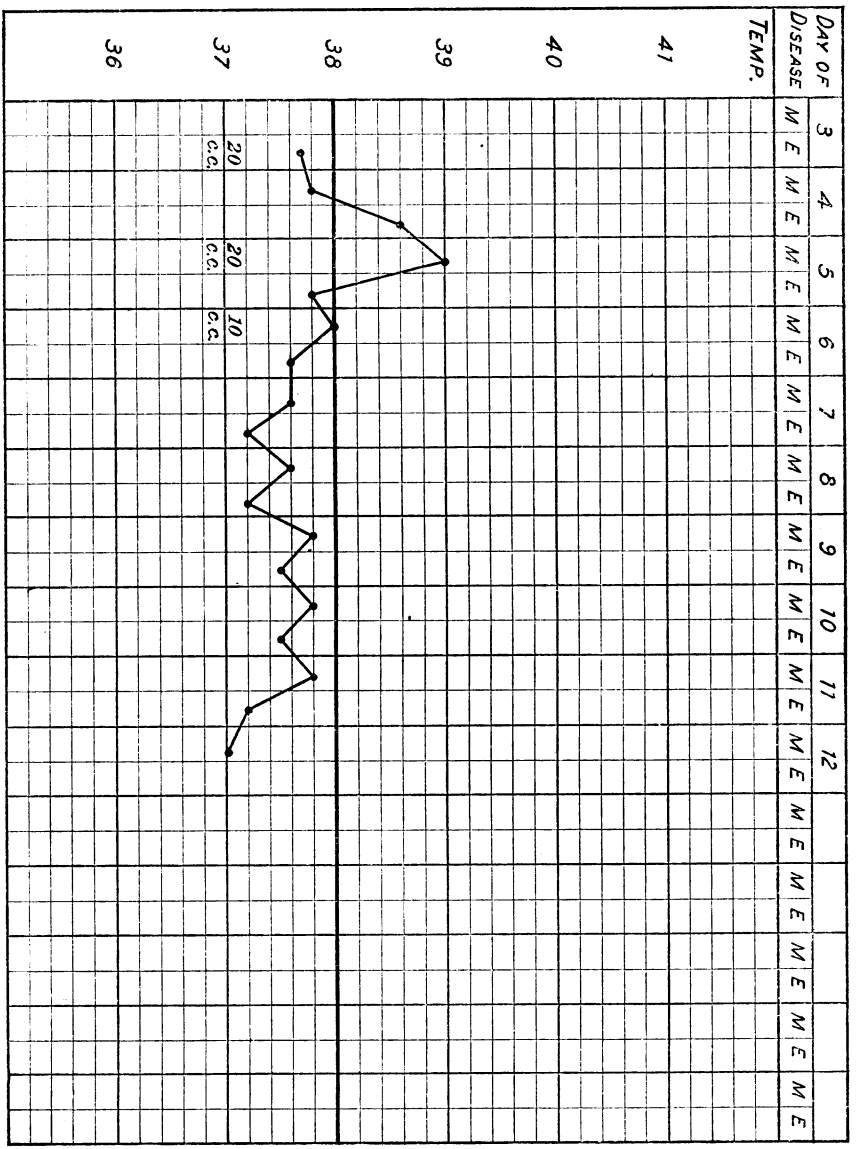
CASE V. *Age 3 years. Faucial and tracheal diphtheria.*



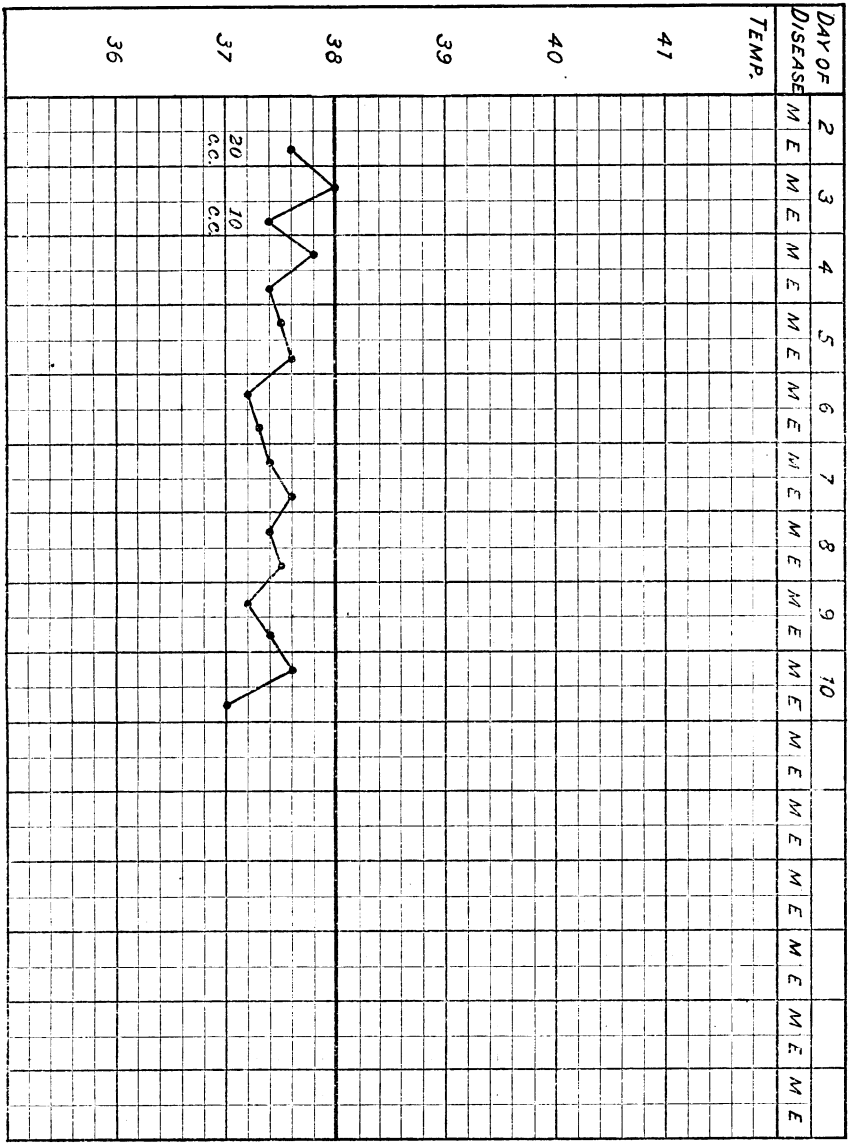
CASE VI. *Age 4½ years. Faucial diphtheria.*



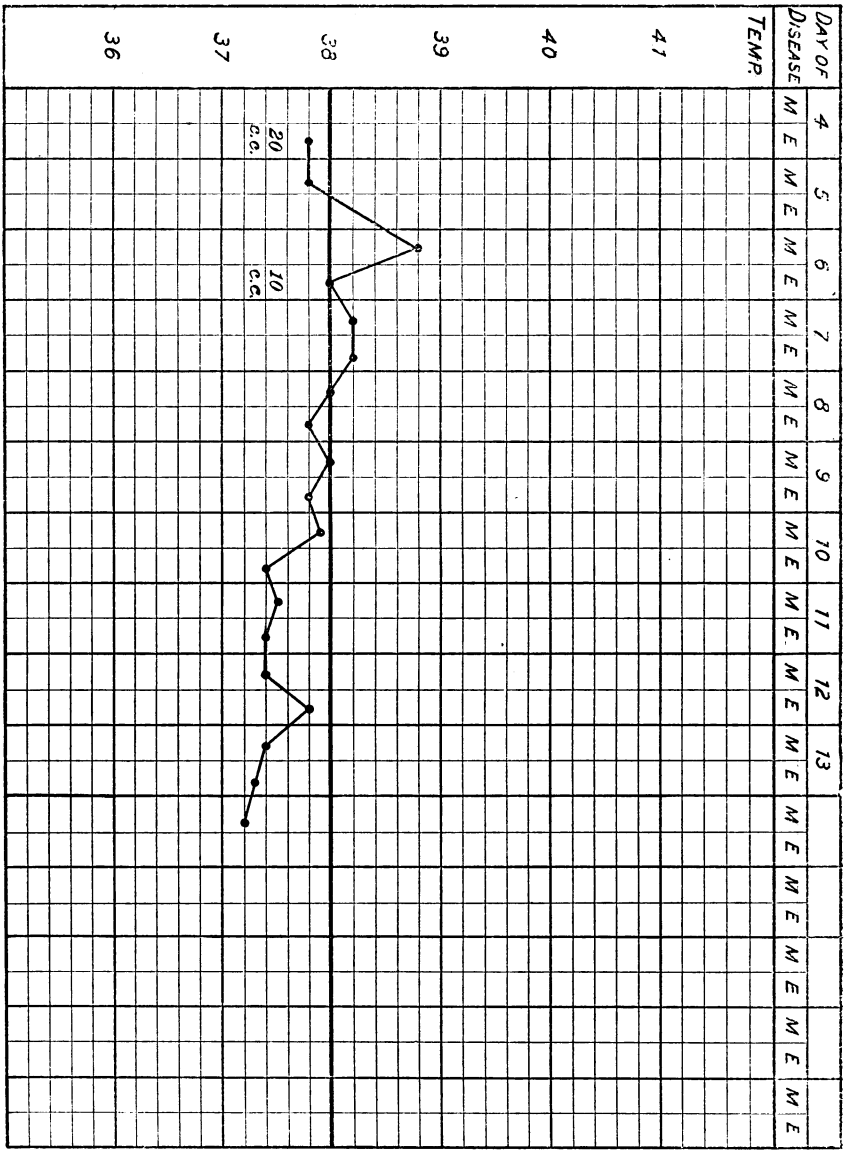
Case VII. *Age 2½ years. Faucial diphtheria.*



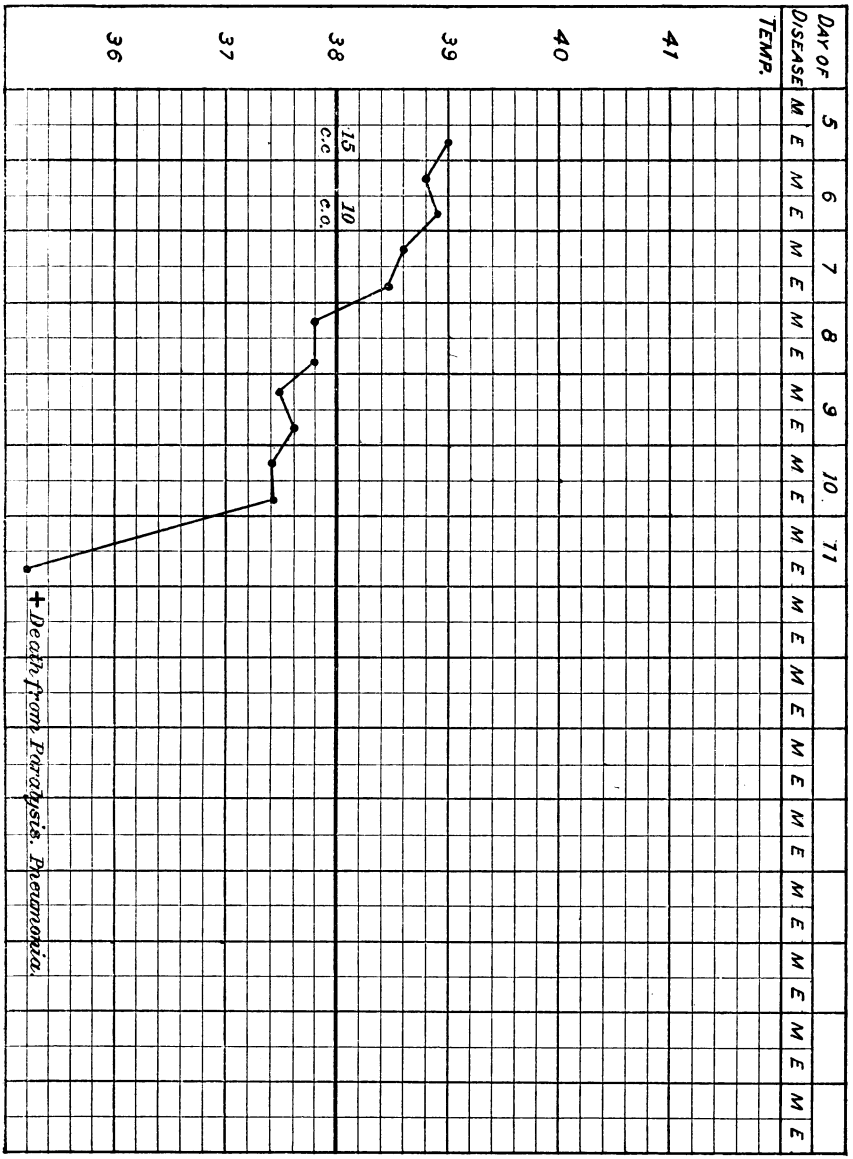
CASE VIII. *Age 5 years. Faucial diphtheria.*



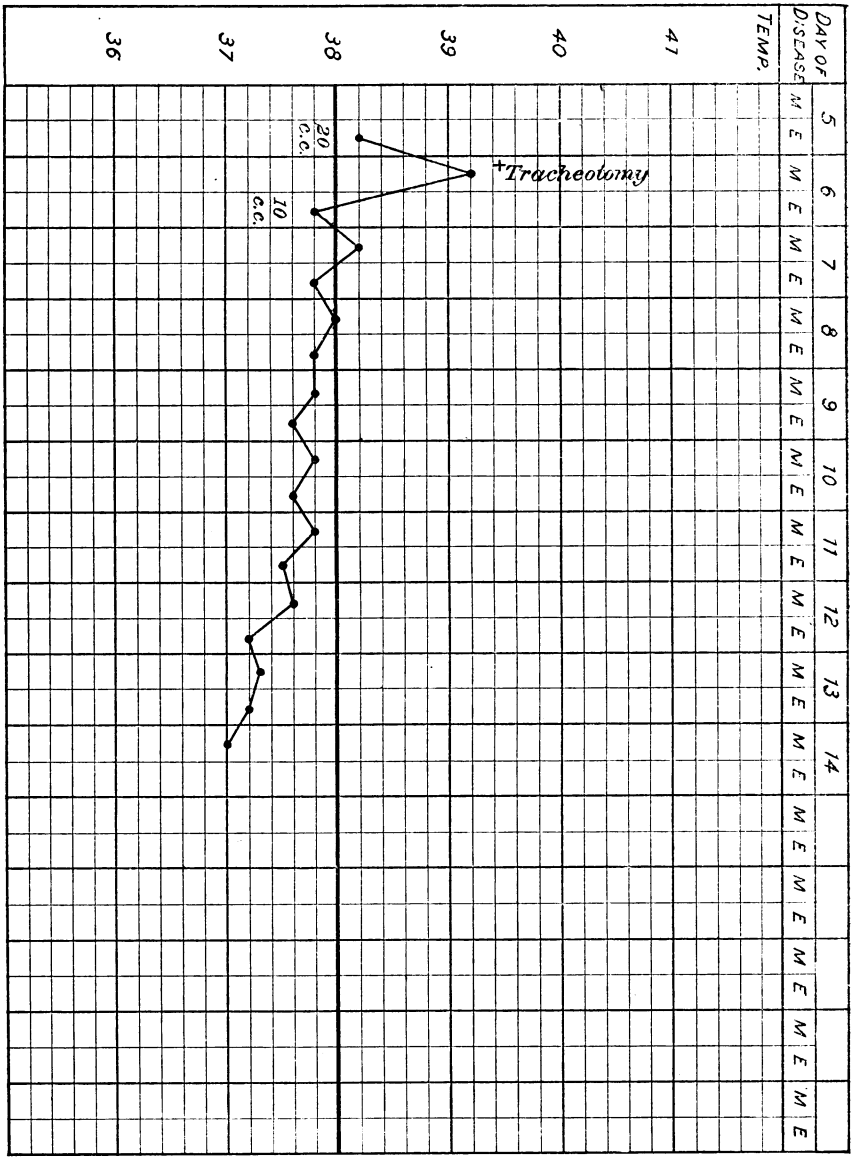
CASE IX. *Age 2½ years. Faucial diphtheria.*



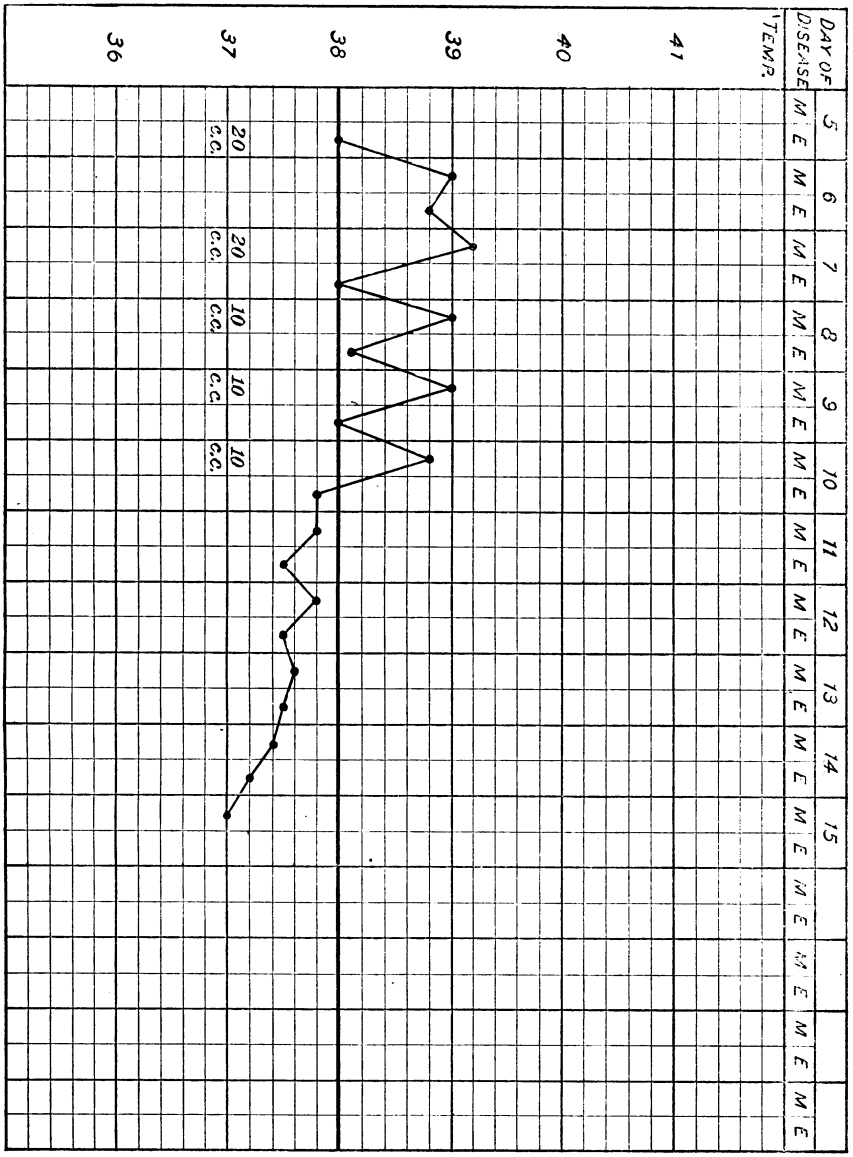
CASE X. *Age 18 months. Faucial and tracheal diphtheria, associated with streptococcus and staphylococcus.*



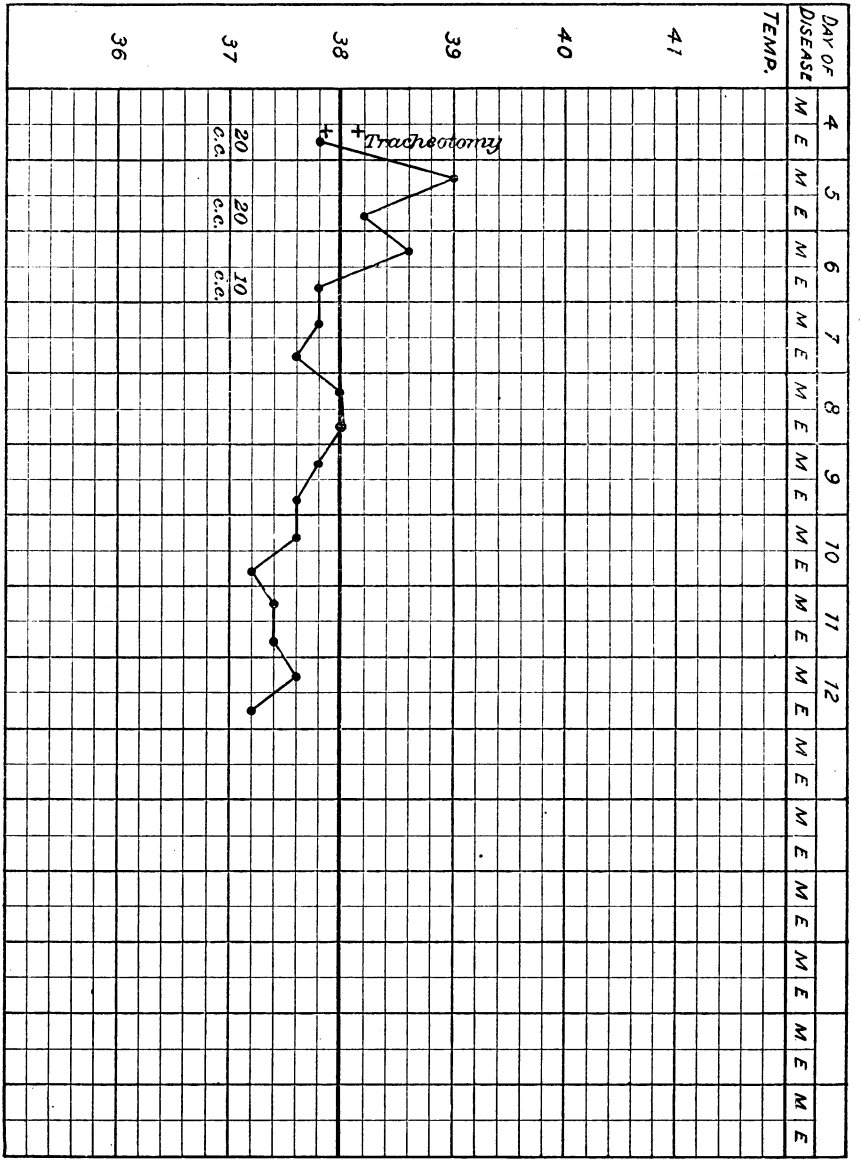
CASE XI. *Age 3½ years. Diphtheria—Tracheotomy.*



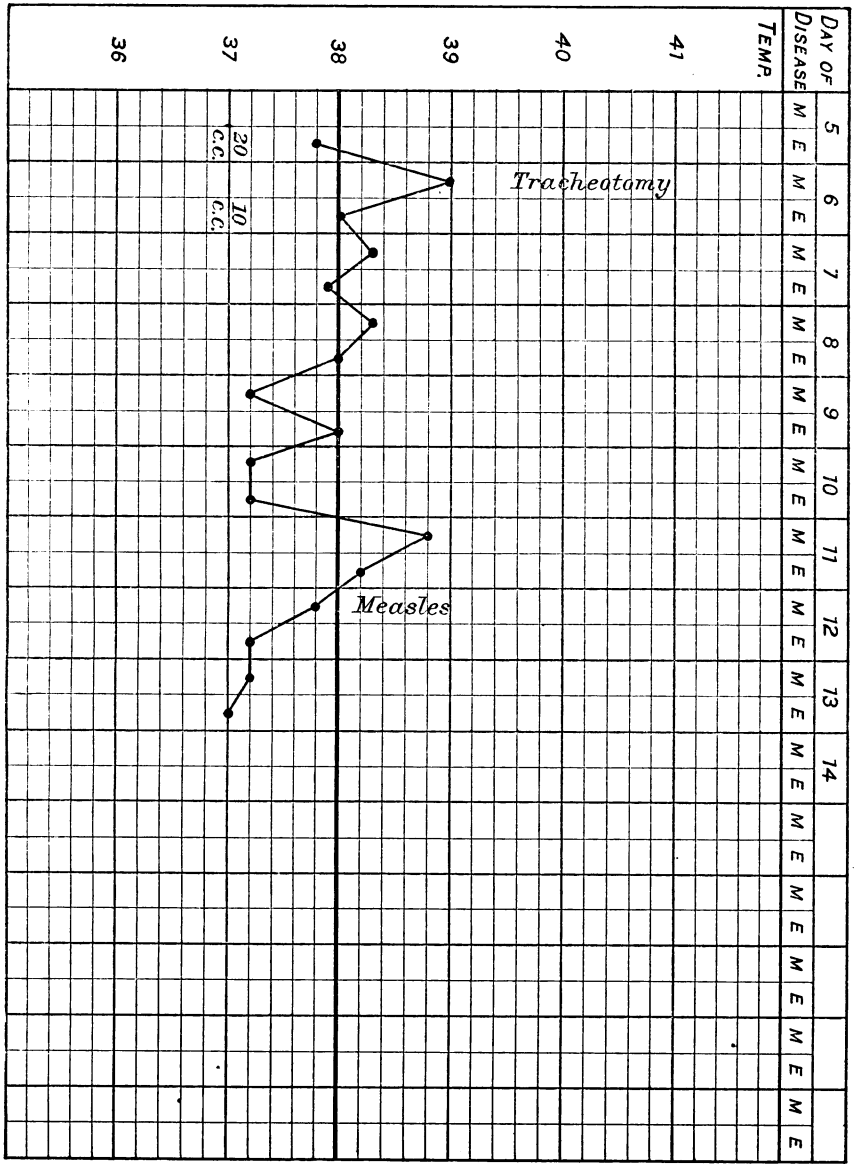
CASE XII. *Age 5½ years. Diphtheria associated with streptococcus—Tracheotomy.*



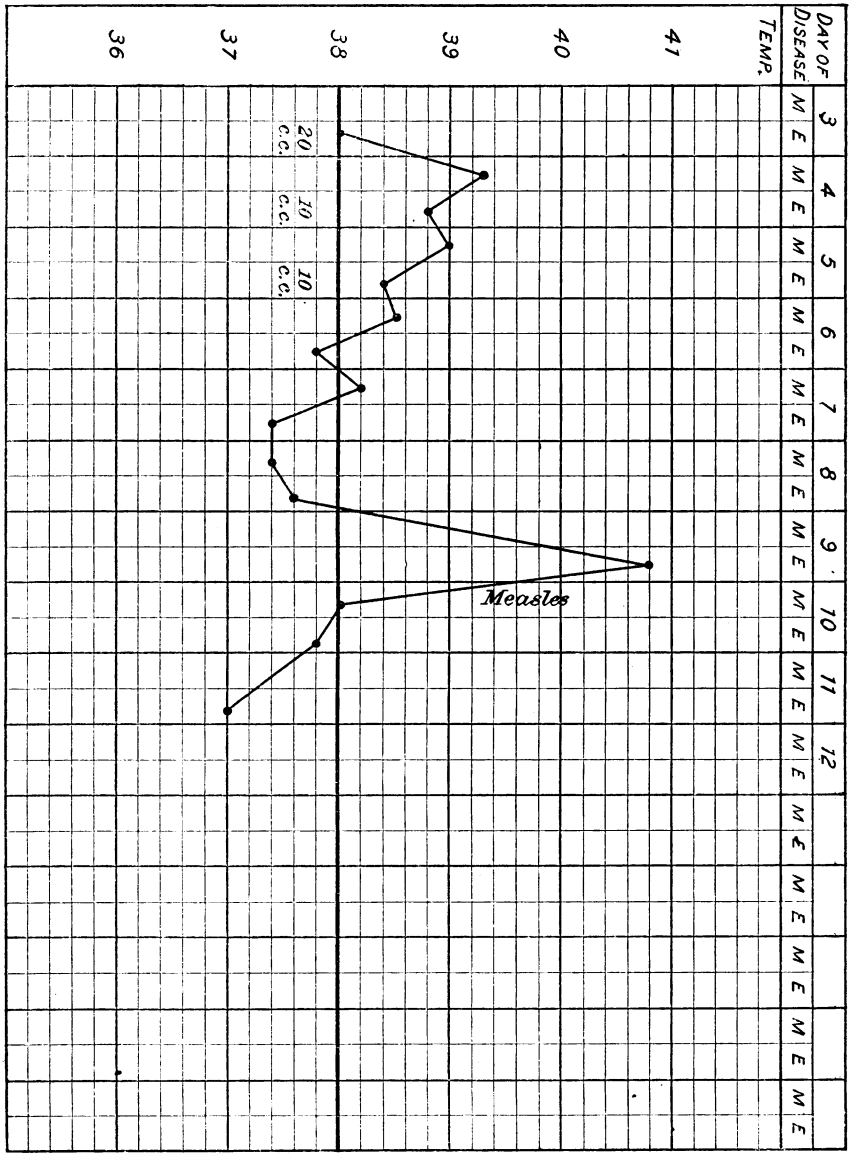
CASE XIII. *Age 3½ years. Diphtheria—Tracheotomy.*



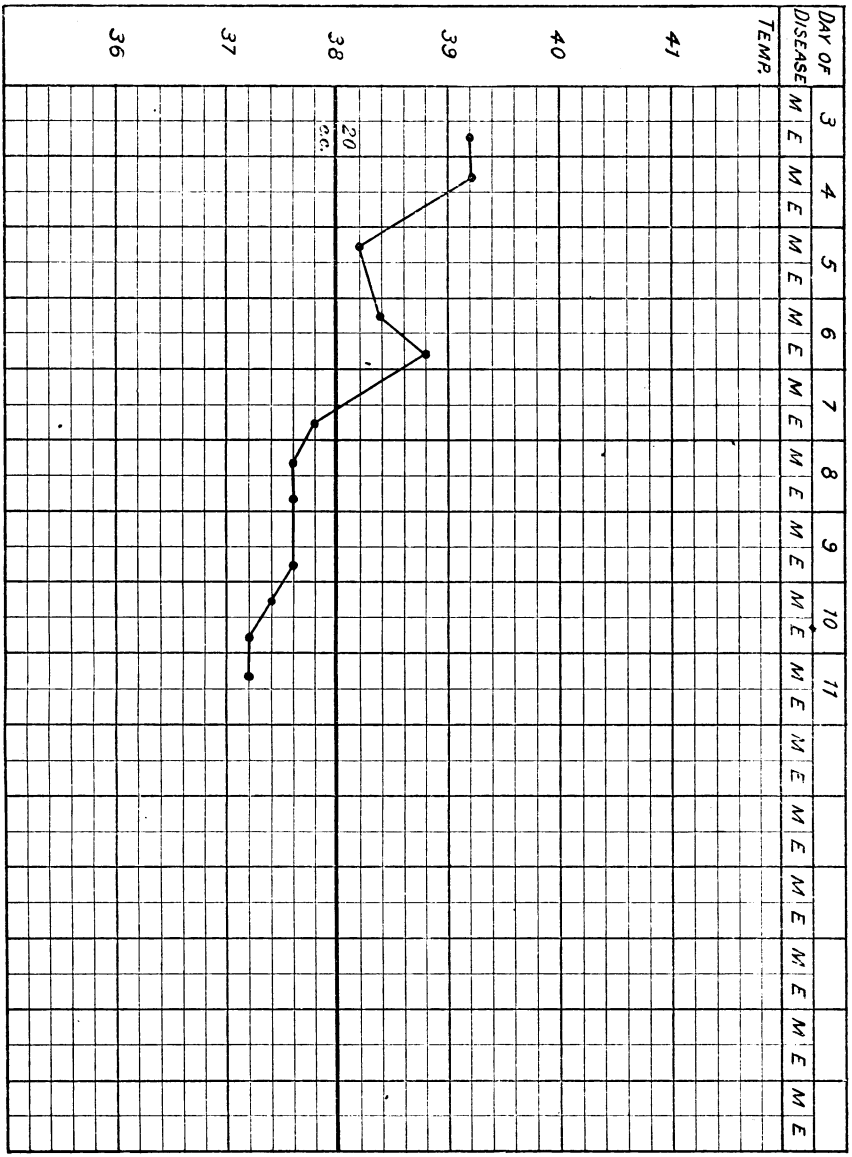
CASE XIV. *Age 4 years. Diphtheria—Tracheotomy.*



CASE XV. *Age 2½ years. Diphtheria—Tracheotomy.*

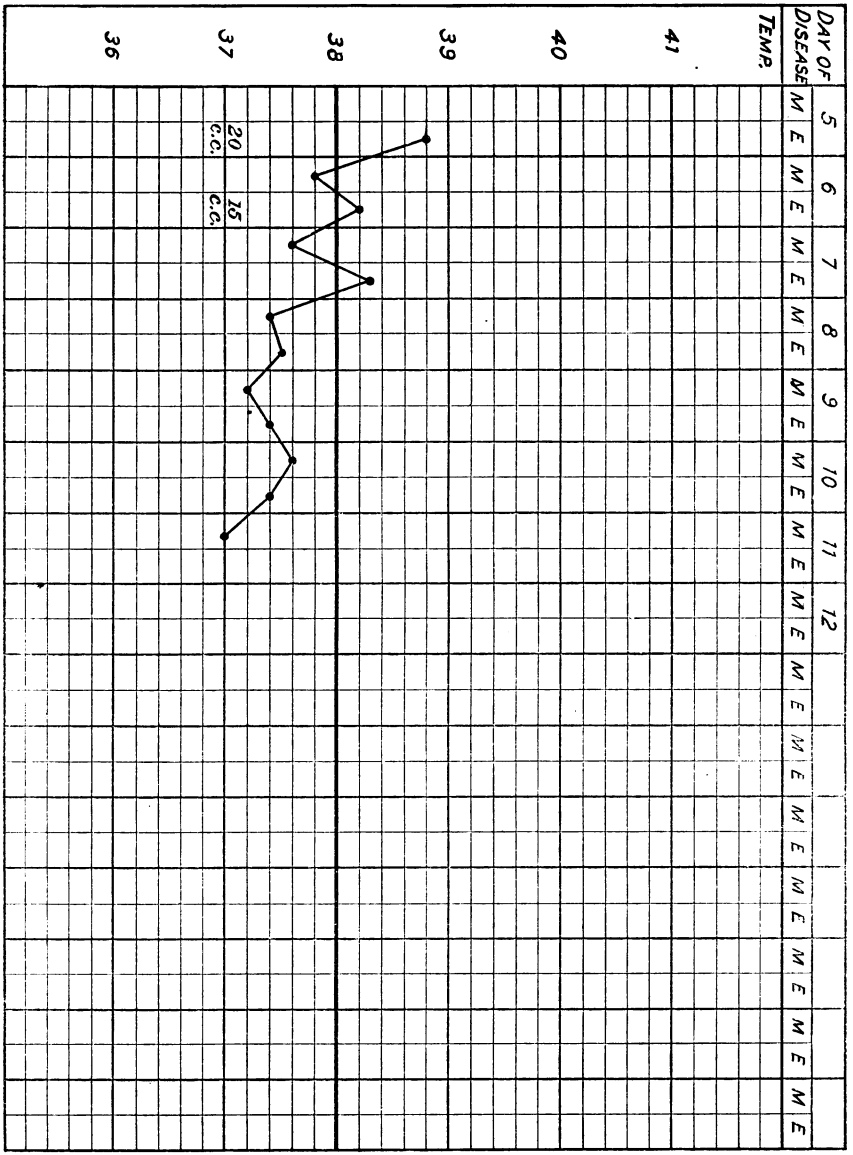


CASE XVI.* *Age 1 year. Not diphtheria—Simple angina.*

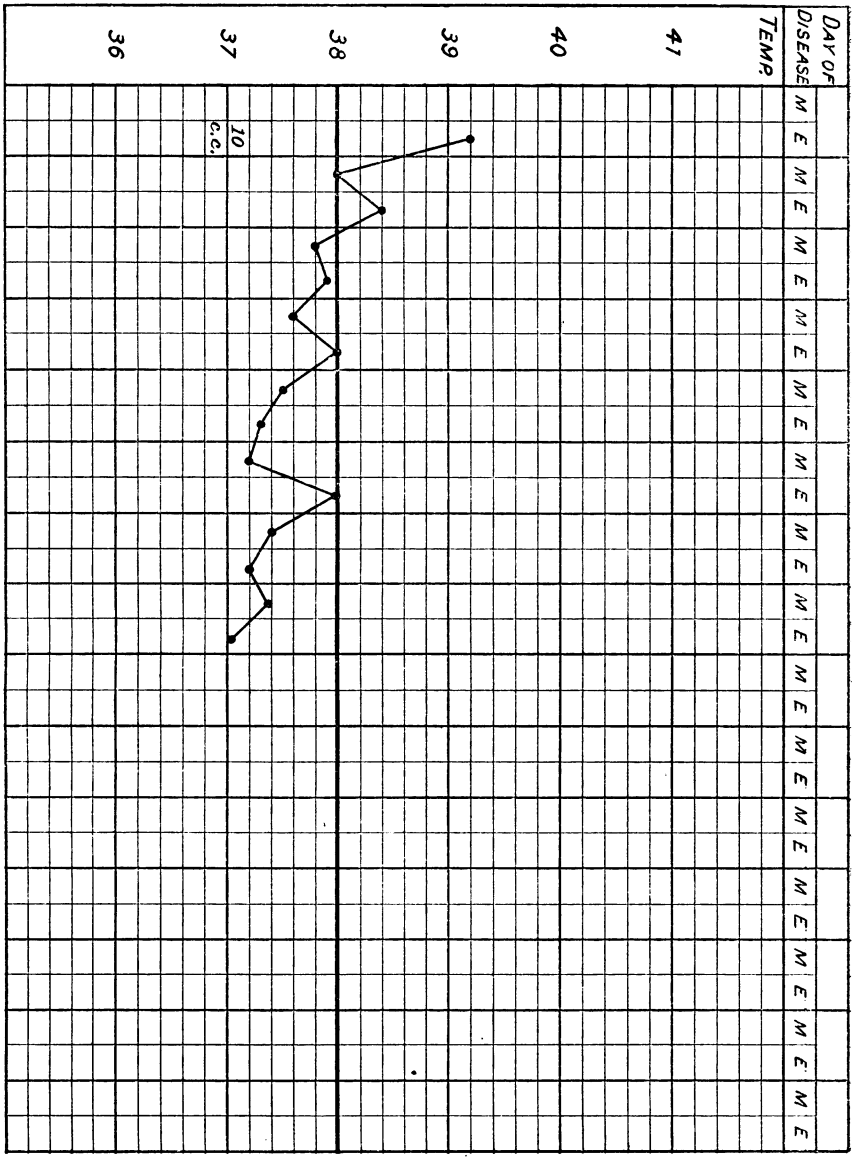


*This case was placed alongside another of the most virulent diphtheria, the same nurse ministering to the wants of both. No special precautions to prevent infection were taken.

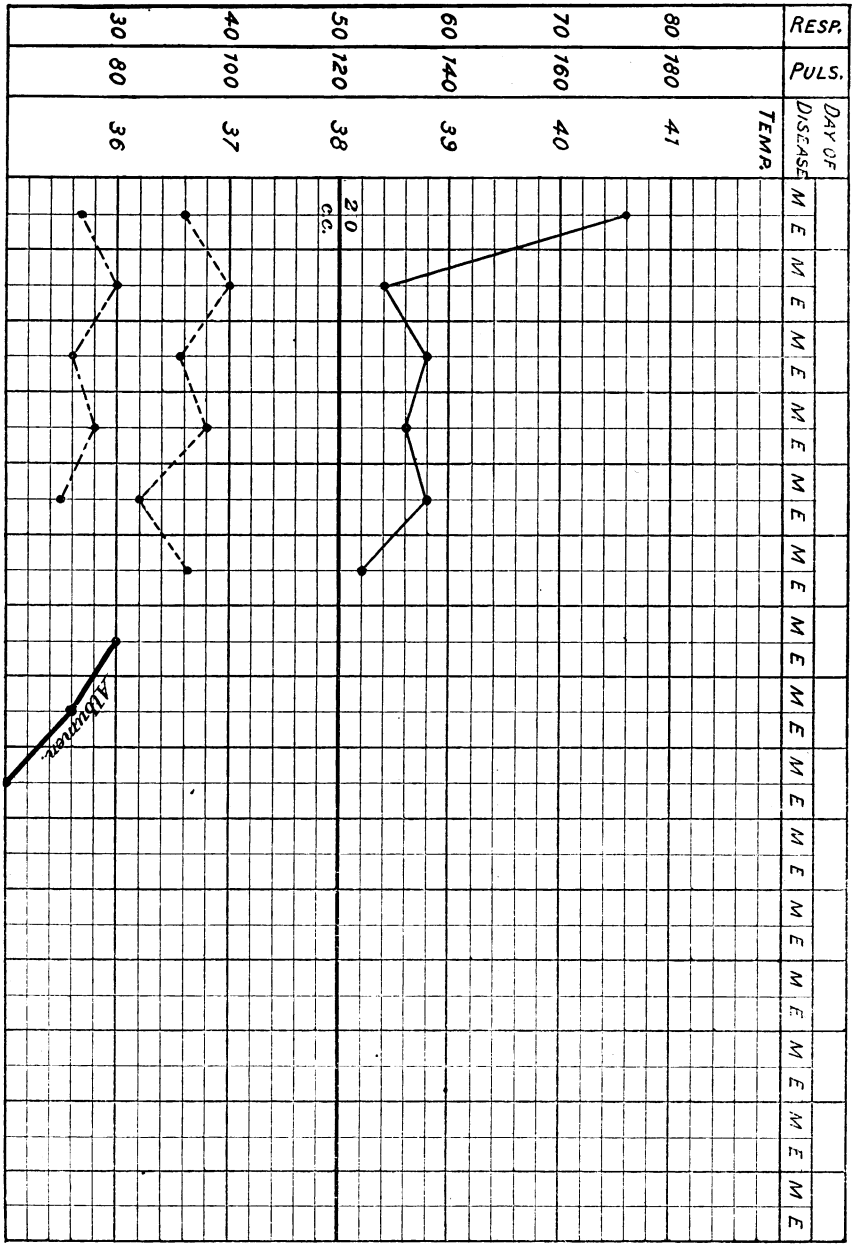
CASE XVII. *Age 3 years. Not diphtheria—Short bacilli found—Faucial exudate.*



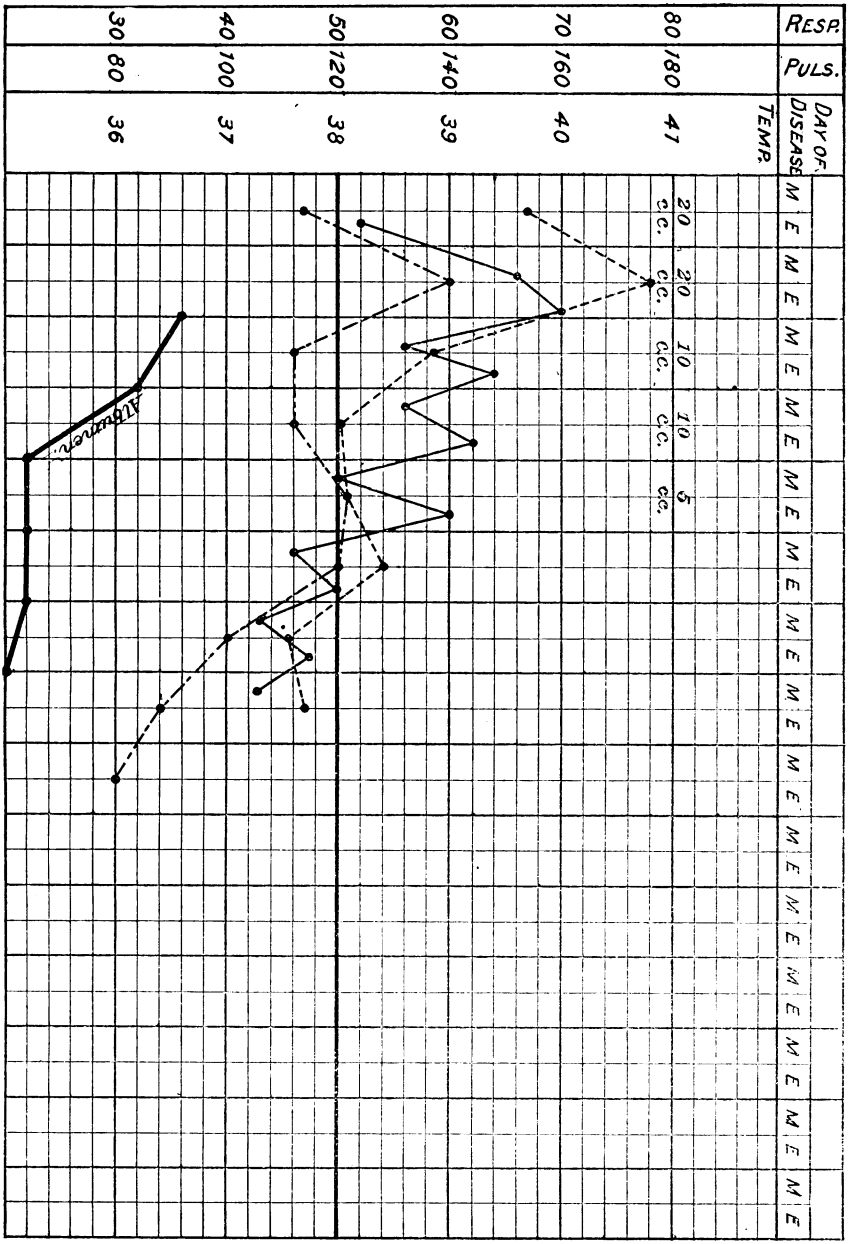
CASE XVIII. *Age 18 months. Not diphtheria.*



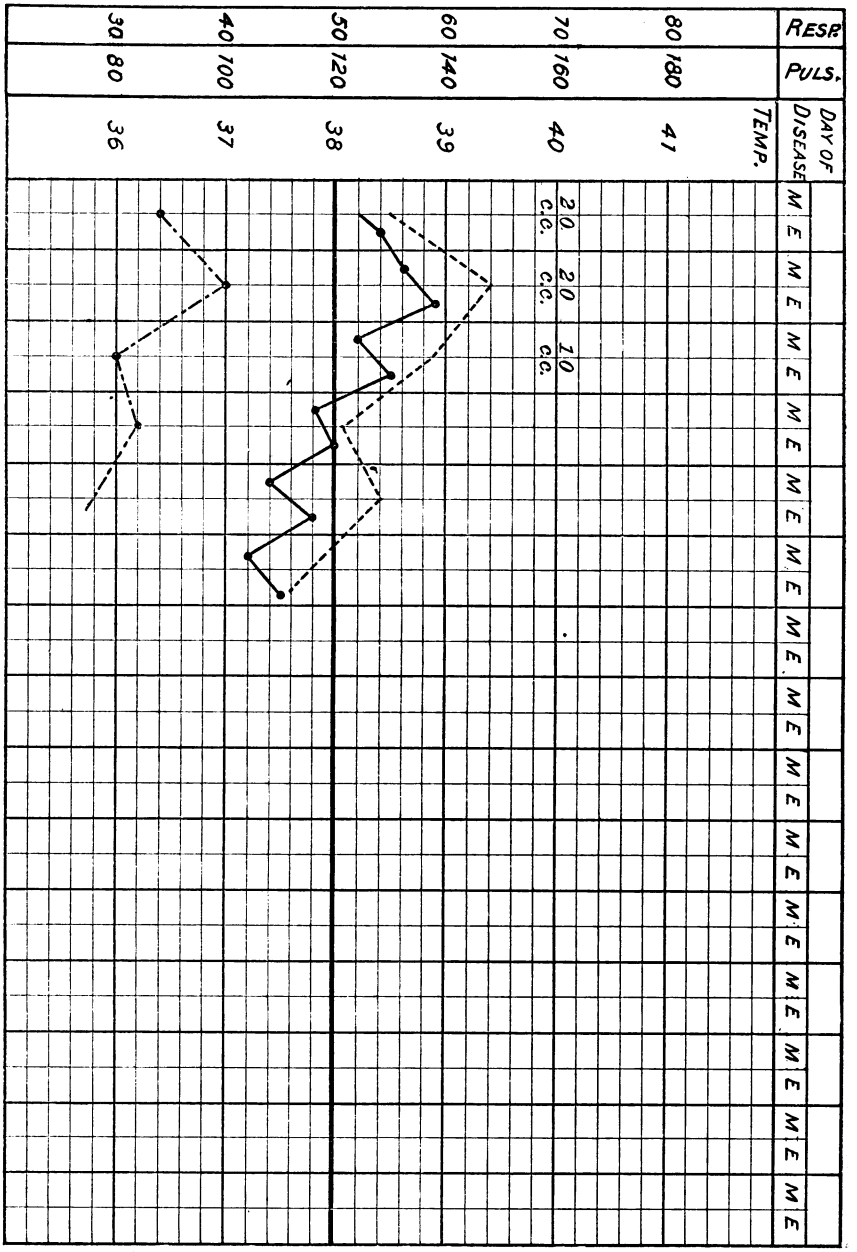
Diphtheria pure (chart given by Dr. Martin).



Diphtheria associated with streptococci (chart given by Dr. Martin).



Diphtheria pure—Tracheotomy (chart given by Dr. Martin).



BERLIN, *November 6, 1894.*

SIR: On completion of my observations in Paris on the serum therapy of diphtheria, I immediately set out for Berlin for the purpose of investigating this subject further. While at Budapest I met several gentlemen from Berlin, who had a more or less intimate knowledge of the mode of preparation of the antitoxine and of its uses in the treatment of diphtheria. It was asserted by some of these that the statistics of the treatment in Germany presented a better showing than those of Dr. Roux.

On my arrival I paid my respects to Professor Baginsky, who is the director of the Children's Hospital of Berlin. Here the larger proportion of the cases suffering from diphtheria are treated. Every facility was accorded by the director and his assistants to enable me to observe the cases and their treatment with the new remedy. There were about 35 cases at the time of my visit in the pavilion, in various stages of treatment, the daily admissions being from two to three. The age of the patients was usually less than 6 years, only a few between 7 and 8; so that in this respect it compared with those in the Paris hospitals.

The admission of a case to the diphtheria pavilion is marked with a great deal of care, and it is seldom, if ever, that a simple angina finds its way into the ward. To guard against this possibility there is what is known as the quarantine ward, where doubtful cases are sent until the diagnosis can be made. The same painstaking methods are in vogue here as in other German hospitals in the matter of clinical record and physical examination. As soon as the history has been obtained and a physical examination made, the treatment is mapped out accordingly. If there is the usual appearance of diphtheria present, i. e., an exudate, a direct examination is immediately made. In a considerable number of cases this examination suffices to establish the diagnosis. If the Klebs-Loeffler bacillus is found the case is immediately sent to the diphtheria ward; when this can not be done, a culture is at once made from the exudate or the throat, by means of coagulated blood serum, the patient in the meanwhile kept under observation in quarantine until the culture has developed sufficiently for examination. In the meantime, should the child show further symptoms of diphtheria, a routine course of treatment is prescribed. An injection of the antitoxine from 5 c. c. to 10 c. c. is given, the quantity administered being at least sufficient to immunize the patient. In some cases, where the diagnosis has been confirmed by culture methods and the microscope, no further treatment is found necessary.

When a patient is presented, having suffered from the disease for several days, and the unmistakable clinical signs, both local and constitutional, present themselves, no time is lost, the antitoxine being administered at once in the quantity deemed necessary. The methods of giving the injections and the time for their administration are much the same as here practiced by Drs. Roux and Martin. There can be no question raised against the diagnosis of every case, for nothing is called diphtheria unless the Klebs-Loeffler bacillus is found. Not sufficient importance so far has been attached to those cases of diphtheria wherein there is a mixed infection, the treatment of all forms being about the same. In saying this I do not wish to convey the idea that all cases are given one and the same dosage, but that the antitoxine is administered in such quantities as is indicated by the symptoms of the case.

The death rate is slightly lower than the figures of the Paris hospitals—cases as published by Katz. The mortality was 16.5 per cent. This has

been still further reduced in the cases treated from August 1 until now, it being about 14 per cent. I have taken pains to inquire the reason of the apparent difference in the statistics of Roux and of these, and have, I believe, found a satisfactory solution.

In the first place, the patients, as a rule, are sent to the hospital sooner; the treatment, therefore, is commenced earlier. The next and of equal importance is that the little patients receive here better care than is accorded them in like institutions in Paris. I must state here in justice to Professor Roux and Dr. Martin that they are in no way responsible for the care of the diphtheria patients. This is vested in an entirely separate and distinct body; their control of the cases is limited to the antitoxine treatment only. I know from both that they would have it otherwise if it were in their power. Now, since they have revolutionized the treatment, it is quite certain they will do so. The care of the patients is excellent here, and could hardly be improved upon for this class of cases. They are comfortable and well looked after by a corps of trained assistants and nurses. These two features are responsible for the better statistics. The antitoxine has been used in this hospital since June last, the first being obtained from Dr. Aronson, of Schering & Co., and has been continued by Behring's antitoxine during the summer. For about six weeks none of the cases were given the remedy; the supply was well nigh exhausted, some of the horses under the process of immunization having died and the finances of the hospital being in such a state that the antitoxine could not be purchased. The treatment, therefore, was from necessity interrupted.

I have referred to the general treatment of the patients, and it might be well to state here in a general way what it is and how carried out.

The pavilion for diphtheria is well arranged for the treatment of infectious diseases. The general ward features are wanting. There are instead quite a number of rooms of various sizes, in order to carry out a more complete system of segregation or of isolation, according to the character and gravity of the malady. The cases are classified according to the gravity of the disease; a malignant case is invariably isolated. There is also provision made for the care and treatment of diphtheria associated with the exanthems. So perfect is the system that it is of rare occurrence to have an outbreak in the ward from these latter diseases. The convalescents (save those from eruptive diseases) are kept together in a large ward. A liberal regimen of diet is prescribed and given to every case according to its requirements.

Local applications to the affected parts are still used, but only those agents which have the least irritating effect upon the mucous membrane are now used. Strong solutions of mercuric bichloride, carbolic acid, and the like, have been abandoned. This is especially insisted upon in cases where tracheotomy has been performed. In these cases (tracheotomies) Professor Baginsky thinks that moistened air is essential, not only for the comfort of the patient, but is of great value as a medicament. Facilities are at hand in every room to supply the steam spray with or without these other agents. Tracheotomy is fast becoming a rarity, intubation taking its place in the majority of the cases where tracheotomy was formerly indicated.

The surgical treatment of the tracheotomy cases also deserves mention. Great care is exercised to keep not only the wound but the mucous membrane of the mouth and nose as free as possible from pyogenic infection. Experience has taught them that the subsequent infection by pus micro-organisms is a serious complication.

The method of administering the serum does not differ from an ordinary hypodermatic injection. It is given by means of a large syringe (holding 10 c. c.) on the outer aspect of the thigh, the skin at the site of the injection having been previously disinfected. After the injection the point of puncture is closed with idoformized collodion. The amount injected of course depends upon the body weight, on the gravity of the disease, the pulse, respiration, and temperature being also valuable guides. The dosage is 10 c. c., only one-half the quantity as used by Roux. Behring's antitoxine is put on the market in three strengths, graduated upon a scale of immunity units. Aronson's (Schering & Co.) serum is supplied in one strength, which is claimed by Aronson to be stronger by seven times than Behring's serum known as "No. 1."

Behring has demonstrated that when this antitoxine is present in the blood of an animal in a certain proportion it will be immune to a virulent culture of the bacillus diphtheriæ. Thus a guinea pig having $\frac{1}{20}$ c. c. to the 500 grams will be immune. The antitoxine of Behring is put up in three strengths, 1°, 1 to 600; 2°, 1 to 1000; and 3°, 1 to 1500, i. e., the first strength has 60 immunizing units to each c. c., the second has 100 immunizing units, and the third 150 to each c. c. The antitoxine which Aronson has made is only one strength, which has, judging from its effects, the same potential unit as Behring's "No. 2" (1 to 1000).

The above strengths or immunity units are taken as a guide for administration. For instance, a healthy child of medium size is rendered immune by 10 c. c. of Behring's antitoxine, No. 1 (1 to 600), only 5 c. c. of Aronson's antitoxine. For cases of diphtheria the full dose of Behring's No. 2 (1 to 1,000), or that of Aronson, is given. If the child is large, weighing as much as 40 kilos, the quantity of either is proportionally increased. In very grave cases the initial dose should be large—frequently 30 c. c. is given and repeated at short intervals.

So far not much importance has been attached to the mixed infection; diphtheria with streptococci or staphylococci, or both, the symptoms in general being taken as a guide for the character of the treatment. While the majority of the cases coming under my observation were treated with Behring's antitoxine, a considerable number were also treated with Aronson's antitoxine, sufficient in number for comparison. The results, clinically, were, so far as I could see, identical; the class of cases, their gravity, dosage, general medication, etc., were in all respects similar.

I have neglected to make mention of the fact that Behring's serum No. 1 (1 to 600) is primarily intended by him to be used for immunization. This does not preclude its use for treating cases of the disease, only that a quantity must be used which equals in immunizing units that of the stronger; that is to say, one must use of "No. 1" (1 to 600) 16.6 c. c. to correspond in strength to the "No. 2" (1 to 1000). I can not see the utility in these three strengths as advocated by Behring, when his No. 2 answers every requirement, and when, by increasing or diminishing the dosage, the same results can be obtained, which is a far simpler procedure for the practitioner to follow than to remember all the details concerning the strength, dosage, indications, etc., for each strength of antitoxine. Behring no doubt is quite right from a scientific point of view. But is it a practical one? I like the method indicated by Roux much better than that of the German school, because of its simplicity and directness. The treatment of diphtheria with antitoxine has now been practiced here for over five months, excepting the few weeks when the antitoxine could not be had.

From the very commencement these results have been as remarkable as I have before mentioned about the treatment in Paris, from month to month the mortality has been growing less and less. The same story can be repeated with reference to the tracheotomies, the whole offering an array of facts which are to me indisputable. To emphasize more forcibly than I could do otherwise, I wish to refer to the time, during August and a part of September, when the treatment was suspended. During these six weeks it became necessary to perform 37 tracheotomies, with a result of 5 recoveries and 32 deaths. The mortality was so great that Professor Baginsky made an appeal to the public through the daily press for sufficient money to purchase the antitoxine. On recommencement of the treatment the same results were obtained as before, and during the ensuing six weeks there were only 8 tracheotomies, with 4 deaths. The results speak for themselves. Professor Baginsky thinks that if the cases could be seen during the first forty-eight hours of the attack, seldom, if ever, would recourse be had to tracheotomy, and the greater number, if not all, might be saved.

Through the kindness of Professors Koch and Erlich I was accorded the full privileges of the Institute for Infectious Diseases and of the hospital wards under their direction, where abundant opportunities were given me to observe their laboratory work, as well as the cases of diphtheria under treatment with the antitoxine. At present Drs. Erlich and Wasserman are pursuing their investigations on the subject of the toxines and antitoxines, making therein a full and exhaustive inquiry. Here I witnessed their methods of preparing the toxines for immunization of animals. These methods are identical with those of Behring, both in the growth of the cultures and their subsequent treatment. A number of Florentine flasks are half filled with alkaline peptone bouillon and then sterilized. Soon thereafter they are inoculated with a fresh virulent culture of the bacillus diphtheriæ, and then placed in the thermostat and kept at a temperature of 37° C. and after about three weeks the cultures are killed by the addition of iodine trichloride, or by carbolic acid. After standing from twelve to eighteen hours the toxine is tested as to its strength. Several guinea pigs of about 500 grams weight are given doses of this toxine, commencing with $\frac{1}{10}$ c. c. and increasing to $\frac{5}{10}$ c. c. If none of the doses of the toxine kill the animal within thirty-six hours, they are discarded and other flasks tried until one is found having the desired strength.

It is a curious fact, which I have noticed, that there is such a variability of the cultures in the quantity of the toxines. Erlich informed me that it was frequently the case that out of a dozen flasks of bouillon cultures grown under identical conditions he would find only one would possess the requisite strength. So far this variability has not been accounted for.

The immunization of animals is accomplished in the same manner as in Paris, commencing with a small dose ($\frac{1}{2}$ c. c.) and gradually increasing until a tolerance for large doses is established. From time to time a small quantity of blood is withdrawn, the serum collected and tested for the antitoxine. It requires from five to seven months to immune a horse after this manner—much longer than is taken by Roux. A horse is subcutaneously injected with the toxines containing the dead bacilli. This method is, in my opinion, open to serious objections, for sometimes an abscess is caused at the point of the injection. To have this accident supervene stops for a considerable time the process of immunization and renders it very awkward if you are in a hurry to produce the antitoxine. As the method of filtering the cultures through

unglazed porcelain appears to do away with these objections, I am at a loss to understand why it is not practiced here as in Paris.

Aside from the immunization of horses and goats for the antitoxine, Erlich and Wasserman are still continuing their experiments in immunization of cows, with special reference to the antitoxines given off in the milk.

The same results have been obtained here with regard to the antitoxine in the milk and blood, as stated by Roux. It is quite difficult to bring about a tolerance to the toxines in the cow, and even when this is established the serum is quite weak in antitoxic properties.

It has also been demonstrated here and in Paris that the stronger antitoxine of Behring and of Roux 1 to 1500 and 1 to 100000, respectively, are very difficult to obtain. It requires a much longer time to immunize the animal—usually not under eight or nine months—and not only is it tedious, but attended with risk. There is a certain limit of tolerance of the horse to the toxines, just as is shown in the guinea pig or goat to the cholera spirillum. In these latter a certain tolerance can be established and maintained for a considerable period, whereas if attempts be made to go beyond this the animals succumb, that is to say, you break down the barriers which you have with great difficulty erected, and disaster results.

Professor Roux stated to me that a serum could be procured from a horse in two and a half months having all the properties of a stronger serum, which, even if the dose is larger, should be taken into consideration at a time when it might be desirable to supply all who require it. It was true that a stronger serum could be prepared, but the time required is at least twice as long, not taking into consideration the fact that in doing so you might kill the horse. The importance of supplying a serum which will cure diphtheria is paramount; the quicker this is done the more lives will be saved. A criticism of this character may be made against the time it requires the Germans to produce the serum, but the fiat has gone forth that the serum shall be of 10 c. c. doses, and thus it is so: When a horse has been brought under the influence sufficiently the blood is withdrawn from the jugular vein by means of a special trocar and canula and collected in sterilized jars. When the serum separates from the clots it is pipetted off and transferred to sterilized flasks. A small amount of chloroform water is added to prevent deterioration as well as decomposition. It is then filtered through an unglazed porcelain filter and transferred to the 10 c. c. flasks, when it is ready for distribution. Full directions for the administration accompany each flask.

Diphtheria is treated in the annex to the institute—the Hospital for Infectious Diseases. Here two wards have been set apart for this purpose. The cases under treatment are under the direction and supervision of Professors Koch, Brieger, and Erlich. Dr. Kossel, the efficient and obliging assistant, has charge of the cases and makes all the injections. On admission of the patient a careful physical examination is made, supplemented, when possible, with a direct microscopical examination from the exudate, if present, or from the secretions. The main reliance, however, is placed upon the culture method and subsequent examination of the colonies of bacteria for the bacillus diphtheriæ. I was surprised to see that these examinations were made by the old plate method, using ordinary peptone agar instead of the blood serum. "Plates" of agar are poured in sterilized Petri dishes, and then the surface gently streaked over with the platinum or spatula needle, which has been brought in contact with the suspected exudate

or the secretions. In from eighteen to twenty-four hours the colonies develop sufficiently to make the diagnosis certain. The method is one which gives good results, but is much slower and far more tedious than the use of the blood serum.

During my two weeks' stay it was my good fortune to see thirty cures. Just before my arrival a change had been made in the Chanté Hospital, which has also a service for infectious diseases. On account of certain repairs to the lazaretto of this hospital, all these cases were for the time being sent over to Professor Koch. The condition of the patients on their admission compared favorably with those seen in the service of Professor Baginsky. The treatment here differed in some respects from that followed by Baginsky. So far as the hygienic conditions were concerned, there was no difference. The difference lay in the therapeusis. Aside from a proper regimen and good nursing, no topical applications are made to the throat, nor was there any attempt at internal medication, the antitoxine of Behring being their main reliance. It was the desire of Koch as well as his colleagues to make a scientific test of the remedy, to determine its actual value in these cases without possibility of error. The cures here are classified according to the following: Diphtheria (pure), first to fourth day of duration; diphtheria with toxæmia; diphtheria (mixed infection) with streptococci and staphylococci.

The little patient on admission is given the same careful physical examination, and whenever it is possible a diagnosis is attempted by a direct examination. If the result is in any way unsatisfactory, agar plate cultures are made from the exudate or secretions, the usual methods being brought into requisition. In the meantime a dose of the antitoxine serum is immediately given, the quantity depending upon the size of the child and the clinical appearances, usually a large dose, not less than 10 c. c. to 16 kilos weight, or even this quantity to a smaller should the constitutional symptoms appear to warrant it. The subsequent treatment of the case will largely depend upon the result of the bacteriological examination. The classification above referred to has been in practice for a short time only, beginning, I think, in August, soon after Roux's announcement of the importance of the recognition of the double infection. As these cases require a much more vigorous treatment than if they were pure diphtheria, it is now accepted here that Dr. Roux's conclusions are correct. The treatment now practiced is on the lines as laid down by him. Since the adoption of his methods of treatment there has been quite a different result than formerly; there are less pulmonary complications and more of the patients get well. Further than this, there is a shorter convalescence.

The method of administering the serum is the same as that practiced by Baginsky, the site selected for the injection being the outer portion of the thigh. It is given by means of the Koch syringe, having a large canula. The injections are made under strict aseptic precautions, and on the withdrawal of the canula the puncture is closed by iodoformized collodion. The antitoxine now used in the pavilions is what is known as No. 2, 10 c. c., having a strength of 1 to 1000. Seldom, if ever, the weaker serum is used, and if used it is for immunization only. The strongest, 1 to 1500, is used only in the very severe cases, especially those in which the disease has existed for several days, toxæmia supervening, or in those of double infection. In both these, and especially the latter, it is necessary that the system be rapidly brought under the influence of the antitoxine, to neutralize as quickly as possible the toxines in the system, in order to allow nature to assert itself and reestablish an equilibrium. Kossel has observed this in quite a number of cases

where there was double infection, especially of diphtheria and streptococci. If the toxines of diphtheria are quickly neutralized, nature is able to assert itself and throw off the effects of the other organism. The normal or remaining resistance may be sufficient for one of those poisons, but not for both. The dosage depends largely upon the case. In some, one dose will be found sufficient to bring about a recovery. These cases are those which have been affected for a short time, under four days. When the disease has existed longer, or is one of those very malignant cases from the onset, larger and more frequent doses must be given if it is hoped to accomplish anything.

About twelve hours after giving an injection of the antitoxine there is a rise of about a degree in the body temperature; this is known as the reactionary fever. In nearly all the cases which have come under my observation there is this rise in the temperature. It may be taken as a good guide to the character of the malady. In cases of simple angina it also occurs, but is not the rule. This reactionary temperature is observed in all three sets of cases treated by Roux's, Aronson's, and Behring's serum, respectively. The temperature charts sent with my previous letter will demonstrate this point.

The effect of the antitoxine upon the false membrane of diphtheria is quite characteristic. As a rule, on the third or fourth, and in many as early as the second day of treatment, the œdema and redness around the false membrane, disappear, the membrane itself becomes softened at its periphery, becoming in a short time either detached or absorbed. The false membrane, when caused by the double infection, disappears much more slowly. Those caused by streptococci are not influenced in any appreciable way by the antitoxine. Complications such as bronchitis, pneumonia, and abscesses are infrequent—a marked contrast with former years.

Intubation is practiced here the same as in Baginsky's hospital. A few cases were thus operated upon during my stay. Three tracheotomies (one false, not diphtheria) were all I saw, these latter becoming less frequent as the treatment progresses. The mortality from all classes of cases since August to the present time (November 6) was slightly above 16 per cent. The larger number of the casualties were from those cases in which the disease had existed for several days, death resulting from toxæmia or pneumonia.

In those cases which are sent into the hospital during the first days of the attack (not later than the fourth day) the mortality was slightly over 12 per cent. It is believed by Kossel and others that even a better showing than this can be made if the cases can be under treatment earlier than the fourth day.

Behring's antitoxine is made in Hoest on the Main by the large aniline color works of that place. The work is under the direction of Dr. H. Knorr, the son of the discoverer of antipyrin. At this time the firm has thirty-five horses immuned, and are sending out considerable quantities of the serum. It was my intention to go to Hoest on the Main, but when I found that the process of the preparation was the same here as there, I decided to see as much of the clinical side as possible, and so remained here.

Through the courtesy of Dr. Ditmar, the director of the Schering Chemical Factory, I was also accorded the privilege of visiting their place to observe the methods employed by Dr. Aronson in obtaining the antitoxine, some of which I had seen used in the hospital wards.

At one of their factories near Berlin the firm has a well-equipped bacteriological laboratory for producing the toxines and preparing the

serum. Near by they have well-arranged stables and paddocks for the animals. At this time they have 70 horses, 30 sheep, and a number of goats in various stages of treatment. At first I was told that as a trial venture only a few horses were immunized, and from these considerable antitoxine was obtained. During the summer some of these died, and the work was interrupted. They hoped that they would be able to supply the serum on and after December 1.

The work as carried out by Dr. Aronson and his assistants compares favorably with any which I have seen in Berlin. He has all the necessary appliances in his laboratory, possessing the requisite knowledge and training in this special branch. Being provided with the facilities for good work, I see no reason why he can not produce as good serum as any others here. In some of the technique I am inclined to believe it is better than that practiced by those in the institute, i. e., in the preparation of the serum. Aronson adds a small quantity of trikresol to the serum—0.4 to 0.6 per cent. This causes a slight flocculent precipitate, which is filtered off, and then the serum is passed through an unglazed porcelain filter, when it is transferred into small sterilized bottles and sent out for use.

He has also discovered how the antitoxine can be precipitated from the serum and preserved indefinitely (?). A saturated solution of aluminum sulphate throws down a large precipitate; this is separated and dissolved out from the alumina by the addition of a 0.1 per cent solution of soda; it is then dried at ordinary temperatures in vacuo. When prepared in this manner it can, it is claimed, be preserved in hot climates without deterioration. There is the same drawback as with the inspissated serum—it causes a considerable amount of irritation.

The time required for immunizing the animals is the same as by Behring.

Aronson has not attempted to make more than one strength of the antitoxine. That which I saw used in the hospital had the same effects as Behring's (1 to 1000.) He (Aronson) claims to produce a stronger serum than Behring's. This I can not confirm.

I have just learned that the friends and supporters of Behring have resented the intrusion of Schering & Co. upon the field, and not a few are trying to throw discredit upon the latter by statements that the serum had not the same unit of strength as had been prescribed by Behring.

On Saturday last (November 4) Professor Koch convened a meeting of the Prussian board of health for the purpose of determining what action was necessary to be taken by that body in regard to the control or supervision of the use of the antitoxine. I had been told by Professor Koch a few days before this that he thought that there should be some Government supervision of the serum, so that the serum could always be relied upon. If there was no such supervision, it would not be long before spurious articles would be put on the market, and not only a good remedy would be brought into disrepute, but that lives would be sacrificed when they might be saved. It was decided at the meeting of the board (Behring being present) that all serum intended for use in Prussia should be inspected at the institute, and tested for its purity and strength before it would be allowed to be used. This step, I learn, was satisfactory to all the parties concerned, and will be the means of insuring a good article of standard strength at all times for Prussia.

In this connection I would like to call attention to what will evidently ensue in our country. Many persons will, during the ensuing year, commence to prepare the serum as a business enterprise, and there will,

without doubt, be many worthless articles called antitoxine thrown upon the market. All the serum intended for sale should be made or tested by competent persons. The testing, in fact, should be done by disinterested parties. The danger with us is perhaps greater than could exist here under any circumstances. An unfortunate wrangle has sprung up between Professor Virchow and Dr. Behring over a statement made by the former that the efficacy of the so-called antitoxine in diphtheria was still in doubt, and he for one could not accept all that was said in its favor. This angered Dr. Behring to such an extent that he made a very caustic rejoinder. This aroused Professor Virchow's friends, who came to the rescue, as well as those of Behring, and no little ill feeling has arisen between the two factions. The general sentiment among those who really know anything about the antitoxine is now, however, one of kindly feeling for the distinguished old man who has deservedly won so many laurels too many, in fact, as they have now become a burden.

An eminent professor, speaking of the criticisms which some were making against this new remedy, attributed the cause of this feeling to tuberculin, and expressed it in the following: "Oh! this unfortunate tuberculin! Not only has it poisoned men's bodies but also their minds! Would they only come and see and not criticise a remedy before they know." I am fully satisfied in my own mind that if those who doubt the efficacy of the remedy, as I first did, would go and not only see, but carefully examine the cases and study them, there would be no longer a question as to its value.

The antitoxine will never work miracles; it has its limit like any other agent, and like a perfect piece of machinery will not accomplish the full result unless directed by a skilled hand. Some persons affected with this dread disease will succumb, it matters not how soon we apply the remedy. The majority will, however, I am sure, recover if the antitoxine is given early and properly.

In closing this letter I will state that, so far as my clinical observation goes, the antitoxine prepared by Roux and Martin is the same in its effect as that of Behring and Aronson, and compares favorably with both. The remedy should be satisfactory to the medical profession. It will, of course, fall short of fulfilling all the requirements demanded by the laity. It is to be hoped that soon every State and municipality will take the proper steps to provide facilities to supply the remedy to the people, and by a judicious and timely use be able to stamp out this terrible scourge, which carries off so many thousands, rendering desolate so many homes.

Respectfully, yours,

J. J. KINYOUN,
Passed Assistant Surgeon, M. H. S.

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The prevention of diphtheria.

By J. J. KINYOUN, M. D., *Passed Assistant Surgeon, M. H. S.*

[Read before the Medical Society, District of Columbia, March, 1894.]

It is not the intention in this short paper to attempt to give a résumé of the etiology and pathology of diphtheria, but to consider these only so far as they bear directly upon the prevention, and control the spread, of the disease.

From time immemorial attention has been called to the infectiousness of this malady, which, under favorable conditions, assumed epidemic proportions. Its cause, enveloped in obscurity, became the subject for theories and speculations, which continued until only a few years ago, when the etiology of the disease was announced by Klebs and Loeffler.

These investigators, after a careful study of several epidemics of diphtheria, asserted that the malady could be attributed to a micro-organism which was constantly found in the pathological process.

The announcement of the specific bacterial infection did not bring about a ready acceptance of belief in this important discovery, but it was subjected to the most searching examination and severest criticism, as was that of the cause of tuberculosis soon after Koch announced it in 1882. Following in the footsteps of these investigators during the past decade are the foremost scientists of Europe and America, and the fruits of their labors are now on record. These data are replete with corroboration of their statements and with much information relative to its etiology and pathology, from all of which important and valuable lessons may be learned.

It is one of the cardinal principles in the practice of medicine to establish a diagnosis before commencing treatment. Until this is accomplished our attitude must necessarily be tentative. Rational therapeutics is just in proportion to our knowledge of the cause of the disease, and as rapidly as advances are made in their etiology, so much is accomplished in removing medicine from the domain of speculation and placing it among the positive sciences. Upon these views rest all the measures for the prevention of disease, and no better exemplification of this fact and the principles involved can be shown than in the practical application of our knowledge of the cause of disease in the quarantine practices of to-day as compared with those of hardly a decade ago.

In the domain of surgery results have been equally as brilliant in demonstrating the effect of accurate knowledge.

The same degree of skill and acumen are not so essential in determining the true character of an infectious or contagious malady after the occurrence of several cases, either in a group or seriatim.

It is always in the first cases where the diagnosis may be obscure or in doubt. These are by far the most important of all, and it stands to reason that they should be detected at the earliest moment possible, because each one of such cases represents a focus from which the disease may spread.

This is especially true of that class of diseases termed the minor infectious or contagious—diphtheria and the acute exanthemata of childhood. While some of the above class do not usually present as high a death rate as others, it does not follow that the effects of one or all should be lightly regarded because they are the concomitants of early life.

We have no right as parents or citizens to maintain two standards of excellence—one for ourselves (adults) and one for the children—any more than that the rich when sick require a different course of treatment from the poor. Nor should we incur a risk for our children which we, all things equal, are timorous to assume.

Take, for an example, our attitude against the major infectious and contagious diseases, cholera or yellow fever. Mark the interest we take in the simple fact that cholera is in Europe or yellow fever in Havana, the speculations indulged in as to the probabilities of the spread, and the possibilities of their introduction into this country; and if, perchance, one of these should effect a foothold, even by a few cases, our interest then becomes intense, even verging on the border line of panic. We then can fully appreciate the danger to ourselves, and are willing to do anything possible or impossible to prevent the scourge from spreading. We call for large appropriations to carry on a sanitary warfare. We demand superhuman endeavors, and that every means shall be employed to prevent their spread. And yet, when we take into consideration the number of deaths occurring in one of the epidemics from one of these, or the mortality in aggregate, and compare it with the annual mortality from the minor infectious class, they pale in significance!

When we are confronted with an array of facts as set forth by statistics, they are far more convincing than argument. They should in themselves be a sufficient stimulus to awaken an interest in the most apathetic, and direct our energies to the best advantage to systematized efforts for the suppression of disease.

These diseases (diphtheria, scarlet fever, etc.) are constantly present among us, and as our civilization advances we are constantly being menaced by them from within as well as from without. This danger is becoming more and more increased in proportion to our facilities for intercommunication.

Doubtless there are but few municipalities in this country which are at any time free from these diseases. How they become infected will not be discussed. We know that they are here, and their presence is by far a more serious problem than the speculation as to their origin. Take, for an instance, diphtheria, a disease of the most virulent type of any with which we have to deal. In this, the brilliant discoveries which have been made in regard to its cause, and demonstrating the best means for its control, are due to bacteriology.

Without the bacteriological researches of Klebs and Loeffler, the establishment of its bacilliary origin, the voluminous work of Roux and Yersin and others on its toxic products, of Kitasato and Behring on the effects of the disease upon the blood, the researches of Klein, Prudden, Parke,

and many others on the diagnosis, the means of its propagation and spread, and, lastly, the résumé of the literature by Professor Welch and Dr. Abbott, their confirmation of the claims of the discoverers and their collaborators, we would be yet just as much in the dark concerning its pathology and prophylaxis as before the advent of this important epoch.

Diphtheria is, as is well known, a local disease, and caused by the lodgment and growth of the bacillus diphtheria on a mucous surface.*

The action of the bacillus upon the body is twofold: First, by being an irritant per se to the part, possessing this property to nearly as high a degree as the bacillus tuberculosis, while its virulent effect on the tissues is demonstrated at the point of infection by the rapid cell degeneration which occurs.

The rapid proliferation of the cells, fibrinous exudate, coagulation necrosis, all bespeak its profound local aetion.

The bacillus rarely, if ever, invades the blood, and when this does occur it is usually accidental, caused either by the rupture of a vein or lymphatic, which allows ingress of the bacillus to the circulation.

The pathological effects upon the body are local in the formation of the membranous exudate, and systemic, caused by the absorption of the toxic products, formed by the action of the bacillus on the tissues.

The local effect usually assumes the form of an exudative inflammation, somewhat circumscribed, with the borders of the exudate gradually fading into the healthy tissues. The exudate is composed of cells in the various stages of degeneration, fibrin, epithelium, and bacilli. Other forms of the diphtheritic inflammation so closely resemble that of follicular tonsillitis or pharyngitis that it becomes a difficult task to differentiate it.

A microscopical examination of the exudate or products of inflammation will seldom, if ever, fail to distinguish the presence of the bacilli. The constitutional symptoms are insidious, and variable; in some cases resembling an acute intoxication, in others, the effects of a slow poison.

In the first instance, a large quantity of the bacterial toxine is absorbed into the circulation, and affects the central nervous system, bringing about the fatal result. Secondly, the poison is absorbed slowly in a small quantity, and taken up by the nerve filaments, which undergo a fatty ascending degeneration, which, if it is not arrested, passes on to the vital centers, causing the fatal paralysis. The local effect of this poison is frequently shown, as in the local paralyses.

In the above we have a partial explanation of the cases of sudden death which often occur, and for which we have been at a loss to account. These cases resemble, in a great measure, those of lobar pneumonia, affecting a small portion of the lung where the grave constitutional symptoms are out of proportion to the local condition. Such cases are due to the involvement of the cardiac and respiratory centers, by the toxic products of the micro-organism, which is followed by an acute fatty degeneration of the heart muscle. In those due to diphtheria the same condition exists, the intoxication of the respiratory and cardiac centers, with the additional degeneration of the nerve plexus.

The toxic substances by their action resemble more the characters of an enzyme rather than an alkaloidal ptomaine, because infinitesimal quantities appear to cause a fatal result in animals which have been inoculated with it.

The factors which give rise to exudative inflammation of the mucuous membranes of the upper air passages, resembling diphtheria, are several,

*Diphtheritic infections of wounds are not considered.

and on account of their striking resemblance to this disease in both the local affection and clinical history it becomes a task of no little difficulty to differentiate them. Whether it will be necessary in one instance to institute procedures against an infectious disease, entailing restrictions and perchance hardships upon both patient and family, or treat it as a noninfectious malady in another, becomes a weighty question to decide.

Since there are other factors which cause affections resembling the diphtheritic inflammation, it may be well to consider them in this connection.

The *pseudo-membranous angina*, which not infrequently precedes and accompanies the acute exanthemata, clearly indicates some of the difficulties which stand in the way of a diagnosis. In this instance the affection, serious in its character, resembles diphtheria to a marked degree, but it differs both in its nature and the treatment required.

Until the disease was subjected to a bacteriological examination it was considered the same as the true, and by reason of its apparent tendency not to affect others these cases formed the basis of the argument that membranous croup was a form only of diphtheria, and diphtheria was not highly contagious, as claimed. Fortunately the microscope has been called to our aid, and has established the cause to be quite another thing from the bacillus diphtheria. It has been recently shown that the agent of the exudative inflammation is the streptococcus, classed by some as the streptococcus pyogenes and by others the streptococcus conglomeratus. Whether the micro-organism encountered in scarletinal angina bears a closer relationship to the disease other than its local effect is a question for the future to solve.

Not all the anginas occurring in the exudative inflammations are due to this micro-organism. These diseases (exanthemata) have a marked tendency to render the tissues highly receptive to diphtheritic infection, and many cases of diphtheria do occur, and not infrequently we encounter a mixed form of infection where the streptococcus dies and bacilli are present.

The *bacillus Freidlander*, the micro-organism once claimed to be the cause of acute lobar pneumonia, has been found in cases of faucial and nasal inflammations resembling diphtheria.

The *diplococcus lanceolatus* or pneumococcus (Sternberg) has been found in faucial inflammations, especially in those where the tonsil is involved.

The *streptococcus pyogenes*, already referred to in connection with the exanthemata, plays an independent rôle in faucial affections; in many cases this micro-organism is the only one present.

In follicular pharyngitis and tonsillitis with exudate, the *staphylococcus pyogenes*, *aureus*, or *albus*, is frequently found to be the agent of the inflammatory changes.

Lastly, the most difficult of all—the bacillus of pseudo-diphtheria—occurs in a limited number of cases, and when it does occur it is the most difficult to differentiate from the bacillus diphtheria. It has been identified with the diphtheritic processes, and Loeffler first announced it to be the cause until his subsequent investigations proved the contrary. Morphologically, it so closely resembles the true bacillus that it is impossible to recognize a difference between them, and their clinical behavior are almost identical. Only three points of difference have so far been found. It frequently occurs in the saliva of persons in apparent health, resembling in its biology the diplococcus lanceolatus, its nonpathogenesis to animals which are susceptible to the diphtheritic

bacillus, and its behavior on sterilized culture media, the potato in particular.

Roux and Yersin have asserted that this micro-organism is only an attenuated form of the bacillus diphtheriæ, but now many observations made upon both appear to be in favor of two bacilli rather than one, the attenuated form of the other.

We now come to consider those inflammations of the throat which may be termed for our purpose the atypical anginas.

Clinical observation as well as microscopical examination has demonstrated that diphtheria has a wide range in its appearance and symptomatology. In the majority of cases occurring in an epidemic the typical character will be present, while others may resemble the acute follicular affections. For illustration, a child is taken ill with what appears to be a simple follicular inflammation of the fauces, and soon recovers. Following this case are others in the same family who are affected with sore throats, these differing in appearance, character, and termination from the first, stamping them as malignant diphtheria.

The follicular inflammations are caused by the same agents as those accompanied with an exudate, and so closely do they resemble one another in macroscopical appearance that a diagnosis is out of question. Taking these factors into consideration, and recognizing the prime importance of the one possessing most virulent properties, its control and suppression is more than important. What plan of procedure is the best to attain this end?

Considering this part of the subject, importance will be given to measures looking to the management and control of the disease in municipalities, because herein lies the greatest danger to the largest number. While the measures necessary to be observed may differ in degree according to conditions, the principles upon which these are based are the same, and can be applied to any or all cases, no matter where or when they occur. The essential features in management of this disease resolve themselves into the following: Diagnosis, isolation, notification, and disinfection.

The several causes of the typical and atypical inflammations must be duly weighed, and one by one excluded before a positive diagnosis is assured. As in many if not in all the discoveries of principles perfection in their application is not attained at once; simplicity of method has always been attained by multiplicity of error tinged with truth.

Through the patient plodding labors of the bacteriologist we have at last arrived at a point in our investigation of the causes of these affections whereby the true character can be established with comparative ease.

The diagnosis of diphtheria depends largely if not wholly upon a microscopical examination, and, while it is not intended to place an underestimate upon the value of clinical observation born of long experience, it is believed that on account of the many factors heretofore enumerated, it is almost impossible clinically to determine the nature of the disease. This is especially so in isolated cases, or the first of an epidemic. The accepted cause is the bacillus diphtheria, a micro-organism having a morphology and biological character which readily distinguished it from others. A direct examination of suspected material will not suffice, for in many cases the micro-organism may be present in so few numbers, or associated with so many other kinds, that the characteristics will be masked. It will be necessary to further subject it to biological methods before its presence or absence can be stated.

In regard to its biology and morphology Professor Welch says:

"The bacillus is nonmotile; it varies greatly in size and shape, averaging 2.5 μ in length and 0.5 μ —0.8 μ in thickness. Its morphological characteristics are so peculiar as to render its identification, on cover slip preparations, and on sections from diphtheritic membranes in most cases an easy matter. Sometimes appearing as a regular straight or slightly bent rod with rounded ends, it is especially characteristic to find irregular bizarre forms, such as rods with one or both ends swollen, and very frequently rods broken at irregular intervals into sharp segments either round or oval, or with straight rods; some forms stain uniformly and others in various ways. The bacillus can be cultivated in nearly all the laboratory media. It grows best in the Loeffler blood serum, or media rendered slightly alkaline. When blood serum is inoculated with this bacillus, the surface is studded over with coalescent or scattered colonies, and is so characteristic in appearance that one can anticipate with tolerable certainty the result of examination. The colonies are large, round, elevated, and grayish white, with a center more opaque than the slightly irregular periphery. The surface of the colony is at first moist, and in a day or two rather dry in appearance."

Loeffler found by experience that a mixture of one part of peptone bouillon, containing 1 per cent grape sugar, added to three parts of blood serum, was the best medium for its growth, as well as a substance of greatest value in differentiation of it from other bacilli. The bacillus grows more rapidly on this medium, and at the same time has a restraining effect upon other bacteria. Thus a blood serum tube can be inoculated with a minute portion of a pseudo membrane containing a number of bacteria of several kinds, and in a few hours the bacillus can be separated in almost pure culture; when in this condition the morphological characters are well pronounced, so much so that the bacillus may be easily recognized. The pseudo-diphtheritic bacillus has all the morphological and biological characteristics of the bacillus diphtheria, except with two or possibly three differences: (First) Its nonpathogenesis to susceptible animals; (second) its dirty brownish growth on sterilized potato; (third) the colonies are slightly larger and more granular.

Roux and Yersin claim that this bacillus is only an attenuated form of the diphtheria bacillus, giving their reasons for this that the bacillus diphtheria varies in intensity in different epidemics. The latter has been observed by others in this country. On account of its unsettled status, and the relative infrequency with which it occurs, it would for practical purposes be considered virulent, and be treated the same as diphtheria.

For the purpose of facilitating the diagnosis and determining the cessation of the disease, I know of no plan better devised than is now in operation in the city of New York the essential features of which were inaugurated under Dr. Herman M. Biggs, pathologist to the New York board of health.

From time to time it has received additions and improvements, until now this is a nearly perfect system, and should serve as a model for every city and municipality. The features worthy of note are these:

Facilities are provided for the examination of every case of suspicious sore throat occurring in the city and notification given to the attending physician of the results. Upon this depends the classification of the diseases and the adoption of measures required. Not only does the board make the diagnosis, but require exact data when the patient is free from the disease, i. e., when the diphtheria bacilli are absent from the secretions. The plan of operating the system is as follows:

Culture media in test tubes, containing cotton swab on the end of a steel wire, are prepared and kept on hand at the central laboratory. These are placed in small wooden boxes made for the purpose, and sent to different portions of the city, usually kept at drug stores, so that they can be of easy access to anyone desiring to make a primary inoculation for diagnosis. In this box is inclosed a slip upon which is a printed form for giving the necessary data, which, after being filled in and signed, is inclosed in the box with the tubes. These boxes are collected and sent to the laboratory for examination. As soon as it is completed the physician is notified.

The manner of making the inoculation is of extreme simplicity, and can be followed by anyone. The swab is removed from the test tube and passed into the pharynx or nares, the inflammatory area touched, and after this the swab is drawn lightly over the surface of the blood serum, then removed and replaced in the empty tube. At stated intervals, from three to five days, another inoculation is made from the case and sent in for examination. These subsequent examinations are designed to determine the time when the bacilli disappear and the patient is free from the disease. These examinations, in many instances, have demonstrated that even after the patient has recovered from the attack, and is to all intents and purposes well, the bacillus is present and in a state of extreme virulence. When these conditions exist it may be seen how such persons unwittingly may become a vehicle of contagion.

Isolation.—Pending the result of the bacteriological examination, arrangements should immediately be made to remove the patient to a room where the danger of communicating the disease, if diphtheria, will be reduced to a minimum. If the examination proves its noninfectiousness, your precaution will not reflect detriment to your professional standing with the family. If it prove to be diphtheria, the precaution will be attributed to your foresight.

Little may be said in detail about the special management of a case, save that due precautions should be taken both by the attendants of the sick room and by the physician. As means of prevention of the dissemination of the disease, disinfection should be practiced at all times, so far as possible, during the attack, and thorough disinfection after convalescence. Medical asepsis is as essential as surgical asepsis, and we are just as remiss in our duties as practitioners when we fail to do this as in allowing erysipelas or suppuration to exist in our surgical cases when we can prevent them.

In many of the cases which come under our observation it will be next to impossible to provide suitable accommodations for the comfort of the patient and carry out even a semblance of isolation. These are the cases who give us the greatest concern, and unfortunately will outnumber those occurring where proper measures can be adopted. To allow these to remain under such conditions is to further disseminate the disease, and cause epidemic. The management of these is a serious problem. These cases should be immediately removed to places where they can receive good and careful treatment, and at the same time free the community from the danger of its spread.

We have provided hospitals for the care of those sick with nearly every other disease, and receive the patient without question, but when a case of diphtheria presents itself the doors are closed, and, if perchance, there still remains any charity for this class of sufferers, the accommodations are such as not to be designated as hospital or hospitable. Because one is unfortunate enough to contract a disease, does it

follow that it is not the proper thing to have diphtheria or smallpox, while it is highly so to suffer from erysipelas or pneumonia, or from our time-honored associate, and highly respected protégé, tuberculosis.

This is a serious problem, and one fraught with the deepest interest to all. I am glad to say that the question of providing facilities for the care and treatment of this class of maladies is interesting many. But here and there over our broad land we observe scenes transacted which are in this enlightened age barbaric, and a blot on our civilization.

For the purpose of efficiency, not only in the control of epidemic disease, but in many other ways, it is necessary to have the scope of our work systematized. Every municipality should have its health organization, whose duty it should be to take the initiative in all sanitary reforms and to keep not only for record, but for the information of the medical profession facts regarding the presence of a contagion or infectious disease, simply reporting the presence without doing more, does not control. In addition to this, every health organization should have under its control facilities for diagnosis of infectious diseases. A small and inexpensive laboratory plant appears to me a necessity. A city could not make a better investment.

Disinfection should be considered under the following heads: Disinfection practiced during attack of diphtheria and disinfection of the infected premises after convalescence is established, or as soon as the rooms are vacated. In the first instance, the whole subject may be considered in this manner: Allow nothing to leave the room which has not been properly sterilized or disinfected. Scrupulous cleanliness of all things in the rooms—the prevention, so far as possible, of contaminating objects by the excreta. The nurse and doctor deserve notice. When we admit that textile fabrics may possibly convey the infection, the clothing of such persons may be disseminators of the disease. In some hospitals for the treatment of an infectious disease there is an outer covering for use while attending on the sick. When the rooms occupied by the patients are vacated thorough measures should be at once instituted, under the direction of a competent person; one who knows what cleanliness means and understands the principles which he is to apply in the disinfection. The contents of the room should not be handled save under precautions. All textile fabrics which will not be damaged by the action of disinfecting solutions, or by boiling in water, should have one of these applied before removing them.

Upholstered furniture should have their surfaces thoroughly saturated with a disinfecting solution. Clothing which will be injured by boiling, carpets, rugs, mattresses and pillows, etc., should be disinfected by steam. The room should be rendered mechanically clean, and thoroughly disinfected with one of the standard solutions. In case of a plastered wall a coat of freshly prepared whitewash will perhaps be the best application.

Fumigation by sulphur dioxide gas never should be relied upon as a disinfectant, but when used it should be as an adjunct to more efficient agents, because a larger quantity of the gas is required for a germicidal effect than can be obtained by the ordinary method, by burning it in a closed space. It is an unreliable disinfectant for clothing and bedding, having no action on the diphtheria bacillus when it is in a dried state—a condition which constantly exists in rooms where the disease has occurred.

The manner in which diphtheria is disseminated and the different factors involved therein will be considered only in regard to the first cases. It is believed that if due attention be paid to the immediate

detection of these cases as soon as they occur, and necessary measures instituted, but little will be left to be done in other directions. To attain this end depends entirely upon the cooperation of the medical profession. Rules and regulations for notification and disinfection will avail little unless there is hearty cooperation by one and all.

In conclusion, the points to be observed in the control of diphtheria are essentially these:

First. A positive diagnosis by microscopical examination.

Second. Prompt isolation of suspects, domiciliary or hospital.

Third. Thorough disinfection of articles and apartments infected or exposed to infection.

Smallpox in New York.

NEW YORK, December 17, 1894.—The number of cases and deaths from smallpox for the week ending December 15 is as follows: Cases reported, 3; deaths reported, none.—EMMONS CLARK, *Secretary Health Department.*

Smallpox in the United States as reported to the Supervising Surgeon-General Marine-Hospital Service, October 10 to December 19, 1894.

Places.	Date.	Cases.	Deaths.	Remarks.
Connecticut:				
Groton	Dec. 5	1		
District of Columbia:				
Washington	Oct. 15–Nov. 22	16	5	
	Dec. 11	1		
Illinois:				
Chicago	Nov. 26	65		In smallpox hospital.
Sandwich	Nov. 7–Dec. 10	15		
Indiana:				
Walkerton	Nov. 8	3		
Maryland:				
Charles County, near Glymont	Oct. 27–Nov. 22	3		
Michigan:				
Adrian Township	Nov. 23	1		
Cheboygan	Oct. 19	2		
Danby Township	Nov. 17	4		
Detroit	Oct. 13–Nov. 10	27	7	
	Dec. 1–Dec. 8	4	4	
Manchester Township	Oct. 20			Smallpox reported.
Norvill Township	Oct. 13–Oct. 20			Smallpox reported.
Rives Township	do	1		
Royal Oak Township	Nov. 1	1		
Sebewa Township	Nov. 14	5		
St. Johns Township	Oct. 28	3	1	
Watersmeet Township	Dec. 7	3		
Minnesota:				
Brainerd	Nov. 15	1		
New Jersey:				
Newark	Oct. 6–Oct. 20	6		
Paterson	Dec. 10	2		
New York:				
Brooklyn	Oct. 6–Nov. 17	4	1	
	Nov. 24–Dec. 8	3		
New York	Oct. 27–Nov. 24		10	
	Nov. 24–Dec. 15	27	3	
Ohio:				
Cincinnati	Nov. 23	1		
Deerfield	Nov. 5–Dec. 1	4		
Pennsylvania:				
Philadelphia	Oct. 22–Nov. 27	34	3	
	Nov. 24–Dec. 1	7	1	
Ridley Park	Nov. 17	1		
Vermont:				
Pomfret	Oct. 20–Nov. 14	2		
Washington	Dec. 15	1		

Smallpox in the United States as reported to the Supervising Surgeon-General Marine Hospital Service, October 10 to December 19, 1894—Continued.

Places.	Date.	Cases.	Deaths.	Remarks.
Wisconsin:				
Beaver Dam	Nov. 5–Nov. 26	1	1	
Franklin	Oct. 22–Nov. 19	17	3	
Ellsworth	Oct. 8–Oct. 22	1	1	
Greenfield	Nov. 19	24		
Liberty	Oct. 8–Oct. 22	1	1	
Milwaukee	Oct. 6–Dec. 10	381	122	
Milwaukee Township	Oct. 8–Nov. 19	7	1	
Muskego	Oct. 22–Nov. 19	7	3	
Raymond	Nov. 27–Dec. 3	1		
Rhinelander	Dec. 3–Dec. 10	2		
Rochester	do	1		
Spring Prairie	Oct. 22–Nov. 19	4	1	
Two Rivers	Oct. 22–Dec. 10	14	4	
Wauwatosa	Oct. 8–Nov. 19	18	3	
Wonewec	Oct. 8–Oct. 22	6		

Report of immigration at New York for the week ended December 15, 1894.

OFFICE OF U. S. COMMISSIONER OF IMMIGRATION,
Port of New York, December 17, 1894.

Number of alien immigrants who arrived at this port during the week ended December 15, 1894; also names of vessels and ports from which they arrived.

Date.	Vessel.	Where from.	No. of immigrants from Russia.	No. of immigrants.
1894.				
Dec. 9	Steamship Amalfi	Hamburg	89	196
Dec. 10	Steamship Alesia	Naples		174
Do	Steamship La Champagne	Havre		128
Dec. 11	Steamship Moravia	Hamburg		290
Do	Steamship Anchoria	Glasgow and Moville	89	206
Do	Steamship Amsterdam	Rotterdam	63	231
Do	Steamship Fulda	Genoa and Gibraltar		121
Dec. 12	Steamship Baumwall	Naples		164
Dec. 13	Steamship Teutonic	Liverpool and Queenstown	7	140
Do	Steamship Waesland	Antwerp	5	151
Dec. 15	Steamship Salier	Bremen	104	338
	Total		357	2,139

Dr. J. H. SENNER,
Commissioner of Immigration.

Report of immigration at Philadelphia for the week ended December 15, 1894.

OFFICE OF U. S. COMMISSIONER OF IMMIGRATION,
Port of Philadelphia, December 15, 1894.

Number of alien immigrants who arrived at this port during the week ended December 15, 1894; also name of vessel and port from which it arrived.

Date.	Vessel.	Where from.	No. of immigrants from Russia.	No. of immigrants.
1894. Dec. 11	Steamship Lord Gough	Liverpool	7	127

JNO. J. S. RODGERS,
Commissioner of Immigration.

VESSELS REMAINING, ARRIVING AT, AND DEPARTING FROM UNITED STATES QUARANTINE STATIONS.

BRUNSWICK QUARANTINE.

Week ended December 15, 1894.

Name of vessel.	Date of arrival.	Where from.	Destination.	Treatment of vessel and cargo.	Date of dep'ture
Am. schr. Helen L. Martin	Dec. 10	Havana	Brunswick	Disinfected	Dec. 14
Nor. bark Sweigaard	Dec. 12	Para	do	Held for disinfection.	
Span. bark Felo	Dec. 9	Cienfuegos	do	do	

Four vessels inspected and passed.

DELAWARE BREAKWATER QUARANTINE.

Week ended December 15, 1894.

Four vessels inspected and passed.

PORT TOWNSEND QUARANTINE.

Week ended December 8, 1894.

One vessel inspected and passed.

REEDY ISLAND QUARANTINE.

Week ended December 16, 1894.

Fifteen vessels inspected and passed.

SAN DIEGO QUARANTINE.

Week ended December 12, 1894.

Three vessels inspected and passed.

SOUTH ATLANTIC QUARANTINE.

Week ended December 8, 1894.

Name of vessel.	Date of arrival.	Where from.	Destination.	Treatment of vessel and cargo.	Date of dep'ture.
Spanish bark Constantia*	Nov. 16	Havana	Savannah	Disinfected	Dec. 3
Norwegian bark Noel*	Dec. 1	Rio de Janeiro.	do	Held for disinfection.	

* Previously reported.

Week ended December 15, 1894.

Name of vessel.	Date of arrival.	Where from.	Destination.	Treatment of vessel and cargo.	Date of dep'ture.
Norwegian bark Noel*	Dec. 1	Rio de Janeiro.	Savanah	Disinfected	Dec. 11

* Previously reported.

Reports of States and yearly and monthly reports of cities.

CALIFORNIA—*Alameda.*—Month of November, 1894. Estimated population, 14,000. Total deaths, 19, including phthisis pulmonalis, 2; and enteric fever, 1.

Los Angeles.—Month of November, 1894. Estimated population, 75,-

000. Total deaths, 81, including phthisis pulmonalis, 12; enteric fever, 4; diphtheria, 5; and croup, 2.

Oakland.—Month of November, 1894. Estimated population, 60,000. Total deaths, 57, including phthisis pulmonalis, 9; and croup, 1.

Sacramento.—Month of November, 1894. Estimated population, 30,000. Total deaths, 38, including phthisis pulmonalis, 6; and enteric fever, 3.

San Francisco.—Month of November, 1894. Estimated population, 330,000. Total deaths, 522, including phthisis pulmonalis, 92; enteric fever, 10; diphtheria, 2; croup, 5; measles, 1; and whooping cough, 1.

CONNECTICUT.—Month of November, 1894. Reports to the State board of health from 165 towns, having a population of 811,037, show a total of 953 deaths, including phthisis pulmonalis, 106; enteric fever, 37; diphtheria and croup, 48; scarlet fever, 4; and whooping cough, 8.

FLORIDA.—Month of October, 1894. Reports to the State board of health from 45 counties, having an aggregate population of 391,422, show a total of 306 deaths, including phthisis pulmonalis, 42; enteric fever, 7; croup, 2; and whooping cough, 2.

Tampa.—Month of November, 1894. Estimated population, 16,000. Total deaths, 18, including 2 from phthisis pulmonalis.

ILLINOIS—*Chicago.*—Month of September, 1894. Estimated population, 1,600,000. Total deaths, 2,098, including phthisis pulmonalis, 183; smallpox, 31; enteric fever, 71; scarlet fever, 5; diphtheria, 76; measles, 8; croup, 41; and whooping cough, 38.

Month of October, 1894. Total deaths, 1,916, including phthisis pulmonalis, 165; smallpox, 40; enteric fever, 68; scarlet fever, 8; diphtheria, 104; croup, 81; measles, 7; and whooping cough, 8.

IOWA—*Davenport.*—Month of November, 1894. Estimated population, 35,500. Total deaths, 44, including phthisis pulmonalis, 1; enteric fever, 2; and diphtheria, 5.

KENTUCKY—*Louisville.*—Month of November, 1894. Estimated population, 200,000. Total deaths, 235, including phthisis pulmonalis, 37; enteric fever, 9; diphtheria, 13; and croup, 3.

MARYLAND—*Baltimore.*—Month of November, 1894. Estimated population, white, 384,394; colored, 71,033; total, 455,427. Deaths, white, 562; colored, 170; total, 732, including phthisis pulmonalis, 107; enteric fever, 20; scarlet fever, 3; diphtheria, 37; croup, 6; and whooping cough, 4.

MASSACHUSETTS—*Fitchburg.*—Month of November, 1894. Estimated population, 29,383. Total deaths, 24, including phthisis pulmonalis, 3; enteric fever, 1; and diphtheria, 1.

Northampton.—Month of November, 1894. Estimated population, 16,400. Total deaths, 13, including 1 from phthisis pulmonalis.

Worcester.—Month of November, 1894. Estimated population, 98,000. Total deaths, 132, including phthisis pulmonalis, 18; enteric fever, 3; scarlet fever, 1; diphtheria, 6; croup, 1; measles, 1; and whooping cough, 1.

MICHIGAN.—Week ended December 8, 1894. Reports to the State board of health, Lansing, from 60 observers, indicate that intermittent fever, influenza, tonsillitis, and remittent fever increased, and that diarrhea decreased in area of prevalence. Diphtheria was reported present during the week at 228 places, scarlet fever at 65, enteric fever at 43, diphtheria at 41, measles at 10, and smallpox at 8 places, Adrain, Danby Township, Detroit, Manchester Township, Royal Oak Township, Sebewa Township, St. Johns, and Watersmeet Township.

Grand Rapids.—Month of November, 1894. Estimated population, 80,000. Total deaths, 91, including phthisis pulmonalis, 12; enteric fever, 5; and diphtheria, 3.

MINNESOTA — *Minneapolis.*—Month of November, 1894. Estimated population, 223,700. Total deaths, 141, including phthisis pulmonalis, 14; enteric fever, 10; scarlet fever, 2; diphtheria, 8; and whooping cough, 2.

St. Paul.—Month of November, 1894. Estimated population, 155,000. Total deaths, 130, including phthisis pulmonalis, 4; enteric fever, 6; scarlet fever, 5; diphtheria, 6; and croup, 2.

MISSOURI—*St. Louis.*—Month of November, 1894. Estimated population, 540,000. Total deaths, 670, including phthisis pulmonalis, 83; enteric fever, 20; scarlet fever, 1; diphtheria, 62; and croup, 34.

NEW HAMPSHIRE—*Concord.*—Month of November, 1894. Estimated population, 19,000. Total deaths, 32, including phthisis pulmonalis, 4; and diphtheria, 1.

NEW JERSEY—*Plainfield.*—Month of November, 1894. Population 11,267. Total deaths, 15, including phthisis pulmonalis, 3; and diphtheria, 2.

NEW YORK—*Buffalo.*—Month of November, 1894. Estimated population, 315,000. Total deaths, 354, including phthisis pulmonalis, 39; enteric fever, 16; scarlet fever, 1; diphtheria, 25; croup, 22; and whooping cough, 23.

OHIO—*Hamilton.*—Month of November, 1894. Population, 17,565. Total deaths, 26, including 2 from diphtheria.

RHODE ISLAND—*Newport.*—Month of November, 1894. Estimated population, 20,000. Total deaths, 24, including phthisis pulmonalis, 4; and enteric fever, 2.

TENNESSEE—*Knoxville.*—Month of November, 1894. Estimated population, white, 31,273; colored, 9,112; total, 40,358. Deaths, white, 32; colored, 26; total, 58, including phthisis pulmonalis, 4; scarlet fever, 2; measles, 2; and croup, 1.

UTAH—*Salt Lake City.*—Month of October, 1894. Estimated population, 70,000. Total deaths, 52, including phthisis pulmonalis, 3; and enteric fever, 7.

PUBLICATIONS RECEIVED.

Annual Statement of the Vital Statistics, Meteorological Summary, etc., of Tampa, Fla., year ended October 31, 1894.

MORTALITY TABLE, CITIES OF THE UNITED STATES.

Cities.	Week ended.	Population, U. S. Census of 1890.	Total deaths from all causes.	Deaths from—									
				Phthisis pulmonalis.	Yellow fever.	Smallpox.	Varioloid.	Cholera.	Typhus fever.	Enteric fever.	Scarlet fever.	Diphtheria.	Measles.	Whooping cough.
Allegheny, Pa	Dec. 15	105,287	33	2						1		1		
Amesbury, Mass	do	9,798	4							1				
Ashtabula, Ohio	Dec. 8	8,338	6									1		
Do	Dec. 15	8,338	14									13		
Baltimore, Md	do	434,439	162	15						4		9		4
Bath, Me	Dec. 8	8,723	5											
Baton Rouge, La	do	10,478	1											
Beaver Falls, Pa	Dec. 11	9,735	16	2							1	3		
Bennington, Vt	Dec. 8	6,391	0											
Do	Dec. 15	6,391	3							1				
Binghamton, N. Y	do	35,005	16	1						1	1			
Boston, Mass	do	448,477	222	25						3	5	30		2
Bristol, R. I	Dec. 8	7,382	4											
Do	Dec. 15	7,382	2											
Brockton, Mass	Dec. 8	27,294	10	1										
Brookline, Mass	do	12,103	9	1								1		
Brooklyn, N. Y	Dec. 15	806,343	327	39		1				3	1	34	1	2
Butte, Mont	Dec. 8	10,723	1											
Carlisle, Pa	Dec. 15	7,620	3							11				
Charleston, S. C	Dec. 8	*54,955	†30	4										
Cincinnati, Ohio	Dec. 14	296,908	28	13								4		
Columbus, Ind	Dec. 8	6,719	4	1										
Columbus, Ohio	Dec. 15	88,150	22	4								4		
Dayton, Ohio	Dec. 13	61,220	19	2								1		
Dunkirk, N. Y	Dec. 10	9,416	2									2		
Elgin, Ill	Dec. 8	17,823	4											
Evansville, Ind	Dec. 7	50,756	20	3						1				
Do	Dec. 15	50,756	15	1										
Everett, Mass	do	11,068	11											
Fall River, Mass	do	74,398	22	2						1				
Fitchburg, Mass	Dec. 8	22,037	6											
Fort Worth, Tex	do	23,076	8	1										
Greenville, Miss	Dec. 15	5,473	4											
Haverhill, Mass	do	27,412	6											
Hazleton	Dec. 1	11,872	4											
Do	Dec. 8	11,872	0											
Hoboken, N. J	do	43,648	13	1								3		
Jamestown, N. Y	do	16,038	5											
Lebanon, Pa	do	14,664	4											
Lowell, Mass	Dec. 15	77,696	32	4										
Lynchburg, Va	do	19,709	5											
McKeesport, Pa	Dec. 8	20,741	11											
Manchester, N. H	do	44,126								1		1		
Medford, Mass	Dec. 15	11,079	7								1			
Memphis, Tenn	do	64,495	34	4								1		
Mount Vernon, N. Y	Dec. 8	10,830	2											
Nashville, Tenn	Dec. 15	76,168	34	4						1				
Naugatuck, Conn	do	6,218	1											
New Bedford, Mass	do	40,733	22	3						1		3		
New Brunswick, N. J	do	18,603	10	3						1				
New Haven, Conn	Dec. 13	81,298	16	3						1		3		
New Orleans, La	Dec. 8	242,039	155	18						5		3		
Newport, R. I	Dec. 15	19,457	11	3										
Newton, Mass	do	24,379	5											
New York, N. Y	do	1,515,301	672	93						3	10	42	2	2
Norristown, Pa	do	19,791	2											
North Adams, Mass	Dec. 8	16,074	9											
Northampton, Mass	do	14,990	4											
Omaha, Nebr	do	140,452	23							1	1	1		1
Oneonta, N. Y	Dec. 15	6,272	1											
Ottumwa, Iowa	Dec. 8	14,001	6	1										
Passaic, N. J	Dec. 15	13,028	4											
Peekskill, N. Y	Dec. 1	9,676	3											
Do	Dec. 8	9,676	4	1										
Do	Dec. 15	9,676	6									1		
Pensacola, Fla	Dec. 8	11,750	7							1				
Pittsfield, Mass	do	17,281	6											1
Portage, Wis	do	5,143	1											
Port Richmond, N. Y	Dec. 10	6,290	4	1						1				
Poughkeepsie, N. Y	Dec. 8	22,206	3	1										
Do	Dec. 15	22,206	2											
Providence, R. I	do	132,146	46								2		1	

* Estimated population, white, 28,870; colored, 36,295. Total, 65,165. † White, 10; colored, 20.

MORTALITY TABLE, CITIES OF THE UNITED STATES—Continued.

Cities.	Week ended.	Population, U. S. Census of 1890.	Total deaths from all causes.	Deaths from—									
				Phthisis pulmonalis.	Yellow fever.	Smallpox.	Varioloid.	Cholera.	Typhus fever.	Enteric fever.	Scarlet fever.	Diphtheria.	Measles.	Whooping cough.
Pueblo, Colo	Dec. 8	24,558	12	3	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Putnam, Conn	do	6,512	3	.....	.....	.....	.....	.....	.....	1	.....	1	.....	.....
Reading, Pa	Dec. 17	58,661	25	1	.....	.....	.....	.....	.....	.....	.....	7	.....	.....
St. Louis, Mo	Dec. 1	451,770	158	.....	.....	.....	.....	.....	.....	3	.....	12	.....	.....
Do	Dec. 8	451,770	.....	.....	.....	.....	.....	.....	.....	.....	.....	6	.....	.....
Salt Lake City, Utah	do	44,843	17	1	.....	.....	.....	.....	.....	.....	.....	1	.....	.....
San Francisco, Cal	do	298,997	98	16	.....	.....	.....	.....	.....	3	.....	.....	.....	.....
Santa Barbara, Cal	do	5,864	3	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Sault Ste. Marie, Mich	do	5,760	2	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Seattle, Wash	Dec. 1	42,837	10	2	.....	.....	.....	.....	.....	1	1	.....	.....	.....
Seneca Falls, N. Y	Dec. 8	6,116	0	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Shreveport, La	do	11,979	4	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Sioux Falls, S. Dak	do	10,177	6	1	.....	.....	.....	.....	.....	.....	.....	1	.....	.....
South Bethlehem, Pa	Dec. 16	10,302	6	3	.....	.....	.....	.....	.....	1	.....	.....	.....	.....
Springfield, Mass	Dec. 15	44,179	8	2	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Sterling, Ill	Dec. 8	5,824	2	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Superior, Wis	do	11,983	6	.....	.....	.....	.....	.....	.....	.....	1	.....	.....	.....
Taunton, Mass	Dec. 15	25,448	5	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Tonawanda, N. Y	do	7,145	.....	.....	.....	.....	.....	.....	.....	1	.....	.....	.....	.....
Virginia City, Nev	Dec. 8	8,511	2	1	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Wallingford, Conn	do	6,584	2	1	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Washington, D. C	do	230,392	89	9	.....	.....	.....	.....	.....	4	1	4	.....	1
Winona, Minn	do	18,208	3	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Woburn, Mass	do	13,499	8	1	.....	.....	.....	.....	.....	.....	3	.....	.....	.....
Worcester, Mass	Dec. 6	84,655	21	1	.....	.....	.....	.....	.....	.....	.....	1	.....	.....
Yonkers, N. Y	Dec. 14	32,033	7	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....

Table of temperature and rainfall, week ended December 10, 1894.

[Received from Department of Agriculture, Weather Bureau.]

Locality.	Temperature in degrees Fahrenheit.			Rainfall in inches and hundredths.		
	Normal.	*Excess.	*Defic'ncy.	Normal.	Excess.	Deficiency.
Atlantic Coast:						
Eastport, Me	30	.....	5	.98	.....	.98
Portland, Me	27	0	.....	.83	.....	.74
Northfield, Vt	26	.....	1	.67	.....	.05
Boston, Mass	36	.....	4	.81	.....	.31
Block Island, R. I	39	.....	2	.84	.06	.....
New London	37	.....	3	.77	.00	.....
Albany, N. Y	33	.....	2	.63	.....	.39
New York, N. Y	38	2	.....	.70	.....	.04
Philadelphia, Pa	38	2	.....	.63	.....	.04
Atlantic City, N. J	39	1	.....	.84	.....	.52
Baltimore, Md	40	0	.....	.70	.02	.....
Washington, D. C	40	.....	1	.63	.24	.....
Lynchburg, Va	41	1	.....	.77	.16	.....
Norfolk, Va	46	.....	1	.84	.....	.56
Charlotte, N. C	46	0	.....	1.02	1.26	.....
Wilmington, N. C	51	.....	2	.77	.....	.39
Charleston, S. C	54	3	.....	.77	.....	.77
Augusta, Ga	51	1	.....	.84	.24	.....
Savannah, Ga	55	4	.....	.76	.....	.76
Jacksonville, Fla	59	4	.....	.64	.....	.64
Titusville, Fla	64	2	.....	.70	.....	.70
Jupiter, Fla	69	1	.....	.52	.....	.01
Key West, Fla	71	2	.....	.42	.....	.41
Gulf States:						
Atlanta, Ga	48	3	.....	1.08	.17	.....
Mobile, Ala	54	8	.....	.98	.....	.26
Montgomery, Ala	52	7	.....	1.10	.40	.....
Vicksburg, Miss	53	6	.....	1.13	1.18	.....
New Orleans, La	58	7	.....	1.05	.....	.88
Shreveport, La	52	7	.....	1.12	.85	.....
Fort Smith, Ark	45	4	.....	.70	.12	.....

*The figures in these columns represent the average daily departure.

Table of temperature and rainfall, week ended December 10, 1894—Continued.

Locality.	Temperature in degrees Fahrenheit.			Rainfall in inches and hundredths.		
	Normal.	*Excess.	*Defic'ncy.	Normal.	Excess.	Deficiency.
Gulf States—*Continued.*						
Little Rock, Ark	47	3		1.07	1.53	
Palestine, Tex	53	9		.80	.51	
Galveston, Tex	60	5		1.05		.74
San Antonio, Tex	56	10		.42		.42
Corpus Christi, Tex	60	8		.45		.45
Ohio Valley and Tennessee:					.50	
Memphis, Tenn	46	6		.81		
Nashville, Tenn	44	3		.77	.52	
Knoxville, Tenn	42	5		.88	.95	
Louisville, Ky	41	5		.91	.49	
Indianapolis, Ind	36	6		.77	.06	
Cincinnati, Ohio	39	3		.77	.10	
Columbus, Ohio	36	2		.70	.26	
Parkersburg, W. Va	38	2		.77	.04	
Pittsburg, Pa	38	2		.63	.14	
Lake Region:						
Oswego, N. Y	32	3		.77		.33
Buffalo, N. Y	33	5		.77		.29
Erie, Pa	36	4		.83		.67
Cleveland, Ohio	34	4		.63		.37
Toledo, Ohio	34	5		.56	.12	
Detroit, Mich	34	4		.63	.25	
Port Huron, Mich	31	6		.56	.11	
Alpena	28	6		.56	.30	
Marquette, Mich	26	10		.56		.04
Grand Haven, Mich	32	7		.63		.39
Milwaukee, Wis	29	9		.43		.27
Chicago, Ill	31	7		.56		.14
Duluth, Minn	22	15		.35	.48	
Upper Mississippi Valley:						
St. Paul, Minn	22	13		.28		.02
La Crosse, Wis	28	10		.35		.33
Davenport, Iowa	32	8		.42		.36
Des Moines, Iowa	30	11		.35		.35
Keokuk, Iowa	34	7		.45		.11
Springfield, Ill	36	5		.63	1.06	
Cairo, Ill	42	5		.77	.75	
St. Louis, Mo	39	6		.56	.54	
Missouri Valley:						
Springfield, Mo	39	6		.65		.55
Kansas City, Mo	36	10		.41	.06	
Wichita, Kans	37	9		.21		.20
Concordia, Kans	35	8		.21		.19
Omaha, Nebr	31	9		.26		.22
Valentine, Nebr	29	9		.11		.11
Huron, S. Dak	22	10		.17		.09
Pierre, S. Dak	25	8		.07	.01	
Moorehead, Minn	15	15		.14		.08
St. Vincent, Minn	11	16		.14		.08
Bismarck, N. Dak	18	11		.21		.19
Williston, N. Dak	17	6		.14	.24	
Rocky Mountain Slope:						
Havre, Mont	23	3		.15	.08	
Helena, Mont	26	4		.21		.15
Spokane, Wash	33	3		.63	.10	
Wallawalla, Wash	41		1	.56		.29
Winnemucca, Nev	33		2	.23	.26	
Salt Lake City, Utah	36		1	.35	.35	
Cheyenne, Wyo	31	2		.00	.03	
North Platte, Nebr	30	6		.14		.14
Denver, Colo	36	4		.14		.12
Pueblo, Colo	36	5		.07		.06
Dodge City, Kans	35	7		.16	.08	
Abilene, Tex	49	6		.40		.38
Santa Fe, N. Mex	34	1		.21	.12	
El Paso, Tex	48	3		.14		.06
Tucson, Ariz	53	0		.22	.50	
Pacific Coast:						
Port Angeles, Wash	39		1	1.17		.25
Portland, Oreg	43		3	1.83		.50
Roseburg, Oreg	44		3	1.40	.96	
Red Bluff, Cal	49		2	1.16	2.24	
Sacramento, Cal	50		1	.92	2.18	
San Francisco, Cal	53		3	1.10	2.01	
Fresno, Cal	49		2	.33	1.55	
Los Angeles, Cal	57		4	.96	1.65	
San Diego, Cal	57		2	.52	.39	
Yuma, Ariz	59		4	.14		.10

*The figures in these columns represent the average daily departure.

FOREIGN.

[Reports received from the United States consuls through the Department of State and from other sources.]

Cholera and yellow fever as reported to the Supervising Surgeon-General M. H. S., May 15 to December 19, 1894.

CHOLERA.

Places.	Date.	Cases.	Deaths.	Remarks.
Arabia:				
Mecca	June 11		[illegible]	Cholera reported.
Austria-Hungary:				
Bukowina		863	490	From beginning of epidemic to November 25.
Galicia		14,129	7,733	
Belgium	June 1-Nov. 17	2,694	1,266	
Brazil	Nov. 27			Cholera reported.
Ceylon	Aug. 11			1 death on steamship Natal.
China	June 23-Oct. 11		2	
England	July 28-Aug. 18	5	1	
France	May 28-Oct. 8		170	
Germany	May 25-Dec. 3	988	325	
Holland	July 11-Nov. 10	532	265	
India	May 16-Oct. 16		755	
Italy	Aug. 31-Nov. 6	2	1	
Japan	July 14-Aug. 18	6	3	
Russia		62,661	28,589	
Spain		1	1	
Sweden	July 4-Aug. 19	29	5	Quarantine station.
Turkey		10,565	4,692	

YELLOW FEVER.

Brazil:				
Rio de Janeiro	Apr. 29-Oct. 20		439	
Cuba	June 1-Nov. 22	1,296	490	
Equador	May 4-May 10		3	
Honduras	Apr. 8-Apr. 28		5	
Mexico:				
Vera Cruz	Apr. 27-Nov. 22		200	
Nicaragua	Sept. 14			Yellow fever at Granada and Managua.
Panama	Sept. 13	1		
Salvador	July 14-Nov. 8	193	158	
West Indies	Apr. 29-Nov. 14	185	32	
Port of Spain	July		1	
Yucatan	May 25-May 31		1	
Venezuela	Sept. 15-Nov. 24	8	2	

BRAZIL.

Sanitary reports of Rio de Janeiro.

RIO DE JANEIRO, *November 13, 1894.*

SIR: I have the honor to inclose report for week ended November 10, 1894. The report is very satisfactory, there being 5 deaths from accesso pernicioso, 8 in the previous week; 2 from smallpox, as in last week; 1 from beriberi, none last week, and none from typhoid or yellow fever, the temperature being high and the atmosphere damp. The total from all causes was 215, 18 less than in the previous week.

The health of the town and port is exceptionally good, the few cases of smallpox occurring not being amongst the shipping.

Since last report the following-named ships have been inspected and received bills of health from this office: November 7, steamship *Merida*, English, from Buenos Ayres, to New York; November 9, steamship

Lassell, English, for New York; November 10, steamship *Lancastrian Prince*, English, from Santos to New York; bark *Verveine*, French, for Pensacola, Fla.; and bark *Helena*, German, for Pensacola, Fla.

Respectfully, yours,

R. CLEARY, M. D.,
Sanitary Inspector, M. H. S.

RIO DE JANEIRO, *November 20, 1894.*

SIR: I have the honor to transmit report for week ended November 17, 1894. There were 3 deaths from accesso pernicioso, being 2 less than in the previous week; 1 from smallpox, 1 less; 2 from typhoid fever, none in the foregoing week; 4 from beriberi, an increase of 3; and 2 from diphtheria. The deaths from all causes were 218, an increase of 3. The health of the town compares more than favorably with the same period last year, and may be considered excellent, especially in the shipping. I doubt the 2 cases of diphtheria, as they were reported one as "angina diphtherica" and the other "infective diphtherica," and the disease is so rare in this place that mistakes can well occur.

Yellow fever.—Again I have to report no deaths from this disease, whilst at this time last year we had from 3 to 4 deaths each week, with a gradual increase. A telegram in the morning's paper states that there was a report in Buenos Ayres of yellow fever here, but it was denied, as it should be. There seems to be a chronic yellow-fever scare in Buenos Ayres, and reports from that quarter must be examined very closely before accredited.

Since last month the following-named ships have been inspected and received bills of health from this office: November 14, steamship *Dona Maria*, Portuguese, for New Orleans, La.; November 17, steamship *Turquoise*, British, for New York, from Buenos Ayres; steamship *Leibnitz*, Belgium, for New York; and November 19, bark *Cassandra*, German, for Tybee, Ga.

Respectfully, yours,

R. CLEARY, M. D.,
Sanitary Inspector, M. H. S.

CUBA.

Yellow fever in Santiago.

SANTIAGO DE CUBA, *December 8, 1894.*

SIR: Yellow fever continues to hold on in this city later than usual, and is said to be more than usually fatal. The number of cases has at no time been large, but has been continuous from April to the present time, my own wife having been a victim, but fortunately recovered.

Several cases occurred among the marines on the gunboats lying at anchor in the bay, but for some time past the port and vicinity have been free from the plague, the disease having been prevalent in the more distant parts of the city.

The Ward Line of steamers, that make bimonthly trips between southern Cuba and New York, taking their last bill of health from this port, have been quarantined the entire season at Nassau, the health officers of that British port being governed by the American bill of health rather than that issued by the British consul.

Deaths from yellow fever for week ending December 7 were 7; the number of cases I have not been able to learn.

Respectfully,

PULASKI F. HYATT,
United States Consul.

GERMANY.

Cholera in Silesia.

BRESLAU, *November 7, 1894.*

SIR: I have the honor to make the following report on the present condition of cholera in Upper Silesia for the information of the Surgeon-General of the Marine-Hospital Service:

On the 4th and 5th instant no cases of cholera, bacteriologically determined, were reported to the officials at Oppeln. In the week from October 28 to November 3, inclusive, 11 cases were reported—1 from Klein Dombrowka, 1 from Burowietz, 4 from Brzezinka, and 3 from Myslowitz, all in the Kreis Kattowitz; further, 1 from Imielin, Kreis Pless, and 1 from Adamowitz, Kreis Gross-Strelitz. Only the case in Imielin was fatal. It is to be remarked that, although the presence of cholera bacilli was determined, in the case of 6 of these persons they did not show the corresponding symptoms of the disease.

In Lower Silesia, in the village of Jätschau, Kreis Glogau, a series of cases appeared in the family of a laboror named Zaebe. They were wholly unexpected, and no chain of communication of the disease has yet been discovered. The persons affected are 4 of the 6 children of the man Zaebe, and 2 of them have died. The first attack took place on the 29th ultimo, but a physician was not called in until the 3d instant. The customary precautions are being taken and the cases further investigated. This news has only to-day been made public here.

I have reported these cases already to the seaport consuls, and shall continue to exercise a vigilance which the progress of the disease warrants.

I have, etc., FREDERICK OPP,
United States Consul.

To the Hon. ASSISTANT SECRETARY OF STATE.

ITALY.

Smallpox at Marsala.

PALERMO, ITALY, *November 24, 1894.*

SIR: I have the honor to state that I am this day in receipt of a communication from the United States consular agent at Marsala to the following effect:

"About ten days ago a poor family was allowed to land at Marsala from Tunis with a child suffering from smallpox. The family went to live with relatives in the heart of the town, and in a few days other members of the family were attacked. The authorities at once ordered the removal of the patients to a convent converted for the time being into a smallpox hospital, and the houses in the infected quarter were disinfected. The hospital accommodation being very limited, the patients attacked within the last three or four days have been obliged to remain at their homes. Up to the evening of November 21 there were 22 cases of a mild form reported and only 1 death registered, the child who imported the disease."

Owing to the proximity of Marsala to Trapani and the daily uninterrupted communication between them, I have given orders to the agent at Trapani as well as at Marsala not to allow the crews of vessels bound for the United States to go ashore.

I am, etc., WM. H. SEYMOUR,
United States Consul.

To the Hon. ASSISTANT SECRETARY OF STATE.

STATISTICAL REPORTS.

AFRICA—*Cape Town.*—Two weeks ended November 10, 1894. Estimated population, 55,000. Total deaths, 59; including 1 from enteric fever.

ARGENTINE REPUBLIC—*Buenos Ayres.*—Month of September, 1894. Estimated population, 597,422. Total deaths, 1,341, including enteric fever, 5; scarlet fever, 11; diphtheria, 36; measles, 5; and whooping cough, 6.

BAHAMAS—*Dunmore Town.*—Four weeks ended December 7, 1894. Estimated population, 1,472. One death.

Governors Harbor.—Four weeks ended December 8, 1894. Estimated population, 1,169. One death.

BRITISH COLUMBIA—*Victoria.*—Month of November, 1894. Estimated population, 18,000. Total deaths, 22. No deaths reported from contagious diseases.

FRANCE—*Nice.*—Month of October, 1894. Population, 97,720. Total deaths, 111, including phthisis pulmonalis, 12; enteric fever, 2; and diphtheria and croup, 2.

GREAT BRITAIN—*England and Wales.*—The deaths registered in 33 great towns of England and Wales during the week ended December 1 corresponded to an annual rate of 17.8 a thousand of the aggregate population, which is estimated at 10,458,442. The lowest rate was recorded in Nottingham, viz, 14.2, and the highest in Swansea, viz, 25.1 a thousand.

London.—One thousand three hundred and forty-seven deaths were registered during the week, including measles, 29; scarlet fever, 19; diphtheria, 54; whooping cough, 26; enteric fever, 18; and diarrhea and dysentery, 25. The deaths from all causes corresponded to an annual rate of 16.1 a thousand. In greater London 1,783 deaths were registered, corresponding to an annual rate of 15.6 a thousand of the population. In the "outer ring" the deaths included 22 from diphtheria, 10 from measles, and 10 from whooping cough.

Ireland.—The average annual death rate represented by the deaths registered during the week ended December 1 in the 16 principal town districts of Ireland was 21.1 a thousand of the population. The lowest rate was recorded in Drogheda, viz, 8.8, and the highest in Lurgan, viz, 36.5 a thousand. In Dublin and suburbs 142 deaths were registered, including smallpox, 3; scarlet fever, 1; enteric fever, 2; and whooping cough, 1.

Scotland.—The deaths registered in 8 principal towns during the week ended December 1 corresponded to an annual rate of 21.4 a thousand of the population, which is estimated at 1,482,767. The lowest mortality was recorded in Leith, viz, 14.4, and the highest in Aberdeen, viz, 24.5 a thousand. The aggregate number of deaths registered from all causes was 611, including smallpox, 9; measles, 22; scarlet fever, 11; diphtheria, 14; and whooping cough, 17.

JAMAICA—*Kingston.*—Month of November, 1894. Population, 19,264. Total deaths, 90, including phthisis pulmonalis, 12; diphtheria, 1; and whooping cough, 3.

MEXICO—*Acapulco.*—Month of October, 1894. Population, 4,000. Total deaths, 24. No deaths reported from contagious diseases.

TURKEY—*Constantinople.*—Month of October, 1894. Population, 700,000. Total deaths, 845, including 120 from smallpox.

MORTALITY TABLE, FOREIGN CITIES.

Cities.	Week ended.	Estimated population.	Total deaths from all causes.	Deaths from—								
				Cholera.	Yellow fever.	Smallpox.	Typhus fever.	Enteric fever.	Scarlet fever.	Diphtheria.	Measles.	Whooping cough.
Amherstburg	Dec. 8	2,300	0									
Amsterdam	Dec. 1	449,167	136					1		4		4
Antigua	Oct. 20	16,664	13									
Do	Oct. 27	16,664	20									
Do	Nov. 3	16,664	16									
Do	Nov. 10	16,664	28									
Do	Nov. 17	16,664	16									
Do	Nov. 24	16,664	17									
Do	Dec. 1	16,664	11									
Do	Dec. 8	16,664	22									
Antwerp	Nov. 24	254,370	72			1		1			1	2
Batoum	Nov. 27	28,000	8									
Belleville	Dec. 10	10,201	3									
Birmingham	Dec. 1	492,301	162			3		4	2	4		2
Bologna	do	146,068	50				1			2		
Bombay	Nov. 13	853,926	461									
Brussels	Nov. 24	498,400	177			1		2	1		4	1
Calcutta	Nov. 3	681,560	420	10		1						
Cape Town	Nov. 19	55,000	35					1				
Catania	Dec. 2	120,000	51					1		2		1
Chatham	Dec. 8	9,052	3							1		
Christiania	Nov. 17	167,588	57						3			2
Do	Nov. 24	167,588	62						1	2	1	1
Do	Dec. 1	167,588	57						5	2		1
Cienfuegos	Dec. 8	23,000	23		1							
Cognac	Dec. 3	17,500	8									
Colombo	Nov. 3	130,000	96					2			3	
Crefeld	Nov. 17	106,059	29						1	3		
Do	Nov. 24	106,059	19									1
Do	Nov. 31	106,059	59									
Demerara	Dec. 13	53,176	42									
Do	Dec. 20	53,176	42									
Do	Dec. 27	53,176	58									
Denia	Nov. 24	11,618	4									
Dresden	Nov. 17	316,660	101						2	7	1	2
Do	Nov. 24	316,660	112						1	6	1	2
Dundee	Dec. 1	158,719	55							1	2	2
Edinburgh	Nov. 24	270,588	113			4		2	1	2	1	
Flushing	Dec. 1	15,250	6									
Genoa	do	182,401	104					1		4		
Ghent	do	153,803	56							2		
Gibraltar	Nov. 25	25,800	13									
Do	Dec. 2	25,800	7									
Girgenti	Dec. 24	23,847	12									
Glasgow	Nov. 17	686,820	298					3	5	6		
Do	Nov. 24	686,820	280					5	3	7		
Gothenburg	do	108,000	45						2	3		1
Guelph	Dec. 8	10,689	3									
Halifax	do	38,700	15						2			
Hamburg	Dec. 1	598,372	164					2	2	10	1	4
Königsberg	do	169,200								2		
Leeds	do	388,761	162					2	1	1	22	1
Leghorn	do	102,956	33					1				
Leith	Nov. 24	72,003	19							1		
Liege	Dec. 1	155,898	51									
Madras	Nov. 9	452,518	352								3	
Madrid	Oct. 28	482,816	326			21		11	2	5		

MORTALITY TABLE, FOREIGN CITIES—Continued.

Cities.	Week ended.	Estimated population.	Total deaths from all causes.	Deaths from—								
				Cholera.	Yellow fever.	Smallpox.	Typhus fever.	Enteric fever.	Scarlet fever.	Diphtheria.	Measles.	Whooping cough.
Manchester	Nov. 24	522,365	203	.....	.....	.....	.....	4	3	2	.....	1
Maracaibo	Dec. 1	38,000	22	.....	.....	.....	.....	.....	.....	.....	.....	.....
Marsala	Dec. 24	40,131	16	.....	.....	2	.....	1	.....	1	.....	.....
Matamoras	Dec. 7	8,000	2	.....	.....	.....	.....	.....	.....	.....	.....	.....
Matanzas	Dec. 5	40,000	22	.....	.....	.....	.....	.....	.....	.....	.....	.....
Messina	Dec. 1	87,500	39	.....	.....	.....	.....	2	7	.....	.....	.....
Montevideo	Nov. 3	239,667	51	.....	.....	.....	.....	2	.....	1	.....	.....
Do	Nov. 10	239,667	....	.....	.....	.....	.....	.....	.....	1	.....	.....
Do	Nov. 17	239,667	57	.....	.....	.....	.....	.....	.....	3	.....	.....
Moscow	Nov. 24	800,000	413	.....	.....	2	4	2	11	27	1	3
Munich	do	390,000	153	.....	.....	.....	.....	.....	2	6	3	3
Naples	Dec. 1	540,000	239	.....	.....	.....	.....	.....	.....	.....	.....	.....
Nogales	Dec. 8	1,200	0	.....	.....	.....	.....	.....	.....	.....	.....	.....
Odessa	Nov. 24	324,500	132	.....	.....	.....	.....	.....	7	4	.....	.....
Palermo	Dec. 2	273,000	116	.....	.....	.....	.....	.....	.....	8	.....	.....
Paso del Norte	Nov. 24	7,500	7	.....	.....	.....	.....	1	.....	1	.....	.....
Plymouth	Dec. 1	86,781	28	.....	.....	.....	.....	.....	.....	.....	.....	.....
Puerto Cortez	Dec. 5	1,500	0	.....	.....	.....	.....	.....	.....	.....	.....	.....
Queenstown	Nov. 17	15,000	6	.....	.....	.....	.....	.....	.....	.....	.....	.....
Do	Nov. 24	15,000	3	.....	.....	.....	.....	.....	.....	.....	.....	.....
Do	Dec. 1	15,000	1	.....	.....	.....	.....	.....	.....	.....	.....	.....
Rio de Janeiro	Nov. 10	600,000	215	.....	.....	2	.....	.....	.....	.....	.....	.....
Do	Nov. 17	600,000	218	.....	.....	1	.....	2	.....	2	.....	.....
Rome	Dec. 5	456,664	152	.....	.....	.....	.....	5	.....	.....	.....	.....
Rotterdam	Dec. 1	228,597	101	.....	.....	4	.....	.....	1	.....	.....	.....
St. Georges	Nov. 11	15,013	2	.....	.....	.....	.....	.....	.....	.....	.....	.....
Do	Nov. 18	15,013	1	.....	.....	.....	.....	.....	.....	.....	.....	.....
St. Stephen	Dec. 8	2,700	1	.....	.....	.....	.....	.....	.....	.....	.....	.....
San Juan del Norte	Nov. 18	400	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Do	Nov. 25	400	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
San Pedro	Dec. 1	3,300	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Schiedam	do	25,580	10	.....	.....	.....	.....	.....	.....	.....	.....	.....
Sheffield	do	340,898	117	.....	.....	.....	.....	1	1	1	10	.....
Sonneberg	Nov. 11	12,000	4	.....	.....	.....	.....	.....	.....	.....	.....	.....
Southampton	Dec. 1	67,283	16	.....	.....	.....	.....	.....	.....	.....	.....	1
Stettin	Nov. 24	133,000	50	.....	.....	.....	.....	.....	2	.....	3	.....
Stockholm	do	252,937	87	.....	.....	.....	.....	.....	2	12	19	.....
Tegucigalpa	do	12,000	5	.....	.....	.....	.....	.....	.....	.....	.....	.....
Trapani	Dec. 1	45,095	14	.....	.....	1	.....	.....	2	.....	2	.....
Tuxpan	do	10,280	8	.....	.....	.....	.....	.....	.....	.....	.....	.....
Venice	Nov. 24	158,187	58	.....	.....	.....	.....	.....	.....	.....	.....	.....
Vera Cruz	Dec. 6	25,500	20	.....	.....	.....	.....	.....	.....	.....	.....	.....
Warsaw	Nov. 10	515,654	210	.....	.....	2	1	1	23	10	6	6
Do	Nov. 17	515,654	213	.....	.....	2	.....	2	18	12	2	1
Do	Nov. 24	515,654	236	.....	.....	2	4	.....	11	17	5	4
Winnipeg	Dec. 10	34,981	6	.....	.....	.....	.....	.....	.....	.....	.....	.....

By authority of the Secretary of the Treasury:

WALTER WYMAN,

Supervising Surgeon-General Marine-Hospital Service.

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