

A B S T R A C T S .

D I P H T H E R I A , & C .

Report of the American Pediatric Society's Collective Investigation into the Use of Antitoxin in the Treatment of Diphtheria in Private Practice. "Med. Record," July 4, 1896.

A CIRCULAR-LETTER was issued by the above society to practitioners in North America, asking for detailed information as to the use of antitoxin in diphtheria in private practice. Replies were received from 615 physicians (with 3628 cases) in fifteen different states, in the district of Columbia, and in Canada. In making up the statistics and report certain cases were neglected, because the diagnosis for various reasons seemed doubtful. Reports of private cases were also obtained from the Boards of Health of New York and Chicago. The grand total gives 5794 cases, with 713 deaths—a mortality of 12·3 per cent. If cases moribund or dying within twenty-four hours of the first injection are deducted, the mortality is reduced to 8·8 per cent. The advantages of early injection are very strikingly demonstrated, thus :—

P E R C E N T A G E M O R T A L I T Y .

	Injected on 1st day.	2nd day.	3rd day.	4th day.	5th day, or after.
Committee's Report ...	4·9	8·3	12·7	22·9	38·9
New York Health Board	8·7	12·0	16·6	20·9	29·0
Chicago	0·0	1·5	2·7	14·1	34·0

Thus the mortality per cent. of all cases injected during the first three days was only 7·3; deducting those moribund, or that died within twenty-four hours from the first injection, the mortality is 4·8 per cent.

The age table is much in accordance with ordinary experience, showing that the danger decreases with advancing age. Over fifteen years old there were 359 cases, with only thirteen deaths. The majority of these were either septic cases, or had already cardiac or kidney lesions. Omitting four moribund cases, the percentage mortality is reduced to 2·5.

It is difficult to judge from the returns what influence (if any) antitoxin has in preventing paralytic sequela. If it has any such effect, it is only when given at the very onset of the disease.

With regard to sepsis and nephritis the reports are unsatisfactory, different men calling different conditions by the same name; but there is very little evidence to show that nephritis was caused in any case by the serum.

Bronchio-pneumonia occurred in only 5·9 per cent. of the cases.

Of laryngeal cases, one-half recovered without operation, although in a large proportion the stenosis was severe; and in cases intubated the mortality was only 25·9 per cent.

Only three cases are reported in which unfavourable symptoms were attributed to the serum, and of these only one (viz., the girl Valentine, who died in convulsions ten minutes after receiving the injection) is clearly proved to be due to the serum.

Arthur J. Hutchison.

Diphtheria Treated with and without Antitoxin. "Med. Record," June 30, 1896.

FIVE papers on the antitoxin treatment of diphtheria :—

1. **Winters, Joseph E.**—*Clinical Observations upon the Use of Antitoxin in Diphtheria; and a Report of a Personal Investigation of this Treatment in the Principal Fever Hospitals of Europe during the Summer of 1895.*
2. **Thomson, W. H.**—*How the Facts about the Antitoxin Treatment of Diphtheria should be Estimated.*
3. **Brannan, John Winters.**—*A Critical Analysis of Dr. Winters' Clinical Observations on the Antitoxin Treatment of Diphtheria.*
4. **Stowell, W. L.**—*Diphtheria with and without Antitoxin.*
5. **Ernst, F. H.**—*Personal Experience in the Treatment of Diphtheria with and without Antitoxin.*

The first of these papers is a violent attack on the use of antitoxin on both theoretical and statistical grounds.

The bacillus is not destroyed, is not rendered less virulent, is in no way affected by the antitoxin. Antitoxin is supposed to be an antidote to the bacillary toxins, but to have no influence on the toxins of other bacteria; thus its scope is at once greatly restricted because pure bacillary infection is rare. The duty of the antitoxin is or ought to be to prevent cardiac depression, cardiac paralysis, albuminuria, and post-diphtheritic paralysis, all of which are due to the toxins of Loeffler's bacillus. Has it done so? Behring states that to obtain the maximum result the antitoxin should be applied at the same time and at the same spot (Ruffer) as the toxin. This is impossible in man. "Another consideration of prime importance is: if we are to attribute the reported decrease of mortality of diphtheria to the action of a specific, this decrease must be uniform and constant. There must be the same reduction of mortality in all parts of the world where the remedy is applied.

"The most misleading part of antitoxin literature is the constantly quoted percentage mortality. The mortality from diphtheria in the city of Boston in 1895 was 14.48 per cent.; in 1893, 32.49 per cent.; and yet there were one hundred and twelve more deaths from diphtheria in the city of Boston in 1895 than there were in 1893."

The author next proceeds to deal with the results obtained at the Willard Parker Hospital during the first nine months of 1895, quoting shortly cases in which the treatment was begun early in the disease, and summing up thus:—
"Not one item in the clinical records can be found to indicate that any one of these patients was in any way benefited by the antitoxin. This is particularly noticeable in the laryngeal cases. . . . There are clinical features here recorded which are due to the treatment, and not to the disease. These features are referable to the kidneys, nervous centres, temperature, and respiratory organs."

The next part of the paper is devoted to the injurious effects of antitoxin, used either as a curative or prophylactic agent, large numbers of cases (both from hospital and private practice) being quoted in support of the author's opinion that antitoxin is utterly bad.

The popularity of antitoxin is due largely to the results obtained at the Empress Frederika Hospital (Baginsky), Berlin, and at the Hospital for Sick Children in Paris (Roux and Martin). The methods of obtaining these results do not stand close investigation. Then, probably, we have just been passing through a period of mild diphtheria, and certainly "include many cases which previously (*i.e.*, before bacteriological diagnosis) were not considered as cases of diphtheria."

Dr. P. H. Ernst treated seventy-seven cases of diphtheria since May, 1895; twelve with and sixty-five without antitoxin. Of the twelve treated with antitoxin, five recovered, seven died. Mortality, over fifty-eight per cent. Of those treated without antitoxin, eleven died. Mortality, seventeen per cent.

The author concludes thus:—"When I began the use of antitoxin I had implicit faith in its remedial effects, but careful observation of the cases just enumerated convinced me that antitoxin does not exert the slightest favourable influence on the course of diphtheria. In fact, it is my opinion that the antitoxin patients who recovered had a more protracted convalescence, the anæmia specially being more marked and less amenable to treatment than in those who recovered without antitoxin."

Dr. William L. Stowell's paper, a review of his own cases and partly of the literature of the same period, is also unfavourable to antitoxin. He is convinced—

"That diphtheria is very variable in extent and severity, both epidemically and clinically.

"That the diagnosis of true or false diphtheria requires as much care bacteriologically as clinically.

"That the unusual number of cases recorded is in part due to bacterial cases without symptoms and the general alertness of physicians now to report suspicious cases.

"That the same causes, plus elimination, give the apparently low ratio of deaths." (This refers to the fact that many physicians use antitoxin for mild and moderate cases of diphtheria, but refuse it to very severe or moribund cases.)

"That cleanliness and ventilation will immunize as well as hypodermic serum.

"Diphtheria is a treacherous disease under any treatment. Selected cases and faithful treatment of any reasonable kind lead to success. Jules Simon was correct in saying, 'Efficiency of remedy not only, but fidelity in its use, give results.'"

Dr. W. H. Thomson's paper, after dealing with the difficulties and grounds for doubt in forming an opinion as to the value of antitoxin, shows that no individual's experience or opinions, however loudly he may express them—nothing but the experience of the whole of the medical profession throughout the world—should influence us in favour of or against antitoxin. From the published hospital statistics of practically the whole civilized world he proves quite clearly (as clearly as the above quoted papers disprove it) that antitoxin is the best treatment yet devised for diphtheria. He does not claim that antitoxin is a specific, because "there are no specifics;" but antitoxin treatment of diphtheria has reduced the death rate, so far as hospital experience goes, by fully fifty per cent.

J. W. Brannan's paper is a reply to that of Dr. Winters', first analysing, and in most cases proving the incorrectness and misleading nature of, his statements with regard to the Willard Parker Hospital results, then showing up the one-sided nature of his personal European investigation.

Dr. Winters, in citing cases from the hospital, uses a formula somewhat as follows:—"Patient, M. C.; one day sick; small bit of membrane on the tonsil; favourable prognosis; antitoxin injected; death on the fourteenth day." It ought to have been: "M. C., two years old; two days sick. No membrane visible, marked croup, retraction of chest, cyanosis. Intubation required. Prognosis doubtful. Antitoxin injected. Death on fourteenth day. Broncho-pneumonia on autopsy," etc.

One case—"J. L., thirty-two years old; three days sick; intoxicated on admission, with marked tremor"—is cited to show a type of case in which antitoxin should not be used,

“Dr. Winters insists that we should study the fatal cases, not those that result in recovery. Therefore he has not told you that for every eight first-day cases that died, ninety-two recovered; for every twenty-four second-day cases that died, seventy-six recovered; for every twenty-seven third-day cases that died, seventy-three recovered.”

Dr. Brannan shows from the hospital books that with antitoxin less alcohol is used per head than before antitoxin was introduced, contrary to the statement of Dr. Winters. The broncho-pneumonia observed has been of the usual type; suppression of urine has occurred with about the usual frequency, and has generally been relieved by local applications and diuretics. Albuminuria has been observed more frequently; but the urine has been more carefully and systematically examined. Cardiac weakness has not been more frequent, and post-diphtheritic paralysis (excepting temporary paresis of the palatal muscles) has been noteworthy by its absence.

The rest of Dr. Winters' evidence is similarly disposed of, special stress being laid on the complete absence of *post-mortem* findings in his reports.

As for his European investigation, it is shown that his authorities are either recognized opponents of antitoxin, or young men who never had any experience of diphtheria in pre-antitoxin days, and whose opinions are therefore of little or no value.

Arthur J. Hutchison.

Coakley, C. G.—*Statistics of Diphtheria*. “Med. Record,” June 6, 1896.

THIS is an examination (with tables) of the diphtheria statistics of Boston, New York, and Brooklyn from 1880 to 1895, also of those of the Boston City Hospital and the Willard Parker Hospital, with a view to estimating the value of the antitoxin treatment. Two sources of error have to be allowed for in treating municipal statistics. (1) The neglect to report cases. The busy practitioner will generally report his severe, and specially his fatal, cases, but will often forget to report the mild cases. (2) The variation in character or type of the disease from year to year.

A very marked increase in the number of cases reported took place in each of the three cities in the year in which these cities provided public laboratories for bacteriological investigation of the cases.

Contrasting “percentage mortality” with “number dying per 10,000 inhabitants” in Boston some interesting discrepancies appear. Thus, between 1886 and 1887 there occurred a rise of 2·5 in percentage, but a fall of 0·5 dying per 10,000 inhabitants; again, between 1888 and 1889 a fall of over two in percentage, with a rise of nearly two dying per 10,000 inhabitants; again between 1893 and 1894 a fall in percentage of nearly 5·5 and a rise of 6·7 dying per 10,000 inhabitants. The introduction of bacteriological examination of cultures from the throat, begun in 1894, was the means of discovering many mild cases, and thus increasing the total of cases; and as the patients in these cases mostly recovered the death rate was reduced. In 1895, when antitoxin treatment was used, there was a further very marked fall in the percentage mortality—12·5 of a fall, accompanied by a fall of about five in the number dying per 10,000 inhabitants. Such sudden falls in the number dying per 10,000 have occurred several times in other years, so that one cannot right away give the credit for this reduction to antitoxin. The percentage mortality for 1895 is phenomenally low—about half what it used to be—but in ten out of the sixteen years recorded the number dying per 10,000 inhabitants has been lower than in 1895. Similar results are obtained from the other tables. The conditions in the bacteriological and the pre-bacteriological periods are so different “that any comparison of the death-rate of the one period

“with the death rate of the other period will be apt to lead one to erroneous conclusions.”
Arthur J. Hutchison.

Glaser (Hamburg).—*Reports on Twenty Years' Diphtheria in the Hamburger Allgemeiner Krankenhaus.* “*Zeitschrift für Klin. Med.*,” Band 30, Heft 3, 4.

IN Hamburg from 1872 to 1891 there were 52,938 cases of diphtheria, with a mortality of 8241, or 14 per cent. In the hospital 4358 were treated, with a mortality of 1584, or 36.3 per cent. Only the most important data will be given here. Of 743 cases treated in the hospital before the fourth day of the disease, 280, or 37 per cent., died; of 325 admitted later, 163, or 50 per cent., died. The cases with high temperature gave the worst results, but the duration of the fever had less influence, whilst albuminuria increased the mortality. It is curious that the cases which only had tonsillar diphtheria give worse results than when it is spread on other parts of the mouth; and nasal diphtheria is of grave import. Of 1768 tracheotomies 343 recovered. Of 935 *post-mortem* examinations, 47 cases showed lethal complications which had no relation to the disease. The therapy consisted in ice application, spray of salt or boric solution, antiseptic irrigation of the nose, and nourishing diet. The author concludes: the mortality of Behring's cases is improved by the great number of slight cases, and the per centual mortality diminished.
Michael.

Halderman, S. S.—*Antitoxin in the Treatment of Diphtheria; with Report of a Fatal Result from a Prophylactic Injection.* “*Journ. of the American Med. Assoc.*,” June 13, 1896.

IN an epidemic of diphtheria of great severity the writer treated with antitoxin seventy cases, all presenting the typical signs of diphtheria, and some bacteriologically proved diphtheritic, without losing a single case. He used Behring's serum as a prophylactic in twenty-seven cases, “with the desired result of preventing the development of diphtheria in all but three cases; these three cases manifesting evidence of the disease within less than seventy hours, showing that it was already in their systems and incubating.”

A fatal result occurred in a child of five years old. The child had just wakened from a sound sleep, and the prophylactic dose was injected into the subcutaneous tissue below the right scapula. He made but slight outcry, lay down, and was noticed to try to scratch the spot where the injection had been made. Within four minutes the child was cyanotic, lips swollen and puffy, no radial pulse and no heart beat to be made out. Twenty-five minutes' artificial respiration, etc., was of no avail. No explanation is offered, except “idiosyncrasy.”

Along with antitoxin the writer recommends Loeffler's solution locally, calomel internally pretty freely, for its cathartic effects, free administration of beef tea, sterilized milk, coffee and any carefully prepared food the patient desired. Tr. *erri perchlor.* in syrup and glycerine every hour (to please the nurse); if very restless, chloral and morphia; later on small doses of quinine and strychnine. He never gives potass. chlorate internally, and thinks his good results may be partly due to that fact.
Arthur J. Hutchison.

Kortright, James L.—*The Value of Antitoxin.* “*American Medico-Surg. Bulletin*,” July 4, 1896.

A SHORT paper without figures, in which the author expresses himself in favour of antitoxin in diphtheria. He prefers Aronson's antitoxin, or that prepared by the Brooklyn Health Board, to any other preparation. The risk run is not to be ignored, but should be faced in presence of the disease, but the practice of “immunizing” should be given up.
Arthur J. Hutchison.

Mundorff, Geo. Th.—*Severe Post-Diphtheritic Paralysis in an Adult treated by Antitoxin.* "Med. Record," June 27, 1896.

THE patient, aged twenty, had diphtheria in December, 1895, was treated without serum, and recovered. A few weeks later paralysis began to appear, slight at first, but growing steadily worse, till patient came to hospital, March 2nd, 1896. He was then greatly emaciated, muscles of limbs and trunk atrophied. Two injections of antitoxin were given, and the man recovered.

It should be noted, however, that the first injection was given on March 4th—*i.e.*, two days after admission, and, therefore, before it was possible to judge whether recovery had already commenced, or whether ordinary hospital treatment alone would have been sufficient: it is, therefore, impossible to give the antitoxin any credit for the result.
Arthur J. Hutchison.

Struck, Carl.—*Once more on Antitoxin.* "The Journ. of the American Med. Assoc.," May 16, 1896.

THE first part of this paper quotes and criticises statistics from various sources, apparently in favour of the antitoxin treatment of diphtheria. It points out that percentage mortality is misleading, because in many cases where this has been reduced even as much as half (fifty per cent.), the numbers dying from diphtheria per thousand inhabitants has increased (*e.g.*, Boston); again, because the number of cases reported has simultaneously increased immensely (*e.g.*, Berlin); again, because in some places antitoxin has not been applied to very severe cases, or to cases seen after the third or fourth day of illness (*e.g.*, Chicago); again, because when antitoxin is used the drug treatment is either greatly modified or entirely given up, which alone might produce all the good results ascribed to the antitoxin; again, in one hospital the mortality in 1876 was thirty-four per cent., in 1886 only six per cent., yet no antitoxin was used (Basel Children's Hospital); again, the short experience of two years is not sufficient to determine the value of antitoxin treatment—a severe epidemic may completely change our present ideas on the subject. If no discredit is to be attached to antitoxin because it fails when used on the fourth or a later day, surely no credit should be given it when recoveries take place under similar circumstances.

If antitoxin is a specific for diphtheria, why do its advocates not use it in every case, and why does percentage mortality under its use vary from two (Stockholm) to sixty-three (Trieste)?

In the rest of the paper the ordinary treatment by drugs internally and the local application of antiseptics is briefly criticized and condemned—even the use of antitoxin is likely to be less harmful. With regard to the use of antitoxin in laryngeal diphtheria, the writer points out that it is quite illogical, because the "croup" does not become manifest till the diphtheria has already existed three or four days, *i.e.*, till it is too late to expect any good from antitoxin. Many of these are not cases of diphtheria, but simply of catarrh.

The author maintains that doctors "are enthused on" antitoxin, because diphtheria is an acute disease presenting great and sudden changes in its course and its severity, and because its natural history is not really known: on the other hand, such a fever as "enteric" will never be treated by an enteric antitoxin.

Arthur J. Hutchison.

Vissman, William. — *The Therapeutic Value of Diphtheria Antitoxin.*

"American Medico-Surg. Bulletin," July 4, 1896.

THIS is a short paper, with a table (taken from C. G. Coakley's paper, *vide supra*) of the statistics of diphtheria for Boston, New York, and Brooklyn from 1880 to 1895, in which is shown—

	New York.	Brooklyn.	Boston.
Average number of deaths from 1880 to 1895 ...	1631 $\frac{1}{4}$	824 $\frac{1}{4}$	452 $\frac{1}{2}$
Deaths reported in 1895	1634	1139	588
Average number dying per 10,000 inhabitants,			
1880 to 1895.....	10·84 $\frac{1}{4}$	10·24 $\frac{1}{2}$	10·90
Number dying per 10,000 inhabitants, 1895 ...	8·73	10·35	11·73

New York is thus the only city showing improvement during the antitoxin year. The percentage mortality is, on the other hand, strikingly reduced. This is due to the fact that the number of cases recorded has immensely increased. Physicians no longer diagnose diphtheria, but in any throat case take a swabbing, send it to the Health Department, and leave the responsibility of the diagnosis in their hands. Thus a child may have a white spot in its throat on which by chance one Loeffler bacillus has settled—this in the bacteriological laboratory is sufficient grounds for the diagnosis of diphtheria, which is absurd.

The danger of using antitoxin as a prophylactic is pointed out.

Arthur J. Hutchison.

MOUTH.

Beuermann, J. A.—*The Differential Diagnosis between Benign Lymphomyxoma and Malignant Lymphomyelia.* "New York Med. Journ.," Aug. 8, 1896.

THE author remarks on the extreme difficulty of diagnosis by microscopical examination between benign and malignant neoplasms of lymph tissue, especially when this is not accompanied by a knowledge of the clinical history of the case. He proceeds to describe the two forms quoted in the title, prefaced by the suggestion that "we admit the so-called protoplasm is traversed by a reticulum, the "points of intersection of which, previously termed 'granules,' may grow into "solid lumps of living matter, which in further development become vacuolated, "afterwards reticulated, and, at last, transformed into nucleated protoplasmic "bodies." Also, that we admit the existence of a delicate reticulum in connective tissue tumours, this reticulum being transformed into protoplasm. The small round-celled sarcoma of Virchow is termed lymphomyeloma. He takes a "so-called adenoid growth springing from the mucosa covering the turbinate bone" as an example of the lymphomyxoma, which is thus described: "The "main mass of the growth consists of lymph tissue, *i.e.*, a protoplasmic reticulum, "the meshes of which contain an indistinctly granulated basis substance and a "number of so-called lymph corpuscles, formations of living matter, varying in "size from a small homogeneous lump to a granular corpuscle." Stress is also laid on the fact that the reticulum is always traceable and the appearance of the masses referred to are minutely described, and are said always to exhibit "radiating spokes of living matter, which enter into and inosculate with the reticulum of the basis substance." In the lymphomyeloma, on the contrary, no reticulum is seen in the denser parts, and in others it is extremely delicate—the number of somewhat larger coarsely granulated protoplasmic bodies is far greater, and the number of still larger bodies still more marked, approaching a gliosarcoma in appearance. The more frequent these "lumps" in the reticulum the more rapid the growth and malignancy of the growth; and the fact that the fibrous capsule is unchanged is in favour of the tumour being benign. This is of especial value in tonsillar growths. Finally epithelium is attacked by malignant tumours, and not by benign.

R. Lake.