The value of antitoxin in the treatment of diphtheria.

Issued by the Research Defence Society, May, 1908.

THE VALUE OF ANTITOXIN IN THE TREATMENT OF DIPHTHERIA.

Issued by the Research Defence Society,

May, 1908.

THE VALUE OF ANTITOXIN IN THE TREATMENT OF DIPHTHERIA.

It is sometimes said, by the opponents of all experiments on animals, that these experiments have had no great result in the saving of life; and, by way of example, they point to the antitoxin treatment of diphtheria, denying that this has done anything to diminish the dangers of the disease, or even going so far as to say that diphtheria is often aggravated by the administration of antitoxin.

In support of this statement, they bring forward a number of statistics, obtained from the annual reports of the Registrar-General, shewing that the death-rate from diphtheria in proportion to the whole population has risen rather than fallen since the introduction of antitoxin in 1894. The following extract from a recent magazine article will serve to illustrate their line of reasoning:—

"Average diphtheria death-rate per million persons living "as recorded in the returns of the Registrar-General for the "last thirty years in quinquennial periods:—

1st	Quinquennial	Period	1876-1880	...	121
2nd	,,	,,	1881-1885	...	156
3rd	,,	,,	1886-1890	...	170
4th	,,	,,	1891-1895	...	252
5th	,,	,,	1896-1900	...	272
6th	,,	,,	1901-1905	...	204

"From this it will be seen that the highest death-rate ever "recorded took place in the five years of 1896 to 1900, which "synchronises with the spread all over England of the anti-"toxin treatment. During the last five years, 1901-1905, the "death-rate seems somewhat to have decreased, but it is still "above the death-rate for the whole time from 1876 to 1890, "during which time diphtheria patients escaped the attention "of the vivisectors. . . . All these figures, which can be "verified by anyone capable of simple arithmetical exercises, "show the insidious and malignant inroads the Black Art of "Vivisection has made upon human lives, wherever its "familiars have succeeded in practising their sorceries and "serums. . . . . The Registrar-General records his "dispassionate facts, and proclaims to the world that wherever "the hand of the vivisector is stretched out over a disease, "there that disease increases its hold upon life, and hurries men "faster to the tomb."

These returns of the Registrar-General may seem at first sight to give convincing proof of the uselessness of antitoxin in the treatment of diphtheria. But, if we look below the surface, it will at once become evident that the figures will not for a moment bear this interpretation; and the purpose of this pamphlet is to show that the argument against antitoxin treatment is based on three entirely false premises.

i. *It is impossible to judge of the value of the antitoxin treatment from a study of the death-rate in proportion to the general population.*

The distribution of an epidemic disease such as diphtheria varies widely from time to time. The disease may be very common one year, and very scarce the next; or a cycle of bad diphtheria years may be followed by a cycle of good years.

Supposing, now, that during a period of 5 years the prevalence of diphtheria were to be twice as great as during the preceding 5 years. If the severity of the disease remained unchanged, the death-rate in proportion to the general population would be approximately doubled, and it is absurd to expect that treatment, either by antitoxin or by any other means, could counteract such a largely increased death-rate. Unless, therefore, we know the number of cases of diphtheria during the period under consideration, it is quite impossible, from a study of the death-rate in proportion to the general population, to estimate the efficacy of antitoxin treatment; this can only be deduced from the *case-mortality*, that is to say, the percentage of deaths from diphtheria occurring amongst those who have contracted the disease.

ii. *It is impossible to estimate from any death-rate figures the value of antitoxin, unless we know in how many cases it was given.*

The truth of this statement is obvious. If antitoxin were given only in 5 per cent. of all diphtheria cases, the results, however brilliant, would not be reflected to any appreciable extent in the death-rate; whereas if it were given in every case we ought to be able to discover its effect, whether good or evil, from an examination of the case-mortality. The returns of the Registrar-General contain no information as to the number of cases treated by antitoxin, and the writer just quoted apparently assumes that since its introduction in 1895 it was given in every case of diphtheria. But this is very far from the truth. For, at first, antitoxin was regarded with a good deal of uncertainty and suspicion by the medical profession, so that only a small proportion of patients were treated in this way; and it is only of recent years, after passing

through a long period of probation, that it has come into general use, and is now almost universally given in all municipal fever hospitals. Moreover, in the early days, even those who believed in antitoxin were afraid to use it often enough, or in sufficient amount; the doses then given seem ridiculously small by the light of our present knowledge, and it is certain that they could not have produced the best results.

iii. *The Registrar-General's returns as to the death-rate from diphtheria are admitted to be untrustworthy, on account of the confusion that existed until recent years between diphtheria and croup.*

Sixty years ago, diphtheria was not regarded as a distinct disease, and not till 1855 did it appear in the Registrar-General's returns under its own name. For many years after 1855, there was a great deal of uncertainty as to what was and what was not diphtheria; and, in particular, a large number of cases of true diphtheria were classed as croup. The Registrar-General himself refers to this confusion, and in 1885 writes:—"The registered deaths from diphtheria fell from an annual average of 185 per million to 121; but so much uncertainty attaches to the use of the term diphtheria by medical men, and there is so much confusion in their certificates between diphtheria and simple spasmodic croup, that the returns under this heading are extremely untrustworthy." In addition, each annual return contains some such statement as this:—"In order to obtain an approximate measure of the loss of life caused by diphtheria, it has been found necessary to class the deaths definitely referred to that disease with those referred to croup."

The advance of bacteriology has done much to dispel this

uncertainty; and at the present time, when almost every large town owns a municipal laboratory, any doubtful case of sore-throat is submitted to the crucial test of a bacteriological examination; a culture is made from the throat and examined for the diphtheria bacillus. In consequence of these improved methods of diagnosis, a great number of cases which would previously have been classed as croup, are now returned as diphtheria. This has naturally led to a decreased record of mortality from croup, and a corresponding increased record of mortality from diphtheria, as is shown by the following table:—

	Average annual mortality from (*a*) Diphtheria.	(*b*) Croup.
1861-1870	3,945 ...	5,254
1883-1894	5,617 ...	3,331
1895-1906	7,586 ...	860

It is evident, therefore, that in order to determine from any statistical data the influence of antitoxin in the treatment of diphtheria, three conditions must be satisfied as far as possible:—

i. It is necessary to know the case mortality.

ii. It is necessary to know the number of cases in which antitoxin was given.

iii. The diagnosis of diphtheria in all cases under consideration must rest on the surest foundations.

These conditions are not likely to be fulfilled except in public institutions and hospitals, where

i. Accurate records are kept as to the progress and termination of every case.

ii. Antitoxin is given almost invariably as a matter of routine.

iii. The diagnosis of every doubtful case is verified by a bacteriological examination.

We may turn, then, to the statistics of recognised hospitals, with the assurance that here at last may be found an answer to the question, What is the value of diphtheria antitoxin? A few examples of these statistics are given here; they could be multiplied almost indefinitely.

Statistics of cases of diphtheria treated in the Metropolitan Asylums Board Hospitals† :—

Year.	Cases treated by Antitoxin; per cent. of all cases.	Mortality; per cent. of all cases.
1888-93	—	28·5
1894	—	29·6
1895*	61·8	22·5
1896	71·3	20·8
1897	80·2	17·5
1898	81·4	15·5
1899	—	13·95
1900	—	12·01
1901	—	12·5
1902	—	11·0
1903	—	9·7
1904	—	10·1
1905	—	8·3

† 65 per cent. of all cases of diphtheria in the County of London are treated in these hospitals.

* Commencement of the antitoxin period.

Statistics of cases of diphtheria in New York City from 1891-1899 :—

Year.	Cases.	Deaths.	Mortality per cent.
1891	5,346	1,970	36·7
1892	5,184	2,196	40·6
1893	7,021	2,558	36·4
1894	9,641	2,870	29·7

Year.	Cases.	Deaths.	Mortality. per cent.
1895* ...	10,353 ...	1,976 ...	19·1
1896† ...	11,399 ...	1,763 ...	15·4
1897 ...	10,896 ...	1,590 ...	14·6
1898 ...	7,593 ...	923 ...	12·2
1899 ...	8,240 ...	1,087 ...	13·1

* Antitoxin introduced.

† Use of antitoxin became general.

Statistics of cases of diphtheria treated in the Paris Hospitals, 1893-1898 :—

Year.	Case mortality per cent.
1893	45
1894*	31
1895	12
1896	15·2
1897	13·2
1898	14·5

* Commencement of antitoxin treatment.

The opponents of all experiments on animals object to hospital statistics on the grounds that the cases are selected, that a great many mild and favourable cases are admitted, and that the hospital patient has an advantage over the patient treated at home as regards careful nursing and skilled attention. Those who hold these objections seem to be unaware that until 1894 the diphtheria death-rate in hospital patients was always higher than in cases treated at home, because the former belonged to the poorer classes, who were less able to resist the attacks of any disease. Antitoxin treatment was at first almost confined to the hospitals, with the result that the mortality among hospital patients fell rapidly, and for the period 1895-1900 was slightly lower than among home-cases. Subsequently the death-rate among the

two classes of patients became equalised, coincidently with the general use of antitoxin. This is shown by the following table :—

Case mortality from diphtheria in London.

	Hospital Patients.	Home Patients.
1889-1894 ...	30·1 per cent. ...	24·2 per cent.
1895-1900 ...	16·0 „ ...	17·0 „
1901-1906 ...	10·0 „ ...	10·0 „

The value of antitoxin in laryngeal diphtheria.

In some cases diphtheria spreads from the throat to the larynx, whereby the disease at once becomes more serious, because the diphtheritic membrane may easily block the narrow orifice of the larynx and cause fatal suffocation. Under these circumstances the correct treatment is to perform tracheotomy. The death rate in these laryngeal cases has always been much higher than in others ; consequently, in testing the effect of antitoxin on laryngeal diphtheria, there is no possibility of the inclusion of a number of mild cases, which would have recovered if left to nature. The following figures show the influence of antitoxin under these conditions :—

Previous to 1894, the mortality among 8,927 hospital cases of laryngeal diphtheria was 71·6 per cent.

After 1894, the mortality among 2,374 cases, in which antitoxin was given, was 36·6 per cent., showing a reduction of nearly 50 per cent.

In Germany, an even greater reduction was obtained. There, before the introduction of antitoxin, the death-rate among cases of laryngeal diphtheria was 86 per cent. ; whereas of 2,041 children, treated with antitoxin, on whom tracheotomy had to be performed, 778 died, giving a death-rate of 33·6 per cent. Similar results have been obtained in other European countries and in America.

One other point, having an important bearing on the subject, is the varying effect of antitoxin according to the stage at which it is given. The ideal treatment is to give antitoxin on the first day. If this be done, any risk of death is almost obliterated; unfortunately, this is often impossible, as a diagnosis can rarely be made so soon. The later the administration of antitoxin is deferred, the less will be its effect in checking the disease, as can be seen from this table, compiled from the records of the Brook Hospital, London :—

No of cases treated.	Day of disease on which antitoxin was given.	Fatal cases.	Case mortality.
2,135	1st day	0	0
1,441	2nd „	62	4·3
1,600	3rd „	178	11·12
1,276	4th „	220	17·24
1,645	5th „ or later	308	18·72

If the antitoxin were of no value as a remedy, whether it were administered on the first or on the fifth day of the disease would be immaterial.

We have touched on only a few of the arguments in favour of antitoxin, but it is hoped that enough has been said to show that the claims put forward on its behalf are based on a solid foundation of use and experience. Those who still remain sceptical may be advised to seek the opinion of some officer in charge of a fever hospital.

GEORGE PULMAN AND SONS,
LONDON AND WEALDSTONE.