INTRAVENOUS INJECTION OF DIPHTHERIA ANTITOXIN IN CHILDREN *

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The benefits of the antitoxin treatment of diphtheria are well recognized. From 1878 to 1894 in New York City the deaths from diphtheria per hundred thousand of population ranged from 110 to 264 and from 1890 to 1895 the combined diphtheria deaths in the larger European and American cities from 66.9 to 80.4 per hundred thousand population, while following the general use of diphtheria antitoxin since 1895 the deaths per hundred thousand of population have varied in New York City between 22 and 91, and between 19 and 55.6 in the larger cities of the world.

Diphtheria antitoxin was first used generally in 1895 and in 1896 first manifested its real value in the United States. Gradually fewer deaths from diphtheria have occurred, but it must be evident that in the past few years the death-rate has not been decreased materially. That we still have some deaths due to the disease is too well known. When deaths occur in patients having received antitoxin we generally believe them due to one of three causes: late administration of antitoxin, injection of insufficient amount of antitoxin, or the presence of exceptionally virulent diphtheria bacilli. Knowledge of these facts, however, is of little value in some of the cases of diphtheria seen, for any one having charge of diphtheria patients in a hospital for contagious diseases or doing consultation work in the diseases of children meets with patients who have had diphtheria for some days, but have had little or no diphtheria antitoxin administered. No wonder, then, that the need for further investigation of the treatment of diphtheria should be recognized and that any method which enables diphtheria antitoxin to exert its influence at the earliest possible time after administration should be tried.

We know that it is through the blood that antitoxin is distributed to the places where it binds toxins, and last year Park¹ reported from his experiments that he believed 5,000 units introduced intravenously are as beneficial as 20,000 units injected subcutaneously. His experiments showed that six hours after injection the blood-serum contains twenty units per cubic centimeter of blood when injected intravenously

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1. Park: Boston Med. and Surg. Jour., 1913, clxviii, 73.

and two when given subcutaneously, and after twenty-four hours twelve units when given intravenously and six when injected subcutaneously.

Intravenous injection of diphtheria antitoxin was long ago practiced, but has usually not been followed because the subcutaneous method gives good results and intravenous injection is difficult in children. The veins of the arm are often too small, so in this series antitoxin was administered by way of the external jugular vein. Martha Wollstein² reported obtaining blood for cultures from children

TABLE 1.—GENERAL RESULTS OF DIPHTHERIA ANTITOXIN INJECTIONS

	Subcutaneous Injection		Intravenous Injection	
		Average		Average
Day of disease on which injections were made..	3, 8, 10, 3, 8, 7, 5	6.3	1, 3, 2, 2, 3, 2, 6, 10, 3, 3, 3, 10, 7, 3	4.1
Units injected at one time	3,000 × 2 5,000 × 7	4.555	5,000 × 10 10,000 × 6	6.875
Number of injections made	9	1.3	16	1.1
Days after injection on which fever and membrane were absent and patients felt well.....	13, 6, 4, 5, 10	7.6	2, 1, 3, 2, 1, 2, 1, 2, 4, 2, 2, 3	2.1
Days after injection on which diphtheria bacilli were absent	30, 36, 43, 16, 8	26.6	12, 8, 14, 2, 8, 2, 5, 5, 4, 6, 4, 6	5.4
Total days sick.....	15, 20, 12, 15, 15	15.4	3, 4, 5, 4, 4, 4, 7, 12, 14, 5, 5, 10	6.4
Total days confined.....	31, 44, 38, 22, 37	34.4	18, 20, 22, 11, 16, 14, 11, 23, 26, 7, 16, 13	16.4
Carriers		4.		0.
Serum reactions		0.		4.
Immediate reactions.....	0		4	
Deaths		2.		2.
Laryngeal diphtheria....		2.		7.
Paralysis { Cardiac		3.		0.
{ Palatine		1.		1.

by going into the jugular vein and the method she suggested was employed in the cases reported here. In all, fourteen children received intravenous injections of diphtheria antitoxin. The results and symptoms observed are compared with those obtained in the same epidemic by subcutaneous injection in seven cases. The latter patients were seen in consultation and some had received diphtheria antitoxin before they were seen by me. The general results are shown in Table 1.

2. Wollstein, Martha, and Morgan, Edward: Blood Cultures During Life in Infants and Young Children, with Description of a New Technic, *AM. JOUR. DIS. CHILD.*, October, 1912, p. 197.

It is evident that so small a series does not offer enough evidence on all of the facts detailed. It seems fair, however, to draw some conclusions from the data. It will be observed that following intravenous injections the fever and membrane disappeared sooner and the patients felt well; that diphtheria bacilli disappeared more rapidly; that there were fewer carriers and that paralyses were less frequent than when subcutaneous injections were made.

Two children died in each series; death occurred from seven to fourteen hours after the first injection in each case. All four children who died had laryngeal diphtheria, but there were seven cases of laryngeal diphtheria in the series that received intravenous injections, and only two in the series given subcutaneous injections.

Reactions, however, followed only intravenous injections. The data in regard to this are shown in Table 2. These reactions are classified as "immediate" and "serum" reactions.

TABLE 2.—INTRAVENOUS INJECTION REACTIONS

Immediate Reaction		Average	Serum Reaction		Average
Time after serum injection	1, 1, 1½, ½ hrs.	1 hour	Days after serum injection	9, 10, 10, 6	8.8
Temperature elevation	103.2, 104 103.8, 103.2		Rash		4 cases
Disappeared in...	3 hrs., 20 hrs. 5 hrs., 20 hrs.	12 hours	Glandular enlargement		1 case
Respiratory distress	2 cases		Articular pain.. Days on which symptoms dis- appeared	 2, 2, 2, 3, 1	1 case 2.25

"Immediate Reaction."—Generally, the introduction of diphtheria antitoxin is not believed to be followed by an elevation of temperature, but slight elevations do occur frequently. When given intravenously, four injections out of sixteen were followed in from one-half to one and a half hours by striking symptoms. These were usually ushered in by a marked chill, then an elevation of temperature from 103.2 to 104 F., and in two cases by respiratory distress. All of these symptoms disappeared in from three to twenty hours, when the patients usually felt entirely well. That these were serum reactions did not seem to be the case, as in none did the later serum rashes appear. When serum rashes and reactions did occur they did not differ from those following other serum injections, though none occurred in the small series of patients receiving subcutaneous injections.

SUMMARY

It is not to be inferred that intravenous injections are advocated in all cases, but intravenous injections undoubtedly produce results more rapidly and so are to be preferred in late and severe cases.

Intravenous injection is less painful at the time of administration and later, and because of the smaller number of units necessary intravenous injection is much less expensive. Entrance into the jugular vein in children is not difficult and this vessel affords a ready site for the intravenous injection of diphtheria antitoxin when the median basilic and the cephalic veins are too small. This small series indicates that there are fewer carriers and heart failures are less likely to occur following intravenous injection, but there are more immediate and serum reactions. The immediate reactions never impressed us as being grave and in themselves did not seem to be a contra-indication to intravenous injection of diphtheria antitoxin.

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