

THE TREATMENT OF TETANUS WITH ANTITOXIN*

AN ANALYSIS OF THE OUTCOME IN SIX-HUNDRED FORTY-TWO CASES

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UNEQUIVOCAL evidence for the therapeutic efficacy of antitoxin after the onset of symptoms of tetanus has been obtained only in animal experiments,⁵ and differences between the experimental disease in laboratory animals and the clinical disease in man are sufficient to invalidate any argument by analogy. Most clinicians feel that the results of serum treatment of tetanus have been very disappointing, and data from the World War experience^{2,3} seem to indicate that tetanus antitoxin, invaluable as a prophylactic, is relatively useless as a therapeutic measure. Nevertheless, the continued use of antitoxin in cases of tetanus indicates that the question is not settled, and it appears that further data are desirable.

A series of 642 cases was collected from the records of a group of hospitals.¹ The authors bear the sole responsibility for the presentation and interpretation of the figures; nevertheless, in the truest sense, the work represents a joint contribution of these hospitals, and we wish to acknowledge the great courtesy which we received from their administrative and professional staffs. Particular thanks are due to the record room workers.

Seventy-two cases from preantitoxin days form a control group. The remaining cases have been grouped according to the amount of antitoxin given within 12 hours of admission to a hospital,† and according to the method of administration. Since, in experimental tetanus, serum is apparently most effective if given intrathecally,⁵ special attention has been given to the cases of patients treated in this manner. Such cases have been classified by the amount of antitoxin given by this route, only within 12 hours of admission. The groups and their respective mortalities are given in Table I.

The mortality for the untreated group approximates that of the whole

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† In most instances the dose cited was given within six hours of admission. In the few cases which developed in a hospital, the figures are for treatment given within 12 hours of the first symptoms. Submitted for publication April 17, 1936.

TABLE I
MORTALITY IN UNTREATED CASES, AND IN GROUPS
CLASSIFIED ACCORDING TO TREATMENT

Groups	Total Antitoxin within 12 hrs.	Intrathecal Antitoxin within 12 hrs.	Cases	Deaths	Mortality Per Cent
A	None	None	72	47	65.3
B	Less than 10,000 U	None	116	68	58.6
C	10,000 U or more	None	112	74	66.1
D	Not specified	Less than 2,000 U	74	47	63.5
E	Not specified	2,000-9,000 U	107	70	65.4
F	Not specified	10,000 U or more	161	99	61.5
Totals			642	405	63.0

series, and there are no significant differences among the several groups. Nearly all the patients who received intrathecal antitoxin received large intravenous and intramuscular doses in addition. Of the patients not treated intrathecally, many of those (Group C) received very large amounts of antitoxin within the stated time. All but six of these patients received at least 20,000 units within 12 hours after hospitalization. From these data it is evident that small or large doses of antitoxin have little effect on the mortality.

The figures generally cited as evidence for the therapeutic value of diphtheria antitoxin are those correlating early treatment and low mortality. However, in the study of these tetanus cases it soon became evident that the mortality was highest in patients admitted to the hospital within 24 hours of the first symptoms, in both the untreated and treated groups. In Table II the entire series is analyzed according to two prognostic criteria, the incubation period, and the time between the onset of symptoms and hospitalization. The correlation between the two is interesting.

It will be seen that in the cases of patients admitted on the first day the incubation period is usually short. Both the incubation period and the duration of symptoms to admission must be considered in evaluation of the prognosis, but the latter seems actually the more important. This observation does not mean that early treatment was harmful. It merely shows that the rapidity with which symptoms progress is an important factor in the prognosis. Patients whose symptoms compel them to seek hospitalization within 24 hours of the onset of the disease are patients with severe tetanus. However, these figures confirm the belief that the effect of antitoxin treatment cannot be great.

Since serum treatment, if effective at all, should be chiefly so on the first day of the disease, it seemed desirable to select from the treated and untreated groups cases of patients admitted within this interval whose incubation periods were comparable. The figures are given in Table III.

Here again it is clear that treatment is not associated with a marked diminution of mortality. There is a slight difference in favor of the patients

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TABLE II
AN ANALYSIS OF THE OUTCOME IN 642 CASES OF TETANUS, WITH REFERENCE TO INCUBATION PERIOD, AND THE DURATION OF SYMPTOMS OF TETANUS UP TO THE TIME OF HOSPITALIZATION

Incubation (days)	1		2		3		4		5		6 & +		Uncertain*		Total	
	D	R	D	R	D	R	D	R	D	R	D	R	D	R	D	R
0-7.....	98	10	34	8	8	1	2	8	0	0	1	6	17	3	158	36
8-14.....	45	15	33	17	12	15	10	11	0	1	2	15	25	5	127	79
15-21.....	7	6	7	6	5	5	2	6	1	3	1	15	7	4	30	45
More than 21..	3	0	3	4	1	4	3	1	0	1	0	1	2	1	12	12
?.....	27	5	9	4	14	11	4	12	3	7	7	20	12	6	78	65
Total	180	36	86	39	40	36	21	38	4	12	11	57	63	19	405	237

D = deaths. R = recoveries.
* This column includes cases in which the duration of symptoms was not stated in the history, and the few cases which developed in a hospital.

TABLE III
CASES OF PATIENTS ADMITTED ON FIRST DAY OF
SYMPTOMS OF TETANUS

Group	Incubation 0-7 Days			Incubation 8-14 Days		
	Cases	Deaths	Mortality	Cases	Deaths	Mortality
A.....	11	11	100.0%	1	1	100.0%
C.....	15	14	93.3%	15	13	86.7%
A-D incl.....	57	54	94.7%	36	30	83.3%
E and F.....	51	44	86.3%	24	15	62.5%

receiving over 2,000 units intrathecally. This difference is barely twice the calculated standard deviation;^{6, 7} such a difference is classed as "probably significant" by some statisticians. However, unqualified "significance" is attributed only to differences of a magnitude at least three times that of the standard deviation. The present data might be interpreted as a corroboration of the experimental data in favor of intrathecal treatment, but their evidential value is slight.

TABLE IV
MORTALITY IN PATIENTS ADMITTED ON FIRST DAY OF SYMPTOMS, WHOSE
INCUBATION PERIODS WERE NOT LONGER THAN 14 DAYS

Comparison of Groups A-D with Groups E-F

Groups	Cases	Deaths	Mortality
A-D.....	93	84	90.3%
E-F.....	75	59	78.7%
Difference.....			11.6%
Calculated Standard Deviation...			5.5%

The figures given there confirm those of previous workers,^{2, 3} and indicate that relatively little has been accomplished in the specific treatment of tetanus. Further work may confirm or deny the suggestion as to the desirability of intrathecal treatment. It is hoped that the data in Table II may be of value as a control for further therapeutic experiments. At present it would seem that adequate sedation was the most hopeful line of attack.

REFERENCES

- ¹ Data were collected from the following hospitals: in Boston, Children's, Massachusetts General, Boston City; in Hartford, Conn., Hartford Hospital; in New Haven, Conn., New Haven Hospital; in New York, Presbyterian, Babies', Roosevelt, Mt. Sinai, Bellevue; in Philadelphia, University of Pennsylvania, Children's, Episcopal, Jefferson, Presbyterian; in Baltimore, Johns Hopkins, University of Maryland; in St. Louis, Barnes and St. Louis Children's.
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