ANALYSIS OF CASES OF TETANUS TREATED IN HOME MILITARY HOSPITALS

FROM AUGUST, 1914, TO AUGUST, 1915.

BY

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THE object of this paper is to give medical officers serving in military hospitals at home the result of various methods of treatment in cases of tetanus.

In December, 1914, a return of cases of tetanus was called for from home military hospitals, and an army form issued. Up to the present, notes on 231 cases have been sent in; of these, 98 recovered and 133 died. This gives a mortality of 57.7 per cent. In the *Memorandum on the Treatment of Injuries in War* (July, 1915)¹ it is reported from overseas that 179 cases of tetanus have been treated. Of these 179 cases, 140 died, a case mortality of 78.2 per cent.

The death-rate in untreated cases is stated to be 91 per cent. in those of short incubation, 50 per cent. in those of delayed incubation.

On examining the rate of mortality at the various hospitals where cases of tetanus have been treated, it is seen that at Netley it stands at 81 per cent. This is probably due to the fact that as this hospital is near the port of disembarkation the most serious cases and those already showing symptoms of tetanus would naturally be sent there.

There were 6 cases at Aldershot with 6 recoveries. As this result is very satisfactory, it may be useful to describe the method of treatment employed.

Cases of Tetanus treated at Aldershot.

Case 40.—The wound was in the right arm and caused by a shrapnel bullet. Five days after the wound, on his admission to Aldershot Hospital, he had 1,500 units of antitetanic serum injected subcutaneously as a preventive measure. Symptoms of tetanus occurred nine days after this injection, fourteen days after the date of wound. He now had 3,000 units injected subcutaneously and intrathecally on two days. Recovered.

Case 41.—Gunshot wound of middle finger of the left hand. On his admission to Aldershot Hospital he received 1,500 units as a preventive measure. Symptoms of tetanus occurred fourteen days after this injection and nineteen days after wound. Same treatment as in Case 40. Recovered.

Case 42.—Gunshot wound, scrotum and right thigh. He received 1,500 units on admission, five days after wound. Four days after this symptoms of tetanus appeared, and he received 4,500 units intrathecally in three doses on two days. Recovered.

Case 43.—Shell wound in left hip. On admission, three days after wound, 1,500 units were injected. Symptoms of tetanus appeared seven days after this injection, about ten days after the wound; 3,000 units subcutaneously and intrathecally. Recovered.

Case 44.—Gunshot wound, thorax. No preventive dose was given in this case on admission to the Aldershot Hospital. Symptoms of tetanus appeared six days after wound; 4,500 units in three doses, all intrathecally; 1,500 each, two on one day and one the day following. In addition, 2 c.cm. of a 25 per

cent. solution of magnesium sulphate were injected into the spinal canal with each injection of serum. Recovered.

Case 45.—Gunshot wound of left hand. A preventive dose of 1,500 units was given on admission and thirteen days after wound. Symptoms three days after this injection and sixteen after wound; 3,000 units in one day subcutaneously and intrathecally. Recovered.

It may be that these cases were slight, and would have recovered spontaneously, but two things must be remarked. In five of the cases a prophylactic dose of serum was given immediately on admission to hospital at Aldershot, and in the curative treatment the direct injection into the spinal canal was always used. In England resort to this preventive use of serum seems to have been rare, and it is suggested that in suspicious cases it seems a sound line of treatment. After onset of symptoms the intrathecal way of approach appears also to be by far the most effective.

At Aberdeen there were 3 cases with 3 recoveries. None of these had a preventive dose on admission to the Aberdeen Hospital. One had 147,000 units (140,000 subcutaneously, 4,000 intravenously, and 3,000 intrathecally), another 18,000 units (16,500 subcutaneously, and 1,500 intrathecally), while the third had only 3,000 subcutaneously.

Colchester also had good results—7 cases with 5 recoveries. Here also there was no prophylactic treatment on admission, and nothing noteworthy in the manner of curative treatment.

THE DISTRIBUTION OF CASES OF TETANUS BETWEEN AUGUST, 1914, AND AUGUST, 1915.

The first cases occurred in August, 1914, and the following diagram represents as nearly as possible the number of cases which occurred in each month until the following July. It is impossible to show the proportion of cases of tetanus to the number of wounded, as the information is not at present obtainable.

Diagram I.

From Diagram I it will be seen that most of the cases occurred during September, October, and November, 1914. This may have been due to the fact that the wounded

¹ BRITISH MEDICAL JOURNAL, August 21st, 1915, p. 305.

TABLE I.—Particulars of the Six Cases treated at Aldershot.

No. of Case.	Date of Wound.	Prophylactic Injection of Serum.				Onset of Symptoms.			Curative Treatment by Antitetanic Serum.			
		Date.	No. of Days after Wound.	Method.	Units.	Date.	No. of Days after Wound.	No. of Days after Prophylactic.	Date.	Subcutaneously.	Intrathecally.	Result.
40	1914. Oct. 18.	1914. Oct. 23.	5	Subcutaneously	1,500	1914. Nov. 1.	14	9	1914. Nov. 2 Nov. 3	— 1,500	1,500	Recovered.
41	Oct. 18.	Oct. 23.	5	Subcutaneously	1,500	Nov. 6.	19	14	Nov. 6 Nov. 7	— 1,500	1,500	Recovered.
42	Oct. 18.	Oct. 23.	5	Subcutaneously	1,500	Oct. 27.	9	4	Oct. 27 Oct. 28 Oct. 28	— — 1,500	1,500	Recovered.
43	Oct. 26.	Oct. 29.	3	Subcutaneously	1,500	Nov. 5.	10	7	Nov. 5.	1,500	1,500	Recovered.
44	Oct. 25.	—	—	—	—	Oct. 31.	6	—	Oct. 31 Nov. 1	— —	3,000 1,500	Recovered.
45	Oct. 20.	Nov. 2.	13	Subcutaneously	1,500	Nov. 5.	16	3	Nov. 5.	1,500	1,500	Recovered.

were more exposed to contamination of their wounds at that time, which included the retreat from Mons; that there was less opportunity of receiving surgical treatment as rapidly and as effectually as later on; that during this time the preventive use of antitetanic serum had not been developed, as it has during the last six months, when it is reported that, wherever possible, every wounded man has received a prophylactic dose; and generally that experience has taught medical officers how better to cope with the conditions obtaining in time of war, to unlearn the lessons of modern aseptic surgery, and to revert to the older methods of free incisions, thorough drainage, and constant removal of septic products by baths or irrigation.

At the present time it is impossible to say which of these factors has been the most important.

RELATION OF THE NUMBER OF DAYS WHICH ELAPSED BETWEEN THE DATE OF WOUND AND THE ONSET OF SYMPTOMS, AND THE RATE OF MORTALITY.

It is well known that the rate of mortality depends on the length of time which has elapsed between the date of the wound and the onset of symptoms, and the following diagram shows that the cases of tetanus under consideration follow the same law.

Diagram II.

Diagram II shows that in the cases dealt with, if the symptoms of tetanus appeared within ten days of receiving the wound, the mortality was 66.6 per cent.; if between the eleventh and twenty-fifth day, 39 per cent.

The Incubation Period, or Number of Days which Elapse between the Date of Wound and the Onset of Tetanus Symptoms.

The following curve shows the number of cases which occurred on each day from the third day after date of wound.

Curve 1.

From Curve 1 it will be seen that, in the cases of tetanus under consideration, more occur on the tenth day after the wound than on any other. The incubation period may be as short as three days and as long as 157.

TREATMENT OF TETANUS BY ANTITETANIC SERUM.

A.—Preventive Treatment.

Among the 231 cases, only 37 are noted as having been treated with antitetanic serum before the onset of symptoms: 20 in France, 7 in England, 10 not specified. Of these 37, 18 recovered and 19 died, giving a mortality of 51.3 per cent.

The usual dose was 1,500 units (8 records), but 1,000 were given in 3, 500 in 3, and 4,000 in 2.

TABLE II.

	Recovered.	Died.
8 cases inoculated on day of wound	3	5
3 " " one day after wound	2	1
3 " " two days after wound	2	1
2 " " three days after wound	1	1
2 " " five days after wound	1	1
3 " " six days after wound	3	0
2 " " seven days after wound	0	2
1 " " eight days after wound	0	1
1 " " nine days after wound	2	1
3 " " eleven days after wound	1	0
9 cases were unaccounted for.		

The average incubation period of 17 fatal cases was thirteen days; of 15 cases which recovered, 18.5 days.

B.—Curative Treatment.

Out of the total of 231 cases the numbers treated with antitetanic serum after the onset of symptoms was 215 (93 per cent.). Sixteen cases did not receive curative treatment with antitetanic serum in England. Of these, 3 recovered and 13 died; mortality, 81.25 per cent. Of the 3 which recovered all had been treated prophylactically in France. Of the 13 who died 6 had been treated prophylactically in France.

Of the 215 cases 116 were treated by subcutaneous injections alone; 46 recovered, 70 died. Mortality, 60.3 per cent.

Of the 215 cases 7 were treated by intravenous injections alone; 1 recovered, 6 died. Mortality, 85.7 per cent.

Of the 215 cases 14 were treated by intrathecal injections alone; 8 recovered, 6 died. Mortality, 42.8 per cent.

Of the 215 cases 17 were treated subcutaneously and intravenously; 5 recovered, 12 died. Mortality, 70.9 per cent.

Of the 215 cases 41 were treated subcutaneously and intrathecally; 23 recovered, 18 died. Mortality, 43.9 per cent.

Of the 215 cases 2 were treated intravenously and intrathecally; 1 recovered, 1 died. Mortality, 50.0 per cent.

Of the 215 cases 16 were treated subcutaneously, intravenously, and intrathecally; 8 recovered, 8 died. Mortality, 50.0 per cent.

Of the 215 cases 73 were treated intrathecally with or without subcutaneous or intravenous injections; 40 recovered, 33 died. Mortality, 45.2 per cent.

It would appear from Diagram III, which represents this graphically, that injections of antitetanic serum into

Diagram III.—Treatment of tetanus by antitetanic serum, showing rate of mortality in subcutaneous, intravenous, and intrathecal methods of injection. S., Subcutaneous; I., intravenous; S.I., subcutaneous and intravenous; T., intrathecal; T.S., intrathecal and subcutaneous; S.I. & T., all three; W., intrathecal with or without others.

the spinal canal are more effective than subcutaneous or intravenous injections.

The Influence of Dosage on the Curative Action of Antitetanic Serum.

It is generally held at the present time that success in the treatment of tetanus by antitetanic serum depends on the use of big doses.

Out of the 231 cases under review, in 200 only was the amount of serum recorded. In analysing these 200 cases it must be noted that the amount of serum given is the total amount, not the daily amount or the amount of each dose. For example, if a serious case came into hospital, received 10,000 units, and died at the end of one day's treatment, this would be put down as 10,000, whereas a milder or more chronic case receiving the same treatment for ten days would be returned as having had 100,000 units. It would be false to argue that as the one got ten times as much serum as the other and recovered, the result was due to the larger amount of serum given.

In the returns sent in the daily amount is seldom given; what is recorded is the total amount given from the beginning to the end of treatment.

It is suggested that in the returns sent in in future the daily amounts should be specified, and the mode of injection, intrathecal or otherwise, carefully recorded.

Out of the 200 cases 4 received 1,000 units or under; 2 recovered, 2 died. Mortality, 50 per cent.

Out of the 200 cases 61 received from 1,001 to 5,000 units; 24 recovered, 37 died. Mortality, 60 per cent.

Out of the 200 cases 50 received from 5,001 to 10,000 units; 14 recovered, 36 died. Mortality, 72 per cent.

Out of the 200 cases 20 received from 10,001 to 15,000 units; 12 recovered, 8 died. Mortality, 40 per cent.

Out of the 200 cases 19 received from 15,001 to 20,000 units; 6 recovered, 13 died. Mortality, 68 per cent.

Out of the 200 cases 19 received from 20,001 to 30,000 units; 10 recovered, 9 died. Mortality, 47 per cent.

Out of the 200 cases 14 received from 30,001 to 40,000 units; 9 recovered, 5 died. Mortality, 36 per cent.

Out of the 200 cases 13 received from 40,001 to 147,000 units; 9 recovered, 4 died. Mortality, 38 per cent.

The main conclusion to be drawn from a study of these cases of tetanus treated therapeutically by antitetanic serum is that it seems highly probable that the serum has little or no effect on the course of the disease. There is a little evidence that, if the serum has any effect at all, then the intrathecal method of injection is the most effective. It hence arises that, if serum is to be used at all, then it should first and foremost be injected intrathecally in as large dose as possible, and repeated as often as safe and practicable, as long as symptoms persist. If there is any likelihood that tetanus toxin is still being absorbed into the blood stream from the wound, then, in addition to the intrathecal injection, a further quantity of serum may be introduced intravenously and subcutaneously. In this way 3,000 to 5,000 units could be injected into the spinal canal and 10,000 to 20,000 into a vein and under the skin.

On account, doubtless, of the ease of giving serum by subcutaneous injection, this method is most used. In 116 cases out of the 215 under consideration (54 per cent.) it was the only method used. In 190 cases (88 per cent.) it was one of the methods used. The intrathecal method was only used in 73 cases out of the 215 (33 per cent.).

Now the contention is that the intrathecal path should be used in every case where serum is used, either alone or in conjunction with the other methods.

OTHER THERAPEUTIC REMEDIES.

1. *Carbolic Acid Injections.*

The treatment of tetanus by carbolic acid injections was described by Baccelli in 1888, and consists of the subcutaneous or intramuscular injection of carbolic acid. It is generally used in a 1 in 20 solution, and from 3 grains to 12 grains of the acid constitute a daily dose.

In the present series 33 cases were treated by this drug; 12 patients recovered and 21 died (63.6 per cent.).

In Table III the single injections and daily quantities are expressed in grains of carbolic acid. The cases are arranged according to the amount of carbolic acid given per diem, from 0.45 grain in Case 75 to 80 grains daily in Case 206.

From a study of the table it would appear that there is no evidence that carbolic acid has any favourable therapeutic effect on cases of tetanus. It is also suggested that

small doses, such as half a grain a day, are quite inadequate.

TABLE III.

No. of Case.	Single Dose, in Grains.	Quantity per Diem, in Grains.	Total Quantity Injected.	Recovered.	Died.
75	0.45	0.45	2.25 gr. in 5 days	R	
92	0.2	0.6	1.2 gr. in 2 days		D
214	0.22	5.2	?		D
51	0.9	5.4	5.4 gr. in 1 day	R	
219	0.9	7.2	27.0 gr. in 4 days		D
10	2.6	7.8	?		D
14	0.7	8.4	94.5 gr. in 18 days	R	
20	0.75	9.0	18.0 gr. in 2 days		D
223	0.9	10.8	42.0 gr. in 3 days		D
13	1.0	12.0	?	R	
229	1.1	13.2	26.0 gr. in 2 days		D
231	2.25	13.5	108.0 gr. in 14 days	R	
155	1.35	16.2	24.0 gr. in 1½ days		D
6	1.5	18.0	?	R	
9	0.75	18.0	75.0 gr. in 4 days		D
46	0.75	18.0	144.0 gr. in 18 days	R	
47	0.75	18.0	?	R	
48	0.75	18.0	?	R	
50	0.75	18.0	93.0 gr. in 5 days		D
164	1.5	18.0	?	R	
225	1.5	18.0	36.0 gr. in 4 days		D
228	1.5	18.0	20.0 gr. in 1½ days		D
16	1.0	24.0	72.0 gr. in 3 days		D
216	1.5	36.0	88.5 gr. in 4 days		D
205	10.0	80.0	900.0 gr. in 21 days	R	

Case 206 received altogether 900 gr. of carbolic acid subcutaneously during a period of twenty-one days. The strength of the solution was 2 per cent. He received 10 gr. every 3 hours for 48 hours, every 4 hours for 96 hours, and every 6 hours for 48 hours; then 20 gr. every 12 hours for 9 days, and afterwards every 24 hours for 3 days. At no time were there any symptoms of carbolic acid poisoning. In addition, he had chloral and bromide by the rectum three times a day, the effect of which was augmented by hypodermic injections of heroin and morphine whenever he was restless. The longest general spasm lasted for about two hours, but throughout the course of the illness the spasms were always well under control; the last occurred fourteen days later than the first. The patient developed tetanus six months after the date of wounding. No focus of infection was discovered.

2. *Magnesium Sulphate.*

This method of treatment seems to have been first used in America, and its value depends on its powerful sedative or anaesthetic action on the spinal cord. Few of the cases under treatment in England have received this treatment. One case was given 2 c.cm. of a 25 per cent. solution intrathecally; another, one injection (amount and strength not given) subcutaneously; another received 2 c.cm. of a 25 per cent. solution with each dose of serum intrathecally. Three doses were given, and the patient recovered. Two cases received intrathecal injections, one of them 7 c.cm. of a 25 per cent. solution. In other cases it was given by the mouth and by the rectum, but in these it could not have been intended to exert its action on the spinal cord. Nine cases in all were treated with magnesium sulphate; of these 7 died and 2 recovered.

It would appear that this method of treatment is powerful and not without danger, so that great caution ought to be used in its exhibition. Stromeyer treated 5 cases, giving an injection of 8 c.cm. of a 15 per cent. solution. In 2 of these there was marked anaesthesia of the trunk and lower extremities; in the other 3 no anaesthesia was noted. In all 5 cases after the injection there was a cessation of the spasms and muscular rigidity, the patient slept, and respiration was slowed.

CONCLUSIONS.

The conclusions to be arrived at by this analysis are as follows:

1. In the 231 cases of tetanus under review the mortality was 57.7 per cent.
2. Cases with a short incubation were more fatal than those of longer incubation.
3. Most cases occurred on the tenth day after the wound.
4. There are few allusions to the use of antitetanic serum as a prophylactic.
5. In regard to the therapeutic effect of antitetanic serum, the evidence would go to show that this action is not well marked.
6. If antitetanic serum is used—and in such a fatal disease it would seem wrong not to give the patient the benefit, even if doubtful, of the antitoxin—it ought to be injected in the first place intrathecally, as this method would seem to possess advantages over the intravenous and subcutaneous methods.
7. There is no evidence that any benefit accrued to the cases treated by carbolic acid or magnesium sulphate injections.
8. To sum up, the treatment of a case of tetanus might be as follows:
  - (a) Place in a quiet, darkened room under care of a sympathetic and capable nurse.
  - (b) The best surgical treatment of the wound should be thoroughly carried out to ensure the prompt and complete removal of all septic products.
  - (c) The intrathecal injection of at least 3,000 units of antitetanic serum. At the same time 10,000 to 20,000 units may be injected intravenously and subcutaneously. This procedure to be repeated as frequently as the course of the disease seems to demand.
  - (d) In addition to this the patient should receive sedative drugs, such as chloral or chlorotone, in full doses.

ON THE HAEMOLYTIC ACTION OF THE URINE IN CERTAIN CONDITIONS.

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This article is a summary of two papers read before the Vancouver Medical Association in April, 1914, and April, 1915, and not yet published. The work is based upon material obtained from the Vancouver General Hospital, while Director of the Laboratory of Clinical Pathology in that institution. Since arrival in England, with the concurrence of Surgeon-General Carleton Jones, D.M.S., Canadian Expeditionary Force, and thanks to the help given me by the National Research Committee, facilities have been granted to me to continue the work at Cambridge, under Professor Gowland Hopkins. I had, however, been able to do little more than demonstrate some of the main phenomena here recorded to Professor Hopkins, and, I may add, in the laboratories at St. Bartholomew's and Guy's Hospitals (to which hospitals I would express my gratitude for the opportunity given to obtain material), when I was called to active service overseas.

I would here express my sincere thanks to Professor A. B. Macallum, of Toronto; Principal Westbrook, of the University of British Columbia; Lieutenant-Colonel Adami, C.A.M.C.; and Professor Hopkins, for the encouragement they have given me in this research.

It seems fitting to place on record the following observations, since a careful search through the literature at my command, and also a search by interested friends through that contained in much larger libraries than were at my disposal in Vancouver, has failed to show that the reaction here described has been noted before, or, if noted, published. The only mention made of the action of urine upon the red blood corpuscles is the loss of shape and colour that these cells undergo after standing for some time in urine which tends to become alkaline, together with certain incidental notes upon changes observed in the red corpuscles in some (but by no means all) cases of haematuria.

It is unnecessary here to detail in full the sequence of observations and deductions which led me to this

particular line of inquiry. It will suffice to say that for the last few years I have interested myself particularly in the various forms of anaemia, and after not wholly successful endeavours to find some reaction whereby to separate sharply the conditions of so-called primary and secondary anaemia, it appeared worth while to test whether change in the blood plasma led to change in the corpuscles, whether these changes, if any, were due to the loss of some protective material, to the presence of toxins, or to the presence of something passed into the plasma for the purpose of neutralizing circulating toxic elements—a something which, while neutralizing these toxic bodies, exerted a coincident deleterious action upon the erythrocytes. Should there be bodies of any of the above types in the circulating blood, it seemed deserving of study whether they undergo excretion and are to be detected in the urine; and the first question to be answered was, Can any difference be made out between the action upon the red corpuscles of normal urine and that of urine from cases of grave (pernicious) anaemia?

METHOD EMPLOYED.

The solution of this first problem was not so simple a matter as it might seem. In fact, for a long time I failed to note any difference between them as far as the action on red corpuscles was concerned, red cell emulsions of different strengths and amounts being mixed with varying quantities of urine. The intention was to note if, after the red corpuscles had been exposed to the action of urine, there was any increase or decrease in the resistance of these to the action of a haemolytic serum, or any other change, which could be noted and followed up. Eventually I adopted the following technique by which, while ordinary urines have so far exhibited a complete absence of haemolytic power, those from cases of grave pernicious anaemia show at some period, often daily for a long time, a marked haemolytic activity. I have so far noted it in all cases studied, except in cases of the aplastic type.

The method is as follows:

1. Make an emulsion in the proportion of one drop of blood to 4 c.cm. of 0.85 per cent. salt solution.
2. Collect a dozen or more urines from various cases and take a series of test tubes, 3 in. by $\frac{3}{8}$ in. in size. In each place 15 drops of the urine to be tested.
3. To each tube add 1 c.cm. of the blood emulsion and mix with the urine.
4. Place the tubes in the incubator at 37° C. for two and a half hours, shaking several times during this period, examining at each shaking for evidence of haemolysis.
5. If haemolysis occurs in any of the urines, a series of 1-2-4-6-8-10 drops, added to 1 c.cm. of the emulsion, can then be made up for the purpose of measuring the haemolytic value of the urine giving the reaction.

Notes on Method.

There are certain notes which it is well to make regarding this technique.

I.

To make up the cell emulsion I add the blood—10 or 15 drops—to 15 c.cm. centrifuge tubes filled with 0.85 per cent. salt solution, wash once by centrifuging the cells, and make up the bulk to 40 or 60 c.cm., corresponding to 1 drop of blood to 4 c.cm. of the salt solution, as in the Noguchi-Wassermann system. I have, however, gained the impression that unwashed cells are somewhat more resistant, this being noted best in those cases where very small amounts of urine, say 1 or 2 drops, luke the corpuscles, and it is intended to use both washed and unwashed cells in a series of observations on this group.

II.

For the purpose of dropping the urines into the test tubes I use a dropper made from opsonic tubing drawn out in the flame to a capillary of medium bore, and drop with the tube held almost horizontally. After the first 15 drops are measured a mark may be made on the pipette with a grease pencil, and a sufficiently accurate amount of each of any number of specimens may be measured with the one pipette.

III.

I mention 15 drops as the amount chosen, because experience has shown me that whereas with some urines