TETANUS IN THE BRITISH ARMY DURING THE EUROPEAN WAR (AUGUST, 1914, TO DECEMBER, 1918).

BY COLONEL S. L. CUMMINS, C.B., C.M.G.

The subject of tetanus in the recent war is one of the most interesting of the medical problems raised in that great crisis. The advances in the knowledge of the causation of the disease that had been made from 1884 onwards, consequent upon the discoveries of Carlo and Rattone, Nicolaier, Kitasato and others, the successful production of an antitetanic serum; all these advances had been made during the long interval of peace that visited Europe after the war of 1870.

We entered upon the late war equipped with much new knowledge and inspired by hope that this terrible complication of wounds might, at last, be successfully controlled.

How far has this hope been justified?

I think it may be said that it has been justified to a very considerable extent. There have indeed been moments of disappointment. Tetanus cases, though greatly diminished in numbers, continued to occur; but for those who based their hopes on ascertained fact rather than on optimistic speculation, for those who believed that, with due allowance for quantitative factors, the prophylaxis of tetanus by the administration of antitoxic serum shortly after wounding was certain to succeed in greatly reducing the incidence of the disease, the war has brought the expected confirmation.

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VALUE OF PROPHYLACTIC INOCULATION WITH ANTI-TETANIC SERUM.

On what evidence, it may be asked, is this statement based?

It is true that the prophylactic administration of antitoxin became an almost universal rule from the end of 1914, when adequate supplies of antitetanic serum became available, up to the conclusion of hostilities, and that this universal inoculation deprived statisticians of any large uninoculated "Control Group."

It is possible, however, to compare the first months of war, when very little antitoxin was procurable, with subsequent periods when serum was available for every wounded man.

Let us compare the actual numbers of tetanus cases arising in hospitals in England during the first four months of the war with the numbers during the first four months of 1918.

The periods are comparable in certain particulars, both including heavy fighting under adverse conditions and both including a retreat.

An important difference is that the average strength of the British Expeditionary Force in 1914 was something less than 200,000 men, whereas it was just about 2,000,000 men in 1918. The number of men wounded in the British Expeditionary Force in the first four months of 1918 was greater than the whole British Expeditionary Force that landed in France in August, 1914. Even with these numerical differences the actual number of tetanus cases arising in hospitals in England from the battles in August, September, October and November, 1914, was 163; whereas the numbers arising in hospitals in England from the battles of January, February, March and April, 1918, was only ninety; or less than half the number in 1914. Nor is this comparison in any way unduly favourable to the latter period; quite the reverse. In 1914, the majority of our severely wounded during August and September had to be left in the hands of the enemy, as our horsed ambulance wagons were unequal to the task of evacuation during a rapid retreat. Consequently, we have no record of the incidence of tetanus amongst cases left behind as prisoners; nor have we any accurate information as to the number of cases that arose in British hospitals in France in the early months of 1914, as the work was too heavy to allow of statistical records at that time.

It is certain, then, that the 163 cases arising in England in 1914 represented but a small proportion of the total number. Even if we add to the 90 cases arising in England in the first four months of 1918 the 71 cases that arose in British hospitals in France during the same period, we can only reach a total of 161.

These differences are well shown in Sir David Bruce's statistics, reproduced with his kind permission in chart I.

A known incidence of 163 "home" cases from about seven divisions at a time when only a few selected casualties received antitoxin; an incidence
of ninety cases in home hospitals from about seventy divisions at a
time, when practically every wounded man received an inoculation; these
figures constitute a conclusive proof of the protective value of antitetanic
serum. Nor are other evidences wanting. One striking instance is as
follows: although in 1916 all wounded were given a prophylactic dose
of serum, no such dose was at first given to men suffering from "trench
foot." In November and December, 1916, no less than thirteen cases
of tetanus developed in British hospitals in France amongst uninoculated
soldiers suffering from "trench foot," and the Director General at once
issued an order that a prophylactic inoculation should be given to every
case. This order went forth in December, 1916. During the whole
of 1917, only one case of tetanus arose in a "trench foot" patient in
the hospitals of the British Expeditionary Force in France. Thirteen
cases in two months; one in a year. Here again is a tribute to the
protective value of antitetanic serum.

For the last year of the war, including some of the heaviest fighting
in the history of the world, in areas that had been intensively cultivated
and in which the earth was grossly infected with tetanus spores, the
incidence of tetanus in the British Force in France and Belgium varied
from two to seven cases in every ten thousand wounded men. The disease
was insignificant as a factor in the loss of life from wounds.

It may be claimed, then, that the value of prophylactic inoculation with
antitetanic serum is finally established as a measure for the reduction of the
incidence of tetanus amongst the wounded in war.

The following rules for the prophylactic administration of antitetanic
serum were drawn up by the Committee for the study of tetanus in the
British Army and have given satisfactory results.
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(1) The first prophylactic dose should be given as soon after wounding as circumstances permit, and should be not less than five hundred U.S.A. units of antitoxin.

(2) As there is both clinical and experimental evidence that the immunity conferred by an injection rapidly declines from about the tenth day onwards after administration, and as the appearance of a wound affords no indication whether it is infected with tetanus or not, it is recommended that all wounded men should receive at least four injections of antitetanic serum; a primary injection given at or shortly after the time of the wound and three others.

(3) The second injection should follow the first at an interval of seven days. The third and fourth injections should follow at as nearly as possible the same interval of time.

While these rules are thoroughly sound, they are not always easy to carry out in strict detail when very heavy fighting is in progress. The initial dose is naturally the most important and it has been found possible to give it in practically every case within the first twenty-four or forty-eight hours after wounding. The second and subsequent doses are of undoubted value but they are less easy to ensure. It is often difficult to arrange for re-inoculation at the right interval during the various stages of evacuation of a wounded man from the Front to the Base and thence to Home territory. Again, the condition of the patient may be such that the surgeon may hesitate to add to his burden by even so much as an injection of serum. But it has been found possible to give the re-inoculations at or about the intervals recommended, in the majority of cases with very satisfactory results. Whether these successive injections be given or not, one rule is of cardinal importance.

A precautionary dose of antitetanic serum (500 units) should invariably be given at the time of any operative measures at the site of the wound.

A point on which some difference of opinion has arisen is that of the quantity of serum to be recommended for the initial prophylactic dose. The War Office Committee for the Study of Tetanus which, under the able Presidency of Major-General Sir David Bruce, contributed so successfully to our knowledge of this disease throughout the whole course of the war, has recorded the opinion that an initial dose of 500 U.S.A. units is sufficient for all practical purposes. It must be admitted that there is no conclusive evidence to show that a larger dose is necessary and, where it is quite certain that the subsequent re-inoculations can be given, it may be assumed that this initial dose of 500 units will give very satisfactory results. It is impossible, however, for the reasons above mentioned, to be sure that the patient will always receive the later injections.

It must be conceded, also, that the whole question of toxin and antitoxin is a matter in which quantitative factors play a large part. The fact that tetanus has continued to appear, though in greatly reduced degree, even in inoculated men, must necessarily raise the question of sufficiency
of dosage. The serum supplied to the British Army contains 1,500 U.S.A. units to ten cubic centimetres, the volume contained in one phial.

It has usually been found convenient to give five centimetres or 750 units, for the first dose, and even this quantity may often be increased with nothing but benefit to the patient.

These considerations led the Director General of Medical Services in France to issue in 1917 an instruction to the following effect.

"It is recommended that an initial prophylactic dose of 1,000 to 1,500 units shall be given in all deep wounds, in those which are contaminated by dirt, and in those in which there is fracture of bone."

In the opinion of the writer, this instruction expresses a view which will be widely endorsed by those with practical experience of the prevention of tetanus in modern warfare.

But, while the effect of the routine use of prophylactic injections of antitetanic serum has been so great in diminishing the case-incidence of the disease, its value is by no means confined to mere prevention of tetanus. It can be confidently claimed that these injections have acted beneficially in at least four ways:

(1) In reducing the case-incidence of tetanus.
(2) In diminishing the case mortality.
(3) In extending the incubation period.
(4) In modifying the severity of the disease.

The last three headings are all closely inter-dependent. The mortality is less because the cases are not so severe; the cases are less severe because the incubation period is prolonged.

It might seem more reasonable to express all three tendencies by merely saying that the use of prophylactic injections has led to the production of a modified type of tetanus in the late war. This is undoubtedly true.

But, in order to fully appreciate the change that has taken place, it will be more convenient to discuss each tendency separately, as this will lead to a clearer grasp of the factors that have to be considered when the question of the effects of treatment comes to be examined.

**Reduction of Mortality.**

In order to realize the change in the character of tetanus in the recent war, it is necessary to examine, for a moment, the tetanus records of previous military operations. Baron Larrey, in Napoleon's Egyptian Campaign, recorded a mortality of 82 per cent. In the American War of Secession, there were 505 cases with a mortality of 89.3 per cent. In 1870-1871 in the German Army, the gross mortality of 350 cases was 90 per cent, while Richter recorded a mortality of 82 per cent in 228 observed cases.

While it is true that, in the first months of the late war, when supplies
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of serum were inadequate, the mortality from tetanus was of somewhat the same order as formerly, the percentage of deaths steadily diminished and soon reached a figure not much more than half that of previous campaigns.

In 1914-1915, Sir William Leishman recorded in the hospitals of the British Expeditionary Force, France, 178 observed cases with 140 deaths, a mortality of 78.2 per cent, while Sir David Bruce, collecting his figures from hospitals in Great Britain, reported 231 cases with 133 deaths, a mortality of 57.7 per cent.

Adding these early and late cases together as a sample of the tetanus mortality of the first year of the war, there were 410 cases with 273 deaths, or a mortality of 66.6 per cent.

In 1916-1917, in a series of 376 cases reported from France by Colonel Cummins and Major Gibson, there were 252 deaths or 67 per cent. For the same period, Sir David Bruce reported, from England, 400 cases with 79 deaths, or 19.7 per cent. Adding these early and late cases together, we get a record of 776 cases with 331 deaths; a mortality of 42.6 per cent.

<table>
<thead>
<tr>
<th>Former Wars</th>
<th>European War 1914-18</th>
</tr>
</thead>
<tbody>
<tr>
<td>War of Sec.</td>
<td>64 3%</td>
</tr>
<tr>
<td>1970</td>
<td>81%</td>
</tr>
<tr>
<td>1970</td>
<td>87 7%</td>
</tr>
<tr>
<td>1970</td>
<td>19 4%</td>
</tr>
<tr>
<td>1970</td>
<td>42 8%</td>
</tr>
<tr>
<td>1970</td>
<td>48 8%</td>
</tr>
</tbody>
</table>

CHART II.—Tetanus case mortality per cent.

The total mortality in a third group of cases from British hospitals in France and England in 1918 shows a slight rise to 48.8 per cent, owing, doubtless, to the unfavourable conditions for the treatment of wounded necessitated by the retreat in the Somme area in March.

The three series, representing the tetanus mortality in the British Expeditionary Force at selected periods of the war, are graphically represented in comparison with former war records, in Chart II.

It must be allowed that other factors besides antitetanic serum have played a part in this reduction of mortality. Critics hostile to protective inoculation might ask, at this point, whether the whole of this improve-
ment could not be explained in terms of the increased experience in surgical technique and in the methods of evacuation of wounded that were such features of the latter half of the war period. As will be shown later, these developments played an important part in diminishing tetanus mortality; but there is reason to believe that the most potent agent in reducing the death-rate was antitoxin.

Here again, the absence of an adequate uninoculated "control group" deprives us of a complete answer. The cases of tetanus arising in uninoculated persons during the war were, after the first few months, most frequently from scratches or other accidental injuries, so slight that the patients never "reported sick" until tetanus developed. These slight injuries, unaccompanied by shock or extensive sepsis, were such as to initiate a less severe type of tetanus and they do not make good material for comparison.

Of fifty cases of tetanus in non-inoculated persons arising in France in 1918 only nineteen were in men wounded in battle. Of these nineteen cases sixteen died, a mortality of eighty-four per cent; just such a mortality as characterized the tetanus of older wars before serum was introduced.

In the same period 136 wounded and inoculated men developed tetanus. Of these seventy-five proved fatal—a mortality of 55.1 per cent.

If we take the mortality in the whole series of 50 uninoculated persons, including only 19 battle wounds, we find that 35 died, or seventy per cent, as compared with 55.1 per cent amongst the inoculated wounded group. These results are shown in Table I.

<table>
<thead>
<tr>
<th>Description</th>
<th>Total</th>
<th>Died</th>
<th>Recovered</th>
<th>Per cent case mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoculated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-inoculated, battle casualties</td>
<td>136</td>
<td>75</td>
<td>61</td>
<td>55.1</td>
</tr>
<tr>
<td>Total Not-inoculated</td>
<td>50</td>
<td>35</td>
<td>15</td>
<td>70.0</td>
</tr>
</tbody>
</table>

Including non-inoculated battle casualties.

Another significant comparison may be made between those to whom antitoxin was given within twenty-four hours of wounding and those to whom it was given at a later period.

Of 269 men inoculated within twenty-four hours of wounding, 170 or 63.2 per cent died.

Of sixty-nine men inoculated at a longer interval than twenty-four hours after wounding, fifty-three or 76.8 per cent died. These results are illustrated in Table II.

<table>
<thead>
<tr>
<th>Description</th>
<th>Total</th>
<th>Died</th>
<th>Recovered</th>
<th>Per cent case mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoculation within twenty-four hours</td>
<td>269</td>
<td>170</td>
<td>99</td>
<td>63.2</td>
</tr>
<tr>
<td>Inoculation later than twenty-four hours</td>
<td>69</td>
<td>53</td>
<td>16</td>
<td>76.8</td>
</tr>
</tbody>
</table>

Again, where cases have received only one protective inoculation, the mortality has been less amongst those who received the larger doses. For
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instance, in 1917, there are records of 119 tetanus cases in men to whom a single dose of 500 units was given; of these, ninety died; a mortality of 75.7 per cent. In the same period thirty-nine cases had received 750 units or more. Of these seventeen died; a mortality of 43.5 per cent (see Table III).

<table>
<thead>
<tr>
<th>Description</th>
<th>Total</th>
<th>Died</th>
<th>Recovered</th>
<th>Per cent mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 units</td>
<td>119</td>
<td>90</td>
<td>29</td>
<td>75.7</td>
</tr>
<tr>
<td>750 units or over</td>
<td>39</td>
<td>17</td>
<td>22</td>
<td>43.5</td>
</tr>
</tbody>
</table>

While giving these figures for what they are worth, I feel obliged to add that they are calculated on small numbers and subject to many factors of error. The fact that they all point in the same direction is significant.

It may be stated as a proved fact that the mortality of tetanus was definitely less in those cases to whom prophylactic inoculation had been given, and especially in those to whom it had been given early and in large quantity.

Incubation Period.

But the most profitable mode of investigation as to the effects of antitoxin upon tetanus mortality and severity still remains to be examined. It has always been admitted that the mortality and the severity of tetanus is markedly less in those cases in which the incubation period has been prolonged. This inverse relation was well known to surgeons in previous wars.

If it can be shown that one of the effects of prophylactic inoculation of antitetanic serum is to lengthen the incubation period, and if it is also proved that the prolongation of incubation is actually associated with a lessened death-rate, then it will follow that the prophylactic inoculations have led to a diminished case mortality.

Let us now consider the evidence available on this point.

Chart III shows the incubation periods in the Franco-German War of 1870-1871. It will be seen that only about twenty per cent of all cases had an incubation period of fifteen days or upwards. About eighty per cent developed within the first fortnight after wounding. This may be taken as typical of former wars. Was this associated with the fact that antitetanic serum was then unknown? If it can be shown that similar, or somewhat similar, incubation periods arose amongst uninoculated men in the recent war, and that the incubation periods amongst inoculated men were much more prolonged, then we shall have gone far to prove our point.

Chart III shows the incubation periods in seventy cases of tetanus in persons receiving no prophylactic inoculation.

It will be seen that eighty per cent arose within the first fortnight after injury.

The same chart shows the incubation periods in a group of whom only a few had been given a prophylactic dose, the men reaching hospitals in
England during 1914 (Bruce). Here it will be seen that seventy-six per cent arose within the last fortnight.

As a contrast to these figures let us examine a group of 452 inoculated cases, 342 arising in British hospitals in France in 1916-1917 and 109 arising in British hospitals in England in 1916. Here only 59.5 per cent arose in the first fortnight. Over forty per cent were delayed to the fifteenth day or more. No less than twenty-five per cent of the whole number had an incubation period of three weeks or more.

The comparisons in Chart III will suffice to show that the incubation period of tetanus cases has been very markedly prolonged amongst those receiving prophylactic inoculation of antitoxin in the late war, while it has retained its original character in uninoculated patients.

The conclusion seems inevitable that the use of antitoxic serum has been a factor of the greatest importance in prolonging the incubation period of tetanus.

Does this delay in the onset of tetanus lead to a decrease in mortality? The figures at my disposal on this point deal only with cases arising in British hospitals in France. The inclusion of statistics from hospitals in England, where most of the delayed cases occurred, would make the charts more striking still, but these statistics are not yet available.

The first column in Chart IV, from cases arising in 1917, shows that while the mortality amongst cases developing within ten days of wounding was 70.1 per cent, it was only 48.3 per cent in cases developing on and after the twenty-first day.

The second set of columns in Chart IV for 1918 are still more striking. In this the mortality at the three periods, ten days and less, eleven to
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twenty days, and twenty-one days and over, are, respectively, 71.7 per cent, 49.1 per cent, and 31 per cent.

These charts prove that a "delayed tetanus" means mild tetanus and a low death-rate.

We are, then, in a position to state definitely that the prophylactic use of antitoxin not only diminishes the case-incidence of tetanus, but also leads to a prolongation of the incubation period and a reduction of case-mortality.

<table>
<thead>
<tr>
<th>Periods of Incubation</th>
<th>1917</th>
<th>1918</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10 Days and Under</td>
<td>80</td>
<td>70</td>
</tr>
<tr>
<td>11-20 Days</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>21-30 Days</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>31-40 Days</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>41-50 Days</td>
<td>10</td>
<td>4.5</td>
</tr>
<tr>
<td>51-60 Days</td>
<td>2</td>
<td>1.5</td>
</tr>
</tbody>
</table>

CHART IV.—The relation between incubation period and per cent mortality.

MODIFICATION OF CLINICAL TYPE.

This lengthening of the incubation period seems to go hand in hand, not only with a diminution of case-mortality, but with a marked amelioration of the clinical course of the disease in a large number of cases.

If there is one feature that marks out the tetanus of the recent war from that of all previous campaigns, it is the frequent appearance in human beings of "local tetanus."

An excellent, though brief, account of tetanus as it was known in previous wars, is given by F. Golla in his paper, "An Analysis of Recent Tetanus Statistics" (Lancet, December 29, 1917), from which I may quote to make my point clearer. He says "the symptomatology of tetanus in pre-serum days is characterized by the initial symptom of trismus."

"A certain number of cases are recorded with history of local onset, gradually going on to secondary trismus, but they were cases of very great rarity. If would seem that, although the term 'local tetanus' was used sometimes by the surgeons in the War of Secession, it was used to designate not tetanus confined to the segmental wound area, but tetanus confined to trismus without a tendency to spread."

A good idea of the accepted view of clinical types in tetanus before the late war may be gleaned from text-book accounts of the disease. In "A Manual of Surgical Treatment," by W. Watson Cheyne and F. F. Burghard, part 1, page 220, 1901, it is stated that "tetanus may be acute
or chronic. The acute form, accompanied by a high temperature, usually ends fatally in four days, and of those affected with this form only about one per cent recover under ordinary treatment. In the more common chronic variety the convulsions are less frequent and not so general, but this form may become acute and death then rapidly takes place; about twenty per cent of the patients recover." G. A. Gibson, in his "Text Book of Medicine," (1901) says, "the disease is characterized by the occurrence of tonic spasms of the voluntary muscles, commencing in those of the face and neck and gradually extending to all the muscles of the body." There is no mention of "local tetanus" in these works. For practical purposes, such a condition was so rare as to be ignored.

Let us now examine the types noted in the late war. Information as to clinical types was collected on the tetanus case sheets under the headings drawn up by the War Office Committee for the study of tetanus. These headings were as follows:—

Type A. I. Trismus the earliest symptom. Tetanus with complete closure of jaws, developing within twenty-four hours from onset of symptoms.

Type A. II. Trismus the earliest symptom. Tetanus with complete closure of jaws, developing after more than twenty-four hours.

Type A. III. Trismus the earliest symptom, with incomplete closure of jaws. Mouth can be partially opened.

Type B. Trismus occurring after other symptoms of tetanus have shown themselves.

Type C. General tetanus without trismus.

Type D. Local tetanus without trismus.

In Table VI is shown an analysis of 489 cases, 300 from Sir David Bruce's records of cases arising in hospitals in England, 189 from cases arising in British hospitals in France.

<table>
<thead>
<tr>
<th>TABLE IV.—PERCENTAGE OF INCIDENCE OF THE DIFFERENT CLINICAL TYPES.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Origin</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>In France</td>
</tr>
<tr>
<td>In England</td>
</tr>
<tr>
<td>Per cent</td>
</tr>
</tbody>
</table>

In this table, in which the cases are grouped according to the types laid down by the War Office Committee for the investigation of tetanus, it will be seen that no less than twenty-three per cent of all the cases in the series were "local tetanus."

Types A I and A II, corresponding to the classical acute tetanus of former wars, together amount only to 16·6 per cent of all the cases analysed. Type A III, in which the trismus is incomplete and in which the mortality is low, forms 35·5 per cent of all the cases and is the commonest manifestation of the disease.

It is clear, therefore, that some factor, absent in former wars, has completely altered the character of tetanus.
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It is not possible to claim all this improvement for any one factor acting alone. The surgical treatment of wounds in the late war was efficient to a degree without precedent in any previous campaign and I shall attempt to prove that excision of wounds had a very great influence in lessening the danger of tetanus. In no previous war were the wounded evacuated with so little shock or suffering. The influence of transport in motor vehicles and in smoothly running ambulances must have been considerable as a factor in conserving the resistance of wounded men to bacterial disease. But the figures already given show that, over all and above all ancillary influences, the general use of prophylactic inoculation has been the prime factor in lessening the severity of tetanus in the war.

Factors Diminishing the Success of Prophylactic Inoculation.

While fully admitting, however, that antitoxin has led to these very remarkable results, it is well to retain a critical attitude of mind as to the degree to which it has failed as well as to the measure of success to which it has attained.

The fact remains that, in spite of the almost universal administration of antitoxin, tetanus cases continued to arise, though in relatively small numbers; and it is also true that the severe and fulminating types A I and A II, though reduced from about eighty per cent to less than twenty per cent of all cases, still occurred in patients in whom a prophylactic dose had been given shortly after wounding.

We must therefore examine the information furnished by the war to ascertain, if possible, why the success of antitoxin, admittedly very great, was not greater still.

As a preliminary to this inquiry, it will be advantageous to examine into the mortality in each clinical type. In doing so, it will be necessary to examine separately the figures for cases arising in the British hospitals in France and Belgium and those arising in England. The cases in France were, naturally, more severe, since they included the cases of shortest incubation and the cases arising in patients whose wounds were so severe as to prevent their early transfer to England.

<table>
<thead>
<tr>
<th>Type</th>
<th>Total cases</th>
<th>Deaths</th>
<th>Recovery</th>
<th>Per cent mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>A I</td>
<td>17</td>
<td>10</td>
<td>7</td>
<td>58.7</td>
</tr>
<tr>
<td>A II</td>
<td>19</td>
<td>3</td>
<td>14</td>
<td>26.3</td>
</tr>
<tr>
<td>A III</td>
<td>111</td>
<td>26</td>
<td>85</td>
<td>23.4</td>
</tr>
<tr>
<td>B</td>
<td>57</td>
<td>11</td>
<td>46</td>
<td>19.2</td>
</tr>
<tr>
<td>C</td>
<td>19</td>
<td>3</td>
<td>16</td>
<td>15.7</td>
</tr>
<tr>
<td>D</td>
<td>77</td>
<td>0</td>
<td>77</td>
<td>0</td>
</tr>
</tbody>
</table>

The mortality by types in British hospitals in France and in England is given in Table V.

It will be noticed that the mortality is much higher in cases arising in France than in England. This is due, in part, to the fact that other factors,
such as shock; acute sepsis, and gas gangrene were operative to a greater extent in the early cases in France than in the cases evacuated to home territory. But the difference is too marked and too constant to be completely accounted for in this way.

At this point, it is instructive to go back for a moment to the question of "incubation period."

In Chart V the incubation periods in France in 1916-1917, and in England in 1916, are contrasted with those of Richter's series in 1870-1871.

![Chart V](chart.png)

**CHART V.**—Comparison between incubation periods in home hospitals, hospitals in France, and previous wars.

It will be apparent that the severer types of cases in hospitals in France approximated fairly closely, both in their high mortality and also in their relatively short period of incubation, to the types already shown to be characteristic of previous wars in which serum was not used. How is this to be explained?

The protective effects of a prophylactic inoculation only last for about ten days. For those cases in which a heavy contamination of the wound with tetanus spores has taken place and in which the wound condition is favourable to their development, the effects of the initial dose of antitoxin will already be disappearing at the very moment when the tetanus infection is approaching the end of its normal incubation period of eight to ten days. This is the most critical period in the course of a septic wound. The bulk of the cases in hospitals in France arose at a moment when the immunity following the first inoculation was on the
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wane, and when the second dose had not yet been given or, if given, was too small and too late to modify the effects of a volume of toxin already great and already combining with nerve tissue.

The marked amelioration of type and prolongation of the incubation period in hospitals in England was probably due to the fact that the wounds were at a less recent stage and that the reinoculations had had time to be effective.

It is possible, too, that active immunization played a part. Given the presence of tetanus infection in a wound, and it is now well known that such infections are present in a high proportion of war wounds, even where tetanus does not develop, it is to be assumed that the production of immune substances will proceed in the tissues of the patient.

The prophylactic inoculations, may have played an important rôle in helping on this process by neutralizing toxins and thus giving the body cells the protection necessary to enable them to form antibacterial substances. But there are still other factors, of a more complicated nature, to be considered.

The bacteriology of tetanus has been re-investigated during the war and, in this field of research, new questions, that may prove to be of fundamental importance, have been raised.

Captain W. J. Tulloch, R.A.M.C., working for the War Office Committee for the investigation of tetanus, has been able to show, by serological differentiation, that there are at least four separate types of tetanus bacilli operative in war wounds. Of these, Type I corresponds to the organism employed for the preparation of the toxin used in manufacture of antitetanic serum.

Tulloch has shown that, while serologically distinct, all four types produce exactly the same toxin. The antitoxin in general use, is, therefore, equally effective in neutralizing the toxin in all four types of infection.

But further work by this investigator has pointed strongly to the conclusion that it is not only the toxin that matters but that the power of invasion by the bacteria themselves plays an important part in the production of tetanus. Tulloch has isolated all his bacterial types both from tetanus cases and also from septic wounds in patients in which tetanus did not develop.

His findings are well illustrated by two diagrams published by Sir David Bruce in "War Medicine," vol. ii, p. 759, which are here reproduced (Chart VI).

In the diagram it will be noted that in the case of bacilli of Type I the proportion of positive findings in "indifferent" wounds is much higher than in the wounds of patients suffering from tetanus. With bacilli of Type II, III and IV, the proportion of positive findings is much greater in tetanus patients than in patients suffering from "indifferent" wounds.

This finding certainly suggests that the protection afforded by antitetanic serum has been more effective where the wounds were infected by the homologous bacilli of Type I.
The diagram gives the death-rate expressed as a percentage of the number of cases in which each type of the bacillus was isolated from men suffering from tetanus. All the cases had received prophylactic inoculations of antitetanic serum.

These diagrams illustrate results which point strongly to the conclusion that the serum used afforded a higher measure of protection against the homologous strain, Type I, than against the heterologous types.

Further work by Captain Tulloch, as yet unpublished, still further supports this suggestion.

It is along these lines that we must look for still greater development of efficiency in antitetanic serum in the future.

**INFLUENCE OF EFFICIENT SURGICAL TECHNIQUE.**

In a previous paragraph it was indicated that prophylactic inoculation was not the only factor in the prevention and amelioration of tetanus cases. It has been constantly observed that the proportion of tetanus cases to the total wounded has risen during times of heavy fighting.

Chart VII, in which the numbers of tetanus cases per 10,000 wounded is given, graphically illustrates the marked increase in case incidence during times of mobile battle, the retreat in March and the advance in November, 1918.

Naturally, the administration of antitoxin tended to be less constant at such periods, but, from information that has come to hand, it is certain...
Tetanus in the British Army during the European War

that medical officers very seldom failed to give a prophylactic injection even at these strenuous and difficult times.

But the chances of deliberate and thorough surgery are always much less when the casualty clearing stations have to be moved rapidly in retreat or advance. It is to this interference with early surgical intervention that I incline to attribute the increase in tetanus cases in times of heavy fighting.

CHART VII.—Tetanus incidence per 10,000 wounded, 1918. (Cases arising in France and Belgium).

<table>
<thead>
<tr>
<th>Jan</th>
<th>Feb</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>August</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.50</td>
<td>1.98</td>
<td>7.99</td>
<td>2.26</td>
<td>17</td>
<td>6.3</td>
<td>2.16</td>
<td>1.26</td>
<td>1.88</td>
<td>2.43</td>
<td></td>
</tr>
</tbody>
</table>

It may be asked whether the statistics collected in the British Army afford any support to this view. It is very difficult to produce effective figures in support of what must depend on such a varying factor as good surgical technique. An attempt has been made to ascertain the effect of excision of wounds upon tetanus case-mortality in British hospitals in France during 1918. The results are shown in Table VII.

TABLE VI.—Excision of Wounds and Mortality.

<table>
<thead>
<tr>
<th></th>
<th>Total number of cases</th>
<th>Died</th>
<th>Recovered</th>
<th>Per cent mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not excised</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excised</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It will be observed that the case mortality was definitely less amongst the thirty-three cases whose wounds were excised than amongst the seventy-six cases in which no excision was practised. A further effort has been made to evaluate the effect of excision on the type of tetanus that subsequently developed and this is shown in Table VII.

TABLE VII.—Excision and Severity of Type.

<table>
<thead>
<tr>
<th></th>
<th>A1</th>
<th>AII</th>
<th>AIII</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>Total number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per cent not excised</td>
<td>22.3</td>
<td>3.9</td>
<td>34.2</td>
<td>14.1</td>
<td>5.3</td>
<td>10.7</td>
<td>76</td>
</tr>
<tr>
<td>Excised</td>
<td>6.2</td>
<td>3.9</td>
<td>27.2</td>
<td>31.2</td>
<td>3.1</td>
<td>34.2</td>
<td>33</td>
</tr>
</tbody>
</table>

Here, too, the figures appear to indicate that, when tetanus develops after excision of the wounds, it tends to assume a benign rather than a severe type. It is not desired to claim too much for these very small figures. All that can be said is that, as far as they go, they support the
conclusion that effective surgical intervention helps very largely in lessening the incidence, the severity and the case-mortality of tetanus.

This conclusion is so obviously in agreement with bacteriological and physiological facts, that it is unlikely to be seriously questioned.

**Antitetanic Serum in Treatment.**

Before attempting to discuss this very difficult question, I desire to explain that I have not been personally concerned with the treatment of tetanus cases during the late war. It has been my duty to collect and examine the tetanus case sheets rendered by all the hospitals with the British Army in France and Belgium and I have had access to those received by my predecessor, Sir William Leishman.

Under these circumstances, I am in no way fitted to formulate a definite opinion for or against the value of specific treatment in tetanus. My object is merely to put before you, in as simple a form as possible, the results of an examination of the case sheets received by me. As to the actual value of any given method of treatment, the best judge must always be the surgeon who sees the progress of the case throughout its course and who can weigh the different factors that make for recovery or determine a fatal issue.

Nevertheless, the collection and examination of a number of reports, all rendered on the same form, is not without interest and the results may perhaps assist in supplying a basis for discussion by those with actual experience of cases.

Time has not permitted me to get together a full account of the treatment in England and in France. I can merely indicate, in general terms, the effects of treatment upon the mortality in a certain number of cases in British hospitals in France, and summarize for you the opinions formed by some of those who had occasion to investigate cases in hospitals in England.

Before attempting to discuss these questions, it will be well to consider, for a moment, what can and what cannot be expected from the use of antitoxin in treatment.

(1) It is now generally admitted that, once tetanus toxin has entered into combination with nerve tissue, the presence of antitoxin in the circulating blood and lymph cannot lead to dissociation of the toxin.

(2) It is known that the presence of antitoxin in the circulation can neutralize its equivalent of circulating toxin.

(3) The experiments of Meyer and Ransom have shown that the toxin travels along the axis cylinders of motor nerves. Teale and Embleton, while confirming this observation, have shown that the toxin also travels along the perineural lymphatics. Antitoxin cannot travel along the axis cylinders, but it can and does travel along lymphatic vessels and circulate in the blood-stream.
It seems probable from these considerations that the most that can be hoped from antitoxin in treatment is that it will, if given in sufficient quantity, neutralize all circulating toxin.

Whether recovery can take place will depend on how much toxin has already combined with nerve tissue, and how far the antitoxin can neutralize the poison formed at the infected site and prevent its effective passage along motor nerves. One very hopeful feature is the success attained in preventing a fatal issue in animals, to which a lethal dose of toxin has been given, by means of subsequent injection of antitoxin.

The experiments of William H. Park and H. Nicoll, of New York, published in 1914, demonstrated clearly that guinea-pigs, inoculated with two fatal doses of toxin and kept untreated until spasm had developed in the inoculated leg, could be cured by the intrathecal inoculations of 250 units of antitoxin. No success was obtained by these observers by antitoxin given subcutaneously nor by intracardial injections except, in the latter case, by doses of twenty times the amount of antitoxin that had led to cure by the intrathecal route.

Perhaps the most remarkable and convincing experiments yet done in this connexion were those of Professor C. S. Sherrington for the "War Office Committee for Investigation of Tetanus," published in the Lancet of December 29, 1917.

Sherrington inoculated a series of monkeys with eight times the lethal dose of tetanus toxin. Control monkeys invariably passed through a period of thirty to thirty-six hours without symptoms of any kind. Then spasm commenced in the inoculated limb, increased, became general, and led to trismus and spasm of all four limbs by the end of the fourth day. Death invariably took place on the fourth or fifth day.

Of twenty-five animals so inoculated, an injection of 2,000 U.S.A. units of antitoxin was administered, by different routes, after spasm had commenced; the interval after the injection of toxin varying from forty-seven to seventy-eight hours.

Of twenty-five animals to which the antitoxin was given subcutaneously, two recovered. Three recovered out of twenty-five treated by intramuscular injection. Seven out of twenty-five were cured by intravenous inoculation.

No less than fourteen monkeys out of twenty-five recovered after the intrathecal inoculation of antitetanic serum. All the control animals died within five days.

These very striking results are, in the opinion of the writer, the strongest argument yet available in favour of the value of antitoxin in treatment. They definitely show that, under controlled conditions, antitoxin can cure tetanus.

Unhappily, the factors entering into death or survival in human cases are so numerous and so difficult to evaluate that we cannot hope to obtain any results as clear-cut and definite as those of Sherrington in monkeys.
Turning from animal experiments to the published observations of British investigators on the results of antitoxin treatment of tetanus cases during the war, we find that opinions are by no means unanimous. Amongst those who believe that they have obtained satisfactory results with serum therapy, there are marked differences as to the best route for the administration of the inoculation.

The most convinced upholders of the value of antitoxin in treatment are those who have actually used it in their own practice. On the other hand, those who have examined large series of case sheets sent to them from groups of hospitals have been much more guarded in drawing favourable conclusions.

A very important paper on serum therapy is that published by Professor H. R. Dean in the Lancet of May 5, 1917. He treated twenty-five cases with serum with only four deaths. Of five mild cases treated by intramuscular and subcutaneous inoculation, all recovered. Of five treated by intrathecal doses with or without other injections, three recovered. One patient to whom both intravenous and intrathecal inoculations were given, died. The most remarkable results were obtained with intravenous inoculation. Of fourteen severe cases, with trismus, to whom 30,000 units of antitoxin were given intravenously under chloroform anaesthesia, thirteen recovered. The serum of patients thus treated was proved by animal experiment to contain free antitoxin up to thirty-nine days after the intravenous inoculation of 30,000 units.

This record, taken by itself, would go far to show that serum given intravenously in large doses is of very great curative value. But there are other records that point to a different conclusion.

Sir William Leishman and Major Smallman; in an analysis of 160 cases in British Hospitals in France (Lancet, January 27, 1917) condemn the intravenous route as highly dangerous and of little utility and advocate intramuscular inoculations as the method of election.

Dr. F. W. Andrewes, in the Lancet of May 5, 1917, gives a careful analysis of twenty cases treated with serum with five deaths. Of sixteen cases treated by the intrathecal method, two died of tetanus and one later from septic complications. Dr. Andrewes examines critically the relative severity of the cases and, while regarding some of them as so mild as to have, perhaps, recovered without treatment, considered that at least five of them were of a degree of severity great enough to warrant the conclusion that the serum turned the scale in their favour.

In the "Memorandum on Tetanus" issued by the War Office Committee for the Study of the Tetanus (fourth edition, 1919) the following recommendation is made:

"The Committee is of the opinion that, in acute general tetanus, the best method of treatment lies in the earliest possible administration of a large dose of antitoxic serum by the intrathecal route, repeated on the following day; combined with, and followed on succeeding days, by subcutaneous and intramuscular injections."
On the other hand, Dr. F. Golla, from a careful study of a series of reported cases, shows that, in cases of tetanus in men to whom no prophylactic injection has been given, but who were treated with antitetanic serum, the rate of mortality approached closely to that of tetanus cases in pre-serum days. He concludes that there is no evidence to show that the employment of antitetanic serum in treatment is of any value at all.

Sir David Bruce, whose successive series of analysis of tetanus cases in hospitals in England have been such a valuable contribution to this subject, remains, at the end of the war, uncertain whether serum therapy in tetanus is of any use. In an Address to the American Red Cross Society, in October, 1918, he says:

"Whereas there can be no shadow of doubt as to the benefit of prophylactic injection of antitoxin, we are on much less firm ground when we come to consider antitoxin as a curative agent. In fact there does not seem to be any statistical evidence that serum given therapeutically has marked effect on the rate of mortality."

As regards the reports that have come to my own notice, these have been in two series. With regard to the first series of 376 cases arising in France, between November, 1916, and December, 1917, the full figures have already been published by Major Gibson and myself, in the Lancet of March 1, 1919. I need, therefore, only quote the conclusion to which Major Gibson and I were forced by an examination of the records. Briefly we were unable to find in these records any clear indication as to the value of antitoxin treatment in tetanus. The mortality was less amongst those patients who had received the largest doses and we were at first inclined to think that, in this, we had evidence for a favourable action of the serum. But an argument of this kind is liable to serious fallacy. The cases that die soon after treatment has been commenced can only receive a relatively small amount of serum. The cases that recover continue to receive inoculations until convalescence is well established. Under these circumstances, the total dosage given to recovering cases must always tend to be greater than that given to fatal cases. To avoid this factor of error, we decided to make comparison only of dosage within the first forty-eight hours.

When this was done, we were unable to find any association between the larger dosage and a lessened mortality. It even seemed as if the reverse were the case. The death-rate in 265 cases treated with fairly large doses of serum within forty-eight hours of the onset of tetanus was sixty-four per cent, while the death-rate in twenty-eight patients to whom no serum was given within the first forty-eight hours was only forty-two per cent.

With these results in our minds, we decided that it was our duty to advocate still larger doses of antitetanic serum as we were at a loss to explain the poor results of serum treatment except on the ground that the dosage given had been insufficient. We personally expressed this view to
many of the surgeons working in the hospitals in France and the result was a tendency, during 1918, to larger doses of serum than previously.

In evaluating the results of treatment, it is necessary to take into account the clinical types of tetanus as well as the size of the dose given.

In Table VIII are given the numbers of recovering cases of each type treated with serum and the approximate dosage, the cases that died being shown in Table IX.

<table>
<thead>
<tr>
<th>Type</th>
<th>1,000 to 10,000 units</th>
<th>10,000 to 20,000 units</th>
<th>20,000 to 50,000 units</th>
<th>50,000 to 100,000 units</th>
<th>over 100,000 units</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>13</td>
<td>1</td>
<td>34</td>
</tr>
<tr>
<td>AII</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>AIII</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>26</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>2</td>
<td>20</td>
<td>24</td>
<td>30</td>
<td>79</td>
</tr>
</tbody>
</table>

It will be seen that there were 116 deaths and seventy-nine recoveries, a death-rate of sixty-eight per cent.

A glance at Table VIII will show that the number of cases recovering grows steadily greater, for all the types, as the dosage increases, and this is especially marked in type A III. This is the type that runs the most chronic course; the type that lasts longest; the type, therefore, that gets the greatest total quantity of serum.

It was clear that this tendency to an association of recovery with larger dosage might be only apparent in this instance also. To get a correct view of the situation it is necessary to compare the groups as to dosage within the first forty-eight hours after the onset of tetanus. This is done for a group of ninety-one cases in Tables X and XI.

In these tables, in which the mortality for the whole group is sixty per cent, it will be noticed that, of the seventeen cases receiving no serum treatment within forty-eight hours of the onset, the mortality is only forty-seven per cent.

On the other hand, there is a tendency for the larger number of recovering cases to be found amongst those getting the largest doses.
Tetanus in the British Army during the European War

It is interesting to note that, of the three recoveries out of eighteen "type A I" cases, all had received upwards of 20,000 units within the first forty-eight hours and two of them had received over 100,000 units in that time. Of these recovering cases, one was in an American soldier and two in German prisoners accidentally wounded and given immediate treatment.

TABLE X.—Serum Treatment. Recovered.

<table>
<thead>
<tr>
<th>Type</th>
<th>No serum</th>
<th>1,000 to 10,000 units</th>
<th>10,000 to 20,000 units</th>
<th>20,000 to 50,000 units</th>
<th>50,000 to 100,000 units</th>
<th>Over 100,000 units</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AII</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>AIII</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>9</td>
<td>5</td>
<td>36</td>
</tr>
</tbody>
</table>

TABLE XI.—Serum Treatment. Died.

<table>
<thead>
<tr>
<th>Type</th>
<th>No serum</th>
<th>1,000 to 10,000 units</th>
<th>10,000 to 20,000 units</th>
<th>20,000 to 50,000 units</th>
<th>50,000 to 100,000 units</th>
<th>Over 100,000 units</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AII</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>AIII</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>13</td>
<td>10</td>
<td>10</td>
<td>55</td>
</tr>
</tbody>
</table>

But, taken as a whole, the figures do not amount to evidence of the least statistical importance in favour of serum therapy. As to the different routes of administration, practically every case received serum in more ways than one, but very general use was made of the intrathecal and intramuscular routes.

There is no evidence to show that one method was markedly superior to another, but the tendency was evidently to conform to the recommendation of the War Office Tetanus Committee and make use, for preference, of intrathecal and intramuscular injections.

The conclusions which I would draw from the information gained upon the subject of tetanus in the late war are as follows:

1. The almost universal use of antitoxin for prophylactic inoculation has greatly diminished the incidence of tetanus as a complication of war wounds.
2. There is reason to hope that, by following up and applying the new knowledge gained by Dr. Tulloch as to types of tetanus bacilli, it may be possible to still further increase the prophylactic efficacy of antitetanic serum in the future.
3. The prophylactic use of antitoxin has not only reduced the inci-
dence of tetanus but has also led to a modification of the clinical type of the disease. Tetanus, in inoculated persons, tends to assume a milder form characterized by a longer incubation period and a greatly decreased case mortality. "Local tetanus," without trismus, is common.

(4) The improvement in surgical technique, notably the introduction of early excision of wounds, has favourably influenced the incidence, severity and mortality in tetanus cases.

(5) There is as yet no statistical evidence to show that antitoxin has been valuable in the treatment of tetanus.

(6) Good results from serum therapy have been claimed by many surgeons, and recent experiments on animals show clearly that under controlled conditions serum therapy can cure tetanus even though administration had been withheld until the onset of spasm. It is therefore advisable to give every tetanus patient the chance of benefit from specific treatment.

(7) If serum is given it should be given in large doses and as early as possible after onset. Intrathecal injections should be given and these should be supplemented by intramuscular and subcutaneous inoculations.
Tetanus in the British Army during the European War (August, 1914, to December, 1918)

S. L. Cummins

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