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Tetanus

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TETANUS

by

J. B. Henriksen

1932.
INTRODUCTION

The inspiration for this paper was furnished by a case of tetanus which the writer was fortunate in being able to follow from the time of admittance to the hospital to the death of the patient.

There seemed to be some hesitancy as to the proper course of treatment to pursue and the treatment was later rather severely criticised. This resulted in a desire for a more complete knowledge as to the present day ideas on treatment and prophylaxis and I believe these are fairly well reflected in the following discussion. I did not limit the paper to an exhaustive review of the literature on any one particular phase of the disease as I felt that a more comprehensive knowledge of all aspects would be of more value to me.

Many more authors could have been quoted but, in the main, it would have been but a repetition of the information already set forth.

J.B.H.
Definition.

Tetanus (3) is a disease caused by an infection with the Bacillus tetani, and characterized clinically by a toxemia in which the central nervous system is attacked, producing tonic spasm of the muscles.

Etiology.

Predisposing causes.

The most important predisposing cause of tetanus is the wound. This is generally traumatic but may be of any type, from the large wound of the shell fragment, to the minute wound of the hypodermic needle (49). However, the tetanus bacilli and spores unaccompanied by other bacteria do not develop readily if located in healthy tissue. If the tissues are injured, or they are accompanied by other bacilli or by foreign materials, the tetanus spores then develop, multiply and poisoning occurs. This is especially apt to take place in a ragged penetrating wound when the tissues adjacent to the infection are somewhat lacerated. The presence of a foreign body as catgut, the waste from a blank cartridge, shreds of clothing or simply dirt add to the danger. The addition to the wound of a few pathogenic or putrefactive bacteria add still further to the probability of infection. Another predisposing cause is the richness with which the soil of the particular territory is infected with B. tetani, some
soils being rich, others poor in tetanus spores.

Exciting causes.

(3) The direct cause of tetanus is the B. tetani, generally as a wound infection.

The modes of entry are many: Tetanus is liable to occur in any wound which has been contaminated with manure or soil. It has occurred as the result of contaminated catgut and sera and following operations and umbilical cord infections in the new born. Tetanus occasionally follows operations on the intestinal canal due probably to the presence of the organism in the contents of the intestinal canal, tho Kerrin (29) in an examination of 204 stool specimens taken mainly from children in the Royal Hospital for Sick Children, and the City Hospital, Aberdeen, found B. tetani in no instance either by repeated plating or by the method of Fildes (16). Fildes examined 200 stools and found the number of carriers of tetanus spores was 1%. However, Ten Broeck and Bauer (44) in China found that the stools of Chinese patients was positive for B. tetani in 34.7% of cases. Kerrin concludes that the habitat of the patients examined probably influence the results to a marked degree. While his results were negative in town dwellers, farm workers would probably show a considerable degree of positives.
Bacteriology.

Nicolaier (4) in 1885, showed that inoculation of mice and other animals with samples of earth caused tetanic symptoms and he recognized the probable causal agent in a slender bacillus which he grew in mixed culture with other organisms on blood serum. In 1889 Kitasato obtained pure cultures of Nicolaier's organism under anaerobic conditions; he grew mixed cultures and then heated these at 80 degrees centigrade for one hour by which means the other organisms were killed.

As regards the manner in which the disease effects are produced, Knud Faber, in 1889, produced tetanic symptoms by the injection of bacterium-free filtrates of impure fluid cultures of B. tetani mixed with other organisms; he showed that, as in the case of diphtheria toxin, the filtrates were deprived of their power by heating at 65 degrees centigrade. Kitasato then completed the proof by demonstrating the presence of toxin in sterile filtrates from pure cultures of B. tetani. In 1890 Behring and Kitasato (4) showed that when an animal was injected with repeated doses of tetanus toxin in non-lethal doses, it gradually acquired marked tolerance to the poison; in addition, the blood serum of such an actively immunized animal neutralized tetanus toxin when mixed with it in vitro. The mixture of many times the fatal dose of tetanus
toxin with a suitable amount of such "antitoxin" immune serum proved quite harmless when injected into a susceptible animal. This observation constitutes the basis of serum therapy.

(15) The tetanus bacillus in the non sporing condition has slightly rounded ends varying in width from 0.6 microns to 0.3 micron. Length varies from a few micron to over two diameters of the field. The morphology of the spore depends upon its stage of development. Spores do not appear until after about 10 hours of incubation. At first there is a slight oval enlargement of one end of the bacillus not capable of retaining fuchsin. It gradually acquires a spherical shape and expands to the typical drumstick and stains deeply with fuchsin. Bartley (3) in his description of the organism states that the spore first appears as a slender rod with a round refractive spore at either extremity, giving the bacillus the appearance of a club. As the bacillus grows the rod disappears, leaving only the spore. In the absence of oxygen, mobility may be demonstrated in fresh material. This mobility is very slight and disappears with the formation of the spore. The B. tetani is Gram-positive and will take the basic aniline dyes. Those with spores take the stains only in the rod or bacillary part and around the rim of the spore, the center remaining refractive and without stain.

(15) Cultures of the organism in broth or in broth
containing blood derivatives frequently show no opacity until the second day when a general opacity develops. Fields (15) states that obvious gas formation has not been observed in liquid cultures. Agar shake cultures incubated in air, when heavily inoculated, develop a diffuse opacity below the line to which air has penetrated. In gelatin the growth of most strains of tetanus bacilli at 22 degrees centigrade is absent, or so feeble as to be of little value as a test. Milk is an unsatisfactory medium for the growth of B. tetani as no obvious change has been noted in three weeks incubation. In sugars there is no fermentation of glucose, lactose, maltose or saccharose after a period of four weeks incubation.

For isolation of the B. tetani Fields (15) recommends placing the material suspected in freshly boiled blood-broth and incubating in air for at least two days. Spores do not form readily in the blood-broth and therefore every tube, without microscopical examination, is subcultured (2 drops) to the condensation water of a sloped peptic blood agar tube, which is then incubated anaerobically at 37 degrees centigrade. In 24 hours, or occasionally in 48 hours, it is found that the growth has spread up the surface. As B. tetani will grow higher than other bacteria there may be seen upon the apparently unaffected surface of the medium, an exceedingly fine almost structureless film, with a hand lens. This film should be sub-
cultured to another tube which will usually be found to grow a pure structureless film with filamentous edge. B. proteus which is the only organism resisting this method of elimination can be removed by heat. Bartley (3) states that the vitality of the spore lasts for several years, they resist boiling for four or five minutes and withstand a temperature of 80 degrees centigrade for from five to six hours. He states that Nocar de found organisms, taken from colts dying from tetanus, alive after eighteen months and a splinter taken from the hand of a patient with tetanus and kept two and one half years in a closet caused tetanus when inoculated into an animal (Eiselberg).

Procedures that will sterilize articles infected with B. tetani (4).

1. Steam at atmospheric pressure kills spores in five minutes.

2. 5% phenol requires fifteen hours.

3. 5% phenol with 0.5% hydrochloric acid requires 2 hours.

4. 1 to 1,000 corrosive sublimate requires 3 hours.

5. 1 to 1,000 corrosive sublimate with 0.5% hydrochloric acid requires one-half hour.

Tullock (46) found that of 100 wounded who showed no sign of tetanus there were 19 cases from whom the
tetani bacillus could be isolated. From this one could infer a possible natural or acquired immunity and Ten Broeck and Bauer (45) found that the sera of 26 individuals who carried tetanus bacilli in their digestive tracts all contained appreciable amounts of antitoxin. The sera of thirty individuals in whose stools no tetanus-like organisms were found were with two exceptions, free from tetanus antitoxin. They state that although they were unable to measure accurately the antitoxin content of these human carriers of tetanus bacilli, 0.1 c.c. of serum neutralized 10 or more M. L. D. of toxin and they feel that it is evident from this that an active immunity had been acquired due to the bacilli in the intestinal tract. On the above findings they feel that a possible means of immunization has been found which might be useful in armies or in regions where tetanus infections are common.

Tullock (46) has shown the existence of four distinct serologic types of tetanus bacillus differentiated by the agglutination reaction. The distribution of these among two separate groups of wounded men, all of whom were inoculated prophylactically with antitoxin, was as follows:
TABLE 1

<table>
<thead>
<tr>
<th>TYPE</th>
<th>100 TETANUS CASES</th>
<th>25 NON-TETANUS CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>41%</td>
<td>76%</td>
</tr>
<tr>
<td>2</td>
<td>22%</td>
<td>12%</td>
</tr>
<tr>
<td>3</td>
<td>33%</td>
<td>8%</td>
</tr>
<tr>
<td>4</td>
<td>4%</td>
<td>4%</td>
</tr>
</tbody>
</table>

In a study of the four types of B. tetani he found that while the death rate in the cases of Type 2 and Type 3 infection, is greater than cases infected by Type 1, that Type 1 appeared to be responsible for a greater number of cases. He also found that in 100 wounded men who showed no sign of tetanus that B. tetani could be recovered in 19 and probably in 21 instances.

While Tullock isolated only four different types Coleman and Gunnison (8) have concluded that there are nine distinct serologic types of B. tetani. They also differentiated their types by the agglutination reaction and they feel that such a differentiation should be of great value in the serum prophylaxis and therapeutics of the disease. They also believe that the regional distribution of the different types should be studied as ultimately the control of the tetanus problem will depend upon a more extensive knowledge of as many types as possible.

According to Park (49) the tetanus bacillus liberates two toxins. One, tetanospasmin which causes the characteristic symptoms of tetanus by firm union with the cells of the central nervous system, and the other,
tetanolysin which causes lysis of blood cells. The endotoxins in the protoplasm of the tetanus bacillus are of no importance since the bacillus develops only in small numbers and long before the endotoxins could accumulate in sufficient amount to cause harm the tetanospasmin would cause death. The tetanus bacillus remains almost wholly at the site of the wound, a few only are carried to the blood and scattered throughout the system. These isolated bacilli apparently do not proliferate.

The tetanospasmin is a very powerful poison, 0.000,005 c.c. or less may be fatal to a mouse weighing 10 grams. Jordon (28) states that Hall has repeatedly produces toxin of which the M. L. D. for guinea pigs was rarely more than .0001 c.c. and usually less. Jordon (28) states that toxic cultures may be freed from bacteria by filtration through filters of the Berkefeld type. The filtered toxin is highly unstable and is destroyed in aqueous solution by exposure to light, heat and chemical actions. Tetanus toxin is destroyed also by gastric and tryptic digestion. It is generally the practice in immunizing horses for the production of the antitoxin to use the toxic filtrate in as fresh a state as possible.

Before the toxin can be so used it must be tested for potency. But the minimal lethal dose need not be determined with great exactness; if 1 c.c. of a 1 to 10,000 dilution kills a guinea pig with tetanus symptoms,
the filtrate may be accepted.

Tullock (46) from his extensive experimental work with tetanus has drawn several important conclusions. From experiments made to determine the point he found that there is no qualitative difference existing between the toxins produced by the different types of bacilli so that one antitoxin neutralizes the toxin of any type or of all types. And no quantitative difference is demonstrable.

Other conclusions that he arrived at are:

1. Antitoxic sera do not stimulate phagocytosis of tetanus bacilli.

2. Anti-bacterial sera, prepared by inoculation of whole culture, markedly stimulate phagocytosis; and the relationship between serum and organism is specific to the serological type.

He also found that in whole cultures of B. tetani there appeared to exist three antigens. First the bacillary substance itself; the inoculation of this leads to the development of agglutinins which are specific to the types. Second, an antigen, which is antiphagocytic, is present in young unfiltered cultures; but if present at all, is only found in small quantities in filtrates. The presence of this antigen in an inoculum evokes the development of "opsonins", which are specific to the types of bacilli. Third, the spasm-producing toxin, an antigen which is
filtrable and which, in laboratory animals at least, does not appear to be specific to the types. These findings suggest, that improvement might be looked for in serum prophylaxis and serum therapeudics from the employment of sera possessing anti-bacterial as well as antitoxic properties.

He also found in experiments on laboratory animals that the spasm-producing toxin of B. tetani, when employed in sublethal doses, does not produce sufficient local devitalization of tissue to permit of the growth of the B. tetani when inoculated along with it but that the toxin of Bacillus welchii and to a less extent that of Vibrion septique, when used in sub-lethal doses, do produce sufficient devitalization of tissue to allow of the developement of tetanus infection. Antitoxins to the products of these organisms protect animals against infection with B. tetani when such products are used as tissue debilitants. Whether the spores of B. tetani develope or not depends greatly upon the substance producing the devitalization. He also found from examination of the blood of patients suffering from tetanus that agglutination could not be employed as an aid to the diagnosis of the disease.

Symptomatology.

Period of Incubation.

(3) The period of incubation of tetanus is
generally from four to ten days, but it may vary from two days to seventy or more. Patients who have received prophylactic injections show a longer incubation period, as do also the atypical forms of tetanus, especially local tetanus. The symptoms of the incubation period, or the prodromal symptoms, are of the utmost importance in early diagnosis and in determination of treatment. The cure of acute tetanus can only be hoped for by early treatment. The onset of tetanus is often insidious and early symptoms are easily overlooked. For a description of an attack of tetanus we will go to Curling (11) whose Treatise on Tetanus won the Jacksonian Prize in 1834. He states that, "at the commencement of an attack of tetanus, the patient generally complains of stiffness or uneasiness about the muscles of the jaws, throat, or neck, which is frequently attributed by him to having caught cold, and described as a sore throat or a stiff neck. A difficulty is experienced next in rotating or moving the head, and in masticating or swallowing food, attempts to expand the jaws occasioning considerable distress, the nature of the disease often being first detected on requesting the patient to show his tongue. A painful traction or sense of tightness is soon felt about the cartilage ensiformis, passing backward to the spine, and the muscles along the spine and those of the abdomen become affected with spasms, which may afterwards extend to the limbs. The patient is bathed with profuse perspiration, and suffers greatly from thirst; but the attempt to swallow often causes such a distressing paroxysm that
there is complete inability to drink or take any nourishment. The larynx becomes raised, the angles of the mouth drawn up, the alae of the nose elevated, the nostrils expanded, the eyes fixed and prominent, the brow contracted, and the forehead wrinkled, giving to the countenance an expression of great distress and anxiety, and frequently a peculiar grin, called by the earlier writers 'risus sardonicus.' The voice is sometimes altered, being harsh and disagreeable, and, in the violent paroxysm, the tongue, being forced between the teeth, frequently becomes severely lacerated and torn, rendering the mouth bloody, and adding very much to the frightful appearance of the countenance. The shoulders are drawn forward, and the body forced into different postures, according as one set of muscles is more strongly contracted than their antagonists, is sometimes, during the paroxysms, so violently thrown about as only to be protected from injury by the care of assistants. The pain at the precordium increases, respiration is embarrassed and hurried, and the pulse becomes quick and irregular. As the disease advances, the highly painful and distressing paroxysms recur more frequently, being renewed every ten to fifteen minutes. They also become more violent and painful, and are induced by the most trivial circumstances as opening the door, a draught of air or the least attempt to move or swallow. An agonizing sense of suffocation is experienced, the face appears livid, and in a state violent convulsion life frequently terminates suddenly; or sometimes all symptoms
are abated just previous to death and the patient afterwards sinks as if all the powers of the system were exhausted by the long and violent contractions of the muscles and by the excess of pain and suffering."

Bartley (3.) gives as the early subjective symptoms, the following:

1. A slight feeling of tension or contraction, especially in the region of the wound.
2. Insignificant pain in the facial muscles.
3. Pain in the back without apparent cause.
4. Slight difficulty or pain in swallowing, with negative throat inspection.
5. Frequent urination with pain.
6. Constipation.
7. Cramp-like pains in the muscles, especially near the wound. Cramps arising when the patient is startled by a noise.
8. Headaches.
9. Restlessness, especially at night.

The early objective symptoms are:

1. A tendency toward sweating.
2. A slight increase in pulse rate.
3. Restlessness, especially during sleep.
4. Retention of urine.
5. Twitching of the muscles in the region of the wound, which may show irregular clonic contractions.
A slight tap with the finger or an instrument may cause clonic contractions, spreading to other muscles.

6. A tonic spasm of the muscles, especially the flexors, in wound regions.

7. An increase of reflexes; those in the wounded limb often show "double jerk" throwing the muscles of that limb into tonic spasm.

8. Anxious expression of the face.

He states that, "these prodromal, classical symptoms of tetanus, although trivial, may last for days before the acute symptoms occur; generally the increase in severity is in proportion to the toxemia. At times the localized muscle symptoms exist for weeks before becoming generalized, especially in cases which have had prophylactic treatment."

Altho Graves (20) feels, "that the administration of one prophylactic dose of antitetanic serum will greatly prolong the incubation period in those cases destined to develop tetanus is improbable. The antitoxin remains in the blood stream approximately eight days and is thus rapidly and completely excreted by the 10th day." "It is, therefore reasonable," according to him, "that such a prophylactic dose can only prolong the incubation period for the short time that it is in the blood stream, and for that reason the antitetanic serum should always be repeated on about the 7th day whenever a wound is a favorable one for the development of tetanus."
Bartley continues, stating that, "in other cases, with short incubation periods, the onset may be rapid and more severe. Sooner or later, as the disease progresses, the signs become generalized and acute tetanus develops." He gives the objective symptoms of acute tetanus as:

1. Tonic muscle-groups distant from the site of the wound become involved; at first, there are general spasms, generally of the masseters, posterior cervical, abdominal wall, spinal muscles, and of the flexors of the extremities. These tonic contractures are acutely painful and occur spontaneously or following sensory stimuli, either optic, acoustic, or tactile. These contractures may produce the classical opisthotonos of tetanus.

The muscles of the face may contract, the forehead becomes wrinkled, the lips drawn back, the teeth bared, giving the classical facies risus sardonicus.

2. These symptoms are accompanied by a rise in temperature, generally slight. The pulse becomes rapid and poor in tension and volume. It is 100 to 130 in most cases with low temperature. Rare cases show hyperpyrexia.

3. Sweating is profuse and the patient shows varying amounts of cyanosis.

4. Trismus may occur early or late in the disease. The jaws become firmly set and the patient cannot open his mouth. Trismus is not always complete; it may be possible to open the mouth half an inch. When trismus
developes, the muscles of the neck stand out like whip-cords and are rope-like to palpation.

5. As the disease progresses in severity, involvement of the diaphragm and laryngeal muscles may occur. The diaphragm becomes fixed in inspiration, occurring with general convulsions. The larynx contracts, the patient becomes very cyanotic, and asphyxiation may occur. These respiratory symptoms are very severe and give an unfavorable prognosis. Their onset is usually forewarned by epigastric pain, which may occur days in advance, and is a valuable prognostic sign.

6. Hydrophobic symptoms occur in severe cases and these also give an unfavorable prognosis.

7. Laryngeal stenosis may occur from contractures of the larynx and may, if continuous demand tracheotomy.

Subjectively the patient complains of severe thirst and exhaustion. Pain is felt with each spasm and the patient states that he feels "as if held in a vice". All external stimuli cause convulsions; pain and discomfort. The mentality is not altered and the patient is very anxious about his condition. He suffers horrible mental and physical anguish.

The physical findings are mostly those obtained by observation of the above symptoms. Palpation of the groups of muscles involved reveals a board-like rigidity
which is increased by percussion. Any examination of the patient causes a spasm of the muscles involved. Of the special tests the reflexes are of interest, as they are almost always exaggerated. The knee jerk is generally violent and is followed by tremors of the thigh muscles. In other cases a violent spasm of the hamstring muscles may occur, giving a "double jerk". Exaggerated plantar stimulation and ankle clonus may be obtained, the spasm extending as far up as the thigh. The reflexes of the arm are not commonly increased. Occasionally patients show crossed reflexes in the lower limbs. Any group of muscles involved show a marked hypertonicity to mechanical stimulation.

Examination of the wound at this time shows nothing typical of tetanus. The situation of the wound may be of value, as wounds of the extremities and head are more liable to tetanic infection. Puncture wounds are always suspicious. The degree of suppuration and surrounding inflammation of the tissues is not in any way characteristic. The cases with a prolonged incubation period may, upon examination, show the wound to be completely healed.

The laboratory findings in tetanus are usually meagre. The urine is generally diminished in amount, is of high specific gravity and may contain albumin and hyaline casts, if the kidney has been damaged by the elimination of the toxins. Cultures of the wound should always be made in all cases of suspected tetanus. B. tetani cannot
always be demonstrated, and a negative culture does not rule out tetanic infection.

The presence of other organisms in wound cultures is important data, as certain bacteria inhibit and others help the growth of tetanus spores. Blood cultures are negative, as tetanotoxin has a special affinity for the central nervous system and but few of the organisms get into the blood stream.

X-ray examination of all wounds should be a routine procedure, especially in gunshot wounds of any type as small fragments may remain even after the main projectile has been removed.

Diagnosis.

The diagnosis according to Bartley, in the early stages is not always easy. To save the life of the patient early diagnosis is essential, for treatment with serum must be established before too much tetanotoxin has combined with the nerve cells, and in order to prevent the fixation of subsequent toxins.

The diagnosis is made on the basis of the clinical history, a wound, especially of the extremities, an operative wound, or in rare cases even on the basis of a needle puncture followed by an incubation period of from one to twenty-one days or more. After this the development of the prodromal symptoms takes place as previously described, followed by tonic or clonic spasms, trismus and the classical symptoms. Cultures from the wound showing the presence of B. tetani or
of spores confirm the diagnosis.

In the early stages the symptoms may be confused with strychnine poisoning or tetany. However, in strychnine poisoning a history of the use of the drug is important. Besides the contractures of strychnine intoxication begin with clonic spasms, which quickly become tonic. The muscles of the jaw are never involved early, if at all. Between single paroxysms there is complete relaxation of the muscles, instead of a diminution in the degree of contraction, as in tetanus.

Tetany may cause more confusion in the diagnosis. The spasms of tetany are bilateral and symmetrical. They are chiefly confined to the muscles of the distal portions of the extremities. There is a peculiar involvement of the hands, which are conical in shape; the fingers extended as far as the interphalangeal joint but flexed at the ends. The thumb is flexed and tucked inside the fingers. The feet are semi-flexed at the ankle and the toes strongly flexed. Tetany occurs most generally in children and is a symptom complex manifested in constitutional toxemia more frequently than in metabolic pathology. If a wound is present with symptoms of tetany, cultures should always be made.

Wilmoth (47) reports a case of tetanus which he mistakenly diagnosed as acute appendicitis. The patient was a male Indian, age 20, who gave a history of vomiting two days previous to examination and vague abdominal pain
which rapidly became agonizing. Temperature on admission was 102.4 degrees, pulse 156, respiration 36. The white blood count was 17,250. Physical examination revealed board-like rigidity in the lower right quadrant with extreme pain on pressure. Diagnosis was acute appendicitis. On operation no abdominal pathology was found. He was given the usual post operative treatment but continued to complain of severe abdominal pain. Rigidity and spastic contraction of the back muscles was next noted. Abdominal reflexes were hyperactive and Kernig's sign on both sides was positive. History of frozen toes two weeks previously was elicited, with exposure to tetanus infection; the patient having worn no shoes and walked about on the dirt floor of the Indian hut. 61,000 units of tetanus antitoxin was given but to no avail.

Reuter (40) reports a case of tetanus that only narrowly escaped operation for appendicitis. The patient, age 17, complained of severe pain in the right lower quadrant of the abdomen and in the right lumbar region, growing progressively worse from the onset. His physician had diagnosed the case as acute appendicitis and the patient was immediately taken to the hospital for operation. At time of entrance his temperature was 100.2 degrees, pulse 84, respiration 24. The white blood count was 13,000. Tetanus was suspected because it was observed that firm pressure upon the abdomen caused the patient to arch his back
and straighten out his legs. Further questioning revealed a history of a puncture wound in the foot two weeks previously. The following day well marked signs of tetanus had developed. Antitoxin was given intramuscularly and intravenously in 10,000 unit doses with sedatives and a nourishing diet given every two hours.

It is evident from these two reports that the possibility of making a mistaken diagnosis of acute appendicitis is not slight especially if a careful history is not obtained or the early symptoms properly evaluated and interpreted.

Complications.

Classical tetanus is not associated with any other disease, except that it may be superimposed in sepsis from wounds. According to Bartley (3) lobular pneumonia is the chief complication of tetanus, especially in cases with diaphragmatic and laryngeal spasm and in cases showing suffocation symptoms. It is usually fatal. Cardiac de-latation also occurs in some cases and is generally a terminal manifestation.

High (24) reports a case of tetanus in a boy 8 years old complicated eleven days after injury by the onset of measles: The two diseases ran concurrently and by the tenth day the rash had almost disappeared. The boy recovered.

Armstrong (1) presents an interesting report of 98 vaccination cases complicated by tetanus. He concludes from epidemiologic evidence that large vaccination insertions
and the use of shields and dressings predispose to post-vaccination tetanus in man. He states that extensive tests of commercial vaccine virus both by the manufacturers and by the Hygienic Laboratory have uniformly failed to demonstrate the presence of B. tetani. Needles, tubes, dressings and antisepsics have been repeatedly examined for tetanus but with negative results except in two instances. In one instance B. tetani were found on bone-point scarifiers and in 1925 the organism was demonstrated in bunion pads and as he states, "one is therefore left to conclude that the infection is due to accidental contamination of the lesion".
<table>
<thead>
<tr>
<th>Method of Insertion abrasions (1/4 -5/8&quot;) or scarification.</th>
<th>Shields</th>
<th>Gauze</th>
<th>Bunion Pads</th>
<th>Gauze &amp; Shield</th>
<th>No dressing early, Shield later dressing.</th>
<th>Adhesive banding.</th>
<th>No dressing</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>22</td>
<td>13</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Multiple linear incisions 2-12 in one locality.</td>
<td>7</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Single linear incision.</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
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<td>0</td>
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<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>32</td>
<td>15</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>98</td>
</tr>
</tbody>
</table>
He states, "that a proper vaccination is defined as one in which the insertion is not more than 1/8 inch in its greatest diameter and which is made by some method that does not remove or destroy the epidermis. Such insertions, when treated openly, have never, as far as we are aware, been followed by postvaccination tetanus.

Moir (31) reports a case of tetanus in a girl 13 years of age which was complicated by a gas gangrene infection (B. welchii) that was treated successfully with 102,000 units of antitoxin administered intrathecally, intravenously and subcutaneously and 1,300 c.c. of anti-gas gangrene serum.

Clinical Varieties.

Not much is said in the English literature of the clinical varieties of tetanus.

Cumston (10) gives the following clinical types of localized partial tetanus in addition to the classical form:

1. Splanchnic tetanus - following visceral inoculation.

2. Localized cephalic tetanus.
   a. Non-paralytic type characterized by trismus, stiffness of the neck muscles and slight contracture of facial muscles.
   b. Type with facial paralysis.
c. Type with paralysis of the hypoglossus.

3. Unilateral forms characterized by paralysis of different groups of muscles of the limbs.

Bartley feels that splanchnic tetanus cannot be classified as atypical, for if trismus does not become generalized it is only because death occurs within from twenty-four to forty-eight hours.

He gives the following description of the localized cephalic types:

1. Simple cephalic tetanus occurring following a wound of the head. Trismus and contractions are established unilaterally or bilaterally, and localized in the muscles of the face and in some cases in the cervical region also. Dysphagia, hydrophobic, or paralytic symptoms never occur in simple cephalic tetanus.

2. In cephalic tetanus, accompanied by dysphagic or hydrophobic symptoms the trismus occurs unilaterally on the same side as the head wound, remains unilateral for four to six days and is continuous. Pharyngeal spasms are established, giving rise to the dysphagic symptoms, which may increase until hydrophobic symptoms appear.

3. Cephalic tetanus with facial diplegia or hemiplegia occurs following a wound of the face in a region close to the facial nerve or any of its branches, especially the superior division. Contractures of the neck muscles appear shortly after trismus and these are tonic in character but may become spasmodic. These contractures extend
with the progress of the disease to the muscles of the back, abdomen and limbs.

4. Facial paralysis is rare in classical tetanus cases; but in this form of the disease it is always present. Its character is that of a peripheral paralysis, except that the phenomena of contracture and paralysis occur in the same muscle. The condition must be differentiated from severance of the facial nerve and Bell's palsy.

5. In cephalic tetanus with ophthalmoplegia the wound is usually situated in the orbitosuperciliary region. Altho the eyelids and eyeballs may also be sites of the infection. The symptoms may be unilateral or bilateral. The paresis is generally incomplete. The patient appears drowsy, the upper lid falling and hiding the cornea.

6. Local tetanus of the limbs is an entity in itself as general tetanus does not later develop. There are two forms of local tetanus, the early and the late forms. In the first variety, the incubation period is five to ten days. In the late variety the incubation period varies. The course of the disease is chronic. The first stage of painful contractions and fixation of the limb generally extends over a period of from ten to twenty days. The second stage then follows, in which the painful contractures cease but the limb still remains rigid and is fixed by the board-like rigidity of the muscles. This period lasts from twenty-five to fifty days. During this time, the muscles may become atrophied; tendon contractures, trophic ulcers and
vasomotor disturbances may become established. The third period, that of recovery, may be extended over a long time. From three to four months is not excessively long for this period of recovery.

Pathology.

It is generally conceded that B. tetani and its spores always remain at the site of the wound, generally in company with other pathogenic bacteria. The bacillus rarely if ever invades the blood stream or parts of the body distant from the wound. However, the course that the tetanospasmin, produced by the B. tetani, takes in reaching the central nervous system is much in dispute.

Park (49) states that, "it is a matter of great practical importance to discover the course of the toxin from the wound to the cells of the brain and spinal cord, because our methods of injecting the antitoxin will be greatly influenced by the location of the toxin in the tissues at the time symptoms develop. Much experimental work has been done in investigating this subject. All agree that the toxin is taken up to some extent by the nerves. Some believe this is wholly thru the end nerve plates and that the toxin passes along the nerve fibers until it reaches the spinal cord. Others think the toxin passes up the lymph vessels of the nerves. There can be no doubt that a considerable amount of the toxin passes up the nerve trunk, supplying the region of infection, but probably a much larger part is taken up by the tissue lymph spaces and carried thru the
lymph channels to the blood stream and thereby distributed thru the body and taken up by the nerve endings. Camprech and Stintzing conclude from their experiments that the toxin from the wound passes to the central nervous system, partly directly by the perineural and endoneural lymph spaces of the nerves of the infected region, which directly connect with the subdural spaces and partly thru other nerves obtaining it indirectly from the blood. The local tetanus they consider as due to the contact of the poison with the motor end plates.

Hall (22) concludes that, "although tetanus toxin passes rapidly from the blood stream into the connective tissue spaces and thence to the thoracic duct, the toxin does not pass from the capillaries of the central nervous system to the tissue thereof. Neither does it pass from the choridal plexus to the cerebrospinal fluid". It is perhaps important that, "although bacteria can pass through the posterior root ganglion to the cord, colloidal pigments and tetanus toxin are prevented from doing so."

In a review of the literature Freedlander (18) also finds that there is considerable disagreement over the path which the tetanus toxin takes in getting to the central nervous system, it being either conducted by means of the axis cylinders or by the neural and perineural lymphatics. He states, "from a therapeutic standpoint it matters greatly as to which of these absorption paths is correct, as obviously
if tetanus toxin is conducted by the axis-cylinders only, antitoxin can be of little value, while if the lymphatics carry it vigorous antitoxin therapy is indicated. As a bases for therapy it would be safest to take the position that the tetanus toxin appears in the blood stream and other tissues and can be neutralized by antitoxin at any stage in its passage before its final and relatively indissociable union with ganglion cells. Consequently, the greatest indication for treatment is to maintain as high a concentration as possible of antitoxin in the blood and lymph stream. This can best most readily be done by large frequently repeated injections intravenously.

Robertson (41) performed an experiment based on the theory that tetanus toxin is conveyed by the axis-cylinder of the peripheral nerves to the spinal cord, it must also pass up the cord by the same means, while if conveyed to the cord by the lymph channels it must likewise spread by means of the lymph channels. The spreading of toxin by means of the lymph channels can be prevented by a previous administration of antitoxin, which same, on the other hand, should not prevent the passage of toxin along the axis-cylinder. Then by injecting toxin into the lower end of the spinal cord substance of a passively immunized animal he found that this toxin, even in doses which were sufficient to provoke symptoms in control animals, neither produced any marked local effect nor advanced in the spinal cord toward the more sensitive centres of the medulla, in short,
that it was not taken up by the axis-cylinder but was prevented by antitoxin from spreading along its natural customary route, namely, the lymph channels. He feels also that the experiment supports the observation made on the occurrence of local tetanus when toxin is injected into the sciatic nerve or into the muscles of an animal's hind leg. In the presence of antitoxin in the system, tetanus toxin, no matter where it is injected, does not travel far in the cord, because manifestly as it becomes more diluted, the antitoxin which is present in the lymph spaces of the spinal cord as well as in the lymph channels of the nerves, has an opportunity to neutralize fully the less concentration of the antitoxin as compared with that of the toxin.

Ransom (39) concludes that, "tetanus toxin travels to the central nervous system along motor nerves because if by means of lumbar puncture the toxin is injected into the subarachnoid space without injury to the pia or cord it passes rapidly into the bloodstream, and after the usual period of incubation, general tetanus occurs. If, however, the toxin is injected intravenously and immediately afterwards the spinal cord is injured by injection of a drop of normal salt solution, then the general tetanus is preceded by a local tetanus in the muscles, corresponding to the injured segment of the cord. If an animal is first protected by the administration of a large dose of antitoxin so that no free toxin can exist in the blood, and then a small dose
of toxin is injected into a motor nerve, a local tetanus corresponding to the distribution of the injected nerve results. Injection of toxin into a purely sensory nerve does not cause either local or general tetanus."

From these and other facts Ransom has concluded that tetanus toxin is transported to the central nervous system along motor nerves. Ransom has his conclusion well substantiated by experimental evidence and most writers are inclined to agree with his views.

Considerable study has been made of the contractures resulting from local tetanus. Davenport et al (12) found that, in advanced stages of local tetanus, the extensor muscles fail to relax after section of the motor nerves. This myostatic contracture was studied histologically in the gastrocnemius and soleus muscles of white rats. There is no increase in connective tissue and the contracture is not due to fibrosis. The muscle fibers undergo changes, but what relation these bear to the shortening of the muscle is not obvious. The muscle fibers show a blurring of the cross striations and a mottled staining. The blurring of the cross striations appears to be due, in part, to a disruption of whatever holds the myofibrils in close juxtaposition and accurate transverse alignment. The fibers acquire a wavy longitudinal striation due to the greater evidence of the individual fibrils. The mottling is due to changes in staining reaction of different parts.
of the same fiber, some areas staining more heavily, others
more lightly than normal.

A small percentage of the muscle fibers undergo
degeneration. Where the separation into light and dark
areas has been pronounced, the light fields may disintegrate
while the dark ones become granular. A few other fibers
become replaced either for short distances or throughout
their lengths by nuclei, which fill the old sarcolemma.
These appear to be derived, in part, from the nuclei of the
muscle and, in part, from mononuclear cells that have
invaded the fibers from without."

(38)

S. Ranson and S. W. Ranson conclude that, "the
gastrocnemius muscle of the white rat, which has been set
at a shortened length in the myostatic contracture of local
tetanus, may after from eight to twelve weeks recover ap­
proximately its normal length and be used again normally
in locomotion. The muscle acquires again a normal histologic
appearance. The muscle fibers show regular and well defined
cross striations and nuclei of the normal number and dis­
tribution. There is no obvious increase in connective
tissue."

According to Ranson (37) in a study he made on
muscle tonus and contracture, "when local tetanus is fully
developed, the extensor muscles in the affected limb are in
a state of contracture and do not relax after all nerve
impulses have been interrupted by section of the motor nerves
or death of the animal. This contracture is not due to
fibrosis nor to any change in the muscle fibers which can be recognized by the microscope. It must be due to some change in the physical condition of the muscle fibers, possibly the formation of an irreversible sarcoplasmic gel. Muscles in tetanus contracture show a decreased height of contracture and a delayed relaxation. A muscle in advanced contracture is only slightly shortened when its motor nerve is stimulated, but this is due to changes in the muscle rather than to a paralysis of the nerve or nerve endings.

In addition to its action on the central nervous system, tetanus toxin has also a peripheral action, which appears to be exerted directly on the muscle fibers rather than on the nerve endings. This causes a change in the physical condition of the muscle fiber, which seems to be in the nature of an increased viscosity. It decreases the resistance of a muscle against permanent elongation, when the muscle is stretched with moderate leads, and is in all probability partly responsible for fixing the muscles in a state of permanent contracture. The fact that tetanus does not develop in a muscle the motor nerve of which has been cut cannot be taken as evidence against this peripheral action of the toxin; it shows only that the tonic contractions are of central origin. He also states that, "the sympathetic nervous system does not take part in the production of the tonic contractures of tetanus." He concludes that, "while the dorsal roots have some influence, they do not
play the important role in the genesis of tetanus which has been assigned to them by some investigators. Typical tonic contraction occurs in deafferented muscles under influence of tetanus toxin. This appears, at first sight, to be contrary not only to Frank's hypothesis of the antidromic conduction of tonic impulses in the dorsal roots but also to Sherrington's conception of tonus as a proprioceptive reflex. The occurrence of such tonic contractions in deafferented muscles seems to find at least a partial explanation in the direct action of the toxin on the muscle fibers.

The post mortem findings in tetanus are very meagre. The blood vessels show an over filling with cellular exudate in the perivascular spaces. The ganglion cells of the spinal cord may show chromatolysis. The B. tetani may be demonstrated in the pus from the wound. The negative findings in the tissues are of pathological importance.

Treatment.

In the literature the treatment of tetanus is considered considerably more than any other phase of the condition.

As will be seen from the following reports the concensus of opinion is that prophylaxis is of major importance while massive therapeutic doses of antitoxin ranks second. All agree that early diagnosis and immediate instigation of treatment are of primary importance and offer
our best means of combating the disease after it is acquired. There is some disagreement as to when prophylactic treatment should be used. Considering the tremendous numbers of wounds of all types it would seem practically impossible for all to receive prophylactic injections of antitoxin tho no doubt we should strive for that ideal.

The treatment of tetanus may be divided into prophylactic, and curative:

Prophylaxis.

The prophylaxis for tetanus consists of from one to three or more injections of 1500 units of tetanus antitoxin subcutaneously. The variations and different conditions influencing prophylaxis will be taken up later in the reports by different authors.

No doubt before continuing the discussion of treatment we should take up the manufacture of tetanus antitoxin. According to Park (49) antitoxin is developed by inoculating the tetanus toxin in increasing doses into horses. The horse receives 5 c.c. as the initial dose of toxin, of which one c.c. kills 250,000 grams of guinea pig, and along with this, twice the amount of antitoxin required to neutralize it. In five days the dose is doubled. This over neutralized toxin stimulates the production of antitoxin. Another method is to inject the horses subcutaneously with 5,000 units of tetanus antitoxin, and then after a lapse of 24 hours, give, at short intervals,
increasing doses of straight toxin, after four to five months of this treatment the blood of the horse contains enough antitoxin to be of therapeutic use. The serum is then refined, leaving only the pseudoglobulins to which is bound the antitoxin. A unit of antitoxin is defined as the amount of antitoxin required to just neutralize 1,000 M. L. D. of tetanus toxin for a 350 gram guinea pig.

The United States Government's (2) method for testing the strength of tetanus antitoxin is: "The immunity unit for measuring the strength of tetanus antitoxin shall be ten times the least quantity of antitetanic serum necessary to save the life of a 350 gram guinea pig for 96 hours against the official test dose of the standard toxin furnished by the Hygienic Laboratory of the Public Health Service." The official test dose of toxin is one hundred times the smallest quantity of toxin which will kill a guinea pig within 96 hours.

Mac Conkey (30) concludes from experience gained during the first year of the war that 500 to 1000 U. S. A. units of tetanus antitoxin is a sufficiently large prophylactic dose for the majority of cases, and that it is advisable, in severe wounds, to repeat the dose once or twice at intervals of a week.

The statement that it is often valuable to administer more than one prophylactic dose of antitoxin is substantiated by Cummins (9) who found that one
A prophylactic dose of serum does not greatly influence the length of incubation period as in 343 cases which occurred in British soldiers in France the average incubation period was 13.2 days, while in the British "home hospitals" when prophylaxis was adequately repeated and where there was the influence of other factors, the average (5) incubation period was 45.5 days.

To emphasize the importance of repeated prophylactic injections we will cite a case reported by Hoge (25). This case had suffered a severe laceration of the hand. 1500 units of antitoxin were given immediately on entrance to the hospital. The patient was dismissed in 10 days feeling very well. The patient was readmitted the following day, eleven days after injury, unable to open his mouth; muscles of the neck and back were rigid. A diagnosis of tetanus was made and 10,000 units of antitetanic serum was given intravenously, followed immediately by a convolution, collapse, and death in about ten minutes from an anaphylactic reaction.

Hoge concludes from consideration of this case that antitetanic serum should be administered as soon after the accident as possible, if there is a laceration or puncture wound and that the dose should be repeated in ten days if the wound contains necrotic material. A third dose should be given if it is found necessary, at a later date, to carry out operative procedures upon the wounded parts.
From a study of 1,669 cases of tetanus, of which 262 cases were analyzed critically, Nicoll (34) has concluded that:

1. "Deaths from tetanus in the state of New York from 1907 to 1925 are but one-third the number which occurred eighteen years ago. This can be attributed to no other cause than the more general use of tetanus antitoxin as a preventative."

2. Deaths from tetanus as a result of Fourth of July celebrations are increasing.

3. The fact that tetanus occasionally occurs after a single preventative dose of antitoxin strongly suggests that the advisability of repeating the dose one or more times in all severe and extensive wounds, and possibly the advisability of administering twice the standard preventative dose at the first inoculation.

McGregor (33) feels that in comparison with the prophylaxis used in the army, the prophylaxis used by physicians in civil practice is very inadequate with the result that many more cases of tetanus occur in civil practice. He advocates prophylactic antitoxin in every wound, no matter how slight, especially if it has been exposed to contamination by the B. tetani. As for treatment he feels that both the specific and symptomatic should be heroic, accompanied by excision or incision with cautery of the wound and infiltration about the wound with antitetanic serum.
Nothing has been said so far as to the prophylactic value of incision of puncture wounds.

Wainwright (48) disagrees with McGregor as to when prophylaxis should be used, stating that he does not believe that the tetanus bacillus is often if ever (except possibly in barnyards and stables) on the puncturing body itself, not even on the classical rusty nail. He feels that the organisms are on the skin, stocking or shoe, and are driven in at the time of puncture, or get in later from want of proper surgical dressing, so that if a puncture wound gets prompt and efficient treatment, routine prophylaxis is not necessary unless contamination is present from street dirt, soil from the garden or farm, or from the stable or barnyard. He concludes from the reports of a large number of industrial physicians that routine prophylaxis is not practical and that the possibility of tetanus arising in the most unexpected cases will have to be accepted and the possibility of improved curative treatment be relied upon.

Bartley (3) feels that all wounds under suspicion must be cleansed early, contending this is of as great value in the prevention of the disease, as is the use of serum. Mechanical sterilization should take place by the removal of all traumatized tissue which has been devitalized, and all devitalized skin and fascia should be cleanly removed. All dirt, clothing, pieces of bone denuded partially or completely of their periosteum, and foreign bodies
of all kinds should be removed by cleancut surgery. The mechanical sterilization by surgery should be augmented by the use of antisepsis. Tincture of iodine neutralizes tetanus toxin while hydrogen peroxide, magnesium peroxide or calcium peroxide are of value as dressings and are perhaps the best chemicals at our disposal because of the oxygen which they liberate which kills the anaerobic B. tetani. The ultra-violet rays are also an effective means of killing spores.

Park (49) advocates washing with soap and water followed by a disinfectant. Possibly packing the wound lightly with antiseptic gauze.

Curative Treatment.

This may be divided into:
1. General management.
2. Local surgical treatment of the wound.
4. Antitoxin therapy.

We shall not consider each phase separately but shall consider them as a whole as each author sees fit.

Freedlander (17) in a series of 25 cases treated used the following regime.
1. Local treatment of the wound consisted of making all parts accessible to the air by the removal of devitalized tissue. A small amount of antitoxin was injected about the wound.
2. Within the first 24 hours a total of
50,000 to 150,000 units of antitoxin was given intravenously, divided into three to five injections. Thereafter a daily dose of from 15,000 to 150,000 units intravenously in from two to three injections. This was continued from 12 to 15 days depending upon muscle rigidity.

3. Morphine was given hypodermically every 6 hours and cloretone every 6 hours by rectum.

Rationale of treatment.

"It has been shown" he states, "that tetanus antitoxin appears early in the blood stream and it is from here that it is taken up by the motor nerve endings. It has also been shown that antitoxin can only neutralize the toxin which is in the blood stream. Toxin already bound by the central nervous system cannot be influenced. Furthermore antitoxin is excreted very rapidly.

The aim of the treatment should be to maintain a high concentration of antitoxin in the blood in order to neutralize whatever toxin is already there and also that which is being given off by the focus of infection. Thus the toxin would be neutralized before being taken up by the nerve endings. The most practical way to maintain a high concentration in the blood stream is by repeated intravenous injections. Intraspinous injections, theoretically, offer the slight advantage of neutralizing more directly the small amount of toxin in the spinal fluid, which would also
be neutralized from the blood stream, while practically, there is the difficulty of doing repeated spinal punctures on spastic tetanus patients. Antitoxin is not taken into the central nervous system from the spinal fluid.

**TABLE 3**

Results of intravenous treatment - large doses.

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>Cured</th>
<th>Died</th>
<th>Mortality %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Incubation period 10 days</td>
<td>11</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>2. &quot; 10 days or more</td>
<td>8</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>3. &quot; Unknown</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>16</td>
<td>9</td>
</tr>
</tbody>
</table>

Wainwright (48) not only supports Freedlander's ideas as to the efficiency of intravenous therapy but contends intrathecal injections are harmful. Both advocate massive injections. Wainwright states that his review of English literature shows a marked degree of pessimism in the reports of English physicians on the efficiency of antitoxin treatment of tetanus and he believes their bad results have occurred due largely to two factors, first, that antitetanic serum given intraspinally is harmful and diminishes the chances of recovery; second, that when antitetanus serum is given by less harmful methods, it is given in doses so small that it cannot be expected to do any good. He supports his first contention on a physiological basis by stating, "first, it seems universally agreed by laboratory workers
that once tetanus toxin unites with the cells of the central nervous system the antitoxin has no power to break up the union and so it would do no good to bathe the cells in antitoxin even if we could do so. Second, there is no evidence that the antitetanus serum injected into the spinal canal gets into the tissues of the cord and brain whether it would do any good or not. Third, it is established that during the disease the toxin is not present in the cerebrospinal fluid so that no. toxin is neutralized by spinal injections." Also his first contention is supported on a statistical basis as he shows by citing several groups of cases. In British army patients in hospitals in France in 360 cases treated by intrathecal injection, alone or in combination with other methods, the mortality rate was 68.2% while in 164 cases not treated intrathecally the mortality was 64.5%. In British army patients in Home Hospitals in 804 cases treated intrathecally alone or in combination, the mortality rate was 32.9% while in 585 cases not treated intrathecally the mortality was 20.6%.

The following table shows increase in deaths when intrathecal treatment is added to any other method of treatment. (Personally communicated cases).
He feels therefore that the first thing to do to cut down the tetanus mortality is to eliminate intrathecal injections. His conclusion that intravenous injection of from 30,000 to 50,000 units of tetanus antitoxin given promptly will divide the present mortality rate by two or three is supported by the following table.

1. Thirty-eight hospitals using intrathecal or small intravenous doses report 515 cases.
2. City Hospital, Cleveland, using average initial dose of 78,000 units intravenously, reports 20 cases only.
3. Ninety compiled cases in which treatment was given 30,000 units or more intravenously the first day of treatment

### TABLE 4

<table>
<thead>
<tr>
<th>Method</th>
<th>Mortality in %</th>
<th>Method</th>
<th>Mortality in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td>63</td>
<td>TV</td>
<td>71</td>
</tr>
<tr>
<td>S</td>
<td>39</td>
<td>TS</td>
<td>63</td>
</tr>
<tr>
<td>M</td>
<td>54</td>
<td>TM</td>
<td>63</td>
</tr>
<tr>
<td>VS</td>
<td>28</td>
<td>TVS</td>
<td>51</td>
</tr>
<tr>
<td>VM</td>
<td>52</td>
<td>TVM</td>
<td>56</td>
</tr>
<tr>
<td>SM</td>
<td>50</td>
<td>TSM</td>
<td>80</td>
</tr>
</tbody>
</table>

V - Intravenous  
S - Subcutaneous  
M - Intramuscular  
T - Intrathecal
46.

(Table Continued)

Mortality in %

4. Seventy-three compiled cases in which treatment was given 30,000 units intravenously the first 3 days. 55%

As a symptomatic treatment for the relief of tonicity he states his opinion that chlorbutanol, given in 30 grain doses per mouth or 75 grain doses per rectum, often enough to keep the patient relaxed, is the best sedative.

A table compiled by Nicoll (34) in 1926 appears to support Wainwright's opinion concerning intrathecal injections tho he draws a different conclusion stating that, "grouped according to the results obtained by each method whether alone or in combination, gives the most favorable place to that series of cases in which the intravenous method was used, namely 56% mortality while those cases in which intraspinous injection were used showed a mortality of 62%. This is somewhat contrary to Nicoll's (35) opinion in 1915 when in reporting a series of 20 cases he felt that the low death rate of 20% must be attributed to the intraspinal use of large doses of antitoxin.

Altho Wainwright and Freedlander are strongly opposed to the intrathecal use of antitoxin there are many more men who strongly advocate that method.

Ashhurst (2) advocates very strongly the intrathecal use of tetanus antitoxin but feels that the use of
magnesium sulfate to relieve spasms is dangerous, it being efficient for that purpose only in lethal doses.

Park and Nicoll (36), performed a series of experiments on guinea pigs in an attempt to determine the efficiency of the intrathecal administration of tetanus antitoxin in comparison to other methods of administration. They injected guinea pigs with two lethal doses of tetanus toxin then gave antitoxin to one series into the heart, another subcutaneously and another series intraspinaly. They came to the conclusion after observing the comparative low death rate in those animals treated intrathecally that that method was greatly superior to any other and that the subcutaneous method was the most inefficient.

They advise the following course of treatment:

1. 3,000 to 5,000 units intraspinaly each 24 hours as early as possible after injury.
2. 10,000 to 15,000 units intravenously.
3. 15,000 units subcutaneously or intramuscularly three of four days later.
4. Proper and thorough surgical treatment of wound.
5. Sedatives and stimulants as necessary.

From a series of experiments on animals in which animals were inoculated with 2 M. L. D. of tetanus toxin then treated with tetanus antitoxin by the different routes, Andrews (26) feels that the intrathecal is the most efficient
with the intravenous method a close second. In 20 cases of tetanus seen by him, his impression was that the intrathecal route gave the better results.

Denyer (13) reports a case in a man aged 21, who was given antitoxic serum in large doses, intrathecally, intramuscularly and subcutaneously for five days with no apparent improvement. He was then given 10,000 units intracistemally and 10,000 units intramuscularly and in 18 hours considerable improvement could be noted. Improvement progressed steadily for a month when the patient was discharged. A total of 192,000 units was given.

We have seen, in the previously cited cases and papers, both the intrathecal and intravenous methods of administration advocated and condemned. There are some men who question the therapeutic value of tetanus antitoxin given by any method.

Suvansa (43) states that becoming discouraged with the unsuccessful treatment of tetanus by antitoxin and the ineffective subcutaneous phenol treatment he decided to try the injection of phenol intrathecally. He obtained fresh leucocytes from a lumbar puncture and found that a 1-to 400 dilution of phenol in normal salt was the strongest solution that would not affect the leucocytes. The dosage used was 30 to 40 c.c. in adults; 12 to 20 c.c. in children. He reports the results of this phenol treatment
in fourteen cases. Of the fourteen cases treated four died but these were severe cases, having reached the final stage of cardiac and respiratory failure, and one of the four cases probably died of uremia rather than tetanus.

Sequelae of the treatment:

1. Rigidity of the back muscles due to irritation of the motor nerve roots from the first to the seventh day of injection.

2. A rash, varying in character and intensity, appears between the first and seventh days and lasts 4 to 14 days. It abates without treatment and probably is due to the elimination of carbolic by the skin.

3. Three of the fourteen cases developed an acute nephritis due no doubt to elimination of carbolic by the kidneys. The treatment would be contraindicated in patients having chronic nephritis. A follow up of the recovered cases gave no evidence of late nervous complications.

Suvansa concludes from this series of cases that the phenol treatment is better than the antitoxin because,

(a) First, it is more certain in action.

(b) Second, one injection suffices.

(c) Third, the cost is almost nil.

The only disadvantage is the danger of chronic kidney disease.

In an analysis of tetanus occurring in the British
armies in France from November 1st, 1916, to December 31st, 1917, Cummins and Gibson feel that while the statistics do not show a marked decrease in mortality due to the therapeutic use of antitoxin, that it is still of great value and they recommend that it be given in large doses as the toxin antitoxin union is a quantitative one. They found in their series of cases that the incubation period for fatal cases was 12.5 days while the average incubation period was 13.2 days.

In support of antitoxin as a therapeutic agent, Hall (21) in a study of fifteen cases of tetanus occurring in Colorado during the years 1924, 1925, and 1926, feels of the fourteen fatal cases, nine might possibly have been saved by the early recognition of the danger of tetanus and the timely use of tetanus antitoxin. He also feels that all deep lacerated or puncture wounds should receive prophylactic treatment.

Ireland (27) in a recent paper states that the tendency now is to give larger doses of tetanus antitoxin than previously. Many patients, however, given extremely large doses, do not recover because of the marked severity of the infection and the greater number of days the infection lasts. There seems to be little or no evidence of untoward results from these extremely large doses of antitoxin. He cites a case of a boy, aged 8 years, who was given 265,000 units followed by recovery.

Graves (20) gives tables showing the comparative effect of small doses of serum and no serum treatment and
comparison of results obtained by use of small doses with that obtained by using large doses.

TABLE 5

<table>
<thead>
<tr>
<th>Doses of serum</th>
<th>Cases</th>
<th>Discharged</th>
<th>Died</th>
<th>Mortality in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 to 1000 units</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>75.0%</td>
</tr>
<tr>
<td>1000 to 10,000 units</td>
<td>202</td>
<td>68</td>
<td>134</td>
<td>66.3%</td>
</tr>
<tr>
<td>10,000 to 20,000 &quot;</td>
<td>32</td>
<td>9</td>
<td>23</td>
<td>71.8%</td>
</tr>
<tr>
<td>20,000 to 50,000 &quot;</td>
<td>27</td>
<td>10</td>
<td>17</td>
<td>63.0%</td>
</tr>
<tr>
<td>50,000 to 100,000&quot;</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>66.6%</td>
</tr>
<tr>
<td>Over 100,000 &quot;</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>50.0%</td>
</tr>
<tr>
<td>No serum used</td>
<td>304</td>
<td>97</td>
<td>207</td>
<td>68.0%</td>
</tr>
<tr>
<td>Serum used</td>
<td>273</td>
<td>91</td>
<td>182</td>
<td>66.6%</td>
</tr>
</tbody>
</table>

Average dosage 13,000 units.

This table indicates that the use of serum lowered the mortality 1.4% but this could be expected from the small average amount of serum given. In the following series the average dosage was 48,000 units with average death rate of 41.5% in contrast to 65.8% of the previous table.
TABLE 6

<table>
<thead>
<tr>
<th>Units of Serum</th>
<th>Cases Discharged</th>
<th>Died</th>
<th>Mortality in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 to 20,000 units</td>
<td>11</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>20,000 to 40,000 units</td>
<td>27</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>40,000 to 50,000 units</td>
<td>24</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>50,000 to 60,000 units</td>
<td>11</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>60,000 to 90,000 units</td>
<td>26</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>90,000 to 120,000 units</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>120,000 to 155,000 units</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>180,000 units</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>No serum used</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Summers (42) in a very good outline of treatment states that careful antisepsis is of the greatest importance as a prophylactic, and besides, all puncture and other kinds of wounds likely to have carried the germs of tetanus into tissues should be freely opened and all foreign bodies removed. His treatment is to first cleanse the wound using hydrogen peroxide because of the anaerobic character of the bacillus; then thoroughly antisepticize with pure carbolic acid; wash this away with 95% alcohol. All such wounds should be treated on the open, free drainage, antiseptic plan. Beside the surgical treatment the patient should be given the benefit of a prophylactic dose of 1500 units of antitoxin. After development of symptoms the wound should be given the same surgical treatment with the addition of massive doses of antitoxin, intraspinously,
intravenously and intramuscularly.

In severe cases of tetanus, Summers advocated the use of 1 c.c. of 25% magnesium sulphate per 25 pounds of body weight, injected slowly into the spinal canal to produce rapid and prolonged muscle relaxation. Calcium chloride injected intravenously will control any depressing respiratory symptoms caused by the intraspinal injection. He also believes that phenol given subcutaneously in a 2% or 3% water or oil solution is of definite value. The dose being one to one and one half grams every 24 hours, divided so as to be administered every one to three hours.

Summary of a case of tetanus presented by Henry (23). A penetrating wood splinter in the foot with a partially closed wound and incubation period of eight days followed by the outstanding symptoms of trismus and rigidity of the neck muscles, irritability, localized tonic and clonic spasms. The treatment consisted of thorough excision and drainage of the wound with 1500 units of antitoxin injected locally, 15,000 units intrathecally and 40,000 units intravenously, cloral hydrate and pantapone when indicated. The patient left the hospital completely recovered after a period of 25 days.

He concludes that:

1. Prophylactic doses of antitoxin should be given in every case of penetrating wounds, particularly with soil contamination.

2. On development of symptoms, large doses
of antitoxin should be given.

3. Intrathecal administration is preferable early in the attack. Intravenous and intramuscular are effective later.

4. Opiates should be given freely to control nerve irritability.

Moschocowitz (32) from an excellent review of the literature for the 10 year period previous to 1900 A.D. concludes that all forms of tetanus are caused by the bacillus of Nicolaier, hence diagnosis of rheumatic or idiopathic should have no room in our nosology. Second, tetanus toxins appear to have a distinct affinity for the anterior horns of the spinal cord, which may be distinctly recognized by Nissl's method of staining. Three, cerebrospinal fluid of tetanus patients is more toxic than the blood. Four, antitoxin therapy appears to have a distinct beneficial influence upon the course of tetanus. Five, with the antitoxin treatment the mortality has been reduced from 90% to 40%.

Of historical interest is a method of treatment suggested by Krokuwitz which consisted of the injection of an emulsion of brain substance. This was based on the theory that the brain substance of all animals have a definite tetanus antitoxic power and so would bind the toxin preventing it from uniting with the cells of the central nervous system of the patient. Several cases of recovery were reported. An instrument, possibly of some importance,
used in the treatment of trismus is described by Dorrance (14). He states that trismus is a condition in which the jaws cannot be opened, due to either mechanical or nervous irritation of the muscles of mastication.

To correct this he has devised an instrument known as the Dorrance-Webster jaw separator. This exerciser consists of two flat plates conforming to the dental arches, covered with heavy soft lead sheets and connected on either side to a spring which extends out to a distance of approximately six inches. These springs are further connected to each other by two rods running transversely, to stabilize the appliance and prevent any play. An additional spiral spring is placed on either. This is so constructed that it can be regulated by a nut to produce a change in the force of the springs, so that the desired pressure upon the flat plates which are placed between the opposing teeth may be applied.

After the jaws have been sufficiently separated by a suitable instrument, the patient places the flat plates in apposition by grasping the springs on either side and introducing them between the upper and lower jaws. He then gradually relaxes the pressure to the point that he can bear. He gradually opens and closes the jaws until he tires. Trismus may very rapidly be overcome by means of this appliance if used for 10 minutes each hour of the day.

My impression of this instrument, from the description given is that it would probably be of value in
those cases in which no great difficulty was encountered in opening the jaws far enough to permit insertion of the plates. This, of course, would limit its field of usefulness to a marked degree.

As to the general management of patients with tetanus Bartley (3) states that they should be isolated in a quiet, dark room and kept free from reflex irritation. Care should be taken that other patients are not infected from wound discharges as the tetanus is infectious. Patients with severe or well developed tetanus cannot be fed by mouth so nutrient enemas should be given and intravenous glucose may be used. Warm baths give many patients much relief. The bath should be started at 97 degrees F. and increased to 106 degrees to 108 degrees F. As the toxin is eliminated by the kidneys the urine should be watched and fluids forced. He recommends as sedative drugs, chloral hydrate, chloretohe, morphine sulphate, magnesium sulphate intraspinally, one c.c. of 25% solution per kilogram of body weight, using calcium chloride to combat respiratory paralysis if such occurs. Magnesium sulphate may also be given subcutaneously in doses of 12 to 16 c.c. of a 25% solution three times a day.

In a discussion of Dr. Gessner's paper (13), Dr. S. J. Meltzer of New York reviewed the several experiments in which magnesium sulphate was used to relax trismus and opisthotonos in dogs. He strongly advocated its use
In cases of tetanus to control spasms stating that it is the best palliative remedy we have.

Light chloroform anaesthesia may be used for spinal injections if opisthotonus is present or in case of frequent spasms.

Prognosis and Mortality.

Robertson (41) states that the most frequent causes of death are asphyxia, exhaustion and cardiac failure and that the mortality rate depends greatly upon the length of the incubation period. He gives the following table.

<table>
<thead>
<tr>
<th>Incubation period</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>of 10 days or less</td>
<td>94</td>
<td>94.7%</td>
</tr>
<tr>
<td>&quot; over 10 days</td>
<td>57</td>
<td>70.8%</td>
</tr>
<tr>
<td>&quot; Unknown</td>
<td>48</td>
<td>58.3%</td>
</tr>
</tbody>
</table>

In graves (20) report of 217 cases he found that the mortality rate in cases where the wound occurred in the upper extremity was 67.6% while those of the lower extremity had a mortality of 55%.

He gives the following table of types of wounds and mortality in 157 cases.
<p>|</p>
<table>
<thead>
<tr>
<th>Type of Wound</th>
<th>Number of Cases</th>
<th>Mortality %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Splinter</td>
<td>50</td>
<td>46</td>
</tr>
<tr>
<td>Nail</td>
<td>52</td>
<td>67.3</td>
</tr>
<tr>
<td>Tetanus neonatorium</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>Puncture wounds (excluding nails)</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>Blank Cartridges</td>
<td>24</td>
<td>83.3</td>
</tr>
<tr>
<td>Abortions</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Postpartal</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Morphine addicts</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>Compound fractures</td>
<td>2</td>
<td>56</td>
</tr>
<tr>
<td>Ulcer</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Gangrene of toe</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Amputation of stump</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Extraction of teeth</td>
<td>3</td>
<td>33.3</td>
</tr>
<tr>
<td>Gunshot wounds</td>
<td>3</td>
<td>100</td>
</tr>
</tbody>
</table>

According to Calvin and Goldberg (7) "the most important factor in the prognosis of tetanus is the length of the incubation period. Specific therapy has not altered this fact. An incubation period under 10 days has a mortality of around 84% whereas an incubation period between fourteen and twenty-one days has a mortality of 25%. The duration of the disease after it is established is of extreme importance in the prognosis. Hippocrates stated that persons seized with tetanus die within four days or if they pass these they recover."
Anders gives the following figures in his 1,246 collected cases: "If the duration of the disease was 5 days or less the mortality was 81%; between five and ten days, 63%; between ten and fifteen days, 30% and over fifteen days 8%.

Gessner (19) found in a study of 368 cases of tetanus that during the period from 1840 to 1889 when there was no antitoxin that the death rate was 79.1% while for the period from 1890 to 1917 the mortality was 70.1%.

He found 12 patients in his series who had prophylactic injections of antitoxin who developed the disease and four of these died. Two of these patients should have had repeated injections of antitoxin as they had suppurating wounds.

He states that he has never known of a case of death from anaphylaxis tho Braunlick (6) reporting a case of anaphylaxis following the injection of 1500 units of tetanus antitoxin, questions the advisability of giving tetanus antitoxin in trivial injuries.

Bartley (3) states that the prognosis in local tetanus is usually good. However, diaphragmatic and laryngeal involvements give a bad prognosis as do also a high temperature and pulse rate. The development of pathological conditions in wounds demanding radical surgery increases the severity of the disease. He states that in reviewing the statistics of the Great War and of some of the previous
wars occurring before the discovery of tetanus in 1883 and subsequently, of the antitoxin of von Behring, one is struck by the lack of difference in the prognosis and incidence of tetanus. It is only in 1916 and 1917 that an appreciable lowering of the incidence and mortality has been accomplished by rigid prophylaxis and massive doses of serum given on early diagnosis.

He gives a table from a report of Surgeon-General Sir David Bruce of the English War Office Committee for the study of tetanus which accurately presents the mortality of a representative number of cases.

**TABLE 9**

<table>
<thead>
<tr>
<th>Years</th>
<th>No. of Cases</th>
<th>Recovered</th>
<th>Died</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1914-15</td>
<td>231</td>
<td>98</td>
<td>133</td>
<td>57.6%</td>
</tr>
<tr>
<td>1915-16</td>
<td>195</td>
<td>99</td>
<td>96</td>
<td>49.2%</td>
</tr>
<tr>
<td>Aug.-Oct. 1916</td>
<td>200</td>
<td>127</td>
<td>73</td>
<td>36.5%</td>
</tr>
<tr>
<td>Oct.-Dec. 1916</td>
<td>100</td>
<td>69</td>
<td>31</td>
<td>31.0%</td>
</tr>
<tr>
<td>Dec.1916 to Mar. 1917</td>
<td>100</td>
<td>81</td>
<td>19</td>
<td>19.0%</td>
</tr>
</tbody>
</table>

These were cases treated in "Home Hospitals".

In the first year of the war 47 per cent of the cases had short incubation periods; in the last reports this had fallen to 10%. Also the cases with long incubation periods had risen from 6.4% to 69%. 
CASE REPORTS

Case 1

L. W. aged 6 years, entered hospital June 21, 1926. Some time during previous week the patient had cut his foot on a bone laying in the yard. This was not noticed until Thursday, June 6, 1926, three days ago. At this time a muscular stiffness also was noticed and the child was not feeling well. During the evening of June 20, 1926 he had five convulsions before being brought to the hospital.

On entrance temperature was 102.4 degrees rectally, pulse 108, respirations 36. No laboratory work was done as quiet and no stimulation was considered the best policy.

Examination showed a colored boy of stated age, lying in opisthotonus. Breathing rapidly and stertorously. Convulsions before antitetanus serum was given, were initiated by a generalized stiffening of the muscles. The typical risus sardonicus was present. Diagnosis of tetanus was made from the type of convulsions and the definite history of a dirty stab wound.

Eyes were partially open. Mouth was open except when in convolution, and breathing was through the mouth. Breathing was partly obstructed by contraction of throat muscles.

On inspection of the right foot a longitudinal cut was located in about the middle of the plantar surface about one half inch long and apparently one half to one inch
Case 1 (contd.)

Deep.

Progress and treatment as follows: June 21, 1926
Diagnosis of tetanus confirmed by staff doctor who recommended wider incision of local lesion with insertion of drain and application of A. B. C. dressing.

Soon after being admitted the patient was given 10,000 units of tetanus antitoxin subcutaneously. The wound was opened by initial incision, washed out with peroxide and soaked with iodine. Within the next three hours 10,000 units of antitoxin were given intraspinally and 1,500 units were injected at the site of injury. Morphine gr. 1/8 given to quiet. Later choral and bromides per rectum.

In evening patient's condition considered moribund and treatment discontinued. The following day, first day after entrance, patient died in a generalized tonic convulsion.

Discussion: This case again serves to illustrate the fact that prognosis is bad in cases having a short incubation period. We might criticize the treatment in that the injections were relatively small considering the severity of the symptoms although it is doubtful whether larger doses would have been of any avail as the disease had progressed too far for any treatment to have been of much value.
Case 2

B. G. D. a girl aged 3 years was admitted to the University Hospital August 6, 1926. Two days previously the child had seemed irritable and complained of headache. The following day the Mother noticed stiffness of muscles and took her to a doctor. It was thought to be a lung involvement.

August 6, 1926 another doctor was seen and the child hurried to the hospital. During previous nite the child cried out in her sleep several times.

On admission the temperature was 100 degrees rectally, pulse 120, respirations 24. White blood count 16,400. Urine negative.

Examination revealed a well nourished girl, about 3 years of age. All muscles were stiff especially those of the back, there were no involvement of the muscles of mastication. Reflexes normal - Kernig's sign negative. Toe nail of second toe of right foot had come off due to an injury received ten days before entrance. No apparent infection. Her progress was as follows:

August 6, 1926 Staff physician felt that a diagnosis of meningismus could be made with something developing in the right chest.

August 7, 1926 spinal puncture done. Fluid clear with a cell count of 9. Flexion of long muscles brought on a severe generalized convolution during which patient became very cyanotic. Definite physical findings of pneumonia in right chest.
Case 2 (contd.)

In evening there seemed to be very little change. pulse staying from 130 to 140. R rigidity seemed about the same.

August 9, 1926 condition did not seem good in the morning. She perspired profusely and about 8 o'clock she began having convulsions, in which there were tonic contractions of all muscles and jaws would become set, seriously embarrassing her respirations. These convulsions kept recurring and there was a gradual filling up in the bronchi. Death occurred at nine twenty-five a.m.

Tetanus was suggested as being the most probable cause of death.

A complete autopsy was done and no apparent cause of death could be found.

The only treatment was phenacetin, salol and caffeine every three hours.

This is evidently a case having a short incubation period and demonstrates the previously made statements that death occurs more rapidly and more surely in such cases. The question must be asked, "why wasn't a diagnosis of tetanus made earlier considering the history of injury and the physical findings?"
Case 3

C. A., aged 9, was admitted to the hospital April 30, 1929. On April 25, 1929 at noon he stepped on a rusty nail, which punctured his right foot. That evening it was quite sore, so much so that he couldn't bear weight on it, and hasn't been able to since. The following day about eleven a.m. he came to his Mother and complained of soreness in his neck and back. She noticed that he didn't talk as plainly as usual. Examination revealed that he couldn't open his mouth more than about one-half inch. This condition became progressively worse and the evening of April 30, 1929 they decided to see a doctor who brought him to the hospital.

On admission, temperature was 99.8 degrees rectally, pulse 116, respirations 26. White blood count 24,200.

Examination showed a boy of about stated age lying in bed in a position of extreme extension, head back, neck rigid, back bowed, extremities flexed, mandible fixed, abdomen board-like and the right foot showed a nail wound about one-half inch deep on the ball of the foot.

Progress and treatment as follows:

April 30, 1929, wound incised and 11,500 units of tetanus antitoxin given, 10,000 intravenously and 1,500 subcutaneously. Morphine and luminal given to control convulsions.

20,000 units tetanus antitoxin given intracisternally.
Case 3 (contd.)

1,500 units subcutaneously.

1,500 units intramuscularly.

5 c.c. of magnesium sulphate 5% given intramuscularly without noticeable effect.

Chloral hydrate and bromides given.

Patient died at three thirty-five p.m.

Autopsy findings:

1. Abscessed mediastinal glands.
2. Abscess at base of left lung.
3. Infected wound of right foot.

This is an interesting case in that death occurred but six days after injury. It seems that the complicating lung infection must be given strong consideration as playing an important part in the fulminating character of the condition.

Case 4.

Mr. R. N., aged 17, was admitted to the University Hospital October 30, 1931, complaining of backache and rigidity of the masseter muscles. He gave the following history. On October 16, 1931, the patient stepped on a nail which entered the left foot on the lateral surface, going in about one-half inch. This wound healed without a doctor's care. On October 25, 1931, the patient complained of backache and inability to open his mouth. He worked Monday and Tuesday with continuation of symptoms. Friday patient went to a doctor who gave him tetanus antitoxin and sent
Case 4 (contd.)

him to the hospital.

On admission temperature was 100 degrees F., pulse 84, respiration 20, white blood count 15,200. Physical examination showed marked rigidity of the abdominal muscles and spasticity of the jaws and extremities.

The diagnosis of tetanus was made.

On November 1, 1931, the patient showed definite signs of trismus, abdominal rigidity and generalized spasticity.

Antitoxin given as follows:

1. 15,000 units intrathecally.
2. 10,000 " intravenously.
3. 5,000 " in site of local lesion after excision (foot).

November 2, 1931 patient symptomatically improved.

Antitoxin given:

1. 15,000 units intrathecally.
2. 10,000 " intravenously
3. 5,000 " in hypothenor space right hand after excision of area (local lesion at this site).

November 3, 1931 Less rigidity today.

Antitoxin given:

1. 10,000 units intravenously at eleven a.m.
2. 10,000 " intramuscularly at one p.m.
3. 10,000 " " six-thirty p.m.
Case 4 (contd.)

November 4, 1931, Symptomatically much improved. Antitoxin given:

1. 10,000 units intravenously two p.m.
2. 10,000 " intramuscularly eight-thirty p.m.

Chill and temperature to 104.2 degrees following intravenous injection.

Temperature down to 100 degrees F. by twelve o'clock mid-night.

November 5, 1931, Improved. Mentally more acute. Lower abdomen softening.

1. 10,000 units intramuscularly at one-thirty p.m.

November 6, 1931, Much improved.

1. 10,000 units antitoxin intramuscularly.

November 10, 1931, Only complaint is stiffness of knees.

Abdomen still moderately rigid.

November 14, 1931, Dismissed - complete recovery.

Total serum:

Intraspinal 30,000 units.
Intravenous 40,000 units.
intramuscular 52,500 units.
Total 123,500 units.

Morphine, chloral hydrate and bromides given as necessary to control muscle spasms.
Case 5

G. V. age 19, entered Methodist Episcopal Hospital January 19, 1932, complaining of aching in jaws, difficulty in opening his mouth, pain in back and restlessness. History was that on January 15, 1932 the patient did not feel entirely well, but worked all day. He only complained of an aching in his jaws, which he attributed to "cutting his wisdom teeth". The following day he also felt ill but was able to go to town with his family. It was on this day that he noticed some difficulty in opening his mouth wide. January 18, 1932 he noticed soreness and pain in his back and also some soreness in his chest. The following day his physician recommended that he be brought to the hospital. He gave no history of any recent injury or infection. Last July he had an infected thumb, with no injury primarily. The patient was very restless, especially at night.

On admission his temperature was 100.2 rectally, pulse 82 and respirations 32. White blood count 8,450, spinal fluid count 10. Examination showed a young man of about stated age, lying in bed, very restless and having profuse diaphoresis. Risus sardonicus evident. Mouth could be opened only about 1/4 inch. Neck quite rigid and held in extension.

Abdominal muscles rigid. General rigidity of extremities.

Progress and treatment.

January 19, 1932 patient given 10,000 units
antitoxin intratheca1ly and 10,000 units intramuscularly on entrance.

Chloral hydrate grains 35 p.r.n. for rest.

avertin as a sedative and intravenous glucose.


January 22, 1932, patient died respiratory failure.

This is an unusual case in that there was a reaction to the antitoxin given intratheca1ly resulting in a rapid rise in the spinal fluid count. No doubt more vigorous antitoxin therapy should have been instituted.

Case 6

Mr. P. H. aged 15, entered the University Hospital July 21, 1925 complaining of contraction of jaw muscles, inability to eat and pain in the back. The patient gave a history of having developed blisters on the heels and big toes, due to wearing shoes that were too tight, three weeks before entrance. He disregarded the sores, removed the shoes and went down the railroad tracks with other boys to go swimming. Three days before entrance his jaw muscles became
sore and stiffened. Parents considered the condition lightly believing it to be due to mumps. Jaw muscles gradually stiffened, face became swollen until on the third day the jaws were set and patient could not open his mouth to take nourishment. The day before entrance the patient complained of soreness and stiffness of the muscles of the neck. These contractures of the neck muscles were noted at intervals last night. The parents still believed that the condition was probably caused by wrestling or by excessive smoking, disregarding any relationship to troublesome sores that had persisted on heels.

Physical examination showed the patient to be laying flat on his face in bed with his head drawn back, spine arched and feet extended backward, a typical opisthotonus position. Touching the body produced no results until the muscles of the neck and chest were felt. This produced a muffled cry. The jaws were set, and trapezius muscles were tense. On admission the temperature was 99 degrees, pulse 92 and respirations 24.

Progress and Treatment.

July 21, 1925 a spinal puncture showed the spinal fluid to be clear, pressure 8 m.m. Hg. with a cell count of 4.

10,000 units of antitoxin given intravenously.

10,000 units of antitoxin given intrathecally.

Chloral hydrate gr. 15 and sodium bromide gr. 30
given rectally every 3 hours.

No immediate relief was given by any medication.

July 22, 1925, tonic convulsions, trismus and opisthotanuss continued throughout the night. Pulse weaker, patient cyanotic. Apparently has spasm of the respiratory muscles.

10,000 units of antitoxin given intravenously.

Patient died a respiratory death at 10 a.m.

Post mortem examination was negative.

About the only comment we can make on this case is that the parents should have consulted a physician earlier so that treatment could have been instigated before the patient had advanced to the stage of cardiac and respiratory collapse.
CONCLUSIONS

1. The causative agent is the Bacillus tetani.

2. An early diagnosis should be made on history, symptoms and physical findings.

3. The tetanus toxin reaches the central nervous system by passing along the motor nerves and by passing into the blood stream through the lymphatics.

4. Treatment should consist of massive doses of tetanus antitoxin plus sedatives and supportive treatment. Antitoxin should be given intrathecally and intravenously. Phenol may possibly be of value.

5. Prophylaxis should consist of early injection of 1,500 units of tetanus antitoxin plus proper surgical treatment of the local wound and should be used particularly in contaminated wounds.

6. The incidence and mortality have been decreased by present day rigid prophylaxis and antitoxin treatment.

7. Prognosis may be based upon length of incubation period, severity of symptoms and presence or absence of complications.
BIBLIOGRAPHY


11. Curling, T. B., A Treatise on Tetanus, 1834, p. 11.

12. Davenport, H. K., Ranson, S. W. and Stevens, E., Microscopic changes of muscle in myostatic contracture caused by tetanus toxin, Arch. Path. 7:978-992, June 1929.


31. Moir, J. C., Case of tetanus combined with gas gangrene, Brit. m. J. 2:748, October 27, 1928.
34. Nicoll, M., Survey of our present knowledge of tetanus and its treatment, New York State J. Med. 26:379-383, May 1, 1926.
37. Ranson, D. W., Local tetanus; study of muscle tonus and contracture, Arch. Neurol. and Psychiat. 20:663-701, October 1928.
38. Ranson, S. and Ranson, S. W., Recovery from myostatic
contracture caused by tetanus toxin, Arch. Path. 7: 949-954, June 1929.


47. Wilmoth, L. H., Mistaken diagnosis of appendicitis, Colorado Med. 27:143-144 April 1930.
