

Tetanus: Evaluation of Treatment at Charity Hospital, New Orleans, Louisiana *

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"INDEED, I am inclined to believe that if the patient be placed in a suitable situation, remote from all excitement, with a proper allowance of food and drink, the recovery will be perhaps more frequent."—Hester—1846.

The tragedy of tetanus is not its dreadful symptoms nor high mortality, but the fact that it could have been eradicated within the past 25 years by a vigorous program of immunization with tetanus toxoid. Yet the disease still occurs, with frequency in some areas, and remains a challenge to therapy.

It is often assumed that new treatment is better treatment because it is different. Nowhere is this assumption more in evidence than in the therapy of tetanus, for within the past 100 years new therapeutic agents, one after another, have been applied to this disease with apparent good results, implying that the mortality has been reduced.

Charity Hospital in New Orleans has been identified with the treatment of tetanus for more than a century. Serving an area to which tetanus is endemic, a large experience with the disease has accumulated here over the years. The first report from Charity Hospital¹⁴ covers the period from 1840 to 1916, although records for the first ten years were incomplete. This series of cases included two periods in the treatment of tetanus, namely, the pre-serum epoch from

1840 to 1889, and the period in which serum was first employed, from 1890 to 1915. Subsequent reports from this institution^{3, 4, 7, 9, 15-17, 28} appearing at five to ten year intervals have served to keep the statistical data relating to tetanus current and to introduce new therapeutic measures. With this long and extensive experience as a background it seemed timely to review the cases of tetanus observed during the period 1943 to 1956 and compare the results with those of previous years. The experience of this period of 14 years is particularly suited to analysis because the cases fall naturally into two categories covering seven years each. The first period is from 1943 to 1949, when treatment was essentially the same as that employed for many years previously. In the second seven year period, from 1950 to 1956, additional therapeutic measures consisting of antibiotics, tracheostomy, muscle relaxing agents and gastrostomy were used. This report is an attempt to evaluate the effects of these newer therapeutic measures in terms of mortality and morbidity and to compare the results with those reported from Charity Hospital since 1906.

ANALYSIS OF CASES

Incidence

There were 558 cases of tetanus admitted to Charity Hospital from January 1, 1943, through December 31, 1956. The yearly incidence varied from 0.3 to 1.1 cases per

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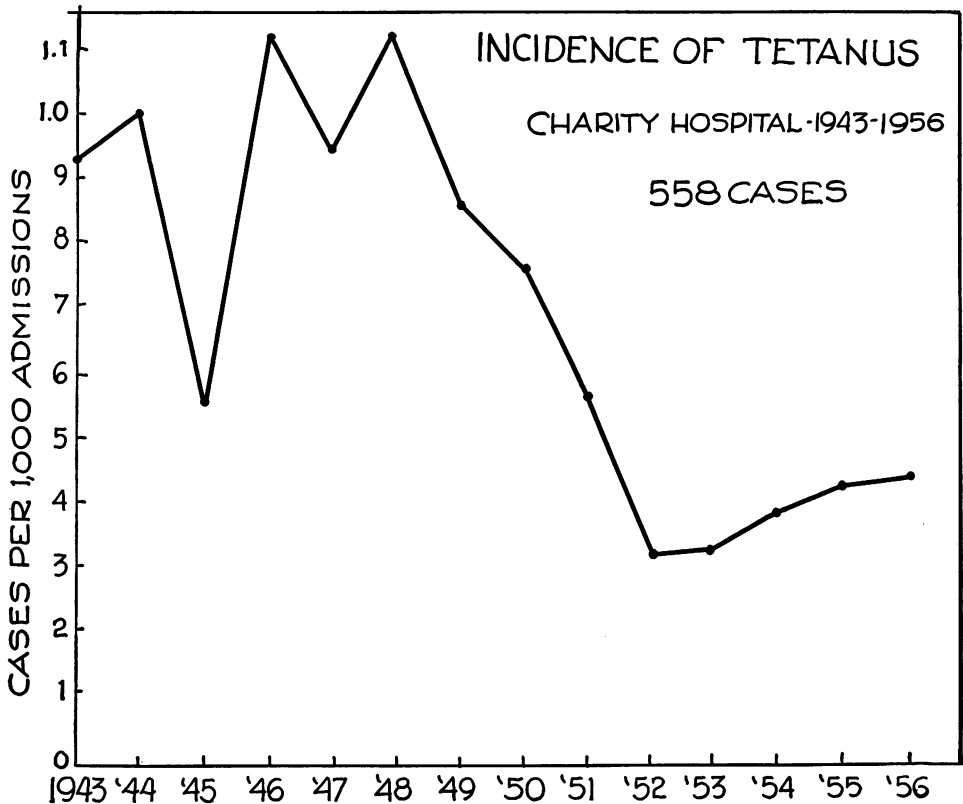


CHART I.

1,000 hospital admissions (Chart I). An average of 39 cases were admitted each year. This approximates the average annual incidence in each of the previous series reported from this institution since 1916. On the basis of hospital admission, however, the yearly incidence has progressively decreased (Chart II). This, no doubt, is a result of many factors, not the least of which are the more frequent prophylactic use of tetanus antitoxin following injury and the programs of active immunization with toxoid carried out in the Armed Forces and in pre-school children.

The average age of patients with tetanus varied from 22 years to 39 years (Chart III). A comparison of the incidence since 1906 among children 12 years of age and under, and patients above the age of 12 reveals a disproportionate decrease in the

younger age group (Chart IV). This may be accounted for in part by the increasing use of diphtheria-pertussis-tetanus vaccines in pre-school children since 1940.

Until recently males have been affected by tetanus more frequently than females in a ratio of two to one. Since 1943, however, there has been a decrease in the incidence in males so that the disease occurred with equal frequency in both sexes during the period 1950-1956 (Chart V). This trend is to be expected in view of the mass immunization program carried out by the Armed Forces since 1940 primarily affecting young adult males. An increased incidence of tetanus among negroes has been noticed in each of the reports from Charity Hospital and is out of proportion to the ratio of negroes to whites in the patient population here (Chart VI).

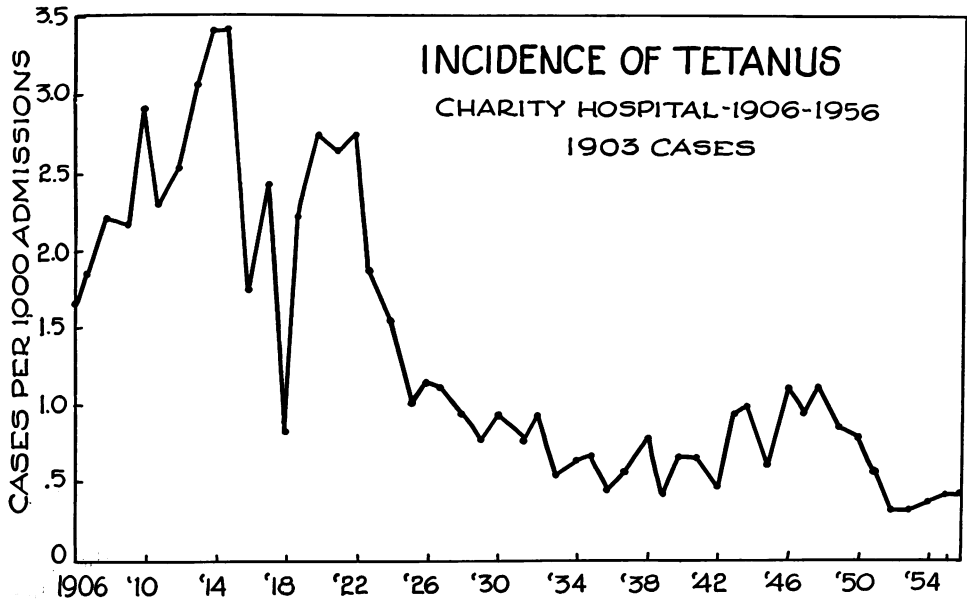


CHART II.

SITE AND TYPE OF INJURY

The sites of injury in decreasing order of frequency are as follows: foot, leg, upper extremity, scalp, face, and uterus. This distribution is similar to that noted in previous reports. A majority of injuries were the result of puncture wounds; other injuries were lacerations, scratches, abrasions, burns, compound fractures, and gangrene of the extremities. In some instances injury had been so trivial, apparently, that it was forgotten by the patient and a definite portal of entry was not determined.

PROPHYLAXIS

Among the 558 cases, one patient had received a complete immunizing course of tetanus toxoid and another had received an incomplete course consisting of the initial dose only. Neither of these was given a booster dose of toxoid at the time of injury. In one case, tetanus antitoxin had been administered in a dose of 1,500 units at the time of injury, 14 days before the develop-

ment of tetanus. There were two patients who were treated for open wounds in the emergency room of Charity Hospital, did not receive tetanus antitoxin because of the nature of the wound, and subsequently developed tetanus.

INCUBATION PERIOD

The observation that a short interval between injury and onset of tetanus is usually followed by severe symptoms and high mortality has been repeatedly confirmed. Thus, in this series the incubation period for survivors was almost 40 per cent longer than for those who succumbed to the disease (Chart VII). However, there were survivors with an incubation period of only four days and death occurred in patients with incubation periods of 20 days or more.

TREATMENT

The treatment of tetanus varied little in the period from 1906 through 1949. The



CHART III.

essentials of treatment consisted in care of the wound, administration of tetanus antitoxin and sedation. Early in this period, wounds were treated by incision and drainage when necessary and, in a few instances, by cauterization with carbolic acid. Debridement or total excision of the wound was not usually performed, however, and not until 1925-1926 did careful attention to the site of injury become routine. Since that time cauterization, debridement, and total excision have been employed prefer-

entially at one time or another. Current therapy calls for excision when feasible; when not, the wound is opened widely and debrided if necessary.

The amount and route of administration of tetanus antitoxin have varied from year to year. In a report covering the period from 1906 to 1923, Graffagnino and Davidson¹⁶ found that 273 of 627 cases received tetanus antitoxin. Of this group more than half received from 1,000 to 5,000 units, primarily by the subcutaneous route, and most

RELATIVE INCIDENCE OF TETANUS

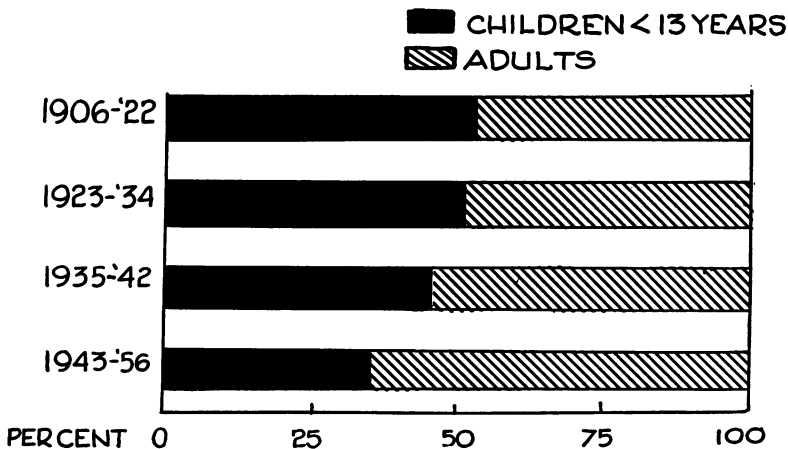


CHART IV.

SEX INCIDENCE

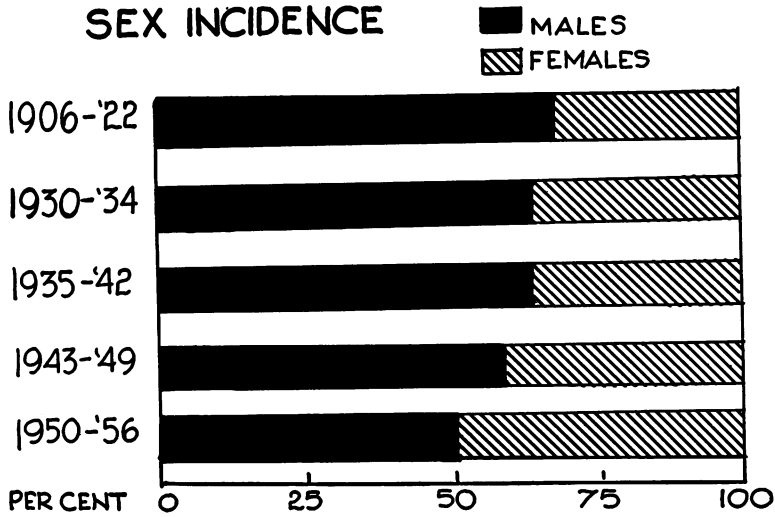


CHART V.

of the remaining cases received between 5,000 and 50,000 units administered in a variety of ways (intramuscular, subcutaneous, intravenous, intraneural, and intrathecal routes). Only one patient received more than 100,000 units of tetanus anti-

toxin. These authors observed that the death rate for patients receiving antitoxin was 66.6 per cent, and for cases treated without antitoxin 68.6 per cent. Furthermore, there were as many deaths and recoveries when only small units (500 to

RACE INCIDENCE



CHART VI.

INCUBATION PERIOD

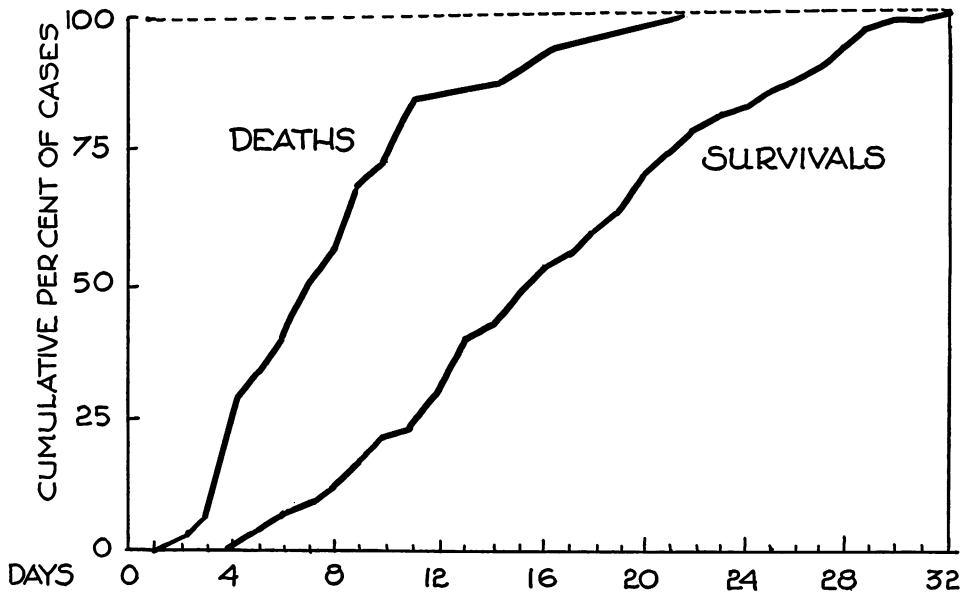


CHART VII.

1,000) of antitoxin were given as when larger amounts were administered.

After 1923, relatively large doses of serum were administered averaging 48,000 units total dose for children and 52,400 for adults.¹⁷ Since then the amount of tetanus antitoxin administered has been gradually increased. In 1934 Boyce and McFetridge⁷ recommended the administration of 20,000 units intravenously and 20,000 units intramuscularly with an additional 2,000 to 5,000 units injected locally into the wound. Vinard,²⁸ in 1944, stated that during the preceding three or four years most of the tetanus patients at Charity Hospital had received 40,000 to 60,000 units of tetanus antitoxin intravenously and an equal amount intramuscularly on admission. Subsequent doses of antitoxin ranging from 10,000 to 40,000 units daily were given for one to eight days. Currently, tetanus antitoxin is administered to the patient immediately after admission in a dose of 100,000 units divided equally between the intravenous

and intramuscular routes. Subsequent daily administration of 5,000 to 10,000 units of tetanus antitoxin for six to eight days was routinely practiced until about 1952 when it was discontinued.

In the initial report on tetanus at Charity Hospital by Gessner and Adiger,¹⁴ Chloretone® (tri-chlor-tertiary butyl alcohol) and magnesium sulphate were the principal agents used for sedation and muscle relaxation. Other agents employed for purposes of sedation were morphia, bromide, Amytal®, chloral hydrate, and Luminal®. In 1932, tribromoethanol (Avertin®) was introduced for the control of muscle spasm.⁷ It was administered in an initial dose of 80 to 100 mg./Kg. of body weight with somewhat smaller subsequent doses. This agent together with the barbiturates was employed routinely until 1947 for purposes of sedation and for the control of convulsions. At this time, curare was used in the treatment of five cases of tetanus and the results reported by Adriani and Ochsner.³ On the

basis of this limited experience it was felt that the use of curare in the treatment of tetanus was hazardous. At about the same time, intravenous procaine hydrochloride was utilized to alleviate pain and control muscle spasm.⁹ It was administered in a 0.1 per cent solution and the rate of administration was adjusted to relieve symptoms without inducing hypotension. In order to prevent the central stimulation accompanying intravenous administration of procaine, Avertin® was given simultaneously. In 1949, a synthetic curare-like drug, mephenesin (3-ortho-toloxyl-1,2-propanediol) or Tolserol®, was first employed as an anticonvulsant in the treatment of tetanus at Charity Hospital. In a review of experience with procaine, barbiturates, Avertin®, curare, and mephenesin, Godman and Adriani,¹⁵ in 1949, concluded that the combination of phenobarbital and Tolserol® was exceedingly satisfactory in the control of muscular rigidity and spasm in cases of moderately severe tetanus. In 1954, Adriani and Kerr⁴ reported a series of 100 cases of tetanus observed between February 1951 and August 1954. Sedation and control of convulsions were maintained with mephenesin and phenobarbital. The results of the use of chlorpromazine were also reported and it was concluded that this drug was a valuable adjunct which enhanced the effect of the other drugs without producing circulatory or respiratory depression. Currently, sedative and anticonvulsive therapy consists of mephenesin, barbiturates, and chlorpromazine.

It was observed in 1949, that there was a high incidence of respiratory complications among the patients who succumbed to tetanus. This was not an original observation, for Hester¹⁸ had reached a similar conclusion in 1846, on the basis of experience at Charity Hospital. Indeed, he suggested tracheotomy or bronchotomy as a preventive measure. More recently, tracheostomy was performed in severe cases of

tetanus complicated by bronchopneumonia and the favorable outcome suggested that maintenance of an open airway and frequent removal of tracheal and bronchial secretions were at least partially responsible. Thus, tracheostomy became almost a routine measure in the treatment of tetanus. In a report in 1950,⁹ the authors stated: "Although some patients with tetanus still will succumb, most will be saved by the prompt performance of tracheostomy because death in tetanus is due largely to pulmonary complications which can be prevented by maintenance of an adequate airway."

Sulfadiazine was added to the treatment of tetanus about 1941. In 1948, this drug was replaced by penicillin for selected cases in a dose of 300,000 to 400,000 units daily, and in 1950, the routine administration of penicillin in large doses was begun. These chemotherapeutic and antibiotic agents were administered for whatever direct effect on the *Clostridium tetani* they might have, but mainly as prophylaxis against pulmonary infections.

Although tube feeding had been utilized for about 20 years, the occurrence of fatal aspiration of gastric contents in several cases resulted in the adoption of gastrostomy in 1953, as a routine measure in the treatment of severe tetanus.

Thus, the essentials of the therapy of tetanus, namely, removal of the source of toxin, neutralization of circulating toxin and control of muscle spasm, have remained the same for over 50 years. To be sure, the methods for accomplishing these objectives have varied but the principles of therapy have generally been the same. During the past seven years, however, some newer measures, consisting of tracheostomy, antibiotics, muscle relaxants and gastrostomy have been employed in addition to the routine treatment described above. These newer adjuncts represent the only attempt in more than half a century to attack directly the complications of tetanus.

CASE FATALITY RATES

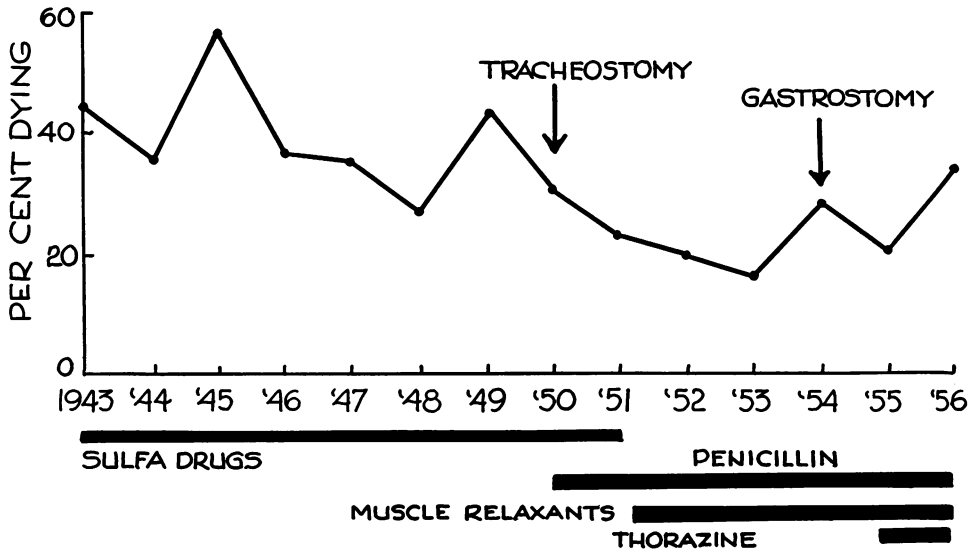


CHART VIII.

RESULTS

Among the 558 cases of tetanus treated from 1943 to 1956, there were 171 deaths, a mortality rate of 30.6 per cent (Chart VIII). Comparison of the two seven year

periods covered by this series reveals a mortality rate for the period 1943 to 1949, of 36.8 per cent and for the period 1950 to 1956, of 24.4 per cent. However, when the experience of these 14 years is contrasted

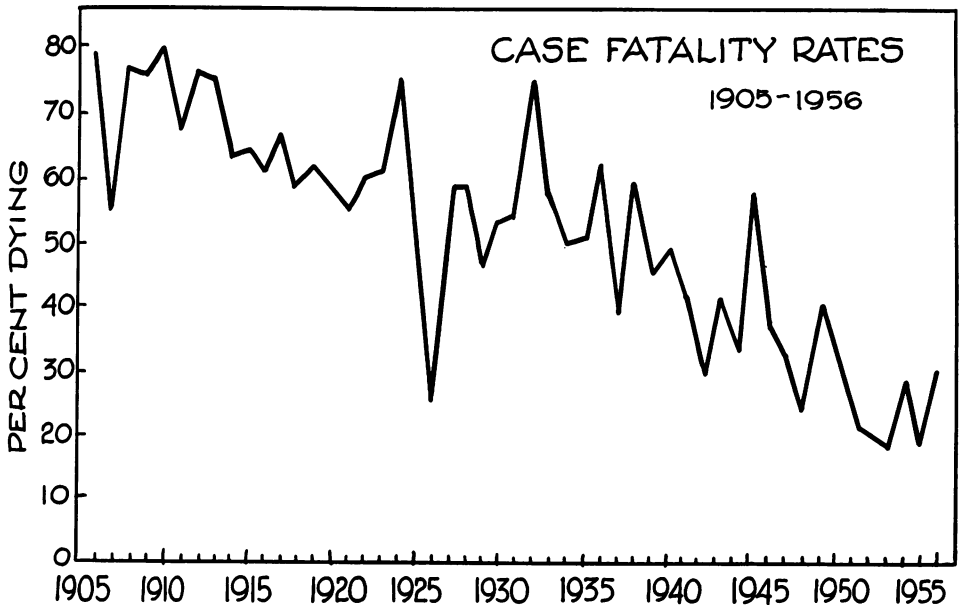


CHART IX.

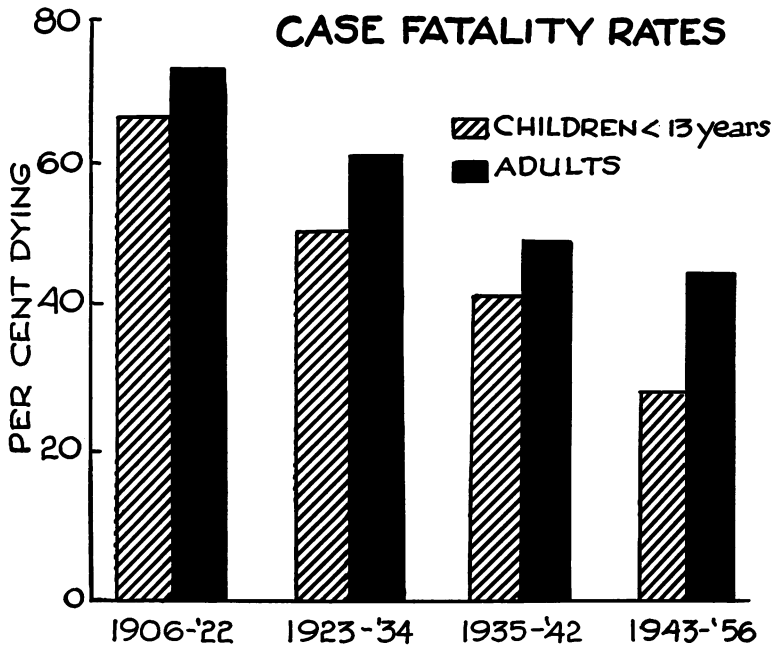


CHART X.

with that of the previous 36 years (1906-1942) it becomes apparent that the recent decrease in mortality from tetanus is simply a continuation of a trend which began 50 years ago (Chart IX). A lower mortality rate in children was also observed in this series (Chart X) as well as those reported by Graffagnino and Davidson,¹⁶ Graves,¹⁷ Boyce and McFetridge,¹⁷ and Vinnard.²³ In general, the results of treatment appeared to be better for patients below the age of 40. In fact, the mortality rate for patients in the fifth, sixth, seventh and eighth decades was about 50 per cent during the period from 1943 to 1949, and although this mortality was reduced during the second seven year period, tetanus still was most hazardous during these later decades.

Among those dying of the disease, 75 per cent succumbed within four days after admission to the hospital and after seven days the mortality was extremely low (Chart XI). There was no significant difference in

morbidity in terms of hospital days for the two seven year periods. Thus, in 1943-1949, the average period of hospitalization was 25 days, while for 1950-1956, it was 23 days.

The causes of deaths were essentially the same for the two periods covered by this series (Chart XII). Respiratory complication were responsible for 81 per cent of the deaths from 1943-1949, and for 70 per cent from 1950-1956. Of the three instances of cardiac arrest, two occurred while tracheostomy was being performed.

The relationship of incubation period to survival was essentially the same for the two periods. Thus, for the first seven years the average incubation period for 199 survivors was 14.7 days, and for 116 patients dying of tetanus, 9.2 days. Among the 161 survivors during the second seven years of this series, the average incubation period was 13 days, and among those dying of the disease, 8.2 days. This factor is of questionable prognostic value, however, for of the fatal cases, 15 had incubation periods of

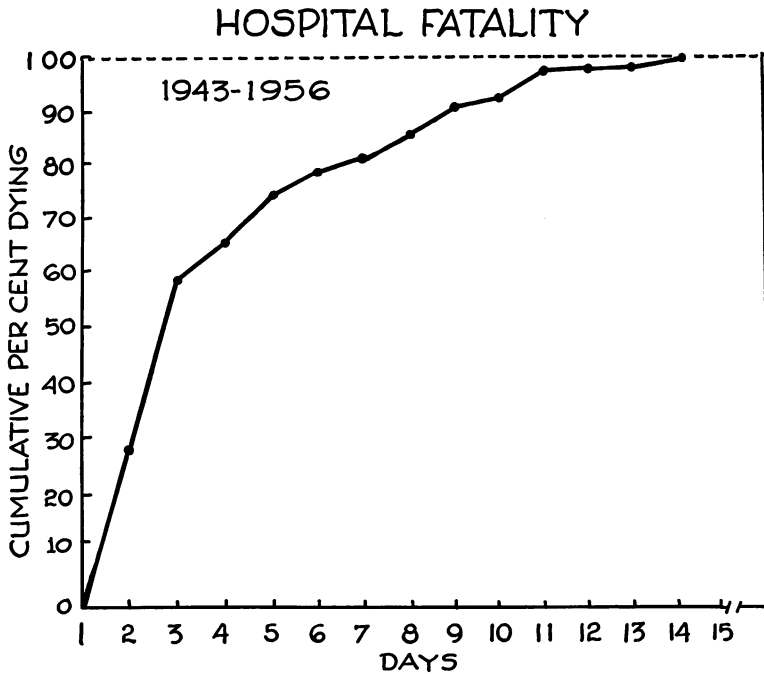


CHART XI.

14 days and over, and about the same number of survivors had incubation periods of six days and less.

There was no indication that the site of injury had any particular influence on the outcome of the disease since the incidence of the various sites of injury were essentially the same for survivors and those dying of the disease.

DISCUSSION

An understanding of the etiologic agent and the physio-pathology of a disease is essential to effective treatment. Although the discovery of the causative organism of tetanus was reported in 1889,^{19, 20} and the characteristics of the organism and its exotoxins have been studied extensively,⁵ the pathogenesis of the disease is still not entirely clear. This, together with the uncontrolled variables which alter the course of clinical tetanus, makes it difficult if not impossible to accurately assess the effectiveness of various forms of therapy. This

is particularly true when one attempts to evaluate the results of treatment in small series.^{6, 8-11, 21} For instance, Forbes and Auld¹³ reported 15 consecutive cases treated successfully with central depressants. They were of the opinion that these agents were highly effective in the management of the patient with tetanus. In 1949, there were 52 cases of tetanus observed at Charity Hospital and of these, 19 consecutive patients survived. Yet, the mortality for that year was 42 per cent. It is apparent that the treatment employed in the 19 consecutive survivors might have been credited with the successful outcome. The fact is, however, that cases prior and subsequent to these 19 were treated essentially in the same fashion but with singularly poor results.

Although the prophylactic value of tetanus antitoxin and tetanus toxoid has been established beyond question, the therapeutic value of the former is less evident.¹² In animal experiments, Sherrington²² reported that antitoxin was therapeutically

effective. Clinical experience likewise suggests that antitoxin is efficacious in the treatment of tetanus, but as observed by Abel and Chalian¹ tetanus antitoxin does not mitigate or abolish existing and clearly evident symptoms and since serum fails to save life, it cannot be thought of as having a specific curative action. These authors are of the opinion, however, that tetanus antitoxin should be employed in all cases and at the earliest possible moment in order to save as many patients as possible. A study of the mortality rate from tetanus at Charity Hospital clearly indicates a decrease during the past 50 years and at a fairly constant rate. From 1906 to 1923, an increasing number of patients received tetanus antitoxin therapeutically in doses ranging from 1,500 to 5,000 units in the majority of cases, although in a few instances as much as 50,000 units of antitetanic serum was administered. All cases were treated with tetanus antitoxin from 1923 to 1935, and in amounts which were increased yearly to a routine dosage of 40,000 to 50,000 units in 1935. From 1935 to 1956, the amount of tetanus antitoxin remained constant at a dose of 80,000 to 100,000 units. On the basis of this experience, therefore, it might be assumed that the increasing use of tetanus antitoxin in progressively larger doses from 1906 to 1935, was in some measure responsible for the reduction in mortality rate; however, this factor was probably not responsible for the continued reduction in mortality after 1935, since the dose of antitoxin remained essentially the same.

The routes of administration of tetanus antitoxin have been the subject of considerable discussion. At Charity Hospital the antitoxin was administered primarily by the subcutaneous route from 1906 to 1923, and after that time it was administered in equal amounts via the intravenous and intramuscular routes. An occasional patient was treated with antitoxin intrathecally and the results were uniformly poor. In addition to the initial dose of tetanus antitoxin,

CHART XII. *Causes of Deaths*

	1943-49	1950-56
Respiratory		
Pneumonia	54	17
Atelectasis	18	8
Aspiration	10	8
Pulmonary edema	6	2
Asphyxiation	6	4
Septicemia	3	2
Convulsion	8	4
Cardiac arrest	0	3
Unknown	11	7
	<hr/> 116	<hr/> 55

small amounts were given daily intramuscularly for seven to ten days until 1952, when this procedure was abandoned. Since that time antitoxin has been given in a single dose at the time of admission to the hospital, one-half of the amount being given intravenously and the other half intramuscularly. Thus, the effectiveness of routes of administration cannot be determined from this study.

The importance of local wound care in the treatment of tetanus has been repeatedly emphasized. However, there is some question as to whether or not this constitutes therapy for the clinical manifestations of tetanus. From 1906 to about 1925, the local care of the wound was somewhat haphazard and was employed mainly when needed for incision and drainage or removal of foreign bodies. From 1925 to 1956, however, debridement or wound excision where feasible were practiced. In fact, in many instances it appears that overzealous adherence to the policy of wound excision resulted in sacrifice of normal tissue. As with the use of tetanus antitoxin, the application of routine wound care to all cases of tetanus since 1925, has not appeared to alter the relatively constant yearly decrease in mortality rate.

The chemotherapy of tetanus began in 1941, with the use of sulfadiazine and the routine administration of this agent was continued until 1949, when it was replaced

with penicillin. On the basis of experimental and clinical reports,^{8, 10, 11} it was hoped that penicillin in large doses would significantly alter the course of tetanus by specific effect on the organisms, and reduce the incidence of pulmonary complications, thereby reducing the mortality rate. A comparison of the results from 1950 to 1956, with the preceding seven years indicates that, while the mortality rate was reduced somewhat, the morbidity in terms of hospital days was not altered (Chart VIII). As observed earlier by Altemeier,² there is no evidence that penicillin acts in any specific way upon tetanus.

As published reports indicate, tracheostomy was applied to the treatment of tetanus with great enthusiasm.⁹ Surely, many patients with this disease die of pulmonary causes and it was assumed that prevention or amelioration of these complications would naturally bring about a significant improvement in results. Perhaps the 10 per cent reduction in mortality occurring in the years 1950-1956, was in part due to the almost routine performance of tracheostomy (Chart VIII). Yet, a similar decrease in mortality occurred in each of the preceding seven year periods since 1906 (Chart IX).

Although a variety of agents have been employed as sedative and anticonvulsants in the management of tetanus, in no instance has it been demonstrated that a drug was specifically effective in reducing the death rate. To be sure, the intensity and frequency of spasm may be reduced, resulting in a quieter patient, but the value of drugs producing this effect may be questioned. For example, comparison of the results obtained during the two seven-year periods from 1943 to 1956, indicates a decrease in mortality during the second seven year period comparable to that which had occurred in any preceding seven year period (Chart VIII). This occurred in spite of the fact that a routine for the administration of sedatives and anticonvulsants (barbiturates, mephenesin (Tolseram®)

and chlorpromazine) had been developed and proven highly effective for the relief of symptoms. On the basis of this experience, therefore, it may be concluded that any type of sedative or hypnotic agent when properly administered so as to avoid respiratory depression has the same effect, or lack of effect, upon the outcome of tetanus.

This study of the results of treatment of tetanus at Charity Hospital confirms the prophetic observations of Doctor Hester¹⁸ a century ago, that the most important factor is good supportive care of the patient. Simply stated, tetanus is a self-limiting disease, the outcome of which is largely determined before treatment can be instituted. In the absence of a lethal amount of toxin, the majority of patients will survive. On the basis of this study it appears that some patients in this latter group would succumb to the complications of tetanus, and thus might be saved by the recently introduced measures of antibiotics, muscle relaxants and tracheostomy. It may be that the most important feature of these newer measures is that they complicate the care of the tetanus patient to the point where constant nursing attention, the really significant factor in therapy, must be provided.

Thus, the mortality from tetanus at Charity Hospital has been steadily declining for half a century. This has been the result of many factors, not the least important of which has been continuous improvement in supportive care of the patient. During this long experience, no single therapeutic agent nor combination of agents have been demonstrated to be specific. Therefore, control of the disease must come by way of prevention, not cure.

SUMMARY

1. Experience with tetanus at Charity Hospital for the past 14 years has been analyzed and compared with that previously reported.

2. There were 558 cases treated from

1943 to 1956, with an average yearly incidence of 0.3 to 1.1 per 1,000 hospital admissions. Comparison with previous years reveals a gradual decrease in incidence since 1906.

3. The average age of patients with tetanus has increased as has the incidence of the disease in females.

4. Only one of 558 patients had received a complete immunizing course of tetanus toxoid and one had received tetanus antitoxin at the time of injury.

5. The incubation period was 40 per cent longer for survivors than for those who succumbed.

6. Treatment employed for the two seven year periods 1943-1949, and 1950-1956, was essentially the same except that in the latter period antibiotics, tracheostomy, muscle relaxants and gastrostomy were added. From 1950-1956, the mortality was 10 per cent less than for 1943-1949. However, review of the mortality since 1906, reveals a continuous and steady decrease throughout this 50 year period.

7. A review of the various components of therapy emphasizes the lack of specificity of any of the agents employed and suggests that the most important single factor is good supportive care of the patient.

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