RECURRENT TETANUS

JOHN B. PACE,
M.D., B.PHARM., F.R.C.S.,
Department of Surgery,
Royal University of Malta
and
ANTHONY BUSUTTIL, M.D.*
Department of Pathology,
Royal University of Malta

Summary

Tetanus may recur in 0.5 - 1.0% of cases, months or years after the initial infection. A review of the literature uncovered 98 cases of recurrent tetanus reported to date. Three cases of recurrent tetanus encountered in Malta between 1954 and 1965 are presented. The recurrent illness has a lower mortality rate than that of tetanus in general, but its treatment presents some difficulties and hazards, mainly of an immunological nature. The possible reasons for recurrence of this disease are reviewed and prophylactic measures are suggested.

It has been known for over half a century that a clinical attack of tetanus can occur in the same individual more than once. A review of the world literature showed that ninety-eight cases of recurrent tetanus have been recorded. Vener and Bower (1940) found five documented cases and described an additional case. By 1950, fifty-four cases had been reported in the German and French literature (Möbus, 1950). In an analysis of 202 cases of tetanus, Garcia Palmieri and Ramirez (1957) included five instances of recurrence of the disease. Thirty-three other cases were added to the literature by various authors between 1954 and 1968 (Martin and McDowell, 1954; Gunaratna, 1958; Alhady, 1961; Wickramasinghe and Malinie Fernando, 1967; and Sahadevan, 1968).

* Present address: Pathology Department, Western Infirmary, University of Glasgow.

A recent survey of cases of tetanus encountered in Malta during the period 1954-1968 uncovered three instances of recurrence. The purpose of this paper is to report these three cases and to discuss the possible underlying aetiological factors and therapeutic problems of recurrent tetanus. The details are taken from the records of St. Luke's Hospital, Malta.

Case Reports

Case I.

(1) The patient was V.M., a 56-year-old field labourer. Some twelve days after sustaining a punctured wound in the right foot through the spines of a sea urchin, he developed lock-jaw, dysphagia and neck stiffness. He was admitted to hospital on 21st May, 1954, three days after the onset of symptoms.

On examination, he was apyrexial and had a pulse-rate of 82 per minute. Marked trismus and neck rigidity were evident. The punctured wound in his right foot was hardly detectable.

Treatment for tetanus was instituted. The patient was placed in a darkened, quiet room and sedated by means of Paraldehyde retention enemata. After the uneventful injection of a test-dose of anti-tetanic serum, 100,000 I.U. of tetanus antitoxin were administered intravenously. Fluid balance and adequate nutrition were maintained by means of intravenous dextrose-saline infusion and naso-gastric tube feeding.

Steady improvement occurred on this treatment. The trismus and dysphagia receded in a few days, allowing the discontinuance of intravenous and tube feed-

ing; and all the signs of tetanus disappeared within a fortnight. The patient was discharged from hospital on 5th June, 1954.

(2) Sometime in November, 1956, V.M. sustained a punctured wound in the left sole and, a few weeks later, he noticed a septic fissure in the first interdigital cleft of the right foot; he ignored both lesions. On the 7th January, 1957, he developed increasing stiffness in the lower limbs followed by inability to open his mouth, difficulty in swallowing and painful neck stiffness. When admitted to hospital, on 10th January, 1957, he was running a temperature of 100° F. (37.7° C.) and his face was flushed and exhibited a typical 'risus sardonicus'. Marked rigidity was present in the muscles of the neck, abdomen and lower limbs. The tendon reflexes were very brisk. Generalised muscular spasms occurred periodically.

Treatment followed the previous lines. After intra-dermal, subcutaneous and intramuscular test-doses of A.T.S. had been given without producing any hypersensitivity reaction, 195,000 I.U. of tetanus antitoxin were given very slowly by intravenous drip. One million units of crystalline Penicillin intramuscularly twice daily and 5ml. of Paraldehyde intramuscularly 6-hourly were also administered.

The intermittent spasms ceased within days and the patient made a full recovery within two weeks. He was discharged from hospital on 25th January, 1957.

Case II.

(1) M.G., a farmer aged 70 years, was admitted to hospital on May 4, 1959. He gave a two-day history of lumbo-dorsal backache and increasing stiffness, the latter commencing in the back and spreading to become generalised. He also experienced difficulty in articulation and swallowing. There was no history of wounding but a healed punctured wound was discovered on the plantar aspect of the right big toe.

The patient was pale and sweating, and presented the typical facies of tetanus. Trismus was present, abdominal and back rigidity was marked and the tendon reflexes were exaggerated.

Initial treatment consisted in Chlorpromazine, 25 mg. every 8 hours; crystalline Penicillin, 1 million units twice daily; and Streptomycin, 0.5 Gm. twice daily.

No improvement was recorded on this treatment. Five days after admission the patient developed painful generalised muscular spasms. At this stage, 200,000 I.U. of tetanus antitoxin were administered intravenously at the rate of 15,000 I.U. every half-hour. Following this, the symptoms and signs of tetanus gradually subsided over a period of two weeks. The patient's discharge from hospital was delayed until August 10, 1959 because investigations and treatment had to be carried out for coincidental urogenital and arterial disease.

(2) M.G. was re-admitted to hospital on April 1, 1960 complaining of epigastric discomfort of a few days' duration, associated with ingravescent stiffness of the abdominal muscles, followed later by progressive spasticity of both lower limbs and rigidity of the back muscles. Twenty-four hours before admission he developed dysphagia and intermittent generalised muscular spasms. He could not recall having received any wounds within the preceding few days or weeks.

On examination, the patient was afebrile and had no obvious wounds; he had trismus and muscular rigidity of the abdomen and back. 'Flare-up' of tetanus was diagnosed and treatment commenced. In view of the patient's previous experience of horse serum, three test-doses (intradermal, subcutaneous and intramuscular) of A.T.S.: were given at half-hourly intervals: although there was no hypersensitivity reaction, the therapeutic dose of tetanus antitoxin was restricted to 10,000 I.U. and administered intramuscularly under antihistaminic cover (Diphenhydramine hydrachloride 50mg. t.d.s.). Intramuscular injections of Penicillin (1 million units every 6 hours) were also given.

During the first two days of treatment the muscular rigidity became more severe, but no further spasms were recorded. The symptoms then slowly regressed and recovery was complete in 26 days. The pa-

tient was discharged from hospital on April 27, 1960.

(3) The same man (M.G.) was referred to hospital for the third time on October 28, 1960, with a 6-day history of increasing difficulty in masticating and swallowing solid food. Again, there was no history of recent injury.

On examination, there was obvious trismus and general muscular rigidity; the tendon reflexes were brisk and sustained. The temperature was within normal limits. Tetanus was suspected with some reserve in view of the two previous attacks, and treatment was witheld during the first twenty-four hours of observation. By the second day of admission, however, the progression of the rigidity had made the diagnosis of tetanus obvious.

Treatment consisted in the intramuscular injection of 10,000 I.U. of tetanus antitoxin, with the usual precautions, Penicillin (1 million units twice daily), Streptomycin (0.5 Gm twice daily) and Paraldehyde (5 ml 6 hourly).

The symptoms and signs gradually subsided over a period of two weeks and the patient was finally discharged home on November 19, 1960, twenty two days after admission.

Case III.

(1) M.A., a nine-year-old schoolboy, was referred to hospital as a case of tetanus on July 17, 1964. Nine days previously he had sustained a cut in his left big toe while unpacking cases in a warehouse. He gave a four-day history of increasing limitation of jaw movement, pain on swallowing, stiffness of the neck and pain in the back.

On admission, the patient ran a temperature of 99° F (37.2° C) and had a pulse rate of 100 per minute. He had a typical 'risus sardonicus', trismus and rigidity of the neck and abdominal muscles. Generalised muscular spasms occurred from time to time. A healing incised wound was present on the plantar aspect of his left big toe; in addition he had bilateral otitis with purulent discharge. An aural swab gave a mixed growth of non-specific organisms.

Initial treatment consisted in 105,000 I.U. of tetanus antitoxin by intravenous infusion; Penicillin 0.5 Megaunit 6 hourly; Streptomycin, 0.5 Gm a day; and Paraldehyde, 5 ml six hourly.

During the first few days generalised convulsions took place frequently and, on the fourth day, a further intravenous dose (50,000 I.U.) of antitoxin was given. Thereafter, the muscular spasms became milder and less frequent, until they ceased by the ninth day of treatment. The trismus and general rigidity took longer to clear up. By August 27, 1964 there were no residual signs of tetanus and the patient was discharged.

(2) On July 1965, the same boy (M.A.) was referred to hospital with a two-day history of jaw stiffnes, inability to swallow and voice-change to the nasal type. This time there was no history of recent injury.

On examination, he had a temperature of 100° F (37.7° C) and a pulse-rate of 96 per minute. Trismus was considerable and the tendon reflexes were brisk and sustained. No local cause in the head and neck was found to account for the presenting symptoms; no enlarged cervical lymph nodes were present; and no wounds were detected.

In view of the patient's previous experience of A.T.S. and the mildness of the symptoms, only a fractionated dose of 1,500 I.U. of tetanus antitoxin was given initially, but Penicillin, Streptomycin and Paraldehyde were administered as usual.

During the first two days, the trismus increased and a progressive painful rigidity developed in the muscles of the neck, abdomen and lower limbs. On July 21, the third day after admission, the full treatment regime for tetanus was instituted: an intravenous infusion of dextrose-saline was set up, a naso-gastric tube was inserted for feeding purposes; Paraldehyde was administered more frequently and the Penicillin dosage was increased; tetanus antitoxin (200,000 I.U.) was infused very slowly intravenously, with the usual precautions against anaphylaxis. In spite of this, the signs of tetanus increased in severity during the next few days. Further intravenous doses of antitoxin were given

on July 22 (100,000 I.U.), on July 25 (50,000 I.U.) and on July 29 (50,000 I.U.).

Following the last dose of antitoxin, the patient's recovery from tetanus was rapid, but his discharge from hospital was delayed until August 17, 1965 because of infection at one of the sites used for intramuscular injections.

Discussion

It is, perhaps, not widely known that tetanus may recur in the same individual. In one of our cases (II) the illness recurred twice. A recent survey (Pace, Busuttil and Muscat, 1968) has shown that the incidence of tetanus in the Maltese Islands averages 19.4 cases a year; on the basis of this figure, the three cases of recurrent tetanus reported above represent an approximate incidence of 1% of all cases of tetanus. In their series of 2,007 cases of tetanus, Patel *et al.* (1961) recorded a recurrence rate of 0.84% while Vakil *et al.* (1964) estimated an incidence of 0.5%.

The interval between consecutive attacks of tetanus ranged, in our cases, from 6 to 32 months. A distinction has been made in the past between 'relapse' and 're-infection', on the basis of this time interval. Vener and Bower (1940) defined 'relapse' as recurrence of the manifestations of tetanus within one month of recovery from the previous attack through persistence of the original infection; while Patel *et al.* (1961) considered as relapse any recurrence within six months. In our view, the distinction between relapse and re-infection cannot be made on the grounds of an arbitrary time factor. In fact, there may be three kinds of recurrence, namely:

(1) *recrudescence* of symptoms and signs within a few days of apparent recovery, due to incomplete control of the initial infection; (2) *relapse* of the illness as a result of reactivation of persisting dormant infection in the original causative lesion, weeks or months after control of the previous attack; or (3) *re-infection* of the recovered patient with *Cl. tetani* through the primary unhealed lesion or through a fresh wound, followed by the reappearance of clinical tetanus. With the exception of the first, it is very difficult in practice to distinguish between these various types of recurrence. In the first instance, the apparent wound may not be the portal of entry of *Cl. tetani;* while several cases of tetanus have no demonstrable wound. The possibility of asymptomatic residual clostridial contamination of wounds is well known, and the longevity of *Cl. tetani* spores in such lesions is notorious. Moreover, clostridial spores may be present in trivial, healed, long-forgetten or unknown wounds, where they are very often undetectable, and their reversal to the pathogenic vegetative form is unpredictable. On the other hand, of course, fresh infection through new overt or occult wounds is an ever-present possibility and may occur at any time after recovery from tetanus. Therefore, any attempt to differentiate relapse from reinfection on the basis of the length of the sympton-free period between attacks of tetanus, as suggested by the above-mentioned authors, would have no scientific foundation. In clinical practice, the allocation of given cases of recurrent tetanus into one or other of the three theoretical types proves impossible in the majority. In our view, such a classification is only of academic interest and serves no practical purpose, since it has no bearing on diagnosis, course, treatment or prognosis.

There is now ample evidence that one or more attacks of tetanus do not guarantee immunity from recurrence, nor do they necessarily render any subsequent attack(s) less severe. Turner *et al.* (1957) and Vakil *et al.* (1964) have shown that there is little or no active immunity, as measured by the amount of circulating endogenous antitoxin just after the initial attack and during the recurrent bout of tetanus. It is possible that the surviving cases of tetanus have been exposed to only a small dose of toxin, insufficient to be lethal and inadequate to elicit a significant immune response (Turner *et al.*, 1957). It is also possible that the large therapeutic doses of antitoxin administered during the survived attack depress the patient's active immune response by neutralising toxin before it can exert its antigenic effect (Cook & Jones, 1943;

Oakley, 1963). A very small minority of individuals may be subject to recurrent infection because they possess an incompetent immune system (Soothill and Squire, 1963). The ten antigenic strains of *Cl. tetani* all produce an immunologically identical exotoxin (A. Trevor Willis, 1964); but, in spite of this qualitative similarity, some strains may provide a quantitatively weaker antigenic stimulus than others and, therefore, are less likely to produce a significant degree of active immunity. Finally, Patel *et al.* (1961) consider that, even if some immunity is acquired as a result of the first attack of tetanus, it is likely that a highly virulent infection would swamp the defences and result in a second attack of the disease.

The mortality from recurrent tetanus seems to be lower than that from tetanus in general: none of the cases reported in this paper ended fatally. Vakil *et al.* (1964) ascribed this to a tendency for earlier admission to hospital of those patients with recurrence. We feel, however, that the first infection confers a certain degree of active immunity which, although inadequate to prevent the reappearance of the clinical manifestations of tetanus, is sufficient to afford some protection.

Recurrent tetanus presents important clinical problems. It is uncommon and is relegated to further obscurity by the failure of many textbooks to include a few words acknowledging its existence. This fact, coupled with the occasional absence of an obvious portal of entry of infection may lead to a harmful delay in diagnosis and treatment.

The patient with recurrent tetanus may have received therapeutic doses of Antitetanus Serum (A.T.S.) during the preceding infection. This previous experience of horse serum results in the rapid elimination from the patient's circulation of any antitoxin administered during the recurrent illness, with serious reduction of its therapeutic efficacy (Payling Wright, 1963). Therefore, large doses of Antitetanus Serum, repeated at short intervels, would seem to be required for effective antitoxic therapy in recurrent tetanus. In the circumstances, the danger of anaphylactic reactions looms large (vide Cox, 1963). Although, fortunately, none of our patients developed untoward reaction to A.T.S., Vakil *et al.* recorded hypersensitivity reactions in 6 out of 11 patients. In view of this, if A.T.S. has to be used, the routine employment of repeated test doses followed by fractionation of the therapeutic dose should be the rule; concommitant cover with antihistaminics or corticosteroids may also have to be considered. Ideally, Human Tetanus Hyperimmune Globulin should be used as this would be safe and effective, but it is still rare and expensive.

In the light of the foregoing, prophylaxis emerges, as always, the ideal to be aimed at. Active immunisation by means of adsorbed toxoid should be offered to all recovered cases of tetanus. It would seem particularly advisable in 'high-risk' individuals, such as children, field labourers and patients suffering from chronic ulceration or undergoing self-administered parenteral therapy, particularly diabetic

Acknowledgements

We wish to thank Professor V. G. Griffiths, Head of the Department of Surgery, Professor A. P. Camilleri, Dean Faculty of Medicine, and Dr. A. Cuschieri, Chief Government Medical Officer, for kind permission to publish.

References

ALHADY, S.M.A. (1961). Med. J. Aust., *2*, 219.

COOKE, J.V. and JONES, F.G. (1943). J. Amer. Med. Ass., *121*, 1201.

COX, C.A., KNOWELDEN, J. and SHARRARD, W.J.W. (1963). Brit. Med. J., *2*, 1360-1366.

GARCIA PALMIERI, M.R. and RAMIREZ, R. (1957). Ann. Intern. Med., *47*, 721.

GUNARATNA, N.P.S. (1958). J. Lady Ridgeway Hosp. Child. Colombo., *7*, 3.

LITTLEWOOD, A.H.M., Mant A.K. and PAYLING WRIGHT, G. (1954). Brit. Med. J., *2*, 444.

MARTIN, H.L. and McDOWELL, F. (1954). Ann. Intern. Med., *41*, 159.

MÖBUS, L. (1950). Ztscht. Kinderheilk. *68*, 427.

OAKLEY, C.L. (1963). (Blackwell Scientific Publications, Oxford) "Clinical Aspects of Immunology" 771.

PACE, J.B., BUSUTTIL, A. and MUSCAT, J. (1968).

Paper read Ass. Surg. and Phys., Malta.

PATEL, J.C., MEHTA, B.C., DHIRAWANI, M.K. and MEHTA, V.R. (1961) J. Ass. Physcns. Ind.a, *9*, 1.

PAYLING WRIGHT, G. (1958). Proc. R. Soc. Me!., *51*, 999.

SAHADEVAN, M.G. (1968). Brit. Med. J., *2*, 492.

SCOTHIL, J.F. and SQUIRE, J.P. (1963). Clinical Aspects of Immunology. (Blackwell Scientific Publications, Oxford), p. 307.

TURNER, T.B., VELASCO-JOVEN, E.A. and PRUDOVSKY, S. (1957). Bull. Johns Hopkins Hosp., *102*, 71.

VAKIL, B.J., MEHTA, A.J. and TULPULE, T.H. (1964). Post. Grad. Med. J., *40*, 601.

VENER, H.I. and BOWER, A.G. (1940). J. Amer. Med. Assoc., *114*, 2198.

WICKRAMASINGHE, S.Y.D.C. and MALINIE FERNANDO (1967). Brit. Med. J., *4*, 530.

WILLIS, A. TREVOR (1964). "Anaerobic Bacteriology in Clinical Medicine". (Butterworth) 2nd Ed. p. 179.

WILSON, G.S. and MILES, A.A. (1964). "Principles of Bacteriology and Immunity". (Edw. Arnold), *2*, 1096.