REFRESHER COURSE FOR GENERAL PRACTITIONERS**THE PREVENTION AND TREATMENT OF TETANUS**

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Tetanus or lockjaw is one of those comparatively rare diseases which are liable to crop up unexpectedly in practice. In England and Wales the Registrar-General's Review shows that for the decade 1940-9 an average of 84 fatal cases occurred per annum, which probably represents a total case incidence of between 160 and 200 per annum. For comparison in 1949 there were 79 deaths from tetanus and 84 from diphtheria. Since prevention among civilians depends on giving antitoxin as soon as possible after wounding, and the successful outcome of treatment may depend on early diagnosis, it is clear that a considerable burden of responsibility falls on general practitioners. What happens subsequently after the patient has been admitted to hospital, though more dramatic, has less effect in deciding the issue of prevention or cure.

In considering this subject the logical sequence would be to study first the causal organism, the type of individual at risk, and the kind of wound likely to cause the disease: next to describe methods of prevention; and finally the symptomatology, diagnosis, treatment, and prognosis of the disease. This sequence will be followed here, with particular emphasis on prevention and diagnosis.

Clostridium tetani, the causal organism of tetanus, produces spores which are highly resistant and may remain dormant for years outside the body and for months in the tissues when conditions for development are unsuitable. They are commonly present in cultivated soil and also in the intestinal tract and excreta of man, the horse, and other animals. Manure and horse ploughing may help to disseminate infection, and the degree of infectivity of the soil is one of the factors which determines the incidence of the disease. Germination of spores only takes place under anaerobic conditions. In wounds it is helped by tissue trauma, necrosis, foreign bodies, and pyogenic or other anaerobic infection, but the determining factor is a sufficiently low oxygen tension. When growth occurs an exotoxin is produced which is absorbed by the blood stream and reaches the nervous system producing the characteristic symptoms. The evidence suggests that once the toxin has become "fixed" to the motor cells it cannot be neutralized by antitoxin. Circulating antitoxin can only prevent further absorption of toxin from the wound and neutralize toxin which has not already reached the motor cells.

Type of Wound and Type of Patient

In civilian practice in this country tetanus hardly ever follows serious wounds because prophylactic antitoxin is almost always given to such and affords protection. Instead it is caused by relatively slight injuries in patients who for one reason or another have not been given antitoxin. Thus it commonly follows septic infections such as whitlows, dirty abrasions, or slight penetrating wounds as from a thorn, splinter, garden fork, or nail in boot. Such injuries have usually become infected and sealed by scabs forming

a cavity where anaerobes can grow, and injuries such as these account for about 80% of all cases. Occasionally clean cuts sustained in a field or garden are a cause. The remainder arise from a miscellaneous collection of lesions such as umbilical sepsis causing tetanus neonatorum, puerperal sepsis, infection in body cavities such as the middle ear or maxillary antrum, and septic skin lesions such as impetigo, dermatitis of the scalp, or varicose ulcers. Abscesses or ulcers in the intestinal tract may be the source and probably account for some of the so-called idiopathic cases. Sometimes the wound is so slight that it has healed before the disease develops. Finally there is a small group, now happily becoming smaller, in which tetanus is due to infected materials used in medicine or surgery. These have included surgical instruments, catgut, wool or felt, material for intramuscular injections, vaccination lymph, or even sulphonamide dusting-powder infected by the cardboard containers in which it was packed.

Tetanus may occur at any age, and men are affected three times more commonly than women chiefly because of their greater liability to infected wounds. The majority live and work in agricultural districts in occupations such as farm labourers, grooms, farmers, gardeners, which involve manual contact with soil or manure. Children develop it as a result of abrasions or cuts which have not been kept clean, and old people from uncleanness combined with slight wounds of the hands and feet.

Passive Immunization

Two methods of prevention are now known: by passive and by active immunization. In civilian practice the former is the only method in general use, and this will be considered first.

Passive immunization by injection of antitoxin as soon as possible after a wound has been sustained was first introduced on a large scale in the war of 1914-18 on the Western Front. As a result the incidence of tetanus fell from 9 to 1.4 per 1,000 in three months in 1914, and later in the war it was reduced still further partly by increasing the initial prophylactic dose and repeating it at weekly intervals after severe and heavily infected wounds. Ever since then this method has been used in civil life, but, although the incidence of tetanus has been considerably reduced thereby, many cases still occur which might be prevented. The reasons for this are several: (1) country people are not yet sufficiently aware of the importance of keeping slight wounds clean; (2) some wounds which cause tetanus are not considered sufficiently severe to show to a doctor; (3) others which receive medical attention are not considered severe enough to merit prophylactic antitoxin; (4) prophylactic antitoxin is given, but the dose is too small or not repeated even though the wound is severe or heavily infected, and so modified tetanus develops; and (5) tetanus occasionally follows wounds in which the possibility could not reasonably be suspected or no wound at all, and no antitoxin is given.

Passive immunization could give better results only if the type of wound likely to cause tetanus were more generally appreciated by doctors. One reason for the omission of prophylactic injections may be that most medical students are trained in large cities where tetanus is almost unknown, so that they do not have the salutary experience of seeing the actual disease to impress on them the impor-

tance of prevention, or of seeing the type of wound in the type of person who would be likely to develop tetanus.

After every severe wound, and after every wound of the type described as likely to cause tetanus, 3,000–5,000 I.U., according to the severity, should be injected intramuscularly as soon as possible, and this should be repeated at weekly intervals if chronic suppuration continues, or before further operation. To guard against reactions to horse serum in allergic subjects, or those who have had previous antitoxin, a solution of 1:1,000 adrenaline should be kept at hand and 0.5 ml. injected if required. With care on the above lines it is possible that the incidence might be reduced still further, but many cases would inevitably slip through the net of passive immunization.

Active Immunization

Ramon and Zoeller showed that active immunization against tetanus could be produced by injection of formolized toxin, called "toxoid," and a modification of this method was used and perfected during the war of 1939–45.

To produce immunity two injections of 1 ml. were given at an interval of not less than six weeks to soldiers before they went on active service and a further similar injection once a year while serving. In the British Army an injection of prophylactic antitoxin was also given directly a man was wounded, but in the American Army a further injection of toxoid. The results by both methods were wholly satisfactory, and tetanus was practically stamped out.

While it is true that active immunization of the whole civilian population would eliminate tetanus, its practical application presents economic difficulties, for it would be a heavy undertaking to prevent the comparatively small number of cases which do occur. Conybeare and Logan have suggested that active immunization would be justifiable and practical for schoolchildren at the age of entry in rural districts, and Boyd has recommended it for agricultural workers, grooms, and those exposed to occupational risk of infection. Even limited application of active immunization on these lines would undoubtedly do more to eliminate tetanus than anything else.

Classical Symptoms and Signs

To understand the clinical picture of tetanus it is essential to have a clear idea of the march of the disease and to appreciate that it follows the same sequence whether it is mild or severe. The difference is that in mild cases the march is slow and in severe ones it is rapid. Symptoms first appear from two days to several weeks after injury. The longer the incubation period the milder the attack.

The presenting symptoms are so important for early diagnosis that they will be considered first. In a few cases vague prodromal symptoms which are not diagnostic may occur for twenty-four hours. These include a feeling of nervousness, unaccountable weariness, fleeting pains in the back and limbs, irritability, muscular twitchings, and malaise. Much the most important early symptom which is present in about 90% and should immediately suggest the diagnosis of tetanus is painless stiffness of the jaw or trismus. This is produced by tonic spasm of the masseters, so that the patient experiences difficulty in opening his mouth and masticating food. It is sometimes accompanied by difficulty in swallowing, and occasionally this is the first symptom. At this stage, too, a peculiar facial expression appears—the risus sardonicus. In this the corners of the mouth are drawn upwards and backwards and the forehead wrinkled transversely, the effect becoming more marked when the patient attempts to open his mouth. At the same time, or shortly after, the tonic rigidity spreads to the neck and spine and muscles of the trunk. The spine is arched backwards in the position called opisthotonos, and the abdominal muscles are affected with board-like but painless rigidity. This is usually so marked that when the patient is lying on a flat bed the hand can be passed easily under the lumbar arch—a very useful confirmatory sign. The tonic rigidity can often be increased by manipulation of the limbs or making the patient try to sit up or open his mouth, but the limbs usually remain

relatively relaxed. Other presenting symptoms and signs are local tetanus and cranial nerve palsies. Local tetanus consists in slight pain and stiffness in the injured limb and may be the very first symptom. It occurs only in very chronic cases with a long incubation period—usually in those who have been incompletely protected by passive immunization. Its presence heralds a mild attack, provided that treatment is given without delay. Cranial nerve palsies in which usually the 3rd, 4th, or 7th cranial nerves are affected, giving rise to diplopia or unilateral facial weakness of the lower motor neurone type, may be the presenting symptom following wounds of the head and neck. This, too, is probably a form of local tetanus, and the prognosis is also good, provided the treatment is given without delay. Both local tetanus and cranial nerve palsies are accompanied or followed by trismus and generalized tonic rigidity, and the subsequent course is similar.

Progress

Following the initial symptoms tonic rigidity persists throughout the illness until death or recovery. In severe cases it reaches its maximum in a few days; in mild chronic cases it comes on more slowly and passes off gradually after three to six weeks. It is not in itself dangerous, although it limits respiratory movements to some extent. With the increase of tonic rigidity there is an increase in reflex excitability which is shown by increased tone on manipulation or attempted movement. This reflex excitability is the prelude to reflex spasms or convulsions. In very severe cases these first appear about 24 hours after the first appearance of trismus. When a reflex spasm occurs the whole body suddenly becomes rigid; the jaws are tightly clenched; the neck and trunk are arched backwards, the limbs extended, and respiration may be stopped. Such an attack may last from a few seconds to three or four minutes, and the patient foams at the mouth and becomes cyanosed. To begin with these attacks are brought on by external stimuli, such as an attempt to move or drink, noise, or bright light, and they are mild and of short duration. Later they become more violent, of longer duration, and occur spontaneously and with greater frequency. The longer their onset is delayed the better the prognosis. If they are occurring within 48 hours of the onset of trismus the prognosis is bad, and the patient is unlikely to recover. If they are delayed for three days or more the prognosis is relatively good, and the longer they are delayed the better the prognosis. In a severe case when they are established in less than 48 hours death usually occurs within six days. In less severe cases which survive they may continue for any period up to three weeks. After they have ceased, the residual tonic rigidity gradually passes off. Reflex spasms are an indication that the disease is severe, and they are dangerous in that they exhaust the patient, predispose to aspiration pneumonia, and may kill by prolonged respiratory spasm. Tonic rigidity alone is harmless, provided that sufficient antitoxin has been given.

In mild or medium cases the pulse rate is only slightly raised except during reflex spasms, and the temperature remains normal unless some intercurrent infection such as pneumonia develops. In fatal cases terminal hyperpyrexia to 105–108° F. (40.6–42.2° C.) often occurs a few hours before death. Pneumonia is the most frequent and dangerous complication and should always be watched for, and retention of urine is occasionally troublesome.

Diagnosis

The onset of painless stiffness of the jaw in the presence of a recent wound or septic infection of the hands, feet, or head should always suggest the possibility of lockjaw. The characteristic facial expression, stiffness, and arching of the lumbar spine and painless rigidity of the abdomen made worse by manipulation are additional evidence. Local tetanus involving a limb has to be distinguished from fibrositis, neuritis, and local bone or joint lesions; cranial nerve palsies from Bell's palsy, polio-encephalitis, or tuberculous

meningitis. Local lesions of the mouth or throat, such as an impacted wisdom tooth or peritonsillar abscess, although they may cause difficulty in opening the mouth, are painful and can usually be distinguished from true trismus on careful examination. The abdominal rigidity of tetanus has simulated that due to acute abdominal conditions, but the absence of tenderness and presence of trismus should prevent this mistake. At a later stage reflex spasms, accompanied as they are by severe trismus and opisthotonos, are characteristic, but occasionally they have to be distinguished from other causes of fits such as meningitis, encephalitis, epilepsy, and hysteria, and the convulsions of strychnine poisoning are similar except that they do not cause trismus.

The diagnosis of tetanus is essentially clinical, and special investigations are of little value. Lumbar puncture should be avoided except in cases of real doubt. The isolation of the organism from the wound is difficult, often impossible, and too slow to be relied on.

Treatment

This is best considered under four headings: (1) antitoxin and wound toilet; (2) prevention of intercurrent infection; (3) sedation and control of reflex convulsions; and (4) nursing, feeding, and general management.

The aim of giving antitoxin in tetanus is to prevent further absorption of toxin from the wound and to neutralize any toxin in the tissues or circulation before it can reach the nerve cells. If this can be given before a lethal dose has reached the nervous system the patient's life may be saved. To this end a large dose of 200,000 I.U. should be given, preferably intravenously, at the earliest possible moment. If the whole of this dose is not available when the patient is first seen a smaller dose should be given and the rest as soon as possible. A smaller dose given early is probably more effective than a larger dose some hours later. In patients with slight wounds it is unnecessary to give further antitoxin after the single large initial dose, but with severe infected wounds 50,000 units should be given intramuscularly once a week until healing has occurred. This is hardly ever necessary after civilian wounds. Nothing is gained by giving intrathecal antitoxin, and lumbar puncture is liable to excite spasms.

When antitoxin has been given the wound should receive appropriate treatment. Broadly the aim should be to convert an anaerobic into an aerobic infection, with the minimum disturbance of tissues, by thorough drainage and removal of necrotic tissue and foreign bodies.

One of the great risks of tetanus is secondary lung infection. As a prophylactic measure against this 500,000 units of penicillin should be given daily from the outset, and if infection develops in spite of this other appropriate antibiotics may be necessary.

It cannot be too strongly emphasized that the control of reflex convulsions by sedatives and relaxants is only symptomatic treatment. Complete control has little effect in prolonging life in a patient who has already absorbed a lethal dose of toxin. The aim should be to control the severe spasms which exhaust and are dangerous, without depressing respiration so much that the risk of chest complications is increased. Tonic rigidity alone is relatively harmless and can be left alone. In the early stages or in mild cases slight reflex excitability is best treated by large doses of ordinary sedatives such as potassium bromide, chloral, or phenobarbitone. For reflex convulsions bromethol is the drug of choice, but at present is difficult to obtain. This is given rectally as for basal anaesthesia in doses of from 0.07 to 0.1 ml. per kg. of body weight (estimated) twice or even three times daily in severe cases. As an alternative paraldehyde may be given rectally in normal saline in doses of 30 minims per stone of body weight (0.25 ml. per kilo.) two or three times daily or in one-quarter of this dose intramuscularly. Mephenesin antagonizes the convulsions produced by strychnine, probably by depressing reflex activity in the spinal cord, and has been favourably reported on in tetanus. It may be given either intra-

muscularly or orally in doses of 0.5 to 1 g. for an adult, repeated every few hours according to the effect produced. Opinions vary as to which route is better, but it seems to be relatively more effective in mild than in severe cases. Tubocurarine appears to be liable to excite respiratory spasm and is dangerous. In using sedatives and relaxants in tetanus the first dose should be on the small side and the increment judged by the response.

Because reflex convulsions are excited by stimuli of all kinds tetanus patients should be nursed as quietly as possible in a darkened room. All manipulation such as feeding and giving injections should be done while the patient is most deeply under the influence of sedatives. Nourishing fluid feeds should be given as regularly as possible, and a special nurse is essential in severe cases. When trismus is severe nasal feeding is necessary and intravenous fluids may be required. The mouth should be kept as clean as possible to lessen the risk of aspiration pneumonia, and cyanosis controlled by warmed nasal oxygen. Good nursing may have great influence in turning the scales in borderline cases.

Prognosis

In assessing prognosis the factors which have to be considered are whether passive immunization has been given, the length of the "incubation period," the length of the "period of onset," the severity and site of the wound, the violence of the spasms, the age and physique of the patient, and the presence of intercurrent disease. The "incubation period" is the length of time between the receipt of the wound and the first symptom, which is usually trismus. If infection with *Cl. tetani* has occurred some time after the wound was received this may be shorter than it appears, and therefore misleading. An incubation period of less than seven days means a bad prognosis, but when more than 10 days it is relatively good. When the "period of onset" is less than 48 hours the chances of recovery are slight, but when more than three days relatively good, and they improve with every day convulsions are delayed. If prophylactic antitoxin has been given the attack is usually mild. A severe or heavily infected wound makes the prognosis worse, and it is bad in infants or the aged or those enfeebled by intercurrent disease. The best prognostic yardstick is the period of onset, and this should always be used in assessing the result of any new form of treatment.

It will be seen that tetanus still presents many practical problems in prevention, diagnosis, and treatment. The ideal relaxant has yet to be found, and there is no specific remedy against toxin in the nervous system. The paradox remains that, although preventable, tetanus still occurs in civilian practice. Notification with details of age, sex, occupation, type of wound, and whether active immunization had been given might yield useful data which would make it easier to apply active immunization to certain limited sections of the population.

Next Refresher Course Article.—"Antenatal Care," by Professor W. C. W. Nixon.

A special programme of health education by World Health Organization teams was recently carried out under the auspices of the Egyptian Government in an isolated village in Upper Egypt (*Chron. Wld Hlth Org.*, 1952, 6, 355). Here a venereal disease control campaign included a complete serological survey of the population of about 9,000 persons and treatment with penicillin of all infected persons and their contacts. Social workers had the task of visiting homes and obtaining the co-operation of village people. Though there had never before been a public meeting for women in the village the team was successful in arranging shows of films and other meetings for them. While blood samples were being taken a rumour went round the village that the blood was being used in the manufacture of certain beverages, but it was successfully dispelled. In the end about 85% of the population submitted to blood tests.