TETANUS AS A RESPIRATORY PROBLEM*

RESULTS OF TREATMENT BY MEANS OF INTERMITTENT-POSITIVE-PRESSURE RESPIRATION

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In the past, attention has largely been focused on controlling the rigidity and the spasms of tetanus, and opinions have varied as to how this may best be achieved. Over the past 7 years we have compared the phenothiazine derivatives chlorpromazine and acetylpromazine with other drugs used for this purpose in a series of random clinical trials,[1-3] but none has significantly reduced the high mortality rate. During this time we have come more and more to appreciate the dominant role played by respiratory failure in this disease. It is the purpose of this paper to show in what respects tetanus may be regarded as a respiratory problem and to discuss the management of severe cases by means of tracheostomy with total paralysis and intermittent-positive-pressure respiration (IPPR).

Prognosis can be judged by the length of the incubation period and by the period of onset of reflex spasms, but probably the most valuable information comes from observation of the patient for the occurrence of reflex spasms, their frequency and severity. Patients with so-called 'mild' tetanus, in which there is muscular rigidity but no spasms, seldom have respiratory difficulty. The prognosis on conservative treatment is relatively good, with a mortality rate under 20%. The reverse is true of 'severe' tetanus, in which there are frequent reflex spasms and respiratory complications are common. Here the death rate in our hands on conservative treatment was about 60% in children and adults, and over 90% in neonates.

Why we regard severe tetanus as largely a respiratory problem may be judged from its natural history. Since 1956 we have observed about 1,000 cases during conservative treatment, and we have gained a fair experience of the clinical course of the disease.[4, 5] Muscular rigidity and reflex spasms are characteristic and colour the clinical picture. By conservative means both can usually be controlled, but seldom abolished. Reflex spasms (especially if frequent), rigidity of the abdomen and thorax, and excessive secretions in the naso-pharynx undoubtedly impede respiration but, unless there is acute obstruction of the airway, cyanosis does not often occur and hypoxia and CO_2 accumulation may easily be missed while the drama of the spasms and the pain they cause are being observed. In a severe case spasms increase in the first few days, and for a week or ten days the condition is often critical, with many hazards. Spasms may sometimes be uncontrollable and, after a severe bout seriously restricting thoracic and diaphragmatic movements, cyanosis may be observed. Respiration may also be embarrassed by thick tenacious secretions in the upper respiratory passages, or by pneumonia, which is often, though not in all cases, promoted by aspiration of food or secretions. Atelectasis is also not uncommon. And at any time laryngeal spasms or apnoeic attacks may occur, and either may be fatal. Whether these apnoeic attacks are caused by previous episodes of hypoxia or by direct action of tetanus toxin on the respiratory centre is not known.

Previously these hazards were recognized and treatment attempted. Oxygen was administered for hypoxia and cyanosis; tracheostomy was performed to obviate laryn-

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geal spasms, reduce the dead space, and facilitate the removal of secretions; and antibiotics were given to prevent or minimize infection; yet the results were very poor indeed, particularly in tetanus neonatorum. A more vigorous approach seemed to be indicated.

Before discussing intermittent-positive-pressure respiration as applied to tetanus it is worth while examining the value of tracheostomy alone.

Tracheostomy

This procedure has much to commend it in many types of acute respiratory failure. It reduces the dead space by about 100 ml. and relieves obstructive laryngeal dyspnoea; it isolates the respiratory tract from the digestive tract and lessens the aspiration of secretions, thus reducing the risk of aspiration pneumonia; and, last but not least, it permits the speedy application of IPPR should this become necessary.

Tracheostomy was first suggested in tetanus more than a hundred years ago.[6] It certainly would appear to be a logical procedure where secretions are copious or laryngeal spasms have occurred, and when there is difficulty in swallowing it prevents aspiration of food. Recently a neurologist in Britain stated that there was 'no doubt at all that the mortality from tetanus would be much less if all cases had a tracheostomy at the beginning of the illness'.[7] A review of the work of others and an analysis of our own experience, however, shows no conclusive evidence in its favour. Like most of the literature on the treatment of tetanus, opinions on tracheostomy are usually based on small series without adequate controls. In New Orleans, where tetanus is common, Creech *et al.*[8] fell into this trap in 1950 when they advocated tracheostomy on the strength of a series of 6 cases, yet their own critical analysis later showed that the drop in tetanus mortality over the seven-year period after its introduction was similar to that which had occurred in each of the preceding seven-year periods since 1906.[9]

We attempted to assess the place of tracheostomy in the treatment of tetanus by conducting a random clinical trial on 37 infants, admitting only the most severe cases and using the same standard conservative method of controlling spasms in both groups. The trial was imperfect and humidification inadequate, but the mortality rate was 100% in those submitted to tracheostomy as well as in the controls, and so we concluded that conspicuous benefit could not be expected from tracheostomy alone. We came to the same conclusion in a trial of similar design in adults, which we stopped after 15 cases because only 3 survived, 2 in one group and 1 in the other.

I believe that the disappointing results after tracheostomy alone, despite obvious theoretical advantages, are due to the particular hazards of the procedure in tetanus, where the tracheostoma has to be maintained for many weeks until the spasms cease and rigidity decreases. They should not be allowed to distract attention from the value of the procedure in other conditions where the respiratory hazards are likely to be of shorter duration. Inadequate humidification of the inspired air leads to crusting of secretions and blocked tubes, and vigilant supervision is vital if unnecessary deaths are to be avoided. On several occasions we have been called in to see cases of tetanus elsewhere, to find tracheostomy already performed but the patient doing badly because of inadequate attention to the tube. Tracheostomy should therefore only be performed in tetanus if proper care can be given to the tube and the secretions, and preferably if mechanical respiratory aids are available should they be required.

IPPR IN TETANUS

During the severe poliomyelitis epidemic of 1952 in Copenhagen, Danish workers developed the technique of tracheostomy and IPPR for patients with paralysis of the muscles of respiration. Later they applied the method to a patient with tetanus, completely abolishing spasms (and respiratory movements) with curare.[10] Encouraging reports soon appeared from other centres, such as Oxford and Leeds,[11-13] and in Durban and Cape Town the method has been extensively used.[14-16]

Since the effects of the toxin on the spinal cord in severe cases usually begin to wear off after about 10 days, and since most of the respiratory difficulties occur during this period, this might be expected to be the minimum time for total curarization and IPPR in tetanus; and in fact trial and error have shown it to be so. Moreover, if intoxication of the medullary centres is one of the causes of acute respiratory failure in this disease, and if the effects of the toxin are reversible here as they are in the cord, respiratory assistance may be necessary for longer than this—for 3 weeks or more—until spontaneous respiration is re-established satisfactorily. Experience with neonatal cases, too, has borne this out.

The advantage of IPPR is that two of the major problems of management may be dealt with simultaneously, viz. controlling rigidity and spasms, and preventing respiratory failure and other pulmonary complications. The disadvantage is that the technique carries special dangers of its own. Because the patient is paralysed he needs individual attention for, as Smith[12] stated, 'he cannot move, breathe or eat and—probably most difficult of all—he cannot communicate'. Fully-equipped units are necessary and constant vigilance over patients and machines imperative.

We have described our methods elsewhere.[16] Briefly, tracheostomy is performed under local anaesthesia in neonates and general anaesthesia in adults, and total paralysis is induced and maintained for 10 days with curare, IPPR being supplied by Radcliffe or Smith-Clarke respirators. We regularly aspirate the trachea after percussing the chest vigorously and we see that the inspired air is humidified. We estimate the efficiency of respiration clinically, aided by P_{CO_2} estimations done in the ward by a rebreathing technique. At the end of the period of curarization in neonates we continue with mechanically assisted respiration for some days without giving curare, leaving one limb of the suction connector open to the air, and this we find to be most helpful in weaning the infant from the respirator.

(a) *Results in Tetanus Neonatorum*

There is clear evidence in favour of this treatment in tetanus neonatorum. In a random clinical trial on 50 cases we compared treatment by means of a phenothiazine derivative (acetylpromazine or chlorpromazine) with total paralysis and IPPR. The infants were allotted to their

treatment groups by opening a sealed envelope after the diagnosis had been made and the severity agreed upon by two observers. Other factors that might have influenced the outcome, such as feeding, dosage of antitetanus serum, and prophylactic penicillin, were standardized. Of those treated conservatively 84% died, compared with 44% on IPPR, and this difference is statistically significant.[14]

We have now treated 114 cases of tetanus neonatorum by IPPR with 41 deaths, a mortality rate of 36%. Previously we had recorded a death rate of over 90% in a series of 193 consecutive cases treated conservatively,[5] which is in accord with experience elsewhere. There is therefore little doubt that IPPR is the method of choice for severe tetanus neonatorum.

(b) *Results in Children and Adults*

In contrast to the neonates, we have been unable to prove conclusively that the same holds for all children and adults with severe tetanus. Nevertheless, the trend in favour of IPPR is there. The design of our trial was similar to that used with the neonates, but we had to stop at 42 cases because the results of the trial in the infants were generally known at this stage, and some of the staff of the unit felt that it was unethical to continue. In this controlled series there were 14 deaths among the 21 non-neonates treated conservatively (death rate 67%) but only 9 died among the 21 on IPPR (death rate 43%). Altogether we have now treated 40 patients in this way with 17 deaths (43%). Our own previous experience had taught us to expect a mortality rate of 59% in severe tetanus apart from tetanus neonatorum,[5] so that the favourable drop to 43% suggests a therapeutic advance here too. Numbers, however, are small, and no definite claims are made. After some failures at first, the later striking success of the tetanus team in Leeds—34 cases of tetanus treated by means of curarization and IPPR without a death—confirms the value of the treatment.[17]

DISCUSSION

There is little doubt that total paralysis and IPPR represents a considerable advance in the treatment of tetanus, but it must be carried out in specialized units. The use of mechanical aids to respiration demands a high ratio of staff to patients, and should not be employed for isolated cases of tetanus except when skilled supervision is available, backed by experience in respiratory work. The first 10 neonates treated by IPPR in this unit all died, yet the total mortality rate after several years of experience is now under 40%, having dropped progressively with each additional 10 patients treated.

King Edward VIII is a busy hospital carrying a heavy patient-load and it can ill afford the luxury of a staff of 2 doctors and 20 nurses for the respiratory unit, most of the work of which is for tetanus patients. Often there are 15 infants and older patients to be treated at the same time, and all 7 respirators may be in use simultaneously. Work under such circumstances is an exacting experience—and mistakes may be costly. Deaths due to blockage of the tracheostomy tube and mechanical failure of the respirator are not infrequent and difficulties are encountered during extubation which may be fatal. The mortality rate is still too high. Given fewer patients—or more staff—it could certainly be reduced, perhaps to the 20% level achieved in Cape Town by Smythe and his colleagues.[15]

Tetanus is usually common where medical services are poorly developed, and few centres can afford the luxury of a respiratory unit fully staffed to treat a large number of cases of tetanus. Moreover, if mortality rates in 3 centres such as Leeds, Cape Town and Durban are compared, the results of treatment with IPPR are found to be best where the admission rate of tetanus is lowest (Leeds) and worst where it is highest (Durban). In the last world war active immunization with tetanus toxoid clearly demonstrated the efficacy of this preventive measure, and in areas where the incidence of tetanus is high it would seem far better to attempt to immunize the whole population against tetanus—and virtually eradicate the disease—than to concentrate medical services on treatment.

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REFERENCES

1. Laurence, D. R., Berman, E., Scragg, J. N. and Adams, E. B. (1958): Lancet, **1**, 987.
2. Adams, E. B., Wright, R., Berman, E. and Laurence, D. R. (1959): *Ibid.*, **1**, 755.
3. Wright, R. (1960): Trans. Roy. Soc. Trop. Med. Hyg., **54**, 270.
4. Adams, E. B. (1958): Proc. Roy. Soc. Med., **51**, 1002.
5. Wright, R. (1960): *The treatment of tetanus*, M.D. Thesis, University of Cape Town.
6. Curling (1837): Quoted by Drew, A. L. (1954): Neurology, **4**, 449.
7. Russell, W. R. (1956): Brit. Med. J., **1**, 517.
8. Creech, O., Woodhall, J. P. and Ochsner, A. (1950): Surgery, **27**, 62.
9. Creech, O., Glover, A. and Ochsner, A. (1957): Amer. J. Med., **18**, 947.
10. Bjornboe, M., Ibsen, B. and Johnsen, S. (1953): Ugeskr. Laeg., **115**, 1535.
11. Honey, G. E., Dwyer, B. E., Smith, A. C. and Spalding, J. M. K. (1954): Brit. Med. J., **2**, 442.
12. Smith, A. C. (1958): Proc. Roy. Soc. Med., **51**, 1006.
13. Garland, H. and Ablett, J. J. H. (1958): Lancet, **1**, 1107.
14. Wright, R., Sykes, M. K., Jackson, B. G., Mann, N. M. and Adams, E. B. (1961): *Ibid.*, **2**, 678.
15. Smythe, P. M. (1963): Brit. Med. J., **1**, 565.
16. Mann, N. M., Jackson, B. G. and Holloway, R. (1963): Arch. Dis. Childh., **38**, 251.
17. Ellis, M. (1963): Brit. Med. J., **1**, 1123.