SOME MODIFICATIONS IN METHOD OF TREATING TETANUS NEONATORUM WITH INTERMITTENT POSITIVE-PRESSURE RESPIRATION

BY

E. B. ADAMS, R. HOLLOWAY and A. K. THAMBIRAN

From the Department of Medicine, University of Natal and King Edward VIII Hospital, Durban, South Africa

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In a previous paper we showed that the treatment of severe tetanus neonatorum by means of total paralysis and intermittent positive-pressure respiration (I.P.P.R.) represents a real therapeutic advance (Wright, Sykes, Jackson, Mann and Adams, 1961), and this has since been confirmed in Cape Town by Smythe (1963). Mortality rates of over 80% on conservative treatment have been reduced by this technique to under 40%.

Experience with 100 infants with tetanus neonatorum admitted to our unit in a 12-month period shows that the majority (77%) need respiratory assistance of some sort, judged by the occurrence of apnœic and cyanotic attacks. Such numbers indicate not only the high incidence of this disease in Natal but also the size of the problem if all severe cases are to be treated by the full I.P.P.R. method. We admit all patients with tetanus to a special unit, staffed by two doctors, a nursing sister, 19 nurses, and a medical technologist. Seven respirators and ancillary equipment are available for treating acute respiratory failure. Elsewhere in Africa and in other parts of the world where tetanus is common, medical services are sometimes less well developed than they are in South Africa. We therefore felt justified in conducting further clinical trials in search of simpler or more economical methods. In this paper we report the results with two modifications of our standard method described by Mann, Jackson and Holloway (1963).

Trial of Selective Tracheostomy and I.P.P.R.

We had previously observed that infants with severe tetanus neonatorum occasionally settle down well on conservative treatment with chlorpromazine and phenobarbitone and survive, although the majority respond poorly, either because spasms cannot be controlled or because apnœic attacks and cyanosis occur. Our experience with tracheostomy alone has been very disappointing (Wright, 1960), but since humidification was not used and others have stressed the importance of tracheostomy in adults and children with tetanus, another trial of this procedure seemed to be justified. It was desirable to determine whether all infants with severe tetanus neonatorum require treatment with full I.P.P.R. (as our previous trial suggested) or whether a substantial number can be successfully treated more conservatively using chlorpromazine and phenobarbitone, and tracheostomy if necessary, but keeping I.P.P.R. as a last resort.

A trial was therefore designed to compare immediate curarization and I.P.P.R. with a more conservative 'selective' method, allotting infants with severe and frequent reflex spasm at random to the two treatment groups.

All received 50,000 units anti-tetanus serum immediately, and prophylactic penicillin; other antibiotics were used later when indicated.

Infants in group 1 ('I.P.P.R.') were treated by the standard I.P.P.R. method. Those in group 2 ('conservative method with selective tracheostomy and I.P.P.R.') were treated initially with chlorpromazine 5 mg. by intramuscular injection, the aim being to control spasms by subsequent similar doses at four- or six-hourly intervals, with intramuscular phenobarbitone sodium, gr. 1, in addition when spasms were still not controlled.

If there were uncontrolled spasms, laryngeal spasms, apnœic attacks with or without cyanosis, or episodes of flaccidity with or without hypothermia, tracheostomy was performed. If respiration was still inadequate as judged by clinical observations and $P_{O_2}$ estimations, these infants were curarized and I.P.P.R. was instituted.
When the trial was stopped at 28 cases the results were as follows:

Of 15 cases in Group 1 there were six deaths (40%); and of the 13 cases in Group 2 there were eight deaths (62%).

Only one infant in Group 2 was treated conservatively throughout and survived. All the remainder required tracheostomy, but in none did this procedure suffice. Two died after episodes of severe spasms and cyanosis before the need for I.P.P.R. was appreciated by the staff. The remaining 10 infants required curare and I.P.P.R., but only four survived.

We concluded that the conservative method with chlorpromazine and phenobarbitone to control spasms, selective tracheostomy and later I.P.P.R. has nothing to commend it as an alternative to immediate curarization and I.P.P.R. in severe tetanus neonatorum. The trial also confirmed our belief that tracheostomy without total paralysis and I.P.P.R. is inadequate.

**Trial of Assisted Respiration**

We use this term to mean I.P.P.R. without total paralysis, a technique we had previously employed in tetanus neonatorum, sometimes for 10 days or longer after stopping curare and before spontaneous breathing was re-established (Wright et al., 1961; Jackson, 1962; Mann et al., 1963).

This trial began at a time when we had more patients with severe tetanus neonatorum than respirators, and we were forced to watch infants die on conservative treatment. Two old Radcliffe Mark I respirators, unsuitable for the full I.P.P.R. régime, were available. We started by using them to treat infants admitted with continuous reflex spasms who then became flaccid, apnoeic and cyanosed on conservative treatment and whose prognosis we judged to be otherwise hopeless, since the mortality rate of such patients in our hands had previously been 99% (Wright, 1960). All were given antitetanus serum, antibiotics, chlorpromazine and phenobarbitone (as in Group 2 above); tracheostomy was performed and I.P.P.R. instituted without curarization, one limb of the suction connector being opened to the air through a small hole in the stopper.

The early results were encouraging (six survivors out of 10) so we proceeded to a longer trial. We could not use a randomized method of comparison with a second group treated by total paralysis and I.P.P.R. because respirators were not available. Although this was therefore not a strictly controlled trial, we admitted to it only those infants with frequent and severe spasms, known from our experience with 193 similar cases in the same unit to carry a mortality rate of over 90% when treated conservatively (Wright, 1960). At some time on conservative treatment such infants would almost always have continuous spasms, followed by apnoea and then gasping respiration. Other patients with severe tetanus neonatorum were being treated concurrently with Smith-Clarke and Mark V Radcliffe respirators and I.P.P.R., and these results are used for comparative purposes.

We attempted to treat 41 infants by means of assisted respiration, but in four we could not control the continuous spasms and we proceeded to full I.P.P.R.: two of these four died. Assisted respiration was employed for the remaining 37 infants: 20 died, giving a mortality rate of 54%. This compares favourably with the results of conservative treatment, but unfavourably when compared with the series of 40 cases treated concurrently by total paralysis and I.P.P.R. or when judged against our full series of 114 cases treated by this method (see Table).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Cases</th>
<th>No. of Deaths</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative</td>
<td>193</td>
<td>178</td>
<td>92</td>
</tr>
<tr>
<td>Assisted respiration</td>
<td>37</td>
<td>20</td>
<td>54</td>
</tr>
<tr>
<td>Total paralysis and I.P.P.R.</td>
<td>40</td>
<td>13</td>
<td>33</td>
</tr>
<tr>
<td>(concurrent series)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full series</td>
<td>114</td>
<td>41</td>
<td>36</td>
</tr>
</tbody>
</table>

It was not always possible to attribute a definite cause of death. In seven infants death could be attributed to mechanical causes (tube blocked or slipped out, and failure of the respirator), while bronchopneumonia was thought to be the main cause of death in eight others. One infant died of haemorrhage from a tracheal ulcer, while another died who had numerous cyanotic attacks on the respirator, histological sections of the brain-stem showing ghost nuclei and chromatolysis.

Those who survived were kept on the respirator for variable periods. Two were doing well after only two days and were then taken off. Another needed assistance for six days, but the remainder required assisted respiration for periods ranging from nine to 18 days.

**Discussion**

From the evidence of our own series of 114 cases of tetanus neonatorum treated by total curarization and I.P.P.R. it is seen that this method can offer
a chance of survival of about two in three. At present it appears to be the method of choice, but it is time consuming and expensive and may be impractical in most countries where tetanus is common.

An attempt to treat infants conservatively at first, followed by tracheostomy if there were episodes of acute respiratory failure or flaccidity, and followed if necessary by full I.P.P.R., failed since the results were worse than those of a control group treated by our standard method. We believe, however, that the method of assisted respiration we have described has certain potential advantages, particularly where the incidence of the disease is high and respiratory units are unable to cope with large numbers of cases because of shortage of staff. Failure of the respirator or blockage of the tracheostomy tube, if not immediately detected, is fatal within a few minutes when the infant has been curarized. With assisted respiration, however, there is more time for an overworked staff to discover and avert such a disaster, for the infant can continue to breathe spontaneously through the open end of the suction connector if the respirator fails; and when the tube begins to block warning is given by the infant's facial expression. We therefore intend to carry out a fully-controlled clinical trial comparing assisted respiration with total paralysis and I.P.P.R.

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