Assisted Respiration in the Treatment of Neonatal Tetanus*

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Conservative management of severe tetanus neonatorum is attended by a very high mortality (Tompkins, 1958; Wright, 1960a; Adams, Holloway, and Thambiran, 1964). Tracheostomy in addition to sedation has not been successful in preventing respiratory failure, which necessitated mechanical ventilation (IPPV) in about 90% of the patients described by Holloway (1967). Although IPPV has been shown to be the treatment of choice in this disease (Wright *et al.*, 1961; Smythe, 1963), this technique requires a team of medical personnel and an efficient nursing staff to cope with the special hazards introduced by the use of mechanical apparatus and the practice of tracheostomy. These facilities are not readily available in countries where tetanus occurs frequently, and modifications of IPPV would be of value in these areas.

This paper reports on a clinical trial which compares the management of severe tetanus neonatorum by two techniques: (a) tracheostomy, total paralysis, and IPPV; (b) tracheostomy, sedation, and assisted respiration. Assisted respiration is defined as IPPV without total paralysis, using chlorpromazine and phenobarbitone to control reflex spasms (Adams *et al.*, 1964).

Purpose of Present Trial

The trial of assisted respiration was designed to evaluate its use in the treatment of severe tetanus neonatorum. Encouraging results obtained in the earlier series (Adams *et al.*, 1964) seemed to indicate that a trial comparing controlled and assisted ventilation was necessary.

In theory, preservation of cough and laryngeal reflexes in infants receiving assisted respiration is an advantage. Aspiration pneumonia and retained secretions resulting in collapse of lung segments should occur less frequently than in curarized infants. Conscious babies are able to signify

respiratory distress by facial contortions, and in the event of machine failure can maintain unaided respiration for some time. Measurements of partial pressure of carbon dioxide in the arterial blood (P_aCO_2) need not be done routinely, as the infant's facial expression can be an index of respiratory sufficiency. Machine failure, which must be detected within seconds when the baby is totally paralysed, need not be fatal even after 10 or 15 minutes.

During controlled respiration curare is given for 10 days, but a state of partial paralysis exists for a further 2 to 3 days because decurarization in infants is a slow process. Some infants are capable of adequate breathing before this time as spasms can be much reduced in severity by the 8th day. Thus, a further advantage of assisted respiration is that it obviates the need for prolonged respirator treatment, since patients can be allowed to breathe on their own as soon as they are ready to do so.

If the period of artificial respiration were reduced, then extubation, a procedure often attended by difficulties in the infant, could be performed earlier. This form of treatment would make less demands on the medical and nursing staff, both of which are invariably insufficient in areas where tetanus occurs commonly.

Design of the Trial

Selection of patients. Only infants with frequent and severe, or continuous reflex spasms (Wright, 1960b), or cyanosis associated with spasms, as judged by 2 or more observers, were admitted to the trial.

Randomization. When a patient was chosen for the trial, treatment was determined by opening the next of a series of 60 sealed envelopes containing cards randomized for the following groups: (a) IPPV and high tracheostomy; (b) IPPV and low tracheostomy; and (c) assisted respiration and low tracheostomy.

A provision was made for changing the treatment to controlled ventilation if uncontrolled spasms, cyanosis, apnoea, or lung infection occurred during assisted respiration. It was felt that these complications could

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FIG. 1.—Diagram showing components of the tracheostomy assembly.

FIG. 2.—Diagram showing assembled tracheostomy components.

influence the prognosis adversely. Apnoea was defined as spontaneous breathing not being resumed when respirator assistance was discontinued at intervals during assisted respiration.

Standard Treatment in Two Groups

Tracheostomy. Tracheostomy as described by Mann, Jackson, and Holloway (1963) was performed on all infants. The operation in the IPPV group was performed at the level of the 2nd and 3rd tracheal rings on 20 infants, and at the level of the 5th and 6th on the remaining 20 patients. This was done to assess only whether the site of tracheostomy influenced extubation. Shortened nylon-reinforced tubes (3.0–3.5 mm. internal diameter) held in a special clamp (Sykes, 1960a) were used for tracheal intubation. The tracheostomy assembly is shown in Fig. 1 and 2.

Drugs. Initial sedation for all infants consisted of either 10 or 12.5 mg. chlorpromazine and 60 mg. phenobarbitone. A single dose of 50,000 units of tetanus antitoxin was given (Laurence and Webster, 1963). Procaine penicillin 150,000 units was given daily for 10 days but other antibiotics were prescribed when indicated. All drugs were given by intramuscular injection.

Feeding. The infants were fed with expressed breast milk at 3-hourly intervals through a polyvinyl

tube. During the first two weeks 120 ml./kg. per day was given; thereafter the feeds were increased to 150–220 ml./kg. per day. The feeds were reduced during the acute phase of the illness to prevent abdominal distension and gastric stasis.

If distension or stasis was present, a reduction in the volume, or omission of a feed was tried. If no improvement resulted, intravenous fluids (300 ml./24 hr.) were given and the milk feeds discontinued. After each 24–36-hour period, milk feeds in small quantities (30 ml. 3-hourly) were given. As absorption improved, the quantity of milk per feed was increased and intravenous therapy discontinued. From the second week onwards, when severe spasms had ceased, the infants were offered milk feed from a Belcroy feeder (Mann *et al.*, 1963).

Position of infant during artificial ventilation.

The infant was placed in a cot with a rolled napkin under his neck so that his head was at a lower level than his thorax. This position prevented pharyngeal contents flowing past an uncuffed tube into the trachea. The patient's position was changed hourly using the supine, right, and left lateral positions in rotation.

Adequacy of ventilation during IPPV. Adequate ventilation was judged clinically by good bilateral chest excursions and air entry, and the absence of cyanosis. Measurements of P_aCO_2 and P_aO_2 were also used as indicators. The inflation pressure and rate of the

respirator were set to maintain the P_aCO_2 between 25 and 40 mm. Hg. Initially, P_aCO_2 values were determined by a rebreathing method (Campbell and Howell, 1960), as modified for infants by Sykes (1960b). Later in the trial, blood gas analysis using a microtechnique (Desai *et al.*, 1967) was possible. These procedures were undertaken regularly during the first 10 days of treatment.

While P_aCO_2 levels were maintained easily at satisfactory levels, oxygen pressures were low when infants were ventilated with air (Holloway *et al.*, 1966). For this reason, the oxygen concentration of the inspired air was increased to 35%.

Technique of assisted ventilation. After tracheostomy, the respirator was connected to the tracheostomy assembly, the screw cap (Fig. 1 and 2) being removed or replaced with a perforated one. The ventilator was set to generate 15–20 cm. water pressure at rates between 25–35 cycles per minute. Although the volume of air during each cycle was reduced by the leak in the screw cap, the respirator continued to inflate the lungs. The patient adapted rapidly to an imposed pattern of ventilation slower than his own, and continued to breathe in between machine inflations. At intervals during the day, the respirator was disconnected to observe whether the infant could maintain spontaneous respiration.

Chlorpromazine, 10 or 12.5 mg., supplemented by phenobarbitone, 30 or 60 mg., was given to control reflex spasms. Chlorpromazine was given regularly at 4–6 hourly intervals, but phenobarbitone was used only when spasms were not adequately controlled during the first 5–6 days of treatment. The dose of chlorpromazine was reduced as spasms became less frequent and less severe.

During this time weaning from the respirator was tried. The ventilator was stopped if the patient's breathing appeared to be adequate. He was observed by a nurse sitting at the bedside. If cyanosis, rib recession, or apnoea occurred, his respiration was aided for another 24 hours before a further attempt at weaning was made.

'Failed' assisted respiration. Assisted ventilation begun in 20 patients was unsuccessful in 12 infants. This technique failed in 9 patients because severe or continuous reflex spasms persisted despite sedation. In addition to the spasms, apnoea, cyanosis, or tachycardia had been observed. Bronchopneumonia in 2 patients, and cyanosis, flaccidity, and bradycardia in one other were reasons for starting controlled respiration.

Controlled respiration. Forty patients were managed by the total paralysis régime (Mann *et al.*, 1963), instituted immediately after tracheostomy had been performed. The nursing care was identical to that in the assisted respiration group.

Results

Results are shown in the Table. The combined mortality in the assisted respiration group was 50%

(10 deaths). Of the 8 infants treated by sedation and assisted respiration, 5 (62%) died. There were 5 deaths (42%) in the 'failed' assisted respiration group.

In the group treated by controlled ventilation, the mortality was 25% (10 deaths). The over-all death rate in this study was 33% (20 deaths). The difference in mortality between assisted and controlled respiration groups was not statistically significant ($p > 0.05$).

TABLE

Mortality in 60 Cases of Neonatal Tetanus Treated by Two Methods

Treatment Group	No. of Patients	No. of Deaths	% Mortality
Assisted Respiration Group			
(i) Sedation and assisted respiration ..	8	5	62
(ii) 'Failed' assisted respiration ..	12	5	42
			50
Controlled Respiration Group (high and low tracheostomy groups) ..	40	10	25
Total	60	20	33

Discussion

Several problems occurred during treatment in both groups of patients. While most complications were common to both, the one peculiar to assisted respiration was the difficulty in controlling reflex spasms.

Control of reflex spasms. Reflex spasms were not well controlled by the use of chlorpromazine and phenobarbitone. Although the dose of chlorpromazine was almost ten times that recommended for infants, tetanic spasms were not adequately suppressed. Adams *et al.* (1964) used heavier doses of chlorpromazine than those given in the present study without achieving satisfactory control of reflex spasms.

The combination of chlorpromazine and phenobarbitone in high doses to suppress convulsions resulted in drowsiness and flaccidity. Thus, it was impossible to assess respiratory distress by the infant's facial expression. Severe spasms occurred even when the infant was flaccid. Physiotherapy, manipulation of the tracheostomy, feeding, collection of blood and gas samples, and injections induced spasms, in addition to those occurring spontaneously. Physiotherapy and tracheal suction were probably the most potent and frequent

stimuli. Consequently, these procedures were often inadequately performed or delayed until spasms abated after additional sedation.

Lung infection. The diagnosis of pulmonary infection during IPPV was made if abnormal signs (diminished air entry, crepitations and rhonchi) persisted after physiotherapy and if the tracheal aspirate became purulent. Fever was not a prominent feature of infection; this is not an uncommon observation both in premature infants (Crosse, 1957) and in severely ill full-term infants (Mann and Elliott, 1957). The value of radiography was limited because a portable unit had to be used and many films were not of diagnostic quality. Two-thirds of the infants in this study had clinical evidence of infection, but radiological confirmation was obtained in only 15 infants. In another 9 patients pulmonary infection was confirmed at necropsy.

Tracheostomy and intubation of the trachea for periods of a month or longer, repeated tracheal suction, and impaired ciliary action undoubtedly contributed to infection in the lungs. Recently, evidence to suggest that sepsis of the tracheostomy is a common cause of pulmonary infection has been presented (Bolton, 1966).

Tracheostomy. Proper care of the tracheostomy is one of the most important factors in reducing morbidity and mortality during respirator treatment. The complication of misplaced tracheostomy tube (total or partial dislodgement or displacement of the tube into the right main bronchus) occurred in 27 patients, while partial or complete obstruction was encountered in 19 infants. Obstruction of the tubes occurred despite attempts to maintain adequate humidification through humidifiers connected to the respirators, and through modified heat moisture exchangers incorporated in the tracheostomy assembly (Toremalm, 1960). A dislodged tracheostomy tube was the cause of death in 2 infants, and obstruction of the tube was responsible for 1 fatality.

Difficulty in extubation is the most common problem of tracheostomy in infants under 1 year (Holinger, Brown, and Maurizi, 1965). Of the 40 survivors in the present study, 24 were extubated when the attempt was first made. The average duration of tracheostomy in this group was 30 days. The remaining 16 infants presented problems in extubation; the mean duration of tracheostomy was 97 days, and extubation was achieved only after several attempts. In the group of patients treated by IPPV, there was no significant difference

($p > 0.4$) in the extubation time between the high and low tracheostomy groups. Cyanosis alone or a combination of cyanosis, rib recession, and inspiratory stridor accounted for the failure of extubation. Cyanosis alone probably indicated failure of the infant to adapt to laryngeal breathing, while the association of rib recession and inspiratory stridor with cyanosis suggested that tracheal weakening might be an added complication. Tracheal ulceration was severe in the majority of survivors, some of whom were nevertheless extubated successfully at the first attempt. Tracheal weakening, thought to be the result of severe ulceration, was commonly encountered in those infants in whom initial extubation failed.

Duration of artificial ventilation. For the reasons mentioned earlier it was hoped that treatment by assisted respiration might reduce the duration of respirator assistance. In this study there was no difference whether infants were treated by assisted or controlled respiration.

Modes of death. The modes of death were similar in each of the groups treated during the present trial. It was difficult to determine the exact cause of death in some patients, while in others it was likely that a combination of complications was responsible. In the former group were 3 infants who were found dead while being ventilated by normally functioning machines. Necropsy in all 3 infants revealed patchy atelectasis which was thought to be insufficient to account for the fatal outcome. The possibility of fatal brain-stem intoxication by tetanus toxin precipitating cardiac arrest could not be excluded (Kloetzel, 1963; Adams *et al.*, 1966).

In 10 infants mechanical faults (faulty respirator connexions, dislodged tracheostomy tubes, and airway obstruction) were associated with fatality, but in only 3 could death be attributed to the fault with reasonable certainty. Respiratory complications (infection and atelectasis) which could contribute to the hypoxia caused by the mechanical fault were present in the other infants.

Although mechanical faults were numerous in the controlled respiration group, it cannot be concluded that total paralysis contributed to death in all, because only 3 patients were curarized at the time of death. The remaining 4 fatalities occurred between the 21st and 40th days.

Place of assisted respiration in treatment of severe tetanus neonatorum. Although the requirements for carrying out assisted respiration

are similar to those for full IPPV, hopes that the former technique would make less demands on the medical and nursing staff were not fulfilled. Nor were the other predicted advantages realized, largely because reflex spasms were inadequately controlled. However, the results of this trial and those of Adams *et al.* (1964) show that the mortality is lower than with conservative treatment. On this evidence it is felt that assisted ventilation merits further investigation for use in those parts of the world where facilities for controlled ventilation are not available. The use of preparations other than chlorpromazine and phenobarbitone to control tetanic spasms may be more rewarding.

Summary

A clinical trial to assess the value of assisted respiration in severe tetanus neonatorum is described. 60 infants were allotted at random for treatment by (a) sedation and assisted respiration, or (b) total paralysis and IPPV. The results suggested that IPPV might be superior to assisted respiration, but the difference in mortality between the two groups was not significant.

It was difficult to control reflex spasms adequately with chlorpromazine and phenobarbitone in the group treated by assisted respiration. The other complications—severe tracheal ulceration, difficulty in extubation, lung infection—and the modes of death were common to both groups of infants.

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