TETANUS NEONATORUM*

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Despite the high incidence of tetanus neonatorum in South Africa a large series of cases has not been recorded. Friedlander,[1] and Klenerman and Scragg,[2] drew attention to the frequency of the condition in Durban, and there have also been reports from the other large centres.[3-5] During the 3-year period May 1956 to April 1959, 246 cases of tetanus neonatorum were admitted to King Edward VIII Hospital, Durban. Of these, 217, admitted to a special tetanus unit, are the subject of this report.

Race, sex and age. The average age on admission was 7 days. There were 198 African and 19 Indian infants, a ratio of approximately 10 to 1, and males outnumbered females by 129 to 89. The seasonal incidence was not striking, though there was a slight increase during the summer months.

Infection. The organism was rarely isolated, but the umbilicus was always presumed to be the source of infection, though in a few instances it did not appear septic.

Clinical features. The appearance of an established case is unmistakable. The face is pursed up in risus sardonicus and the limbs are partly flexed and stiff, with fists clenched around the thumb and toes plantar-flexed. There is usually some degree of opisthotonus and characteristically stiffness of the abdominal muscles. By placing one hand on the infant's abdomen and the other over the spinal muscles we have found the simultaneous contraction of these antagonistic muscle groups to be a sign pathognomonic of reflex tetanic spasms.

Diagnosis. This picture is so characteristic that we agree with Jelliffe[6] that there is no valid differential diagnosis, and differentiation from conditions causing convulsions in the neonatal period is easy. Some difficulty may occur in the minority of patients (7% in this series) who are not having typical reflex spasms when first seen. Infants suffering from meningitis, birth trauma or sclerema have shown sufficient resemblance to tetanus to be admitted with this diagnosis. Necropsies were performed in all deaths and in none of them was the clinical diagnosis of tetanus disproved.

Treatment. The general principles of treatment remained constant throughout the series. One hour after sedation a single dose of 50,000 international units (i.u.) of antitetanus serum was given intramuscularly. Benethamine penicillin, 300,000 i.u., was injected by the same route and repeated every third day unless signs of pneumonia supervened, when soluble penicillin or a broad-spectrum antibiotic was substituted. Local treatment of the umbilicus was restricted to cleaning with hydrogen peroxide and the application of merthiolate.

Feeding. When spasms had been reasonably well controlled, an intragastric rubber or polyethylene tube was passed by the nasal or oral route and feeds of expressed breast milk given. However, because poor absorption and aspiration of feeds occurred quite commonly, intravenous feeding by intermittent scalp-vein infusion has been recently attempted in a few infants. Most of these were hypothermic and their fluid requirements low, so that overhydration with the development of oedema was a constant danger. Difficulty in providing adequate nutrition during the stage of reflex spasms and rigidity resulted in death from marasmus and bronchopneumonia as late as the 5th or 6th week.

Sedation. Chlorpromazine has been compared with barbiturates and a mixture of barbiturate and chloral hydrate in two random trials which have been reported elsewhere.[7,8] Chlorpromazine (or acetylpromazine, another phenothiazine derivative) was used in combination with a barbiturate in a large number of cases in an attempt to reduce the toxic effects of both drugs. Table I shows the various combinations and the dosage of the drugs used. When once spasms had been controlled, particularly in the phenothiazine-barbiturate groups, the dosage required was usually at the minimum of the daily range.

TABLE I. DRUG COMBINATIONS AND DOSAGES USED

Drug	*Size of Dose (mg. intramuscularly)*	*Daily Range (mg.)*
Chlorpromazine ..	25	100—200
Phenobarb. sod. ..	60	60—300
Phenobarb. sod.* + chloral hydrate..	120 orally	240—720
Phenobarb. sod. .. + chlorpromazine	30—60 $12\frac{1}{2}$—25	30—180 $12\frac{1}{2}$—100
Phenobarb. sod. .. + acetylpromazine	30—60 5—10	30—180 5— 40

*300 mg. (intramuscularly) maximum for 1st 24 hours.

Tracheotomy. Tracheotomy was performed on 17 patients, 13 of whom were compared in a random clinical trial with a conservative method, a mixture of chlorpromazine and barbiturate for sedation being used in both groups.

DISCUSSION

Incidence. It is difficult to compare accurately the incidence of tetanus neonatorum in Durban and district with that elsewhere. Table II has been constructed from reports in the literature to emphasize the alarmingly high incidence at Durban. Table III shows the figures for the past year for neonatal deaths in King Edward VIII Hospital, Durban, indicating that tetanus is one of the major killers. Because of the rapid period of onset and early death if spasms are uncontrolled, it is likely that many more infants die before reaching hospital.

TABLE II. INCIDENCE OF TETANUS NEONATORUM

Area	*Period under Review*	*No. of Deaths or Cases*
Great Britain[9] ..	1938—47	36 deaths
United States[10] ..	1951—55	370 deaths
Singapore[11]	1946—50	254 cases
Ibadan[12]	1953—56	141 cases
Durban	1956—59	246 cases

Aetiological factors. Though no specific custom or method of delivery can be incriminated, about a third of the mothers gave a history of the application to the umbilicus of a 'black powder' obtained from a witch-doctor, and in a few cases *Clostridium tetani* has been cultured from this substance. Confinement on a mat in a hut or shack with an earthen floor, and the use of an unsterilized razor blade, pair of scissors or sharp reed for cutting the cord, has not surprisingly resulted in umbilical sepsis. However, quite frequently the

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TABLE III. NEONATAL DEATHS AT KING EDWARD VIII HOSPITAL FOR THE YEAR ENDED 30 JUNE 1959

		%
Prematurity	167	26·2
Tetanus	90	14·2
Asphyxia neonatorum and atelectasis	87	13·2
Bronchopneumonia	79	12·4
Gastro-enteritis	72	11·3
Miscellaneous	61	9·6
Haemorrhagic disorders	49	7·7
Cerebral haemorrhage	18	2·8
Meningitis and septicaemia	12	1·9
Total	635	

delivery took place in a location or domestic servant's quarters, and some of the mothers, occasionally with teaching or nursing experience, had obviously made some attempt at an hygienic confinement, or had even been delivered in hospital.

Prognostic criteria and criteria of severity. Spivey *et al.*[13] have used a 7-day incubation period as the critical level for prognosis. In the present series only 7% of deaths had an incubation period greater than 7 days and only 8% a period of onset of more than 24 hours. While a short incubation period and a short period of onset usually indicate a poor prognosis, as many as 24% of the recoveries had an incubation period of less than 6 days, and 30% a period of onset of under 6 hours. The most useful prognostic sign is the severity of reflex spasms on admission; only 1 of 64 cases in which they were *spontaneous* recovered, whereas 12 of the 15 infants who were not having typical spasms on admission survived. In 8 of these, reflex spasms as described above were never observed, but stiffness and facies were so typical that they are classed in a small group corresponding to mild tetanus in non-neonatal patients. The existence of this type of case, as well as another small group in whom spasms were only moderately severe, though together comprising less than 10% of the series, nevertheless emphasize the need to randomize when comparing different treatment groups.

Complications and mechanism of death. We have found considerable difficulty in deciding on the exact cause of death in the majority of cases. In general terms there would appear to be 4 groups, viz:

1. Uncontrolled spasms, usually in those dying within the first 48 hours, anoxia and exhaustion being largely responsible.
2. Respiratory failure, occurring between the 3rd day and the end of the 2nd week; the action of the toxin on the medullary centres, over-sedation and pulmonary infection and atelectasis being factors in its causation.
3. Marasmus with terminal bronchopneumonia between the 3rd and 8th weeks.
4. A miscellaneous group including tracheo-oesophageal fistula from prolonged tube feeding, neonatal peritonitis and aspiration of feeds.

Necropsies on those dying early usually show acute congestion of the lungs and liver with intra-alveolar haemorrhages and cerebral oedema. Histological evidence of bronchopneumonia was present in 37% of deaths, its incidence being directly proportional to the survival time. Two of the infants who recovered showed radiological evidence of compression of the mid-thoracic vertebrae.

Comparison of sedatives used. Table IV shows the mortality, and the average survival time, in those dying within 14 days in the different treatment groups. Experimentally the phenothiazine derivatives have been shown by Laurence and Webster[14] to have a potent antitetanic action in animals, and this has been confirmed clinically in non-neonatal tetanus.[7,8]

TABLE IV. COMPARISON OF DIFFERENT TREATMENT GROUPS

No. of Cases	*Treatment*	*Percentage Mortality*	*Survival Time* (days)*
17	Barbiturate	72	2·2
34	Chlorpromazine	94	2·0
20	Barbiturate + chloral hydrate	90	3·8
77	Chlorpromazine + barbiturate	76	4·0
34	Acetylpromazine + barbiturate	74	5·2
17	Tracheotomy	100	4·1
18	Miscellaneous	92	
217	(Recoveries 38)	82·5	

* Average survival time in deaths under 14 days.

In two clinical trials in the present series phenothiazine derivatives used alone have not been effective in controlling reflex spasms in 75% of cases, even if given in large doses, and the mortality has been high and the survival time short. In this respect we have not been able to confirm the findings of other workers.[15,16] When they have been combined with barbiturates, spasms have been controlled in all but 30% of cases, with some reduction in mortality, but in general death from uncontrolled spasms within the first 48 hours has been replaced by death from respiratory failure a few days later. In Table V our average mortality throughout the series is compared with that in other large series published recently. With one surprising exception,[20] in which full details of cases are not given, the similarity of the results with different conservative methods of treatment suggests that there is little to choose between the sedatives used.

TABLE V. COMPARISON OF MORTALITY WITH THAT IN OTHER LARGE SERIES

Series	*No. of Cases*	*Sedative used*	*Percentage Mortality*
Present series	217	acetylpromazine chlorpromazine barbiturate etc.	82·5
Jelliff *et al.*[17]	26	barbiturate	96
Spivey[13]	25	paraldehyde chloral hydrate	77
Loh Siew Gek[11]	174	paraldehyde chloral hydrate	92
Sarrouy *et al.*[18]	20	chlorpromazine barbiturate relaxant	80
Pinheiro[19]	256	barbiturate chloral hydrate myanesin	84
Tompkins[12]	141	paraldehyde chloral hydrate barbiturate	89·6
Earle *et al.*[20]	32	barbiturate chlorpromazine	25

In an attempt to reduce the mortality from respiratory failure, a random trial was conducted to assess the value of tracheotomy in preventing pneumonia and anoxia. The sedative used was a barbiturate-chlorpromazine combination and tracheotomy was performed under local anaesthesia, a metal tube being inserted through a window cut in the trachea. Oxygen was administered when required by means of a funnel or catheter but without artificial respiration or humidification of the inspired air. Only very severe cases were selected for

trial. Though the mortality was 100% in both groups, the survival time in the conservatively treated group was longer than in those on whom tracheotomy was performed, two cases in the former dying of late complications at 42 and 37 days respectively. It is apparent that some form of assisted respiration is necessary in the treatment or prevention of respiratory failure, and a trial is now in progress of total curarization, tracheotomy, and intermittent positive-pressure respiration. The constant medical and nursing attention required may alone be an important factor in reducing mortality, making it essential to randomize when assessing the value of this form of treatment. While our own and other preliminary findings[5] indicate a striking increase in survival time, care should be taken in confining such a radical procedure to severe cases; even if it is shown to be effective its use on a large scale will be limited by the expense and the need for specially trained personnel.

Preventive treatment. The only practical method of reducing the high death rate from this disease lies in its prevention. While this can only come with radical changes in the educational and socio-economic status of our African and Indian populations, a few measures may be advocated under present circumstances. A campaign by the local authorities should be directed against the current tribal customs of applying foreign material to the cord, and advice given on simple methods of hygiene at the time of delivery. Active immunization of mothers during pregnancy in an attempt to produce protective antibody levels in their newborn infants has been suggested,[21] and transplacental transmission has been demonstrated experimentally.[22] At least 2 inoculations are given at an interval of 6 weeks during pregnancy. Mothers delivered in hospital should be carefully instructed in the care of the cord; the development of tetanus in hospital-born infants who are discharged prematurely has been well documented,[10,13] and has occurred in this series. Lastly, in view of the high incidence and appalling mortality from the disease, it may well be that the administration of prophylactic tetanus antitoxin, which has become a routine in the treatment of surgical wounds, is as strongly indicated in newborn infants at risk in areas where tetanus neonatorum is endemic.

SUMMARY

Over 200 cases of neonatal tetanus have been admitted to a special unit of the Department of Medicine, King Edward VIII Hospital, Durban, during a 3-year period. The alarmingly high incidence of the disease in the area is emphasized, and possible aetiological factors mentioned. The diagnosis, clinical features, prognostic criteria and mechanism of death in these cases are discussed. Various forms of therapy are described, some of which were investigated in randomized clinical trials, and the value of phenothiazine derivatives and other drugs in the suppression of tetanic spasms compared. The literature is briefly reviewed and the problems of therapy discussed, with special reference to the control of reflex spasms and the treatment and prevention of respiratory failure.

In view of the high mortality, public-health measures are urged in an attempt to prevent the disease.

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