Short reports

Cause of death in tetanus neonatorum

Study of 233 cases with 54 necropsies

Tetanus with its high incidence and mortality is one of the greatest public health problems in most developing countries (Veronesi, 1967). The aim of this prospective study was to study hypothermia and bronchopneumonia, with the common complications of tetanus neonatorum, and also the cause of death.

Materials and methods

Tetanic infants in Sahr-Azad Children's Hospital were admitted to a special nursery built for these infants. Each case received horse antitetanic serum 5000 units IM, antibiotics (benzyl penicillin and kanamycin), and sedation with amobarbital 12.5 mg and chlorpromazine 2 mg, each 3-hourly via nasogastric tube. The dose was increased 3-hourly as necessary, the highest dosage used was amobarbital 112.5 mg plus chlorpromazine 10 mg each 3-hourly. Phytomenadione 1 mg was given on admission (Salimpour, 1971). Low reading thermometers have been used routinely since 1973. The infants are cared for by nurses aids.

The clinical part of the study began on 1 May 1971, and lasted one year. Of 125 consecutive cases of tetanus neonatorum admitted, 75 died of whom 31 had a sudden onset of hypothermia. 26 infants from this latter group had a chest x-ray which showed bronchopneumonia in 23. Of 53 children who were x-rayed, 31 showed evidence of pneumonia, of whom only 9 survived. In 2 cases there was diffuse bilateral pulmonary disease and in 5 there was bilateral lobular involvement. The remaining 24 patients showed unilateral pneumonia mainly involving the right lung, with a marked predilection for right upper lobe, the right lower lobe being rarely involved.

Bronchopneumonia was detected more commonly during the 4th and 5th days after admission, and rarely after the 7th day. The lowest temperature

was observed on the 3rd day in hospital. A sudden drop in the amount of sedation required and loss or diminished tetanal signs were associated with hypothermia (i.e. rectal temp. 35 °C or below) in most such infants, so that a sudden drop in temperature proved almost certain to indicate the onset of bronchopneumonia.

The pathological part of the study started on 1 June 1973 and lasted one year. 108 tetanic infants were admitted and studied during this period. 33 infants recovered (31%). Permission for necropsy was given in 54 cases (34 males, 20 females). The weight of the 54 on admission ranged from 2.2-4.0 kg (mean 3.05 kg). 14 had suffered hypothermia within the first 7 days in hospital (mean 3.1 days), of whom 11 had radiological evidence of bronchopneumonia. Bodies were kept at 0-1 °C until transferred to the Children's Medical Centre within 3 days for necropsy.

Results

Table 1 summarizes the necropsy findings. Con-

Table 1 *Necropsy findings in 54 cases of tetanus neonatorum*

Neonatorrham		Associated pathology	
Main findings	No. of cases	Pulmonary aspiration	Others
<i>Pulmonary pathology</i> (n = 46)			
Pulmonary haemorrhage	14	4	Ruptured inferior vena cava 1
Pulmonary haemorrhage + bronchopneumonia	7	3	Adrenal haemorrhage 3
Bronchopneumonia	21	13	Adrenal haemorrhage 2 Renal vein thrombosis 2
Pulmonary oedema	2	—	—
Aspirations only	2	(2)	—
<i>No pulmonary pathology</i> (n = 4)			
Hepatitis	1		
Omphalitis	1		
Cerebral haemorrhage	1		
Renal vein thrombosis	1		
Cause of death not determined (n = 4)	4		

gestion of the brain, liver, spleen, and other viscera was a common finding. Patent foramen ovale was found in 22, persistent ductus arteriosus in 15, and both in 10. 46 showed gross pulmonary pathology. Bronchopneumonia was found in 28 patients of whom 16 showed evidence of pulmonary aspiration and 7 also showed intrapulmonary haemorrhage. In 14 patients pulmonary haemorrhage was the main finding and in 4 of these there was evidence of aspiration. One patient in this group had a ruptured inferior vena cava. Adrenal haemorrhage was an associated finding in 3 patients with bronchopneumonia and pulmonary haemorrhage, and in 2 patients with bronchopneumonia. 2 patients showed only pulmonary oedema and 2 others showed evidence of pulmonary aspiration but no other pathology. In 4 cases necropsy failed to record any obvious cause of death. Pulmonary complications were not more common in infants who had persistent ductus arteriosus or patent foramen ovale. Regarding the 5 infants with adrenal haemorrhage (Table 2), there was no clinical clue to the onset of this complication.

Table 2 Details of 5 infants with adrenal haemorrhage

Weight on admission (kg)	Age at death (d)	Severity of tetanus	Hypothermia	Pneumonia	Other
2.35	8	Severe	+	+	—
2.5	11	Severe	+	+	—
3.3	11	Severe	+	+	—
3.0	13	Severe	—	—	—
3.3	33	Moderate	—	—	Laryngospasm before death

The cause of death was restudied in 3 groups (Table 3). Group A who died during the first 5 days of admission, group B who died during the second 5 days, and group C who died from day 11 onwards. This division was of particular interest in view of the high incidence of hypothermia and bronchopneumonia observed clinically during the first 5 days of hospital admission.

Table 3 Pathological findings related to time of death

Group	Time of death after admission (d)	Age at onset of tetanus (d)		Aspiration pneumonia	Broncho-pneumonia	Pulmonary haemorrhage	Other complications
		Range	Mean				
A (n = 33)	0-5	4-10	(7.3)	++++	+++	++	Cerebral haemorrhage 3 Adrenal haemorrhage 1 Renal vein thrombosis 1
B (n = 9)	6-10	5-12	(6.3)	++	++++	+++	Adrenal haemorrhage 3 Renal vein thrombosis 2
C (n = 12)	11+	4-12	(7)	+	++	++++	Atelectasis and pulmonary oedema 1

Group A 33 infants (21 male, 12 female). Age at onset of disease was from 4 to 10 days (mean 7.3 days). Aspiration pneumonia, bronchopneumonia, and pulmonary haemorrhage were the commonest causes of death in order of frequency. Additional findings were cerebral haemorrhage 3 (2 subdural), adrenal haemorrhage 1, renal vein thrombosis 1, biliary stasis 1, and fatty liver was found in 2 cases.

Group B 9 infants (6 male, 3 female). Age at onset of disease 5 to 12 days (mean 6.3 days). Apart from the 3 main causes of death as above, renal vein thrombosis was found in 2, desquamative alveolar lesion in 1, adrenal haemorrhage in 3 (1 thrombosis of medullary vessels, 1 renal vein thrombosis) fatty liver in 3, and ruptured inferior vena cava in 1.

Group C 11 cases (9 male, 3 female). Age at onset of disease 4 to 12 days (mean 7 days). Pulmonary haemorrhage was the commonest cause (9 cases). Biliary stasis and bronchopneumonia were present in 4 each, aspiration pneumonia in 2, atelectasis and pulmonary oedema 1, and bilateral adrenal haemorrhage in 1.

Thus, pulmonary haemorrhage and bronchopneumonia were the most common cause of death and equally fatal.

Discussion

The cause of death is not clear in most cases of tetanus, but the respiratory system is affected in the vast majority of patients (Adams *et al.*, 1969). Creech *et al.* (1957) attributed death to pneumonia in 42% of 171 patients who died at the Charity Hospital, New Orleans, between 1943 and 1956. Infections in the respiratory tract were the most common findings (49%), bronchopneumonia being the predominant lesion in 139 necropsies studied by Patel *et al.* (1965). Wright (1960) found bronchopneumonia in 38% of tetanic infants who died later than 48 hours. These infants were cold, flaccid with irregular gasping respiration, bradycardia, and peripheral cyanosis.

Several factors seem to contribute to the develop-

ment of pneumonia in this condition. (1) Spasms and convulsions, the main signs of tetanus, both cause contraction of the stomach, resulting in aspiration pneumonia. (2) Apnoea, the direct effect of tetanus toxin upon respiratory centres. Though most drugs used for sedation in tetanus cause respiratory depression, so that shallow respirations might contribute to pulmonary collapse and secondary infection, we see bronchopneumonia predominantly among convulsing infants.

To detect this severe and common complication, any clue would be valuable. Cough is rarely seen in the heavily sedated infant, and lung signs are hard to detect as tetanic manifestations tend to obscure them. Feeble respiratory movements, cyanosis, hypothermia, sudden loss of tetanic signs, and/or a drop in the amount of sedation required, have proved to be the best indications of developing bronchopneumonia. It is uncertain whether hypoxia, caused by chest infection, or the toxic effects of secondary infection increases the central nervous system's sensitivity to drugs, or suppresses drug metabolism in the liver and so causes drug accumulation and increased sedation of the infant.

Since infants were nursed flat in bed, the pathological distribution of pulmonary lesions could be an indication of a mechanical factor. Furthermore, the heavy sedation could be an important cause of respiratory depression leading to anoxia and eventually to pulmonary haemorrhage (mechanical ventilation was not used).

Most of these infants were under-fed to avoid aspiration of intragastric content. This state of dehydration could have contributed to development of 3 cases of renal vein thrombosis.

This study confirms the importance of pulmonary complications, in particular pneumonia and pulmonary haemorrhage, as causes of death in neonatal tetanus and emphasizes the need for adequate pulmonary ventilation and frequent change of position of the infant, and the hazard of oversedation. In addition, there are problems related to feeding which include aspiration of vomit and dehydration from too vigorous restriction of fluid intake.

Summary

Of 125 newborn infants with tetanus studied clinically, 75 died. Hypothermia and bronchopneumonia were the commonest events leading to death. A sudden drop in the amount of sedation required, loss of or diminished tetanic signs, and hypothermia usually indicated the onset of bronchopneumonia.

A later series of 108 cases with 75 deaths (54

necropsies) formed the basis of a pathological study. Pulmonary pathology was found in 46 out of the 54 necropsies: mainly pulmonary haemorrhage, aspiration pneumonia, and bronchopneumonia, particularly of the right upper lobe. Adrenal haemorrhage and renal vein thrombosis also occurred.

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Intestinal damage in rotavirus and adenovirus gastroenteritis assessed by D-xylose malabsorption

There is increasing evidence that rotavirus (Flewett *et al.*, 1974) is an important aetiological agent in acute infantile gastroenteritis (Davidson *et al.*, 1975). These viruses have been recovered from the proximal small intestine of infected infants in association with mucosal damage (Bishop *et al.*, 1973). Adenovirus has been implicated as a cause of gastroenteritis in sporadic cases (Ramos-Alvarez and Olarte, 1964), and in South African infants