Tetanus and its complications: intensive care and management experience in 150 Indian patients

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SUMMARY

A total of 150 patients were treated for tetanus in the tetanus ward of the J. J. Hospital, Bombay, between October 1983 and January 1986. The complications of tetanus and the mode of management in the presence of restricted resources are outlined. Intensive care, proper nutrition, early tracheostomy and ventilator support in severe tetanus were chiefly responsible for an overall reduction in mortality from 30 to 12%. The mortality in severe tetanus was reduced from 70 to 23%.

Sudden death due to unexpected cardiac arrest was an important complication in severe tetanus. We observed that an abrupt marked rise in rectal temperature ($> 107^{\circ}\text{F}$, 41.7°C), if undetected, could lead to sudden circulatory collapse and death. Well-marked hypoxaemia was observed in all patients with severe tetanus, and was related to ventilation perfusion inequalities and to an increase in the true venous admixture (increased Q_s/Q_t) in the lungs. Bronchopulmonary infections and the adult respiratory distress syndrome added significantly to morbidity and mortality. Autonomic cardiovascular disturbances included bradycardia alternating with tachycardia, and hypertension which was either labile, paroxysmal or sustained. Persistent hypotension was of ominous significance. Amongst numerous complications involving other systems, sepsis and septic shock were associated with a high mortality.

INTRODUCTION

Tetanus constitutes one of the major public health hazards in developing countries, and still carries a high morbidity and mortality. The problem in India is far greater than appears, because the organization for collecting health data is inadequate, and tetanus occurring in the many villages of this country largely goes unreported. The fatality rate in various reported series from different countries ranges between 20 and 60% (Kerr *et al.* 1968; Hollow & Clarke, 1975; Clifton, 1964; Nicholson, 1976). Until recently the overall mortality from tetanus in Bombay was between 25 and 30%, and the mortality from severe tetanus occurring in adults at the J. J. Hospital, Bombay, was well over 70%. This high mortality was in our opinion due to failure to grasp the importance of critical care and ventilatory support in severe tetanus. This paper presents the experience of

the authors in the management of 150 consecutive cases of tetanus (excluding tetanus neonatorum) admitted to the eight-bed tetanus ward at the J. J. Hospital, Bombay from October 1983 to January 1986.

MATERIAL AND METHODS

A total of 150 patients with tetanus were admitted to the special eight-bed ward of the J. J. Hospital, Bombay during a 27-month period from October 1983 to January 1986. The male:female ratio in the 150 patients was 4:1 and the age distribution was from 5 years to 74 years. There were 6 patients in the age group 5–12 years; 64 patients aged 13–29 years; 33 patients aged 30–39 years; 20 patients aged 40–49 years; 20 patients aged 50–59 years and 7 patients aged 60–74 years.

Allowing for minor modification, the severity of tetanus was graded according to the criteria devised by Ablett (1967).

Grade I (mild). Mild to moderate trismus, general spasticity, mild or no respiratory embarrassment; no spasm; little or no dysphagia – 49 patients.

Grade II (moderate). Moderate trismus and well-marked general spasticity; mild to moderate but short-lasting spasms; moderate respiratory embarrassment with tachypnoea < 30/min; mild dysphagia – 36 patients.

Grade IIIA (severe). Severe trismus and severe general spasticity; severe prolonged spasms both spontaneous and on stimulation; severe respiratory embarrassment with tachypnoea > 40/min; apnoeic spells – 36 patients.

Grade IIIB (very severe). Features of grade IIIA plus autonomic dysfunction – 29 patients.

The above grades were given when the disease was at its most severe and not necessarily at the time of admission or immediately prior to death. This is because some patients admitted with grade II, and at times even with grade I severity progressed within a varying period of time (1–6 days) to grade IIIA or grade IIIB.

All patients were given intensive care by a team of house doctors and by a small but dedicated group of nurses. Vital signs and ECG were monitored, and the mode of management, clinical observations, complications and results of investigations entered on a standard proforma.

Serial investigations were as with any critically ill individual and included blood chemistry, serum electrolytes, cultures of blood, tracheal aspirates, frequent chest X-ray, serial blood gas and acid–base analysis. A central venous line (generally percutaneously through the subclavian vein) was inserted and maintained in all grade II and grade III patients for the purpose of administering i.v. fluids and drugs and also to measure the central venous pressure. A Swan Ganz catheter was inserted in 12 patients with very severe tetanus (grade IIIB) to help in management and to allow haemodynamic studies and measurement of mixed venous oxygen content. The Q_s/Q_t ratio and the venous admixture was determined in these patients by the conventional formula

$$Q_s/Q_t = C_{c,O_2} - C_{a,O_2} / C_{c,O_2} - C_{v,O_2}$$

(where C_{c,O_2} was the O_2 content of capillary blood; C_{a,O_2} was the O_2 content of arterial blood; C_{v,O_2} was the O_2 content of mixed venous blood.

The V_D/V_T ratio was determined in 39 patients with severe tetanus who were given ventilatory support, by using the formula of Lavesquel & Rosenberg (1975).

$$V_D/V_T = \frac{\text{measured ventilation per minute } (V_M)}{\text{predicted ventilation per minute } (V_E)} \times \frac{P_{a,CO_2}}{40} \times 0.33.$$

Mode of management

All patients were given 10000 units horse antitetanus serum intravenously, after a test dose, on admission. They were also given 1 megaunit of crystalline penicillin 6-hourly for 5 days. Wounds were dealt with by a surgical unit on basic surgical principles with cleaning, debridement and drainage being done after administration of antitoxin. Patients were managed on three basic treatment regimes depending on the severity of disease.

(1) Regime S. (sedation). This was used for grade I tetanus and 9 of the 36 patients of grade II tetanus. Sedation was achieved by the use of diazepam 40–150 mg/day orally or intravenously.

(2) Regime ST (sedation + tracheostomy). This was used for 26 (of 36) patients with grade II tetanus and 26 (of 36) patients with grade IIIA tetanus.

(3) Regime STR (sedation + tracheostomy + mechanical ventilator support). This was the regime employed for all 29 grade IIIB patients and 10 of the 36 grade IIIA patients. The use of ventilator support was coupled with the induction of neuromuscular blockade or paralysis by the use of a curare-like drug. The drug available to us was gallamine, 20–40 mg i.v. being administered every $\frac{1}{2}$ to 1 h. Neuromuscular blockade often had to be continued for over 3–4 weeks.

Our mode of management in severe grade III tetanus was constrained by paucity of material resources (to quote an example, there were just two ventilators available in the eight-bed ward), and by the paucity of trained nursing staff (two staff nurses on duty at any one time in the eight-bed ward). The indications for inducing neuromuscular paralysis with the use of ventilator support that we followed would therefore interest doctors in developing countries working under similar restraints. These indications were as follows.

(1) All patients with grade IIIB tetanus.

(2) All patients with grade IIIA whose spasms were uncontrolled by i.v. diazepam. (The dose of diazepam was pressed to a point where the patient was still arousable; it was never pushed to the point where the patient could not be fairly easily aroused or was rendered unconscious.)

(3) Patients with grade IIIA whose breathing between muscle spasms was very shallow, whose P_{a,O_2} was < 60 mmHg whilst on 5–8 l/min of tracheal oxygen, or who developed a respiratory complication – atelectasis or pneumonia.

(4) Complications requiring ventilator support, e.g. septic shock. This was the reason for the use of a ventilator in one patient with grade I tetanus and in one with grade II tetanus.

In addition to critical pulmonary care, critical care of the patient as a whole was vital in reducing the morbidity and mortality in tetanus. Particular stress was laid on the following.

(a) Nutrition and fluid electrolyte balance. A daily caloric intake of 3500–4500 calories was provided through the nasogastric tube from the day of admission in moderate and severe tetanus.

(b) Circulatory support in critically ill hypotensive patients – either using a volume load or a slow i.v. infusion of dopamine at 5–10 $\mu\text{g/kg/min}$.

(c) Use of appropriate extra sedation or small ‘titrated’ doses or oral beta blockers in grade IIIB tetanus.

(d) Prevention, early detection and prompt control of infection and sepsis with appropriate antibiotics.

(e) Detecting (by frequent monitoring) and treating (by physical methods and the use of paracetamol) hyperpyrexia.

RESULTS AND DISCUSSION

Mild (grade I) tetanus posed no serious problem except when complicated by a serious septic wound that in itself could lead to death, as was seen on one of our patients. It needs to be stressed, however, that grade I tetanus can graduate over a period of a few days to grade II or even grade III, and therefore needs careful observation.

The course and management of moderate and in particular severe tetanus is often bedevilled by complications that can involve almost any organ or system of the body. Many complications are inherent in the management of any critically ill individual who requires a tracheostomy with prolonged ventilator support, who requires prolonged neuromuscular blockade extending for 3–6 weeks and who is severely catabolic through the greater part of the illness. The complications observed and discussed below pertain only to grade II and grade III tetanus (101 patients).

Respiratory complications

The most frequent pulmonary complications were infections, atelectasis, and complications related to tracheostomy. In fact the first five complications listed in Table 1 were incidental to prolonged mechanical ventilation in febrile critically ill individuals; their incidence could be reduced by more meticulous patient care. Laryngeal spasm is not listed in Table 1; it occurred in almost all patients with grade II and every patient with grade III tetanus. The importance of an early tracheostomy in such patients was brought home to us by death in one patient (before a tracheostomy could be done) from prolonged laryngeal spasm.

The organisms responsible for bronchopulmonary infection and tracheostomy wound infections were *Klebsiella* sp. (40%), *Pseudomonas aeruginosa* (32%), *Enterobacter* sp. (15%), pneumococcus (5%), staphylococcus (5%) and other organisms (3%). Respiratory infections usually responded to appropriate antibiotic therapy, but even so were responsible for a great deal of morbidity and significant mortality in tetanus.

An unusual respiratory complication observed in eight patients (four with grade II and four with grade III tetanus) was sudden episodes of severe respiratory distress not associated with increase in hypoxia or carbon dioxide retention, nor with bronchospasm, blocked airways or any increase in muscle spasms. The explanation for these episodes was obscure, and suggested a form of release of inhibitory control over the respiratory centre probably due to the action of the tetanus toxin.

The adult respiratory distress syndrome (ARDS) was observed in four patients

Table 1. *Respiratory complications in tetanus*

	Number of patients
Bronchopulmonary infection	
Pneumonia and bronchopneumonia	20
Lung abscess	1
Pyopneumothorax with a bronchopleural fistula	1
Significant pulmonary atelectasis	17
Pneumothorax (iatrogenic)	2
Pneumomediastinum	1
Complications related to tracheostomy	
Serious stomal infection	6
Fatal bleed due to perforation of the innominate artery	1
Episodes of unexplained respiratory distress	8
Adult respiratory distress syndrome	4

with grade III tetanus. In two it occurred early in the natural history of tetanus (within 5 days) and in the absence of infection, sepsis or other causes of this syndrome. It was therefore conceivably related to tetanus. In the remaining two patients ARDS occurred as a complication of severe sepsis.

Disordered pulmonary function has been reported in 25 adult cases of mild to moderate tetanus (Kokal *et al.* 1984). The detailed results of our lung-function studies in severe tetanus are being reported separately. The relevant features observed in this study were:

(a) the presence of significant hypoxia ($P_{a,O_2} < 60$ mmHg in all patients with severe tetanus;

(b) an increase in the alveolar arterial gradient whilst breathing air in all grade IIIA and grade IIIB tetanus – mean gradient 41.76 ± 0.07 s.d.;

(c) an increase in the true venous admixture (Q_s/Q_t) on 100% oxygen in 12 patients with grade IIIB tetanus on whom this was measured (mean value of Q_s/Q_t 21.75 ± 5.94 s.d.);

(d) an increase in V_D/V_T ratio to a mean of 0.477 ± 0.11 s.d. in the 39 patients with severe tetanus who received ventilator support (Fig. 1).

The hypoxia, increase in alveolar arterial oxygen gradient, increase in shunt and the V_D/V_T ratio were observed at a time when no respiratory complication was manifest clinically or radiologically.

Cardiovascular complications in severe tetanus

These were particularly observed in grade IIIB tetanus. Sustained sinus tachycardia of between 150 and 200/min occurred at some stage in every patient with severe tetanus. Persistent hypotension (systolic B.P. < 90 mmHg) occurred in 18 patients, and in our study was more frequent than sustained hypertension, which occurred in 5 patients. Episodic hypertension was however very frequent, and to an extent was present in almost all patients with severe tetanus. A significant rise in blood pressure was evident on suction, physiotherapy and during nursing care (e.g. turning the patient). Sudden cardiac arrest occurred in 6 patients; 2 of these were successfully resuscitated with ultimate survival, whilst 4 died. The cause of cardiac arrest in tetanus remains perplexing. We feel that sudden almost paroxysmal hyperpyrexia is an important cause of sudden

Fig. 1. Q_s/Q_t (%) in 12 patients with grade IIIB tetanus. V_D/V_T ratio in 39 patients with severe tetanus on mechanical ventilation.

circulatory collapse. The latter follows a sudden rise in rectal temperature to $> 107^\circ\text{F}$ (41.7°C); this rise is easily missed as the axillary temperature is not unduly raised. We have prevented disasters after being aware of this problem. Paroxysmal supraventricular tachycardia occurring in short bursts was observed in five patients; ventricular extrasystoles occurred frequently but no ventricular tachycardia was observed. An alternating bradycardia (pulse rate $< 60/\text{min}$)–tachycardia (pulse rate $> 150/\text{min}$) syndrome of sinus origin was observed in ten patients with grade IIIB tetanus.

Severe sweating occurred in 25 patients, hyperpyrexia (rectal temperature $> 106^\circ\text{F}$, 41°C) in 15 patients. Peripheral vasoconstriction as judged by cold peripheries was observed in six patients, and in combination with persistent hypotension was of ominous significance.

Many of the clinical features described above have been attributed to overactivity of the autonomic nervous system, in particular to excessive sympathetic discharge (Kerr *et al* 1968; Hollow & Clarke, 1975; Tsueda, Oliver & Richffer, 1974; Corbett, 1969; Kerr, Corbett & Spalding, 1969; Kanarek, 1973).

The management of persistent hypotension involved use of a fluid challenge and/or the use of dopamine support. The effect of a fluid challenge on blood pressure was often transient, and excessive volume overloading was avoided because of the danger of ARDS, particularly in patients with sepsis. Sustained hypertension was managed by the use of a small dose of propranolol (10 mg thrice daily). Exquisite sensitivity to beta blockers was observed in most of these patients, necessitating meticulous monitoring of heart rate and blood pressure.

Table 2. *Cardiovascular and autonomic complications in grade III A and III B tetanus*

	Number of patients
Sustained tachycardia (> 150)	38
Hypotension (systolic < 90 mmHg)	18
Extreme sensitivity to β -blockers	4
Hypertension	5
Episodic labile hypertension	10
Paroxysmal SVT	5
Ventricular extrasystoles	15
Sudden cardiac arrest with death	4
Sudden cardiac arrest with complete resuscitation	2
Suspected pulmonary embolism	1
Hyperpyrexia (> 106° rectal)	15
Severe sweating	22
Vasoconstriction (clinical)	11

Table 3. *Other complications in tetanus*

Gastrointestinal		Fluid electrolyte disturbances	
G.I. bleeds	45	Hypokalaemia	15
Ileus	30	Hyponatraemia	10
Diarrhoea	20		
		CNS complications	
Septic shock with DIC	4	Unexplained coma	2
		Peripheral neuropathy	4
Renal failure			
Related to sepsis	4	Miscellaneous	
Related to gentamicin	1	Thrombophlebitis	15
		Bed sores	8
Pre-renal and mixed causes	10	Corneal abrasions	8
		Fracture thoracic vertebra	3

Supraventricular arrhythmias spontaneously reverted to sinus rhythm and required no treatment. Careful monitoring and symptomatic treatment of hyperpyrexia was an important feature of management.

Other complications

These were varied and involved many organ systems. They are summarized in Table 3. The most frequently observed were gastrointestinal complications and the most dreaded were septicaemia and septic shock. The organisms cultured from the blood in patients with septicaemia were *Klebsiella* sp. and *Pseudomonas aeruginosa*. The sepsis was iatrogenic, the potential sources being the tracheostomy wound, pulmonary infection, a contaminated central venous line, an infected bedsore, or thrombophlebitis in a peripheral vein. Coma in patients unrelated to the use of diazepam was difficult to explain. In one, recovery occurred after 4 days; in the other, deep coma persisted for 26 days before death. Autopsy did not throw light on the cause of coma. Anaemia and hypoproteinaemia were frequently observed in long critical illnesses.

Table 4. *Mortality figures*

	Treatment regime			Number of patients	Number of deaths
	S	ST	STR		
Grade I	48	Nil	1	49	1
Grade II	9	26	1	36	2
Grade III	Nil	26	39	65	15
Total	57	52	41	150	18

Overall mortality rate 12%, mortality rate in Grade II, Grade III 17%.

Mortality

The single most striking feature in our study was a sharp reduction in overall mortality to 12% (18 deaths out of 150 consecutive patients) compared to the earlier existing overall mortality of 30% in the same hospital's tetanus ward. Our mortality for combined moderate (grade II) and severe (grade III) tetanus was 17% and for severe tetanus 23%. This is a sharp improvement from the earlier near-70% mortality for severe tetanus from the same ward. It is difficult to compare mortality figures in tetanus reported by different workers in different parts of the world. The grading of tetanus is clinical, and unquestionably the line between moderate and severe tetanus is not always sharp. There is a possibility that most patients considered by us to be grade II would be placed by workers who see tetanus less commonly as grade III. It is otherwise difficult to understand why in a series gathered in 1961-77 by Edmondson & Flowers (1979) at Leeds Infirmary, UK, 90 out of 100 patients were graded as severe and 10 as mild, with no in-between or moderate (grade II) tetanus observed. Trujillo *et al.* (1980) reported an overall mortality of 11% in 232 patients studied over a 10-year period in Venezuela. Here again the grading of severe tetanus was chiefly related to muscle spasms that interfered with respiration. All our patients graded as moderate (grade II) would qualify under severe (or grade III) tetanus if judged chiefly by this criterion.

The reasons for improved mortality in our present series were: (1) early tracheostomy in grade II and III tetanus; (2) early ventilatory support in severe tetanus; (3) critical intensive care in patients with moderate and severe tetanus; (4) maintenance of adequate nutrition through a nasogastric tube in a disease known to cause excessive catabolism; (5) prevention, prompt recognition and treatment of complications occurring in the course of treatment.

Cause of death

The age, severity of tetanus, treatment regime used, and the cause of death in each of the 18 patients who died are tabled below in Table 5.

Nine (the first nine listed in Table 5) of these 18 deaths could be directly attributed to tetanus, and nine (10-18 listed in Table 5) could not. Sudden death due to cardiac arrest was the most important and the single most frequent mode of death directly due to severe tetanus. It was not related to tracheal suction nor was it preceded by bradycardia as reported by other workers (Kerr *et al.* 1968; Benedict & Kerr, 1977). Though the cause of sudden death is obscure, its

Table 5. Cause of death in the 18 patients who died during the study

Cause of death	Age and sex	Severity	Treatment regime*	Time since admission days
1 Sudden death	26 M	III B	STR	10
2 Sudden death	55 F	III A	ST	4
3 Sudden death	60 F	III B	STR	7
4 Sudden death	50 F	III A	STR	26
5 Hypotension ; ? terminal pulmonary embolism	32 M	III B	STR	3
6 Hypotension with respiratory distress	48 M	III B	ST	1
7 Hypotension with ARDS	40 F	III B	STR	7
8 Asphyxia following laryngeal spasm	28 M	II	S	1
9 Prolonged unexplained coma with terminal pneumonia	30 F	III B	STR	37
10 Generalized septicaemia causing shock	72 M	III B	STR	8
11 Bronchopneumonia/ARDS/DIC	20 M	III B	STR	30
12 COPD with bronchopneumonia with septic shock	55 M	III A	STR	11
13 Lobar pneumonia (present on admission) with shock	40 M	III A	STR	6
14 Bronchopneumonia + septicaemia with massive tracheal haemorrhage	23 M	III B	STR	15
15 Complete heart block with shock	52 F	III B	STR	1
16 Primary wound sepsis with shock	30 M	I	STR	3
17 Primary wound sepsis with shock	50 F	II	STR	3
18 Primary wound sepsis with shock	50 M	III A	STR	3

*S, sedation; ST, sedation and tracheostomy; STR, sedation, tracheostomy and mechanical ventilation support.

association with undetected hyperpyrexia has already been stressed. Three of the nine deaths directly attributable to tetanus were related to hypotension and shock. In two of these the severity of tetanus was responsible for hypotensive shock and in the third the cause of shock was massive pulmonary embolism. The most important cause of death not directly attributable to tetanus was infection and septic shock that was iatrogenic or that occurred during the course of management of severe tetanus.

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