Not to be forgotten: tetanus
不要忘記：破傷風

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We describe a patient presenting with altered mental state, generalised stiffening of the body and limbs as a result of acute generalised tetanus. Discussion of the clinical manifestations, diagnosis, initial management in the emergency department and complications is put forth. *(Hong Kong J Emerg Med*. 2007;14:119-124)

我們描述一名因急性全身化破傷風而全身及肢體僵硬，呈現神智不清的病者。並討論臨床徵象、診斷、急症室初步治理及併發症。

**Keywords:** Acute disease, *Clostridium tetani*, tetanus, tetanus toxin

**關鍵詞:** 急性疾病、破傷風梭狀芽胞桿菌、破傷風、破傷風毒素

**Introduction**

Tetanus was first described in Egypt some 3,000 years ago and it was common in the ancient world.¹ The clinical manifestations of the disease are caused by the action of a potent neurotoxin, tetanospasmin, produced by *Clostridium tetani* during its growth in the body at the site of injury. The disease can be prevented by immunisation with tetanus toxoid.² The latter was introduced in the 1940s and since then the incidence of tetanus has declined in many developed countries where effective immunisation programmes have been implemented.²⁻⁴ For that reason, residents of these countries are rarely if ever afflicted with this scourge with high mortality.⁵ We recently treated a patient with acute generalised tetanus presenting to the emergency department.

**Not to be forgotten: tetanus**

A 38-year-old unemployed Indonesian Chinese presented to the Department of Emergency Medicine in February 2005 with symptoms of altered mental state (Glasgow Coma Scale Score: 9), intermittent stiffening of all four limbs and trunk, stiffness of the jaw and inability to ingest food and fluids as well as foaming at the mouth.

He had a history of hypertension but defaulted therapy. Eleven days ago in Indonesia, he had been involved in a road accident and had sustained injuries to his lower limbs. He was transported to Singapore from the Indonesian Island of Tanjung Batai on a ferry with no ventilatory or other medical support en route.

When transferred to the resuscitation room, his vital signs were: blood pressure 167/111 mmHg, heart rate 109/min, temperature 37.3°C and oxygen saturation of 89%. He was non-communicative, generally stiff with opisthotonous and trismus. There was a lot of saliva and secretions in his oral cavity which required immediate suctioning. Muscle spasms and stiffening

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were brought on with stimulus. There were healing abrasions with surrounding bruises over his left foot and knee (Figures 1 & 2).

In view of his poor oxygenation, preparation for intubation was made. As he had trismus, a small dose of diazepam was given as premedication. Rapid sequence intubation was done with the use of intravenous etomidate and suxamethonium. He was then paralysed and sedated with rocuronium and diazepam respectively. The other medication administered included intramuscular (IM) tetanus toxoid 0.5 ml, intravenous (IV) crystalline penicillin 5 MU, IV metronidazole 500 mg, IV magnesium sulphate, IV diazepam (a total of 30 mg in divided doses) and Human Tetanus Immunoglobulin 500 IU.

His electrocardiogram (ECG) showed sinus tachycardia and the initial chest X-ray showed early consolidation in both perihilar regions. The results of the other initial investigations (Table 1) showed acidosis and elevated white cell count. His wounds were cleaned and dressed.

The patient was admitted to the Intensive Care Unit (ICU) for further management after initial stabilisation. In the ICU he had a stormy course where he developed labile blood pressure, paralytic ileus (which resolved spontaneously) and pneumonia which resulted in fever. As his abrasions were minor, clean and already healing, no debridement was performed. Tracheostomy was also done in view of the prolonged period of ventilator support. (The patient was ventilated for a total of 14 days). He progressively improved and responded to therapy and was discharged well on the 21st day.

Discussion

There are ten distinct serological types of Clstonium tetani and only some of these strains produce tetanospasmin at the end of the germination phase under anaerobic condition. The spores are highly resistant and can survive exposure to phenol, merbromin, boiling water and many chemical disinfectants.1

Tetanus is now encountered largely in underdeveloped, overcrowded countries where there are no

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Table 1. Results of the initial investigations in the emergency department

| Arterial Blood Gas (on arrival): |
| pH: 7.006 (7.35–7.45) |
| pCO₂: 57.9 (35–40 ) |
| pO₂: 84.4 (95–100) |
| Base excess: -17.0 (-2→+2) |
| HCO₃: 14.2 (22–25) |
| O₂ saturation: 90% (95–100) |

| Cardiac Markers: |
| All in the normal range |

| Full Blood Count: |
| Total white cell: 18.38 x 10⁶; Neutrophil: 79.3%, Lymphocyte: 12.8% |
| Haemoglobin: 18 g/dl |
| Platelet: 267 X 10⁹ |

| Electrolytes/Renal Panel: |
| All in the normal range |
effective immunisation programmes.\textsuperscript{6} \textit{C. tetani} spores are normally introduced into the body through cuts, wounds or burns. The incubation period ranges from a few days to three weeks. Since these spores cannot germinate until oxygen is depleted, the focal anaerobic conditions in wounds with tissue necrosis and foreign bodies serve as suitable sites. The longer incubation periods are usually associated with injury further away from the central nervous system, while centrally located, cephalic wounds may produce symptoms after a shorter incubation period. The interval between the injury and the onset of symptoms is another determinant of severity. The cases presenting within one week of injury are usually more severe with higher case fatality rate.\textsuperscript{7-10}

\textbf{Clinical manifestations}

Four different forms of tetanus have been described:\textsuperscript{1,5,10,11}

1. \textbf{Local-tetanus}

This is an uncommon form of the disease where persistent contractions of the muscles occur in the same anatomic area as the injury. These contractions persist for many weeks before gradually subsiding. Local tetanus may precede the onset of generalised tetanus. Only about 1\% of these cases are fatal.

2. \textbf{Generalised-tetanus}

This is the commonest type, representing 80\% of the reported cases. It usually presents with a descending pattern, the first sign being trismus (lockjaw), followed by stiffness of the neck, difficulty in swallowing, rigidity of the abdominal muscles and then, the rest of the muscle groups. The other symptoms include elevated body temperature, sweating, labile blood pressure and episodic tachycardia. Spasms can continue up to three weeks and complete recovery may sometimes take months. Our patient had this form of tetanus.

3. \textbf{Cephalic-tetanus}

This is a rare manifestation and occurs with middle ear infections or otitis media following head injury. There is involvement of the cranial nerves, especially those of the facial area.

4. \textbf{Neonatal-tetanus}

This is generalised tetanus in the newborn infant. These are infants born without protective passive immunity, as the mothers are not immune. It usually occurs through infection of the unhealed umbilical stump, particularly when it has been cut with a non-sterile instrument. This form of tetanus is common in developing countries.

\textbf{Diagnosis}

The diagnosis of tetanus is most frequently made on clinical manifestations rather than on biologic findings. This is relatively easy in areas where tetanus is common, but may be delayed in the developed world where cases are infrequent.\textsuperscript{1}

In addition to trismus, there may be marked hypertonicity of muscles, hyperactive deep tendon reflexes, clear mentation, low grade temperature, absence of sensory involvement, local or generalised paroxysmal spasms, as well as evidence of an injury or wound in the past two weeks.\textsuperscript{1,4,5}

Bacteriologic studies confirm the presence of \textit{C. tetani} in only a third of all patients with clinical manifestations of the disease. The isolation of the organism from contaminated wounds does not mean that the patient will contract or has contracted tetanus.\textsuperscript{1,4}

Laboratory investigations usually show mild leucocytosis. Cerebrospinal fluid is normal but the pressures may be elevated by the muscle contractions. Electromyography and electroencephalography are normal and not helpful in the diagnosis. The commonest electrocardiographic change is sinus tachycardia, and T wave inversion may be seen in cases with cardiac involvement.\textsuperscript{12}

The differential diagnoses to be considered include: strychnine poisoning (which is usually associated with homicide or suicide), dystonic reaction such as that seen with phenothiazines (these patients usually have tremors, athenazines, trismus and also torticollis) and rabies (this can also affect the muscles of respiration and deglutition, but trismus is classically
absent). Alveolar abscess can also present with trismus and in children under the age of 2 years, hypocalcaemic tetany should be considered as well.

**Treatment and management**

Tetanus has been aptly described as a third world disease where the treatment requires first world technology, as heavy sedation and ventilatory support represent the mainstay of management and these are not readily available in many third world and developing countries where the disease is prevalent.\(^1\)\(^2\)\(^3\)

The main objectives of the therapies carried out for the tetanus patient are as follows:\(^1\)\(^2\)\(^4\)

1. The provision of supportive care until the tetanospasmin that is fixed to tissues has been metabolised;
2. Neutralising the circulatory toxins and;
3. Removing the source of tetanospasmin.

The acute tetanus patient is managed in the intensive care unit setting. A dark quiet room will help minimise stimuli that trigger paroxysmal spasms and proper positioning can help reduce aspiration pneumonia. Electrolytes and blood gas results guide intravenous fluid therapy.

Penicillin is the standard therapy in most parts of the world and the recommended dose is 100,000 to 200,000 IU/kg/day for 7-10 days. Lately however, metronidazole has been considered the first line drug and a superior alternative to penicillin, which has been noted to cause myoclonic convulsions in many. The recommended dose of metronidazole is 500 mg intravenously (or 400 mg rectally) every 6 hours for 7-10 days.\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)

Aggressive management of the muscle spasm is the cornerstone of therapy. This is achieved with the use of central nervous system (CNS) depressants that produce muscle relaxation and sedation (the higher doses can cause depression of respiratory function), or neuromuscular blocking agents (NMA) such as d-tubocurarine or pancuronium bromide. The CNS depressants include the short acting barbiturates such as secobarbital and phenobarbital and these are used in combination with diazepam, which helps with the control of seizures if any. The use of NMA makes it compulsory for the patient to be mechanically ventilated for proper airway management and to prevent aspiration pneumonia.\(^1\)\(^7\)

The judicious use of tracheostomy is important in maintaining adequate ventilation among patients with opisthotonus and involvement of back and thoracic muscles. It helps to ensure good bronchopulmonary toilet.

Magnesium is a physiological calcium antagonist. There is significant correlation between depression of neuromuscular transmission and serum magnesium concentration. This dose dependent and controllable effect is a great advantage that magnesium has over the use of muscle relaxants. It is used in the control of spasms in eclampsia and the safety of the therapeutic range (2-4 mmol/l) has been well-established. Areflexia can be useful as a monitor, as it only happens at levels over 4 mmol/l and muscle paralysis will occur at levels over 6 mmol/l. It is therefore possible for magnesium to control the spasms of tetanus without paralysis and thus, reducing the need for ventilation. The recommended loading dose is 5 grams of intravenous magnesium sulphate over 20-30 minutes and this is followed by an infusion of about 2 grams per hour. The patient, who will be in ICU, will have the vital signs, pulse oximetry and ECG monitored, whilst the patellar reflex may serve as a clinical monitor of the magnesium levels. Serum calcium must also be monitored.\(^7\)\(^10\)

Cardiovascular disturbance is a frequent cause of death in tetanus.\(^1\) Autonomic dysfunction appears to be the cause for this. Sympathetic overactivity, usually more evident in younger patients (<55 years), is characterised by fluctuating tachycardia, alternating hypertension and hypotension, peripheral pallor and sweating.\(^10\) The manifestations of autonomic dysfunction is usually picked up by close monitoring in the ICU and is managed accordingly e.g. for hypotension, the judicious use of fluid together with inotropic agents
will be recommended. The incidence of sympathetic overactivity appears to be less in patients who have been treated with large doses of drugs that depress the central nervous system. With the use of diazepam and phenobarbital, cardiac function needs to be monitored especially if beta blockers are used concomitantly. However, due to drug interaction, they are not recommended to be used simultaneously. It is safer to control the sympathetic activity by further dampening the CNS activation rather than initiating peripheral autonomic blockade.7,8,10

As tetanus is associated with clinical and biochemical evidence of sympathetic overdischarge and thus, protein catabolism, the maintenance of nutritional support is essential. Otherwise, the consequence of protein depletion will result in reduced host defences.

Upon diagnosis, human tetanus immune globulin (TIG) must be administered intramuscularly. A total dose of 3,000 units should be injected in 3 equal portions at 3 separate sites. The half life of TIG ranges from 25 to 30 days, therefore, only a single treatment is required. The earlier it is given, the more efficacious it is. TIG does not neutralise tetanospasmin already fixed to the CNS, nor does it have any effects when administered locally in the wound.4,6,16

Hypersensitivity reactions to TIG have not been documented and thus a test dose is not necessary. Active immunisation must be instituted concomitantly with the passive immunisation. This combined active and passive prophylaxis of tetanus does not reduce the subsequent development of antibodies from tetanus toxoid.16

Anticoagulation is often given as well to reduce the chance of developing deep vein thrombosis and pulmonary embolism.1,6 Wounds must be properly cleansed, irrigated and debrided, removing all traces of necrotic tissue. Any abscesses must be drained and foreign bodies removed expeditiously.

Complications
The possible complications of tetanus would include laryngospasm, fracture of the spine or long bones (from sustained contractions and convulsions), hypertension, sweating and arrhythmia (from hyperactivity of the autonomic nervous system), nosocomial infections from prolonged hospitalisation, e.g. sepsis from indwelling urinary catheter, hospital acquired pneumonia, pulmonary embolism and aspiration pneumonia. Some of these complications result from long term heavy sedation and mechanical ventilation.1,11,12,16 Occasionally, muscles can rupture from the very forceful contractions and as a result of this, intramuscular haematoma can develop and may be a source of infection or fever.10

Prevention
There is no natural immunity to tetanus toxin. The only effective way to control tetanus is by prophylactic immunisation. Universal primary immunisation with subsequent maintenance of adequate anti-toxin levels by means of appropriately timed boosters is necessary to protect all age-groups (Table 2).

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<th>Table 2. Guide to tetanus prophylaxis</th>
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<tr>
<td>History of tetanus toxoid</td>
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<tr>
<td>TT</td>
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<tr>
<td>Uncertain or &lt;3 doses</td>
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<td>3 doses or more</td>
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*Should be ‘Yes’ if it has been more than 10 years since the last dose; †Administer booster if >5 years have elapsed since last dose

NB: when TT and TIG are to be given concurrently, separate syringes and injection sites should be used.
Conclusion

A high index of suspicion is important even in first world countries, especially where imported cases are a reality. Tetanus is highly preventable through both routine vaccination and appropriate wound management. The recommendations for good management include: (1) wound care, (2) neutralisation of toxins, (3) antibiotic therapy, (4) supportive measures, including good nursing care and control of convulsions and (5) completion of active immunisation.

Every contact with the healthcare system that patients have should be used as a platform to review and update their vaccination status. The solution to the problem of tetanus is still adequate prophylaxis.

References