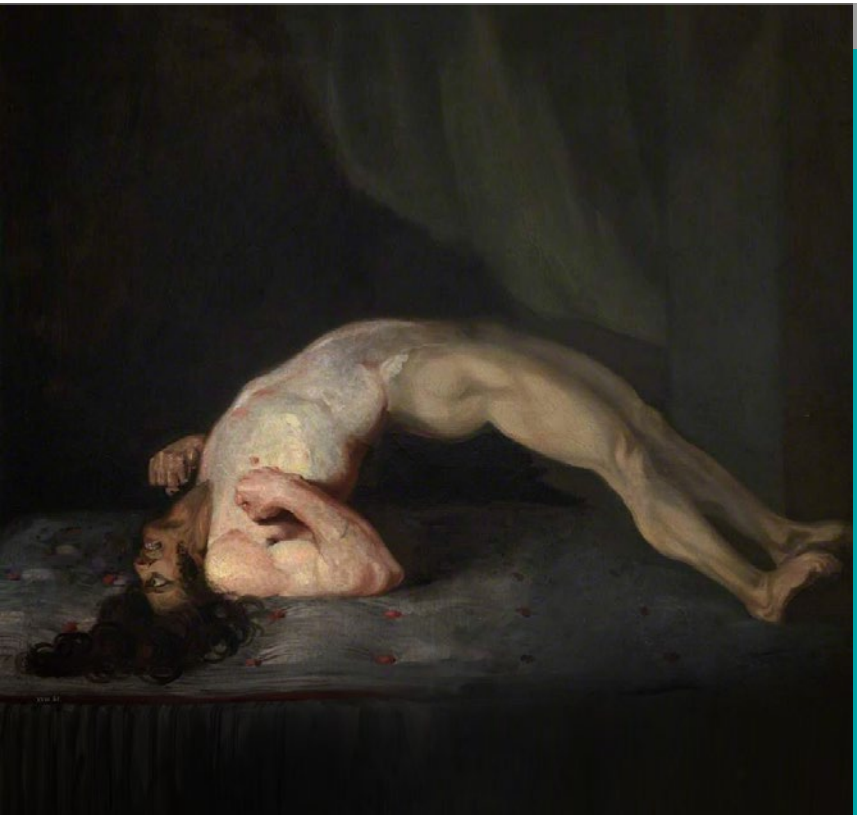
SWISS SOCIETY OF NEONATOLOGY

Neonatal tetanus – still a threat



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Title figure:
Soldier dying from tetanus, painting by Charles Bell (1808).
(Source: www.reddit.com)

INTRODUCTION

Elimination of maternal and neonatal tetanus is a key area in global health policy. In maternal tetanus, infection occurs after abortion, miscarriages, or unhygienic delivery practices, whereas neonatal tetanus infection usually occurs through the umbilical stump after delivery. Inadequate maternal vaccination and poor perinatal hygiene contribute to the occurrence of the disease (1).

Without medical care, mortality from neonatal tetanus is close to 100%, often exceeding 50% even with hospital care (2, 3). In 1988, the World Health Assembly passed a resolution to eliminate neonatal tetanus by the year 2000, then estimated to kill roughly 800'000 neonates a year. The Maternal and Neonatal Tetanus Elimination Initiative involved three main strategies: immunization, birth hygiene and surveillance (1). While it has been remarkably successful, WHO estimated that 58'000 and 49'000 neonates still died in 2010 and 2013, respectively (1, 4).

In their review article, Farrar et al. wrote: "If any one disease epitomizes the healthcare disparities between the developed and developing world, and the difficulties in overcoming that inequality, then tetanus is that disease. It is entirely preventable worldwide." (5)

This 13-day-old male infant presented to a local clinic and was referred to Rundu State Hospital in September 2018 with a history of excessive crying, irritability, poor feeding, generalized body stiffness, fever, and not having passed stools for 4 days.

On admission to the hospital, the infant weighed 2200 g and had a body temperature of 41.5 °C. His heart rate was 150 bpm and his respiratory rate was 42 bpm without signs of distress. There was impressive generalized body stiffness with scissoring of the lower extremities with dorsi-flexed feet, clenched fists and generalized muscle spasms (Fig. 1, 2 and movie part 1).

Fig. 1

Patient on day of life 16: generalized body stiffness with scissoring of lower extremities and clenched fists.

Fig. 2

Patient on day of life 16: when lifting up the baby, very hard muscles could be felt especially on his back.

In addition, a septic umbilical cord was noted. The patient was initially treated with broad-spectrum antibiotics assuming a diagnosis of omphalitis and sepsis, possibly with CNS involvement. Another diagnostic consideration was spastic cerebral palsy following (undocumented) birth asphyxia.

When his muscle spasms worsened and became virtually relentless, the possibility of neonatal tetanus was considered. Treatment with diazepam was started, and – as best as possible, given the hospital's infrastructure – the infant was protected from visual and acoustic stimuli. Fortunately, the baby continued to tolerate enteral feeds through a nasogastric tube.

On further history, the infant had been delivered at home (a village in Angola across the Kavango river). As is custom in this village, the cord had been cut with a simple blade, and the mother had applied ash to the umbilical cord from the time of birth until present. The mother had not received antenatal care and had not been immunized.

Fortunately, after a 30-day-course of diazepam and a 7-day-course of penicillin (tetanus antitoxin and IVIG were not available), the patient made a full recovery (Fig. 3, 4 and movie part 2) and was discharged home.

Fig. 3

The baby's condition gradually improved with normalization of muscle tone, and diazepam could be weaned off after 30 days.

Fig. 4

Prior to discharge (age 6 weeks), the baby's arms could be extended (left) and would stay in that position without force being applied (right).

DISCUSSION

Tetanus is acquired through the spores of Clostridium tetani, universally present in the soil. This organism is an obligate anaerobe; the spores, by contrast, are highly resistant and can tolerate air, extremes of temperature, and common disinfectants. The spores enter the body through contamination of both deep and superficial wounds, and can transform in anaerobic conditions. The bacteria do not multiply in healthy tissue with normal oxygen tension, but are able to grow and multiply in the low-oxygen-tension environment in devitalized or necrotic tissue.

Tetanus toxin (tetanospasmin) is one of the most potent toxins identified with a median human lethal dose of less than 2.5 ng / kg (6). The toxin is released during the stationary phase of bacterial growth or after cell lysis. It enters the nervous system at the neuromuscular junction and is then transcytosed to preganglionic inhibitory interneurons (7), preventing the release of inhibitory neurotransmitters (GABA, glycine), ultimately resulting in disinhibition of motor neuron discharge (8). Once inside neurons, tetanus toxin cannot be neutralized by tetanus antitoxin.

The diagnosis of neonatal tetanus is based on history and clinical manifestations. As outlined above, infection occurs via the umbilical cord, which can become contaminated during cutting with unsterile instruments or because of substances being applied to the cord (animal feces, ashes). The WHO case definition

for confirmed neonatal tetanus is "a neonate with the normal ability to suck and cry during the first two days of life, and between 3 and 28 days of age cannot suck normally and becomes stiff or has spasms (i.e., jerking of the muscles)" (9). Typically, muscle spasms are exacerbated by sensory stimuli such as noise, light or touch. The differential diagnosis of neonatal tetanus includes birth asphyxia, hypoglycemia, hypocalcemic tetany, and seizures (1).

Treatment strategies include toxin neutralization (human or equine-derived anti-tetanus serum or normal human immunoglobulin if tetanus immunoglobulin is not available), bacterial elimination (penicillin or metronidazole, appropriate wound care) and symptom control (chlorpromazine, phenobarbitone, diazepam) combined with supportive care.

Tetanus can take 6 – 8 weeks to resolve completely with spasms often lasting 2 – 3 weeks. Mortality rate is high, particularly when intensive care is not available. Respiratory failure is the most common cause of death: laryngeal spasm and rigidity and spasms of the abdominal wall, diaphragm, and chest wall muscles cause asphyxiation. Among survivors, long-term sequelae are common. Low birth weight, young age at presentation, fever, generalized rigidity, and risus sardonicus are associated with worse outcome in neonatal tetanus (10).

Unimmunized pregnant women or those with no documentation of immunization should receive two doses of tetanus toxoid given one month apart, with the first dose as early as possible in pregnancy. Further doses should be given in subsequent pregnancies (or at intervals of at least a year) up to a total of five doses, considered to ensure life-long protection (11). Of note, HIV infection is associated with a reduced response to maternal tetanus vaccination (12).

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