International Journal of Clinical Science and Medical Research

ISSN(print): 2770-5803, ISSN(online): 2770-582X

Volume 04 Issue 04 April 2024

DOI: https://doi.org/10.55677/IJCSMR/V4I4-01/2024, Impact Factor: 7.606

Page No : 119-124

Tetanus Update: Latest Diagnosis and Management

Bayu Saputera[1], Desy Puspa Sari[2]

[1]H. Andi Abdurrahman Noor General Hospital, Tanah Bumbu Regency, South Borneo, Indonesia

[2]Resbaharti Clinic, Tanah Bumbu Regency, South Borneo, Indonesia

ABSTRACT

Tetanus still contributes to a large number of deaths with a case fatality rate (CFR) of 11.76% in 2019. The increase in the number of cases and inadequate reporting are the reasons why tetanus management remains an important part of reducing patient mortality. Tetanus almost always occurs in patients who are not immune, partial or immune is inadequate. The diagnosis is made only from clinical manifestations, where the rigidity and spasm can be generalized (including neonatal tetanus) or local. Management of tetanus is divided into general management - with the administration of human tetanus immunoglobulin (HTIG) or serum anti-tetanus (ATS), antibiotics, magnesium, and wound care - and special management - which conforms to Ablett's classification system: mild, moderate, severe, and very heavy. Meanwhile, management in primary health care still adjusts the guidelines given by taking into account the availability of drugs. Prevention is carried out by giving immunizations to pregnant women, neonates and babies, as well as giving a booster every time an injury occurs.

Published Online: April 08, 2024

KEYWORDS

Diagnosis, lockjaw, management, neonatal, tetanus.

1. INTRODUCTION

Tetanus occurs sporadically and almost always affects people who are not immune, partially immune, or people who are fully vaccinated but fail to maintain adequate immunity with a vaccine booster dose. In 2017, the United States reported 33 cases with 2 patients dying from this disease. From 2009 to 2017, 264 cases and 19 deaths have been reported, of which 60 (23%) cases were aged over 65 years, 168 (64%) cases were aged 20 to 64 years, and 36 (13%) cases occurred at ages younger than 20 years, including 2 cases of neonatal tetanus. Meanwhile, reported cases of death occurred in people over 55 years of age (1). Although the incidence of tetanus is almost always associated with acute injuries, such as stab wounds, lacerations and aberrations, drug abuse appears to be an important risk factor, especially in developed countries such as United States and England (2).

In Indonesia itself, an increase in the number of cases of neonatal tetanus has been reported in 2019, namely 17 cases, compared to the previous year which was only 10 cases. The increase in cases of neonatal tetanus is also associated with improper care or cutting of the umbilical cord, where 9 (53%) cases were treated traditionally, 5 (30%) cases were related to other treatments, and 3 (17%) cases had no clear type of treatment. The number of deaths in 2019 was 2 cases, with a case fatality rate (CFR) of 11.76% (3).

The large risk at vulnerable ages, the increasing trend in the number of cases, and the still high CFR in cases of neonatal tetanus in Indonesia, encourage seriousness in preventive and curative efforts to overcome this problem. This burden is also added to by incomplete case reporting, so that vigilance in tetanus management must be increased.

2. DISEASE DESCRIPTION

Tetanus is a neurological disorder caused by tetanospasmin – a powerful neurotoxin produced by *Clostridium tetani* – characterized by increased muscle tone and spasms. Tetanus can be generalized (including neonatal tetanus) or localized (2).

3. ETIOLOGY

C. tetani is a gram-positive anaerobic bacterium, where this species is unable to use oxygen as a final hydrogen acceptor. This germ does not have cytochrome oxidase and cannot break down hydrogen peroxidase, therefore if oxygen is present, H_2O_2 tends to accumulate until it reaches toxic concentrations. Clostridia spores are usually larger than the diameter of the stem on which the spores are formed. Several types of *C. tetani* can be distinguished by specific anti

Corresponding Author: Bayu Saputera

****Cite this Article: Bayu Saputera, Desy Puspa Sari (2024). Tetanus Update: Latest Diagnosis and Management. International Journal of Clinical Science and Medical Research, 4(4), 119-124***

flagellates. All have encapsulated O (somatic) antigens and all produce tetanospasmin of the same antigenic type (4).

The vegetative cells of *C. tetani* produce the toxin tetanospasmin (molecular weight 150,000) which is composed by a bacterial protease in two peptides (molecular weight 50,000 and 100,000) linked by a disulfide bond. Initially the toxin binds to receptors on the presynaptic membrane of motor neurons, then moves upstream via the retrograde axonal transport system to the cell bodies of these neurons to the spinal cord and brain stem. The toxin diffuses to the terminals of inhibitory cells, including glycinergic interneurons and gamma-aminobutyric acid (GABA) - secreting neurons of the brainstem. This toxin also reduces synaptobrevin (vesicle-associated membrane protein, VAMP), a protein that plays a role in binding neurotransmitter vesicles to the presynaptic membrane. The toxin inhibits the release of the inhibitor glycine and GABA is blocked so that the resting firing rate of motor neurons increases, causing rigidity and spasms. This fact means that very small amounts of the toxin can be deadly to humans (3,4,5).

4. PATHOGENESIS

Contamination of wounds with spores may occur frequently. However, germination and toxin products only occur in wounds with low oxidation-reduction potential, such as wounds containing devitalized tissue, foreign bodies, or active infections. C. tetani itself does not cause inflammation, and infected wounds appear clean unless there is infection from other organisms (2).

In these anaerobic conditions, tetanus bacilli secrete two toxins, namely tetanospasmin and tetanolysin. Tetanolysin has the ability to damage tissue, while tetanospasmin, which is a zinc-dependent metalloproteinase, is responsible for triggering tetanus symptoms (5,6). Retrogradely, tetanospasmin reaches the cell bodies of peripheral neurons up to the spinal cord and brain stem. Once inside the inhibitory nerve terminal, tetanus toxin cleaves VAMP, thereby inhibiting the release of GABA and glycine. The partial result is functional denervation of lower motor neurons, which causes hyperactivity and increased muscle activity in the form of rigidity and spasm (5).

Local tetanus occurs if only the nerves supplying the muscle containing tetanospasmin are involved. Meanwhile, generalized tetanus occurs when a number of toxins released from a wound enter the bloodstream and are distributed to other nerve endings. Assuming that the transport time is the same for all nerves, short nerves will be affected more quickly than long nerves. This concept explains the course of rigidity and spasms starting from the nerves of the head, trunk, and then involvement of the extremity nerves is seen.

Little is known about the protein secretion system in clostridia. Until now, it was not understood how tetanus toxin, which lacks a typical N-terminal signal peptide, is exported. Because protein secretion is an important part in the formation of the pathogen phenotype, the secretion system and the secreted proteins of C. tetani need to be studied further (6).

5. CLINICAL MANIFESTATIONS

The clinical manifestations of tetanus are very diverse, they can be local or generalized (Table 1). Local tetanus is a mild manifestation, which only causes rigidity in the area around the focus of infection according to the peripheral nervous system it affects (2,4). However, in some very rare cases, cephalic tetanus can occur due to head injury or ear infection. In cephalic tetanus, there is trismus and dysfunction of one or more cranial nerves (the most common being the seventh nerve), which can lead to muscle spasm of the pharynx and larynx and trigger aspiration or airway obstruction. The prognosis for cephalic tetanus is classified as poor (7,8,9).

Table 1. Clinical classifications of tetanus (14)

Classification	Description
Generalized	Begins with trismus and risus sardonicus (spasm of the facial muscles), then proceeds to generalized spasms and opisthotonos
Localized	Muscle rigidity limited to the site of spore inoculation
Cephalic	Form of localized tetanus affecting cranial nerves, often following a head injury
Neonatal	Generalized tetanus in newborns resulting from infection of the umbilical stump

In generalized tetanus, clinical manifestations begin typically with the appearance of trismus due to increased masseter muscle tone, then the appearance of dysphagia due to stiffness and pain in the neck, followed by abdominal stiffness, and finally the extremities. Facial muscle contraction causes risus sardonicus (like smiling) and back muscle contraction causes opisthotonus (arched back) (Figure 1). These symptoms can occur repeatedly spontaneously or even with very small stimuli. However, tetanus does not affect the patient's mental condition (10). Meanwhile, in neonatal tetanus (generalized tetanus which usually occurs during the first 2 weeks of life), generalized symptoms can occur accompanied by difficulty drinking milk, so that if not treated properly it can cause death (11).

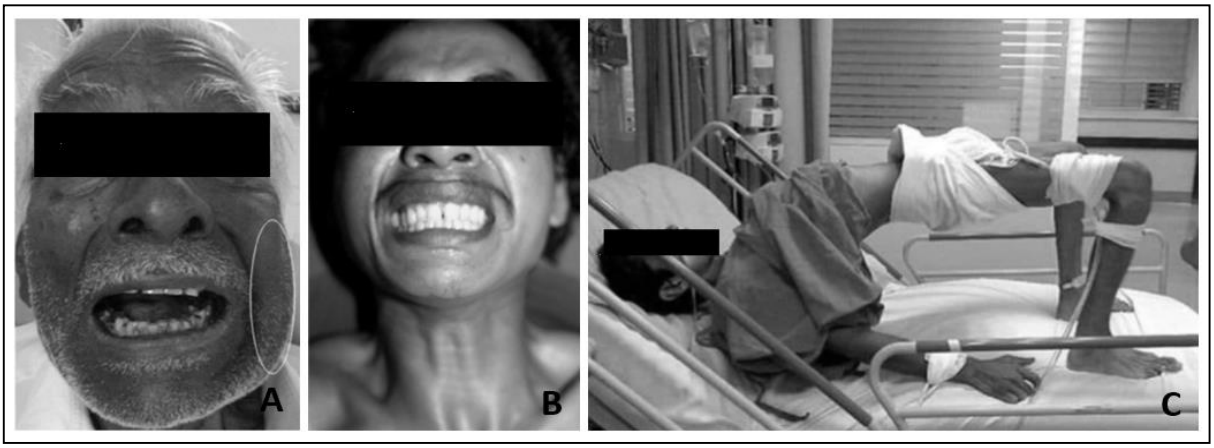

Figure 1. Clinical manifestations of tetanus; (A) trismus; (B) risus sardonicus; and (C) opisthotonus

6. DIAGNOSIS AND PROGNOSIS

The diagnosis of tetanus is made solely based on clinical findings. The incubation period (time from injury to the first symptoms) ranges from 7-10 days, with a limit of 1-60 days. Onset (time from first symptom to first spasm) varies between 1-3 days. Shorter incubation is associated with a worse prognosis (2,12). The first week of the disease is characterized by rigidity and spasms and lasts for 1-2 weeks. Spasms subside after 2-3 weeks, but stiffness may last longer. The recovery period occurs after 4-6 weeks, when the terminal axons grow again and tetanus toxin degradation occurs (Figure 2) (2,13).

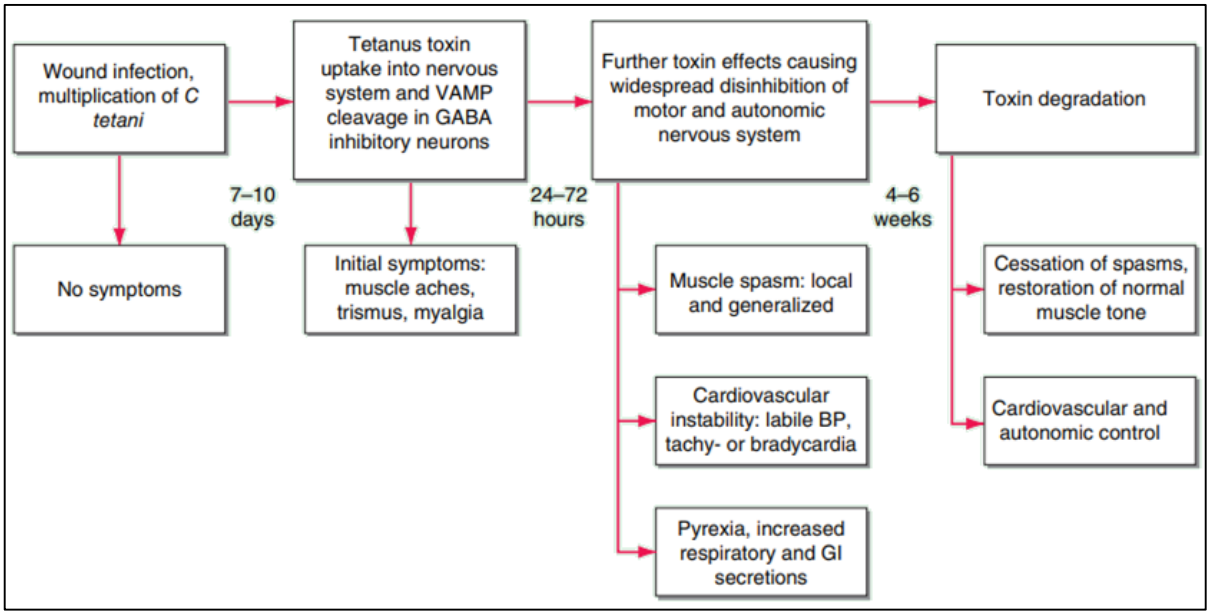

Figure 2. Clinical and pathologic progression of tetanus

There are several systems used to determine the severity of clinical manifestations as well as determine the prognosis of tetanus, as described by Philips, Dakar, and Urwadia. However, among them, the classification system presented by Ablett is the most frequently used system (Table 2) (13,14). This classification system categorizes patients into four levels depending on the intensity of respiratory spasms and autonomic involvement (15).

Table 2. Ablett classification of severity of tetanus (14)

Grade	Clinical features
I	Mild: mild to moderate trismus; general spasticity; no respiratory embarrassment [respiratory distress]; no spasms; little or no dysphagia
II	Moderate: moderate trismus; well-marked rigidity; mild to moderate but short spasms; moderate respiratory embarrassment with an increased respiratory rate greater than 30 [breaths/min]; mild dysphagia
III	Severe: severe trismus; generalized spasticity; reflex prolonged spasms; increased respiratory rate greater than 40 [breaths/min]; apneic spells; severe dysphagia; tachycardia greater than 120 [beats/min]
IV	Very severe: grade III and violent autonomic disturbances involving the cardiovascular system; severe hypertension and tachycardia alternating with relative hypotension and bradycardia, either of which may be persistent

The differential diagnosis includes local conditions that also cause trismus such as alveolar abscess, strychnine poisoning (one of the pesticide ingredients), dystonic drug reactions (such as metoclopramide), and hypocalcemia tetany. Other conditions that may have similar clinical manifestations are meningitis/encephalitis, rabies, and acute intraabdominal processes (due to a stiff abdomen). Increased tone in the central muscles (face, neck, back and abdomen) accompanied by generalized spasm that becomes subtle and symptom-free in the hands and feet, strongly supports the presence of tetanus (2,16,17).

7. TREATMENT

Tetanus management aims to maintain arterial oxygen pressure (PaO_2) and oxygen saturation within an adequate range; maintains acid-base, fluid, and electrolyte balance; and to maintain circulation in hypotensive patients. General management begins with administration of antitoxin, preferably human tetanus immunoglobulin (HTIG) 150 U/kg IM in some places; If not available, anti-tetanus serum (ATS) 10,000 U IV can be given slowly, but with close supervision and preparation in case an anaphylactic reaction occurs (18).

Administration of antibiotics for anaerobic bacteria, such as metronidazole 500 mg PO/IV, is still carried out. If not available, Penicillin G 100,000-200,000 U/kg/day IV can be given, divided into 2-4 doses. If these are also not available, tetracyclines, macrolides (azithromycin or erythromycin), clindamycin, cephalosporins and chloramphenicol are also effective (18,19).

Administration of magnesium can reduce the need for muscle relaxants and sedatives, and may be useful for reducing autonomic dysfunction. Give a loading dose of MgSO4 40mg/kg IV over 30 minutes; followed by IV infusion of 2-3 g/hour for patients weighing >45 kg and 1.5 g/hour for patients weighing <45 kg until spasm can be controlled (18).

Wound debridement is carried out after all the steps above have been carried out. But stitching the wound should be postponed. Specific management for tetanus is based on the severity of the symptoms present.

Grade I

Sedation/muscle relaxants are still given. Give diazepam 5 mg PO/IV (children 0.1-0.3 mg/kg every 1-4 hours). If not available, give chlorpromazine 50-150 mg (adults), 25 mg (children), or 12.5 mg (neonates) IM (phenobarbital can be given if available) (18,19). Stay alert for signs of sepsis. Close observation, because symptoms of grade I tetanus can immediately become severe (18).

Grade II

Treatment is according to grade I, but the dose of sedation/muscle relaxant is increased to 4 times the initial dose in adults (80-100 mg/day, administration of greater than this dose carries a high risk of respiratory depression). Give a slow IV drip with normal saline for 24 hours. Ideally, sedation/muscle relaxant drugs make the patient sleep but can be awakened to receive orders (18,19). Tracheostomy can be performed to prevent prolonged laryngospasm and anoxia. If laryngeal spasm occurs, immediately give chlorpromazine 50 mg IV or diazepam 10-20 mg IV (18).

Grade III

Treatment is according to grade II, but paralysis and ventilation are also given. Reduce the diazepam dose (30-40 mg over 24 hours for adults). Administer pancuronium 2-4 mg IV; if not available, give gallamine 20-40 mg IV. Titration is performed to provide neuromuscular block but maintain effective ventilation. Initially, administer every 1-1.5 hours

(first 1-2 weeks), then extend the interval as the patient's condition improves. Check blood gas analysis (AGD) periodically if available (18). Seizures can occur even if the patient is paralyzed, but do not necessarily affect ventilation. Pancuronium can be discontinued when the seizures stop. Continue ventilation until the patient is stable (18).

Grade IV

Management is appropriate for grade III, but add cardiovascular medications if necessary to stabilize hemodynamics. If hypotensive, administer IV fluids; if ineffective or contraindicated, use dopamine to maintain blood pressure >100 mmHg. If hypertensive crisis occurs (systolic >200 mmHg, diastolic >100 mmHg), administer propranolol 5-10 mg PO or nifedipine 5 mg sublingually. Management of persistent bradycardia or tachyarrhythmia (18).

8. PROCEDURE IN PRIMARY CARE FACILITIES

The principles of management in a primary care setting are not much different from the management described previously. It's just that sometimes the types of drugs available are very limited so knowledge about therapeutic options becomes very important.

General management before the patient is referred; provide IV fluids and adequate oxygen to prevent hypoxia. If HTIG or ATS is available, give it according to the therapeutic dose. Antibiotics and simple wound care are still carried out while preparing facilities for referral to secondary services.

In patients who experience seizures, adjust the diazepam dose according to the patient's symptoms (according to the Ablett classification). If the patient's symptoms are classified as grade I, give diazepam and $MgSO_4$. However, if it is classified as grade II, diazepam drip remains the main choice. In cases of neonatal tetanus; If an IV line is not installed, diazepam can be given rectally (2,18).

9. PREVENTION

Tetanus can be prevented with good wound care and immunization. In neonates, the use of safe and clean delivery and umbilical cord care practices as well as maternal vaccination are essential. The World Health Organization (WHO) guidelines for tetanus vaccination consist of a primary series of three doses in infancy, a booster at ages 4–7 and 12–15 years, and one booster in adulthood. In the United States, the CDC recommends an additional dose at 14-16 months and an additional dose every 10 years (2).

Passive immunization should be given to patients who have not received immunization or patients with unclear immunization status, when contaminated wounds occur or there is tissue devitalization (Table 3). HTIG administration is recommended at 250 U IM; if it is not available, or the patient chooses another alternative, ATS 1,500 U can be given. Active immunization with tetanus toxoid (TT) should be carried out simultaneously (20).

Table 3. Guide to tetanus prophylaxis in wound management (20)

History of Absorbed Tetanus Toxoid	Clean, Minor Wounds		All Other Wounds	
	Tdap or Td	TIG	Tdap or Td	TIG
Unknown or < 3 doses	Yes	No	Yes	Yes
3 or more doses	No	No	No	No

10. CONCLUSION

Considering the high CFR rate of tetanus and the increasing trend of cases, attention to tetanus management should be increased. Meanwhile, in the background of primary health care, the choice of therapy must be adjusted to the type of drug available, so that before a referral is made, the patient has received initial treatment which can be useful in reducing the risk of death.

REFERENCES

1. Faulkner AE, Tiwari TSP. Tetanus. In: Roush SW, Baldy LM, Hall MAK, editors. Manual for surveillance of vaccine-preventable diseases. Atlanta: CDC; 2020. Chapter 16. p. 1-6.
2. Thwaites CL, Yen LM. Tetanus. In. Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, editors. Harrison's principles of internal medicine. 19th ed. New York: McGraw-Hill Education; 2015. p. 984-7.
3. Primadi O, Budijanto D, Hardhana B, Sibuae F, Widiantini W. Profil kesehatan Indonesia tahun 2019. Jakarta: Kementerian Kesehatan RI; 2020. p. 170-2.
4. Carroll KC, Hobden JA, Miller S, Morse SA, Meitzner TA, Detrick B, Mitchell TG, McKerrow JH, Sakanari JA. Jawetz, Melnick, & Adelberg's medical microbiology. 27th ed. New York: McGraw-Hill Education; 2016. p. 184-6.
5. Hassel B. Tetanus: pathophysiology, treatment, and the possibility of using botulinum toxin against tetanus-induced rigidity and spasms. Toxins. 2013;5:73–83.
6. Rind NA, Taj MK, Taj I, Jan S, Ali SA, Mohammad G, Hussain A, Ali M, Rafeeq M, Zafar U, Essote SA, ul-Haq A, Samreen Z. Clostridium tetani as a

pathogenic organism. International Journal of Biosciences. 2019;14(4):207–13.
7. Bernardes M, Presti SL, Ratzan K. A case of cephalic tetanus in elderly patient with trismus. Case Reports in Infection Diseases. 2018;1:1–3.
8. Kotani Y, Kubo K, Otsu S, Tsujimoto T. Cephalic tetanus as a differential diagnosis of facial nerve palsy. BMJ Case Report. 2017;1:1–3.
9. Sesama M, Gomber S, Yadav M. Cephalic tetanus presenting as ptosis. Indian Pediatrics. 2020;57(1):72–3.
10. Fan Z, Zhao Y, Wang S, Zhang F, Zhuang C. Clinical features and outcomes of tetanus: a retrospective study. Infection and Drug Resistence. 2019;12:1289–93.
11. Nyong EE, Udoh JJ, Inyang IJ, Oloyede IP, Udoh PA. Cluster of neonatal tetanus: case series from one traditional birth attendant's home in Uyo, South-South Nigeria. Journal of Public Health and Epidemiology. 2020;12(4):305–9.
12. Yadav YR, Kala PC, Yadav S. Relative significance of incubation period and period of onset as a prognostic factor in tetanus. Rajasthan Medical Journal. 1987;24(4):167–70.
13. Cook TM, Protheroe RT, Handel JM. Tetanus: a review of literature. British Journal of Anaesthesia. 2001;87(3):477–87.
14. Srigley JA, Haider S, Johnstone J. A lethal case of generalized tetanus. Canadian Medical Association Journal. 2011;183(9):1045–8.
15. Bravo TE, Siregar ML, Jamil KF. Diagnosis and management of tetanus outside the intensive care unit: a case report. Earth and Environmental Science. 2018;125:1–3.
16. Moniuszko A, Zajkowska A, Tumiel E, Rutkowski K, Czupryna P, Pancewicz S, Rutkowski R, Zdrodowska A, Zajkowska J. Menigitis, clinical presentation of tetanus. Case Report in Infectious Disease. 2015;1:1–2.
17. Rampengan NH. Rabies post exposure prevention. Bali Medical Journal. 2017;6(2):449–55.
18. Davidson R, Brent A, Seale A, editors. Oxford handbook of tropical medicine. 4th ed. Oxford: Oxford University Press; 2014. p. 454-7.
19. World Health Organization. Current recommendation for treatment of tetanus during humanitarian emergencies. Geneva: WHO; 2010. p. 1-6.
20. Tierney LM, McPhee SJ, Papadakis MA, editors. Current medical diagnosis & treatment. 61th ed. New York: McGraw-Hill Education; 2022. p. 1469-71.