POST-EXPOSURE PROPHYLAXIS OF TETANUS IN CASES OF INJURY – RULES OF CONDUCT

Profilaktyka poekspozycyjna tężca w zranieniach – zasady postępowania

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Abstract: This article presents the management of injuries aimed at preventing tetanus. The epidemiology and pathomechanism of tetanus, clinical forms and symptoms, and non-specific and specific post-exposure prevention principles are discussed. A management algorithm supplements the article.

Streszczenie: W artykule przedstawiono postępowanie w zranieniach mające na celu zapobieganie rozwojowi tężca. Omówiono epidemiologię i patomechanizm tężca, postacie i objawy kliniczne oraz zasady profilaktyki poekspozycyjnej nieswoistej i swoistej. Artykuł uzupełnia algorytm postępowania.

Key words: immunisation, vaccine, wound infections, *Clostridium tetani*, tetanus antitoxin.

Słowa kluczowe: szczepienia, szczepionka, zakażenia przyranne, laseczka tężca, antytoksyna.

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Introduction

Tetanus is a life-threatening neurological disease caused by a potent neurotoxin produced by anaerobic *Clostridium tetani* rods. It can be effectively prevented by vaccination. Therefore, tetanus is found in unvaccinated populations, primarily in poor countries in Asia, Sub-Saharan Africa and South America, frequently in the form of neonatal tetanus. According to the World Health Organization, in 2015, 36,806 people and 19,937 neonates died due to tetanus worldwide [1, 2]. Based on the most recent data from 2018, 15,103 cases of tetanus were reported globally, including 1,803 in neonates [3]. Due to widespread vaccination, the incidence of this disease has been very low for years in well-developed countries. According to the data of the National Institute of Public Health – National Institute of Hygiene, in Poland 17 cases in 2019, and only 2 cases in 2020 of wound tetanus were reported (the annual incidence was 0.01 and 0.04/100,000 people, respectively); no cases in neonates were observed [4, 5].

Resistant to environmental conditions spores of tetanus rods are commonly present in the environment, including gastrointestinal systems of humans and animals. The spores may contaminate wounds and the umbilical stump. In most cases, tetanus is caused by small cuts and abrasions of the skin.

The excellent epidemiological situation in developed countries is due to widespread vaccination and effective post-exposure prophylaxis. Wound tetanus threatens unvaccinated and elderly people with weakened post-vaccination immunity. Other risk groups comprise intravenous drug users and immunosuppressed patients. Mortality due to generalised tetanus is 10 to 70%, depending on the age of the patient and access to treatment at an Intensive Therapy Unit. Recovered patients may suffer neurological complications for a long time.

Clinical forms of tetanus

Tetanus usually develops as a result of small skin injuries and abrasions and, in small children, as a result of chronic otitis media, so in 20 to 50% of cases the entry point of infection cannot be identified. The clinical course of the disease is probably determined by the amount and rate of toxin production, and its severity is highest in puerperal women, patients with deep wounds and intravenous drug users [6]. Following the prodrome period, one of four characteristic, different clinical forms of tetanus develops. Localised forms are characterised by muscle stiffness in the area of the wound that is the entry point of infection. However, local symptoms may forecast generalised tetanus – the most common, classic form of the disease, found in the majority of cases (80%). Its incubation period is 3 to 21 days, and the symptoms develop gradually, usually for a week, starting with the jaw muscles. Therefore, the first symptom is trismus. Then muscle spasms occur in a descending pattern, and

they may persist for a few weeks. Their tension increases, and paroxysmal, strong and painful contractions of large muscle groups, triggered by various sensory stimuli, occur. It leads to the typical clinical signs, such as hyperextension of the dorsal muscles (*opisthotonus*) and wince due to the spasm of facial muscles (*risus sardonicus)* which are, characteristically, not associated with consciousness disorders [6, 7]. The spasms are accompanied by the symptoms of autonomous nervous system impairment: heart rhythm disorders, disturbed thermoregulation and variations in arterial pressure. Contractions of the laryngeal muscles (epiglottis) or diaphragm may result in quick death. The rarest clinical presentation, cerebral tetanus, develops within 1–2 days as a result of head trauma or chronic otitis media, and it affects the muscles supplied by the cranial nerves. A special form of the disease is neonatal tetanus. A severe generalised form develops typically within 3 to 7 days after birth, usually due to infection of the umbilical stump [8]. The typical symptoms of the disease include difficulties with feeding, impaired suckling and swallowing reflexes and excessive crying of the neonate. Both localised and cerebral tetanus may be complicated by generalised tetanus [7].

The type of the wound largely determines the risk of tetanus. Small and clean injuries with good blood supply, without necrotic tissue occurring at home are associated with low risk. Whereas risk factors for the development of tetanus include:

- crush wounds, deep wounds, puncture wounds, shot wounds, wounds containing a foreign body, wounds that are considerably contaminated with soil, faeces or saliva, slaughterhouse waste or aerobic bacteria (they consume oxygen, thus supporting the anaerobic bacteria), wounds associated with shock (ischaemia), burns or frostbite,
- wounds that have not been treated within 24 hours,
- injuries occurring during work in soil (especially enriched with natural manure), e.g. while gardening, growing vegetables, taking care of farm animals (especially horses) and injuries caused by tools contaminated with soil,
- intravenous drug use,
- obesity (due to weakened response to vaccination).

Pathophysiology of tetanus

Clostridium tetani rods are non-invasive, anaerobic, Gram-positive bacteria commonly found across the world, particularly in soil contaminated by animal faeces, especially horses (saprophytes in the gastrointestinal system). They create spores that can survive dozens of years, and are resistant to environmental factors, high temperatures and disinfectants.

Tetanus is a wound infection, limited to the place of entry. Typically, the bacteria enter the body through a damaged skin. In anaerobic conditions, the spores transform into a vegetative form and produce a potent, polypeptide neurotoxin (tetanospasmin) which causes the symptoms. The toxin blocks the release of acetylcholine and inhibitory neurotransmitters in the spinal cord. The development of fully symptomatic tetanus is preceded by a prodrome period, characterised by patient anxiety, feeling unwell, minor increase in muscle tone, increased sweating, headache, insomnia, as well as pain and paraesthesias in the wound area. The incubation period of generalised tetanus is 3 to 21 days (a mean of 8 days), and in rare cases it may extend to a few months. Shorter incubation usually is associated with a more severe course of the disease and worse prognosis [9].

Due to the mentioned pathophysiology, tetanus patients do not pose a threat to others, as the disease is not transmitted between people, but on the other hand, population immunity cannot develop.

Post-exposure tetanus prophylaxis

Post-exposure tetanus prophylaxis consists in wound debridement (non-specific prophylaxis) and using a specific anti-tetanus immunoglobulin (antitoxin), as well as vaccination. It should be introduced as soon as possible. The principle applies both to the specific and non-specific prophylaxis.

1. Non-specific prophylaxis

Regardless of the history of vaccinations, each injury requires non-specific prophylaxis, i.e. wound care. The wound should be cleaned immediately, and if necessary, surgically debrided to remove the damaged or necrotic tissues and foreign bodies. It should be emphasised that extensive debridement may have adverse consequences in the case of deep puncture wounds [9]. Subsequently, depending on the risk of tetanus, specific prophylactic measures should be applied.

2. Specific prophylaxis

Specific prophylaxis consists in post-exposure use (active prophylaxis) of tetanus toxoid (tetanus anatoxin) or a vaccine combined with a tetanus component (toxoid) or human anti-tetanus immunoglobulin (anatoxin – TIG – passive prophylaxis). The decision regarding the use of specific prophylaxis and its type (active or active-passive) is determined by two main factors: the anti-tetanus immunity status of the exposed person (interview related to the vaccination history) and the risk of developing the disease (type of wound and time from the injury). The general immunity status of the exposed patient is also an important factor. The basic principles of specific post-exposure prophylaxis of tetanus are presented in Table 1 along with the enclosed algorithm with a check list.

2a. Active prophylaxis

It consists in administration of a single dose of a vaccine containing tetanus toxoid (deactivated toxin). The toxoid dose is the same, regardless of the patient's age.

Unvaccinated patients, those with incomplete vaccination or without documented vaccination, continue to receive vaccination from their family doctor. The following products are available on the Polish market: monovalent tetanus toxoid vaccines (T) and combined vaccines containing tetanus toxoid and diphtheria toxoid (Td), vaccines against diphtheria, tetanus and pertussis (DTP and dTpa – a capital D or P in the abbreviation refer to a higher dose of diphtheria toxoid or pertussis antigens, respectively, and a lowercase d and p denote lower doses), typhoid and tetanus vaccine (against tetanus and typhoid – TyT), as well as multi-combination vaccines 4-in-1, 5-in-1 and 6-in-1

for infants and young children. All of these vaccines contain similar doses of tetanus toxoid. According to the current Polish Protective Vaccination Programme for 2021, T and Td vaccines are of key importance in the post-exposure prophylaxis of tetanus. However, both the American CDC (*Center for Disease Control and Prevention*) and AAP (*American Academy of Pediatrics*) recommend to use preferentially the products that contain not only tetanus toxoid but also a pertussis component, to offer protection against whooping cough [10].

Table 1. Post-exposure prophylaxis of tetanus

Patient's vaccination history	Risk of tetanus infection	
	Low	High
Unvaccinated or incompletely vaccinated patients, or those with uncertain vaccination history	Tetanus and diphtheria or tetanus vaccine, then continue basic immunisation (0; 1; 6 months)	Tetanus and diphtheria or tetanus vaccine and antitoxin (TIG 250/500 IU), then continue basic immunisation (0; 1; 6 months)
Basic or booster immunisation – last dose more than 10 years ago	Tetanus and diphtheria or tetanus vaccine – one booster dose	Tetanus and diphtheria or tetanus vaccine – one booster dose and antitoxin (TIG 250/500 IU)
Basic or booster immunisation – last dose 5–10 years ago	Tetanus and diphtheria or tetanus vaccine – one booster dose	Tetanus and diphtheria or tetanus vaccine – one booster dose
Basic or booster immunisation – last dose less than 5 years ago	Not required	Not required In particularly high-risk cases, administration of one dose of tetanus and diphtheria or tetanus vaccine should be considered

Check list and explanation of the algorithm of "Specific post-exposure tetanus prophylaxis"

Qualification for specific prophylaxis has two stages. First, the patient's immunity against tetanus at the moment of exposure (previous vaccination) is assessed, as current vaccination allows specific prophylaxis to be omitted in immunocompetent patients. Then, in stage two, the risk of tetanus development is evaluated, based on the circumstances and type of wound, and the decision regarding the type of specific tetanus prevention is made.

1. Assessment of the tetanus vaccination status and of general immunity

- Did the patient receive a full course of tetanus vaccine ?
- When did the patient receive the last booster dose?
- Is the vaccination documented or highly probable (e.g. based on military service, surgically treated injury)?
- Which group does the patient belong to?
  - Lack of tetanus vaccination, unvaccinated or incompletely vaccinated patients, or those with uncertain vaccination history.
  - Basic or booster immunisation – last dose 5–10 years ago.
  - Basic or booster immunisation – last dose less than 5 years ago

Assessment of general immunity:

- Is the patient's immunity significantly compromised (HIV or SCID infection, severe antibody deficiency)?
  - **If yes, the risk is high –** administration of TIG is required after every injury

2. Assessment of the risk of tetanus based on the wound

- Is the wound clean, with good blood supply or is it a small and clean superficial wound that occurred in a domestic environment and does not contain necrotic tissue?
  - **If yes** – the risk of tetanus is low.
- Is it a crush wound, a deep wound, a puncture injury, a shot wound, does it contain a foreign body, is it contaminated with soil, faeces or saliva, slaughterhouse waste or infected by aerobic bacteria?
  - **If yes** – the risk of tetanus is high.
- Was the patient in the state of shock during or after the injury?
- Does the wound result from a burn or frostbite?
- Was the wound treatment delayed by more than 24 hours?
- Did the injury occur while working in soil, e.g. growing flowers or vegetables, taking care of farm animals (especially horses)?
- Was the wound caused by a tool contaminated with soil?
- Is the patient an intravenous drug user?
  - **If yes** – the risk of tetanus is high.

Table 2. Vaccines with a tetanus component registered in Poland that can be used in post-exposure tetanus prophylaxis.

Type of vaccine		Commercial name	Comments
Tetanus vaccine	T	Tetana	Routinely used
Tetanus and diphtheria vaccine	Td	Clodivac	Routinely used
		Td-pur	In a pre-filled syringe
Diphtheria, tetanus and pertussis vaccine	dTap	Adacel	For children from 4 years of age and adults, including pregnant women
		Boostrix	For children from 4 years of age and adults, including pregnant women
		Tdap – SSI	For children from 4 years of age and adults, including pregnant women
Diphtheria, tetanus and polio vaccine	dT-IPV	Dultavax	For children from 7 years of age and adults, including pregnant women
Diphtheria, tetanus, pertussis and polio vaccine	DTPa-IPV	Tetraxim	For infants from 2 months to children 12 years of age
	dTpa-IPV	Boostrix-Polio	For children from 3 years of age and adults, including pregnant women
Typhoid and tetanus vaccine*		Ty T	For children from 6 years of age and adults up to 60 years of age. Practically not used in post-exposure prophylaxis.

*Packaging of 20 doses

It applies to post-exposure prophylaxis following injury in children aged 5 to 7years and adolescents, as well as adults who were not vaccinated in the recent years (usually 5) against pertussis and demonstrate no contradictions preventing this vaccination [11]. Depending on the manufacturer's recommendations, the vaccine is administered by a deep subcutaneous or intramuscular injection. Table 2 presents the vaccines registered in Poland for use in tetanus prevention [12–18]. The table does not include the multi-combined preparations used in children up to 3 years old. When selecting a vaccine, it is important to consider the summary of product characteristics regarding the age groups for which the product is approved.

2b. Passive specific prophylaxis

It consists in the administration of hyperimmunised immunoglobulin containing specific antibodies binding the tetanus toxin. The antitoxin (TIG) is injected deeply into the muscles at a dose of 250 IU or 500 IU, at a different anatomical site than the previously administered vaccine. The dose does not depend on the patient's age or body weight, but is determined by the risk of tetanus infection. If the wound is infected and cannot be surgically treated within 24 hours, the injury is deep, the access to oxygen is restricted, and in certain types of injuries, e.g. caused by animals (e.g. bites, stings) or by foreign bodies (e.g. shot wounds), a higher TIG dose (500 IU) should be used, following the relevant SPC. If a wound is associated with a lower risk of tetanus infection, half of that dose (250 IU) will be sufficient [19]. When TIG is not available, normal human immunoglobulin or equine tetanus-specific immunoglobulin may be used (the product is not available in Poland) [9]. Following CDC recommendations, normal human immunoglobulin (IVIG) should be administered at a dose of 0.2–0.4 g/kg b.w.; however, it is worth mentioning that the FDA (Food and Drug Administration) has not approved such treatment, and it has not been included in the Polish Protective Vaccination Programme [10, 20]. If there are any indications for using tetanus-specific immunoglobulin, it should be administered as soon as possible. It is also used in patients who come to the doctor with a delay, regardless of the time from the injury. This is due to the therapeutic properties of the immunoglobulin (it is also used to treat tetanus) and a potentially long period of tetanus incubation.

3. Prophylactic antibiotic therapy

Routine antibiotic therapy is not recommended in tetanus prevention. However, wound monitoring is advised, as well as selection of appropriate antibiotic therapy in case the wound area becomes infected [20].

Conclusions

Due to common protective vaccination against tetanus, improved sanitary conditions, widespread access to healthcare and routine post-exposure tetanus prophylaxis, in developed countries – including Poland – tetanus is only occasionally observed. However, despite the favourable epidemiological situation, we should bear in mind that tetanus spores are common in the environment, and in the case of tetanus infection, the mortality rate in Poland is up to 30%. Moreover, recovered patients often suffer from chronic complications that significantly reduce the quality of life [21]. After exposure, routine management should include both an effective, non-specific post-exposure prophylaxis, i.e. wound treatment, and specific prophylaxis: passive – administration of TIG antitoxin, or active – administration of a vaccine containing tetanus toxoid. Post-exposure tetanus prophylaxis should be introduced as quickly as possible, immediately after the risk assessment. As part of post-exposure prophylaxis, patients who were vaccinated against tetanus should continue the tetanus immunisation, following the recommendations in the current Protective Vaccination Programme.

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