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Review | Обзор



# Tetanus in unvaccinated persons: A review of case reports

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### **ABSTRACT**

**INTRODUCTION.** Tetanus cases are registered annually throughout the world, mainly in unimmunised or incompletely immunised populations. Analysis of tetanus cases and identification of the reasons for non-vaccination, including refusal to vaccinate, are important for drawing attention of health professionals to this issue.

**AIM.** This study aimed to review case reports of tetanus in unvaccinated or undervaccinated individuals, analyse reasons for non-vaccination, and identify problems associated with preventive vaccination against tetanus.

**DISCUSSION.** According to epidemiological data, tetanus cases are recorded every year in almost every country in the world. In 2023, the World Health Organisation (WHO) reported 21,830 cases of tetanus worldwide, and the Russian Federation reported eight tetanus patients, including children. The main issue with diagnosing tetanus lies in the lack of reliable laboratory tests confirming tetanus. Tetanus-specific therapy with tetanus antitoxin (equine) is associated with the risk of allergic reactions. Traditionally, tetanus is considered an infection that develops only in patients with deep and soil-contaminated wounds. However, unvaccinated or undervaccinated individuals are at high risk of tetanus, even with minor wounds. This study involved an analysis of tetanus case reports (13 cases) in unvaccinated or undervaccinated individuals with minor wounds or wounds minimally contaminated with soil. In all the paediatric tetanus cases discussed in this article, the parents had not vaccinated their children for religious and/or personal reasons. Analysis of tetanus case reports in adults showed that the patients had not taken their wounds seriously and had not sought medical help before the onset of the disease.

**CONCLUSIONS.** The concerning tetanus incidence is attributed to insufficient public awareness of the disease threats and the increasing number of people refusing vaccines. Health professionals, public organisations, and religious communities should work together to promote vaccination and improve health education. This will enhance public confidence in vaccination, increase preventive vaccination coverage, and reduce the incidence of tetanus.

#### **Keywords:**

tetanus; tetanus vaccine; vaccination; unvaccinated persons; case report; tetanus antitoxin (equine); tetanus immune globulin; vaccination refusal; anti-vaccination movement; vaccine hesitancy; tetanus toxin; wound infection; trismus

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# Столбняк у непривитых лиц: обзор клинических случаев

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## **РЕЗЮМЕ**

**ВВЕДЕНИЕ.** Случаи заболевания столбняком ежегодно регистрируются в различных странах мира, главным образом среди невакцинированных или частично вакцинированных лиц. Анализ случаев заболевания столбняком и выявление причин отсутствия вакцинации, включая отказы от ее проведения, имеют большое значение для привлечения внимания специалистов системы здравоохранения к данной проблеме.

**ЦЕЛЬ.** Обзор клинических случаев столбняка у непривитых или частично привитых лиц, анализ причин отсутствия вакцинации и выявление проблем, связанных с профилактической вакцинацией от данного заболевания.

**ОБСУЖДЕНИЕ.** Анализ эпидемиологических данных показал, что случаи заболеваемости столбняком ежегодно фиксируют практически во всех странах мира. В 2023 г. в мире было зарегистрировано 21830 случаев столбняка (по данным ВОЗ), в Российской Федерации – 8 случаев. Основной проблемой при диагностике столбняка является отсутствие надежных методов лабораторного подтверждения диагноза. Специфическая терапия с применением лошадиной противостолбнячной сыворотки сопряжена с рисками развития аллергических реакций. Несмотря на то, что столбняк традиционно считается инфекцией, которая может развиваться в случаях появления глубоких и загрязненных почвой ран, у непривитых или частично привитых лиц даже незначительные травмы могут привести к развитию инфекции. Проведен анализ 13 клинических случаев столбняка, развившегося у невакцинированных или частично вакцинированных лиц вследствие незначительных травм или травм, ограниченно загрязненных почвой. В описанных случаях все заболевшие дети не были вакцинированы из-за религиозных и/или личных мотивов родителей. Анализ клинических случаев у взрослых выявил, что заболевание развивалось из-за небрежного отношения к травме и несвоевременного обращения за медицинской помощью.

**ЗАКЛЮЧЕНИЕ.** Проблема заболеваемости столбняком связана с недостаточной информированностью населения об опасности заболевания и ростом числа противников вакцинации. Необходимо активное взаимодействие специалистов системы здравоохранения, представителей общественных организаций и религиозных общин с целью улучшения пропаганды вакцинации и санитарно-просветительской работы, что позволит повысить доверие населения к вакцинопрофилактике, увеличит охват профилактическими прививками и снизит риски инфицирования столбняком.

#### Ключевые слова:

столбняк; вакцины против столбняка; вакцинация; непривитые лица; клинический случай; противостолбнячная сыворотка; противостолбнячный иммуноглобулин; отказ от вакцинации; антипрививочное движение; столбнячный токсин; раневая инфекция; тризм

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#### INTRODUCTION

Tetanus is an infectious disease successfully managed by vaccination. Tetanus vaccine is deemed highly safe and effective. However, current global statistics (for countries with high vaccination coverage as well) knows registered tetanus cases in all age groups, including fatal outcomes [1, 2]. According to WHO, there were 9,828, 6,705, and 21,830 global cases in 2021, 2022, and 2023, respectively¹. In Russia, eight (8), eleven (11), and eight (8) cases were reported in 2021, 2022, and 2023, respectively, among them children (aged 0 to 17 years)². In Europe, 53 cases were registered in 2022, of them seven (7) fatal outcomes³.

Tetanus mostly progresses in children either not vaccinated yet or undervaccinated, as well as in young adults that were not revaccinated (no booster doses). Disease incidence also includes the adults not revaccinated every 10 years. Anti-vaccinationists (vaccination refusal) are the highest-risk group.

Tetanus antibody titre monitoring showed low vaccination coverage in population aged 65 and older<sup>4</sup>, as well as preterm infants [3, 4]. Considering the impossibility to fully eliminate the infectious agents and high disease severity, strong vaccination coverage of all age groups is needed.

Numerous publications are dedicated to tetanus incidence<sup>5</sup> [5–11]. Still, there is a need for an analysis of tetanus case reports over the last 15 years following the publications, including unvaccinated/undervaccinated patients, as a result of minor or atypical wounds, as well as children whose parents intentionally refused to have them vaccinated.

The aim of the study is to review tetanus case reports in unvaccinated or undervaccinated persons; to analyse the cause of non-vaccination and the challenges that preventive vaccination faces.

Data search was performed in eLIBRARY.RU, PubMed, and ScienceDirect bibliographic databases using Russian and English keywords: «клинические случаи столбняка», «столбнячный токсин», «заболеваемость столбняком», tetanus cases, tetanus toxin, and tetanus incidence. Review articles, original articles, and case reports published in 2009–2024 were analysed. The review did not include neonatal tetanus. Additionally, the authors used data from WHO, Centers for Disease Control and Prevention (CDC), European Centre for Disease Prevention and Control (ECDC), and Unified

Interdepartment Information and Statistics System (EMISS) websites.

# MAIN PART Tetanus intoxication

Clinical symptoms are caused by tetanus toxin produced by spore-forming bacterium *Clostridium tetani. C. tetani* endospores are spread virtually everywhere and long-lived. Thus tetanus cannot be fully eradicated.

C. tetani typically enters the body through a wound. In anaerobic conditions, the spores sprout and begin producing the toxin. The toxin is released from the wound during autolysis and carried by blood and lymph to the central nervous system (CNS; includes spinal cord and the brain stem) [12–15]. Tetanus neurotoxin (tetanospasmin) blocks the release of inhibitory neurotransmitters in the neuromuscular junction and the CNS neurons, causing uncontrolled muscular contractions.

Tetanospasmin is a protein (molecular weight ca. 150 kDa) including a heavy chain (100 kDa) and a light chain (50 kDa) coupled via disulfide and non-covalent bonds. Heavy toxin chain interacts with a receptor on presynaptic membrane of a motor neurone and allows the light chain to penetrate the cell [12–15]. First, the toxin reaches peripheral motor nerve endings – the main neuron aperture. After penetrating the neuron, disulphide bonds between the heavy and the light chain are destroyed. Within endocytic vesicles, the light chain moves along the axon (retrograde motion) into the CNS. The process can take from 2 to 14 days. After reaching the spinal cord, the toxin enters central inhibitory neurons and blocks the release of gamma-aminobutyric acid and glycine. Tetanus toxin disrupts inhibitory effect on motor and autonomic neurons, causing vegetative hyperactivity, uncontrolled muscle contractions, and spasms triggered even by weaker stimuli, such as light or sounds. The resulting muscle tensions and spasms are manifested as trismus (lockjaw), risus sardonicus, dysphagia, and opisthotonus (back arching); in case of rigid and spastic respiratory, laryngeal, and abdominal muscles, respiratory paralysis and respiratory failure can occur [12–15].

Humans are extremely sensitive to the tetanus toxin. Tetanus does not interfere with the higher nervous activity. A tetanus patient suffers terrible pains caused by muscular spasms, while being fully awake.

Tetanus reported cases and incidence. WHO; 2023.

<sup>&</sup>lt;sup>2</sup> ЕМИСС. Государственная статистика. Число зарегистрированных случаев инфекционных заболеваний. <a href="https://fedstat.ru/">https://fedstat.ru/</a>

Surveillance Atlas of Infectious Diseases. ECDC; 2023.

Tetanus – Annual epidemiological report for 2022. ECDC; 2024.

https://ourworldindata.org/tetanus

### **Diagnosis and treatment**

Lack of reliable laboratory diagnostics is the major diagnostic challenge. Laboratory examinations of wound materials are recommended for inoculating *C. tetani* or detecting the agent by polymerase chain reaction (PCR) method<sup>6</sup>. However, negative analysis does not exclude clinical diagnosis of tetanus. Moreover, it is recommended to determine serum tetanus antibodies (protective titre 0.1 IU/mL)<sup>7</sup>. However, clinical cases were registered even for protective levels of antibodies [8, 16–19]. In this regard, the established protective titre of tetanus antibodies is a subject of discussion [16].

When initiating tetanus treatment, the first measure is a thorough data collection, including immunisation history, wound aetiology, clinical manifestations, and immunity status<sup>8</sup>. Especially concerning are wounds contaminated with soil or foreign objects; complicated wounds; cold injuries or burns; animal bites (including snakes); wounds resulting from industrial and traffic accidents; poor childbirth hygiene and non-sterile medical instruments; and illegal abortions. Clinical cases described in this review clearly show that any injury creates a hazard of infection (see *Table 1*).

Hospital admission is binding for tetanus cases. The treatment requires immediate injection of specific antitoxins – tetanus immune globulin (TIG) or tetanus antitoxin (TA), immunisation with tetanus toxoid (TT; post-exposure prophylaxis), anticonvulsant therapy, and treatment for complications and concurrent infections (antibiotics)<sup>9</sup>. Anti-toxins should be administered quickly and effectively, within hours after assumption for tetanus, since the treatment loses its effect as soon as the toxin reaches the target cells.

One of the crucial aspects of the used antitoxins is their origin: heterologous (equine tetanus antitoxin, TA) or homologous products – tetanus immune globulin (TIG). Some countries (US, Can-

ada, Great Britain, and several EU countries) have already stopped producing heterologous antitoxin products.

Injection of TA heterologous protein bears risk of immediate and delayed hypersensitivity, as well as late serum sickness, therefore TIG is preferred. However, compared to TA, TIG has lower activity, thus it requires higher injection volume (250–500 mL). A therapeutic dose of purified concentrated equine serum (tetanus antitoxin)<sup>10</sup> requires a small volume (2–3 mL) due to production specifics. In order to achieve high serum activity (titre), horses are immunised with native tetanus toxoid (TT) derived from tetanus toxin (not applicable for humans). TIG is produced by immunising healthy donors with TT (adsorbed tetanus toxoid)<sup>11</sup>.

TIG and TA provide short-lived passive immunity – antibodies circulate in the human body for 2 to 4 weeks and then gradually disappear; native antibodies are not produced. To induce immunogenesis and specific antibodies, tetanus toxoid is used (for example, adsorbed tetanus toxoid<sup>12</sup>) that provides long-lasting protection.

Notably, post-exposure patients do not gain natural immunity and can become infected again<sup>13</sup>. The reason is the agent located solely within the wound and producing the toxin, while the body immune system cannot recognise the agent. It defines the nature of the acquired immunity, which is antitoxic, not antibacterial.

#### **Preventive measures**

Timely immunisation is the only reliable protection. Routine vaccination is included in the approved national immunisation schedule<sup>14</sup>. Data show decreasing tetanus incidence in Russia and the world, thus proving immunisation effectiveness<sup>15</sup>. For example, in Russia (USSR), the period prior to immunisation (1951–1955) showed the incidence of 0.87 per 100,000,000 population; af-

- Guidance on the management of suspected tetanus cases and the assessment and management of tetanus-prone wounds. UK Health Security Agency; 2024.
- The immunological basis for immunization series Module 3: Tetanus. WHO; 2018.
- <sup>8</sup> Clinical Guidance for Wound Management to Prevent Tetanus. CDC; 2024. Tetanus. WHO; 2024.

Эпидемиологический надзор за столбняком: Методические указания. М.: Федеральный центр гигиены и эпидемиологии Роспотребнадзора; 2009.

- <sup>9</sup> Там же
- 10 Государственный реестр лекарственных средств. https://qrls.rosminzdrav.ru
- <sup>11</sup> Там же.
- <sup>12</sup> Там же.
- https://www.who.int/ru/news-room/fact-sheets/detail/tetanus
- Приказ Минздрава России от 06.12.2021 № 1122н «Об утверждении национального календаря профилактических прививок, календаря профилактических прививок по эпидемическим показаниям и порядка проведения профилактических прививок».
- https://ourworldindata.org/tetanus
  https://ourworldindata.org/tetanus
  https://www.statista.com/statistics/1121381/tetanus-cases-worldwide-by-region/
  https://gateway.euro.who.int/ru/indicators/hfa\_333-2110-incidence-of-tetanus-per-100-000/#id=19264

ter mass immunisation porgramme began (since the 1960s), this index was steadily decreasing and reached 0.026 per 100,000,000 population by 2000. Currently, single tetanus cases are registered in Russia<sup>16</sup>.

Adsorbed TT is used for tetanus prevention; it is produced by detoxification tetanus toxin with formaldehyde and then heating the compound. Then the preparation goes through several purification stages (acid-salt deposition, chromatography, ultra- and microfiltration). Purified TT is rigorously controlled for quality compliance with WHO standards<sup>17</sup>.

Tetanus vaccine is included all national immunisation schedules worldwide. According to WHO<sup>18</sup>, every newborn should be immunised with three (3) vaccine doses starting with six (6) weeks of age, and then three (3) revaccinations at the age of 4–15 years for long-lasting protection. Antitoxic tetanus immunity of a fully vaccinated person lasts for about 10 years. Thus, adults should be immunised once every 10 years. Children are usually immunised with a combined vaccine that includes not only diphtheria and tetanus antitoxins, but other components as well (pertussis, hepatitis etc.). Adult vaccines usually include only diphtheria and tetanus antitoxins, or solely tetanus antitoxin. Adult vaccines are not age-related.

In the countries maintaining wide immunisation coverage for several decades, tetanus incidence is quite low<sup>19</sup>.

# Review of tetanus cases in unvaccinated or undervaccinated persons

Tetanus cases are registered every year in all age groups; unfortunately, fatal outcomes are quite frequent. Analysed mass media, social networks, blogs, and popular literature showed lack of awareness in tetanus prevention and vaccination hesitancy<sup>20</sup> [20, 21]. The sources show that bathing a minor injury (abrasion, scratch, or splinter) at home followed by surgical debridement fully eliminates the risk of tetanus infection. However, timely and full debridement is not always possible, while at-home bathing of even a small wound does not decrease infection risk. Moreover, many patients with domestic injuries

do not seek for timely medical help, thus exacerbating the process and the outcome. Some publications (including official websites) offer misinformation, such as showing major tetanus risk only for injuries of the lower limbs<sup>21</sup>. Moreover, anti-vaxxers spread wrong information that distorts the modern scientific achievements and public healthcare success and causes fear of vaccines. Anti-vaccination activism reduces common adherence with preventive immunisations, which decreases immunisation coverage in all age groups<sup>22</sup> [20, 21].

Table 1 shows tetanus cases in undervaccinated or unvaccinated children and adults. All tetanus cases described were caused by lack of post-vaccinal immunity due to vaccination refusal or breach of vaccination schedule. Eligibility criteria used for paediatric patients: lack of vaccination, minor injury (splinter, abrasion), fatal outcome; for adults: minor injury, unusual traumatising conditions (firecracker, toothpick), poor hygiene of wound debridement, and uncommon clinical manifestations (abnormal urination).

The analysed clinical cases in adults often show irresponsible treatment of the injuries and inattentive wood bathing. In some cases, the patients were late to seek for medical help. It is noteworthy that urgent post-exposure immunisation of a wounded patient is important for maintaining high protection level, alongside with scheduled immunisation.

Paediatric cases are often associated with parents influenced by anti-vaccination propaganda. Anti-vaccination advocates spread the idea of supposedly useless immunisation while fully disregarding cutting-edge data on vaccine safety and efficiency, as well as their essential role in decreased incidence of severe infections causing disabilities and fatal outcomes [20, 21, 35]. According to CDC, in 2019, a case of severe tetanus was registered in an unvaccinated child whose parents actively supported anti-vaccine activism. The incident gained public resonance due to several reasons: anti-vaccine activism of the parents, prolonged and complicated treatment, and high treatment expenses (approximately \$800,000)<sup>23</sup>.

<sup>&</sup>lt;sup>16</sup> ЕМИСС. Государственная статистика. Число зарегистрированных случаев инфекционных заболеваний. <a href="https://fedstat.ru/">https://fedstat.ru/</a>

WHO Expert Committee on Biological Standardization. 40th report. WHO; 1990.

Immunization, Vaccines and Biologicals. Tetanus. WHO.

<sup>&</sup>lt;sup>18</sup> Tetanus reported cases and incidence. WHO; 2023.

https://vaccina.info/

History of vaccines. History of Anti-Vaccination Movements.

https://34.rospotrebnadzor.ru/content/202/9711/

History of vaccines. History of Anti-Vaccination Movements.

Notes from the Field: Tetanus in an Unvaccinated Child – Oregon, 2017. CDC; 2019.

Table 1. Clinically confirmed cases of tetanus in children and adults Таблица 1. Клинически подтвержденные случаи столбняка у детей и взрослых

Year, country Год, страна	Age (sex) Возраст (пол)	Vaccination status Иммунный статус	Inoculation site and wound characteristics Локализация и характер травмы	Post-injury period, clinical manifestations Период после травмы, клинические проявления	Treatment and outcomes Лечение и исход заболевания
2023, Brasil Бразилия	16 (male) (муж)	Unvaccinated Не вакцинирован	The patient sustained a hand injury while carrying iron construction materials Повреждение руки при переноске строительных материалов из железа	In 10 days: trismus, gener- alised muscle spasms Через 10 сут: генерализованные спазмы, тризм	Treatment received: TA, TIG. The treatment was successful [22] Введено: ПСС и ПСЧИ. Полностью восстановлен [22]
2023, Belarus Беларусь	8 (female) (жен)	Unvaccinated (parents' religious and personal beliefs) Не вакцинирована (религиозные и личные убеждения родителей)	The patient had a splinter in the foot. The splinter was removed by the parents Заноза в стопе. Занозу родители самостоятельно удалили	Within 7–10 days: trismus, head and neck pain, speech impairment, fever (no exact measurements, no thermometer in the household). At admission: hypertonus В течение 7–10 сут: тризм, боли в области головы и шеи, нарушение речи, лихорадка (температуру не измеряли – в семье не было термометра). Поступила в состоянии гипертонуса	The girl's parents refused TA or TT. After a long hospital stay, the treatment was adjusted, and TA was administered. The patient was discharged in stable condition [23] От введения ПСС и СА родители девочки отказались. После длительного пребывания в стационаре лечение было скорректировано, введен СА. Выписана в стабильном состоянии [23]
2023, Кугдуzstan Кыргызстан	5 (male) (муж)	Unvaccinated (parents' religious beliefs) Не вакцинирован (религиозные убеждения родителей)	The patient stepped on a nail with his foot. The wound was 0.5 cm deep and healed quickly. The patient did not seek medical attention Стопа. Наступил на гвоздь (глубина раны 0,5 см). Рана быстро затянулась, за медицинской помощью не обращался	In 10 days: fever (39.8 °C), opisthotonus Через 10 сут: температура (39,8 °C), опистотонус	Treatment received: TA (90,000 IU), intensive care. The patient died on day 3 of treatment [24] Введено: ПСС 90 тыс. МЕ, интенсивная терапия. На 3 сут лечения констатирована биологическая смерть [24]
2022, Indonesia Индонезия	44 (male) (муж)	No data (no recollection of having been vaccinated) Нет данных (пациент не мог вспомнить)	The patient had tetanus of odontogenic origin. He often used a toothpick to poke his interdental gingiva Столбняк одонтогенного происхождения. Пациент часто использовал зубочистку для чистки межзубного пространства	At admission: lockjaw and difficulty swallowing, rictus grin, pain and stiffness in the neck and jaw Обратился в больницу с жалобами на невозможность открыть рот, трудности при глотании, сардоническую улыбку, боль и скованность в области шеи	Treatment received: TIG (3,000 IU). The patient was successfully treated and discharged in 2 weeks [25] Введено: ПСЧИ 3000 МЕ. Через 2 нед. выписан с выздоровлением [25]

Table 1 (continued) Продолжение таблицы 1

Year, country Год, страна	Age (sex) Возраст (пол)	Vaccination status Иммунный статус	Inoculation site and wound characteristics Локализация и характер травмы	Post-injury period, clinical manifestations Период после травмы, клинические проявления	Treatment and outcomes Лечение и исход заболевания
2021, Indonesia Индонезия	7 (female) (жен)	Unvaccinated (low body weight at birth, parents' religious beliefs) Не вакцинирована (низкая масса тела при рождении; религиозные убеждения)	The patient had a forehead laceration from falling and hitting her head on the cement floor in a public restroom. She was brought to a healthcare facility immediately and underwent wound suturing Травма головы (рана на лбу). Ударилась головой о цементный пол в общественном туалете. Сразу обратились за помощью — рана была зашита	In 10 days: nuchal rigidity, trismus, motoric spasticity, a purulent scalp wound (2 × 1.5 × 0.5 cm). Diagnoses: tetanus and skull fracture Через 10 сут: ригидность затылочных мыши, тризм, двигательная спастичность, на черепе гнойная рана (2×1,5×0,5 см). Поставлены диагнозы: столбняк и перелом черепа	Treatment received: TIG (3,000 IU), skull fracture repair surgery. The patient was successfully treated and discharged in 3 weeks [26] Введено: ПСЧИ 3000 МЕ. Проведена операция по устранению перелома черепа. Через 3 нед. выписана с выздоровлением [26]
2021, Russia Россия	11 (male) (муж)	Unvaccinated (mother's religious beliefs) Не вакцинирован (мать противница вакцинации)	The patient stepped on a nail with his foot and was brought to a healthcare facility immediately. The wound was treated, and Td was administered Стопа. Наступил на гвоздь. Сразу обратился в травмпункт, проведена санация раны, введен АДС-М-анатоксин	On day 8: trismus, back rigidity На 8 сут развился тризм, спазм мышц спины	Treatment received: TA (60 IU). The patient was discharged in 26 days [27] Введено: ПСС 60 МЕ. Выписан на 26 сут [27]
2019, Canada Канада	33 (male) (муж)	Fully vaccinated as a child Вакцинирован полностью в детстве	The patient injured his hands in an altercation (minor hand cuts and abrasions). The patient worked as a soil testing technologist; he was regularly exposed to dirt and soil. He did not seek medical attention Травмы рук, полученные в результате драки (небольшие порезы и ссадины на руках). В связи с профессиональной деятельностью (технолог по исследованию почв) пациент регулярно контактировал с почвой и грязью. За медицинской помощью не обращался	In 10 days: nausea, vomiting, pain and spasms in the lumbar region. At admission: intense spasms that were triggered by sound and movement and progressed to opisthotonus  Через 10 сут: тошнота, рвота, боли и спазмы в области поясницы. При осмотре в отделении – интенсивные спазмы, прогрессирующие до выгибания спины, и связанные с определенными триггерами – звук и движение	Treatment received: TIG (500 IU), intensive care. The patient was discharged in 34 days. Tetanus resulted in a slipped disc for which the patient required operative repair. Two years post-incident, he has fully recovered [28] Введено: ПСЧИ 500 МЕ. Интенсивная терапия. Выписан через 34 сут. Перенесенное заболевание привело к смещению межпозвоночного диска, что потребовало оперативного вмешательства. Полностью восстановился спустя два года [28]

Table 1 (continued) Продолжение таблицы 1

Year, country Год, страна	Age (sex) Возраст (пол)	Vaccination status Иммунный статус	Inoculation site and wound characteristics Локализация и характер травмы	Post-injury period, clinical manifestations Период после травмы, клинические проявления	Treatment and outcomes Лечение и исход заболевания
2018, Ireland Ирландия	22 (female) (жен)	Fully vaccinated as a child Вакцинирована полностью в детстве	The patient presented with a dog bite to her hand. She did not wash the wound or seek medical attention Рука. Укус собаки. Рану не промывала. За медицинской помощью не обращалась	In 3 days: feeling intermittently hot and cold, headache, and palpitations. TT was administered. Afterwards, difficulty opening the mouth and walking developed Через 3 сут: приступы холода и жара, головная боль, сердцебиение. Введен СА. Развились трудности с открыванием рта и ходьбой	Treatment received: TIG (3,000 IU). The patient was discharged in satisfactory condition in 10 days [29] Введено: ПСЧИ 3000 МЕ. Через 10 сут выписана в удовлетворительном состоянии [29]
2015, Япония Јарап	34 (male) (муж)	No data Нет данных	The patient was scratched by a stray cat. The patient did not seek medical attention Царапина нанесена дикой кошкой. За медицинской помощью не обращался	In 1 month (at admission): bladder dysfunction, difficulty walking Через 1 мес. поступил в стационар с дисфункцией мочевого пузыря, жалобы на трудности при ходьбе	Treatment received: TIG. The patient fully recovered in 1 week [30] Введено: ПСЧИ. Через неделю полностью восстановился [30]
2012, Sri-Lanka Шри-Ланка	13 (female) (жен)	Fully vaccinated before 5 years of age Получила полную иммунизацию до 5 лет	The patient injured her eye by falling on a tree stump and had minor bleeding. The patient was admitted to hospital Глаз. Повреждение при падении на пень дерева, было небольшое кровотечение. Обратились за медицинской помощью и оставлена в стационаре	In 2 days: pain on eye movements, fever. On day 7: neck spasms, opisthotonus Через 2 сут: боль при движении глазом, лихорадка. На 7 сут — спазмы мышц шеи, опистотонус	Treatment received: TIG (4,000 IU), intensive care. The patient was immunised after recovery [31] Введено: ПСЧИ 4000 МЕ. Интенсивная терапия. После восстановления проведен курс вакцинации [31]
2012, Јарап Япония	49 (male) <i>(муж)</i>	No data Hem данных	The patient suffered a traumatic amputation of his right middle finger at the distal interphalangeal joint region. His gloved hand was caught between a gas cylinder and a concrete floor at work Травма руки в результате несчастного случая на работе. Ампутация среднего пальца правой руки в области дистального межфалангового сустава (рука в перчатке была зажата между газовым баллоном и бетонным полом)	The surgery was performed. No TT was injected since there was no soil contamination. In 21 days after surgery: tetanus with trismus and back pain Проведена хирургическая операция. Поскольку раны не были загрязнены почвой, специфическую противостолбнячную иммунную терапию не проводили. На 21 сут после операции появились признаки тризма и болей в спине	Treatment received: TIG (12,000 IU). The patient fully recovered in 12 weeks after surgery [32] Введено: ПСЧИ 12000 МЕ. Полностью восстановлен через 12 нед. после операции [32]

Table 1 (continued) Продолжение таблицы 1

Year, country Год, страна	Age (sex) Возраст (пол)	Vaccination status Иммунный статус	Inoculation site and wound characteristics Локализация и характер травмы	Post-injury period, clinical manifestations Период после травмы, клинические проявления	Treatment and outcomes Лечение и исход заболевания
2009, Netherlands Нидерланды	4 (male) <i>(муж)</i>	Unvaccinated (parents' religious beliefs) Не вакцинирован (религиозные убеждения родителей)	The patient had his big toenail torn off and a small local haematoma present Нога. Содран ноготь на большом пальце ноги, небольшая гематома	In 3 days: weakness, dysphagia, sore throat, salivation. Tetanus not diagnosed. The condition worsened, difficulties with opening the mouth increased Через 3 сут: слабость, дисфагия, боль в горле, слюнотечение. Диагноз не установлен. Состояние ухудшалось, появились трудности при открывании рта	Treatment received: TIG (3,000 IU), intensive care. The patient fully recovered in 30 days [33] Введено: ПСЧИ 3000 МЕ. Интенсивная терапия. Полностью восстановлен через 30 сут [33]
2008, China Китай	37 (female) <i>(жен)</i>	No data Hem данных	The patient had a fire-cracker wound (2 cm diameter) in the chest. She did not seek medical attention Грудная клетка. Ранение при взрыве петарды (диаметр 2 см). За медицинской помощью не обращалась	Gradually: stiffness in the neck and muscle cramps in all limbs Постепенно появились скованность шеи и судороги мышц всех конечностей	Treatment received: TA (1,500 IU), TIG (150 IU/kg), intensive care. The patient fully recovered in 57 days [34] Введено: ПСС 1500 МЕ, ПСЧИ 150 МЕ/кг. Интенсивная терапия. Полное восстановление на 57 сут [34]

The table is prepared by the authors / Таблица составлена авторами

*Note.* TA, tetanus antitoxin; TIG, tetanus immune globulin (human); TT, tetanus toxoid; IU, international units; Td, diphtheria-tetanus toxoid (low-dose antigen formulation).

Примечание. ПСС – противостолбнячная сыворотка (лошадиная); ПСЧИ – противостолбнячный человеческий иммуноглобулин; СА – столбнячный анатоксин; МЕ – международные единицы; АДС-М – анатоксин дифтерийно-столбнячный с пониженным содержанием антигенов.

Sometimes religious beliefs cause vaccination refusals, being second most popular reason for refusal. Importantly, these arguments were repeatedly denied by many religious communities<sup>24</sup>. However, the parents continue ignoring these explanations despite the risk of infections due to active anti-vaccine movement that is often more large-scale than medical and scientific efforts opposing these beliefs.

# **CONCLUSIONS**

Despite high-potency tetanus vaccines widely spread, every year the disease affects tens of thousands of people worldwide. Unvaccinated or undervaccinated people are at a high-risk group. In this regard, particularly important is a regular vaccina-

tion of all age groups based on national guidelines.

Tetanus intoxication specifics, lack of effective laboratory tests that would confirm or exclude the diagnosis, and complicated specific therapy increase the risk of fatal outcomes or disability.

The reviewed cases show that minor wounds and abrasions bear a risk of tetanus infection, alongside with severe injuries and damages.

Case analysis of unvaccinated or undervaccinated persons highlights the necessity of public health education aimed at:

- popularising timely scheduled immunisations according to national guidelines, including newborns;
- placing emphasis on regular revaccination of adults according to vaccine schedules;

Religious concerns: resources and information. Immunize.org; 2024.
Прививки и мировые конфессии. ЮНИСЕФ; 2022.

- explaining the need of timely post-exposure prophylaxis for any injuries;
- consistently disproving false allegations from the anti-vaxxers.

Successfully handling these tasks requires a close cooperation of health care experts, non-

profit organisations, and religious communities with the required competence and authority. This will allow to increase the vaccination adherence, enhance the coverage and reduce the incidence of vaccine-preventable diseases, including tetanus.

# Литература/References

- 1. Якимова ТН, Максимова НМ, Маркина СС, Яцковский КА, Жилина НЯ. Состояние противостолбнячного антитоксического иммунитета у населения Российской Федерации в настоящее время. Эпидемиология и вакцинопрофилактика. 2013;(5):54–9. Yakimova TN, Maximova NM, Markina SS, Yatskovsky KA, Zhilina NY. The present level of the tetanus antitoxic immunity among population of the Russian Federation. Epidemiology and Vaccinal Prevention. 2013;(5):54–9 (In Russ.). EDN: REFCPB
- Salem N, Huang G, Squires SG, Salvadori MI, Li YA. Epidemiology of tetanus in Canada, 1995–2019. Can J Public Health. 2023;114(3):432-440. https://doi.org/10.17269/s41997-022-00732-7
- 3. Schatz D, Ellis T, Ottendorfer E, Jodoin E, Barrett D, Atkinson M. Aging and the immune response to tetanus toxoid: Diminished frequency and level of cellular immune reactivity to antigenic stimulation. *Clin Diagn Lab Immunol*. 1998;5(6):894–6. https://doi.org/10.1128/CDLI.5.6.894-896.1998
- Ходкевич ПЕ, Куликова КВ, Деев ИА, Федорова ОС, Куликов ЕС. Вакцинопрофилактика недоношенных новорожденных: реальная клиническая практика. Инфекционные болезни. 2022;20(3):50–8. Hodkevich PE, Kulikova KV, Deev IA, Fedorova OS, Kulikov ES. Vaccination of premature infants: Real clinical practice. Infectious Diseases. 2022;20(3):50–8 (In Russ.). https://doi.org/10.20953/1729-9225-2022-3-50-58
- 5. Li J, Liu Z, Yu C, Tan K, Gui S, Zhang S, et al. Global epidemiology and burden of tetanus from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019. *Int J Infect Dis.* 2023;132:118–26. https://doi.org/10.1016/j.ijid.2023.04.402
- 6. Mcelaney P, Iyanaga M, Monks S, Michelson E. The quick and dirty: A tetanus case report. *Clin Pract Cases Emerg Med*. 2019;3(1):55–8. https://doi.org/10.5811/cpcem.2019.1.41301
- Abdi H, Caqli I, Mumin M, Osman J, Fricchione G, Chemali Z. Case series of tetanus diagnosis and management in Hargeisa City. Clin Med Rev Case Rep. 2020;7:312. https://doi.org/10.23937/2378-3656/1410312
- 8. Okuda M, Morizane A, Asaba S, Tsurui S, Tsuno R, Hatakenaka M, et al. An unexpected case of tetanus in a fully immunized 20-year-old female: A case report. *Int J Emerg Med*. 2024;17(1):59. https://doi.org/10.1186/s12245-024-00633-1
- 9. Srigley JA, Haider S, Johnstone J. A lethal case of generalized tetanus. *CMAJ*. 2011;183(9):1045–8. https://doi.org/10.1503/cmaj.101121
- 10. Gulamhussein MA, Li Y, Guha A. Localized tetanus in an adult patient: Case report. *J Orthop Case Rep.* 2016;6(4):100–2.

#### https://doi.org/10.13107/jocr.2250-0685.592

- 11. Raia PJ. Tetanus: a case study. *J Am Board Fam Pract*. 2001;14(3):223-4.
- 12. Samaila A, Abdulkadir B, Kabir K, Aliyu S, Umar Z. Pathogenesis and management of tetanus. *UJMR*. 2018;3(1):16–23.
  - https://doi.org/10.47430/ujmr.1831.003
- 13. Ovsepian SV, O'Leary VB, Ayvazyan NM, Al-Sabi A, Ntziachristos V, Dolly JO. Neurobiology and therapeutic applications of neurotoxins targeting transmitter release. *Pharmacol Ther.* 2019;193:135–55. <a href="https://doi.org/10.1016/j.pharmthera.2018.08.016">https://doi.org/10.1016/j.pharmthera.2018.08.016</a>
- 14. Megighian A, Pirazzini M, Fabris F, Rossetto O, Montecucco C. Tetanus and tetanus neurotoxin: From peripheral uptake to central nervous tissue targets. *J Neurohem.* 2021;158(6):1244–53. https://doi.org/10.1111/jnc.15330
- 15. Popoff MR. Tetanus in animals. *J Vet Diagn Invest*. 2020;32(2):184–91. https://doi.org/10.1177/1040638720906814
- 16. Akane Y, Tsugawa T, Hori T, Togashi A, Yoto Y, Inazawa N, et al. Tetanus in a partially immunized child. *J Infect Chemother*. 2018;24(12):980–2. https://doi.org/10.1016/j.jiac.2018.05.002
- 17. Tharu B, Ibrahim S, Shah M, Basnet S, Park T. An unusual case of evolving localized tetanus despite prior immunization and protective antibody titer. *Cureus*. 2020;12(7):e9498. https://doi.org/10.7759/cureus.9498
- 18. Atabek ME, Pirgon O. Tetanus in a fully immunized child. *J Emerg Med*. 2005;29(3):345–6. https://doi.org/10.1016/j.jemermed.2005.06.005
- 19. Hahn BJ, Erogul M, Sinert R. Case report of tetanus in an immunized, healthy adult and no point of entry. *J Emerg Med*. 2004;27(3):257–60. https://doi.org/10.1016/j.jemermed.2004.03.015
- 20. Оффит ПА. *Смертельно опасный выбор.* М.: Corpus; 2022. Offit PA. *Deadly choices*. Moscow: Corpus; 2022 (In Russ.).
- 21. Galagali P, Kinikar A, Kumar V. Vaccine hesitancy: Obstacles and challenges. *Curr Pediatr Rep.* 2022;10(4):241–8. https://doi.org/10.1007/s40124-022-00278-9
- 22. Deniz M, Erat T. Generalized tetanus: A pediatric case report and literature review. *Rev Inst Med Trop São Paulo*. 2023;65:e40.
  - https://doi.org/10.1590/S1678-9946202365040
- 23. Сергиенко ЕН, Романова ОН, Астапов АА, Ключарева АА, Федорова ИВ, Стрижак МИ и др. Столбняк у невакцинированного ребенка: клинический случай. *Клиническая инфектология и паразитология*. 2023;12(1):68–75. Sergienko EN, Romanova ON, Astapov AA, Klyuchareva AA, Fedorova IV, Strizhak MI, et al. Tetanus in an unvaccinated

- child: A clinical case. *Clinical Infectology and Parasitology*. 2023;12(1):68–75 (In Russ.). https://doi.org/10.34883/PI.2023.12.1.028
- 24. Юнусов ТА, Радченко ЕА. Клинический случай генерализованной формы столбняка у ребенка. В кн.: Технологические инновации и научные открытия. Сборник научных статей по материалам XII Международной научно-практической конференции. Уфа; 2023. Yunusov TA, Radchenko EA. Clinical case of generalized tetanus in a child. In: Technological innovations and scientific discoveries. Collection of scientific articles based on the materials of the XII International scientific and practical conference. Ufa; 2023 (In Russ.). EDN: CPCIDM
- 25. Akbar M, Ruslin M, Yusuf ASH, Boffano P, Tomihara K, Forouzanfar T. Unusual generalized tetanus evolving from odontogenic infection: A case report and review of recent literature. *Heliyon*. 2022;8(9):e10810. https://doi.org/10.1016/j.heliyon.2022.e10810
- 26. Hakim DDL, Faried A, Nurhadiya A, Laymena EH, Arifin MZ, Imron A, et al. Infected open depressed skull fracture complicated with tetanus grade I in an unimmunized child: A rare case report with literature review. *Int J Emerg Med*. 2021;14(1):25. https://doi.org/10.1186/s12245-021-00346-9
- 27. Козлов АА, Шевчук ИВ, Завьялов АЕ, Емельянов АН. Генерализованная форма столбняка у ребенка 11 лет: клиническое наблюдение. Российский вестник детской хирургии, анестезиологии и реаниматологии. 2021;11(1):69–75. Kozlov AA, Shevchuk IV, Zavialov AE, Emelyanov AN. Generalized tetanus in an 11-year-old boy: A case report. Russian Journal of Pediatric Surgery, Anesthesia and Intensive Care. 2021;11(1):69–75 (In Russ.). https://doi.org/10.17816/psaic693

28. Medu O, Ogunyemi N, Hennink M, Mawer S, Styles-Mackinnon T, Wong A, et al. Tetanus in a vaccinated soil

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- expert a case report. *BMC Infect Dis.* 2023;23(1):760. https://doi.org/10.1186/s12879-023-08780-1
- 29. Moynan D, O'Riordan R, O'Connor R, Merry C. Tetanus a rare but real threat. *ID Cases*. 2018;12:16–17. https://doi.org/10.1016/j.idcr.2018.02.004
- 30. Kira S, Sawada N, Aoki T, Kobayashi H, Takeda M, et al. Voiding dysfunction induced by tetanus: A case report. *Urol Case Rep.* 2016;5:6–8. https://doi.org/10.1016/j.eucr.2015.12.004
- 31. Karunarathne S, Govindapala D, Fernando H. Tetanus following ocular wooden foreign body in incompletely vaccinated patient: A case report. *Asian Pac J Trop Dis.* 2012;2(6):495–6.
  - https://doi.org/10.1016/S2222-1808(12)60110-8
- 32. Hayashida K, Murakami C, Fujioka M. Tetanus following replantation of an amputated finger: A case report. *J Med Cases*. 2012;6:343.
  - https://doi.org/10.1186/1752-1947-6-343
- 33. de Jong PR, de Heer-Groen T, Schröder CH, Jansen NJ. Generalized tetanus in a 4-year old boy presenting with dysphagia and trismus: A case report. *J Med Case Rep.* 2009;2:7003.
  - https://doi.org/10.1186/1757-1626-2-7003
- 34. Chun P, Ying-Zi H, Yi Y, Hai-Bo Q. Titration of high dose sedation is effective in severe tetanus: A case report. *Cases J.* 2009;2:6865.
  - https://doi.org/10.4076/1757-1626-2-6865
- 35. Комаровская ЕИ, Перелыгина ОВ. Современная ситуация по заболеваемости отдельными клостридиальными инфекциями: газовая гангрена и столбняк. БИОпрепараты. Профилактика, диагностика, лечение. 2021;21(1):31–8. Komarovskaya EI, Perelygina OV. Current incidence of certain clostridial infections: Gas gangrene and tetanus. BIOpreparations. Prevention, Diagnosis, Treatment. 2021;21(1):31–8 (In Russ.).

https://doi.org/10.30895/2221-996X-2021-21-1-31-38

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