

Fighting the Unseen Foe: Tetanus, Anti-tetanus Serum and the Royal Army Medical Corps in World War I

Edward J Wawrzynczak

Redhill, Surrey, UK. Email: e.wawrzynczak@btinternet.com

Abstract

Tetanus has long been associated with wounds and war. Experimental, veterinary and clinical data suggested tetanus following contamination of wounds could be prevented by injecting anti-tetanus serum soon after injury although it was used sparingly in civilian practice before World War I. The British Army's experience of the disease in the early twentieth century was limited and deployment of anti-tetanus serum was not a priority.

In the early months of the war, the British Expeditionary Force experienced a high incidence of tetanus. Following the order that all wounded soldiers should be given a prophylactic dose of anti-tetanus serum the incidence of tetanus-cases dropped. Earlier reports from abroad raised the danger of projectile wounds, contamination by tetanus-containing soils and the need for large amounts of the serum. Such warnings went unheeded and lack of advance planning meant a shortfall in supply. The expanded use of anti-tetanus serum during the war placed great demands on British serum manufacturers, the Royal Army Medical College responsible for issuing sera, and military medical personnel at the front and at home.

Administration of anti-tetanus serum coupled with surgical excision of wounds reduced tetanus incidence significantly but did not eradicate the disease. Tetanus also followed trivial injuries, trench foot and some surgical operations. Prophylaxis was difficult to deliver during times of intense warfare. Shortly before World War II, however, plans were laid to ensure an adequate supply of anti-tetanus serum in the event of hostilities. Moreover, the introduction of active immunisation led to a further reduction in tetanus incidence.

Keywords

Tetanus, Antitoxin, Serum, Prophylaxis, British Army, World War I

Introduction

In the opening months of World War I (WWI), the British Expeditionary Force (BEF) experienced a high number of fatal cases of tetanus in wounded casualties. The Army then sought to inoculate every wounded soldier with anti-tetanus serum (ATS), commonly called tetanus antitoxin or antitoxic serum, to prevent the onset of the disease. This practice continued for the rest of the war.

In his chapter 'Tetanus in its statistical aspects' in the official history of the war, Colonel S Lyle Cummins (1873-1949), formerly Professor of Pathology at the Royal Army Medical College (RAM College) and later Deputy Assistant Director General, Army Medical Service (AMS), BEF in France concluded:

While giving full weight to the importance of efficient surgery in ameliorating the severity and diminishing the mortality of tetanus, more especially when excision of wounds is practised as in the latter part of the war, neither this nor any other factor can be so closely associated with a diminution of incidence, severity and mortality, and with a prolongation of the incubation period, as can the administration of antitoxic serum. The high value of this method of prophylaxis would appear to be the outstanding fact of the history of tetanus in the European war of 1914-18.¹

This paper examines the response of the British Army to the problem of tetanus within a wider historical context and seeks to answer the following questions. What was the basis for using ATS as a mass prophylactic in WWI? Could prophylactic inoculation have been instituted on a wide scale earlier? What were the arrangements for the supply of the serum? What lessons could be learned? Moreover, were the lessons heeded?

Tetanus

Clinical descriptions of disease highly suggestive of tetanus can be found in some of the oldest known medical treatises including the Hippocratic corpus of the fifth century BCE.² The disease often manifested with stiffness of the jaw ('lockjaw') that stopped the mouth opening. The facial muscles next tightened resulting in an exaggerated grin (*risus sardonicus*). Stiffness affected the neck and the ability to swallow. Painful muscle contractions spread to the rest of the body (*tetanus*). Then, extreme rigidity arched the back and left the body resting on the head and heels (*opisthotonus*). The patient suffered repeated, prolonged and intense spasms. Death typically ensued from asphyxia or heart-failure and mortality was high.³

The horror of acute general tetanus affecting many of the major muscle groups was never better depicted than in an oil painting by Sir Charles Bell (1774-1842) shown in

¹ Macpherson WG, Leishman WB, Cummins SL. *History of the Great War based on official documents. Medical Services, Pathology*. London: HMSO; 1923. p.164-187.

² Chalian W. An essay on the history of lockjaw. *Bulletin of the History of Medicine*. 1940; 8: 171-201.

³ Guilfoile P. *Tetanus*. New York, NY: Chelsea House Publishing; 2008.

Figure 1. A talented artist as well as an accomplished surgeon and anatomist, Bell based the painting on sketches he made of three soldiers who had sustained gunshot fractures of the skull and been repatriated to Portsmouth in January 1809 following the Battle of Corunna during the Peninsular War of 1808-1814.⁴



Figure 1. The Wounded following the Battle of Corunna: Tetanus Following Gunshot Wounds. Painting, oil on canvas, by Charles Bell, 1809. The Royal College of Surgeons of Edinburgh. Accession No. 13843. Creative Commons.

Until the late nineteenth century, treatment of tetanus was largely symptomatic as reflected by Sir William Osler (1849-1919) in the original edition of his textbook for practitioners and students of medicine. The patient was kept in a darkened room, absolutely quiet, attended by only one person and shielded from possible sources of irritation. In extreme cases, feeding was accomplished via a catheter passed through the nose or by rectal injections. Spasms were controlled by dosing with chloroform or, more satisfactorily, keeping the patient under the influence of morphine injected hypodermically. A variety of other drugs might be used, including chloral hydrate, potassium bromide, curare, hemp and belladonna.⁵

⁴ Crumplin MKH, Starling PH. *A Surgical Artist at War: The Paintings and Sketches of Sir Charles Bell 1809-1815*. Edinburgh: Royal College of Surgeons of Edinburgh; 2005.

⁵ Osler W. *The Principles and Practice of Medicine*. Edinburgh & London: Young J Pentland; 1892. p.164-165.

Anti-tetanus serum

Tetanus was long known to occur after wounding, especially in cases where the skin had been deeply punctured and contaminated with foreign matter, but its cause was only understood with the advent of bacteriology. Between 1884 and 1890, researchers established that the causative agent was an anaerobic bacillus present as spores in soil which, after infecting a wound, exerted its systemic pathogenic effects by the release of a soluble toxin that affected the central nervous system. The isolated toxin induced the tetanic symptoms characteristic of the disease in experimental animals.⁶

The Japanese bacteriologist Shibasaburo Kitasato (1853-1931) was the first to succeed in isolating the tetanus bacillus while working as a visitor in the Institute of Hygiene at the University of Berlin directed by Robert Koch (1843-1910).⁷ Also in Koch's laboratory at the time was Emil Behring (1854-1917), a former German military doctor who had been investigating ways to treat diphtheria, which also exerted its pathogenic effects by means of a soluble toxin.⁸

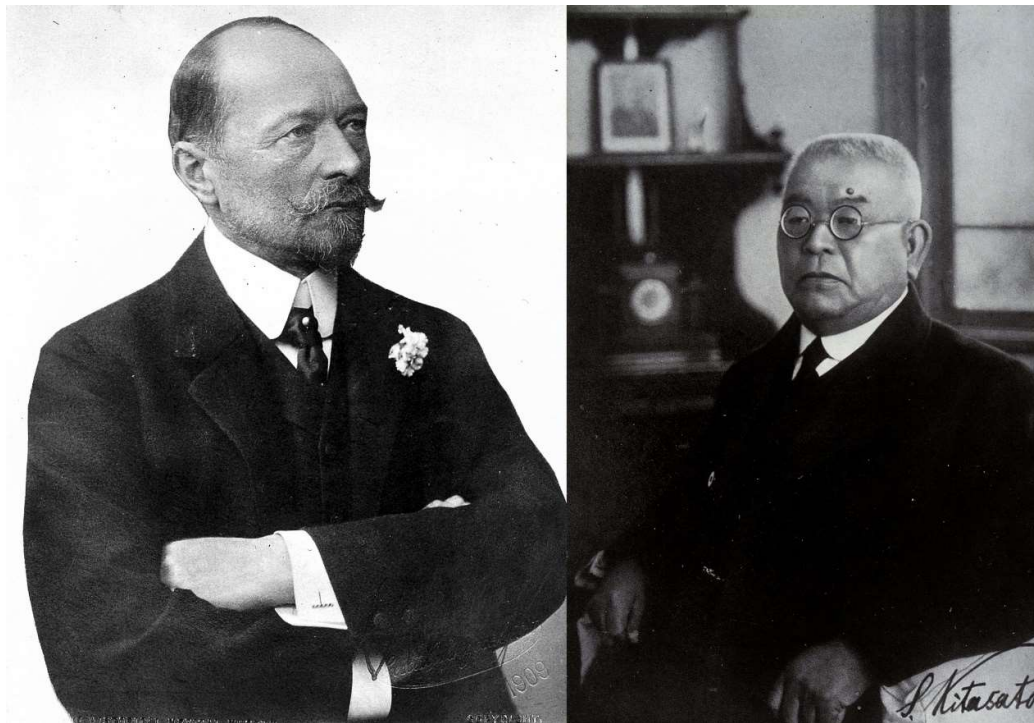


Figure 2. Left: Emil von Behring. Photograph. Wellcome Collection. Reference: 12328i. Public Domain Mark. Right: Shibasaburo Kitasato. Photograph. Wellcome Collection. Reference: 13003i. Public Domain Mark.

⁶ Cavaillon J-M. From bacterial poisons to toxins: the early works of Pasteurians. *Toxins*. 2022; 14, 759; Guilfoile. *Tetanus*, 2008 (Note 3). p.22-26.

⁷ Bartholomew JR. Japanese Nobel candidates in the first half of the twentieth century. *Osiris*. 1998; 13: 238-284.

⁸ Linton DS. *Emil von Behring: Infectious Disease, Immunology, Serum Therapy*. Philadelphia: American Philosophical Society; 2005. p.99-196.

In 1890, Behring and Kitasato (Figure 2) decisively proved that animals repeatedly inoculated with tetanus toxin developed immunity to the toxin and produced a substance in their blood serum which powerfully and specifically neutralised it. When given as prophylaxis, ATS prevented the toxin-induced paralysis of laboratory animals.⁹ As the antidote to tetanus toxin, ATS was one of the earliest medical fruits of bacteriological science, alongside the development of anti-diphtheria serum, or diphtheria antitoxin, as a specific and effective therapy.¹⁰

The horse became the preferred animal for producing ATS. Immunisation involved repeated inoculation with toxin-containing cultures of increasing strength over a matter of weeks or months. However, horses were highly liable to develop tetanus following wounds and, once symptoms set in, ATS rarely brought about a cure. The French veterinarian Edmond Nocard (1850-1903) studied the prophylactic use of ATS in the suburbs of Paris where tetanus was rife and showed that it prevented the disease if animals were injected before planned surgery or after accidental injury. Veterinarians then advised immediate injection for tetanus-prone wounds in localities where the disease was common.¹¹

Clinical use of ATS

A survey of the medical literature between 1890 and 1914, principally case reports and commentaries in the *Lancet* and *British Medical Journal (BMJ)*, shows that attention in Britain was focused on the treatment of tetanus, although the accumulation of reports failed to establish tetanus antitoxin's curative value. In peacetime, tetanus was rare and only occurred sporadically so that few doctors or institutions saw more than a handful of cases. Patients often presented with tetanus symptoms some considerable time after injury by which time the toxin had already acted and it was too late for the antitoxin to intervene.¹²

Using ATS to prevent tetanus from occurring following lacerated wounds had been suggested in Britain as early as 1895.¹³ At this time, however, surgeons were reluctant to practice prophylactic inoculation, believing that the thorough antiseptic cleansing of wounds when patients first presented themselves for treatment was most effective in blocking the development of tetanus.¹⁴ It took until 1910 before the first paper appeared

⁹ Bibel DJ. *Milestones in Immunology: A Historical Exploration*. Madison, WI: Science Tech Publishers; 1988. p.12-15.

¹⁰ Weindling P. From medical research to clinical practice: serum therapy for diphtheria in the 1890s. In Pickstone JV (ed), *Medical Innovations in Historical Perspective*. Basingstoke: Macmillan; 1992. p.72-83.

¹¹ Wawrzynczak EJ. Livesaving serum from horses: The Lister Institute of Preventive Medicine, tetanus antitoxin, and World War I. *Veterinary History*. 2019; 20: 28-52.

¹² Wawrzynczak EJ. *Preventing Tetanus in Wounded Soldiers: Evidence Supporting the use of Tetanus Antitoxin at the Beginning of World War I*. Unpublished Dissertation. Diploma in the History of Medicine of the Society of Apothecaries, London, 2014.

¹³ Hewlett RT. The antitoxin treatment of tetanus. *Practitioner*, 1895; 54: 323-329.

¹⁴ Turner A, Cheate GL. West London Hospital. A case of traumatic tetanus treated by antitoxic serum; recovery. *Lancet*. 1895; 146(3771): 1431-32.

recommending tetanus antitoxin for all accidents where a wound had recently been in contact with dirt from a road, garden or field.¹⁵

The strongest evidence in favour of prophylaxis came from ‘Fourth of July’ injuries sustained annually during celebrations of Independence Day in the US. Large numbers of ‘patriotic tetanus’ cases with very high mortality occurred due to infection of wounds caused by the premature explosion of blank cartridges and fireworks.¹⁶ In 1903, the *Journal of the American Medical Association* began a campaign to eliminate the annual ‘slaughter of the innocents’ by promoting the administration of tetanus antitoxin as well as thorough surgical cleansing of wounds.¹⁷ This was noted in the *Lancet* on a couple of occasions.^{18 19} By 1913, there were only three deaths from tetanus, compared with 406 in 1903, and none by 1916 (Figure 3).

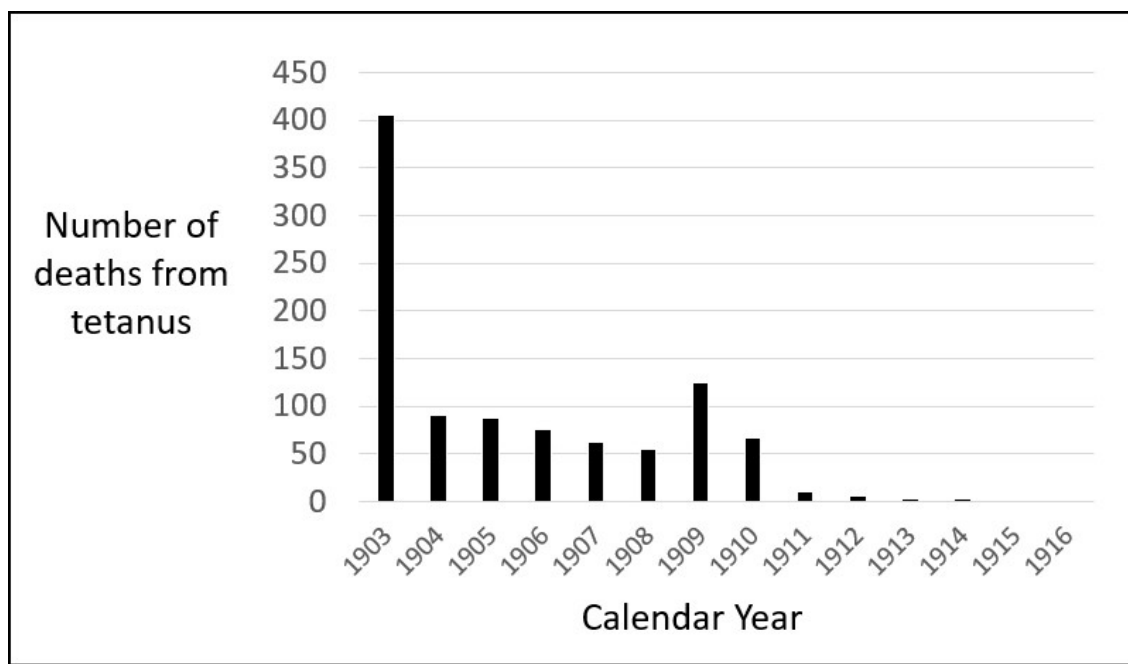


Figure 3. Incidence of tetanus among Fourth of July injuries. Compiled with data from: Smilor. *Creating a National Festival*, 1980 (Note 16).

A 1908 US Public Health and Marine-Hospital Service report noted that, over a five-year period, there were 786 cases of tetanus with 721 deaths, a mortality of 92 per cent. The weight of evidence favoured the view that blank cartridges were rarely

¹⁵ Cheatle GL. Treatment of wounds in road or garden or field accidents. *British Medical Journal*. 1910; 1(2576): 1203.

¹⁶ Smilor RW. Creating a National Festival: The Campaign for a Safe and Sane Fourth, 1903-1916. *Journal of American Culture*. 1980; 2: 611-622.

¹⁷ Anon. The Fourth of July tetanus epidemic. *Journal of the American Medical Association*. 1903; 40: 1654-55.

¹⁸ Anon. ‘Fourth of July’ tetanus. *Lancet*. 1904; 164(4223): 386.

¹⁹ Anon. Fourth-of-July tetanus. *Lancet*. 1905; 166(4271): 97.

contaminated by tetanus bacilli. Instead, the faeces of healthy animals, including the horse, cow, dog, and even man, spread the spores. The danger was evident given that 'street-dust' was largely horse manure. The report recommended that at least 1,500 'American' units of tetanus antitoxin should be given based on the standard measure introduced by the Hygienic Laboratory in 1907.²⁰

In 1912, Osler recommended that tetanus antitoxin should be given promptly in the case of all injuries in tetanus-districts.²¹ An American specialist strongly advocated its use in: wounds contaminated with earth, manure, decomposing vegetable matter and particles of clothing; puncture wounds produced by splinters of wood, rusty nails and broken crockery; all wounds caused by exploding fire-arms, cartridges, fireworks and rockets; and wounds caused by unclean treatments as on battle-fields, after cutting the umbilical cord, and removal of the placenta.²² By contrast, a British practitioner remarked that prophylactic serum was rarely used.²³

Use of ATS in the British Army

World War I has been dubbed 'The Medical War' because of the central role that medicine played in the welfare of the fighting man and the economic efficiency of the military machine.²⁴ Lessons learnt from the South African War of 1899-1902, in which British troops succumbed to typhoid fever in large numbers, led to significant improvements in the AMS. In the years leading up to 1914, the Royal Army Medical Corps (RAMC) emphasised proper sanitation and hygienic discipline as the means to combat infectious diseases, and recent developments in bacteriology and immunology bolstered such practical measures.^{25 26}

Vaccination against smallpox had been common in the British Army for much of the 1800s. Towards the end of the century, vaccines against other infectious diseases became available, of which the most important was a vaccine for typhoid fever. The killed bacterial vaccine developed by Almroth Wright (1861-1947), Professor of Pathology at the Army Medical School, Netley in 1896 had a chequered early history; it was only recommended formally after extensive systematic trials carried out between 1905 and 1909 under the auspices of a War Office Committee provided statistical proof

²⁰ Anderson JF. The danger and prevention of tetanus from Fourth of July wounds. *Public Health Reports*. 1908; 23: 857-861.

²¹ Osler W. *The Principles and Practice of Medicine*, Eighth Edition. New York & London: D Appleton; 1912. p.145.

²² Simon CE. *An Introduction to the Study of Infection and Immunity: Including Chapters on Serum Therapy, Vaccine Therapy, Chemotherapy and Serum Diagnosis*, Second Edition. London: Baillière, Tindall & Cox, 1913. p.234-238.

²³ Murphy JK. *The Practitioner's Encyclopaedia of Medicine and Surgery in All Their Branches*, Second Edition. London: Hodder & Stoughton; 1913. p.104.

²⁴ Harrison M. *The Medical War: British Military Medicine in the First World War*. Oxford: OUP; 2010.

²⁵ Harrison. *The Medical War*, 2010 (Note 24). p.6-9, 123-124 & 142-152.

²⁶ Blair JSG. *In Arduis Fidelis: Centenary History of the Royal Army Medical Corps*, 2nd Edition. Edinburgh: Scottish Academic Press; 2001. p.79-125.

of efficacy. Though used extensively in the colonies, the vaccine was neither compulsory nor routinely provided for troops at home before WWI.^{27 28}

The RAMC training manual of 1911 (reprinted in 1915) advocated personal cleanliness, clean air, food and water, and proper removal of waste, and it accorded protective inoculation a prominent role in strengthening the soldier's resistance to infection. In addition to the vaccines already mentioned, the manual recognised the value of diphtheria antitoxin.

If inoculated with diphtheria germs, the animal does not get ill, but manufactures in its blood an antidote (antitoxin) to the diphtheria germs and their poison. If the animal be bled judiciously, its blood yields a watery fluid rich in antitoxin, which, if injected into man, exercises both a preventive and a curative influence on him against the human disease.²⁹

However, this section on preventive inoculation did not mention tetanus or tetanus antitoxin. Indeed, nothing in the manual suggests that the AMS considered tetanus a problem of particular import, especially compared with common and deadly contagious diseases common in war such as typhoid fever, cholera or malaria.

Before WWI, the *Journal of the Royal Army Medical Corps (JRAMC)* reported few cases of tetanus. In the most prominent example, a young private in the Royal Horse Artillery scratched a thumb on his saddle while vaulting off his horse, developed tetanus after a long interval and succumbed five days after the onset of symptoms despite repeated injections of ATS.³⁰ From an average strength in the UK exceeding 100,000 men there were no cases in 1912, 1913 or 1914 (to 31 July).^{31 32 33} Minutes of the Army Medical Advisory Board in the period before WWI included no particular concerns about tetanus.³⁴

War and tetanus

Tetanus was a regular concomitant of conflicts in the nineteenth century (see Table 1). The statistics of the British Legion during the Peninsular War in Spain recorded an overall incidence of 12.5 cases of tetanus for every thousand casualties. The rate was notably lower among British forces in the Crimean War. There were also marked

²⁷ Worboys M. Almroth Wright at Netley: modern medicine and the military in Britain, 1892-1902. In: Cooter R, Harrison M, Sturdy S (eds). *Medicine and Modern Warfare*. Amsterdam: Rodopi; 1999. p.77-97.

²⁸ Hardy A. 'Straight Back to Barbarism': antityphoid inoculation and the Great War, 1914. *Bulletin of the History of Medicine*. 2000; 74: 265-290.

²⁹ War Office, *Royal Army Medical Corps training, 1911*. London: HMSO; 1911. p.21-22.

³⁰ Begbie FW. A case of tetanus. *Journal of the Royal Army Medical Corps*. 1911; 16: 311-314.

³¹ Army. *Report on the Health of the Army for the year 1912*. London: HMSO, 1913.

³² Army. *Report on the Health of the Army for the year 1913*. London: HMSO, 1917.

³³ Army. *Report on the Health of the Army for the year 1914*. London: HMSO, 1921.

³⁴ War Office: Advisory Board for Army Medical Services: Minutes and Reports, Volume 5. 1913 Jan-1914 Jul. The National Archives (TNA). WO 243/10. 27 July 1914.

geographic variations during the Franco-Prussian War with a rate of 1.6 per 1,000 at Metz and 11 per 1,000 in the northern theatre.³⁵ During the American Civil War, most of the Union cases occurred in a few locations, especially field hospitals established in stables.³⁶

<u>Conflict</u>	<u>Dates</u>	<u>Cases per 1,000 casualties</u>
Peninsular War	1808-14	12.5
Crimean War	1854-56	2.0
American Civil War	1861-65	2.0
Franco-Prussian War	1870-71	3.5
		(1.6 to 11)

Table 1. The incidence of tetanus in nineteenth-century conflicts before the use of ATS. Compiled from data in: Anon. The control of tetanus, 1940 (Note 35).

Tetanus was a rare complication of wounds in the South African War of 1899-1902. Only six cases with three deaths were reported. Surgeon-General WF Stevenson (1844-1922), Professor of Military Surgery at the RAM College, noted that the fatal cases involved considerable lacerated wounds of the lower extremity caused by shell fragments and Martini-Henry bullets. One of these patients was treated with a small amount of tetanus antitoxin injected into the cerebrum but his disease was probably too far advanced to expect any benefit.^{37 38}

Although first-hand experience of tetanus seems to have been infrequent in the British Army, the *JRAMC* carried brief reports on the current literature, which included short translations of articles from military medical journals published abroad that provided the rationale for tetanus prophylaxis. Several were authored by ‘WGM’ – most likely William G Macpherson (1858-1927) – who had been an observer at the Russo-Japanese War of 1904-05 and would go on to write the official history of WWI.³⁹

In 1908, the journal carried a short report of a French article in which the author remarked that now, more than ever, there was a tendency for tetanus to occur in wounds on the battlefield and insisted on the necessity of providing all medical units with large quantities of ATS. ‘The reason for this is that the serum must be injected very soon after the wound has been inflicted if tetanus is to be prevented.’ He believed that, depending

³⁵ Anon. The control of tetanus. *Journal of the Royal Army Medical Corps*. 1940; 74: 36-44.

³⁶ Schroeder-Lein GR. *The Encyclopedia of Civil War Medicine*. Armonk, NY: ME Sharpe; 2008. p.301-303.

³⁷ Stevenson WF. *Report on the Surgical Cases Noted in the South African War, 1899-1902*. London: HMSO; 1905. p.218.

³⁸ Simpson RJS. Medical history of the South African War. *Journal of the Royal Army Medical Corps*. 1910; 15: 659-672.

³⁹ War Office. *The Russo-Japanese War: Medical and Sanitary Reports from Officers Attached to the Japanese and Russian Forces in the Field*. London: HMSO; 1908.

on the nature of the wound, a certain quantity of serum should be injected as a preventive measure.⁴⁰

The following year, a Russian report about the Tsarita's ambulance during the Russo-Japanese War commented that after August 1904, of 592 wounded, 14 (2.3 per cent) developed tetanus and 13 died. Treatment with ATS was unsuccessful and the author hoped preventive injections would give better results as the method had not been properly tried during the war. He noted: 'It is not only open wounds soiled by earth which are likely to induce tetanus, but also wounds which contain fragments of clothing or of the projectile'. He thought it obvious that sufficient supplies would be needed for a large number of wounded.⁴¹

The Austro-Hungarian guide to military surgery on the battlefield included the following recommendation in the case of gunshot wounds of soft tissues: 'In very badly contaminated wounds a prophylactic injection of antitoxin for prevention of tetanus will be administered at the dressing stations'.⁴² Reports from the Balkan War of 1912-13 noted tetanus after wounds of the lower extremities and the futility of treatment with ATS.^{43 44} A French ambulance in Bulgaria 'took 200 doses of antitetanic serum, enough to allow every case in which the wound was soiled to receive a prophylactic injection of the serum' and no cases of tetanus occurred.⁴⁵

The early months of World War I

An early casualty of the war, a driver in the Royal Field Artillery, sustained an injury described in his medical case sheet as a 'shrapnel bullet wound of L Int. condyle of femur [internal condyle of left femur]' at the Battle of Mons on 23 August 1914. Admitted to the Royal Victoria Hospital at Netley on 28 August, the patient was operated on to remove the bullet two days later and seemed to be doing well. However, on 1 September, he showed rapidly worsening signs of tetanus. The injured leg was amputated but the spasms continued the next day when an injection of 1,500 units of ATS was given. William Mailer died on 3 September at the age of 24 and was buried in Netley Military Cemetery.^{46 47}

⁴⁰ WGM. Notes on the necessity of providing field medical units with anti-tetanic serum *Journal of the Royal Army Medical Corps*. 1908; 11: 638.

⁴¹ WGM. Tetanus during the Russo-Japanese war. *Journal of the Royal Army Medical Corps*. 1909; 12: 118.

⁴² Macpherson WG. The Austro-Hungarian regulations regarding the surgical work which is permitted on the battlefield. *Journal of the Royal Army Medical Corps*. 1912; 18: 447-473.

⁴³ CEP. Surgical experiences in Balkan War. *Journal of the Royal Army Medical Corps*. 1913; 20: 607-608.

⁴⁴ CEP. Experiences in the Balkan War. *Journal of the Royal Army Medical Corps*. 1913; 20: 725-726.

⁴⁵ CEP. The Equipment of a French ambulance in Bulgaria. *Journal of the Royal Army Medical Corps*. 1913; 21: 124-125.

⁴⁶ War Office: First World War Representative Medical Records of Servicemen and Servicewomen, 1914-1918. Tetanus. TNA. MH 106/2105, Case sheet No. 383033. The records contain several versions of Army Form I.1237 medical case sheet.

⁴⁷ Driver William Mailer. Commonwealth War Graves Commission. www.cwgc.org

The incidence of tetanus cases rose especially after the Battle of the Aisne in mid-September as reflected in contemporary war diaries. Nursing Sister Kate Luard (1872-1962), then serving with ambulance trains evacuating the wounded from the battlefields, noted three deaths from tetanus on 22 September and mentioned inoculations against tetanus five days later.⁴⁸ Sir Anthony Bowlby (1855-1929), Consulting Surgeon to the BEF in France, recorded a tetanus case in his war diary on 24 September, his first day in the country. Five days later, he visited the Trianon Hospital at Versailles where they had ten cases of tetanus and he saw further cases in subsequent weeks.⁴⁹

Reports of the prevalence of shrapnel wounds, the risk of tetanus, and the prophylactic role of tetanus antitoxin reached the popular press.^{50 51} The *BMJ* of 10 October urged the military authorities to take action to prevent the disease:

The proper use of tetanus antitoxin in war time is prophylactic rather than curative, and it is most important that those responsible for the care of our wounded should realize this fact. A prophylactic dose of tetanus antitoxin should be routine treatment in all cases of shell, bayonet, and other wounds, when there is risk of soil contamination, as soon as possible after their infliction.⁵²

Colonel Arthur Lee (1868-1947), despatched to France to report confidentially on the transport and care of the sick and wounded, wrote to Lord Kitchener (1850-1916) on 12 October: 'I did not find that the serum, even when available, was by any means universally used at the advanced Dressing Stations and hospitals'. Lee found that some medical officers were enthusiastic about serum while others appeared sceptical; he suggested that 'a definite order should be given to RAMC officers to use the serum'.⁵³

The order was apparently enacted swiftly thereafter. In the 17 October issue of the *BMJ*, a special correspondent in France noted that the use of ATS, which had first been restricted to cases in which tetanus had developed already or was deemed likely, was now being used prophylactically as well as therapeutically in a more general way:

An experienced serum worker is stationed at the railhead with instructions to give a prophylactic injection to every wounded man, and in order to avoid any case being overlooked the surgeons lower down the line are directed to inquire as to whether an injection has been made, and if not to make one themselves.⁵⁴

⁴⁸ Luard KE (first published anonymously). *Diary of a Nursing Sister on the Western Front 1914-1915*. Edinburgh & London: William Blackwood & Sons; 1915. p.45 & 53.

⁴⁹ Bowlby A. Wellcome Collection Archives (WCA). RAMC Muniments Collection. RAMC/2008/7/2. Typescript of diary as consulting surgeon to British forces in France during the First World War, 23 Sept 1914-14 Oct 1917.

⁵⁰ Anon. Wounded from the Aisne. *The Times*. 29 Sep 1914 (Issue 40650), p.7.

⁵¹ Anon. Precautions against tetanus. *The Times*. 1 Oct 1914 (Issue 40652), p.5.

⁵² Anon. Tetanus and its prevention. *British Medical Journal*. 1914; 2(2806): 636.

⁵³ War Office. TNA. WO 159/16. Care of the sick and wounded troops in France: copies of letters from Col A Lee, MP, 1914 Oct-1915 May.

⁵⁴ Anon. The War. Medical matters in France. *British Medical Journal*. 1914; 2(2807): 681-685.

Bowlby remarked on the use of ATS on 19 October when he visited No. 6 Clearing Hospital, Bethune: '140 wounded brought in, dressed and injected with anti-tetanic serum'. Three days later he wrote: '900 wounded at Bethune, and I saw a lot coming in and dressed; all getting antitoxin for tetanus'.⁵⁵ On 21 October, Lee was glad to report that: 'the anti-tetanic serum is being universally used, in the case of all wounds and at the earliest possible moment'. By 6 November, however, the supply had run short because of increased fighting at the front.⁵⁶ For some days, after using 30,000 doses, there was not quite enough antitoxin for all cases.⁵⁷

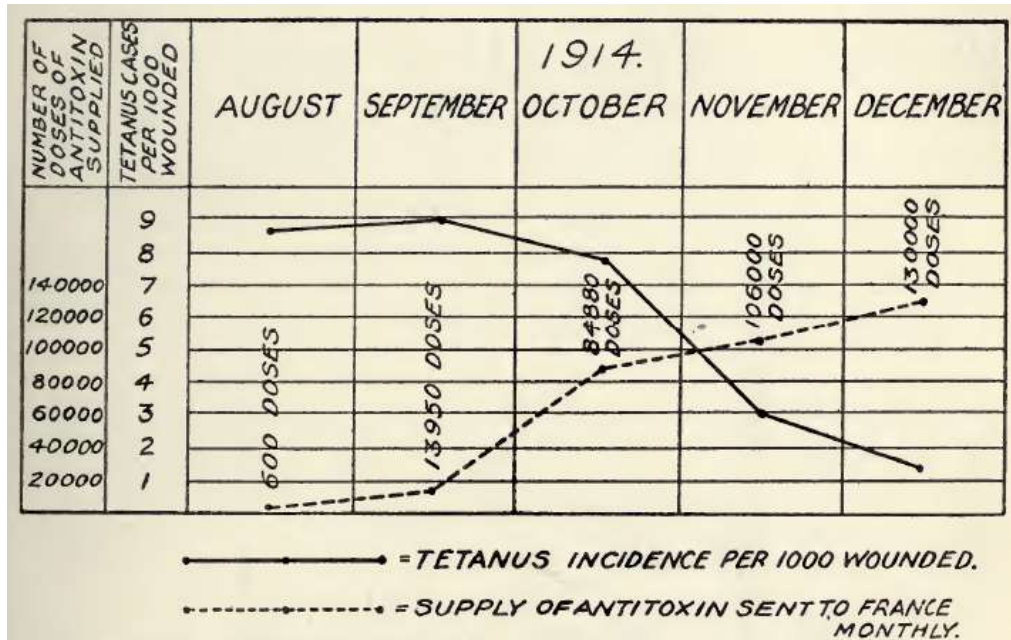


Figure 4. Chart illustrating fall in tetanus incidence as supply of ATS increased during 1914. Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.183.

The BEF had taken a small quantity of ATS designed to be used only in severe wounds of a type especially liable to be complicated by tetanus infection. During August and September, the supply was inadequate given the fact that all wounds offered a potential portal for the entry of tetanus spores. Following the October order that every wounded man should receive a dose of 500 units of ATS, ample supplies became available in the field of operations by the end of November. The incidence of tetanus dropped rapidly, from nearly nine cases of tetanus for every 1,000 wounded in September to 1.4 cases per 1,000 by December (Figure 4).⁵⁸

⁵⁵ Bowlby. Typescript of diary (Note 49).

⁵⁶ War Office. Copies of letters from Col A Lee (Note 53).

⁵⁷ Bowlby A. The work of the 'clearing hospitals' during the past six weeks. *British Medical Journal*. 1914; 2(2816): 1053-54.

⁵⁸ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.181-183.

Sir David Bruce and the Tetanus Committee

Surgeon-General David Bruce (1855-1931) had been commissioned in the Army Medical Service in 1883 and was Assistant Professor of Pathology in the Army Medical School at Netley in 1889-94 (Figure 5). Having made significant scientific contributions by finding the cause of Malta fever (brucellosis), determining the role of the tsetse fly in spreading disease, and establishing the link between trypanosomes and sleeping sickness, he was elected Fellow of the Royal Society in 1899.^{59 60} After the outbreak of WWI, he was appointed Commandant of the RAM College and served until 1919. He also acted as Chairman of the War Office's Pathological Committee, Committee for the Study of Tetanus and Trench Fever Investigation Committee.⁶¹



Figure 5. Sir David Bruce. Process print. Wellcome Collection. Reference: 12400i. Public Domain Mark.

⁵⁹ Anon. Sir David Bruce: 1855-1931. *Obituary Notices of Fellows of the Royal Society*. 1932; 1: 79-85.

⁶⁰ Vassallo DJ. The corps disease: brucellosis and its historical association with the Royal Army Medical Corps. *Journal of the Royal Army Medical Corps*. 1992; 138: 140-150.

⁶¹ Vella EE. Major-General Sir David Bruce, KCB. *Journal of the Royal Army Medical Corps*. 1973; 119: 131-44.

In October 1914, the Director-General AMS at the War Office, Sir Alfred Keogh (1857-1936), drew Bruce's attention to the problem of tetanus.⁶² The first of several successive reports of cases occurring in home military hospitals published a year later noted an 81 per cent mortality at Netley, which received the most serious cases.⁶³ The Tetanus Committee was formed in March 1916 and issued its first *Memorandum on Tetanus* for the guidance of medical officers the following August. Comprising RAMC officers, academic researchers and serum manufacturers, the Committee undertook various clinical and experimental investigations that resulted in a series of publications addressing critical matters relating to both prophylaxis and treatment of tetanus.⁶⁴

One area of concern was the transient nature of protection conferred by a single dose of ATS. This limitation was investigated in experimental animals by Dr Alfred MacConkey (1861-1931), bacteriologist-in-charge of the Lister Serum Department.⁶⁵ He also conducted a study at the Royal Free Hospital involving several 'lady students' who volunteered to receive a dose of ATS and give a series of blood samples for analysis.⁶⁶ The results suggested that the minimum prophylactic dose needed to be repeated about once a week to maintain immunity. The Lister Institute funded the Committee's research work to the tune of £1,350.⁶⁷

Bruce had a long and close relationship with the Lister Institute, having been appointed a member of the Governing Body as nominee of the Royal Society in 1904.⁶⁸ He took up this role again on returning to England, was elected Chairman of Governors early in 1916, and continued in post until his death.⁶⁹ The Institute's headquarters and main laboratories were sited at the end of Chelsea Bridge Road, a short distance from the RAM College. Bruce was a regular visitor and took great interest in the research work on anaerobic microbes undertaken there during the war.⁷⁰

Increasing use of ATS for prophylaxis

The use of ATS intensified as the war progressed. The July 1915 *Memorandum on the Treatment of Injuries in War* reiterated the order that medical officers should give every wounded man a preventive dose of ATS. The prescribed dose was a subcutaneous (sc)

⁶² Bruce D. Tetanus. Analysis of 1458 cases which occurred in home military hospitals during the years 1914-1918. *Journal of Hygiene*. 1920; 19: 1-32.

⁶³ Bruce D. An analysis of cases of tetanus treated in home military hospitals from August, 1914, to August, 1915. *Lancet*. 1915; 186(4808): 901-904.

⁶⁴ War Office Committee for the Study of Tetanus. *Memorandum on Tetanus*, Fourth Edition. London: HMSO, 1919.

⁶⁵ MacConkey AT, Homer A. On the passive immunity conferred by a prophylactic dose of anti-tetanic serum. *Lancet*. 1917; 189(4877): 259-261.

⁶⁶ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.203-204.

⁶⁷ Bruce. Tetanus, 1920 (Note 62). p.3.

⁶⁸ Lister Institute of Preventive Medicine. Governors' Meetings, Minute Book No. 1. WCA. SA/LIS/A.6. 15 January 1904.

⁶⁹ Lister Institute of Preventive Medicine. Governors' Meetings, Minute Book No. 2. WCA. SA/LIS/A.7. 19 January 1916.

⁷⁰ Robertson M. Sir David Bruce: an appreciation of the man and his work. *Journal of the Royal Army Medical Corps*. 1955; 101: 91-99.

injection of 500 units at a distance from the wound at the earliest possible moment. Some medical officers not infrequently injected 1,500 units though there was no evidence the smaller dose was insufficient if given promptly. Experience showed that tetanus sometimes occurred after trivial injuries and frostbite.⁷¹

The revised *Memorandum on Tetanus* of October 1916 suggested that a second sc injection should be given in all cases of septic wounds after a seven-day interval. For long-lasting wounds, especially if caused by shell or bomb, it recommended third and fourth injections at seven-day intervals. The primary injection was to be given at the field ambulance or dressing station as soon as the wounded soldier was removed from the firing line with subsequent injections most likely following at home hospitals. A dose of 500 units was also advised 48 hours before operative surgery at the site of a wound, even if it had healed, because tetanus bacilli could lie dormant for long periods of time.⁷²

In 1916, the BEF's Director-General AMS, Lieutenant-General Sir Arthur Sloggett (1857-1929), issued a circular recommending a dose of 1,000 units in all lacerated wounds and those involving injury to vessels or bone; in December, the occurrence of tetanus deaths among men who contracted trench foot prompted the order that ATS should be used in all such cases, which brought about an immediate drop in the incidence of the disease.⁷³ Following the third edition of the *Memorandum on Tetanus* in June 1917, the order was given that all wounded men, and trench foot cases, must receive at least four ATS injections at intervals of one week.⁷⁴

In June 1918, on the recommendation of the Adviser in Pathology in France, the initial dose for prophylaxis was raised to 1,500 units.⁷⁵ The fourth and final *Memorandum*, published in May 1919, noted that, on account of the exigencies of war, two or more weeks could have elapsed after primary ATS injection before a wounded patient arrived in England. Although multiple prophylactic inoculations had been used for some time, the number who received four inoculations varied from 40 to 90 per cent, depending on the local authority.⁷⁶

Outcome of ATS prophylaxis

The official history records 2,529 cases of tetanus as a result of fighting in France and Belgium, representing more than 99 per cent of all cases in all theatres of war. On average, the incidence of tetanus was 1.47 per 1,000 wounded. The rate was much higher at the start of the war as described above, falling to about 1 per 1,000 from mid-1917, while showing fluctuations throughout the war (Figure 6).

⁷¹ War Office. *Memorandum on the Treatment of Injuries in War based on experience of the present campaign*. London: HMSO; 1915. p.16-18.

⁷² War Office Committee on the Study of Tetanus. *Memorandum on tetanus*. *British Medical Journal*. 1916; 2(2915): 647-649.

⁷³ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.181-184.

⁷⁴ Anon. Fresh light on the treatment of tetanus. *Lancet*. 1917; 190(4900): 128.

⁷⁵ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.182.

⁷⁶ Anon. The revised *Memorandum on Tetanus*. *Lancet*. 1919; 193(5000): 1125.

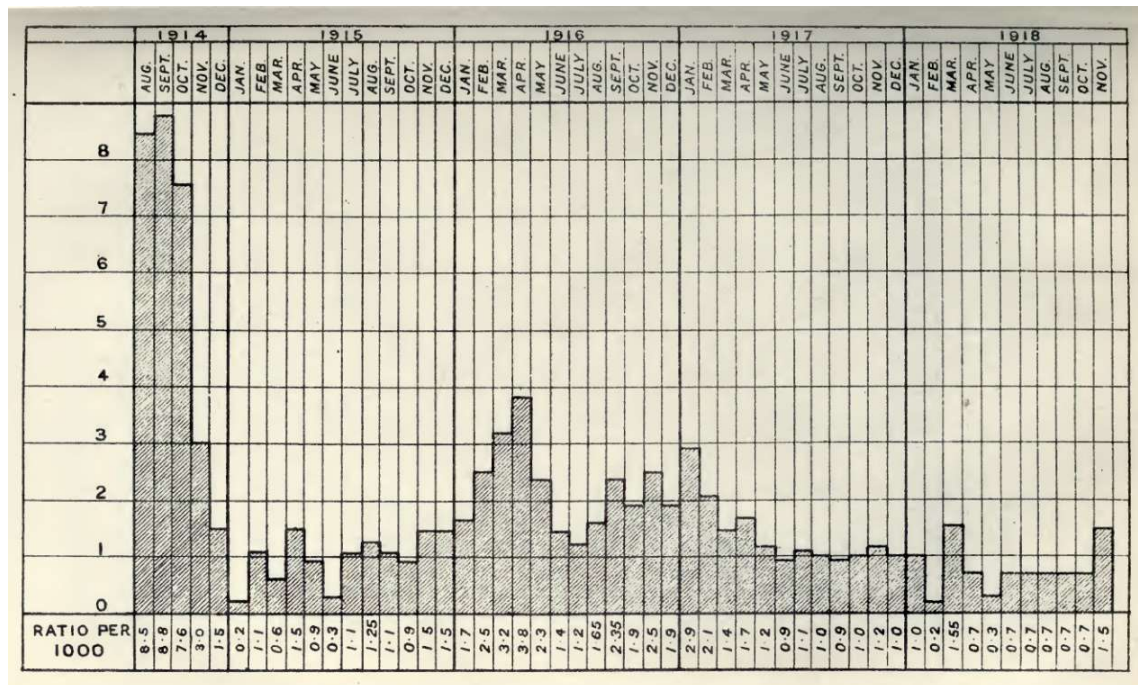


Figure 6. Chart illustrating monthly tetanus incidence during WWI. Includes wounded on the Western Front and in home hospitals but excludes gassed cases and cases linked to trench foot during December 1916. Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.168/169.

The case incidence peaked in the early months of 1916 after the Fourth Army moved into the Somme area where land was still under relatively undisturbed cultivation. Some of the increase may also have been the result of trench foot which had been common in the winter months. From the spring of 1917, the incidence continued at a lower, steadier rate. The peaks seen in March and November 1918 coincided with heavy fighting when rapid movements during the retreat and subsequent advance disrupted the effective evacuation of the wounded.⁷⁷

Prophylactic ATS not only lowered the incidence of tetanus but also prolonged the average incubation period of the disease. At hospitals in England and France alike, mortality fell steadily as the interval between injury and the onset of symptoms lengthened. The clinical nature of the disease also diminished in severity with a substantial increase in the number of cases in which local rather than general tetanus occurred.⁷⁸

The overall mortality of tetanus cases was 50 per cent. It was highest in France where early and more severe cases of tetanus complicated by sepsis and gas gangrene were treated. At the start of the war, the rate approached 80 per cent, comparable with that in previous conflicts (about 80 to 90 per cent); by 1918, it was about 60 per cent. In

⁷⁷ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.168-169.

⁷⁸ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.175-176 & 186-187.

home hospitals, which received more lightly wounded evacuees, mortality diminished from about 60 per cent to below 30 per cent over the course of the war.⁷⁹

Many cases of tetanus occurred among soldiers who had suffered accidental injuries; such cases had not, as a rule, received any ATS and were severe with high mortality. Tetanus also followed ordinary surgical operations such as appendicectomy in unwounded men who had likely ingested tetanus spores in dirt while living in the trenches.⁸⁰

Treating wounds by primary excision was adopted by surgeons only after long experience of less satisfactory methods and was not in common use until the spring of 1917.⁸¹ Surgeons had understood that removing damaged tissues before tetanus spores carried into the wound had time to propagate and release toxins was the most potent factor in preventing the disease. Given that this radical surgery could not be carried out in all cases, the administration of ATS to the wounded remained essential.

The role of the Royal Army Medical College

The RAM College at Millbank officially opened in mid-1907.⁸² During WWI, it served as a centre for research on key aspects of military medical research, including poisonous gases and gas masks, insecticides effective against lice infestation, and nutrition to prevent food deficiency diseases.⁸³ It also housed the Central Cerebrospinal Fever Laboratory that provided instruction to RAMC officers, made novel diagnostic agents and distributed supplies.⁸⁴

The College's laboratory block (Figure 7) was home to the Army Vaccine Department, which was responsible for preparing and issuing vaccines, a task that would expand greatly during the war. To 3 August 1919, the Department supplied more than 34 million doses of vaccines in total, which included over 17 million doses of mixed typhoid/paratyphoid A & B, 7 million doses of cholera and 6 million doses of typhoid vaccines.⁸⁵ The Vaccine Department was also responsible for managing the issue of all sera, which became 'a formidable part of its daily work'.⁸⁶

⁷⁹ Macpherson WG, Bowlby AA, Wallace C, English C. *History of the Great War based on official documents. Medical Services, Surgery of the War, Vol. I*. London: HMSO; 1922. p.154-155.

⁸⁰ Macpherson, Bowlby, Wallace, English. *History of the Great War*, 1922 (Note 79). p.163-164.

⁸¹ Macpherson, Bowlby, Wallace, English. *History of the Great War*, 1922 (Note 79). p.156-157.

⁸² Neal JB. The History of the Royal Army Medical College. *Journal of the Royal Army Medical Corps*. 1957; 103: 163-172.

⁸³ Anon. History of the Royal Army Medical College. *Journal of the Royal Army Medical Corps*. 1950; 95: 374-390.

⁸⁴ Wawrzynczak EJ. Treatment of military cases of cerebrospinal fever during WWI: the concerted efforts of the RAMC, MRC and Lister Institute to make serum therapy work. *BMJ Military Health*. 2020; 166: 347-351.

⁸⁵ Macpherson WG. *History of the Great War based on official documents. Medical Services, General History, Vol. I*. London: HMSO; 1921. p.414.

⁸⁶ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.30-31.



Figure 7. The Laboratory Building, Royal Army Medical College. Image from *The Royal Army Medical College and Laboratory, Millbank, London: description, photographs and plans. Extracted from Architect's Review, 1905.* Wellcome Collection. RAMC/954. p.285. Creative Commons.

To 3 August 1919, the College supplied more than 12 million doses of sera in total, of which the overwhelming majority, that is over 11 million doses, comprised tetanus antitoxin measured in prophylactic doses of 500 units. Of this total, about 6.8 million (62 per cent) were sent to France and 1.7 million (15 per cent) retained for use in home hospitals.⁸⁷ Archive records list the numbers of doses of various antitoxins and sera procured from outside sources and issued monthly during the five years of war to July 1919.⁸⁸ The annual issue of tetanus antitoxin is shown in Figure 8.

The data for the third year are absent but a summary up to 17 January 1917 shows 4.6 million doses, of which 3 million were issued during the first two years, so at least 1.6 million doses were issued during the next half-year. An estimated 2.8 million doses shown for the third year, calculated to make up the official total of 11.1 million doses, appears a reasonable interpolation. Unlike vaccines, however, antitoxins and sera were purchased under contract almost entirely from British and American sources.⁸⁹

⁸⁷ Macpherson. *History of the Great War*, 1921 (Note 85). p.415.

⁸⁸ Museum of Military Medicine Archives. RAMC/CF/3/3/2/62/TYPH.

⁸⁹ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.30-31.

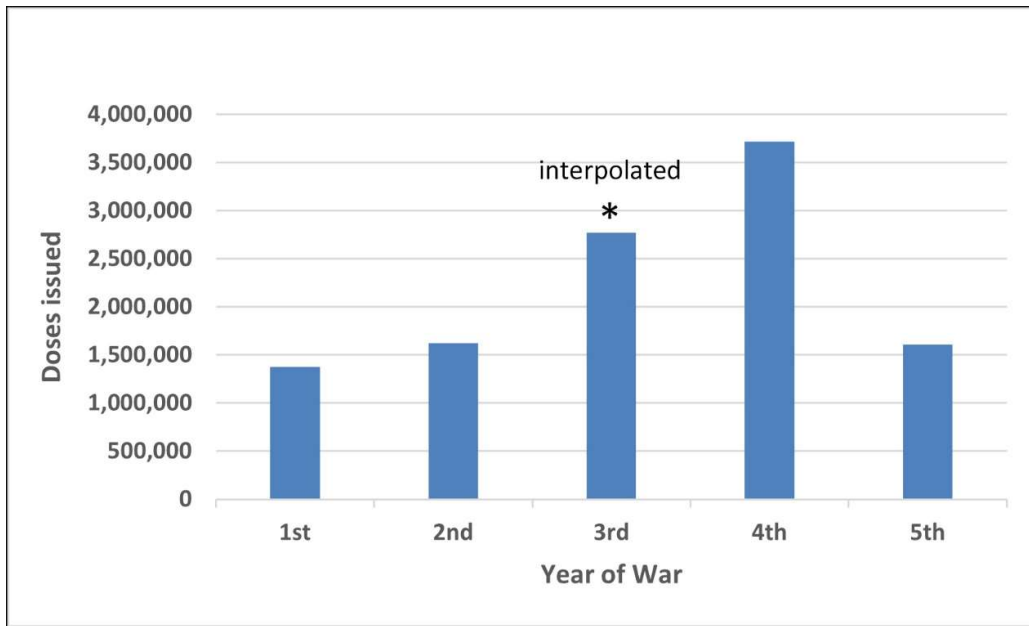


Figure 8. Issue of 500-unit doses of ATS by the RAM College Vaccine Department in WWI. Compiled from archive data at the Museum of Military Medicine (Note 88).

The supply of ATS

Before WWI, there were several British, European and American suppliers of serum products to the British market.⁹⁰ The US company Parke, Davis & Co. recommended a prophylactic dose of tetanus antitoxin of 1,500 units.⁹¹ So did the major US firm HK Mulford Co., which distributed its products via Thomas Christy & Co.⁹² The most important manufacturer of serum products in Britain was Burroughs, Wellcome & Co.⁹³ The other leading supplier, Allen & Hanburys Ltd., acted as agent for sera of the Lister Institute of Preventive Medicine.⁹⁴

The amount of ATS available in the first two months of the war was limited and all sources in England ran short during the Aisne fighting. Supplies came instead from the Pasteur Institute in Paris. Colonel Cummins recalled that the change of bases from the northern ports to St Nazaire interrupted the forwarding of medical supplies. The American Red Cross facilitated the delivery of ATS obtained via the French Army's

⁹⁰ Bosanquet WC, Eyre JWH. *Serums, Vaccines and Toxines in Treatment and Diagnosis*, Second Edition. London: Cassell; 1909. p.354-355.

⁹¹ Parke, Davis & Company. *A Manual of Biological Therapeutics*, Detroit, MI: Parke, Davis & Company; 1914. p.29-32.

⁹² HK Mulford Company. Tetanus Antitoxin Mulford (Advertisement). *The Chemist and Druggist*. 24 Apr 1915. p.72.

⁹³ Burroughs Wellcome & Co. *Price List of Fine Products*. London: Burroughs Wellcome & Co; 1913. p.113-114.

⁹⁴ Allen & Hanburys Ltd. *General List of Drugs, Pharmaceuticals, and The "Allenburys" Specialities*. London: Allen & Hanburys Ltd; 1911. p.252-258.

Central Pharmacy. Although supplies were insufficient for universal use the severely wounded nearly always received serum.⁹⁵

The Lister Institute had immediately offered its expertise and resources, becoming a dedicated supplier of antitoxins and sera to the War Office.⁹⁶ Production of tetanus antitoxin was the priority and the Serum Department began to immunise extra horses. Stocks of ATS were processed promptly and, on 24 August 1914, 25,000 bottles of 500 units were prepared for the use of the Army.⁹⁷ This output was a significant contribution given the archival records show that the RAM College issued just under 27,000 doses in September.

The precise numbers of 500-unit prophylactic doses supplied to the Army were recorded in the Annual Reports of the Lister Institute, which included data to 31 March each year.⁹⁸ Figure 9 shows the annual totals, which reached a high of approximately 250,000 doses in the period 1 April 1916-31 March 1917. The Institute was responsible for just under a million doses, about 9 per cent of the total number of ATS doses issued by RAM College during the war, subject to contracts with the War Office, which also requested large quantities of other types of sera.

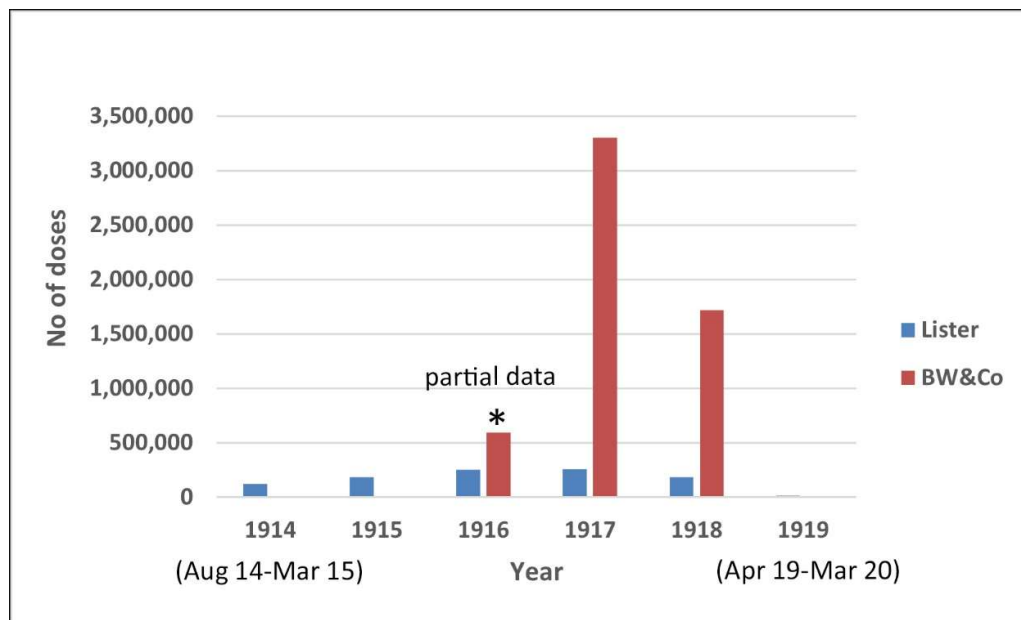


Figure 9. Output of 500-unit equivalent doses of tetanus antitoxin during WWI by British serum producers. Compiled with data from the Lister Institute of Preventive Medicine (Note 98) and Burroughs, Wellcome & Co. (Note 100).

⁹⁵ Research Society Reports. The Eighth Session of the Research Society of the American Red Cross in France. Discussion. *War Medicine*. 1918; 2: 745-746.

⁹⁶ Wawrzynczak EJ. Making serum, saving soldiers: The Lister Institute during World War I. *Vesalius*. 2018; 24: 40-48.

⁹⁷ Wawrzynczak. Lifesaving serum from horses, 2019 (Note 11).

⁹⁸ Lister Institute of Preventive Medicine, Annual Report and Accounts, 1915-1920. WCA. SA/LIS/B.21-B.26.

The form in which Lister tetanus antitoxin was supplied varied during the war. In late 1914, some ATS was bottled as unrefined serum, some had been refined by a process of salt fractionation, and some was a mixture of the two types. Typically, a bottle contained a volume of 5-10 cc and a minimum content of 1,000 units. In late 1915, only unrefined serum was issued in bottles of 8-11 cc containing a minimum of 1,000 or 1,500 units. From early 1916, all serum was refined and dispensed in doses of at least 1,500 units in 4-11 cc. At different times, the Serum Department struggled to maintain sufficient supplies of chemicals, fodder and labour.⁹⁹

Figure 9 also shows the output of tetanus antitoxin based on the surviving monthly reports from the Wellcome Physiological Research Laboratories.¹⁰⁰ The data have been compiled to cover similar time periods to the Lister Institute data and are complete for the two twelve-month periods from 1 April 1917 to 31 March 1919. The recorded output, mainly bottles of 1,500 units, was equivalent to 5.5 million 500-unit doses, about 50 per cent of the number issued by RAM College. Since over two years' data is absent, the total output may have approached 10 million doses, or 90 per cent.

Like the Lister Institute, the work of the Wellcome Laboratories became consumed with the production of ATS for the War Office. In May 1915, there were extreme difficulties in purchasing horses; by October 1918, the number of horses reached a peak of 490.¹⁰¹ Beginning in April 1918, the Wellcome Laboratories also prepared experimental sera against gas gangrene and supplied the Army with a combined serum against tetanus and gas gangrene.¹⁰² In the summer of that year, Colonel Cummins carried out a preliminary trial in the field but found that the dual serum gave no additional benefit over standard ATS.¹⁰³

Some smaller quantities of ATS came from other sources. On one occasion, in April 1915, the Australian Imperial Force in Egypt received a large shipment of medical stores and sent half of the ATS to the War Office due to a shortage in France.¹⁰⁴ In addition, the order book of the Connaught Laboratories in Toronto, Canada shows two orders from the RAM College for 1,500-unit doses: 4,000 on 10 November 1915 and 16,000 on 11 October 1918.¹⁰⁵

⁹⁹ Wawrzynczak EJ. The Lister Institute Serum Department: Wartime, 1914-1918. *Pharmaceutical Historian*, accepted for publication.

¹⁰⁰ Wellcome Bureau of Scientific Research. Monthly Reports. Jul 1914-Dec 1919. WCA. WA/BSR/BA/PrI/A.1.

¹⁰¹ Wellcome. Monthly Reports (Note 100).

¹⁰² Church R, Tansey EM. *Burroughs Wellcome & Co.: Knowledge, Trust, Profit and the Transformation of the British Pharmaceutical Industry, 1880-1940*. Lancaster: Crucible Books; 2007. p.269-273.

¹⁰³ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.95-96.

¹⁰⁴ Butler AG. *The Australian Army Medical Services in the War of 1914-1918. Vol. I*, Second Edition. Melbourne: Australian War Memorial; 1938. p.106.

¹⁰⁵ Connaught Laboratories. Order Book 1914-1923. Sanofi Pasteur Connaught Archives, Toronto, Canada.

Prophylaxis in practice

From early 1916, most ATS came in a glass bottle, which contained a minimum of 1,500 units in a volume of approximately 10 cc, packaged in a protective wooden container. A few examples have survived in museums or private collections; the content of a Parke, Davis & Co. bottle from 1918 was recently tested but found to contain no measurable antitoxic activity after a century.¹⁰⁶

Private Walter George Cook, a medical orderly with 27th Field Ambulance, RAMC near the Hohenzollern Redoubt in late 1915/early 1916 described the need to remove vials from their containers, but the discarded boxes accumulated around his feet: 'There were thousands of men coming in and I had no room to move about ... no-one to help me get the things out of the way, no-one to get me a fresh syringe'. He made sure all were seen to but thought some of the injections must have been a little painful. A sergeant warned him: 'Don't you come near me with that gardening syringe'.¹⁰⁷

A cartoon in the *Gazette of the 3rd London General Hospital* exaggerated the act of serum injection for comic effect (Figure 10).

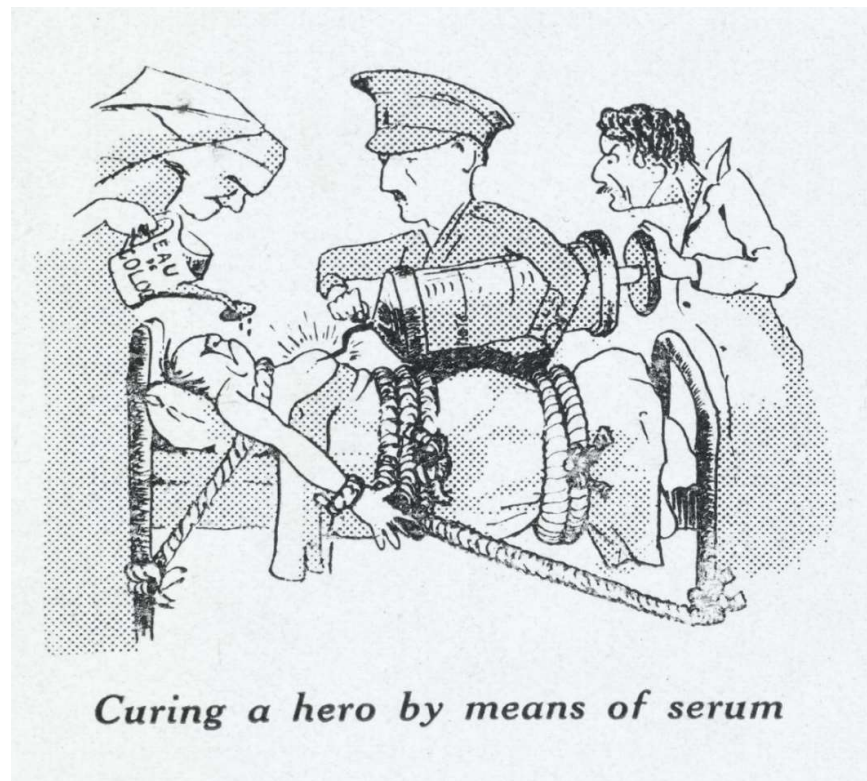


Figure 10. Cartoon by Capt. Harrison. *The Gazette of the 3rd London General Hospital (Territorial Force), Wandsworth*. Oct 1915-July 1919. Wellcome Collection. RAMC/866. April 1916. p.186. CC BY-NC 4.0.

¹⁰⁶ Aubert N, Brachet-Botineau M, de Olivera Preto GE, Benz-de Bretagne I, Watier H, Brachet G. History, extensive characterization and challenge of anti-tetanus serum from World War I: exciting remnants and deceived hopes. *Immunologic Research*. 2020; 68: 7-12.

¹⁰⁷ Cook WG. Imperial War Museums (IWM). Oral History, Cat. No. 9352, Reel 2.

Other oral histories contain accounts of ATS injections in the chest or at the top of the abdomen that involved blunt and dirty needles, or needles that snapped, and men reluctant to be injected.^{108 109 110 111} Such injections were part of the folklore reflected in the humour of the day. For instance, one verse of 'The Medical Corps Alphabet' read:

T is for Tetanus, and I need not here mention
They use a vile weapon just for injection.¹¹²

The intensity of fighting sometimes overwhelmed the dressing stations. Sergeant WR Bland, 97th Field Ambulance, RAMC, attached to 89th Brigade, 30th Division, who ran a special ATS receiving point established at Becordel in November 1916 recorded how his team of dressers injected 2,000 men in 21 hours.

We did them in batch[es] of six at a time, changing syringes alternately. We became very good at these injections and although working at such high pressure very seldom broke a needle.¹¹³

Details of ATS injections along with other relevant details were recorded on the Field Medical Card (Army Form W.3118), which was placed in an envelope attached to the casualty's tunic and accompanied him down the line.¹¹⁴ One alternative was to mark a 'T' on the man's forehead with an indelible marker or iodine solution as shown in some contemporary photographs.¹¹⁵ These procedures were meant to ensure that the wounded received the correct injections mandated by official instructions on reaching casualty clearing stations and hospitals.

Louie Johnson of the Territorial Force Nursing Service at Beckett's Park Hospital, Leeds was responsible for anti-tetanus injections.

... from the field dressing stations where they had been, a label was tagged onto a button, or fixed on in some way, giving their name, because some of them were too ill to know any particular, giving them their name, their number, their regiment ... what their wound was and where, and then, whether they had had anti-tetanus serum or not and, if so, how many units ...

Preparing sterilised syringes and hypodermic needles, and the associated record-keeping, caused a considerable amount of extra work.¹¹⁶

¹⁰⁸ Austin C. IWM. Oral History, Cat. No. 11116, Reel 10.

¹⁰⁹ Reid JPO. IWM. Oral History, Cat. No. 322, Reel 5.

¹¹⁰ Trafford R. IWM. Oral History, Cat. No. 11218, Reel 7.

¹¹¹ Peake G. IWM. Oral History, Cat. No. 10648, Reel 5.

¹¹² 'S Rong'. The Medical Corps Alphabet, *The C.C.S. Review*. Jan 1, 1918. p.8. British Library. Trench Journals and Unit Magazines of the First World War.

¹¹³ Bland WR. *Private Papers of WR Bland*. IWM. Documents. Cat. No. 12069. p.24.

¹¹⁴ War Office. Medical Cards, 1916-1920. TNA. MH106.

¹¹⁵ Wever PC, van Bergen L. Prevention of tetanus during the First World War. *Medical Humanities*. 2012; 38: 78-82.

¹¹⁶ Johnson L. IWM. Oral History, Cat. No. 330, Reel 3.

Side-effects of ATS

James Albert Payne, a British NCO serving with the 16th Battalion, The Manchester Regiment was injured on the first day of the Battle of the Somme and struggled to reach a dressing station along with hundreds of other casualties.

I couldn't speak, you see, yet there was a label on me. They'd tied a label onto me. They ought to have known by that, but they still inoculated me. I was four times inoculated, but they didn't kill me with anti-tetanus.¹¹⁷

However, there were risks to serum injection, including 'serum sickness', an allergic reaction to the horse protein in the serum associated with fever, skin rashes and joint pain. Wounded at the front in August 1918, Harold Joseph Hayward, an officer in the 15th Battalion, The Welch Regiment received ATS more than once and was evacuated home in great discomfort.

And I had it everywhere – every blessed place: in me eyelids, in me privates, on hands and arms. It travelled round the body as though it was trying to find a place where something would absorb it ... Stinging. Stinging.

Hayward resisted having a third injection a fortnight after the first and was threatened with a court martial by the senior medical officer.¹¹⁸

The life-threatening complication of anaphylactic shock was recognised as a possible though unlikely consequence of ATS injection.¹¹⁹ In one unfortunate case, a wounded Canadian soldier, who had been injured previously and injected with ATS on two occasions, was not given a prophylactic jab and subsequently died of tetanus. The surgeon in charge was wary of using ATS after seeing a case of shock following use of anti-diphtheria serum.¹²⁰

However, urticaria and the other phenomena of serum sickness were seen in only a minor proportion of men receiving second and subsequent injections and the condition usually resolved without complication. Although around two million prophylactic doses of ATS were administered in England, only eleven cases of shock were recorded and all the patients recovered.¹²¹

Treatment with ATS

In WWI, ATS was the only specific therapy for tetanus but there was no general agreement on how best to treat patients. In fact, unlike the prophylactic use of ATS mandated by Army order, it was never the policy of the War Office to interfere with the

¹¹⁷ Payne JA. IWM Oral History, Cat. No. 9894, Reel 9.

¹¹⁸ Hayward HJ. IWM Oral History, Cat. No. 9422, Reels 15 & 16.

¹¹⁹ War Office. *Memorandum on the Treatment of Injuries in War*, 1915 (Note 71). p.22-23.

¹²⁰ Cameron K. *History of No. 1 Canadian General Hospital, 1914-1919*. Sackville, New Brunswick: Tribune Press; 1938. p.211.

¹²¹ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.207.

treatment of the sick soldier by his medical officer. Experimental studies in monkeys carried out during the war suggested that intrathecal injection was the most effective route of administration. However, a lack of uniformity in the treatment of patients made it impossible to reach a definitive conclusion based on cases treated in home hospitals.¹²²

The Tetanus Committee advised that a large dose of ATS should be given as early as possible in acute general tetanus. This treatment involved the intrathecal injection of 20 cc of high potency serum (supplied in bottles of 8,000 units in 10 cc) on the first and second days, supplemented and followed on succeeding days by sc and intramuscular injections.¹²³ Intravenous injection was not recommended because of the risk of anaphylactic shock.¹²⁴ About 27,500 doses of 8,000 units were issued during the war. One man received a total of 900,000 units, worth £90 based on the one-shilling cost of a prophylactic dose of 500 units; he was reported to have had a slight serum rash and recovered. Overall, however, 49 cases of shock (3.5 per cent) and twelve deaths (0.8 per cent) were reported following ATS therapy.¹²⁵

Bruce concluded that the risk of anaphylaxis markedly reduced the already questionable usefulness of therapeutic serum. Given the doubts about treating established tetanus, he had earlier underlined the importance of prophylaxis: 'There can surely be no doubt in anybody's mind that an ounce of prophylactic serum is worth pounds of the same serum used therapeutically'.¹²⁶

World War II

In 1936, the Army Pathological Advisory Committee placed advance contracts to ensure sufficient ATS supplies for all medical units in the field in the event of a major war. The Army Veterinary Service kept thirty horses immunised against tetanus and handed them to the Wellcome and Lister Institutes to accelerate production on mobilisation. The dosage for prophylaxis was set at 3,000 International units (1,500 USA units). Additional serum was procured for therapeutic use.¹²⁷

Active immunisation against tetanus was not feasible before WWI because the toxin in its natural form was too dangerous to use in humans. Behring and others had attempted to inactivate diphtheria and tetanus toxins by chemical means but the methods proved unreliable. In the early 1920s Gaston Ramon (1886-1963) at the Pasteur Institute and Alexander Glennie (1882-1965) of the Wellcome Laboratories independently established that formalin attenuated the lethal activity of these toxins by converting them into 'toxoids' that were harmless yet retained their immunising power and so were suitable for safe vaccination.¹²⁸

¹²² Bruce. Tetanus, 1920 (Note 62). p.24-27.

¹²³ War Office Committee. *Memorandum on Tetanus*, 1919 (Note 64). p.8-13.

¹²⁴ War Office. *Memorandum on the Use of Curative Sera*. London: HMSO; 1917.

¹²⁵ Bruce. Tetanus, 1920 (Note 62). p.27-30.

¹²⁶ Bruce D. Notes on the incidence of tetanus among wounded soldiers. *British Medical Journal*. 1917; 1(2926): 118-119.

¹²⁷ Anon. The control of tetanus, 1940 (Note 35). p.39-40.

¹²⁸ Bazin H. *Vaccination: A History. From Lady Montagu to Genetic Engineering*. Esher: John Libbey Eurotext; 2011. p.349-356.

Investigations of active immunisation were undertaken by Major John Boyd (1891-1981) at the Vaccine Department of the RAM College.¹²⁹ With the assistance of the Wellcome Research Laboratories he successfully inoculated human volunteers with tetanus toxoid.¹³⁰ Immunisation against tetanus was introduced into the Army in 1938 on a voluntary basis, initially involving two injections at intervals of six weeks.¹³¹ A third dose was added in January 1941 and an annual booster in November 1942. Every wounded man was also to receive 3,000 International units of ATS and, if non-immunised, a further two doses at weekly intervals.¹³²

<u>Conflict</u>	<u>Dates</u>	<u>Cases per 1,000 casualties</u>
WWI – Western Front	1914-18	1.47
WWII – B.E.F.	1939-40	0.43
– N.W. Europe	1944-45	0.06

Table 2. The incidence of tetanus during WWII after the introduction of immunisation. Compiled from data in: Boyd. Tetanus in the African and European theatres of war, 1946 (Note 133).

The benefit of immunisation was shown by the significant reduction in tetanus incidence compared with WWI, firstly in the BEF of 1939-40 when two doses were given and 90 per cent of troops were inoculated, and secondly in the British Liberation Army (BLA) of 1944-45 when inoculation was practically 100 per cent and boosters were given (Table 2). The small number of cases of tetanus in the BEF were all from the minority who had managed to avoid inoculation. However, in a few cases in the BLA, active immunisation failed to prevent tetanus.¹³³

Tetanus prophylaxis in perspective

Evidence before WWI suggested that tetanus antitoxin could protect against the development of tetanus provided it was administered soon after wounding. Support for prophylaxis came from experimental studies in laboratory animals, field trials in horses and treatment of Fourth of July injuries. Reports in the British medical press suggest

¹²⁹ Goodwin LG. John Smith Knox Boyd, 18 September 1891-10 June 1981. *Biographical Memoirs of Fellows of the Royal Society*. 1982; 28: 27-57.

¹³⁰ Boyd JSK. Active immunisation against tetanus. *Journal of the Royal Army Medical Corps*. 1938; 70: 289-307.

¹³¹ Anon. The control of tetanus, 1940 (Note 35). p.40-44.

¹³² Sachs A. Modern views on the prevention of tetanus in the wounded. *Proceedings of the Royal Society of Medicine*. 1952; 45: 641-652.

¹³³ Boyd JSK. Tetanus in the African and European theatres of war. *Lancet*. 1946; 247(6387): 113-119.

that some doctors had begun to employ tetanus antitoxin for prophylaxis more regularly although it does not seem to have been used widely in civilian practice.

The AMS had limited direct experience with tetanus antitoxin before WWI. The focus on hygiene and vaccination to prevent contagious diseases such as typhoid fever, which ravaged troops in earlier campaigns, was entirely rational and understandable. By comparison, tetanus prophylaxis was not seen as a priority – perhaps a case of ‘out of sight, out of mind’ – as far as the RAMC was concerned. Since tetanus was a known concomitant of war, given the published reports from more recent conflicts, and because of the agricultural land upon which hostilities would take place, the occurrence of the disease among the wounded on the Western Front was predictable.

In hindsight, the low amount of ATS issued by the RAM College at the beginning of WWI can be judged entirely inadequate. Certain types of wounds were considered more tetanus-prone than others and ATS administration was delayed until symptoms had developed. Moreover, the scale and the severity of wounds caused by modern warfare seems to have been greatly underestimated. It should be noted that the German Army also experienced a high incidence of tetanus early in the war which caught its military medical services and serum producers by surprise.¹³⁴

A lack of planning meant that necessary supplies of tetanus antitoxin in Britain were also wholly insufficient in early August 1914. Making increased quantities of ATS in horses was a complex process and there was an inevitable delay between the War Office placing an order and its fulfilment. Engaging with the antitoxin producers would have been necessary several months before the declaration of war on Germany to ensure that adequate amounts had been prepared before hostilities began.

Once the scale of tetanus among casualties was understood the use of ATS ramped up. The diminution in tetanus incidence at the end of 1914 was taken as strong evidence of its efficacy and it would have been unconscionable not to continue administering ATS to all wounded soldiers. However, its almost constant use eliminated any satisfactory non-inoculated control group for comparison.¹³⁵ In consequence, while undoubtedly suggestive, the evidence could not satisfy modern criteria for demonstrating efficacy.¹³⁶

It is unclear if a single dose of 500 units of tetanus antitoxin was sufficient to prevent tetanus in all casualties. Medical officers could use a higher dose at their discretion and it is likely that there was variation in doses administered depending upon local practice. From 1915, men admitted to Canadian hospitals were given 1,500 units.^{137 138} Although this was the accepted prophylactic dose in the US before the war, the American Expeditionary Forces gave an initial dose of 1,000 units, whatever the nature or severity of the wound, followed by at least one further dose of 1,000 units after seven days.¹³⁹

¹³⁴ Linton. *Emil von Behring*, 2005 (Note 8). p.357-362.

¹³⁵ Macpherson, Leishman, Cummins. *History of the Great War*, 1923 (Note 1). p.182-183.

¹³⁶ Adams EB, Laurence DR, Smith JWG. *Tetanus*. Oxford & Edinburgh: Blackwell Scientific Publications; 1969. p.49-52.

¹³⁷ Cameron. *History of No. 1 Canadian General Hospital*, 1938 (Note 120). p.211.

¹³⁸ Macphail A. *Official History of the Canadian Forces in the Great War 1914-19. The Medical Services*. Ottawa: FA Acland; 1925. p.104.

¹³⁹ Siler JF. *The Medical Department of the United States Army in the World War. Volume IX. Communicable and Other Diseases*. Washington: US Government Printing Office; 1928. p.284-289.

As the war progressed, the British serum manufacturers remained under increasing pressure to meet the demands of the War Office for ATS due to more widespread use and increased dosing. Similar demands were faced across the Channel. As principal French producer the Pasteur Institute increased its output of serums five-fold during the war, supplying more than six million doses to France alone and nearly two million in total to Allied troops in Europe and the American Army and Red Cross.¹⁴⁰

The large-scale application of prophylaxis in WWI suggested that ATS helped to lower the incidence of tetanus after wounding, altered the natural course of the disease and reduced mortality. It was also evident that infection was not limited to severe wounds but occurred in the case of trivial injuries, conditions such as frostbite and trench foot, and following certain surgical operations. Although clearly important in reducing the risk of tetanus in casualties, wound surgery alone was not enough to prevent the disease arising through contamination.

Prophylactic ATS also had its limitations. Its use created an additional burden upon medical services in managing the distribution of large numbers of bottles, arranging for the timely inoculation of casualties at dressing stations and ensuring the full course of injections along the evacuation chain and at home hospitals. Compliance with the recommended protocols of multiple injection was not always easy to achieve especially during periods of intense warfare and troop movements. Serum administration was also attended by the risk of potentially fatal side-effects.

The lessons of WWI seem to have been understood and acted upon well before WWII started. Early efforts were made to avoid a shortfall of tetanus antitoxin in the event of war through collaboration with the serum producers. In addition, the introduction of prior inoculation with tetanus toxoid ensured pre-existing immunity to tetanus before injury, replacing the uncertain efficacy of prophylaxis after wounding and further lowering the incidence of tetanus among casualties.

The RAMC's 1911 training manual restricted preventive inoculation to smallpox, diphtheria and typhoid fever, but noted presciently: '... still the principle is right and founded on scientific facts, and, as our knowledge becomes greater, will extend'.¹⁴¹ In 1989 a *JRAMC* editorial reviewing immunisation in the British Army duly concluded that eradication of tetanus '... requires nothing more than the conscientious application of the methods of immunoprophylaxis that have long been to hand'.¹⁴²

¹⁴⁰ Perrot A, Schwartz M. *Le Génie de Pasteur au secours des Poilus*. Paris: Odile Jacob; 2016. p.71-79.

¹⁴¹ War Office. *RAMC training*, 1911 (Note 29). p.22.

¹⁴² Anon. Tetanus immunisation in the British Army. *Journal of the Royal Army Medical Corps*. 1989; 135: 105-106.

Biographical details

Edward J Wawrzynczak PhD DHMSA is an independent writer, lecturer and researcher. He is a Fellow of the Faculty of History and Philosophy of Medicine and Pharmacy of the Society of Apothecaries, President of the British Society for the History of Medicine (BSHM) and acting BSHM Journal Editor.

Acknowledgements

I thank the staff at the British Library, Imperial War Museums, The National Archives and the Wellcome Collection who kindly assisted my research for this paper. Special thanks go to Rob McIntosh at the Museum of Military Medicine, Mytchett and Chris Ruddy at Sanofi Pasteur Connaught in Toronto, Canada who helped me identify rare wartime records. I am grateful to the independent reviewers for their helpful comments and indebted to Anita Hoffmann and David Vassallo for many useful suggestions to improve the manuscript.

Sources of funding

The author did not receive any funding in support of this work.

Wawrzynczak EJ. Fighting the Unseen Foe: Tetanus, Anti-tetanus Serum and the Royal Army Medical Corps in World War I. *Topics in the History of Medicine*. 2023; 3: 157-185.

Topics in the History of Medicine is an Open Access publication of the British Society for the History of Medicine made available under a Creative Commons Attribution-NonCommercial 4.0 International Licence which allows unrestricted redistribution in any medium or format for non-commercial purposes provided the original work is properly credited. <https://bshm.org.uk>

© The Author(s), 2023.