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Infection in a Pre-Antibiotic Era

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Abstract

Aims: This article is designed to demonstrate the problems of infection in a time without antibiotics and to raise awareness and stimulate discussion about the future and the next steps for managing antibiotic resistance.

Methods: Access was gained to original journals and letters of three doctors, who joined the army working as medical officers during the First World War. Transcripts of interviews of the doctors performed after the war, in 1977-1979, were also looked at. These original records were studied and any references to infection were collected. A literature search was then performed to identify research carried out during the First World War on the development of the management of infection and sanitation during that time period. A further literature search was then performed to identify modern day concerns with infection, in particular with regard to antibiotic resistance.

Results: The three doctors made many comments about infection in their journals and letters written during the war. It was clearly a major concern in the treatment of injured soldiers and few effective remedies were available. The literature search demonstrated that this concern was worldwide with massive investment in research between 1915 and 1917. This produced a drive of innervation and development, rapidly improving the management of infection during that time. Now, with concerns of rising antibiotic resistance, infection is again becoming a medical challenge that requires a renewed drive to push research forward.

Conclusions: This article demonstrates that without effective antibiotics infection is massive medical challenge. However when a problem is identified it is possible to produce rapid solutions with research and development. Antibiotic resistance is on the rise. Further research with international cooperation is now required to ensure a simple wound does not become untreatable condition.

Keywords: Infection; Antibiotics; Antibiotic resistance; First World War

Introduction

Today antibiotics are extremely effective and have transformed modern medicine. However sepsis is still a cause of hospital admissions and makes up a significant number of intensive care stays. Antibiotic resistance is making treatment more difficult. The management of infection has been developed and refined over the past 200 years and prior to antibiotics infection was a major cause of morbidity and mortality and treatment a great challenge.

With the rise of antibiotic resistant bacteria, infection is again becoming a concern for modern day medicine. In January 2013 Dame Sally Davies, the chief medical officer in the UK, said the threat from infections resistant to frontline antibiotics was so serious that the issue should be added to the UK government's national risk register of civil emergencies [1]. The World Economic Forum included antibiotic resistance as one of its Global Risks in its 2013 Report [2], and in May 2014, in the journal Nature, Woodhouse and Farrar have called for a coordinated and global effort to act on the problem [3]. In response to the rising concern and calls for international action the World Health Organisation (WHO) produced a report; 'Antimicrobial Resistance: Global Report on Surveillance'. They say 'the problem is so serious that it threatens the achievements of modern medicine. A post-antibiotic era—in which common infections and minor injuries can kill—is a very real possibility for the 21st Century' [4].

This article looks at a pre-antibiotic era, during the First World War. Diaries, letters and transcripts of interviews of three doctors working during the war are used to follow the advances in the treatment of infection that occurred during that time. Table 1 gives details of the three doctors [5-11]. In the diaries and letters tetanus and gas gangrene stood out as particularly common, so these are discussed in more detail. The article then looks to today's concerns with antibiotic resistance and the future. The article is designed to demonstrate the problems in a world without antibiotics and to raise awareness and stimulate discussion about the future and the next steps for managing antibiotic resistance.

Background

A number of studies have investigated the history of the management of infection [12-15]. However it was during the First World War that the most rapid changes in the understanding of infection and development of treatments occurred, prior to the development of antibiotics, and this article discusses this time period in more detail. The First World War presented new problems. There were high numbers of casualties and the horrific nature of the wounds caused by shrapnel and shells contaminated with soil had not been encountered before. Treatment was delayed as it took time to retrieve

soldiers from the frontline and sanitation was poor with crowded living conditions. Many soldiers lost limbs and life due to infected wounds and disease. Many microbes had not yet been identified and named. Alexander Flemming cultured clothing and wounds and described the bacteria grown, for example 'Fine bacillus resembling *C. tetani*, but with slightly oval sprore' and 'Long, stout Gram positive bacilli in threads' [16]. In 1918 a group of surgeons took cultures of wound swabs from their patients and found that 90.3% of the wounds were infected [17]. Captain Pettit looked particularly at gas gangrene and found 53% infected of wounds infected with anaerobic bacteria, however he does not mention numbers infected with aerobic bacteria [18]. Wounds were likely to be contaminated with multiple organisms. Alexander Flemming grew 10 different bacteria from one patient's single wound over a period of 67 days [16]. It was quickly noted that more effective treatments were required.

Doctor	Before the War	During the war	After the War
Sir Henry Platt [5-7]	Born Lancashire UK 1888. Attended medical school in Manchester in 1904, qualifying in 1909. He went to the USA to work in the Massachusetts general hospital orthopaedic department, returning to Manchester a year later.	Joined the Royal Medical Corps and quickly ascended to captain. Due to childhood tuberculous infection of the knee he was not sent on active service. He became surgeon-in-charge at the military orthopaedic unit of the Second Western Hospital, Grangethorpe Hospital, Manchester UK.	In 1916 he was a founding member of the British Orthopaedic Association, becoming president in 1934. President of The Royal Society of Medicine in 1931. In 1932 he was appointed Orthopaedic surgeon to the Manchester Royal Infirmary. In the 1940s Sir Harry Platt was elected to the Council of The Royal College of Surgeons of England, serving on it for 18 years, including as president from 1954-1957. Knighted in 1948 and retired in 1951. He died on the 20th December 1988, aged 100.
Major General Escritt [8,9]	Born in November 1893. Attended Guy's Medical School, London and was in his 4th year when war broke out.	1914 he joined HM Hospital Ship Letitia, as a dresser. They picked up 400-500 seriously wounded soldiers in Gallipoli. In 1917 the Letitia collided with another ship and returned to England for repairs. Escritt went back to Guy's Hospital to finish his medical degree. After qualifying in August 1918 he joined the Royal Medical Corps, becoming a lieutenant. He participated in army training in Blackpool and then joined the 19th Field Ambulance in the 23rd Division, near to Amiens in France.	After the war he remained in the army, in 1920 serving as a medical officer with the British Troops during the Iraqi rebellion and in the 1930s serving in Shanghai during the Sino-Japanese war. He then went to India, and became Assistant Director of Medical Services of the Eastern Army. In 1943 he was appointed an OBE and in the 1950s was Inspector of Training of the Army Medical Services. He retired in 1953 and was appointed Queen's Honorary Surgeon and awarded CBE. During his retirement he worked in a General Practice in Aldershot. He died on March 26th 1993, also aged 100.
Surgeon Lieutenant A.L.P. Gould [10,11]	Unknown	In January 1918 he went to Boulogne in France and from there was sent to Bapaume where he joined the 149th Field Ambulance stationed at Ruyalcourt. In February 1918 he left the Field Ambulance to travel with the 2nd Royal Marine Light Infantry Battalion. He was killed in May 1918	'Buried in Forceville Communal Cemetery Extension, North West of Albert, marked with a durable wooden cross' [11].

Table 1: Background information on the three doctors.

Wound infection

The majority of the comments in the three doctors memoirs and recollections involve wound infection. Escritt described the difficulties on board ship: 'We had quite a heavy death roll through wounds going septic. You see we hadn't got the modern drugs then and all these cases, well, everyone went septic and some very badly so and work was very heavy indeed' [8] and 'After a couple of days, nearly all the cases became septic and the odour of pus was overwhelming' [9]. Sir Platt said 'We delayed operations until certain an operation would not light up latent infection' [5]. The problems were also described by nurses working in a field hospital in Royaumont, where ALP Gould was stationed. They describe the unpleasant nature of the injuries: 'Wounds were pouring in day and night. They were all… horribly infected. I have never seen such wounds, gangrenous and offensive to a degree' [19]. 'I mind the smell, or should I say stink, of the wounds more than anything. I can't seem to get away from it' [19].

Treatments were not adequate. Iodine was given to the soldiers, but it is a weak antiseptic. In the hospitals and casualty clearing stations potassium permanganate, another mild antiseptic, was used on suppurating wounds. Sir Escritt recalls: 'I remember one particular case that had multiple injuries... it involved the genital organs and the anus. That was a very bad case and of course it turned septic like

everything else. We had to, in the end, put him in a bath, slung in a bath of potassium permanganate and kept him in that all the time. Just lifted him out to clean it up and put him back in again. The wound was permanently underneath, immersed in this solution' [8]. Stronger antiseptics; carbolic acid, mercury perchloride and hydrogen peroxide, were also developed but their use was limited due to their corrosive properties. And saline, invented during the first part of the war, was also found effective against infection when soaked in dressings.

By 1915 infection had been identified as a major cause of mortality for which something had to be done. Large numbers of medical trails were set up in Britain and France. H.D. Dakin noted that sodium hypochloride was a very effective germicide but irritating to skin. He found adding boric acid neutralised the solution, making it effective but also non-irritating [20]. In another trial A. Carrel found that the antiseptic action of Dakin's hypochlorite solution was short-lived so had to be renewed frequently [21]. Carrel invented an indian rubber tube with several holes along its length. This could be placed along the wound, covered with towelling and the antiseptic solution continuously poured down it. The fluid was absorbed by the towelling and kept in contact with the surface of the wound [21]. This became known as the Carrel-Dakin treatment. Unfortunately the method took a long time to disseminate out to the hospitals on the front and so was not used until the end of the war. The carbolic acid solutions remaining up till then the most commonly used treatment.

Dressings

Before the First World War Lister detailed the importance of antiseptic dressings [22]. During the war experimentation on different types of wound care and bandaging progressed, particularly at a local level. The nurses in the field hospital described their usual choice, 'Amputation was performed above the seat of the fracture. The usual dressing of 5% salt and 2.5% carbolic acid was applied' [19].The bandages used were generally made of cotton wool pads, but as money became scarce and supplies limited a range of unusual substitutes became more common. Pinewood sawdust was used, packed into muslin bags and sterilised with steam. It was very absorbent and the resin of the wood seemed to act as a deodoriser and probably also as an antiseptic [23]. Sphagnum moss, with its construction of delicate capillary tubes gave it the effect of a fine sponge, making it particularly absorbent. It is also thought to have antiseptic properties. Its use is mentioned by nurses in the field hospital at Royamount; 'Sphagnum moss, collected by volunteers in the boggy areas of Scotland and elsewhere, sterilised, dried and packed, was very useful for the copiously discharging wounds of modem warfare on account of its absorbency and softness' [19]. And 'The Committee were getting worried about the quantity of dressings required. They urged using more sphagnum moss, which cost nothing' [19].

Sanitation and Hygiene

The importance of preventing spread of infection was also evident during the First World War. ALP Gould wrote in his diaries 'Walked round camp. It is vastly improved on last week but as it is based on a dung pit and flies are now coming out in swarms one can hardly call it sanitary' [10]. Flies became such a problem that a committee was set up to deal with them, producing pamphlets advising on the burning of rubbish and on positioning and depths of toilet trenches [24]. In hospitals disinfectants were used and mattresses and beds were sprayed with formalin solution and then steamed. Blankets and woollen articles were soaked in cresol solution and cotton and linen were boiled [25]. Hygiene and sanitation became a high priority in theory, but in practice it was very difficult due to crowded conditions and limited washing facilities.

Tetanus and Gas Gangrene

Tetanus, caused by *Clostridium tetani*, is common in cultivated soils, so contamination of soldiers' wounds was high. In September 1914 there were 15.9 cases of tetanus per 1000 wounded. By the beginning of October 1914 it had increased to 31.8 cases per 1000 [26]. Sir Platt recalls one case; 'Before routine inoculation I myself had a most tragic experience in my unit of the Second Division General Hospital, where I did a bone graft in a fully healed forearm. That soldier died of tetanus' [27].

Tetanus was a well-understood disease even before the First World War. In 1885 Nicolaier produced the disease in mice by inoculating them with garden soil, and he isolated the bacillus from the wound [26,28]. Later in 1890 Behring and Kitasato demonstrated that animals could be immunised against the disease by repeated injection of non-lethal doses of the bacillus toxin [26,28]. But it was during the First World War that this was actually put into practice in people on a large-scale basis. Gould himself had the vaccination. He wrote; 'Felt rotten as a result of anti-tetanus injection' [15]. The 'antitetanic serum' was introduced at the end of October 1914. The number of cases of tetanus dropped to 1.7 per 1000 wounded in November 1914 and 0.9 cases per 1000 in December 1914 [26]. Sir Platt recalls the achievement; 'One great gain was the abolition of tetanus by the compulsory inoculation of every wounded soldier' [27].

Gas gangrene is also caused by the *Clostridium bacillus*, mainly *C. perfringens*, *C.novyi* and *C.septicum*. Treatment is surgical wash and debridement, and these days antibiotics. Escritt recalls trying to treat the disease on the ship. 'We used to get a lot of gas gangrene you know and it was found that the best treatment was cutting wounds round the edges to a depth of about a quarter of an inch and this had to be done within four hours of the injury. In that way you cut out, in those tissues, the organism before they penetrated further' [13]. And it was also a problem in the field hospitals; 'The surgeon's one aim was to open up and clean out the wound, or to cut off the mortifying limb before the dread gangrene had tracked its way into the vital parts of the body' [19].

Work went into finding a cure. Professor Weinberg of the Pasteur Institute in Paris produced a specific anti-gas gangrene serum, which by 1918 was given to most patients suffering with the disease. It was administered subcutaneously along with saline and camphorated oil [29]. Patients given the serum had a greater survival rate than those who did not receive it, but it was not successful in all cases and unfortunately gas gangrene continued to be a major problem until the end of the war. It was not until antibiotics were developed that gas gangrene could be treated effectively, although today it is still a cause of critical illness.

Summary

Over a period of 4 years, through the First World War, the management of infection developed from Lister's basic instructions into a complex system involving sanitation and hygiene, dressings, precise antiseptic solutions, public health and the development of vaccinations. It was a time of massive change. The journals at the time were filled with publications demonstrating research and positive results. By the end of the war our understanding of infection was much

greater and although a cure had not been found treatment has massively improved, saving many soldiers' lives.

The Future

Today bacterial infection is treated with antibiotics. They were manufactured on a large scale just before the Second War World. However infection remains an on-going challenge, particularly in vulnerable people, those with immunocompromise or concomitant illness and those with complicated wounds such as burns. The incidence of antibiotic resistance is rising. The WHO has identified antimicrobial resistance in many common infections including *Escherichia coli*, *Klebsiella pneumoniae*, TB, HIV and Malaria [4]. Sanitation and hygiene are of highest importance in our hospitals but multi-drug resistant bacteria are often contracted by inpatients, and the numbers of cases appear to be on the increase [30]. The WHO found that national data obtained for *E. coli*, *K. pneumoniae* and *S. aureus* showed that the proportion resistant to commonly used antibacterial drugs exceeded 50% in many settings [4]. It is associated with high morbidity and mortality [31,32]. One study found in the wars of Iraq and Afghanistan cases of infection were predominantly due to multi-drug resistant pathogens, likely acquired within the military healthcare system [33]. So despite the advances of the past, wound infection is becoming an increasing worry for modern medicine. Research needs to continue to ensure there is not a return to the conditions of a pre-antibiotic era as multi-drug resistant bacteria become dominant. The loss of antimicrobial action would make modern medicine impossible. It would not only affect infection; simple wounds, UTIs, pneumonia, meningitis, septicaemia. All branches of medicine including trauma, surgery, childbirth, cancer treatments and transplants would become hazardous. Both Professor Farrar of the Wellcome Trust and the World Health Organisation suggest the next step is a coordination global approach [3,4].

Conclusion

We have demonstrated that in the time before antibiotics infection presented a challenge to medicine. The doctors working during the First World War described many difficult cases. However the massive advances in knowledge that occurred during the First World War show that when there is such a need for a solution it creates a drive for results and it is possible for new treatments to be developed rapidly. Now there is a need to raise awareness of antimicrobial resistance, the concerns and risks for the future, and so stimulate research and development and an action plan on a global scale.

References

1. Sample. (2013) Antibiotic-resistant disease pose 'apocalyptic' threat, top expert says. The Guardian 23rd Jaunary 2013.
2. World Economic Forum (2013) The Dangers of Hubris on Human Health. Global Risks 2013.
3. Woolhouse M, Farrar J (2014) Policy: An intergovernmental panel on antimicrobial resistance. Nature 509: 555-557.
4. World Health Organisation. (2014) Antimicrobial Resistance Global Report on Surveillance 2014.
5. Typescript of an interview of Sir Harry Platt by Mr Liddle of Sunderland Polytechnic in Platt's consulting rooms in 1978. Held in the Liddle Collection, Special Collection, Brotherton Library, Leeds University, DF 102.
6. Typescript of 'It Takes All Sorts'. Sir Harry Platt interviewed by Olive Shapley for The British Broadcasting Corporation. Broadcast on Friday 12th May 1971, Radio 4, 0925. Held in the Liddle Collection, DF 102.
7. Obituaries. The Times, 22nd December, 1986, p. 14.
8. Typescript of an interview of Major General Escritt by Mr. Liddle of Sunderland Polytechnic, in Escritt's home, Surry, July 1979. Held in the Liddle Collection, GS 0525.
9. A letter written by Major General Escritt on the 14th July 1978. Held in the Liddle Collection, GS 0525.
10. Typescript of Diary and Letters by Surgeon Lieutenant A.L.P. Gould during 1918. Held in the Liddle Collection, GS 0648.
11. A letter written by the Director of Graves Registration and Enquiries on the 21st July 1918. Held in the Liddle Collection, GS 0648.
12. Eardley WG, Brown KV, Bonner TJ, Green AD, Clasper JC (2011) Infection in conflict wounded. Philos Trans R Soc Lond B Biol Sci 366: 204-218.
13. Manring MM, Hawk A, Calhoun JH, Andersen RC (2009) Treatment of war wounds: a historical review. Clin Orthop Relat Res 467: 2168-2191.
14. Nicoli Aldini N, Fini M, Giardino R (2008) From Hippocrates to tissue engineering: surgical strategies in wound treatment. World J Surg 32: 2114-2121.
15. Cameron HC (1907) LORD LISTER AND THE EVOLUTION OF WOUND TREATMENT DURING THE LAST FORTY YEARS: BEING THE JAMES WATSON LECTURES DELIVERED AT THE FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW IN FEBRUARY, 1906. Br Med J 1: 789-803.
16. Flemming A (1915) On the Bacteriology of Septic Wounds. The Lancet 186: 638-643.
17. Fraser F, Dew JW, Taylor DC, Dennis AW, Oliver MWB, et al. (1918) Primary and Delayed Primary Suture of Gunshot Wounds. Brit J Surg 19: 92-124.
18. Pettit RT (1919) Infections of Wounds of War with special reference to Gas Gangrene. J Amer Med Assoc 73: 494-496.
19. Crofton E (1997) The Women of Royaumont: Scottish Woman's Hospital on the Western Front. Med Hist 42: 270-271.
20. Dakin HD (1915) On the Use of Antiseptic Substances in the Treatment of Infected Wounds. The BMJ 2: 809-810.
21. Editor BMJ (1915) Abortive Treatment of Wound Infection. The BMJ Oct 23rd: 609-610.
22. Sir Lister J (1893) An address on the Antiseptic Management of Wounds. Brist Med J 1: 337-339.
23. Cathcart CW (1914) PINEWOOD SAWDUST AS A SURGICAL DRESSING. Br Med J 2: 661-662.
24. Macpherson WG, Horrocks WH, Beveridge WWO (1923) Medical Services - Hygiene of the War. In: History of the Great War. His Majesty's Stationary Office, London 2.
25. Knox EB (1911) Military Sanitation and Hygiene. Bailliere, Tindall and Cox, London.
26. Hurst AF (1943) Medical Diseases of War. Edward Arnold and Co., London, pp. 250-280.
27. Platt H (1977) Seventy-five years of medicine. Manch Med Gaz 56: 41-48.
28. Macconkey A (1914) TETANUS: ITS PREVENTION AND TREATMENT BY MEANS OF ANTITETANIC SERUM. Br Med J 2: 609-614.
29. Mayo-Robson AW (1918) SOME SURGICAL DEVELOPMENTS IN WOUND TREATMENT DURING THE WAR. Br Med J 1: 1-4.
30. European Centre for Disease Prevention and Control (2015) Annual epidemiological report 2014 – Antimicrobial resistance and healthcare-associated infections. ECDC, Stockholm.
31. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, et al. (2005) The impact of methicillin resistance in Staphylococcus aureus bacteremia on patient outcomes: mortality, length of stay, and hospital charges. Infect Control Hosp Epidemiol 26: 166-174.

32. Tadros M, Williams V, Coleman BL, McGeer AJ, Haider S, et al. (2013) Epidemiology and outcome of pneumonia caused by methicillin-resistant Staphylococcus aureus (MRSA) in Canadian hospitals. PLoS One 8: e75171.

33. Hospenthal DR, Green AD, Crouch HK, English JF, Pool J, et al. (2011) Infection prevention and control in deployed military medical treatment facilities. J Trauma 71: S290-298.

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