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The Role of Scientific Discovery in the Establishment of the First Biological Weapons Programmes

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The Role of Scientific Discovery in the Establishment of the First Biological Weapons Programmes

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This report addresses the scientific and technological discoveries in the biological sciences that enabled the early interest in biological warfare to move from hurling infected corpses into enemy cities in ancient times, through use of small cultures of animal pathogens to sabotage enemy livestock in World War I, to the origins of organised military biological weapons (BW) programmes directed at humans, animals, and plants in the inter-war period. It builds on Dando's 1999 paper: *The Impact of the Development of Modern Biology and Medicine on the Evolution of Offensive Biological Warfare Programs in the Twentieth Century*.[1] For the historical aspects of biological warfare programmes this report primarily draws from the Stockholm International Peace Research Institute volume: *Biological and Toxin Weapons: Research, Development and Use from the Middle Ages to 1945*.[2]

Ancient times and the pre-microbiological era

Prior to the discoveries made in the late 19th century, understanding of the causes of infectious diseases was limited. Three main theories pervaded popular and scientific thought over many centuries. Miasmatic theories emphasised that the 'poisonous fumes' released from rotting flesh or vegetation and stale water were responsible, whilst the theory of contagion suggested that diseases were passed on by person-to-person contact.[3] Theurgic theories related the incidence of disease to notions of good and evil. Those affected were thought to be in receipt of a punishment from God. It is unsurprising, therefore, that early attempts to exploit disease as a weapon were fairly unsophisticated.

Broadly speaking, biological warfare can be defined as the *deliberate* use of microorganisms or toxins to cause illness or death. Establishing this intent is important when looking for early examples of biological warfare in order to distinguish between those acts where the aggressors main aim was to spread disease and those where disease was merely a secondary consequence. Wheelis's study of biological warfare pre-1914 argues that "… intent is assumed if it is consistent with the state of knowledge of the time" but acknowledges the difficulties in determining intent retrospectively.[4] An old military tactic, dating back to ancient Greek and Roman times, was to place human or animal corpses in wells or other sources of drinking water.[5] This tactic may have been used as a method of spreading disease amongst the enemy and could be deemed one of the oldest forms of biological warfare.[6] However, the purpose behind such actions may have been simply to restrict access to potable water.[7] If these actions were biological warfare then the miasmatic theory would have supported the use of such crude delivery systems.

There are several accounts of the use of potentially infected material in siege warfare during the late Middle Ages and Renaissance period.[8] It is unclear whether the intent was to cause disease but as Wheelis argues, it is "… plausible, since the prevailing theory of

infectious disease in medieval times was that disease was a consequence of the bad air resulting from extensive decomposition."[9] Perhaps the most renowned instance occurred at Caffa (now Feodosija, Ukraine) in 1346.[10] During a siege of the city plague broke out amongst the attacking Mongol troops. Subsequently the Mongols are thought to have 'catapulted' the corpses of infected individuals into the city.[11] Plague did emerge amongst the inhabitants but there has been some debate as to the method of transmission. It has been suggested that it may have been carried into the city via the rodent population[12] but Wheelis argues that a biological attack was the most likely cause of the outbreak. A plague epidemic (the Black Death) soon flared up in Europe, killing twenty million people in the space of three years.[13] At the time there were a number of theories on the cause of this outbreak. Some thought it was a punishment from God or the result of certain planetary alignments. The more scientifically minded attributed it to the bad air or miasma from decaying organic matter or stagnant water. Porter notes that some people referred to the idea of contagion,

> "… but most medical theorists, loyal to their Greek learning, stood by constitutional factors: if the body was robust, illness should not result; if not, one would sicken and die."[14]

If the Mongols recognised the miasmatic theory of disease then they would have likely anticipated the transmission of plague through their actions at Caffa.

Two hundred years later there was a significant development in the understanding of disease and contagion. In 1546 Girolamo Fracastoro published a theoretical work entitled '*De contagione et contagiosis morbis curatione*'. He suggested that contagious diseases were characterised by the presence of 'disease seeds', which could infect by contact, by fomites, or from a distance.[15] He defined fomites as materials that could harbour these seeds[16] in some cases for as long as two to three years.[17] The notion of contagion was thousands of years old but it had been non-specific. Fracastoro's work was the first clear suggestion of an infectious agent. His ideas, however, were not revisited for several hundred years.[18] In the 17th century the field of microscopy began to emerge. One of the first uses of a microscope to study disease was in 1656 when Athanasius Kircher used his to study plague victims from an outbreak in Rome and reported seeing 'small worms'.[19] In 1665 Robert Hooke published his *Micrographia*, which "… featured the first biological use of the word 'cell' in describing the 'pores' in wood" and Malpighi pioneered microscopic study of the human anatomy.[20] However it was the Dutchman, Antony van Leeuwenhoek who made the most progress in the late 17th century, in part due to the quality of his microscopes, which he constructed himself.[21] It was van Leeuwenhoek who was the first to see microorganisms, which he called 'animalcules' or 'little animals', thus contributing to the dispute over the theory of spontaneous generation.[22] However, this discovery, which marks the beginning of microbiology, received little attention at the time.[23]

In these early examples of possible biological warfare the intent of the aggressor is unclear. However, in the late 18th century an incident occurred where this intent was unquestionable. During the Indian Wars the English used smallpox as a biological weapon against the Native Americans. Correspondence in July 1763 between the Commander-in-Chief of the British forces in North America, Sir Jeffrey Amhurst, and a regional commander reveals a plan to transmit smallpox by means of contaminated blankets to the Indians who were threatening the British held Fort Pitt.[24] Independently, a

month earlier, the commanding officer, Captain Ecuyer, had apparently authorised such an 'attack'.[25] Relating a meeting between two Indian Chiefs and British officers, one of Ecuyer's subordinates recorded in his diary on 23 June 1763: "Out of our regard to them we gave them two Blankets and a Handkerchief out of the Small Pox Hospital. I hope it will have the desired effect."[26] Interestingly, as Wheelis notes in his account, the use of fomites was an accepted mode of transmission for smallpox.[27] Whether these actions caused the resulting outbreak is unclear since smallpox epidemics had been occurring amongst Native Americans since the Europeans had arrived in the New World 200 years before.[28] Smallpox and other diseases such as measles and influenza were having a devastating effect on the Natives who lacked immunity.[29] Miasmatic theories of disease were popular at the time but theories of contagion were also discussed especially with regard to specific diseases such as syphilis. In the latter years of the 18th century William Cullen, whose work had a great influence on the English speaking world for the next 100 years, embraced both theories and stated that certain diseases, such as smallpox, could be attributed to specific 'contagions' whereas others were the result of environmental miasma.[30]

There is also evidence that the British attempted to transmit smallpox to the Continental Army during the American Revolution. Two such incidences reportedly occurred in Boston and in Quebec in 1775. The British soldiers are thought to have deliberately inoculated some civilians with smallpox, who subsequently acquired a less severe but still highly contagious form of the disease, before sending them to mix with Continental soldiers.[31] It would appear then that both the person-to-person and fomite route of transmission was understood at the time.

There were a number of other possible instances of intentional transfer of smallpox to Native Americans.[32] One of the later events is thought to have occurred in 1831 on the trade route between Saint Louis and Santa Fe, when gifts of smallpox contaminated clothing and tobacco were used in an attempt transmit the disease to the Pawnees.[33] It is interesting because of its timing. As Wheelis notes, Europeans by that time could benefit from vaccination, which had been discovered by Edward Jenner in England in 1798. Jenner had heard that previous infection with cowpox in humans somehow conferred immunity to smallpox. He experimented by inoculating a young boy with cowpox (*Vaccinia*) and subsequently inoculating him with smallpox. The boy did not develop smallpox and thus the practice of vaccination was established. Reportedly the technique was accepted very quickly and, by 1799, 5,000 people in England had been vaccinated.[34]

Some years later, during the American Civil War (1861-65), there was at least one incidence of attempted biological warfare. Dr. Luke Blackburn, who would later become governor of Kentucky, tried to contaminate clothing with smallpox and yellow fever for sale to Union troops.[35] Although smallpox can be transmitted by fomites it was not known at the time that yellow fever is transmitted by mosquitoes. The ancient practice of fouling water supplies with corpses was also employed during this conflict.[36] In one instance during 1863 in Mississippi the retreating Confederates left animal carcasses in wells and ponds to deny Union troops access to water.[37] The same year United States President Abraham Lincoln issued General Orders 100, which contained one of the first legal restrictions applicable to biological warfare. Article 70 stated that "The use of poison in any manner, be it to poison wells, or food, or arms, is wholly excluded from

modern warfare. He that uses it puts himself out of the pale of the law and usages of war."[38]

During the first half of the 19th century a greater understanding of disease aetiology was beginning to emerge, encouraged by challenges to the theory of spontaneous generation. In 1835 the idea that a given disease could be caused by a specific 'agent' was given some credence when Agostino Bassi found that he could cause silkworms to become ill by inoculating them with the fungus found on dead silkworms.[39] A few years later, in 1840, Jacob Henle claimed that diseases were caused by a living agent that entered the body, acting as a parasite. This was a challenge to Liebeg's more popular theories of the chemical nature of fermentation and decomposition.[40] Soon new discoveries would revolutionise the understanding and treatment of disease. These discoveries would in turn have implications for the as yet rare and imprecise science of biological warfare.

The 'germ theory' of disease

During the latter half of the nineteenth century the immature field of microbiology was transformed. The science of bacteriology emerged through the isolation, culture and identification of bacteria. Specific bacteria were found to be the causative agents of numerous human, animal and plant diseases and thus the 'germ theory' of disease was established. The early pioneers in this new field of biology were Louis Pasteur in France and Robert Koch in Germany.[41]

Pasteur (1822-1895) was originally a chemist but he developed an interest in microorganisms and, through appointment as dean of life sciences at the University of Lille in 1854, he came to study the process of fermentation.[42] Challenging the prevailing theory he found that yeast was responsible for alcoholic fermentation and that this was therefore a biological process.[43] He went on to design intricate experiments to show convincingly that microorganisms in the air were the source of the living matter that seemed to appear in flasks of 'broth', thus dismissing the theory of spontaneous generation.[44] His work then concentrated on the relationship between microorganisms and disease. In 1866 he found that a specific microorganism was causing a disease in silkworms.[45] Later, in 1878, he argued for a 'germ theory' of infection at the French Academy of Medicine.[46]

Inspired by Jenner's success with smallpox vaccination, Pasteur set to work on the mechanisms of disease prevention. In 1880 he published a paper showing that attenuated or weakened microbes that were responsible for chicken cholera could be used to protect chickens against infection.[47] Later he worked on rabies and managed to produce a weakened version of the 'poison', or 'virus' as he called it, that was responsible for the illness, using it to successfully immunise a boy who had been bitten by a rabid dog in 1885.[48] Despite this accomplishment he had been unable to distinguish or isolate the causative agent.[49] Prior to this work with rabies, Pasteur had used his attenuation technique to produce a vaccine for anthrax that he had shown to be effective in animals during a public demonstration in 1881.[50] His success with anthrax was enabled largely due the efforts of Robert Koch, who was simultaneously advancing the understanding of microbiology in Germany.

In 1876 Koch had published the results of his work with anthrax, showing that a bacterium, *Bacillus anthracis*, was the causative agent of the disease and thus validating the 'germ theory'.[51] In 1882 he went on to isolate *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis.[52] He soon published his landmark work on the aetiology of tuberculosis in which he defined three conditions that had to be fulfilled in determining that the tubercle bacillus was responsible for the disease.[53] These conditions later came to be known as Koch's Postulates and were used in determining whether a specific microorganism was the causative agent of a given disease.[54]

An important aspect of this new science was the isolation and culture of these microorganisms. Koch and his team also led the way in this respect. It was not possible to obtain pure cultures of microorganisms using liquid media and so Koch and his team looked to solid media.[55] In 1881, building on the work of Schroeter and Brefeld, Koch succeeded in using sterile potato slices and then culture media solidified with gelatin as solid media that could sustain pure bacterial colonies.[56] The following year scientists working in his laboratory proposed the use of the algae extract agar-agar instead of gelatin because it remained solid at temperatures up to 100 degrees centigrade.[57] Several years later, in 1887, another of Koch's colleagues, Julius Petri, developed a new culture dish with an overhanging lid, now known as the Petri dish.[58]

The primary outcome of all this work was the identification of the causative agents of many human, plant and animal diseases (see *Table 1* below). Porter notes that:

> The methods he [Koch] had pioneered proved their worth … leading to the rapid discovery, largely by his own pupils, of the micro-organisms responsible for diphtheria, typhoid, pneumonia, gonorrhoea, cerebrospinal meningitis, undulant fever, leprosy, plague, tetanus, syphilis, whooping cough and various other streptococcal infections.[59]

Table 1: Discovery of microorganisms responsible for various diseases.[60]

Date	Disease	Agent
1876	Anthrax	*Bacillus anthracis*
1880	Typhoid Fever	*Salmonella typhi*
1882	Glanders	*Pseudomonas mallei*
1883	Cholera	*Vibrio cholerae*
1887	Malta (undulant) fever	*Brucella* spp.
1894	Plague	*Yersinia pestis*
1896	Botulism	*Clostridium botulinum*
1909	Rocky Mountain spotted fever	*Rickettsia rickettsii*
1912	Tularaemia	*Francisella tularensis*

Koch and his associates were not alone in identifying new microoganisms. In 1892 William Welch and George Nuttall identified Clostridium perfringens as the cause of gangrene.[61] In 1894 it was Alexandre Yersin in France who was the first to identify *Yersina (pasteurella) pestis* as the causative agent of plague. However, Shibasaburo Kitasato, one of Koch's students, independently observed the plague bacterium that same

year.[62] Later, in 1909, the American, Howard Ricketts showed that Rocky Mountain spotted fever was caused by a new type of microbe that was subsequently named after him, a *Rickettsia*.[63]

There were other significant developments during this period of rapid discovery in microbiology, including work on bacterial toxins. Following the discovery of *Corynebacterium diphtheriae* to be the cause of diphtheria, in 1884, Friedrich Loeffler "… shows that the bacterium secretes a soluble substance that affects organs beyond sites where there is physical evidence of the organism."[64] Several years later in France, in 1888, Emile Roux and Alexandre Yersin show that *Corynebacterium diphtheriae* exerts its effects on tissues and organs by means of a toxin.[65]

An understanding of immunology was also beginning to develop. In 1884 Ilya Metchnikoff had observed phagocytosis and proposed a cellular theory of immunity and in 1891 Paul Ehrlich showed that antibodies formed against the plant toxins ricin and abrin and put forward the antibody theory of immunity.[66] A year earlier Emil von Behring and Shibasaburo Kitasato, both working in Koch's laboratory, were quick to make use of the newly identified *Corynebacterium diphtheriae.* In 1890 they produced a serum antitoxin that could prevent infection with diphtheria in animals.[67]

Importantly the new microbiology was having immediate effects in terms of human disease prevention. Immunisation was mounting an offensive on two fronts. On the one hand employing Pasteur's attenuated pathogens and on the other using newly developed antitoxins. Pasteur's rabies vaccine became standard and was used to treat around 20,000 people worldwide during the decade following its development in 1885.[68] Diphtheria antitoxin was first used on a child in 1891 and by 1895 had become common practice e, made possible by Roux and Yersin's use of horses for large-scale serum production.[69] As Porter notes: "In New York, the [diptheria] death rate had peaked at 785 per 100,000 in 1894; by 1920, it has dipped to under 100."[70] However, other factors, namely better hygiene and sanitation, were contributing to a general decline in the number of cases of diphtheria.[71] The same was true for cholera, which had been proven to be a waterborne disease by John Snow in London in 1854.[72] It was not until 1883, however, that Koch identified *Vibrio cholerae* as the causative bacterium.[73]

In 1884 one of Koch's pupils isolated the microorganism responsible for typhoid fever, *Salmonella typhi*.[74] The wait was not long for a successful vaccine for typhoid fever, which was produced in Britain by Almwroth Wright and David Sample using 'killed' organisms.[75] Due to a debate over its efficacy it was not taken up readily. Porter notes that few British troops received the vaccine during the Boer War when "… in South Africa 13,000 men were lost to typhoid as against 8000 battle deaths."[76] The vaccine was administered to troops during the First World War, however, and "… whereas in the Boer War typhoid incidence was around 10 per cent …, in the Great War incidence was down to 2 per cent".[77] Antitoxin for tetanus, which is caused by *Clostridium tetani*, was another successful treatment to emerge at the end of the nineteenth century and to be used to great effect during World War I.[78]

There were some diseases for which a treatment was not forthcoming despite the isolation of the responsible microorganisms. Treatment of tuberculosis (TB) had a false

start in the early 1890's after it emerged that Robert Koch's much-publicised tuberculin was not effective.[79] It was not until 1924 that the BCG vaccine, developed by Albert Calmette and MarieGuerin at the Pasteur institute, was first used in humans to prevent TB.[80] During the late 1890's Waldemar Haffkine, a Russian former pupil of Pasteur, worked on vaccines for cholera and plague using 'killed' organisms but had limited success. [81]

Although the concept of the virus was not fully understood until the mid-twentieth century, the field of virology did have its roots in this period.[82] In 1892 Dmitri Ivanowski demonstrated that the causative agent of tobacco mosaic disease (TMV) passed through bacteriological filters.[83] Similarly, in 1898, Friedrich Loeffler and Paul Frosch showed that the microorganism responsible for foot and mouth disease (FMD) also passed through filters designed to retain bacteria.[84] The same year Martinus Beijerinck described the agent of TMV as a "contagium vivum fluidum", recognising an infectious agent distinct from bacteria.[85] Through the work of Walter Reed in the United States, the first human disease to be attributed to such a 'filterable agent' was yellow fever, which he found to be transmitted by mosquitoes.[86]

The emphasis of this frenzy of discovery at the turn of the century was on the understanding and treatment of infectious diseases. However, it appears that other uses of this knowledge were not lost on Louis Pasteur. As early as 1882 he had the idea of using a microorganism to cause disease in populations of lice.[87] Later he considered this strategy for control of rabbit populations in Australasia and he carried out a field test on his estate in France, attempting to infect rabbits with *Pasteurella multocida*.[88] Whilst this type of biological control would not fall within the contemporary definition of anti-animal biological warfare it was certainly an indication of things to come. Wheelis points to some other research carried out in Germany and the United States in the early 1890's that provides an early example of the dual-use dilemma applicable to defensive research.[89] This work involved the contamination of bullets with bacteria, such as anthrax, and showed, through tests on animals, that the bacteria could survive the blast of the firearm and subsequently cause infection of the bullet wound. Wheelis states that the research was most likely carried out to increase understanding of wound infection but notes "… the conclusions nevertheless invite application to offensive use".[90]

At this point in history biological warfare had not emerged as a distinct form of waging war. Early biological weapons would likely have been categorised with poisons and chemicals in terms of agents of warfare. Towards the end of the 19th century the opinion of the international community in relation to such weapons was becoming clear. At the Brussels conference in 1874 the 'International Declaration Concerning the Laws and Customs of War' included a section forbidding the use of poison or poisoned weapons, although this agreement never entered into force.[91] On July 29 1899 at the first International Peace Conference in The Hague the 'Convention with Respect to the Laws and Customs of War on Land' was signed. Article 23 stated, "Besides the prohibitions provided by special Conventions, it is especially prohibited … To employ poison or poisoned arms".[92] This position was reaffirmed at the second International Peace Conference at The Hague in 1907. Despite these agreements, and the additional Declaration at the 1899 Peace Conference stating that "The Contracting Powers agree to abstain from the use of projectiles the object of which is the diffusion of asphyxiating or

deleterious gases"[93], chemical weapons were used extensively during World War I.[94] It was at this time that the first biological weapons programmes emerged, enabled by the new understanding of microbes.

Biological sabotage programmes in World War I[95]

Germany and France were the first to assemble rudimentary biological weapons programmes. As Wheelis notes, it is possible that the key role scientists from these two countries played in the development of microbiology was a factor in this. Germany ran an organised programme of biological sabotage in neutral countries from 1915-1918 designed to restrict the supply of military livestock to Allied forces during World War I. The German programme was controlled by the General Staff of the Army and had no civilian oversight. The anti-animal operations made use of cultures of *Pseudomonas mallei* (glanders) and *Bacillus anthracis* (anthrax). These microorganisms had been identified for the first time in 1882 and 1876 respectively. Clandestine operations were conducted in the United States, Romania, Spain, Norway, Argentina, and also on the Western Front. Despite two requests during 1916, the German leadership ruled out the use of microorganisms against humans for moral and technical reasons.

The most extensive operations were carried out in the United States before they entered the War. During this period the US shipped horses and mules, which were of significant tactical importance, to France and the UK. In April 1915, on an assignment for the German General Staff, Dr. Anton Dilger, a physician who was born in the United States to German parents, brought cultures of glanders and anthrax from Germany to the United States and subsequently set up a 'laboratory' in the basement of a private house in the Chevy Chase region of Maryland, not far Northwest of Washington D.C.. He and his brother cultured the bacteria on solid media before creating liquid suspensions. This technique would not have been unfamiliar to physicians at the time. These suspensions were used in attempts to infect horses and mules awaiting shipment near the ports of New York, Baltimore, Norfolk and Newport News. Animals were pricked with needles protruding from the glass vials in which the bacterial suspensions were carried. Another delivery method was the addition of the bacteria to food and water supplies. The modes of transmission for these two diseases were understood and these delivery mechanisms could have lead to infection. The sabotage operations in the United States are thought to have begun in the summer of 1915 and ended in the autumn of 1916.

A similar operation to infect horses in Romania also involved the use of glanders and anthrax to infect horses and cattle respectively. Sabotage was also carried out in Spain against both horses and cattle and is thought to have continued late into the War. In Norway reindeer were the focus of the Germans attention because they were used by the British to transport arms to Russia. In late 1916 attempts were made to infect reindeer using sugar cubes containing capillary tubes filled with anthrax culture. Some of these sugar cubes survived having been acquired by the Norwegian police at the time. These museum pieces were analysed in 1998 by scientists who found that they still contained viable *Bacillus anthracis* organisms.[96] This delivery system was also used in German sabotage activities against horses and mules in Argentina in 1916.

The Germans carried out some anti-animal sabotage activities on the Western Front including an attempt in 1917 to infect French horses with glanders by 'brushing' the cultures on their noses but these operations were discontinued due to the capture of agents. A number of other allegations were made against the Germans including an attempt by an agent to spread plague in St. Petersberg in 1915, the reported infection of 4,500 mules with glanders in Mesopotamia in 1917, and the dropping of fruit, chocolate, and children's toys contaminated with bacteria in Bucharest.[97] However, like many allegations of biological warfare, their reliability is questionable. The uncovering of some German sabotage operations may have encouraged other countries to investigate this method of waging war. The French set up a similar programme of biological sabotage although on a much smaller scale. The Germans believed that French agents were infecting horses in Switzerland with glanders and there are reports of biological material being discovered in the possession of French prisoners of war. The British also addressed the possibility of biological warfare but concluded that it was infeasible.

Wheelis argues that the German programme was notable since it was both the first national biological weapons programme and the first to have a scientific basis. In retrospect it is impossible to assess the effectiveness of the sabotage activities especially given the natural outbreaks of glanders amongst livestock.[98] Over 58,000 horses used by the French Army are thought to have contracted glanders through natural causes during World War I.[99]

By 1918, having learned of the German biological weapons programme, the United States conducted its first research in the field.[100] Investigators looked at two ways in which the toxin ricin, which is extracted from castor beans, could be delivered as a weapon: they found that it could be adhered to shrapnel bullets and would maintain its toxicity after detonation; and they also looked into creating ricin 'clouds' for airborne delivery.[101] These delivery mechanisms were tested in the laboratory but they did not produce an operational weapon before the end of the war.[102]

Since the German sabotage activities consisted of covert operations on a small scale, it is not surprising that they only produced small quantities of agents. It is worth noting, however, that the fermentation technology enabling large-scale culture of bacteria was available at the time. In 1915 Chaim Weizmann discovered and isolated *Clostridium acetobutylicum* and found that it could be used to produce acetone and butyl alcohol.[103] Acetone for the production of explosives was in short supply at the time and the large-scale fermentation of *Clostridium acetobutylicum* became an important part of the British War effort.[104]

Regardless of developments in biological warfare, the world soon received a chilling reminder of the power of naturally occurring disease outbreaks. Recent scientific advances were humbled by the 'Spanish' influenza pandemic (1918-19), which swept across the globe causing illness in 20-40% of the worlds population and killing over 20 million people.[105]

Selected developments in the biological sciences in the inter-war period

Advances and discoveries in the field of microbiology continued apace with particular attention to new therapies. As the result of work begun in 1906, Calmette and Guerin in France demonstrated a vaccine against tuberculosis using a live non-virulent strain of the bacteria.[106] The Bacillus Calmette Guerin (BCG) vaccine was first used on calves but the First World War delayed its introduction to humans until 1924. By 1928 it had been used to immunize 116,000 French children but there seems to have been controversy over its efficacy and other countries including Germany and the USA did not initially approve the vaccine whilst its introduction in the UK was delayed. The BCG vaccine played a major part in a Europe-wide vaccination campaign by the Danish Red Cross in the aftermath of World War II.[107] In 1938 Theller's yellow fever vaccine was successfully tested and by 1947 The Rockefeller Foundation in the USA had produced over 28 million doses.[108]

Although certain diseases had been attributed to 'filterable agents', it was not until 1926 that virology was launched as a distinct field when Rivers presented a paper distinguishing between bacteria and viruses.[109] It was known that viruses could not be cultured in the same way as bacteria since they required their host organism or host cells and so there was a search to develop alternative means of cultivation aside from the inoculation of live animals and plants.[110] In the early 1930s scientists developed the technique of growing viruses in chicken eggs, a method that is still used today despite the subsequent emergence of cell culture methods in the 1950s, whereby mammalian cells are removed from the animal and grown in a culture medium to support viral growth.[111] The study of viruses was severely limited initially by the inability to see them through existing microscopes. This changed with the invention of the electron microscope in the 1930s allowing the first pictures of a virus to be taken in 1940[112] and a subsequent acceleration in the understanding of viruses during the 1940s and 1950s. In 1945 Luria and Hershey showed that viruses mutate making it difficult to develop immunity to them.[113]

Treatment of illness with natural or synthetic chemical compounds did not become organised until the nineteenth century when the scientific study of drugs resulted in the new field of pharmacology.[114] In the 1890s Erlich had been the first to use a systematic approach, following on from discoveries in microbiology and his own work on antigen-antibody interactions, to attempt development of chemical therapies for newly discovered infectious diseases. Building on the long history of use of mercury and arsenical compounds from the dye industry, Erlich synthesised hundreds of arsenical compounds and patented one, Salvarsan, which by 1910 had been used to treat 10,000 syphilis sufferers. This was succeeded by a modified version, Neo-Salvarsan or neoarsphenamine. Although effective these compounds were still toxic and further advances were not forthcoming until 1935 with the use of Protonsil.[115] Protonsil, another chemical from the dye industry, was introduced to medicine by a German, Gerhard Domagk, who demonstrated that it was effective for treating streptococcal infections. Later sulphanilamide was shown to be the active compound produced when Protonsil was hydrolysed in the body. It worked by preventing bacterial growth thus enabling the immune system to overcome the infection rather than killing the bacteria themselves. In 1938 a British team of scientists developed a similar compound called M&B 693 (sulfadiazine), which was also effective against pneumococcal infections and more effective than Protonsil against streptococci. It was used to treat Winston Churchill's

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pneumonia during World War II.[116] As Porter notes in his historical study of medicine, such drugs soon became very popular: "These new 'sulpha drugs' began to be prescribed in vast quantities: by 1941, 1700 tons were given to ten million Americans."[117]

In 1929 Alexander Fleming published a paper describing the anti-bacterial effect of an extract of the *Penicillium* mould, penicillin, on gram positive bacteria.[118] However, since penicillin had no effect on gram negative bacteria, and it was difficult to isolate, Fleming did not take this work further.[119] It was not until 1940 that Ernest Chain and Howard Florey, having reviewed the scientific literature for antibacterial substances and discovered Fleming's paper on penicillin, used the substance to cure streptococcal infections in experimental mice.[120] However the same year, in an early indication of antibiotic resistance in bacteria, Chain and Abraham discovered a substance produced by *E. Coli* that could inactivate penicillin.[121] In 1941 penicillin was first tested on a human volunteer and shown to be non-toxic.[122] One of Florey's colleagues Norman Heatley, collaborating with American scientists in Illinois in 1941, worked to improve techniques for penicillin production and subsequently three US companies started large scale production of the drug. British companies followed suit in 1943 and by mid-1944, as Porter describes, "enough was available to allow unlimited treatment of allied servicemen."[123] Porter goes on to note:

> Penicillin proved hightly effective against most types of pus-forming cocci, and against the pneumococcus, gonococcus, meningococcus and diptheria bacillus, the bacilli of anthrax and tetanus and syphilis. Pre-penicillin, the pneumonia fatality rate was around 30 per cent; it dropped to around 6 per cent, and pneumonia, once the old man's friend, ceased to be a major source of death.[124]

In 1940 Waksman and Woodruff had isolated actinomycin from an actinomycete fungus, which led to the discovery of many other antibiotics from that group of fungi.[125] Actinomycin, although antibacterial, was toxic in humans and not used clinically.[126] In 1944, however, Walksman isolated streptomycin from a related fungal species and found that it had an anti-bacterial affect on gram negative bacteria similar to penicillin's effect on gram positive organisms. It was soon used to treat tuberculosis.[127]

Another significant area of biology with its roots in this period is molecular genetics. In 1928 Griffith discovered bacterial transformation. However, the mechanism behind this process, by which bacteria can take up and express foreign genetic material, was not elucidated until the early 1940s when Avery, MacLeod and McCarty showed that DNA was the transforming material.[128]

First generation biological weapons programmes

Whilst the boundaries of the field of microbiology continued to be pushed forward it was during the inter-war period (1919-1938) that the new body of knowledge, having emerged at the turn of the century, was assessed by militaries in a more organised and wide ranging fashion, beyond the realm of the limited biological sabotage activities that occurred in World War I. France, Japan, and the USSR were the first to establish organised programmes incorporating offensive and defensive preparations although making distinctions between the two types of research would be difficult from the outset.

Germany's efforts were fairly limited due to Hitler's ban on offensive research, which is most ironic since perceptions about Germany's "extensive" activities in this area were a major driver for the development of the French programme and later other allied programmes. These initial biological weapons programmes are known as 'first generation', making use of the new bacteriology, simple culture methods, and crude delivery systems. The programmes of the United Kingdom, Canada, and the United States are considered to be 'second generation' programmes due to their increased level of sophistication. The offensive aspects of these programmes were not initiated until after the start of World War II and so they will not be covered here apart from a brief description of the developing interest in the field of biological warfare in these countries during this period.

An important development during this period was the signing in 1925 of the Protocol for The Prohibition of The Use in War of Asphyxiating, Poisonous or other Gases, and of Bacteriological Methods Of Warfare, known as the Geneva Protocol.[129] Thus the prohibition of use of chemical and biological weapons in warfare became part of international law. However, the Protocol did not prohibit research and development and was essentially seen as a 'no first use' agreement as expressed in the reservations given by some signatories. It had originally been focused on chemical weapons due to the events of World War I but the Polish delegation called for the inclusion of 'bacteriological' weapons in the agreement. The Protocol, which came into force in 1928, increased awareness about the issue of biological weapons amongst many countries. In Japan it was seen as confirmation of the utility of such weapons, which even provided encouragement for their offensive biological weapons ambitions.[130]

France[131]

Interest in biological weapons by the French Government moved beyond crude sabotage methods in the early 1920s when Andre Trillat, Director of the Naval Chemical Research Laboratory, was requested to produce a report evaluating the military potential of biological warfare. The Trillat report, completed in 1922, emphasised intelligence on German biological weapons research activities giving impetus to the idea of a French biological programme. According to Lepick's study of the French programme, Trillat viewed biological weapons as distinct from chemical weapons with different military uses, having delayed effects and to be used at long range. He had been studying aerial transmission of diseases for a number of years previously and had published in this area from 1918-20. He argued that the most effective way to deliver this type of weapon was in the form of a microbial 'cloud' of fine droplets. Agents he considered viable included plague, cholera, influenza, typhoid, dysentery, glanders, foot and mouth disease, and particularly brucellosis because of its hardiness and ease of culture.

A Bacteriological Commission was set up in December 1922 and met first in 1923. It drew on the expertise of leading microbiologists including the Director of the Pasteur Institute, Emile Roux, and his Deputy Director, Albert Calmette, one half of the team that developing the BCG vaccine at the time. A veterinarian at the meeting commented on his preparation of infectious biological material for use in sabotage activities against horses during World War I. The commission thought that aerial bombs producing microbial clouds would be the best delivery systems. Research on biological weapons was to be

funded at military as well as civilian laboratories, including the Pasteur Institute. In 1923 dissemination experiments on animals with paratyphoid (salmonella) and cholera were carried out by the military research laboratories including an open-air test. Further work in 1923 and 1924 focussed on practical issues such as methods for maintaining the virulence of pathogens (e.g. varnishing the inside of bombs). From 1925-26 the focus of research was on delivery systems:

> The aim was to develop a device whose burst on ground impact would have the effect of producing clouds consisting of very small droplets containing fragmented microorganisms with the capability, despite their fragmentation, of producing pathogenic effects.[132]

In October such aerial bombs were successfully tested at a naval firing range.

From 1927-34, research was limited due to a commitment to the 1925 Geneva Protocol, which the French ratified in May 1926 although they reserved the right to retaliate in kind. Lepick notes that the Bacteriological Commission did not meet a second time until 1935 and that this initial work on biological weapons was characterised by the 'individual dedication' of some scientists rather than 'firm political will'.

The reinvigoration of the biological programme through the second meeting of the Bacteriological Commission in 1935 was apparently related to deterioration in Franco-German relations. Press allegations about German tests at disseminating bacteria on underground train systems in London, New York and Paris spurred the French to conduct their own experiments on the Paris Metro. At this time there were also experiments conducted on *Clostridium botulinum* resulting in botulinum toxin being added to the list of suitable weapons agents. During 1936-37 Trillat's research focussed on production of aerosols and also on defensive measures (e.g. antiseptic clouds). In 1937 the Prophylaxis laboratory was established to further offensive work in the BW area given tensions with Germany. The Prophylaxis Commission (the renamed Bacteriological Commission) met twice in 1938 and discussed work on ricin as a weapon, vaccines and serum to protect against ricin, botulinum toxin dispersal studies, the Paris metro tests, and concerns over German use of ricin to poison water supplies.

Again spurred on by reports of German activities in this area, a report presented to the Commission argued that pathogens, most effective in the form of aerosols, should be studied on the basis of their virulence, viability, and serious disease causing potential. Research and testing was expanded in 1939 and early 1940, focussing a variety of areas including: ricin aerosols; animal diseases such as bovine plague; dispersion issues; contaminating projectiles with tetanus, gangrene, or anthrax; combining chemical and biological agents; and finally tests of bovine plague-filled munitions on guinea pigs. This research encompassed offensive and defensive considerations. By early 1940 the Secretary of the Prophylaxis commission had stated, in a presentation at a meeting focussing on the issue of defence against biological weapons, that spreading diseases (such as anthrax, tetanus and gas gangrene) using bursting projectiles or spraying from aircraft was feasible and that contamination of food, water, or medicine supplies with biological agents (such typhoid, cholera, dysentery, botulinum toxin, and ricin) was also possible. The biological weapons programme was suspended in 1940 after defeat by Germany although it is thought that some activities continued secretly until Germany occupied the whole of France in 1942.

Despite German biological sabotage operations during World War I, Geissler's study of their activities in this area during this later period notes that "… German biological warfare activities were sporadic, incomplete and largely unsupported by the leadership."[134] Interest in the 1920s apparently arose from concerns over French and Soviet considerations of biological weapons as well as negotiations of the Geneva Protocol, which Germany ratified unconditionally in 1925. In the same year Richard Otto at the Robert Koch Institute in Berlin and Max Reinmer reviewed potential weapons agents and Otto noted that the bacterial agents causing typhoid, paratyphoid fever, dysentery, cholera, plague, glanders, anthrax, and wound infections were the most suitable. They recommended delivery by production of aerosols or contamination of drinking water. However during the 1920s and 1930s the focus in Germany was on chemical weapons and there was scepticism and disagreement over the utility of biological weapons. Initially biological research activities were incorporated into existing chemical weapons research organisations but in 1940 the first BW laboratories were established. One of the main drivers for German work on biological weapons during World War II was intelligence and perceptions of the activities of Canada, France, UK, USA, and the USSR. A leading bacteriologist, Henrich Kliewe, evaluated the French programme significant data from which were uncovered after the German defeat of France in 1940 and was thereby convinced that biological warfare was viable. In 1942, however, Hilter prohibited all biological weapons activities apart from defensive research.

Geissler notes that, although many facilities were involved in biological weapons research activities under this defensive mandate, activities were limited and few scientists were involved in biological weapons work. The Kliewe Laboratory conducted small-scale work on the combined use of chemical and biological agents and studies on survivability of bacteria including anthrax. Elsewhere there was work on: production of plague vaccine; dissemination of agents by aircraft; dissemination of plague using insect vectors; research and vaccine development on foot and mouth disease; vaccines for plague and yellow fever; and sera for anthrax, botulism and tularaemia. Kliewe carried out experiments on aerosols and reported on various other possible dissemination methods including glass containers. Field-tests with the non-pathogenic bacteria as simulants were conducted as well as experiments with aerial spraying of foot and mouth disease (FMD) virus.

Despite the German sabotage activities of World War I, no such activities were conducted during World War II since Hitler's ban also extended to this type of biological warfare. However there were numerous proposals from those interested in the utility of biological weapons for use of contaminated foods and other products. Other proposals centred on the use of biological agents to contaminate water supplies. Although some offensive research and development was conducted under the cover of defensive activities, Geissler argues that the German activities during this period were disorganised, limited and did not constitute an actual 'offensive programme' as such.

Japan[135]

The Japanese biological weapons programme was by far the largest programme during this period and certainly the most ruthless. It is estimated to have involved over 10,000 personnel. Harris describes the main characteristics of the programme as follows:

> The main features of the Japanese biological warfare programme were the unique emphasis on offensive weapons and the willingness to use them against China and the USSR. However, the programme was also spurred by defensive concerns and the belief that China and the Soviet Union were engaging in biological sabotage against Japanese forces…[136]

The impetus for the establishment of the Japanese BW programme came from an army doctor, Ishii Shiro, whose developed an interest in biological weapons in the mid-to-late 1920s and lobbied his military superiors to establish a programme. Having been appointed Professor of Immunology at Tokyo Army Medical School in 1930 he gained support from Koizumi Chikahiko, a leading military scientist, to set up a biological weapons research laboratory, which remained the headquarters of the programme until 1945.

Harris points out that Ishii repeatedly classified biological weapons research into two distinct categories: defensive vaccine research which he called 'B-type' research and offensive 'assault' research involving human experimentation which he called 'A-type' research. The latter was to be conducted outside Japan and so Ishii set up a laboratory in Harbin in the Chinese region of Manchuria. He staffed it with a unit of 300 men, known as The Togo Unit under the ultimate control of the Army General Staff. This site proved unsuitable for the human experimentation he intended to carry out since it was a large town and so the Harbin site was used for defensive research. Soon after, in mid-1932 they built another facility consisting of 100 buildings on the site of a village called Beiyinhe (100km south of Harbin). This facility was called Zong Ma Prison Camp and contained a large building in the centre where prisoners were held (between 500 and 600 at a time). Here they conducted experiments on the prisoners, infecting them with a variety of pathogens and analysing their blood. They focussed their efforts on anthrax, glanders and plague. In 1935 the facility was closed and Ishii set about his search for an even larger site.

The construction of a new facility at Ping Fan nearby started in 1936 and was completed in 1939. It was very heavily financed and consisted of over 150 buildings as well as a private airstrip and railway link. The operation, which was renamed Unit 731 in 1941, recruited hundreds of civilian as well military scientists, although they were aware of the nature of human experimentation being carried out. Prisoners were injected with a variety of pathogens, made to eat contaminated food and liquids, and exposed to prototype biological bombs and shells exploded at various distances. Thousands of people were killed, with some having been dissected whilst still alive. Hundreds of kilograms, of the pathogens responsible for plague, anthrax, typhoid, cholera, and dysentery were produced at Ping Fan using culture equipment developed by Ishii in the early 1930s that, according to Harris, enabled "automatic planting and scratching operations."[137] Large quantities of agents were also produced by Unit 100, which was established in 1936 also in China, and mainly focussed on anti-plant and anti-animal biological weapons research.

In addition there was considerable work carried out to develop vaccines and sera. 20 million doses of vaccine were produced per year at Ping Fan with additional doses produced at other facilities in China. Harris notes that "Ping Fan utilized 50 000 hens and roosters annually to produce the fertilized eggs required for the preparation of the typhus vaccine…".[138] Unit 731 also conducted vaccine research and development in cooperation with various universities and colleges. Plague vaccine was developed at the Kitasato Institute, typhus vaccine was developed at Manchuria Medical College by a professor who was later to become commander of Unit 731, and other vaccine work on gas gangrene, tetanus, anthrax, cholera, dysentery and typhoid was carried out at Tokyo University.

Unit 731 and Unit Ei 1644, which was established in 1939 at a hospital in Nanking and employed around 1500 people, carried out experiments on humans to the establish the ID50 (Infectious dose necessary to infect 50% of those exposed) for anthrax, cholera, dysentery, epidemic haemorrhagic fever, gas gangrene, glanders, influenza, paratyphoid, plague, tuberculosis, tularaemia, typhoid, and undulant fever (brucellosis). Unit 100 studied anthrax and glanders and there were limited efforts to study toxins such as tetrodotoxin. Anthrax and plague were considered the most suitable biological weapons agents because of their high mortality. Artillery shells, aerial bombs and aircraft spraying were the three methods considered for agent delivery. By 1940 the Japanese programme had developed nine different biological bombs, large numbers of which were used in tests on humans at a test site in Anda, however none proved satisfactory according to Ishii's testimony after World War II. Shells filled with bacterial suspension and an explosive charge also proved ineffective.

In 1939 Ishii was given permission to carry out field tests that involved spreading quantities of the pathogens responsible for salmonella and typhoid along the shoreline at the border of Manchuria and the USSR. 2000 biological shells were delivered to the front lines and were fired against Soviet troops during battles in the summer of 1939. As Harris notes their effectiveness is unclear:

> Many Japanese and Soviet soldiers were felled by cholera, dysentery and plague. It remains uncertain, however, whether the casualties were caused by biological warfare, or perhaps more likely, by the primitive sanitary conditions in the area.[139]

From late 1939 to late 1942 Ishii coordinated extensive field tests in Manchuria and other areas of China. These involved sabotage of wells, release of plague infected rats, and scattering of plague infected fleas and contaminated cotton and grain. Aside from plague, other material used included the causative agents of cholera, salmonella, typhoid, anthrax, typhus, paratyphus, and glanders. Although epidemics occurred, affecting Japanese as well as Chinese troops, the effectiveness of these tests remains unclear. Ishii's successor, Kitano Masaji, preferred laboratory work on human subjects and so field tests were curtailed after 1942.

Although the size of the Japanese programme was unprecedented it did not produce an effective biological weapon system before the close of the programme at the end of the Second World War. Harris argues that this was mainly due to organisational deficiencies:

The Japanese biological warfare programme was uncoordinated, often amateurish and highly compartmentalized. There was no inter-service coordination, and within the programme secrecy isolated specialized workers from one unit to another, thereby cutting down on essential sharing of information.[140]

USSR[141]

The USSR's Military Chemical Agency (MCA) was established in 1925 with responsibility for chemical and biological weapons. Its director, Jacov Fishman, produced a report in 1928 stating the feasibility of biological warfare based upon initial experimental work with anthrax and botulinum toxin. He argued that biological weapons could be used for sabotage and for battlefield operations using biological shells and bombs. This research at the MCA included work to increase the virulence and stability of anthrax, which was considered a suitable warfare agent, and dispersal tests with this agent. Botulinum toxin was considered more applicable to sabotage. He proposed an organisational structure encompassing the MCA responsible for offensive research, the Institute of Chemical Defence for defensive research, and the Ministry of Health for vaccines and prophylaxis. As Bojtzov and Geissler describe in their study of the programme:

> The ministries of Health and Education became involved in BW research. They became the main base for coordinating, executing, controlling and distributing military requests concerning biological warfare. … The entire effort was managed by the MCA and controlled and coordinated by the Ministry of Defence.[142]

Existing research institutes such as the Moscow Institute of Epidemiology and Microbiology, and the Charkov Scientific Research Institute of Microbiology provided a source of expertise and facilities. A small research laboratory in Moscow established in 1926 carried out the orginial experiments on *Clostridium botulinum* and *Bacillus anthracis* discussed in Fishman's report. Other research efforts were distributed amongst medical and university laboratories. Facilities in the Leningrad area included: the Zlatogrov-Maslokovich Laboratory and the Bacteriological Institute in Leningrad. In and around Moscow were: the Scientific Research Institute of the Red Army working on protection against infectious diseases, the Scientific Research Institute of Health carrying out BW research for the Army, the Moscow Chemical-Pharmaceutical Institute, and the Saratov Institute for Microbiology and Epidemiology.

Bojtzov and Geissler note that the programme involved the study of a variety of agents:

> The MCA decided to prioritise research into the agents of: anthrax, brucellosis, encephalitis, glanders, plague, tuberculosis and tularaemia. Agents studied in the MCA laboratories and subsequently tested in field tests were *Bacillus anthracis*, *Clostridium botulinum*, *Yersinia pestis*, *Vibrio comma asiaticae*, *Mycobacterium tuberculosis* and the agents of cholera, glanders, tetanus, tularaemia and typhoid fever.

Testing grounds used for biological weapons experiments included Tomka, which was primarily a chemical weapons testing area, and two islands, Gorodomlia in Lake Seliger and Vozrozhdeniye in the Aral Sea. On Gorodomila dissemination tests were conducted and the Velikonovski Institute on the island evaluated anthrax, cholera, glanders and typhoid. The Public Health Institute of Dnepropetrovsk University conducted other

experiments there with plague and tularaemia, including dissemination of 'clouds' of the tularaemia bacillus. In 1935, tests with foot and mouth disease, leprosy and plague were carried out on the island by the Moscow Institute of Foot and Mouth Disease. Large-scale field tests were conducted on Vozrozhdeniye island including, in 1937, aircraft drops of containers filled with the causative agents of cholera, leprosy, plague, and tularaemia.

Bojtzov and Geissler's study discusses the negative effects of the The Great Terror of the late 1930's on the Soviet biological weapons programme. During Stalin's 'purges' dozens of leading microbiologists were executed or imprisoned, included Jacov Fishman, the originator of the programme, who was not released until 1954.

Reports about biological weapons research and development in other countries, particularly Germany, led to increased Soviet activity in this area during World War II. There were accusations of Soviet biological sabotage activities during 1942 and 43. The USSR also had concerns over biological sabotage directed against it and considerable attention was given to the production of vaccines against anthrax, plague, brucellosis, and tularaemia although their purpose may have been use against natural outbreaks of disease.

Bojtzov and Geissler conclude that in the period before the end of the Second World War:

> … there is substantial evidence that the Soviet Union was interested in biological warfare, carried out numerous test experiments, was sensitive regarding the BW programmes of other nations, was fully aware of the sabotage potentialities of these weapons and may indeed have used them in certain limited operations.[143]

They go on to say that the Soviet Union considered biological weapons as feasible militarily but it is unclear whether they had integrated BW capability into military doctrine by the time of the German invasion in June 1941.

The United Kingdom[144]

Further to reports of biological sabotage activities during World War I, intelligence reports during the 1920s and 1930s indicated that other countries such as Italy and the USSR were pursuing biological weapons. Increased interest in biological weapons was also due to the agreement of the Geneva Protocol in 1925 prohibiting the use of poisonous gas and 'bacteriological' weapons in warfare, which the UK ratified in 1930. However it was 'revelations' brought forward by Henry Wickham Steed in 1934 relating to German biological weapons research and development including tests on the Paris Metro and London Underground that led the UK to investigate the field. Maurice Hankey, then Secretary of the Committee of Imperial Defence, contacted three eminent scientists through the Medical Research Council (MRC): John Ledingham, Director of the Lister Institute; William Whiteman Carlton Topley, Professor of Bacteriology at the London School of Hygiene and Tropical Medicine; and Stewart Rankin Douglas, Deputy Director of the National Institute for Medical Research at the MRC. They assessed the information in the documents obtained by Wickham Steed. The scientists were cautious about the contents but they did point out the vulnerability of the underground system to

such attacks. Subsequently, as Carter and Pearson write in their study of the UK programme:

> In November 1936 the Bacteriological Warfare Subcommittee was set up by the Minister for the Coordination of Defence, Sir Thomas Inskipp, to 'report on the practicability of the introduction of bacteriological warfare and to make recommendations as to the countermeasures which should be taken to deal with such an eventuality.'[145]

Canada[146]

Canada signed the Geneva Protocol in 1925 and waited to ratify it until the UK ratified it in 1930 but there was little interest in biological weapons until the publication of Wickham Steed's revelations about German activities in 1934.   More serious consideration of BW began in 1937 when Fredrick Banting, a leading defence scientist, prepared a report for Andrew McNaughton, President of the National Research Council (NRC), discussing the threat from biological warfare waged with various agents and methods of dissemination. As Avery discusses in his study of the Canadian programme, Banting pressed McNaughton on this issue again in 1938 and during a mission to the UK to meet British experts, McNaughton requested him to prepare a detailed report on the biological weapons threat which emphasised the need for defensive measures and a retaliatory capability which he presented in January 1940. Banting received little support for his appraisal when he returned to Canada but eventually persuaded the Canadian Minister of Defence Colonel Ralston to allow him to proceed with limited biological weapons experiments on delivery systems and suitable agents amongst other relevant issues.

The United States[147]

The United States signed and promoted the Geneva Protocol but the senate did not ratify it at the time.   In the inter-war period the US military was sceptical about the feasibility and utility of biological weapons although they were of course aware of Wickham Steed's allegations about German activities. As Van Courtland Moon's study of the US programme notes:

> A September 1939 conference between CWS [Chemical Warfare Service] officers and members of the Surgeon General's Office and US Public Health Service condluded that the immediate threat to the USA was minimal although further consultations on biological warfare should be held between the participants and other concerned agencies.

With the advance of World War II, and intelligence reports indicating that Japan and Germany considered biological warfare to be feasible, attitudes changed and in 1941 a meeting was held between the Chemical Warfare Service (CWS), the Surgeon General's Office and the War Plans Division of the General Staff to allocate responsibilities for defensive and offensive aspects of a US biological weapons programme.

Conclusion

As events during World War I illustrate, it did not take long for the revolutionary discoveries and advances in bacteriology from the late 1800s and early 1900s to be

incorporated into military operations. The German biological sabotage programme against livestock made use of bacterial agents that had only been identified for the first time some 30 to 40 years previously. Their operations required only small quantities of agent and so simple culture methods were used. Interest in the feasibility of biological warfare expanded in the inter-war and early World War II periods with the development of a number of offensive programmes including a Japanese effort involving a huge number of people and resources as well as thousands of victims of human experimentation. The desire to develop these weapons was influenced by the imminent conflict (World War II) and misperceptions, from intelligence or other reports, about biological warfare preparations underway in other countries. This led to an initial arms race that intensified during World War II.

All this was made possible by civilian advances in the biological sciences, particularly in the field of bacteriology, which provided an understanding of the causative agents of numerous diseases from which the majority of weapons agents were selected. Militaries made full use of the expertise in the civil sector with the same minds applied both to the development of offensive weapons and to defences against them. With the exception of the Japanese programme, these early efforts were at the research and development stage and so did not employ the emerging industrial equipment for large-scale fermentation. In Japan they improvised using basic culture methods and adding elements of automation in order to produce hundreds of kilograms of agent. Aside from contaminating food, water or other materials for sabotage, the dissemination of airborne 'clouds' of bacteria 'sprayed' from bombs, artillery shells or other containers was considered the best route for delivering biological weapons agents. However, the science of aerial transmission of disease, or more broadly aerobiology, was in its infancy and so effective delivery systems were elusive even in the vast Japanese programme.

The timing of two major conflicts may have catalysed the process of applying the new bacteriology for military purposes but the fact remains: Following some of the greatest advances in the history of infectious disease prevention and treatment, this new science was soon applied for nefarious purposes.

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