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REVIEW PAPER

Bio-Warfare : A Mini Review

TRIPTI YADAV

Department of Biotechnology, Mahatma Jyoti Rao Phoole University, Jaipur
S.S. Jain Subodh College of Global Excellence, Sitapura Jaipur
email : rubyharshita@gmail.com

ABSTRACT

Human experimentation, modern nightmares and lone madmen in the twentieth century

Key words *Bio-Warfare, Mini Review*

During the past century, more than 500 million people died of infectious diseases. Several tens of thousands of these deaths were due to the deliberate release of pathogens or toxins, mostly by the Japanese during their attacks on China during the Second World War. Two international treaties outlawed biological weapons in 1925 and 1972, but they have largely failed to stop countries from conducting offensive weapons research and large-scale production of biological weapons. And as our knowledge of the biology of disease-causing agents—viruses, bacteria and toxins—increases, it is legitimate to fear that modified pathogens could constitute devastating agents for biological warfare. To put these future threats into perspective, I discuss in this article the history of biological warfare and terrorism.

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Man has used poisons for assassination purposes ever since the dawn of civilization, not only against individual enemies but also occasionally against armies. However, the foundation of microbiology by Louis Pasteur and Robert Koch offered new prospects for those interested in biological weapons because it allowed agents to be chosen and designed on a rational basis. These dangers were soon recognized, and resulted in two international declarations—in 1874 in Brussels and in 1899 in The Hague—that prohibited the use of poisoned weapons. However, although these, as well as later treaties, were all made in good faith, they contained no means of control, and so failed to prevent interested parties from developing and using biological weapons. The German army was the first to use weapons of mass destruction, both biological and chemical, during the First World War, although their attacks with biological weapons were on a rather small scale and were not particularly successful: covert operations using both anthrax and glanders.attempted to infect animals directly or to contaminate animal feed in several of their enemy countries (Wheelis, 1999). After the war, with no lasting peace established, as well as false and alarming intelligence reports, various European countries instigated their own biological warfare programmes, long before the onset of the Second World War (Geissler& Moon, 1999).

History related to biological warfare

In North America, it was not the government but a dedicated individual who initiated a bioweapons research programme. Sir Frederick Banting, the Nobel-Prize-winning discoverer of insulin, created what could be called the first private biological weapon research centre in 1940, with the help of corporate sponsors (Avery, 1999; Regis, 1999). Soon afterwards, the US government was also pressed to perform such research by their British allies who, along with the French, feared a German attack with biological weapons (Moon, 1999, Regis, 1999), even though the Nazis apparently never seriously considered using biological weapons (Geissler, 1999). However, the Japanese embarked on a largescaleprogramme to develop biological weapons during the Second World War (Harris, 1992, 1999, 2002) and eventually used them in their conquest of China. Indeed, alarm bells should have rung as early as 1939, when the Japanese legally, and then illegally, attempted to obtain yellow fever virus from the Rockefeller Institute in New York (Harris, 2002).

The father of the Japanese biological weapons programme, the radical nationalist Shiro Ishii, thought that such weapons would constitute formidable tools to further Japan's imperialistic plans. He started his research in 1930 at the Tokyo Army Medical School and later became head of Japan's bioweapon programme during the Second World War (Harris, 1992, 1999, 2002). At its height, the programme employed more than 5,000 people, and killed as many as 600 prisoners a year in human experiments in just one of its 26 centres. The Japanese tested at least 25 different disease-causing agents on prisoners and unsuspecting civilians. During the war, the Japanese army poisoned more than 1,000 water wells in Chinese villages to study cholera and typhus outbreaks. Japanese planes dropped plague-infested fleas over Chinese cities or distributed them by means of saboteurs in rice fields and along roads. Some of the epidemics they caused persisted for years and continued to kill more than 30,000 people in 1947, long after the Japanese had surrendered (Harris, 1992, 2002). Ishii's troops also used some of their agents against the Soviet army, but it is unclear as to whether the casualties on both sides were caused by this deliberate spread of disease or by natural infections (Harris, 1999). After the war, the Soviets convicted some of the Japanese biowarfare researchers for war crimes, but the USA granted freedom to all researchers in exchange for information on their human experiments. In this way, war criminals once more became respected citizens, and some went on to found pharmaceutical companies. Ishii's successor, Masaji Kitano, even published postwar research articles on human experiments, replacing 'human' with 'monkey' when referring to the experiments in wartime China (Harris, 1992, 2002).

Although some US scientists thought the Japanese information insightful, it is now largely assumed that it was of no real help to the US biological warfare programme projects. These started in 1941 on a small scale, but increased during the war to include more than 5,000 people by 1945. The main effort focused on developing capabilities to counter a Japanese attack with biological weapons, but documents indicate that the US government also discussed the offensive use of anti-crop weapons (Bernstein, 1987). Soon after the war, the US military started open-air tests, exposing test animals, human volunteers and unsuspecting civilians to both pathogenic and non-pathogenic microbes (Cole, 1988; Regis, 1999). A release of bacteria from naval vessels off

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the coasts of Virginia and San Francisco infected many people, including about 800,000 people in the Bay area alone. Bacterial aerosols were released at more than 200 sites, including bus stations and airports. The most infamous test was the 1966 contamination of the New York metro system with *Bacillus globigii*— a non-infectious bacterium used to simulate the release of anthrax—to study the spread of the pathogen in a big city. But with the opposition to the Vietnam War growing and the realization that biological weapons could soon become the poor man's nuclear bomb, President Nixon decided to abandon offensive biological weapons research and signed the Biological and Toxin Weapons Convention (BTWC) in 1972, an improvement on the 1925 Geneva Protocol. Although the latter disallowed only the use of chemical or biological weapons, the BTWC also prohibits research on biological weapons. However, the BTWC does not include means for verification, and it is somewhat ironic that the US administration let the verification protocol fail in 2002, particularly in view of the Soviet bioweapons project, which not only was a clear breach of the BTWC, but also remained undetected for years.

Even though they had just signed the BTWC, the Soviet Union established Biopreparat, a gigantic biowarfare project that, at its height, employed more than 50,000 people in various research and production centres (Alibek&Handelman, 1999). The size and scope of the Soviet Union's efforts were truly staggering: they produced and stockpiled tons of anthrax bacilli and smallpox virus, some for use in intercontinental ballistic missiles, and engineered multidrug-resistant bacteria, including plague. They worked on haemorrhagic fever viruses, some of the deadliest pathogens that humankind has encountered. When virologist Nikolai Ustinov died after injecting himself with the deadly Marburg virus, his colleagues, with the mad logic and enthusiasm of bioweapon developers, re-isolated the virus from his body and found that it had mutated into a more virulent form than the one that Ustinov had used. And few took any notice, even when accidents happened. In 1971, smallpox broke out in the Kazakh city of Aralsk and killed three of the ten people that were infected. It is speculated that they were infected from a bioweapons research centre on a small island in the Aral Sea (Enserink, 2002). In the same area, on other occasions, several fishermen and a researcher died from plague and glanders, respectively (Miller et al., 2002). In 1979, the Soviet secret police orchestrated a large cover-up to explain an outbreak of anthrax in Sverdlovsk, now Ekaterinburg, Russia, with poisoned meat from anthrax-contaminated animals sold on the black market. It was eventually revealed to have been due to an accident in a bioweapons factory, where a clogged air filter was removed but not replaced between shifts (Fig. 1) (Meselson et al., 1994; Alibek&Handelman, 1999).

The most striking feature of the Soviet programme was that it remained secret for such a long time. During the Second World War, the Soviets used a simple trick to check whether US researchers were occupied with secret research: they monitored whether American physicists were publishing their results. Indeed, they were not, and the conclusion was, correctly, that the US was busy building a nuclear bomb (Rhodes, 1988, pp. 327 and 501). The same trick could have revealed the Soviet bioweapons programme much earlier (Fig. 2). With the collapse of the Soviet Union, most of these programmes were halted and the research centres abandoned or converted for civilian use. Nevertheless, nobody really knows what the Russians are working on today and what happened to the weapons they produced. Western security experts now fear that some stocks of biological weapons might not have been destroyed and have instead fallen into other hands (Alibek&Handelman, 1999; Miller et al., 2002). According to US intelligence, South Africa, Israel, Iraq and several other countries have developed or still are developing biological weapons (Zilinskas, 1997; Leitenberg, 2001).

Potential dangerous microbes utilized for biowarfare

Apart from state-sponsored biowarfareprogrammes, individuals and non-governmental groups have also gained access to potentially dangerous microorganisms, and some have used them (Purver, 2002). A few examples include the spread of hepatitis, parasitic infections, severe diarrhoea and gastroenteritis. The latter occurred when a religious sect tried to poison a whole community by spreading *Salmonella* in salad bars to interfere with a local election (Török et al., 1997; Miller et al., 2002). The sect, which ran a hospital on its grounds, obtained the bacterial strain from a commercial supplier. Similarly, a right-wing laboratory technician tried to get hold of the plague bacterium from the American Tissue Culture Collection, and was only discovered after he complained that the procedure took too long (Cole, 1996). These examples clearly indicate that organized groups or individuals with sufficient determination can obtain dangerous biological agents. All that is required is a request to 'colleagues' at scientific institutions, who share their published materials with the rest of the community (Breithaupt, 2000). The relative ease with which this can be done explains why the numerous hoaxes in the USA after the anthrax mailings had to be taken seriously, thus causing an estimated economic loss of US $100 million (Leitenberg, 2001).

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Another religious cult, in Japan, proved both the ease and the difficulties of using biological weapons. In 1995, the AumShinrikyo cult used Sarin gas in the Tokyo subway, killing 12 train passengers and injuring more than 5,000 (Cole, 1996). Before these attacks, the sect had also tried, on several occasions, to distribute (non-infectious) anthrax within the city with no success. It was obviously easy for the sect members to produce the spores but much harder to disseminate them (Atlas, 2001; Leitenberg, 2001). The still unidentified culprits of the 2001 anthrax attacks in the USA were more successful, sending contaminated letters that eventually killed five people and, potentially even more seriously, caused an upsurge in demand for antibiotics, resulting in over-use and thus contributing to drug resistance (Atlas, 2001; Leitenberg, 2001; Miller et al., 2002).

Necessity to develop drugs and vaccines

We are witnessing a renewed interest in biological warfare and terrorism owing to several factors, including the discovery that Iraq has been developing biological weapons (Zilinskas, 1997), several bestselling novels describing biological attacks, and the anthrax letters after the terrorist attacks on 11 September 2001. As history tells us, virtually no nation with the ability to develop weapons of mass destruction has abstained from doing so. And the Soviet project shows that international treaties are basically useless unless an effective verification procedure is in place. Unfortunately, the same knowledge that is needed to develop drugs and vaccines against pathogens has the potential to be abused for the development of biological weapons (Finkel, 2001). Thus, some critics have suggested that information about potentially harmful pathogens should not be made public but rather put into the hands of 'appropriate representatives' (Danchin, 2002; Wallerstein, 2002). A recent report on anti-crop agents was already self-censored before publication, and journal editors now recommend special scrutiny for sensitive papers (Mervis&Stokstad, 2002; Cozzavelli, 2003; Malakoff, 2003). Whether or not such measures are useful deterrents might be questionable, because the application of available knowledge is clearly enough to kill. An opposing view calls for the imperative publication of information about the development of biological weapons to give scientists, politicians and the interested public all the necessary information to determine a potential threat and devise countermeasures.

A need for awareness

The current debate about biological weapons is certainly important in raising awareness and increasing our preparedness to counter a potential attack. It could also prevent an overreaction such as that caused in response to the anthrax letters mailed in the USA. However, contrasting the speculative nature of biological attacks with the grim reality of the millions of people who still die each year from preventable infections, we might ask ourselves just how many resources we can afford to allocate in preparation for a hypothetical human-inflicted disaster.

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