Biological Weapons

For the purposes of this discussion, define a **biological weapon** as either a pathogen or a substance produced by a microorganism (including viruses) used with the intent of harming or killing. Such weapons can be used against humans, animals raised for food, and/or food-crops.

A Brief History of Biological Weapons

Records of the use of biological weapons go back to at least the sixth century BCE, when the Assyrians poisoned enemy wells with ergot. Ergot is a chemical produced by the fungus *Claviceps purpurea*, which grows parasitically on the grain crop rye. Its effects begin as early as several hours after ingestion. Symptoms include: vomiting, burning sensations, abdominal cramping, tingling and twitching of the extremities, weak and slow pulse, hallucinations, and possibly convulsions. Survivors of these initial symptoms can look forward to an attack of gangrene of the hands and feet.

Also in the sixth century BCE, the Greeks laid siege to the city of Krissa and poisoned its wells by using the potent herb hellebore. Hellebore occurs in two forms: black and green. Symptoms of black hellebore poisoning include nausea, vomiting, diarrhea, dizziness, shortness of breath, and with large intake, cardiac arrhythmias. Folk practitioners also use it to induce abortion. Intake of green hellebore can trigger convulsions, high pulse rate, and respiratory failure. Needless to say, this is not an herb to be trifled with.

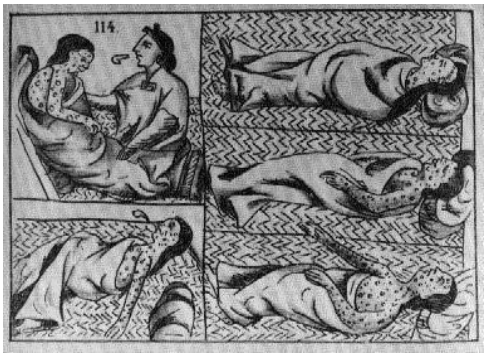
It was customary for Roman armies laying siege to dump dead bodies, animal and human, into the enemy's water supplies. They even went so far as to catapult bodies over the walls of the town.

As mentioned in Chapter 1, the catapulting of dead soldiers into the fortified city of Caffa in 1343 was also a tactic of the Tartars. At that time and location, it seemed to work.

For the sake of expediency, we need to move forward two hundred years to the Spanish conquest of the New World. Most of the microbes the Spaniards brought with them were carried unknowingly—we think—maybe. These germs had used Old World human hosts for hundreds of years but were, for the most part, new to the western hemisphere.

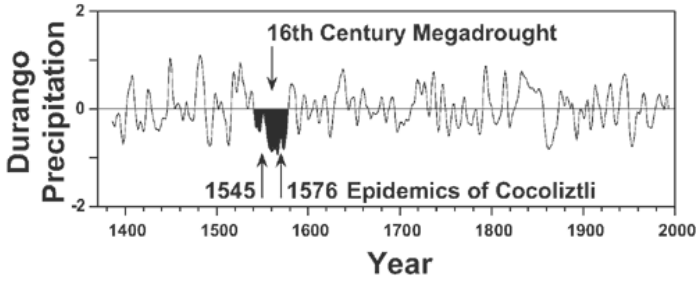
Measles, along with smallpox and a local viral infection, were the likely villains in the partial extermination of the Amerindians.

Cortez's initial foray into the New World might have met with disaster were it not for these diseases. After his first militarily successful encounter with Montezuma's armies, he captured Montezuma. Cortez then took his army to confront a Spanish enemy. Upon return to the Aztec empire, Cortez's forces were outnumbered and soundly defeated. Awaiting a second attack from the Aztecs that would wipe out his entire troop, he was reinforced with men from smallpox-ridden Cuba, including a slave with a mild case of the disease. Once his 300 men were up to the march, he headed back to Tenochtitlán with some native allies, where he laid siege in July and August of 1521. The capital fell on August 31 and upon entering the city, he found most of the population dead, dying, or gone to parts unknown. Montezuma and his son had died. This had caused a small civil war over the succession. Corpses were everywhere; even the famous Aztec canals were filled with the dead.



Aztec drawings of the sufferers of the new diseases.

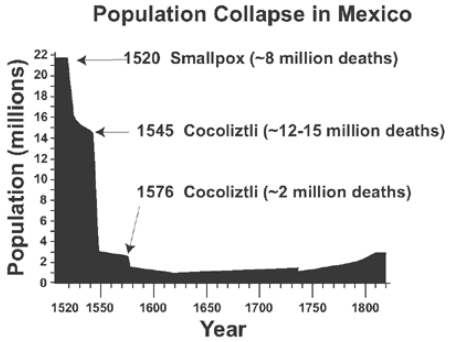
The pox reached the Mayas before the Spanish. This and other diseases swept through the continent like wildfire in dry grass on a windy day. *Dry* is the operative word because the 16th century was a time of unprecedented drought; the worst in five hundred years. This together with the *encomienda* system of New Spain, which treated the natives as less than slaves to be worked nearly to death, and a native hemorrhagic viral infection called *cocolitzli* caused a huge number of deaths.



Cocolitzli developed as a result of that major period of drought, which enhanced its spread through what is most likely a rodent host. This unfortunate confluence of factors contributed to the extraordinarily high mortality rates.

From an estimated population of 20–25 million, fewer than two million survived in Mexico. The Inca population plummeted from 8 million to one million. After all forms of European "germ warfare," the Amerindian population was reduced to about 5% of what it was before "discovery" of the New World. The most extreme estimates are of 130 million indigenous people living in Mexico, Central, and South America before the new diseases and a mere 1.6 million after!

Other research presented in the 2002 book *The Backbone of History: Health and Nutrition in the Western Hemisphere* edited by Steckel and Rose, indicates that based on skeletal remains, the health of the native Amerindians living in large cities was not all that idyllic as was once thought. In fact, pre-Columbians living under Mayan rule were the least healthy of the 12,500 or so skeletons analyzed.



The British were no better than the Spanish in terms of the deliberate infection of native peoples. Lord Jeffery Amherst, for whom the Massachusetts town of Amherst was named[1], was the commanding general of British forces during the last years of the French and Indian War. Amherst was particularly averse to the presence of the indigenous population. Perhaps they did not fit his notion of humanity as defined by then current British standards. Some quotes from letters by and to him illustrate the point.

- "...that Vermine...have forfeited all claim to the rights of Humanity" (Bouquet to Amherst, 6/25/1763)
- "I would rather chuse the liberty to kill any Savage..." (Bouquet to Amherst, 6/25/1763)
- "...Measures to be taken as would Bring about the Total Extirpation of those Indian Nations" (Amherst to Johnson, 7/9/1763)
- "...their Total Extirpation is scarce sufficient Atonement..." (Amherst to Croghan, 8/7/1763)
- "...put a most Effectual Stop to their very Being" (Amherst to Johnson, 8/27/1763)
- "to try Every other Method that can serve to Extirpate this Execrable Race." (Amherst to Bouquet, 7/16/1763)
- "inoculate the Indians" (Col. Bouquet to Amherst, 7/13/1763)
- "Could it not be contrived to send Small Pox among those disaffected Tribes of Indians? We must on this Occasion use Every Stratagem in our Power to reduce them."

It seems indisputable that Amherst authorized the distribution of smallpox-infected blankets to the Ottawa Indians during Pontiac's Rebellion following the surrender of the French.

The French get no medals for honor in this business either. When French trappers felt the locals were infringing on their territory, it was not uncommon to include infected blankets in the trade for furs[2].

Prior to the entry of the US into World War I, one Anton Dilger, an MD with microbiology training, served as an agent of German Kaiser Wilhelm in Washington, DC. He used a basement *room* in his home in Chevy Chase, MD[3], as a facility for growing anthrax and glanders bacteria. His associates, American stevedores he recruited, transported his deadly (liquid) brew to the stockyards at the Baltimore docks where it was applied to mules and horses awaiting transport to aid the anti-German war effort in Europe. Several thousand animals died and hundreds of battlefield soldiers were infected.

Japan's Unit 731

After World War I, Japan aspired to world-class status. The Imperial Army was being prepared for its role on the global stage. It chose to research both biological and chemical weapons for their effects on animals and humans. The modes of experimentation were beyond even the most loathsome acts of the Nazi researchers.

Let us begin with a brief chronology of events.

- 1925: Japan refused to sign the Geneva Convention ban on biological weapons.
- 1932: Japan launched the so-called *Mukden Incident*, which enabled its troops to invade Manchuria. At the end of the year, Shiro Ishii, a physician and army officer who was intrigued by germ warfare, toured Manchuria for a possible experimental site. The *Epidemic Research Laboratory* is formed under him and this group began preliminary experiments.
- 1936: Unit 731, a biological-warfare unit, officially named *Epidemic Prevention and Water Purification Department of the Kwan Tung Army*, is formed. Ishii built a huge compound—more than 150 buildings over six square kilometers—at Pingfang, 20 kilometers south of the city of Harbin, Manchuria. The construction and maintenance of the facility was done by some 10,000 Chinese laborers. Nearly 3000 other people worked under Ishii.
- 1942: Ishii began field tests of germ warfare on Chinese soldiers and civilians. Tens of thousands die of bubonic Plague, cholera, anthrax, and other diseases. Some U.S. soldiers captured in Philippines were sent to the compound at Pingfang.
- 1945: Japanese troops demolished the headquarters of Unit 731 in the final days of the Pacific war. Ishii ordered the 150 remaining "subjects" killed to cover up the experimentation. Nearly 3000 others had already died because of the experiments conducted by Unit 731.

[1] There is also the Lord Jeffery Inn prominently situated on the town's green.
[2] One reason for the very long muskets, other than purported accuracy, was that the traders exchanged these weapons for an equally high pile of furs. Clearly, an inflationary period for the "currency" of the day.
[3] A mere six miles from the White House.

- 1946: U.S. negotiated with Ishii for germ warfare data[4] based on human experimentation in exchange for immunity from war-crimes prosecution.

Shiro Ishii was the Doctor Mengele of the Japanese Imperial Army. Japanese medical personnel were invited to his compound to practice surgery. Chinese locals, patriots, anti-Japanese underground workers, communist party members, and POWs from China, Russia, and Mongolia were usually used for this purpose and they were dehumanizingly referred to as *marutas*, meaning *wooden logs*. They could be men, women (even pregnant women), and children.

A victim was given a general anesthetic, then various surgical techniques were performed, after which they were killed by lethal injection of 5 mL of ether. Such vivisections were exclusively for practice and no research knowledge was gained.

The army was anxious for information on human reactions to various conditions or traumas. Experimentation was carefully designed and sufficient measurements were taken to assure the researchers of the validity of their conclusions. The research "subjects" were usually tied spread-eagle to stakes driven into the ground. Some of them were shot with various munitions, in various body parts, at various angles, and subjected to various treatments. Their responses and times to death, along with other variables, were carefully recorded.

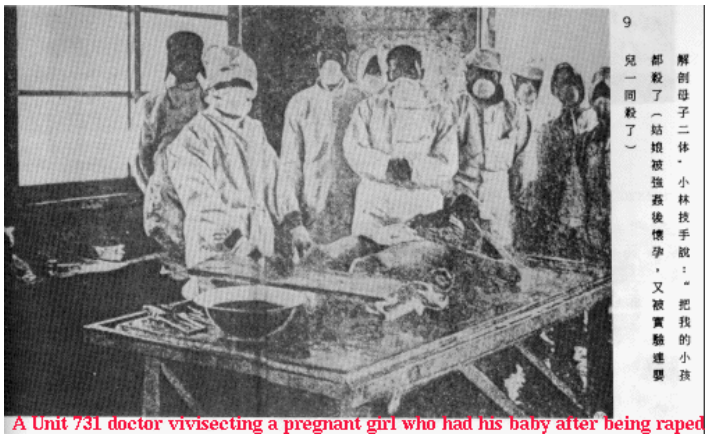
Human subjects were hung upside-down until death, subjected to high and low atmospheric pressures, given blood transfusions from animals or other humans, had stomachs surgically removed, and even more bizarre experiments were conducted.

During winter, "subjects" were tied down outside[5] with various limbs exposed. The exposed areas would be soaked with water and left to freeze until the guard overseeing the test had determined that frostbite had set in. From testimony by an officer, we know that this could be ascertained by listening because

> *frozen arms, when struck with a short stick, emitted a sound resembling that which a board*[6] *gives when it is struck.*

The standard treatment of rubbing the frozen limb, they concluded, should be supplanted by immersion in water at just above 100° F but no hotter than 122° F. This procedure remains in use today.

One woman was deliberately impregnated, i.e., raped, by a syphilitic Japanese medical technician, and both her and her infected child were subjected to *live* dissection.



A Unit 731 doctor vivisecting a pregnant girl who had his baby after being raped

All organs obtained from such dissections were carefully labeled and stored in jars filled with preservative.

Others were subjected to explosions of bombs carrying pathogens. To prevent them from being killed, their bodies were partially protected by metal shields and heavy blankets. Only their legs and buttocks were left exposed to the shrapnel contaminated with many microbes, one of which was *Clostridium perfringens*, the agent that causes gas gangrene. The experimenters carefully followed the progress of their subjects' diseases, until they succumbed.

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[4] The latest information tells that these data were stored away and barely studied at all.
[5] A normal winter low in this part of Manchuria was 40° F *below* zero.
[6] Hence the term *maruta*.

Experiments were also conducted with anthrax, Plague, typhoid, cholera, brucellosis, and wheat smut and nematosis (the last two are plant diseases). Pathogen production was also a major part of Unit 731's normal workload. Especially hardy species of fleas were grown, harvested, and infected with an extremely toxic version of *Yersinia pestis*. Their production facilities were capable of producing hundreds of kilograms of dried *Y. pestis* and billions of fleas in a matter of days. This would have been sufficient to kill every person on the planet at that time.

Particularly cruel bacteriological research took place at the camp. Victims were injected with various pathogens, sent to "the Square Building," locked into cells from which they could be monitored until they died. Some were singled out for special treatment: unanesthetized dissection! Still others, who had been infected, were put with healthy people, to determine the extent of human-to-human transmission. Testimony given in international court by an officer tells us that about 600 people died each year, for a total of about 3000 such deaths. As in the Nazi death camps, all bodies were destroyed in crematoria.

Biological research was not all Unit 731 did. Gas and germ warfare were practiced against the Chinese. During the course of the war, Japan used various poison gases 1131 times in fourteen Chinese provinces. At least five times, the Japanese tried to use germ warfare on the Chinese: on October 4, 1940 they dropped *Y. pestis* that killed 21 people; on October 29, 1940 they air-dropped *Y. pestis* that killed 99 people; on November 2, 1940 there was another drop, but with no reported fatalities; in January of 1941 more Plague was spread on two separate occasions, causing serious outbreaks in three provinces, but the attacks were suspended due to the large number of deaths among Japanese soldiers who were exposed due to the vagaries of the wind.

During the early summer of 1945, Japanese generals came up with the idea of launching 9000 balloons toward the US. The debate centered on the payload; some suggested anthrax or Plague, others wanted cattle viruses or plant diseases. Finally, several hundred balloons were launched; each carrying one antipersonnel bomb and four incendiary devices. Far-fetched though this may seem, seven Americans were killed by these bomb-laden balloons.

Perhaps even more incomprehensible, operation *Cherry Blossoms at Night* proposed that 20 twenty kamikaze pilots be transported by submarine to southern California. Once there, they were to fly sub-carried seaplanes to distribute Plague over the San Diego area. Fortunately, the sub was diverted to the battle of Ulith where it was sunk.

As the war ended, the Unit released all its Plague-infected animals. This led to major outbreaks that resulted in 30,000 human deaths in the surrounding area during the three years following the termination of hostilities. As mentioned before, the US agreed to exchange the Unit's data for a promise not to prosecute the Japanese officers that were captured by the Allies.

Allied Biological Warfare Efforts During World War II

The British set out to produce anthrax bombs and anthrax-contaminated feed cakes to drop on Germany for the purposes of destroying its meat cattle. The research and testing took place on the island of Gruinard, off the Scottish coast. After the war, the project was abandoned. Scientists thought the spores would not be long-lived, but they were *very* wrong. Forty-one years after the war ended the British government embarked on a cleanup project of the still viable spores. An elaborate irrigation system was installed over the entire test range. 280 tons of formaldehyde in solution with 2000 tons of seawater were pumped through the system 24/7 for more than a year. The 500-acre island was officially declared decontaminated in 1990.

Of course, the US also had elaborate programs in place, partly as a response to Japan's threat. In particular, the military had designed, tested, manufactured, and stored anthrax cluster bombs.

The First Modern Bio-Attack in the US

In 1981 the disciples of Bhagwan Shree Rajneesh bought a 64,000-acre ranch in Wasco County near the county seat The Dalles in Oregon. This was the beginning of friction between the cult members and the local planning and zoning board. As the cult members applied for various zoning variances and were denied again and again, relations between them and the local residents deteriorated at an even more rapid rate.

Unbeknownst to many of the cult members, there was a radical subgroup bent on removing all opposition to its desires. The subgroup electronically eavesdropped on visitors and other members. This subgroup eventually hatched a plot to "poison" townspeople prior to voting day, so that the cult could dominate the local boards and get its way without external interference.

The cult was extremely well organized, even having a separate Rajneesh Medical Corporation for tending to its members' needs. Unfortunately, the conspirators used this façade to order samples of pathogenic microbes from the companies American Type Culture Collection and VWR Scientific. These were available in so-called "bactrol disks." These samples were meant for comparison in laboratory testing for disease. In fact, they were used for growing bacteria, such as *Salmonella typhimurium*, which is responsible for some serious food poisoning. The

equipment available to the perpetrators for growing these microbes was quite sophisticated, including a quick freeze-dryer.

The conspirators had used these bacteria to contaminate salad bars at several restaurants in The Dalles area. The number of cases of food poisoning filled the local hospital to overflowing. A second wave of attacks sickened many others. Many people had been near death, but there were no fatalities. The worst case occurred in a pregnant woman who prematurely delivered an infected baby.

After fleeing the US for Germany, the two conspirators were extradited back to the US. They were sentenced to 20 years in prison and required to pay considerable fines. But, in the style of bizarre TV programs, both served less than four years in federal prison in California, were released, and fled the country before the state of Oregon could begin further prosecution.

Although food poisoning doesn't sound very bad, cultures of much more deadly microbes had been undertaken before they were discovered. Neither of the women had any graduate training in microbiology or related fields. One can only wonder at the havoc they could have wreaked with a just a little more knowledge.

Biological Experiments Involving Americans

There are many cases of unethical infection of uninformed patients by medical personnel. This section will give but a very short list of some of these acts.

In 1900 an American doctor working in the newly acquired colony of the Philippines, deliberately infected prisoners with Plague and also induced the deficiency disease beriberi in others. Under the rubric of searching for a cure, another doctor induced the deficiency disease pellagra in twelve Mississippi prisoners.

In 1931, one Cornelius Rhoads, MD, under the sponsorship of the Rockefeller Institute of Medical Investigations, began the *Puerto Rican Cancer Experiment*. Subjects were purposely infected with cancer cells and thirteen died. Oddly, he was entrusted with running this experiment despite the fact that he had previously written that Puerto Ricans should be eradicated (?). Once his experiment was made public, rather than suffer the shame and ignominy he so richly deserved, he went on to a new and even more successful career in establishing the US Army Biological Warfare facilities (which is now USAMRIID – **US A**rmy **R**esearch **I**nstitute for **I**nfectious **D**iseases), served on the Atomic Energy Commission, and conducted illicit radiation experiments on unwitting patients, prisoners, and active duty US soldiers.

The Tuskegee Experiment and Withholding of Treatment

It wasn't until 1905 that Fritz Schaudinn and Erich Hoffman discovered the microbe responsible for syphilis. They called it *Spirochaeta pallida* (since renamed *Treponema pallidum*). In the year 1906 August von Wassermann developed a blood test that was specific to the microbe. Prior to this time, syphilis was diagnosed, for the most part, by its characteristic symptoms. From that time forward, diagnosis was easy, but no cure was yet at hand. By the time the Wassermann test was available, Paul Ehrlich had tested over 600 arsenic-based compounds for their effect on *T. pallidum*. He patented compound #606, but then dropped his investigations. In 1909 Sahachiro Hata started work as Ehrlich's assistant. He retested the entire group of compounds and found that #606 was active against the spirochete. Ehrlich's research group began injecting the drug, named *Salvarsan*, into the most advanced stage patients. Within a year, they had treated nearly ten thousand patients. In some cases, the improvements were nothing short of incredible. The drug was modified to lessen the severe adverse effects any arsenic compound would have. This modified form, called *Neo-Salvarsan* (neoarsphenamine) was introduced in 1914. It was no miracle cure, insofar as treatment required a yearlong series of fairly painful injections, which were not 100% successful.

"Bad Blood" was a common malady among poor Southern farmers. The term referred to the symptoms of everything from beriberi to syphilis to tuberculosis to ulcers. To call it a catchall diagnosis would be a great understatement.

It was well known in the beginning of the twentieth century that some Americans of African descent reacted differently to malaria than Caucasians. The reason, at that time unknown, for this was the inheritance of the cellular mutation that causes sickle cell anemia. Sickled red blood cells are much less susceptible to full infection by the malaria-causing protozoan *Plasmodium falciparum*. This led to a belief among Southern planters that blacks had different reactions to other diseases, in particular, syphilis.

Prior research on whites had been done by a Norwegian investigator who reviewed medical records of about 2000 syphilitic patients from 1891–1910. Dr. E. Bruusgaard of the Venereal Disease Clinic in Oslo published his results in 1929. He had found neural involvement was rare compared to cardiac involvement, which was common. Nevertheless, many American medical people felt that blacks had a totally different course of the disease and because of this belief, there was a need for further research. Whether these beliefs were based on fact or racism, we will never know.

Drs. Clark and Parran sent a proposal to the Rosenwald Fund. Its goals were to train private physicians in the treatment of venereal diseases. The Fund voted in 1929 to join the Public Health Service in this program. Six sites were chosen. One was Macon County, Alabama.

Macon County was dirt poor. Most farmers were sharecroppers. Water came from shallow wells subject to contamination from surface run-off. Pellagra was rampant as a result of poor nutrition. The researchers applied to the Public Health Service (PHS) in January of 1930 for further funding. County planters granted the PHS permission to test their workers without so much as a *by-your-leave*. Their workers were rarely, if ever, consulted or even told of the nature of the study. Some of the patients were told they were being tested for "bad blood." In this initial period, all workers were tested for syphilis, but none of them were informed of the results of their tests, except to be told if they had "bad blood." Doctors gave them mercury salves to rub on their backs and to be applied under rubber belts wrapped around their waists. They were told to leave the belts on and then wash at the end of the week. Most patients without "bad blood" had other serious conditions that were left untreated. Among those tested, the prevalence rate of syphilis was 36%—astonishingly high.

After the first year, the Rosenwald Fund withdrew its support. The doctors applied to the PHS for additional funding, got it, and began the *Tuskegee Study of Untreated Syphilis in the Negro Male*. Historian James H. Jones referred to it as the "Longest nontherapeutic experiment on human beings in medical history." The study began with 399 men with tertiary syphilis and 201 syphilis-free controls. Despite the title of the study, some treatment was given, details of which were not recorded, and no new drugs were tested. No formal experimental design was employed, no randomization was ever done, and there is no record of there having been anything resembling an experimental protocol. None of the men were ever told they had syphilis, nor were their wives or lovers ever informed of the dangers of transmission.

The day-to-day activities of the "study" fell on nurse Eunice Rivers. She worked between fourteen and fifteen hours per day, five days a week. Despite the initial high value, further testing settled at a 17% prevalence rate. Part of her job was to tend to the men, keep some records, take whatever samples were needed, and talk them out of dropping out of the study. The last was made difficult by the medical belief that blacks suffered more neural involvement than whites. This necessitated regular lumbar punctures—a particularly painful procedure in that time and place.

Even after the advent of penicillin for the treatment of syphilis in the 1950s, no one in the study group was given the new drug. Countless sexual partners of the study group were infected as well as their newborn children. The study's existence was revealed by Jean Heller writing for the Associated Press in July of 1972 to great public outcry about the ethics of such "research." The participating doctors continued to extol the merits of the study. In 1973 a class action suit was filed by the NAACP on behalf of the experimental subjects and was settled for $9 million. Finally, in 1976, the Tuskegee experiment was terminated, the survivors were treated, and in the year 1997 apologies were given by then President Clinton.

Military Experiments

Before the end of World War II, human radiation experiments began. Knowing full well the dangers posed by radioactive substances, experimenters at Oak Ridge National Laboratory injected, fed, applied topically, and caused to be inhaled by *unknowing* subjects the radioactive elements plutonium, polonium, americium, uranium, and other radioactive materials. News of these actions was kept from the public until 1972. Of the original 18 people injected with plutonium, four were still alive in 1973 when researchers measured the amount of radioactive material remaining in their bodies. This had been done without prior informed consent. An internal memo from the researcher to the Center for Human Radiobiology at Argonne National Laboratories explicitly said, "Please note that outside of CHR we will never use the word 'plutonium' in these cases." The group told relatives that the original research was an experimental treatment for the patients' diseases. Unfortunately, that statement was totally untrue. In 1995 and 1996, then President Clinton announced that the federal government had settled claims worth $6.5 million with the families of those 18 test subjects

It took until 1986 for Congress to investigate such matters. Representative Edward Markey of Massachusetts chaired the committee that spent over a year investigating claims made by some researchers. In October 1986, *American Nuclear Guinea Pigs: Three Decades of Radiation Experiments on U.S. Citizens* was released to the public[7]. The report is available at

http://raleigh.dis.anl.gov/roadmap/overview/070350/index.html

[7] Perhaps this is too conspiratorial, but after the release of the so-called Markey Report, DOE destroyed many of the relevant documents that were used in preparation of the report.

An April 20, 1994 staff memo sent to Markey said, "The Reagan administration Department of Energy declined to take any action on your 1986 report, and the report gained little further attention at the time."

Another committee released a 1000 page report in October of 1995. Recently, the Department of Energy has listed what it claims are all such experiments on which it has files. They can be accessed at

http://www.ohre.doe.gov/roadmap/roadmap/part3.html

By October 31, 2002, the US Department of Defense released summaries of 41 biological and chemical weapons tests conducted in Alaska, Florida, Hawaii, Maryland, and the Panama Canal Zone as part of Projects 112 and Red Oak, Phase 1, designed to test these weapons and possible defenses against them. The new documents claimed that all exposed military personnel wore "protective gear," but no mention was made of possible civilian exposure nor was the quality of the "protective gear" addressed. The tests conducted in Alaska released the nerve gases sarin and VX. Those conducted in April and May of 1967 in the Upper Waiakea Forest Reserve on the island of Hawaii used 155-mm artillery projectiles and 115-mm rocket warheads that released sarin.

Project SHAD (Shipboard Hazard and Defense) exposed unknowing sailors to both chemical and biological weapons. As of November 2002, some information concerning more than 100 experiments had been released. The extent of exposure of naval personnel is still being studied. More details are awaited (but dwon't hold your breath).

Many of the at least 5500 exposed veterans are pushing for compensation and further release of reports on such experiments beyond those released to date, 4/2005.

In their infinite wisdom, American military researchers also released bacterial simulants in the New York and other subway systems (shades of Aum Shinrikyo). The simulant was *Bacillus globigii*, then thought to be innocuous, but now known to cause acute respiratory problems in anyone with decreased immune function.

The Biological Warfare Treaty of 1972

On November 24, 1969, President Richard Nixon stunned the world by announcing

> *Biological warfare - it may produce global epidemics and profoundly affect the health of future generations. Therefore I have decided that the United States of America will renounce the use of any form of deadly biological weapons that either kill or incapacitate.*

This was a watershed event and it came like a bolt from the blue—completely unexpectedly. Working behind the scenes, diplomats from Russia, the United Kingdom, and the United States had put together a treaty to end the production of all biological weapons and banning any research that would lead to their development. Eventually, there were an additional 140 signatories. This Biological Weapons Convention explicitly prohibits developing, producing, or possessing "means of delivery designed to use such agents or toxins for hostile purposes." It seemed the world was rid of one class of weapons of mass destruction.

The US disassembled its bio-warfare labs almost immediately after signing the treaty. Unfortunately for humanity, the Soviet Union did not follow suit. Rather it embarked on a major program of development, testing, and production. Hidden in the city of Novosibirsk in far-off frozen Siberia was a massive effort administered by the military but populated primarily by civilian scientists. The program was called *Biopreparat*.

American intelligence got word of a major biological accident at a facility in the city of Sverdlovsk in 1979. Many people downwind of the facility came down with anthrax and died. Then President Boris Yeltsin claimed that it was the result of contaminated meat. This explanation was not all that far-fetched, insofar as that region[8] of Asia has long had large outbreaks of the disease among cattle because it is an inveterate focus for the disease. Adding to the mystery was the information that some victims did not develop symptoms until two months after the alleged accident. Then current medical knowledge was that victims entered the prodromal stage in a matter of days. No one pushed to investigate this incident and news of it eventually faded.

Although the Sverdlovsk incident disappeared from the news media, it had an effect on the bioweapons community. Pressure was brought to bear and President Reagan restored funding for "defensive" research.

The Soviets used huge fermenters to grow *tons* of weapons grade anthrax in the mammoth facility at Stepnogorsk in Kazakhstan. Although the US continued its research, production was at nowhere near the level of that of the Soviet Union.

[8] Russia, Ukraine, and Kazakhstan.

Biological Warfare Agents

Several Study groups were formed to assess the possibility of the use, by terrorists, of biological agents on the US civilian population. A select group of scientists was commissioned to search all previous research and report to the government, which they did in May and June of 1999[9]. The group singled out five possible agents: anthrax bacteria, smallpox virus, Plague bacteria, botulinum toxin, and tularemia bacteria. They addressed medical aspects of each, available immunizations, therapy, infection control, and decontamination.

More recently, since the 2001 anthrax-laced letters sent to media and government figures, the CDC has compiled a longer listing of prospective biological agents, their public health threat level, and other factors. The results were published in 2002[10].

Criteria and Weighting Used To Evaluate Potential Biological Threat Agents

The CDC rating scheme ranges from highest threat (+ + +) to lowest threat (+) to no threat (0). The dissemination potential is in quantities sufficient to affect a large population, assuming the most effective route of transmission and environmental stability, i.e., no major degradation of pathogens by air, humidity, sunlight, or ambient temperature. Category A is the highest priority for preparedness, B is lower, and C is reserved for those "emerging" diseases for which the threat to large populations is, as yet, unknown.

Disease	Public Health Impact		Dissemination Potential		Public Perception	Special Preparation	Category
	Morbidity	Mortality	Production-Dissemination	Person-Person Transmission			
Smallpox	+	++	+	+++	+++	+++	A
Anthrax	++	+++	+++	0	+++	+++	A
Pneumonic Plague	++	+++	++	++	++	+++	A
Botulism	++	+++	++	0	++	+++	A
Tularemia	++	++	++	0	+	+++	A
Viral Hemorrhagic Fevers	++	+++	+	+	+++	++	A
Viral Encephalitis	++	+	+	0	++	++	B
Q Fever	+	+	++	0	+	++	B
Brucellosis	+	+	++	0	+	++	B
Glanders	++	+++	++	0	0	++	B
Melioidosis	+	+	++	0	0	++	B
Psittacosis	+	+	++	0	0	+	B
Ricin toxin	++	++	++	0	0	++	B
Typhus	+	+	++	0	0	+	B
Cholera	+	+	++	+/-	+++	+	B
Shigellosis	+	+	++	+	+	+	B

Cryptosporidiosis

Although not on the CDC's list of rated biological threat agents, this protozoan agent has certain advantages. First, it is easily grown and readily available as a normal constituent of soil and infects many dairy cattle. Secondly, it is not removed from municipal water supplies by the usual treatments of sedimentation and chlorination. A 1993 outbreak in Milwaukee, Wisconsin caused several deaths among the immune-suppressed and the aged and resulted in the hospitalization of about 4400. About 400,000 people developed diarrhea from infection with this parasite. Other symptoms for susceptible people include abdominal cramps, nausea and vomiting, and a low-grade fever. These can persist for as long as two weeks and there is no safe and effective cure.

The havoc this could wreak in a population would be very significant.

[9] All five of the reports are currently freely available on the JAMA website.
[10] *Emerging Infectious Diseases* 8(2), 2002.

Anthrax

Historically, anthrax was considered to be predominantly a veterinary disease neither easily transmitted nor very widespread. That turns out to have been inaccurate, at best. In 1770, there was an epidemic of anthrax in Saint-Dominique (now called Haiti). An earthquake had laid waste to the city of Port-au-Prince and many slaves escaped from their masters. Consequently, the food sources were damaged and a major famine descended on the northern part of the island. Desperate people were driven to consuming salted and smoked meats that would not normally have been eaten. Neither process destroys pathogens in the meat, so a common source epidemic resulted. Infection due to the consumption of this uncooked beef was rapid and 15,000 people died. The accompanying famine also killed a large number of people.

Anthrax is caused by the bacterium *Bacillus anthracis*. This is an aerobic, Gram-positive, spore-forming, nonmotile *Bacillus* species. Its spores will germinate quite well within a human or animal host. There are three forms of disease caused by *Bacillus anthracis*: cutaneous, gastrointestinal, and inhalational anthrax. The anthrax genome consists of a single chromosome together with two plasmids. The more copies of the plasmids (up to 243 of the first pX01 and up to 32 of the second pX02), the more virulent the strain. Besides this, variation in the genes can alter the virulence of the previously 89 known strains of the bacteria.

The bacteria produce a toxin that interferes with the molecular signaling that occurs within macrophages and dendritic cells. Both types of inactivated cells become immortal, as their programmed cell death mechanisms are no longer operative. Since they are unable to stimulate the lymphocytes, the adaptive immune system has received a major blow and can no longer mount a fully effective defense.

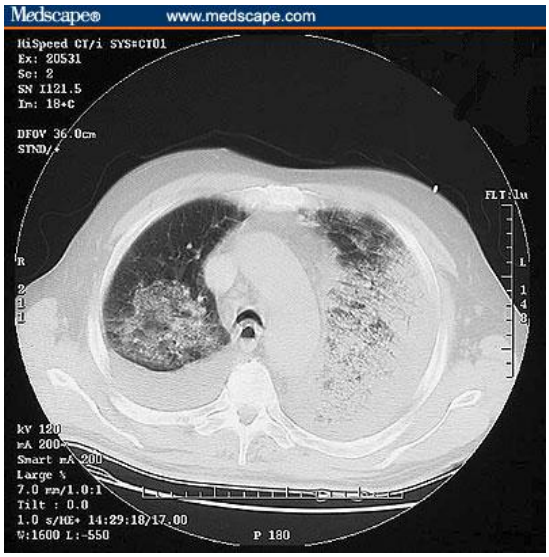
Cutaneous anthrax results when the bacteria are deposited on the skin on which there are nicks or cuts. The resulting lesion is coal-like in color (called eschar) and mortality rates among untreated victims can be as high as 20%.

Eschar due to cutaneous anthrax.

Gastrointestinal anthrax comes from eating the meat of infected animals and is very rare in this country.

Inhalational anthrax follows the deposition of the spores in the lungs. Once there, the immune system sends macrophages to phagocytize them. Spores that are not killed, and there are many of them, make their way through the lymph system and germinate in the lymph nodes. Disease follows in short order. Initial symptoms include fever, shortness of breath, cough, headache, vomiting, chills, weakness, abdominal pain, and chest pain. Second stage symptoms are more specific and can lead to death in as little as one hour. The untreated mortality rate could possibly

be as high as 90%, but research is limited[11]. There have not been any reported cases of human-to-human transmission. Best estimates are that one would need to inhale 10,000 spores to develop a clinical presentation of the disease.



MRI image of lungs infected with anthrax. White coloration indicates damaged tissue.

The LD_{50} (lethal dose capable of killing 50% of those exposed) is thought to be somewhere from 2,500–55,000 spores. Considering that spores are about 1,000–10,000 nm in diameter, that means that a really lethal dose (say 100,000 spores) would occupy a volume of no more than one ten thousandth (10^{-4}) of a cubic millimeter. For reference, that could be easily placed on the head of a pin! You don't need a snootful of this stuff to ruin your entire day.

Anthrax can produce spores, so there is a high likelihood that after the initial dispersal of a weaponized version, that subsequent action of machinery and/or weather could re-aerosolize these spores. This would lead to a set of secondary infections.

All known forms of anthrax can be treated with high doses of amoxicillin, penicillin VK, ciprofloxacin, or doxycycline. Since the incubation period for the disease may be as long as 60 days, anyone who has been exposed must take their medications for at least two months. Nausea and diarrhea are common adverse effects of all four drugs, especially when taken for this length of time. If disease symptoms have developed, these drugs must be supplemented within a week or two with corticosteroids to reduce inflammation.

There is an inactivated cell-free vaccine that was initially licensed in 1970. It consists of a series of six injections. A similar vaccine, but *not* this particular vaccine, was shown to be effective against *cutaneous* anthrax in humans. There have been ***no*** human clinical trials showing efficacy of the vaccine against inhalational anthrax. A 1996 study using rhesus monkeys showed that the vaccine, administered within 2 weeks of birth, was 100% effective against aerosol challenges given at 8 and 38 weeks of age. It was 88% effective against exposure at 100 weeks. The military has mandated this vaccine for all service personnel. They claim there have been no *causally related*[12] serious adverse events. This contention is currently being challenged in court and many service persons have retired or resigned, rather than submit to the vaccine that they claim produces symptoms similar to Gulf War Syndrome. Outside experts hired to analyze the data available on the 500,000 doses given found 1530 FDA-reported reactions. Of these, only 16 were found to be serious "adverse events." This rate is low even by the standards of the usual childhood immunizations, such as DPT, MMR, and polio[13]. Nevertheless, the question of efficacy for humans exposed to aerosol anthrax has not been answered.

Of course, the whole issue of genetic modification of the bacteria has not been raised. Even minor alterations in the anthrax genome (or its adjoined plasmids) could render the bacteria resistant to the one currently available vaccine and/or various antibiotics. The same holds true for any pathogen.

[11] Would you volunteer to be exposed to anthrax???
[12] From a statistical point of view, it is very difficult to establish causality without a fully designed and controlled experiment.
[13] DPT=diphtheria, pertussis, and tetanus. MMR=measles, mumps, and rubella.

Since anthrax bacteria are commonly found in the soil of many locations, collecting samples is far from an impossible task. Once collected, growing the bacteria requires an adequate supply of culture material. Growing large amounts requires some care in terms of temperature control and continual redistribution, oxidation, and supplementation of the growth medium. Bear in mind that serious home-brewers of either beer or wine grow their own yeast in much the same way. Once you have a sufficient quantity of the microbe, the growth medium needs to be slowly dried, usually spray-dried. The dried mixture must then be combined with a carrier substance, fumed silica would be best[14], and ground into fine particles that do not adhere to each other. (Think of a coffee bean grinder, where the grounds cling to the top and sides of the grinding chamber.) Since most grinding generates an electrostatic charge, specialized milling machines and containment vessels are required to prevent such adhesion. Such (large and expensive) devices are readily available on the open market. Distribution of the resulting powder can be done using special industrial sprayers mounted on a moving vehicle or small airplane.

If one's goal were to cause anthrax of cattle raised for meat, several steps in the growth procedure could be eliminated. A liquid culture medium containing the bacteria could be sprayed onto the noses of the animals. Complete coverage would not be necessary since a number of contaminated steers would require a quarantine or recall of an entire feedlot. Some feedlots have a capacity of over 100,000 cattle. The US Department of Agriculture reports that in 2001 there were 118 of the largest category of feedlot, those with 32,000 or more head of cattle, and this group encompasses half of all cattle fattened in feedlots.

A scenario validated by extensive computer simulation showed that if an airplane sprayed 100 kg of weaponized anthrax spores fairly uniformly over a city of five million, then

- Sunny day with a light breeze: 130,000–460,000 killed
- Overcast day or night with a moderate wind: 420,000–1,400,000 killed
- Calm, clear night: 1,000,000–3,000,000 killed

This does not include the possibility, which is the current military and terrorist tactic, of a secondary dispersal targeting emergency personnel responding to the disaster. You should contrast this with the explosion of a one-megaton nuclear bomb, which could result in at least 23,000–80,000 killed.

The costs of responding to such a scenario would run into billions of dollars. Consider the possibilities: (a) insufficient medical personnel to deal with all the victims, (b) insufficient supply of drugs for all victims and others who feel they may have been exposed, and (c) no single agency to organize the response.

Decontaminating a site contaminated with anthrax spores is done by sealing the building, filling it with chlorine dioxide gas and then neutralizing the gas with sodium bisulfite vapor. Applying these steps to the Senate Office Building cost $27 million. Cleaning the Brentwood postal facility, from which the anthrax-laced letters originated, cost $130 million and took 26 months. An alternative method using x-rays and ultraviolet-C light promises to be both less expensive and faster.

Detecting anthrax spores previously required a "wet" laboratory analysis (requiring from 30 minutes to several days to perform), but in June of 2009 a new methodology was announced. Veritude, Ltd. presented a handheld optical device using ultraviolet light which can be operated by persons with no special skills and very little training. Results are available in a matter of minutes. The device, called the *Ceeker*, uses very small amounts of the sample, which is neither consumed nor destroyed (unlike "wet" lab testing). The *Ceeker* is more accurate than other "wet" lab techniques, insofar as it identified 100% of the anthrax samples and correctly identified 95% of the hoax substances.

Smallpox

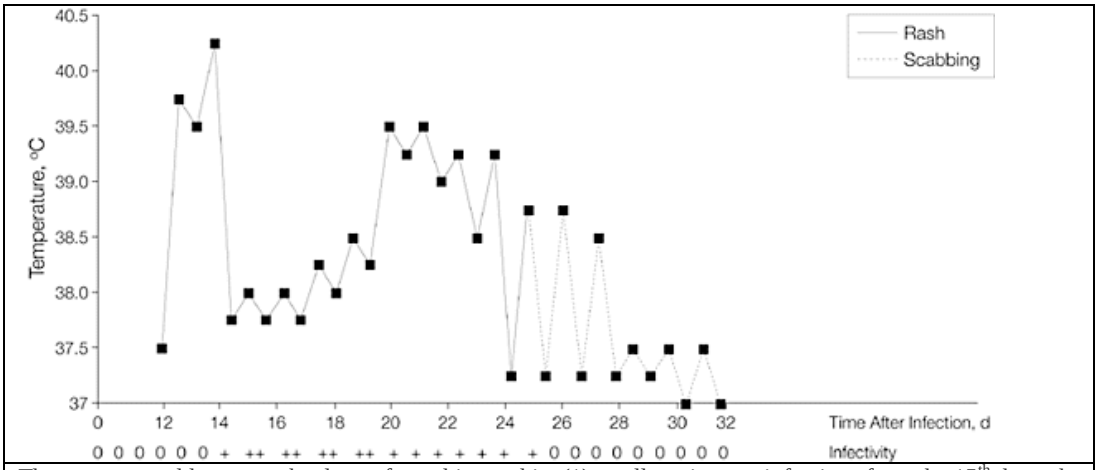
Unlike anthrax, producing smallpox virus can be safely (for the producers) done at very few facilities in the world. From what we are told by the World Health Organization (WHO), the only sources of the virus are the CDC lab in Atlanta and the Russian State Research Center of Virology and Biotechnology in Koltsovo, Novosibirsk. Since a sample of the virus can be frozen and stored for years with no reduction in virulence, there may be many other sources. Some intelligence experts estimate that China, Cuba, France, India, Iran, Iraq, Israel, North Korea, Pakistan, and/or the former country of Yugoslavia may have stores of the virus.

The smallpox virus is a member of the orthopox genus and it is extremely stable in aerosol form. The disease occurs in two common and two uncommon forms: variola major with an untreated mortality rate of 30–40%, variola minor with an untreated mortality rate of only 1–2%, malignant and hemorrhagic smallpox, both extremely rare with mortality rates approaching 100%. All four can be spread from one person to another by the transfer of aerosol droplets, as in coughs and sneezes, or through contact with contaminated clothing, bed linen, or other fomites. Recall, that humans are the only natural reservoir for this disease.

[14] One brand name of the substance is Aerosil.

It is a host-to-host disease, so natural transmission is slow. A deliberate seeding of the atmosphere with weaponized virus would have the same effect as a common source epidemic, speeding the spread. The best estimates for transmission rate are that 1 person would infect at least 10 others.

After exposure to variola major[15] there is a 7–17 day (average of 13 days) incubation period. After that the victim develops a high fever, general feeling of tiredness, headache, and backache. A lumpy rash forms around the mouth and throat, which spreads to the face, arms, legs, and sometimes the trunk. Within the two days the lumps on the skin develop a crusty head and are filled with pus. The lesions around the mouth and throat release a large number of virus particles that becomes part of the saliva. It is during this time that the disease is most contagious. Death usually occurs during the second week of symptoms. The following graph shows the patient's temperature in degrees Celsius (37°C is normal) as a function of the number of days after infection. Below the time axis is a rating of infectivity, ranging from 0 = none to ++ = most infective.



There are several lessons to be drawn from this graphic: (1) smallpox is most infectious from the 15th through the 19th day after infection, (2) it is not infectious before the 13th day or after the 25th day, (3) the pustules scab over around the 25th day.

Since each generation of the disease lasts about two weeks and transmission is about 1:10, the second-generation transmission could increase the number of infections ten-fold, and a third-generation could lead to a hundred-fold increase. In just two months there would be four generations and an initial group of 3000 terrorist-caused infections could grow to as many as 3,000,000 infections. Of these, fully one-third could die. Those one million American deaths would dwarf all such, even the numbers from the Civil War. And that's only the fourth generation! Only a massive vaccination program could mitigate the effects of such an attack (assuming a non-genetically altered strain was responsible for the infection—which is very likely wishful thinking).

Since smallpox was eradicated in the late 1970s, exposure to this disease of severely immune-suppressed people has never been studied. It is likely that **AIDS** patients, cancer patients undergoing either chemotherapy or radiation therapy, transplant patients, the very young, and the very old would be much more susceptible to all forms of the disease. The last case recorded in the US was in 1949. Those born after 1972 were not immunized against the disease, so the lion's share of the population is highly susceptible.

Although medical personnel trained in the US after 1970 are not likely to have ever seen variola major in a living person, the symptoms are so unique that their ability to diagnose this disease should not be greatly impaired; but this may be unlikely because of the disease's initial similarity to chickenpox. Verification of a diagnosis may take some time because, currently, there is no universally available, accurate, approved, reliable, and rapid diagnostic test for the virus[16].

Although there appeared not to be sufficient vaccine even for emergency medical personnel, 86 million more doses were "found" in 2002 by the French firm Aventis Pasteur. Although this would not cover everyone in the US, tests using a 1:5 diluted version of this cache have shown that there is a significant immune response, so this supply

[15] There is virtually no published Western research on the symptoms and spread of malignant, hemorrhagic, or recombinant smallpox. One thing that is known is that pregnant women are unusually susceptible to the hemorrhagic and malignant forms.
[16] The MiraWell™ Rapid Vaccinia Antibody Detection Test (2003) claims to be able to detect the presence of protective antibodies against smallpox in less than three (3) minutes.

together with Wyeth's *Dryvax* would be able to immunize the entire population (9/2002). Unfortunately, there has been no testing of this diluted vaccine on children[17]. Some good news is that the British pharmaceutical manufacturer Acambis together with Baxter Pharmaceuticals has been commissioned to produce a newer version of the vaccine. Currently, their Massachusetts manufacturing facility is producing 2 million doses per month.

Previously, the plan for vaccination in the event of a release was the so-called "ring approach," which called for the federal government to vaccinate all of those who had contact with anyone in the infected group. On September 23, 2002, the administration revised its recommendation to vaccination of all people with supervision occurring at the state level. Mathematical models of disease spread concur with this recommendation insofar as they predict a much higher incidence rate for this "ring approach."

On October 7, 2002 the American Medical Association issued a statement saying that it endorsed government recommendations of a "ring approach." This statement was also taken by the American Academy of Family Physicians and the American Academy of Pediatrics. These statements were based on studies conducted in the 1960s. The results obtained at that time indicated that for every one million people over the age of one year who were vaccinated for smallpox, 1 or 2 died, 9 suffered a serious brain infection, more than 100 developed eczema vaccinatum (a severe illness and skin rash that can leave sufferers with deep scars), and hundreds of cases of rashes, dermatological problems and infections. They expect rates of adverse effects to be higher now because many more people are on some form of chemotherapy, have weakened immune systems, suffer from autoimmune diseases, and have had organ transplants. Dr. James R. Baker, a spokesman for the American Academy of Allergy, Asthma and Immunology, also expressed a need for caution in considering widespread vaccination, because his group had concerns about the increased risks to people with the skin conditions atopic dermatitis and eczema, which affect up to 15 percent of all Americans[18].

On March 25, 2003 the CDC recommended the halt of vaccination of people with known cardiac problems. This action resulted from reports of 7 cases of cardiac-related problems including two deaths following vaccination[19].

It remains to be seen whether any of this discussion of vaccination strategies is even remotely relevant to real-life, insofar as the virus a terrorist group might use is likely to have been genetically engineered to be resistant to current attempts at immunization.

Although decontamination should not be an issue, bodies of victims of this disease still carry the virus, so it has been recommended that they be cremated and all mortuary workers be vaccinated.

Plague

Naturally occurring Plague is carried by fleas living on infected rodents. The disease is transmitted to humans when the fleas leave their normal host to take a blood meal on a person. Transmission is slow. When used as a biological weapon, it is likely that the weaponized bacteria would be released as an aerosol, so that most cases would be pneumonic Plague—the deadliest kind. It has been estimated that such a release would be infective for up to one hour. Once infected, symptoms would develop in 1–6 days at the outside, 2–4 at the inside, and death would follow quickly.

Diagnosing Plague would not be an easy task. The severe respiratory infection would be similar to many other diseases. More to the point, there is no *readily available approved* rapid diagnostic test[20]. Cultures of bodily fluids would take between 24 and 48 hours to show results, by which time the patient could have died. Once Plague was identified in a subpopulation, then all respiratory illnesses from that group would be treated as if they were Plague.

Although streptomycin is the recommended treatment for Plague, it has been little used in the US due to its side-effects, consequently, supplies are limited. Tetracycline and doxycycline are both FDA-approved for treatment. Gentamicin has been used successfully, but is not FDA-approved for this use. Clinical trials have shown that

[17] By 12/08/02 the FDA was to decide whether or not to approve a research project using 40 toddlers, aged under 3 years, to determine the safety of Dryvax. The children would have been kept from daycare/preschool for 30 days or until the rash heals. A new form of bandage was be used that is supposed to prevent the kids from touching the rash, which could cause serious adverse effects. The ethics of the experiment are in question for obvious reasons. Whether it took place is not known.

[19] Between January 24, 2003 and August 8, 2003 there were 77 serious adverse events and 653 nonserious adverse events in 38,257 vaccinations of civilian health care and public health workers. Although there were no civilian to civilian transmissions, there were 16 military to civilian transmissions of vaccinia. If all persons at risk were omitted from a general population vaccination program of those aged from one to 65 years-of-age, there would be around 8800 people having serious side effects and there would be more than 500 deaths.

[20] A collaboration between researchers at the Pasteur Institute (France) and Antananarivo (Madagascar) announced the development and field testing of a 15 minute test for Plague with 100% sensitivity and specificity (*Lancet*. 2003;361:191–192).

ciprofloxacin, levofloxacin, and ofloxacin are as good as or better than tetracycline. Other drugs could also be used. Thus, medical management of the disease is not impossible unless the attack involved a recombinant form of the bacteria that was resistant to most antibiotics.

Transmission from person-to-person of pneumonic Plague does occur. Person-to-person transmission of the other forms of Plague has not been extensively studied. But it is not impossible if there are open cuts or sores. The question then is: what do you do with exposed people who have yet to develop symptoms? Especially if they refuse prophylactic medication?

To our good fortune, weaponized *Y. pestis* does not survive very long; it does not form spores and it is sensitive to both heat and sunlight. Thus, secondary infections are not likely and decontamination would not be necessary. But … if the bacteria-infected rodents (which is likely since all major urban centers have large rat populations—and large rats), then they could be carried into underground burrows where they can survive for as long as thirty years in either soil or animal dung (What a wonderful inheritance for future generations!).

Botulinum Toxin

The first use of botulinum toxin was by Japan's Unit 731 in Manchuria at their research site in Pangfang. It was fed to prisoners in order to study the effects on humans. During World War II, the Allies prepared over one million doses of botulinum toxoid vaccine in the light of intelligence estimates that Germany had weaponized the toxin and was about to use it. Mercifully, the need to use the vaccine did not arise.

It has been claimed that botulinum toxin, BT, is the most poisonous substance known to mankind (by weight). One gram, the weight of one thin dime, evenly distributed over a major city and inhaled by most of its inhabitants would result in over 1,000,000 deaths. If administered directly to each person, it could kill 4 million people! Although these are totally hypothetical (and improbable) situations, it gives you some idea of the potency of the substance.

Surprisingly, BT has many therapeutic uses, not the least of which is the so-called "botox" treatment for the removal of facial wrinkles, which it does by *paralyzing* facial muscles. This is the basis of a $300,000,000 industry in the US.

Between 1990 and 1995 the cult Aum Shinrikyo sprayed BT in downtown Tokyo. For unknown reasons, there were no reported ill effects. United Nations inspectors, UNSCOM, working in Iraq after the 1991 Persian Gulf War did not initially find any BT, but after being informed of its existence by high-ranking defectors, the Iraqis admitted to the manufacture of 19,000 liters of concentrated BT, of which 10,000 liters had been loaded in various weapons systems. As of 1998, when UNSCOM withdrew from Iraq prior to US and UK bombing raids, all the BT had not been accounted for. As a point of reference, 6,000 liters of their BT store would be sufficient to kill every human being on this planet if it were dispersed uniformly and ingested by everyone. Careful scrutiny by the American investigators set to find weapons of mass destruction after the Iraq invasion of 2003 has **failed** to find any biological, chemical, or nuclear weapons.

Terrorist use of BT would probably be in the form of multiple simultaneous contaminations of processed foods. Although there would be recalls, the incidence of botulism would be significant and the economic dislocation would be monumental. Contamination of a city's water supply would require a rather large volume of BT and due to the speed, or lack thereof, that water flows through the sedimentation beds, together with the chemical treatments; it is highly unlikely very much BT would survive intact.

BT can produce muscle paralysis. Research to determine the lethal dose has involved nonhuman primates (monkeys). The estimates for the amount needed to kill a 70 Kg human are: 70 μg ingested orally, less than 1 μg inhaled, and less than ¼ μg injected.

There are three types of botulism: foodborne, intestinal, and wound. BT cannot penetrate intact skin, but it can be absorbed through the mucosa of the gut or the lung and an open wound in the skin. In naturally occurring botulism the symptoms are abdominal cramps, nausea, vomiting, and/or diarrhea. Once BT gets into the bloodstream it produces neurologic symptoms by blocking the release of neurotransmitters. There is no fever; paralysis occurs symmetrically on the body and it starts at the head and moves downward. There is no impairment of brain function, although communication may be difficult because of the paralysis.

All tolled, there are seven forms of botulinum toxin, A–G.

The toxins take between 12 to 72 hours to produce symptoms, but that depends on the amount ingested, i.e., there is a clear dose/response curve.

Diagnosis of this intoxication is difficult because there are several, more common, diseases that present in the same way. Laboratory testing is rather specialized and not available at other than the CDC and about half of the state health departments. Once diagnosed, treatment consists of administration of an antitoxin (grown using horses) and

supportive care. Antibiotics have no effect on the toxin, but could be used for other secondary infections, if the person can survive the toxin. Some antibiotics can make the paralysis worse.

The equine antitoxin has produced some significant adverse effects of which medical personnel should be aware. For this reason, it is recommended a small test dose be given prior to the full dose.

Recent research (8/2002) has produced a new drug, fashioned from three different antibodies, that is much more effective at preventing death in mice exposed to BT. Now all we need to do is see if it works in humans! Of course, producing this drug in sufficient quantity to make a difference is another question entirely.

An airborne release of BT is estimated to decay at a rate of at least 1% per minute and possibly as high as 4% per minute. That translates to 5 parts in 10 million remaining after one day and 3 parts in 10 trillion after two days. In plain English, it would be undetectable after a little more than two days. Thus decontamination of the affected area should not be an issue.

Tularemia

Once again, Imperial Japan's Unit 731 experimented with the bacterium *Francisella tularensis* as a biological weapon. Ken Alibek (former director of the Soviet Union's Biopreparat) has suggested that tularemia outbreaks on the eastern front during World War II were deliberately spread. He also tells of the production of an antibiotic- and vaccine-resistant variant by Soviet scientists.

The CDC predicted total costs to society to be $5.4 billion for every 100,000 people infected due to an aerosol attack. These figures are based on an older, less refined World Health Organization aerosol attack model that predicted if 50 kg of *F. tularensis* were dispersed over a metropolitan area of 5 million people, there would be 250,000 cases of tularemia, of which 19,000 would prove fatal.

The disease is endemic in the US, everywhere except Hawaii. Most cases occur in Missouri, Arkansas, Oklahoma, South Dakota, and Montana. It is carried by small mammals that are infected by bites of infective arthropods like flies, mosquitoes, and/or ticks. Lab technicians can contract the disease simply by inhaling near an open culture plate. There is no known case of person-to-person transmission.

The incubation period is 1–14 days and symptoms would be expected to appear in 3–5 days. The disease would present very much like many other upper respiratory infections: abrupt fever (38°–40°C), sore throat, cough, swollen lymph nodes, and lung involvement. The usual diagnosis follows a sputum or throat culture.

A live-attenuated vaccine is available, but is not yet FDA-approved. Its protection takes two weeks to develop and it is not completely effective against inhalational infection.

Intravenous streptomycin is the treatment of choice for isolated cases but gentamicin, doxycycline, ciprofloxacin, and chloramphenicol can also be used. Mass casualty cases could be treated with oral doxycycline and ciprofloxacin[21].

During natural outbreaks, the bacteria can survive for quite some time in a cold and moist environment. Hopefully, weaponized bacteria would succumb to environmental degradation within days, but, for obvious reasons, there has been no published study to verify this is the case.

Medical Response

As we look back in our history for similar biological/chemical events, several stand out.

During the winter of 1947, there was an outbreak of smallpox in New York City. The public health officials immediately organized a rapid deployment force to vaccinate 2.5 million people who may have had any contact with the infected patients, who had already been quarantined in various hospitals. Only 12 additional cases resulted. The speed of the response may very well have been affected by the fact that the nation had only two years prior been under wartime conditions.

The Aum Shinrikyo use of (neurotoxic) sarin gas in the Tokyo subways in 1995 resulted in over 5500 injuries and completely engulfed all 260 of the hospitals in Tokyo. Some patients were required to go to medical facilities 500 miles away.

The SARS outbreak of 2003 hit Toronto, Canada particularly hard. There were a total of 251 confirmed cases and 27000 people were exposed to the responsible virus. The hospitals were overwhelmed. As many as 7000 patients and health care workers were hospitalized at one time.

In contrast to Toronto, Singapore had only 39 cases and about 600 people quarantined, but the use of surgical masks and sterile gloves added $14000 per day to the regions medical costs.

[21] Research announced in April of 2005 points to the possibility of using interleukin-12 to induce protective immunity against this microbe.

Currently, the US has 5800 hospitals with 700,000 beds covering 35 million admissions per year. A physician's average caseload is 2500 people. In the event of a major outbreak there are many issues with which this country will need to deal. Looking back at the response to Hurricane Katrina in 2005, does not inspire confidence in our ability to cope.

Summary

As far back as 1970, the World Health Organization evaluated a scenario whereby 50 kg of aerosolized Plague bacteria were dispersed over a city of 5 million people. The rather primitive, by today's standards, mathematical model predicted as many as 150,000 cases of primary pneumonic Plague, with at least two-thirds of those needing hospitalization. As many as 36,000 could die. Scaling this down to 10 kg over a metropolitan area of one million, we could expect as many as 30,000 cases and 7,000 deaths. This would generate a need for at least 23,000 hospital beds. Serving such an area, typically there would be from six to ten hospitals with about 3500 beds, nearly 13,000 health care workers, and perhaps 1600 physicians. Even without counting the number of health professionals stricken with the disease, nor the number withdrawn from service while they tend to their family members, we see that we are short 19,500 hospital beds and each doctor would need to minister to at least ten to fifteen severely ill patients. To say that the medical facilities would be completely overwhelmed is to understate the case by several orders of magnitude. The whole question of the availability of drugs in sufficient quantities to treat these numbers of patients is left to the reader's imagination.

Perhaps the best defense against a biological attack would be early detection of the offending microbe(s). Although instantaneous detection is not currently possible, there is an alternative. The Handheld Nucleic Acid Analyzer (HANAA) is about the size of a brick and weighs one kilogram[22]. It is based on the polymerase chain reaction, PCR, and compares sampled DNA to a stored DNA probe. It can test up to four samples simultaneously and signal detection is good, providing the operator knows what s/he is looking for. Although the Lawrence Livermore scientists who developed HANAA are rather tight-lipped, a lab spokesman said that the system could detect as few as 10 bacteria in 0.01 mL of liquid within 30 minutes. The use of readily available DNA microarrays could vastly increase the number of pathogens tested for and lower the threshold for detection. Although many such devices have been proven in concept, there are no operational models *known* to be commercially available (4/2008)[23]. Such microarray testing devices are being developed as smaller, faster, and more effective alternatives.

The lower the detection threshold for a device, the more sensitive it is. Just as with disease testing, increasing sensitivity without a corresponding increase in specificity will result in a larger number of false positives. As science advances on that front, will the response of the population to a large number of false alarms be forgiving or will they disregard them to the point of total apathy?

[22] That was the case in 2005. By now much, much smaller, lighter, and more effective devices are available.
[23] What is available to the military may very well outperform these numbers by several orders of magnitude.