Welcome to the lecture entitled “Historical Perspective on Biological Warfare”.

We are going to discuss how biological warfare has been used throughout history, citing examples from the U.S. program as well as other countries' biological weapons or biological warfare programs. We will also discuss the disadvantages of using biological warfare and illustrate these disadvantages from throughout the historical perspective from pre-modern times to the present.

Let’s first start with the definition for biological warfare. It’s very important in this definition as you read it to emphasize that it is the employment *in the time of war* of microorganisms to injure or destroy not only people but animals or crops. Biological warfare has also been called germ warfare or bacteriological warfare. It's important to not mix this definition with bioterrorism, which we will be covering in the next lecture.

The abbreviation “BW” will stand for either Biological Warfare or Biological Weapons, and it’s very important to point out that throughout history there have been 4 disadvantages of using biological warfare, which contribute thankfully to the fact that it has not been used in major battles or to cause major mortality. These 4 disadvantages are: First, because BW is often done in a clandestine or secretive manner, it may never be possible to determine how effective its use was. The second disadvantage is that if a country or army is going to use a BW, it is very important that they protect their own troops from this agent or agents. The third disadvantage is that many countries use remote areas or islands to test the dispersal of BW. When this is done, it may be difficult to fully decontaminate this area, making it safe for habitation. The fourth disadvantage of BW, as illustrated throughout this lecture, when a naturally occurring disease is the same one as being used in a BW attack, occur concurrently, it may be difficult to determine if it is the naturally occurring disease or the biological agent that is causing the damage.
We will now proceed chronologically from the furthest point in time that we have recorded information to the present regarding biological warfare or biological weapons. It is important to point out that only examples that have been documented historically will be used in this lecture. Between the 6th and 4th century B.C., there were three recorded episodes of BW use. In 600 B.C., there is evidence that Syrians poisoned the water supply with a fungal derivative from the rye plant. In 500 B.C., Greco-Romans poisoned the water supply with dead animals thus making it unfit for human consumption. And finally, in 400 B.C. a historian recorded that during the siege of Athens, by the Spartans, an epidemic among the food and water supply was “most certainly caused by the Spartans”.

There were a group of warriors depicted in this picture with a black pointed helmet. The Scythian warriors, around 400 B.C., were nomads who had a very unique weapon that they used. It consisted of a very long arrow that they could shoot at a rate of 10 per minute for a range of a quarter of a mile. What was the biological component of this weapon was the unique dip that they used for their arrows. They would take a combination of fecal material, human blood and dead animals, put it in earthen jars and bury it for a time period, during which it would putrefy even more thus making a very poisonous tip for their arrow.

In history, Hannibal was most notable for using the elephant to cross the Alps. What he is not well known for is that he was the first person to use naval biowarfare. And in this strategy, he took earthen vessels filled with venomous snakes and went up alongside the enemy ships, throwing the vessels onto the decks. When they broke open, they would release the venomous snakes and thus his enemies would have to contend not only with arm to arm combat, but with poisonous snakes as well.

Throughout history, plague has experienced 3 pandemics and has played a significant role both in biological warfare and as a naturally occurring disease.

The first pandemic of plague occurred between 542 and 543 A.D., otherwise known as the Justinian age. The emperor Justin is depicted on this coin in this slide. This was known as the first cycle of plague and is recorded in the history of the wars. On average, plague during this time period killed 10,000 persons a day and caused 50-60% mortality from Egypt to Europe.
The second pandemic of plague occurred over 3 centuries between the 14th and 17th centuries. It is also known at this time as the Black Death. With significant mortality between 20 and 30 million or 1/3 of Europe’s population. On this slide, the plague is depicted in art history as a big black creature with a long tail carrying a scythe or curved sword and standing over one of its many victims who would fall very quickly in the streets.

On this slide, we have a modern day depiction of the plague. Very similar to that of the 14th-17th centuries but in the background a metropolis, and very importantly in the bottom right, a cute little squirrel. This is to remind us that plague is still endemic in many countries including the southwest U.S. and is something we cannot forget about.

The first recorded event involving BW and the plague is recorded in an account by Gabriele de’ Mussi (aka Gabriel de Mussis) in 1346, talking about episodes that happened in 1345. During this time, the Mongol army was trying to overcome the city of Kaffa. This was a city surrounded by brick walls. During this time, the Mongol army succumbed to the plague and many of its members were dying of the plague. In frustration and in an attempt to use this as a weapon, they used catapults to hurl the bodies of plague infected persons over the walls and into the streets.

Please read this slide as it is an interesting excerpt from deMussi’s text discussing how these machines were used to hurl cadavers over the walls.

We ask the question, could plague have been caused by biological warfare? And it illustrated disadvantage #4 where naturally occurring plague from the 14th-17th century clouds the issue of whether it could have been used as a BW effectively. The most likely scenario is that BW was used at this incident at Kaffa, but certainly did not contribute to 3 centuries of a pandemic.
Slide 15

This slide, again from art history, depicts a street scene in Marseilles, France in the 1700’s where people were dying in hundreds and thousands where there were not even enough carts to pull away and remove and bury the bodies.

Slide 16

The nursery rhyme “Ring Around the Rosey” is actually considered to be about the plague. And where some of the verse comes from, “ring around the rosey” refers to infected red circular sores that people infected with bubonic plague would have on their bodies. Because these sores produced an odor, in order to cover that odor, People would put flowers or posies in their pockets to cover that smell. And thus the term “a pocket full of posies”. Once someone died from the plague, they were burned to prevent spread and thus the term “ashes, ashes, we all fall down”. So the next time you hear this nursery rhyme, it doesn't sound so cute anymore, does it?

Slide 17

A Polish artillery official named Siemienowics in 1650 was actually one of the early designers of a rocket technology. Siemienowics' other claim to fame was his unique use of artillery shells. The picture in the slide is one clue, and what actually was done was filling round pellets with the saliva from rabid dogs as a weapon to make the bullet more effective.

Slide 18

There was an outbreak of smallpox at a British fort during the French and Indian War. Fort Pitt is depicted here in this slide.
Intentional Use of Smallpox

• 1763 smallpox at Fort Pitt
• Correspondence to “reduce” Native American tribes
• What they did
• Disadvantage #4??

During this smallpox outbreak at Fort Pitt, Sir Jeffrey Amherst, who was the commander of British forces in North America, formulated a plan to “reduce,” as he so clinically expressed it, the size of the Native American tribes that were hostile to the crown. In general, during a smallpox epidemic, handkerchiefs and blankets used by the victims were burned because they could be a mode of transmission for this disease. In this situation, however, some blankets and a handkerchief were collected. On June 24, 1763, one of Amherst’s subordinates, Captain Ecuyer, ceremoniously gave the blankets and one handkerchief to the Delaware tribe after inviting leaders of the tribe to confer at the Fort. How we know this happened was by several lines of correspondence, in particular, one that said “out of our respect for them, we gave them 2 blankets and a handkerchief from the smallpox hospital”. An entry from Ecuyer then states “I hope it will have the desired effect.” We ask the question, “was smallpox in native Americans the result of biological warfare or a naturally occurring disease in a non-immune population?” Certainly, in this instance, there was a deliberate attempt to infect this native American tribe with smallpox, and that did occur. The use of inanimate objects, or fomites, to transmit smallpox, although it can happen, is not very efficient. However, we also have to be aware that Europeans coming across to America brought many rash illnesses including measles, rubella, varicella, and smallpox to a virtually non-immune population. This again illustrates Disadvantage #4 of a naturally occurring disease that was brought over from the Europeans to the Native Americans who were not immune to this. A devastating decrease in their population occurred, but how much of this was intentional is difficult to ascertain.

Contaminating Water Supplies

During the Civil War, we have a similar episode to that which occurred between 400 and 600 B.C. We have Confederate General Joseph E. Johnston who used a strategy of driving farm animals into the drinking supplies of the Union Army, shooting these animals and leaving their putrefied bodies to contaminate the water from further consumption. We know this happened because in the journal of Union General William Sherman, there are references to having to “remove the stinking carcasses from the water supplies”.

Alleged Plot to Infect Union Army

Dr. Luke Blackburn was a worldwide expert in yellow fever, working in the Caribbean to quell an outbreak of this disease. He concocted a plot to contaminate clothing used by the Union Army with smallpox and yellow fever. The evidence for this plot comes from signed affidavits from clients who were contracted to deliver trunks of this contaminated clothing, and a journal entry from a union army soldier talking about soldiers who had died from contaminated clothing.
The efforts of Johnston and Blackburn were difficult to quantify, illustrating disadvantages #1 and the fact that more soldiers died of disease during the Civil War than on the battlefield. This also illustrated disadvantage #4.

The third pandemic of the plague occurred starting in the 1860’s into the 1900’s. It began in China, killing over 12 million people in China and India alone and virtually spread to all inhabited continents. The picture on this slide is from the Glass-works temporary hospital during the Hong Kong bubonic plague in 1894.

We will now discuss biological warfare use in the 20th century. This discussion will include the German program in WWI, Japan and Great Britain's programs in WWII, the start of the U.S. biological program and the Soviet biological weapons programs.

In 1915, there was a plot by the Germans to use 2 diseases, anthrax and glanders, to infect horses and cattle. The very first attempt to use these agents was from Erich von Steinmetz, who came over from Germany on a boat disguised as a woman, carrying a vial containing glanders. The organisms did not survive, and therefore the first attempt to infect using BW failed. In 1915, Dr. Anton Dilger together with his brother Carl, in Chevy Chase, Maryland, had a laboratory which has been referred to as “Tony's lab”. They cultivated anthrax and glanders for use as biological weapons against the U.S. It has also been reported that a Captain Frederic Hinsch provided materials to infect 3,000 animals. In this attempt, it is reported that several hundred military personnel were secondarily infected.

The 1915 start of the 20th Century credited the Germans with an Anti-animal Bioweapons Program. This program is very poorly documented and very much debated, but there are recorded instances of anthrax in animals and as well as glanders at this time. This illustrates disadvantage #1, the difficulty of determining effectiveness of a clandestine operation using biological warfare.
During the influenza pandemic of 1918, as we learned in the first class, from 30 to up to 100 million people worldwide were killed. What many people don’t realize is that this is greater than more than 4 years of the Black Death’s mortality. And we also know that the highest mortality rate was in those aged 20 - 34. Why we have as a bullet point questionable BW was that some texts will state that the Germans were suspected to have engineered and released this virus to cause this influenza pandemic. This is highly unlikely however, as the technology of the time was not that advanced, but I list it here because it was questioned in several texts.

Next we will discuss BW used in WWII. Let’s begin by describing Japan’s biological weapons program. Japan’s program consisted of 150 buildings in 5 camps and approximately 3,000 staff members. This program conducted biological and chemical warfare in Manchuria between the years 1942-1945. It had 2 units most famous in historical perspective for this topic. First was Unit 731. It had a false name, which was “the Epidemic Prevention and Water Purification Department of the Kwantung Army”, when its real purpose was to prepare for the potential use of BW agents that might occur against the Japanese people. The second unit, #100, had a false name, “the Department of Veterinary Disease Prevention of the Kwantung Army”, when in fact its purpose was to ready the use of BW.

Japan’s Unit 731 consisted of activities with numerous biological agents against prisoners. These agents included anthrax, meningitis, shigella, cholera and plague. It’s estimated that more than 3,000 prisoners died following experimentation with these agents.

Unit 100’s activities included field trials, up to 12, of weaponized biological agents. It’s estimated that up to 11 Chinese cities were attacked and in these attacks it included contaminating food and water supplies. The leader of Japan’s program was Dr. Shiro Ishii. He was known for inventing a ceramic water filter to purify water and he was a world traveled physician.

In 1941, there was an attack on Changteh using cholera, resulting in 10,000 cases. In this same attack, it is estimated that 1,700 deaths occurred among Japanese troops. This illustrates the 2nd disadvantage of using BW and that is the difficulty in protecting one’s own troops from whatever agent is being used.
There was a very unique use of plague as a BW in the Japanese program. In the laboratory, fleas were fed on rats that had been infected with plague. These fleas, up to 15 million, were then released over China. Although complete bacteriological and epidemiological data are not available, there are historical records of increased #s of animals and people who died from plague at that time. Because plague was also naturally occurring from the 3rd pandemic, and the fact that this was also a clandestine effort, it illustrated disadvantages #1 and #4 about BW use. The unique way that the fleas were released related back to Dr. Shiro Ishii’s invention of the ceramic water filter. In these filters they put grain and fleas and released them from planes that were flying low. The balls would then break open on the ground. Animals would feed on the grain and the fleas would infect the animals and subsequently the people caring for the animals.

Luckily, Unit 731 did come to an end, but it’s an interesting way that that happened. The physical structure was captured by the Soviets. Unfortunately, the Japanese executed the remaining 150 prisoners before this happened. The U.S. captured both Dr. Shiro Ishii and his 2nd in command, Dr. Misaji. In this whole episode, only 9 medical staff out of almost 3,000 employees were convicted. No other senior official was charged, and you may wonder why. The reason is that these officials were granted immunity in exchange for their information, which helped to form the basis for the U.S. BW program.

The exterior remains of Unit 731 can be seen in this picture.

Great Britain had their own BW program located in Porton Down. They secretly developed this program and the area they used to test these agents was known as Gruinard Island. This island was located off the Scottish coast. In 1943, while testing the dispersal of anthrax on Gruinard Island, there was an outbreak of anthrax in sheep and cattle on the nearby coast of Scotland, facing that island. When you ask experts today, it’s questionable whether this area has been completely decontaminated, because as you know, anthrax spores can live in the soil, and depending on how deep you dig, under areas where hooved animals lived, you might always be able to find anthrax spores.

This episode illustrates disadvantage #3 from using BW. When using BW in a remote area, it is difficult to decontaminate that area after exposure.

Operation Anthropoid was a 1942 British plot to assassinate Reinhard Heydrich, the person credited with the idea of using cyanide to exterminate the Jewish population and who many thought Hitler was grooming to be his predecessor. Some Czech patriots went over to Britain for several months and then were parachuted back into Czechoslovakia. They observed Reinhard's movements and travel patterns over several weeks. When he drove with his top up, there was a signal and when he drove with his top down there was a signal, which was in the form of someone in the group having their hat on or off. The idea was to attack Reinhard when the top was down in his car. One day, the time was right, the top was down, and he was only with his driver, so the signal was given and someone in the group came and stood in front of the car as it came around the corner with a submachine gun. Unfortunately, the submachine gun jammed so plan B was to throw a grenade into the car. This happened, ripping off the door and sending shrapnel into Reinhard, but he was not originally considered very ill.

However, a few days later, his condition worsened and he died. The grenade used against Reinhard weighed about 1 lb, whereas a regular grenade weighs about 4 pounds. It is suspected that perhaps the botulinum toxin was used in the grenade. At that time, the director of Porton Down was a Dr. Paul Fildes, and he is known, according to an affidavit of one of his workers, to have said “I had a hand in Heydrich’s death, he was the first notch on my pistol”. Unfortunately, the files on this case are still sealed so we may not know the whole story for quite some time.

Unfortunately, Hitler was enraged by this assassination and retaliation included attacking several thousand in the town of Lidice, Czechoslovakia immediately after Reinhard’s funeral resulting in the death of thousands of people.
During WWII, Germany was known to forcibly infect prisoners with different agents including *Rickettsia*, *Plasmodia*, typhus, and hepatitis A. In this picture is a victim that during that time had an unknown substance injected into one of his eyes. Although the purpose of Germany’s program during this time was to develop vaccines and drugs, they are still known to have experimented, particularly under Dr. Joseph Mengele with different biological agents and on twins. The purpose was not to weaponize agents.

Now let’s talk about the U.S. Offensive BW program. Beginning in 1942, Camp Detrick, MD became a U.S. bioweapons facility. At that time it employed about 3,900 army, navy and civilian personnel and consisted of 4 different program divisions for different biological agents. The 4 plants to produce BW consisted first of Plant 1 to produce botulinum toxin. Interestingly, this plant was under contract with Great Britain and thus strengthens the theory that the attack against Reinhard Heydrich was a British plot. Pilot plant 2 produced a simulant to anthrax, one with the same genus, but did not produce disease like *Bacillus anthracis* does, but to be able to test to see the properties of anthrax. Plant 3 produced pathogens against plants, and plant 4 against animals including brucellosis and psittacosis. In addition, there was a large production facility in Indiana, which today is a pharmaceutical company. The picture from the Textbook of Military Medicine, shows one of the buildings at Camp Detrick. The other shows the entrance gate.

This slide shows photos of the BW program, also taken from the Textbook of Military Medicine. On the left, we have a picture of a biological safety cabinet, whose design has changed very little since that time. Workers would insert their arms into large gloves and negative air would remove the air away from those working there. The picture on the right shows workers at one of the plants inoculating eggs, which was a very time consuming activity, with brucellosis or psittacosis.

The U.S. Biological Warfare/Weapons program conducted several activities. One, they investigated use of anthrax, botulism, tularemia, plague, Q fever, Venezuelan Equine encephalitis, brucellosis, & Staphylococcus enterotoxin B. The U.S. Program conducted animal & human studies. They also tested the aerosolization & “dispersal” methods for biological agents in U.S. cities.
On this slide, is a structure called the “Eight-Ball”, a 1 million liter, hollow metallic sphere used to test vaccines and other agents on military and civilian volunteers. The scientists would stand on the outside and the subjects would be on the inside of this large sphere. The building around the Eight Ball burned down but the Eight Ball still stands today (see the photo on the bottom right).

During this time, there were some conscientious objectors approached by the U.S. war service because of some very desirable physical characteristics of a group known as the 7th Day Adventists. The desirable characteristics were that they refrained from tobacco, alcohol and caffeine making them very physically fit. They were asked to be part of the war effort by volunteering to be part of Q-fever tests to test both the efficacy of the vaccine and the antibiotic treatment of this disease. These tests were conducted in Utah at a place called Dugway Proving Ground. This experiment was known as “Operation Whitecoat”, and the first experiment, 30 volunteers were infected with Q-fever after either receiving a placebo or a vaccine. They were then put in isolation and those that developed Q-fever were given antibiotics. There were no fatalities from this experiment and from it we were able to determine what vaccine efficacy was and also what doses of antibiotics were needed to treat Q-fever.

During the development of the U.S. biological weapons program, there were instances of the release of supposedly harmless organisms to simulate what would happen if deadly ones were released. In the 1950s, *Serratia marcescens*, a bacteria which is known by its characteristic orange color, was released from a naval ship in the San Francisco Bay. In 1966, a simulant of *Bacillus anthracis*, called *Bacillus subtilis*, was dropped out of light bulbs into the NYC subway to see how long that would take to disperse through the system. In that instance, it took 10-20 minutes. There are other instances of dispersal and many are just becoming known in the U.S. public in the past few years.

Shortly after this time, there was an outbreak of *Serratia* at Stanford hospital involving 11 cases and 1 death. Also, after the release of a simulant into the Gulf of Mexico, there was an increase in cases of pneumonia in Alabama and Key West. These instances illustrate disadvantage #2, the difficulty of protecting your own troops or citizens when there is a release of an agent.
This slide illustrates figures that were kept on the U.S. biological weapons program. They had 456 occupational infections that occurred between 1943 and 1969. This was put into a formula of less than 10 infections per 1 million hours worked. There were also 3 fatalities: 2 from anthrax that happened in 1951, and one caused by Bolivian Hemorrhagic fever that occurred in 1964. Both of these were at Ft. Detrick. At the other testing sites, including Dugway Proving Ground, there were 48 occupational infections and no fatalities.

During the Vietnam war, it is suspected that Agent Orange and other herbicides and chemical weapons were used. This lecture is only covering biological agents, so it is not to argue that this activity occurred. However, the biological agent used at that time was Punji sticks. These were sharpened bamboo sticks that were placed in pits and contaminated with fecal material, so that soldiers and civilians would step on these and get very ill or die from infections from these puncture wounds.

In 1973, a treaty prohibiting the stockpiling of biological agents for offensive military purposes and research was signed by 103 nations. These nations included Iraq and the former Soviet Union. It was also built into this treaty that if violations were suspected, the security council could inspect facilities and they could also veto the inspection of facilities suspected to violate this treaty.

It is important to point out that as of today, the U.S. program is considered a defensive program against potential biological weapon use. It has been a defensive program since 1969, and as such, it is considered an open institution, not classified. Its acronym is USAMRID, or United States Army Medical Research Institute of Infectious Diseases. USAMRIID follows a strict program to ensure the safety of the biological materials they work with and the personnel who work with those materials. The **biological safety** component emphasizes safety training, risk management, environmental surveillance, and occupational health screening. **Physical security** refers to multiple security layers to allow only authorized employees to access areas in which biological materials are stored or used. **Personnel Reliability** refers to the requirement that all individuals with access to biological materials meet the highest standard of reliability, including completion of medical screening, safety training, and background investigations. Lastly, the **agent accountability** component involves inventory control, shipping, transfer and destruction records, and observation of laboratory procedures.
These pictures show the United States Army Research Institute of Infectious Diseases or USAMRIID as it appears today in Maryland. On the bottom left, at USAMRIID, is someone on a stretcher that is a self-contained isolation unit, being transferred into a BSL-4 (Biosafety level 4), the highest level isolation suite.

Now let’s talk about the Soviet BW program. Note that this program, whose name was Biopreparat, began in 1973, which is when they signed the 1972 treaty. This facility contained 6 research and 5 production facilities, and is estimated to have between 55,000 to up to 70,000 scientists. Its chief purpose was to carry out offensive BW research and development and this was concealed behind a civilian biotech research façade.

In this picture, the building on the left, Compound 19, was a biological agent production facility. The picture in the center is the headquarters of Biopreparat located in a residential district in Moscow. Although blurry in this illustration on the top right, the important thing is that every black speck is a separate biological production facility at Biopreparat. Products included agents such as anthrax, Marburg hemorrhagic fever, smallpox, plague, tularemia and Venezuelan Equine Encephalitis (VEE).

As would be expected in a facility of this size, accidents happen. The first occurred in 1971, in the town of Aralsk, in the former Soviet Republic, now known as Kazakhstan. A research scientist, working on a ship in the Arial Sea became ill, returned to the mainland and was found to have smallpox. Her brother and 8 others came down with this illness. The Soviet Ministry of Defense, unknown to the public at this time, used “Voz” Island, as it was called, as a site for biological warfare field testing of smallpox. This accident resulted in 10 cases and 3 fatalities, but we may never know the full scope of this situation. An analysis of this outbreak can be found in the reference listed on this slide.

The 2nd accident occurred in Sverdlovsk in 1979 at an anthrax production facility. There is more information on the following 2 slides regarding the accidental release of anthrax in the Sverdlovsk episode.

On this slide is an epidemic curve of the onset of anthrax cases in Sverdlovsk. Between April-May 1979, there were 79 infections and 66 deaths, with an 86% mortality rate.
The original claim about this event was that it was the result of contaminated meat ingestion. It was not until 13 years later that Yeltsin admitted that it was an accidental aerosol release. The cause of this outbreak was the failure to replace a filter that had been removed at the change of shift. The final death toll for the accident was recoded as approximately 200, but may reach numbers of 1,000 or more. This is also a situation where we may never know the whole story.

In this slide, there are 2 aerial maps. The one on the left goes out as far as 10 km and you can see that the line still continues. This is to show that animal cases of anthrax occurred in a line pattern up to 10 km out from Sverdlovsk production facility. The picture on the right, which also doesn’t end with the line, shows the # of human cases, again in a line, up to 1 km from the production facility.

In summary, we began by defining biological warfare. We then outlined how different countries, including our own, have used biological warfare or weapons. We will focus on bioterrorism in the next lecture.

There are numerous on-line resources and journal articles on this topic. Probably one of the best references that I can recommend are the Textbooks of Military Medicine, available on-line. Within those textbooks, I recommend “Medical Aspects of Biological Warfare”. It is updated on a regular basis. Your third Supplemental Reading is from that text. This concludes the lecture entitled “Historical Perspective on Biological Warfare”.