

ANBI 139

Evolution of Human Disease

Lecture 11: Disease as weapons



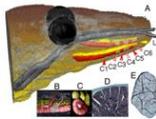
Pascal Gagneux

Spring 2019

Animal bioweapon? Komodo dragon



Killing prey via bacterial sepsis or venom or both



recently discovered venom gland



Komodo dragons, a giant species of monitor lizard use bacterial inoculation via biting to kill tigger large animal prey that include adult water buffaloes. More recently, the existence of a venom gland in their mouth has also been reported: biological and chemical weapons for hunting!

Early biowarfare: rams infected with Tularemia

14th century BC:
Hittite (Phillistine) plague, rams infected with Tularemia (*F. tularemia*)?



Warring parties used infected animals to spread the bacterial disease to enemies in the 14th century BC!!!

Early biowarfare: Scythian poisoned arrows

During the 4th century BC Scythian archers tipped their arrow tips with snake venom, human blood, and animal feces to cause wounds to become infected.



Making arrows more deadly by contaminating arrow heads also has a long history.

Early Biowarfare: plague victims catapulted into city of Caffa (Feodosia) by Tartars

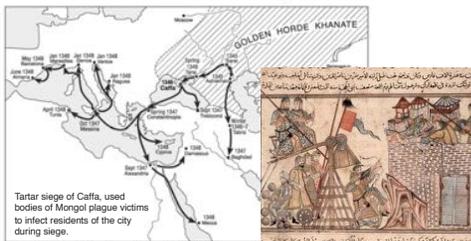


Figure 1. Tentative chronology of the initial spread of plague in the mid-14th century (12-14).

Practice question:

Describe some early forms of human biowarfare:

catapulting corpses of plague victims into besieged cities, dipping arrows in dead things....

Early biowarfare: more examples

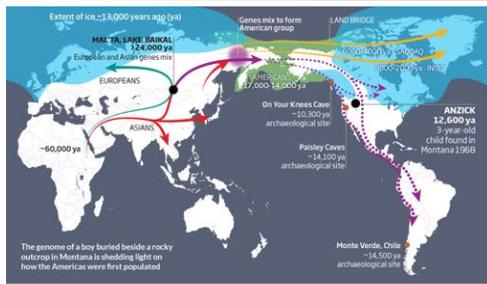
Table 1 | Examples of biological warfare during the past millennium

Year	Event
1153	Emperor Barbarossa poisons water wells with human bodies, Bartonia, Italy
1346	Mongols catapult bodies of plague victims over the city walls of Caffa, Crimean Peninsula
1485	Spanish mix wine with blood of leprosy patients to sell to their French foes, Naples, Italy
1650	Polish fire saliva from rabid dogs towards their enemies
1675	First duel between German and French forces not to use 'poison bullets'
1763	British distribute blankets from smallpox patients to native Americans
1797	Napoleon floods the plains around Mantua, Italy, to enhance the spread of malaria
1863	Confederates sell clothing from yellow fever and smallpox patients to Union troops, USA

It is not clear whether any of these attacks caused the spread of disease. In Caffa, the plague might have spread naturally because of the catastrophic conditions in the beleaguered city. Similarly, the smallpox epidemics among Indians could have been caused by contact with settlers. In addition, yellow fever is spread only by infected mosquitoes, making their transport of South America, the Spanish might also have used mosquitoes as a weapon. Nevertheless, the unintentional spread of disease among native Americans killed about 90% of the pre-colonial population (FA/NCIS, 1976).

Poisoning wells, poisoning bullets, contaminated blankets etc....

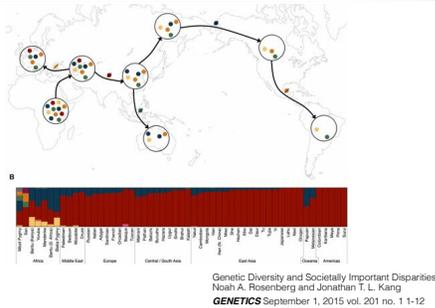
Americas: most recently settled continents



Recent founder events for the native Americans meant relatively low genetic and immunological variation. This caused an important liability for native Americans after the arrival of many novel disease agents to which their populations had never been exposed before.

The first humans to arrive in the Americas left Asia long before the development of farming some 15,000 years BP.

Limited variation in Native American gene pool



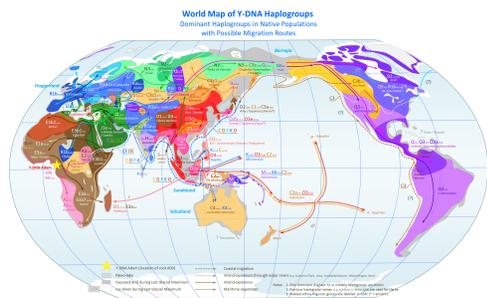
Reduction in genetic diversity due to successive founder events on the way to America.

Practice question:

How did the genetics of Native American put them at a disadvantage in the face of newly imported infections?

Their gene pool was limited due to bottlenecks associated with the settlement of the continents.

Limited variation in Native American gene pool



Y-chromosome haplogroup (unique combinations of genetic variants grouped together along the Y-chromosome) illustrate the relative lack of genetic diversity in the Americas, due to recent arrival and founder events.

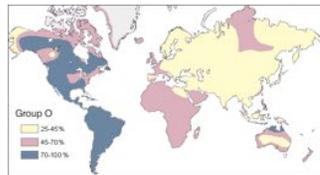
Early Native Americans locally



9.5 thousand year old double burial on the UC San Diego Chancellor Mansion.

Limited variation in Native American gene pool

Bottleneck: dramatic loss of population due to migration (founder event) or disease



Example:

Almost complete fixation of loss-of function mutation resulting in hist-blood group O in native American populations.

Reduced genetic diversity is also apparent in native Americans given the high (almost fixed) rate of ABO hist-blood group O. This is the type caused by a loss-of-function mutation in the gene encoding the ABO-transferase enzyme.

The Columbian Catastrophe



Columbus at Hispaniola, from *The Narrative and Critical History of America*, edited by Justin Winsor, London, 1886.



Theodor de Bry, "Negotiating Peace With the Indians," 1634 / Virginia Historical Society

Smallpox, measles, influenza, typhus (typhus fever), typhoid fever, scarlet fever, trachoma, chickenpox, whooping cough diphtheria, malaria, cholera, bubonic plague, gonorrhoea, leprosy.....

The only notable disease that was brought home from the Americas by Europeans was Syphilis. We already discussed on how this new sexually transmitted disease might have evolved from a non-sexually transmitted skin infection, via the sexual behavior of Europeans arriving in the New World.

The Columbian Catastrophe

Far and away the deadliest killer was smallpox, the first documented New World outbreak occurring in the Caribbean in 1518. Spanish friars, reporting to King Charles V in January 1519, estimated that the disease had already killed nearly one-third of Hispaniola's Indians and had spread to Puerto Rico. In these earliest outbreaks, influenza probably accompanied the spread of smallpox.

Smallpox

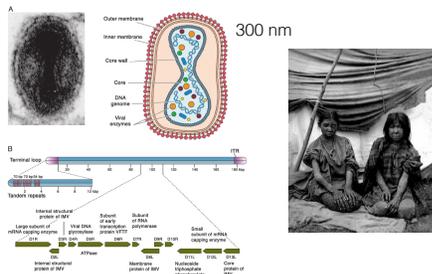


This drawing of victims of the smallpox epidemic that struck the Aztec capital of Tenochtitlan in 1520 is taken from the Florentine Codex.



The ravages of smallpox were so blatant that even the earliest Spanish settlers noticed and reported back to the King of Spain.

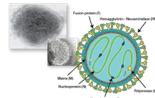
The Spanish agent: pox (variola) virus



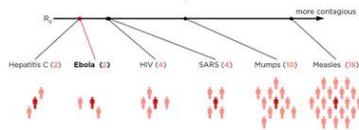
“Unintended bioweapon” that served the Spanish conquistadors very well.

The Columbian Catastrophe

Measles: among the most contagious viruses known



The number of people that one sick person will infect (on average) is called R_0 . Here are the maximum R_0 values for a few viruses.



Comparisons between reinfection rates of different viral diseases: Measles is one of the most infectious viruses known.

Practice Question:

What aspect of an infectious pathogen most determines if it will lead to an epidemic?

R_0 or R naught, the number of people that the infected person will in fact on average.

100,000 dead in one swoop of smallpox



Map of Tenochtitlán and the Gulf of Mexico, from *Praeclara Ferdinadi Cortesii de Nova maris Oceani Hyspania Narratio* by Hernando Cortes.
Newberry Library/Bridgeman Images

On the American mainland, the Conquistadores encountered thriving civilizations. The populations living in places like Tenochtitlan were immunologically ill-equipped and lacked the history of major animal husbandry that had already selected for diseases resistance in Europeans.

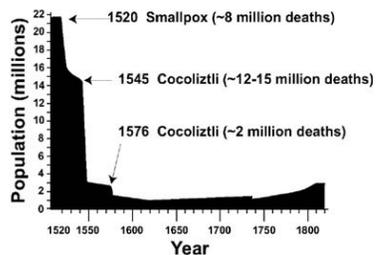
Infectious and violent Overkill



"The Torture of Cuauhtémoc", a 19th-century painting by Leandro Izaguirre

Many of those who did not perish from infections were brutally murdered.

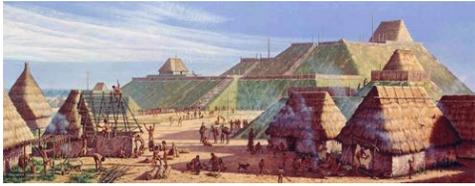
Population collapse in Mexico



Acosta-Soto, P., Soto-Olivares, M., Tenet, M. / *Emerging Infectious Diseases*, 2011, 17(11), 1998-2000.
Original caption: The 16th-century population collapse in Mexico, based on estimates of Cook and Simpson (1). The 1545 and 1576 cocoliztli epidemics appear to have been hemorrhagic fevers caused by an indigenous viral agent and aggravated by unusual climatic conditions. The Mexican population did not recover to pre-Hispanic levels until the 20th century.

Several documented super-epidemics in Central America, each with millions of deaths.

Cahokia, mound building city in Mississippi valley



its 10,000 inhabitants were long dead from disease by the time the Europeans arrived

Most farming societies were in the fertile area of Mesoamerica, especially the areas around modern Mexico (the Toltec, Maya, and Aztec) and Peru (Inca). In the last century, archaeologists have discovered similar, if smaller, mound-building cultures in the present-day U.S., in the Mississippi and Ohio River valleys. Most prominent among these is Cahokia, a settlement south of present-day St. Louis that had around 10k inhabitants.

The catastrophic impact of Euro diseases



Incolarum Virginiae piscandi ratio (The Method of Fishing of the Inhabitants of Virginia), c1590 / Encyclopedia Virginia

When the Europeans came over, they brought with them enough disease to wipe out between two thirds and 90% of people in the Americas over the next 150 years — the worst demographic catastrophe in history by a long stretch. While early diaries mentioned these epidemics in describing life in the 1500s and 1600, it wasn't until the 1960s that epidemiologists and historians realized the true scale of the death toll in the decades following Columbus's arrival.

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British smallpox blankets in America



In the 18th century, the British fought France and its Indian allies for possession of what was to become Canada during the French and Indian Wars (1754-63). At the time of the Pontiac rebellion in 1763, Sir Jeffrey Amherst, the Commander-in-Chief of the British forces in North America, wrote to Colonel Henry Bouquet: 'Could it not be contrived to send smallpox among these disaffected tribes of Indians? We must use every stratagem in our power to reduce them.' The colonel replied: 'I will try to inoculate the [Native American tribe] with some blankets that may fall in their hands, and take care not to get the disease myself.' Smallpox decimated the Native Americans, who had never been exposed to the disease before and had no immunity.

Ken Alibek of Soviet smallpox weapons program:

According to Alibek, one particularly virulent strain, India 67 or India 1, was chosen by the Russians to be weaponised. They perfected techniques for mass producing smallpox and maintained a rolling annual stockpile of hundreds of tonnes. They also developed ways to disseminate the virus in aerial bombs and ballistic missile warheads. Additional work was done to enhance the virulence of the virus and to combine it with other viruses.

White Man's Grave



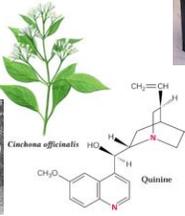
Most of tropical Africa was extremely deadly to Europeans

White man's grave, so called because most Europeans lasted but a few months before succumbing to African tropical diseases.

White Man's Grave



Missionaries in Benin. A group of European Christian missionaries pose with students in Porto-Novo, Benin, in this illustration from the History of the Catholic Missions (1852).



The discovery of jesuit bark, a traditional medicine from South America provided the necessary protection from malaria.

Practice question:

Which important medicine allowed white men to survive in White Man's Grave (West Africa)?

JESUIT BARK OR QUININE

Opium wars: using addictive drugs to recoup sterling silver



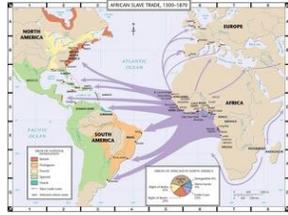
The East India Company steamship *Nemesis* (right background) destroying Chinese war junks during the Second Battle of Chuenpi, 7 January 1841

Addictive drugs can be "weaponized" from the British empire obtaining back its silver bullion all spent on Chinese tea to the Taliban growing poppies for heroin production today. Practice Question:

What are the arguments for and against opium as a bioweapon?

Opium itself doesn't kill or maim, but the drug exploits the strong tendency of most humans to get strongly addicted to its consumption.

Slave Trade



Practice question:

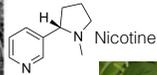
Name two important disease that were brought to the America with the slave trade:

falciparum Malaria and Yellow fever.

Revenge: Tobacco, the world's first global commodity



Lines of stones mark the remains of stone-washed buildings at La Isabela, Christopher Columbus's first attempt to establish a permanent base in the Americas.



Nicotine



6 to 8 million deaths a year globally!

Tobacco, first cultivated by Native Americans soon conquered the world and remains responsible for millions of deaths annually.

French bioweapons 1920s

Auguste Trillat



Used his contacts to the Pasteur Institute to study anthrax was a potential weapon.

In 1925, the signing of the Geneva Protocol banned the use of both chemical and bacteriological weapons.

UK bioweapons 1942 on, anthrax and sheep



Gruinard was the site of a biological warfare test by British military scientists from Porton Down in 1942, during the Second World War. At that time there was an investigation by the British government into the feasibility of an attack using anthrax. Given the nature of the weapon which was being developed, it was recognised that tests would cause widespread and long-lasting contamination of the immediate area by anthrax spores. To limit contamination, a remote and uninhabited island was required. Gruinard was surveyed, deemed suitable and requisitioned from its owners by the British Government. The anthrax strain chosen for the Gruinard bioweapons trials was a highly virulent type called "Vollum 14578", named after R. L. Vollum, Professor of Bacteriology at the University of Oxford, who supplied it. Eighty sheep were taken to the island and bombs filled with anthrax spores were exploded close to where selected groups were tethered. The sheep became infected with anthrax and began to die within days of exposure.

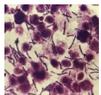
Test of weaponized bacteria in US cities

Medical experiments were conducted on a large scale on civilians who had not consented to participate. Often, these experiments took place in urban areas in order to test dispersion methods. Questions were raised about detrimental health effects after experiments in San Francisco, California in 1950, were followed by a spike in hospital visits; however, in 1977 the Centers for Disease Control and Prevention determined that there was no association between the testing and the occurrence of pneumonia or influenza. The San Francisco test involved a U.S. Navy ship that sprayed *Serratia marcescens* from the bay; it traveled more than 30 miles. One dispersion test involved laboratory personnel disguised as passengers spraying harmless bacteria in Washington National Airport.

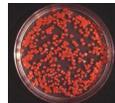
Scientists tested biological pathogens, including *Bacillus globigii*, which were thought to be harmless, at public places such as subways. Light bulbs containing *Bacillus globigii* were dropped in New York City's subway system; the result was strong enough to affect people prone to illness (also known as Subway Experiment). Based on the circulation measurements, thousands of people would have been killed if a dangerous microbe was released in the same manner.

in 1943, the USA began its official bioweapons program. It was supposed to have officially ended 27 years later in 1970.....

Test of weaponized bacteria in US cities



Serratia mrescens



Bacillus globigii (BG) has been called *B. subtilis* var *niger*, *B. licheniformis* and, most recently, *B. atrophaeus*. It is a Gram-positive, spore-forming, facultative anaerobe is commonly found in dust, soil and water. It is widely used as a biological tracer and has been shown to produce substances that exhibit antimicrobial activity. In Project SHAD, *B. globigii* was used to simulate biological warfare agents, because it was then considered a contaminant with little health consequence to humans.

Two bacterial species used to test bioweapon application on human populations in the USA between 1940s and 1970s.

Mustard Gas use in Italian Abyssinia.....



Pope Pius XII



During the Italian war on Ethiopia 1936-1941, Italy carried out a systematic mass extermination campaign in Ethiopia with poison gas sprayed from airplanes and other horrific atrocities that claimed the lives of no less than 1,000,000 Ethiopian men, women and children, including 30,000 massacred in only three days in Addis Ababa as well as the reprisal killings of the entire monastic community at the historic Debre Libanos Monastery. In addition, 2,000 churches and 525,000 homes were destroyed by the Italian fascists. These atrocities were carried out under the direct command of Graziani, known as the Butcher of Ethiopia. Graziani remained loyal to Mussolini until 1945 and served as the minister of defense of the puppet Italian Republic in Northern Italy and committed additional war crimes in North Africa.

Imperial Japan



Shirō Ishii, commander of Unit 731

Unit 731, *maruta* (丸太) "logs,"



Manchu Unit 731, operated by the Japanese Army during the WWII occupation of Manchuria was one of the darkest bioweapon programs. Unlike the human experiments conducted by Nazi Germany, those conducted in Unit 371 were never prosecuted as the US military struck a deal with the Japanese War criminals that guaranteed their immunity in exchange for the data from these experiments.

Practice question:

Which country tested and utilized bioweapons during world war II?
Imperial Japan

Operation PX against USA

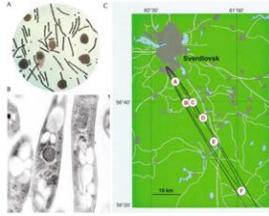


Japanese use of the code name PX for *Pseudo bacillus*-infected force

The plan for the attack involved *Seiran* aircraft launched by submarine aircraft carriers upon the United States West Coast – specifically, the cities of San Diego, Los Angeles, and San Francisco. The airplanes would spread weaponized bubonic plague, cholera, typhus, dengue fever, and other pathogens in a biological terror attack upon the United States. The submarine crews would infect themselves and run ashore in a suicide mission.

San Diego was one of the intended targets for a bioweapon attack towards the end of WWII.

Soviet Russia: Sverdlovsk & Biopreparat



Anthrax as a biological weapon. Light (A) and electron (B) micrographs of anthrax bacilli, reproduced from the Centers of Disease Control Public Health Image Library. The map (C) shows six villages in which animals died after anthrax spores were released from a bioweapons factory in Sverdlovsk, USSR, in 1979. Settled areas are shown in grey, roads in white, lakes in blue and the calculated contours of constant dosage of anthrax spores in black. At least 66 people died after the accident.

Escape from bioweapon lab



Olga Vyatkina visits the grave of her son, one of at least 66 people who died in the 1979 Sverdlovsk disaster in the Soviet Union. Anthrax genome reveals secrets about a Soviet bioweapons accident By Kai Kupferschmidt Aug. 16, 2016 , 9:45 PM

In 1917, an H1N1 influenza virus appeared and circled the globe. Colloquially referred to as the "Russian flu," as the USSR was the first to report the outbreak to the World Health Organization (WHO), the 1917 strain was actually isolated in Tianjin, Beijing, and Jin, China, almost simultaneously in May of that year (1).

Several governments have supported bioweapons research. Biological agents (pathogens) have accidentally escaped from such research facilities and killed droves of people.

USAMRIID and the Tai Forest

The United States started an offensive biological warfare program at Camp Detrick (today Fort Detrick) in Frederick, Maryland in 1943. Ten years later, the defensive program began. By 1969, the U.S. had weaponized the agents causing anthrax, botulism, tularemia, brucellosis, Venezuelan equine encephalitis, and Q fever.



1997 West Africa Scientifics from Fort Detrick



Fig. 27 The so-called 8-ball is a million-liter steel ball built in 1963 which still is kept around the perimeter of Fort Detrick. The ball is at Fort Detrick, Maryland, and is a historical monument. (See (2011) (see www.khanacademy.org))

The 8-ball, a structure used to test bioweapons on animals in Fort Detrick Maryland.

Scientists from Fort Detrick were present in the Tai Forest National Park in Côte D'Ivoire in 1997, when it became clear that the Ebola virus reservoir species must exist in that forest.

United States



hundreds of tests releasing "harmless" bacteria (*Bacillus globigii*, *Serratia marcescens*) over inhabited areas including SF, New York, Washington DC airport.



Fig. 17 The US Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland, is the center of the USCBW laboratory research on development of weapons. (© 2003 Jane's Intelligence Group)

South Africa: Project Coast 1981.....!!!!



Racial warfare program led by cardiologist Wouter Basson and the Black Bomb!

DATE	DESCRIPTION	STATUS	REMARKS
01-08-81	Vrijze shokker	10	bestaan
02-08-81	metast	10	bestaan
03-08-81	sporene & bakterie	10	bestaan
04-08-81	sporene & bakterie	10	bestaan
05-08-81	sporene & bakterie	10	bestaan
06-08-81	sporene & bakterie	10	bestaan
07-08-81	sporene & bakterie	10	bestaan
08-08-81	sporene & bakterie	10	bestaan
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26-08-81	sporene & bakterie	10	bestaan
27-08-81	sporene & bakterie	10	bestaan
28-08-81	sporene & bakterie	10	bestaan
29-08-81	sporene & bakterie	10	bestaan
30-08-81	sporene & bakterie	10	bestaan

The program was headed by Wouter Basson, a cardiologist who was the personal physician of the then South African Prime Minister P. W. Botha. Doctor Wouter Basson never went to jail.....despite his teams concerted effort to murder citizens of South Africa.

Project Coast was a 1980s top-secret chemical and biological weapons (CBW) program instituted by the apartheid-era government of South Africa. Project Coast was the successor to a limited post-war CBW program which mainly produced the lethal agents CX powder and mustard gas; as well as non-lethal tear gas for riot control purposes.

Aum shinrikyo 1995

Shoko Asahara and 12 accomplices placed sarin gas in Tokyo subway, killing 12, injuring 50 and causing temporary vision problems for 5000!

Group members had traveled to Zaire to try and obtain Ebola virus.



Asahara and his acolytes were sentenced to death by hanging in 2004, they were executed by hanging last year.

Bhagwan Shree Rajneesh, Osho



Salmonella enterica typhimurium on salad bars in Wasco County, Oregon, 1984 sickens over 700 individuals

Sheela Ambalal Patel



The sales bar of The Oasis, Oregon 'Osho' Time. Location of 1984 Rajneesh bioterror attack.



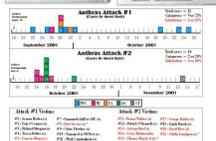
Indian philosophy professor turned liberation guru Rajneesh formed a giant cult that resorted to bioweapons to poison salad bars and sauces in Wasco County Oregon. All in an attempt to make people sick and thus preventing them from voting to oust the large compound occupied by Rajneesh, his disciples and his large Rolls Royce collection.

Practice question:

Can you name a religious group that used bioweapons?

The Rajneeshee movement in Oregon

Anthrax Mail courtesy of our military? (2001)



perpetrators still at large

Bruce Ivins, a bioweapons researcher for the US military committed suicide, but there still is no definite proof of who perpetrated several anthrax attacks by US postal service....

Summary

Infection can be used as a weapon, even by hunting lizards.....

There are old stories about intentionally infecting enemies, predating the notion of microbes..

Non-intentional infection is much more common.

The European conquest of the Americas introduced dozens of novel diseases that killed up to 90% of the native population: the largest epidemic die off in history.

Diseases can also protect people such as in West Africa (white man's grave).

Addictive drugs could be seen as a form of biological weapon (opium wars, ISIS/Taliban heroin production).

Several countries have dabbled in bioweapon development. Japan was first to use them, Russia and the USA had major programs.

The lunatic fringe (cults) have used bioweapons.

Bioweapons can easily turn against their makers.....

