Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Agent Blue
Date: 2012
Source: Wikipedia

Abstract: Agent Blue is one of the "rainbow herbicides" that is known for its use by the United States during the Vietnam War. It was sprayed on rice paddies and other crops in an attempt to deprive the Viet Cong of valuable crops. Agent Blue is a mixture of two arsenic-containing compounds, sodium cacodylate and cacodylic acid. Agent Blue is chemically unrelated to the more infamous Agent Orange and other herbicides used during the war.

As rice is incredibly durable, and difficult to destroy with conventional explosives, and does not burn, the weapon of choice was herbicides. Agent Blue affects plants by causing them to dry out. As rice is highly dependent on water to live, using Agent Blue on these paddies can destroy an entire field and leave it unsuitable for further planting.

Approximately 1.25 million US gallons (4,700 m3) of Agent Blue were used in Vietnam during the war, destroying 500,000 acres (2,000 km2) of crops.

Today, large quantities of the chemical named Agent Blue are still used on lawns and crops throughout the USA. Taken from ZNet Ecology:

"Arsenical herbicides containing cacodylic acid as an active ingredient are still used today as weed-killers. In the US they are used extensively, from golfcourses to backyards. They are also sprayed on cotton fields, drying out the cotton plants before harvesting. So common -- and so profitable -- is the original commercial form of Agent Blue that it was among 10 toxic insecticides, fungicides and herbicides partially deregulated by the US Environmental Protection Agency (EPA) in February 2004. Specific limits on toxic residues in meat, milk, poultry, and eggs were removed." (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Agent Green
Date: 2012
Source: Wikipedia

Abstract: Agent Green is the code name for a powerful herbicide and defoliant used by the U.S. military in its Herbicidal Warfare program during the Vietnam War. The name comes from the green stripe painted on the barrels to identify the contents. It was one of the so-called "rainbow herbicides" that included the more infamous Agent Orange. Agent Green was only used between 1962 and 1964, during the early "testing" stages of the spraying program.

Agent Green was mixed with Agent Pink and used for crop destruction. A total of 20,000 gallons of Agent Green were procured.[1]

Agent Green's only active ingredient was 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), one of the common phenoxy herbicides of the era. It was later learned that a dioxin, 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD), is produced as a side effect of the manufacture of 2,4,5-T, and was thus present in any of the herbicides that used it. Owing to Agent Green's consisting entirely of 2,4,5-T, along with the similar Agent Pink, it contained many times the level of dioxin found in Agent Orange.

The fungus Fusarium oxysporum is also referred to as Agent Green (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Agent Orange
Date: 2012
Source: Wikipedia

Abstract: Agent Orange is the code name for one of the herbicides and defoliants used by the U.S. military as part of its herbicidal warfare program, Operation Ranch Hand, during the Vietnam War from 1961 to 1971. It was given its name from the color of the orange-striped 55 US gallon (208 litre) barrels in which it was shipped, and was by far the most widely used of the so-called "Rainbow Herbicides". A 50:50 mixture of 2,4,5-T and 2,4-D, it was manufactured for the U.S. Department of Defense primarily by Monsanto Corporation and Dow Chemical. The 2,4,5-T used to produce Agent Orange was later discovered to be contaminated with 2,3,7,8-tetrachlorodibenzodioxin, an extremely toxic dioxin compound. Vietnam estimates 400,000 people were killed or maimed, and 500,000 children born with birth defects.

During the Vietnam War, between 1962 and 1971, the United States military sprayed nearly 20,000,000 US gallons (75,700,000 l) of chemical herbicides and defoliants in Vietnam, eastern Laos and parts of Cambodia, as part of Operation Ranch Hand. The program's goal was to defoliate forested and rural land, depriving guerrillas of cover; another goal was to induce forced draft urbanization, destroying the ability of peasants to support themselves in the countryside, and forcing them to flee to the U.S. dominated cities, thus depriving the guerrillas of their rural support base and food supply.

The US began to target food crops in October 1962, primarily using Agent Blue. In 1965, 42 percent of all herbicide spraying was dedicated to food crops. Rural-to-urban migration rates dramatically increased in South Vietnam, as peasants escaped the destruction and famine in the countryside by fleeing to the U.S.-dominated cities. The urban population in South Vietnam nearly tripled: from 2.8 million people in 1958, to 8 million by 1971. The rapid flow of people led to a fast-paced and uncontrolled urbanization; an estimated 1.5 million people were living in Saigon slums.

United States Air Force records show that at least 6,542 spraying missions took place over the course of Operation Ranch Hand. By 1971, 12 percent of the total area of South Vietnam had been sprayed with defoliating chemicals, at an average concentration of 13 times the recommended USDA application rate for domestic use. In South Vietnam alone, an estimated 10 million hectares of agricultural land were ultimately destroyed. In some areas TCDD concentrations in soil and water were hundreds of times greater than the levels considered "safe" by the U.S. Environmental Protection Agency. Overall, more than 20% of South Vietnam's forests were sprayed at least once over a nine year period.

Chemical Description & Toxicology
Chemically, Agent Orange is an approximately 1:1 mixture of two phenoxyl herbicides – 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) – in iso-octyl ester form.

Numerous studies have examined health effects linked to Agent Orange, its component compounds, and its manufacturing byproducts.

Prior to the controversy surrounding Agent Orange, there was already a large body of scientific evidence linking 2,4,5-T to serious negative health effects and ecological damage. But in 1969, it was revealed to the public that the 2,4,5-T was contaminated with a dioxin, 2,3,7,8-tetrachlorodibenzodioxin (TCDD), and that the TCDD was causing many of the previously unexplained adverse health effects which were correlated with Agent Orange exposure. TCDD has been described as "perhaps the most toxic molecule ever synthesized by man". Internal memoranda revealed Monsanto Corporation (a manufacturer of 2,4,5-T) had informed the U.S. government as early as 1952 that 2,4,5-T was contaminated with a toxic contaminant. In the manufacture of 2,4,5-T, accidental overheating of the reaction mixture easily causes the product to condense into the toxic self-condensation product TCDD. At the time, precautions were not taken against this unintended side reaction, which caused also the Seveso disaster in Italy in 1976. In addition to this, 2,4,5-T is hazardous in its own right.

In 1979, the Yale biologist Arthur Galston, who specialized in herbicide research, published a review of what was known at the time about the toxicity of TCDD. Even "vanishingly small" quantities of dioxin in the diet caused adverse health effects when tested on animals.[16] Since then, TCDD has been comprehensively studied. It has been associated with increased neoplasms in every animal bioassay reported in the scientific literature. The National Toxicology Program has classified TCDD as "known to be a human carcinogen", frequently associated with soft-tissue sarcoma, non-Hodgkin's lymphoma, Hodgkin's lymphoma and chronic lymphocytic leukemia (CLL).

While the two herbicides that make up Agent Orange, 2,4-D and 2,4,5-T, remain toxic over a short period—a scale of days or weeks—they quickly degrade.[citation needed] A 1969 report authored by K. Diane Courtney and others found 2,4,5-T could cause birth defects and stillbirths in mice. Several studies have shown an increased rate of cancer mortality for workers exposed to 2,4,5-T. In one such study, from Hamburg, Germany, the risk of cancer mortality increased by 170% after working for 10 years at the 2,4,5-T-producing section of a Hamburg manufacturing plant. Three studies have suggested prior exposure to Agent Orange poses an increased risk of acute myelogenous leukemia in the children of Vietnam veterans.

Starting in 1991, the US Congress asked the Institute of Medicine to review the scientific literature on Agent Orange and the other herbicides used in Vietnam, including their active ingredients and the dioxin contaminant. The IOM found an association between dioxin exposure and diabetes.

Early Development
In 1943 plant biologist Arthur Galston began studying the compound triiodobenzoic acid as a plant growth hormone, in an attempt to adapt soybeans to a short growing season. Galston found that excessive usage of the compound caused catastrophic defoliation — a finding later used by his colleague Ian Sussex to develop the family of herbicides used in Operation Ranch Hand. Galston was especially concerned about the compound's side effects to humans and the environment.

In 1943, the U.S. Department of the Army contracted the University of Chicago to study the effects of 2,4-D and 2,4,5-T on cereal grains (including rice) and broadleaf crops. From these studies arose the concept of using aerial applications of herbicides to destroy enemy crops to disrupt their food supply. In early 1945, the U.S. army ran tests of various 2,4-D and 2,4,5-T mixtures at the Bushnell Army Airfield in Florida, which is now listed as a Formerly Used Defense Site (FUDS).

Use in the Vietnam War
During the Vietnam War, between 1962 and 1971, the United States military sprayed nearly 20,000,000 US gallons (75,700,000 l) of chemical herbicides and defoliants in Vietnam, eastern Laos and parts of Cambodia, as part of the aerial defoliation program known as Operation Ranch Hand. The goal was to defoliate rural/forested land, depriving guerrillas of food and cover and clearing in sensitive areas such as around base perimeters. The program was also a part of a general policy of forced draft urbanization, which aimed to destroy the ability of peasants to support themselves in the countryside, forcing them to flee to the U.S. dominated cities, depriving the guerrillas of their rural support base.

Spraying was usually done either from helicopters or from low-flying C-123 Provider aircraft, fitted with sprayers and "MC-1 Hourglass" pump systems and 1,000 US gal (3,800 L) chemical tanks. Spray runs were also conducted from trucks, boats, and backpack sprayers.

The first batch of herbicides was unloaded at Tan Son Nhut Air base in South Vietnam, on January 9, 1962. Air Force records show at least 6,542 spraying missions took place over the course of Operation Ranch Hand. By 1971, 12 percent of the total area of South Vietnam had been sprayed with defoliating chemicals, at an average concentration of 13 times the recommended USDA application rate for domestic use. In South Vietnam alone, an estimated 10 million hectares of agricultural land were ultimately destroyed. In some areas, TCDD concentrations in soil and water were hundreds of times greater than the levels considered safe by the U.S. Environmental Protection Agency.

The campaign destroyed 5 million acres (20,000 km2) of upland and mangrove forests and millions of acres of crops. Overall, more than 20% of South Vietnam's forests were sprayed at least once over a nine year period.

In 1965, members of the U.S. Congress were told "crop destruction is understood to be the more important purpose ... but the emphasis is usually given to the jungle defoliation in public mention of the program." Soldiers were told they were destroying crops because they were going to be used to feed guerrillas. They later discovered nearly all of the food they had been destroying was not being produced for guerrillas; it was, in reality, only being grown to support the local civilian population. For example, in Quang Ngai province, 85% of the crop lands were scheduled to be destroyed in 1970 alone. Widespread famine occurred as a result, leaving hundreds of thousands of people malnourished or starving.

The U.S. military began targeting food crops in October 1962, primarily using Agent Blue; the American public was not made aware of the crop destruction programs until 1965 (and it was then believed that crop spraying had begun that spring). In 1965, 42 percent of all herbicide spraying was dedicated to food crops. The first official acknowledgement of the programs came from the State Department in March 1966.

Many experts at the time, including Arthur Galston, the biologist who developed and intensively studied TCDD, opposed herbicidal warfare, due to concerns about the side effects to humans and the environment by indiscriminately spraying the chemical over a wide area. As early as 1966, resolutions were introduced to the United Nations charging that the U.S. was violating the 1925 Geneva Protocol, which regulated the use of chemical and biological weapons.

Effects on the Vietnamese People

Health Effects

The Vietnam Red Cross reported as many as 3 million Vietnamese people have been affected by Agent Orange, including at least 150,000 children born with birth defects. According to Vietnamese Ministry of Foreign Affairs, 4.8 million Vietnamese people were exposed to Agent Orange, resulting in 400,000 people being killed or maimed, and 500,000 children born with birth defects. Women had higher rates of miscarriage and stillbirths, as did livestock such as cattle, water buffalo, and pigs.

Children in the areas where Agent Orange was used have been affected and have multiple health problems, including cleft palate, mental disabilities, hernias, and extra fingers and toes.[37] In the 1970s, high levels of dioxin were found in the breast milk of South Vietnamese women, and in the blood of U.S. soldiers who had served in Vietnam. The most affected zones are the mountainous area along Truong Son (Long Mountains) and the border between Vietnam and Cambodia. The affected residents are living in substandard conditions with many genetic diseases.

About 28 of the former US military bases in Vietnam where the herbicides were stored and loaded onto airplanes may still have high level of dioxins in the soil, posing a health threat to the surrounding communities. Extensive testing for dioxin contamination has been conducted at the former US airbases in Da Nang, Phu Cat and Bien Hoa. Some of the soil and sediment on the bases have extremely high levels of dioxin requiring remediation. The Da Nang Airbase has dioxin contamination up to 350 times higher than international recommendations for action. The contaminated soil and

sediment continue to affect the citizens of Vietnam, poisoning their food chain and causing illnesses, serious skin diseases and a variety of cancers in the lungs, larynx, and prostate.

Ecological Effects
About 17.8% (3,100,000 ha) of the total forested area of Vietnam was sprayed during the war, which dramatically disrupted ecological equilibrium. Furthermore, the persistent nature of dioxins, erosion caused by loss of protective tree cover, and loss of seeding forest stock, meant reforestation was difficult or impossible in many areas. Many defoliated forest areas were quickly invaded by aggressive pioneer species, such as bamboo and cogon grass, which make it unlikely the forests will be able to regenerate. Animal species diversity was also significantly impacted: in one study, a Harvard biologist found 24 species of birds and 5 species of mammals in a sprayed forest, while in two adjacent sections of unsprayed forest there were 145 and 170 species of birds and 30 and 55 species of mammals.

Dioxins from Agent Orange have persisted in the Vietnamese environment since the war, settling in the soil and sediment and entering into food chain through the animals and fish that feed in the contaminated areas. Movement of dioxins through the food web has resulted in bioconcentration and biomagnification. The areas most heavily contaminated with dioxins are the sites of former U.S. air bases.
Sociopolitical Effects

The RAND Corporation's Memorandum 5446-ISA/ARPA states: "the fact that the VC obtain most of their food from the neutral rural population dictates the destruction of civilian crops ... if they (the VC) are to be hampered by the crop destruction program, it will be necessary to destroy large portions of the rural economy – probably 50% or more".

Rural-to-urban migration rates dramatically increased in South Vietnam, as peasants escaped the destruction in the countryside by fleeing to the U.S.-dominated cities. The urban population in South Vietnam nearly tripled, growing from 2.8 million people in 1958 to 8 million by 1971. The rapid flow of people led to a fast-paced and uncontrolled urbanization; an estimated 1.5 million people were living in Saigon slums.

Effects on U.S. Veterans
Studies showed that veterans who served in the South during the war have increased rates of cancer, and nerve, digestive, skin and respiratory disorders. Veterans from the south had higher rates of throat cancer, acute/chronic leukemia, Hodgkin's lymphoma and non-Hodgkin's lymphoma, prostate cancer, lung cancer, colon cancer, soft tissue sarcoma and liver cancer. Other than liver cancer, these are the same conditions the US Veteran's Administration has found to be associated with exposure to Agent Orange/dioxin, and are on the list of conditions eligible for compensation and treatment.

Military personnel who loaded airplanes and helicopters used in Ranch Hand probably sustained some of the heaviest exposures. Members of the Army Chemical Corps, who stored and mixed herbicides and defoliated the perimeters of military bases, and mechanics who worked on the helicopters and planes, are also thought to have had some of the heaviest exposures. Others with potentially heavy exposures included members of U.S. Army Special Forces units who defoliated remote campsites, and members of U.S. Navy river units who cleared base perimeters. Military members who served on Okinawa also claim to have been exposed to the chemical.

While in Vietnam, the veterans were told not to worry, and were persuaded the chemical was harmless. After returning home, Vietnam veterans began to suspect their ill health or the instances of their wives having miscarriages or children born with birth defects might be related to Agent Orange and the other toxic herbicides to which they were exposed in Vietnam. Veterans began to file claims in 1977 to the Department of Veterans Affairs for disability payments for health care for conditions they believed were associated with exposure to Agent Orange, or more specifically, dioxin, but their claims were denied unless they could prove the condition began when they were in the service or within one year of their discharge.

By April 1993, the Department of Veterans Affairs had only compensated 486 victims, although it had received disability claims from 39,419 soldiers who had been exposed to Agent Orange while serving in Vietnam.

Legal & Diplomatic Proceedings

US Veterans Class Action Lawsuit against Manufacturers

Since at least 1978, several lawsuits have been filed against the companies which produced Agent Orange, among them Dow Chemical, Monsanto, and Diamond Shamrock.

Hy Mayerson of the law firm The Mayerson Law Offices, P.C. was an early pioneer in Agent Orange litigation, working with renowned environmental attorney Victor Yannacone in 1980 on the first class-action suits against wartime manufacturers of Agent Orange. In meeting Dr. Ronald A. Codario, one of the first civilian doctors to see afflicted patients, Mayerson, so impressed by the fact an M.D. would show so much interest in a Vietnam veteran, forwarded more than a thousand pages of information on Agent Orange and the effects of dioxin on animals and humans to Codario's office the day after he was first contacted by the doctor. The corporate defendants sought to escape culpability by blaming everything on the U.S. government.

The Mayerson Law Offices, P.C., with Sgt. Charles E. Hartz as their principal client, filed the first Agent Orange class action lawsuit, in Pennsylvania in 1980, for the injuries soldiers in Vietnam suffered through exposure to toxic dioxins in the Agent Orange defoliant. Attorney Hy Mayerson co-wrote the brief that certified the Agent Orange Product Liability action as a class action, the largest ever filed as of its filing. Hartz's deposition was one of the first ever taken in America, and the first for an Agent Orange trial, for the purpose of preserving testimony at trial, as it was understood that Hartz would not live to see the trial because of the brain tumor that began to develop while he was a member of Tiger Force, Special Forces, and LRRPs in Vietnam. The firm also located and supplied critical research to the Veterans' lead expert, Dr. Ronald A. Codario, M.D., including about 100 hundred articles from toxicology journals dating back more than a decade, as well as data about where herbicides had been sprayed, what the effects of dioxin had been on animals and humans, and every accident in factories where herbicides were produced or dioxin was a contaminant of some chemical reaction.

In 1984, the class-action suit was settled out of court for $180 million; slightly over 45% of this was ordered to be paid by Monsanto alone. Many veterans who were victims of Agent Orange exposure were outraged the case had been settled instead of going to court, and felt they had been betrayed by the lawyers. "Fairness Hearings" were held in five major American cities, where veterans and their families discussed their reactions to the settlement, and condemned the actions of the lawyers and courts, demanding the case be heard before a jury of their peers. Federal Judge Julius Weinstein refused the appeals, claiming the settlement was "fair and just". By 1989, the veterans' fears were confirmed when it was decided how the money from the settlement would be paid out. A totally disabled Vietnam veteran would receive a maximum of $12,000 spread out over the course of 10 years. Furthermore, by accepting the settlement payments, disabled veterans would become ineligible for many state benefits that provided far more monetary support than the settlement, such as food stamps, public assistance, and government pensions. A widow of a Vietnam veteran who died of Agent Orange exposure would only receive $3700.

In 2004, Jill Montgomery, a spokesperson for Monsanto, said Monsanto should not be liable at all for injuries or deaths caused by Agent Orange, saying: "We are sympathetic with people who believe they have been injured and understand their concern to find the cause, but reliable scientific evidence indicates that Agent Orange is not the cause of serious long-term health effects."

New Jersey Agent Orange Commission

In 1980, New Jersey created the New Jersey Agent Orange Commission, the first state commission created to study its effects. The commission's research project in association with Rutgers University was called "The Pointman Project". It was disbanded by Governor Christine Todd Whitman in 1996.

During Pointman I, commission researchers devised ways to determine small dioxin levels in blood. Prior to this, such levels could only be found in the adipose (fat) tissue. The project compared dioxin

levels in a small group of Vietnam veterans who had been exposed to Agent Orange with a group of matched veterans who had not served in Vietnam. The results of this project were published in the Journal of the American Medical Association in 1988.

The second phase of the project continued to examine and compare dioxin levels in various groups of Vietnam veterans, including Army, Marines and brown water riverboat Navy personnel.

US Congress
In 1991, the US Congress enacted the Agent Orange Act, giving the Department of Veterans Affairs the authority to declare certain conditions 'presumptive' to exposure to Agent Orange/dioxin, making these veterans who served in Vietnam eligible to receive treatment and compensation for these conditions. The same law required the National Academy of Sciences to periodically review the science on dioxin and herbicides used in Vietnam to inform the Secretary of Veterans Affairs about the strength of the scientific evidence showing association between exposure to Agent Orange/dioxin and certain conditions.

Through this process, the list of 'presumptive' conditions has grown since 1991, and currently the U.S. Department of Veterans Affairs has listed prostate cancer, respiratory cancers, multiple myeloma, type II diabetes, Hodgkin's disease, non-Hodgkin's lymphoma, soft tissue sarcoma, chloracne, porphyria cutanea tarda, peripheral neuropathy, chronic lymphocytic leukemia, and spina bifida in children of veterans exposed to Agent Orange as conditions associated with exposure to the herbicide. This list now includes B cell leukemias, such as hairy cell leukemia, Parkinson's disease and ischemic heart disease, these last three having been added on August 31, 2010. Several highly placed individuals in government are voicing concerns about whether some of the diseases on the list should, in fact, actually have been included.

U.S./Vietnamese Government Negotiations
In 2002, Vietnam and the US held a joint conference on Human Health and Environmental Impacts of Agent Orange. Following the conference, the US National Institute of Environmental Health Sciences (NIEHS) began scientific exchanges between the US and Vietnam, and began discussions for a joint research project on the human health impacts of Agent Orange.

These negotiations broke down in 2005, when neither side could agree on the research protocol and the research project was cancelled. More progress has been made on the environmental front. In 2005, the first US-Vietnam workshop on remediation of dioxin was held.

Starting in 2005, the U.S. Environmental Protection Agency (EPA) began to work with the Vietnamese government to measure the level of dioxin at the Da Nang Airbase. Also in 2005, the Joint Advisory Committee on Agent Orange, made up of representatives of Vietnamese and US government agencies, was established. The committee has been meeting yearly to explore areas of scientific cooperation, technical assistance and environmental remediation of dioxin.

A breakthrough in the diplomatic stalemate on this issue occurred as a result of United States President George W. Bush's state visit to Vietnam in November 2006. In the joint statement, President Bush and President Triet agreed "further joint efforts to address the environmental contamination near former dioxin storage sites would make a valuable contribution to the continued development of their bilateral relationship."[68][unreliable source?]

In late May 2007, President Bush signed into law a supplemental spending bill for the war in Iraq and Afghanistan that included an earmark of $3 million specifically for funding for programs for the remediation of dioxin 'hotspots' on former US military bases, and for public health programs for the surrounding communities; some authors consider this to be completely inadequate, pointing out that the U.S. airbase in Da Nang, alone, will cost $14 million to clean up, and that three others are estimated to require $60 million for cleanup. The appropriation was renewed in the fiscal year 2009 and again in FY 2010. An additional $12 million was appropriated in the fiscal year 2010 in the Supplemental Appropriations Act and a total of $18.5 million appropriated for fiscal year 2011.

Secretary of State Hillary Clinton stated during a visit to Hanoi in October 2010 that the US government would begin work on the clean-up of dioxin contamination at the Da Nang airbase.

In June 2011 a ceremony was held at Da Nang airport to mark the start of US-funded decontamination of dioxin hotspots in Vietnam. $32m has so far been allocated by the US congress to fund the program.

Vietnamese Victims Class Action Lawsuit in U.S. Courts
On January 31, 2004, a victim's rights group, the Vietnam Association for Victims of Agent Orange/dioxin (VAVA), filed a lawsuit in the United States District Court for the Eastern District of New York in Brooklyn, against several U.S. companies for liability in causing personal injury, by developing and producing the chemical. Dow Chemical and Monsanto were the two largest producers of Agent Orange for the U.S. military, and were named in the suit, along with the dozens of other companies (Diamond Shamrock, Uniroyal, Thompson Chemicals, Hercules, etc.). On March 10, 2005, Judge Jack B. Weinstein of the Eastern District – who had presided over the 1984 US veterans class action lawsuit – dismissed the lawsuit, ruling there was no legal basis for the plaintiffs' claims. He concluded Agent Orange was not considered a poison under international law at the time of its use by the U.S.; the U.S. was not prohibited from using it as a herbicide; and the companies which produced the substance were not liable for the method of its use by the government. The U.S. government was not a party in the lawsuit, due to sovereign immunity, and the court ruled the chemical companies, as contractors of the US government, shared the same immunity. The case was appealed and heard by the Second Circuit Court of Appeals on June 18, 2007. The Court of Appeals upheld the dismissal of the case, stating the herbicides used during the war were not intended to be used to poison humans and therefore did not violate international law. The US Supreme Court declined to consider the case.

Three judges on the Second Circuit Court of Appeals in Manhattan heard the appeal on June 18, 2007. They upheld Weinstein's ruling to dismiss the case. They ruled that, though the herbicides contained a dioxin (a known poison), they were not intended to be used as a poison on humans. Therefore, they were not considered a chemical weapon and thus not a violation of international law. A further review of the case by the whole panel of judges of the Court of Appeals also confirmed this decision. The lawyers for the Vietnamese filed a petition to the US Supreme Court to hear the case. On March 2, 2009, the Supreme Court denied certiorari and refused to reconsider the ruling of the Court of Appeals.

In a November 2004 Zogby International poll of 987 people, 79% of respondents thought the US chemical companies which produced Agent Orange defoliant should compensate US soldiers who were affected by the toxic chemical used during the war in Vietnam. 51% said they supported compensation for Vietnamese Agent Orange victims.

Help for those affected in Vietnam
To assist those who have been affected by Agent Orange/dioxin, the Vietnamese have established "peace villages", which each host between 50 and 100 victims, giving them medical and psychological help. As of 2006, there were 11 such villages, thus granting some social protection to fewer than a thousand victims. U.S. veterans of the war in Vietnam and individuals who are aware and sympathetic to the impacts of Agent Orange have supported these programs in Vietnam. An international group of veterans from the U.S. and its allies during the Vietnam War working with their former enemy — veterans from the Vietnam Veterans Association — established the Vietnam Friendship Village outside of Hanoi.

The center provides medical care, rehabilitation and vocational training for children and veterans from Vietnam who have been affected by Agent Orange. In 1998, The Vietnam Red Cross established the Vietnam Agent Orange Victims Fund to provide direct assistance to families throughout Vietnam that have been affected. In 2003, the Vietnam Association of Victims of Agent Orange (VAVA) was formed. In addition to filing the lawsuit against the chemical companies, VAVA provides medical care, rehabilitation services and financial assistance to those injured by Agent Orange.

The Vietnamese government provides small monthly stipends to more than 200,000 Vietnamese believed affected by the herbicides; this totaled $40.8 million in 2008 alone. The Vietnam Red Cross has raised more than $22 million to assist the ill or disabled, and several U.S. foundations, United Nations agencies, European governments and nongovernmental organizations have given a total of about $23 million for site cleanup, reforestation, health care and other services to those in need.

Vuong Mo of the Vietnam News Agency described one of centers: "May is 13, but she knows nothing, is unable to talk fluently, nor walk with ease due to for her bandy legs. Her father is dead and she has four elder brothers, all mentally retarded ... The students are all disabled, retarded and of different ages. Teaching them is a hard job. They are of the 3rd grade but many of them find it hard to do the reading. Only a few of them can. Their pronunciation is distorted due to their twisted lips and their memory is quite short. They easily forget what they've learned ... In the Village, it is quite hard to tell the kids' exact ages. Some in their twenties have a physical statures as small as the 7- or 8-years-old. They find it difficult to feed themselves, much less have mental ability or physical capacity for work. No one can hold back the tears when seeing the heads turning round unconsciously, the bandy arms managing to push the spoon of food into the mouths with awful difficulty ... Yet they still keep smiling, singing in their great innocence, at the presence of some visitors, craving for something beautiful."

On June 16, 2010, members of the U.S.-Vietnam Dialogue Group on Agent Orange/Dioxin unveiled a comprehensive 10-year Declaration and Plan of Action to address the toxic legacy of Agent Orange and other herbicides in Vietnam. The Plan of Action was released as an Aspen Institute publication and calls upon the U.S. and Vietnamese governments to join with other governments, foundations, businesses, and nonprofits in a partnership to clean up dioxin "hot spots" in Vietnam and to expand humanitarian services for people with disabilities there. On September 16, 2010, Senator Patrick Leahy (D-VT) acknowledged the work of the Dialogue Group by releasing a statement on the floor of the United States Senate. The statement urges the U.S. government to take the Plan of Action's recommendations into account in developing a multi-year plan of activities to address the Agent Orange/dioxin legacy.

Use Outside Vietnam
While 'Agent Orange' was only used between 1965 and 1970, 2,4-D, 2,4,5-T and other herbicides were used by the US military from the late 1940s through the 1970s.

United States
In 1971 the C-123 aircraft used for spraying Agent Orange were returned to the United States and assigned various East Coast USAF Reserve squadrons, and then employed in traditional airlift missions between 1972-1982. In 1994 testing by the Air Force identified some former spray aircraft as "heavily contaminated" with dioxin residue. Inquires by aircrew veterans in 2011 brought a decision by the US Department of Veterans Affairs opining that not enough dioxin residue remained to injure these post-Vietnam War veterans. On 26 January 2012 the US Center For Disease Control's Agency for Toxic Substances and Disease Registry challenged this with their finding that former spray aircraft were indeed contaminated and the aircrews exposed to harmful levels of dioxin.

In 1978, the U.S. Environmental Protection Agency suspended spraying of Agent Orange in National Forests, due to a threefold increase in miscarriages in women living near forests that had been sprayed.

A December 2006 Department of Defense report listed Agent Orange testing, storage, and disposal sites at 32 locations throughout the United States, as well as in Canada, Thailand, Puerto Rico, Korea, and in the Pacific Ocean. The Veteran Administration has also acknowledged that Agent Orange was used domestically by U.S. forces in test sites throughout the US. Eglin Air Force Base in Florida was one of the primary testing sites throughout the 1960s.

Korea
Agent Orange was used in Korea in the late 1960s. Republic of Korea troops were the only personnel involved in the spraying, which occurred along the Korean Demilitarized Zone (DMZ). "Citing declassified U.S. Department of Defense documents, Korean officials fear thousands of its soldiers may have come into contact with the deadly defoliant in the late 1960s and early 1970s. According to one top government official, as many as '30,000 Korean veterans are suffering from illness related to their exposure'. The exact number of GIs who may have been exposed is unknown. But C. David Benbow, a North Carolina attorney who served as a sergeant with Co. C, 3rd Battalion, 23rd Infantry Regiment, 2nd Infantry Division, along the DMZ in 1968–69, estimates as many as '4,000 soldiers at any given time' could have been affected.".

In 1999, about 20,000 South Koreans filed two separated lawsuits against U.S. companies, seeking more than $5 billion in damages. After losing a decision in 2002, they filed an appeal.

In January 2006, the South Korean Appeals Court ordered Dow Chemical and Monsanto to pay $62 million in compensation to about 6,800 people. The ruling acknowledged that "the defendants failed to ensure safety as the defoliants manufactured by the defendants had higher levels of dioxins than standard", and, quoting the U.S. National Academy of Science report, declared that there was a "causal relationship" between Agent Orange and 11 diseases, including cancers of the lung, larynx and prostate. The judges failed to acknowledge "the relationship between the chemical and peripheral neuropathy, the disease most widespread among Agent Orange victims" according to the Mercury News.

The United States local press KPHO-TV in Phoenix, Arizona alleged that the United States Army has buried Agent Orange in Camp Carroll, the U.S. Army base located in Gyeongsangbuk-do, Korea. It is based on the claim of three U.S. Army veterans. They claimed approximately 250 55 gallon drums of Agent Orange were buried at Camp Carroll in 1978, which was indicated as 'Chemicals type Agent Orange' or 'Province of Vietnam, Compound Orange' with stripe around the barrel dated 1967 for the Republic of Vietnam. The South Korean Ministry of Environment announced that they will request cooperative investigation at Camp Carroll officially. The USFK issued a statement that confirmed that barrels were buried there, but all (plus an additional 60 tons of soil) were removed in 1996.

Currently, Veterans who spent even a single day, or even a few hours, in Vietnam, [as must be established by their military records], and can medically establish that anytime after this 'presumptive exposure' they developed nerve damage, diabetes, or a long list of other medical conditions will receive an 'automatic' VA settlement with a substantial amount of money each month. However, the V.A. fights every similar claim by a Korean Vet. They require added tests: first, that they not only establish they were assigned to S.Korea, [usually this can fairly easily be done, but, not always], for 'some significant time' in the period of clandestine use, 1968-69-70; second, that they were regularly stationed on, or near, the DMZ [This can be almost impossible to prove, as many of the official records only reflect a 'unit' assignment. These orders were often vague, or incomplete, and reflected only a unit assignment of a military organization that might be spread out all over the Korean peninsula. Many have been lost, misplaced, destroyed, or accidentally destroyed in a warehouse fire that destroyed a many old Army records. Most the units where either disbanded, moved, or renamed after the Vietnam Era ended, thus adding to the confusion.]; and lastly, a written opinion by doctor of diagnosis [all that is required of Vietnam Vets], but stating further that disease, or condition, arrises from Agent Orange, and not the other toxic herbasides/chemicals that all Vets are rutinely exposed to.

Canadian Forces Base Gagetown (New Brunswick, Canada)
The U.S. military, with the permission of the Canadian government, tested herbicides, including Agent Orange, in the forests near the Canadian Forces Base Gagetown in New Brunswick in 1966 and 1967. On September 12, 2007, Greg Thompson, Minister of Veterans Affairs, announced that the government of Canada was offering a one-time ex gratia payment of $20,000 as the compensation package for Agent Orange exposure at CFB Gagetown.

On July 12, 2005, Merchant Law Group LLP on behalf of over 1,100 Canadian veterans and civilians who were living in and around the CFB Gagetown filed a lawsuit to pursue class action litigation concerning Agent Orange and Agent Purple with the Federal Court of Canada.

On August 4, 2009, the case was rejected by the court due to lack of evidence. The ruling was appealed.

Veterans Affairs Canada Agent Orange Benefits Rev 1.0

Queensland, Australia
In 2008 Australian researcher Jean Williams claimed that cancer rates in the town of Innisfail, Queensland were 10 times higher than the state average due to secret testing of Agent Orange by the Australian military scientists during the Vietnam War. Williams, who had won the Order of Australia medal for her research on the effects of chemicals on U.S. war veterans, based her allegations on Australian government reports found in the Australian War Memorial museum archives. A former soldier, Ted Bosworth, backed up the claims, saying that he had been involved in the secret testing. The Queensland health department claimed that cancer rates in Innisfail were not higher than those in other parts of the state.

New Zealand
The use of Agent Orange has been controversial in New Zealand, because of exposure of New Zealand troops to it and because of the production of Agent Orange for Vietnam and other users at an Ivon Watkins-Dow chemical plant in Paritutu, New Plymouth. There have been continuing claims that the suburb of Paritutu has also been polluted; see New Zealand in the Vietnam War.[101] There are many cases of New Zealand soldiers developing cancers such as bone cancer from exposure to Agent Orange.

Brazil
The Brazilian government used Agent Orange to defoliate a large section of the Amazon rainforest so that Alcoa could build the Tucuruí dam to power mining operations. Large areas of rainforest were destroyed, along with the homes and livelihoods of thousands of rural peasants and indigenous tribes.

Malayan Emergency
Small scale defoliation experiments using 2-4-D and 2-4-5-T were conducted by the British during the Malayan Emergency in 1951. Areas of jungle close to roadways were cleared using chemical defoliation to help prevent ambushes by Communist Terrorists.

Ontario, Canada
On February 17, 2011, the Toronto Star revealed that the same toxins used to strip the jungles of Vietnam were also employed to clear extensive plots of Crown land in Northern Ontario.[104] The same day, in response to the Toronto Star article, the Ontario provincial government launched a probe into the use of Agent Orange.

On February 18, 2011, Ontario's Ministry of Natural Resources widened the probe of Agent Orange spraying to include all areas of the province where government managed forests on Crown land.

The Toronto Star reported that, "records from the 1950s, 1960s and 1970s show forestry workers, often students and junior rangers, spent weeks at a time as human markers holding red, helium-filled balloons on fishing lines while low-flying planes sprayed toxic herbicides including an infamous chemical mixture known as Agent Orange on the brush and the boys below" (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Agent Pink
Date: 2012
Source: Wikipedia

Abstract: Agent Pink is the code name for a powerful herbicide and defoliant used by the U.S. military in its Herbicidal Warfare program during the Vietnam War. The name comes from the pink stripe painted on the barrels to identify the contents. It was one of the so-called "rainbow herbicides" that included the more infamousAgent Orange. Agent Pink was only used during the early "testing" stages of the spraying program before 1964.

Agent Pink's only active ingredient was 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), one of the common phenoxy herbicides of the era. It was later learned that adioxin, 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD), is produced as a byproduct of the manufacture of 2,4,5-T, and was present in any of the herbicides that used it. Since Agent Pink consisted entirely of 2,4,5-T it contained many times the level of dioxin found in Agent Orange, which also contained 2,4-D, in which there was lower dioxin contamination (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Agent Purple
Date: 2012
Source: Wikipedia

Abstract: Agent Purple is the code name for a powerful herbicide and defoliant used by the U.S. military in their Herbicidal Warfare program during the Vietnam War. The name comes from the purple stripe painted on the barrels to identify the contents. It was one of the so-called "rainbow herbicides" that included the more infamous Agent Orange. Agent Purple and Orange were also used to clear brush in Canada.

Agent Purple is chemically similar to the better-known Agent Orange, consisting of a mixture of the herbicides 2,4-D and 2,4,5-T. It was later discovered that during the manufacture of 2,4,5-T that Agents Orange and Purple were contaminated with varying levels of tetrachlorodibenzodioxin (TCDD), a dioxin that is a toxic and persistent substance. Agent Purple is reputed to have three times the dioxin levels of Agent Orange, 45 parts per million as opposed to 13 parts per million in Agent Orange.

Agent Purple was produced at the Hercules Chemical Plant in Jacksonville, Arkansas. This plant is adjacent to Little Rock AFB. The affluent was delivered to the Little Rock AFB Fire Department and was burned in training fires.

Agent Purple was used only in the earliest stages of the spraying program, between 1962 and 1965 as well as in earlier tests conducted by the US military outside of Vietnam. About 500,000 gallons were sprayed in Vietnam total. (~1.9 million liters). When the need to clear brush around CFB Gagetown in Canada arose, quantities of Agent Purple and Agent Orange were also sprayed there in a testing program during 1966 and 1967 (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Agent White
Date: 2012
Source: Wikipedia

Abstract: Agent White is the code name for a powerful herbicide and defoliant used by the U.S. military in its Herbicidal warfare program during the Vietnam War. The name comes from the white stripe painted on the barrels to identify the contents. It was one of the so-called "rainbow herbicides" that included the more infamous Agent Orange.

Agent White is a 4:1 mixture of 2,4-D and Picloram (also known as Tordon 101). Unlike the more infamous Agent Orange, Agent White did not contain dioxin, which was a contaminant in the defoliants that included 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). However, it appears the Picloram was contaminated with hexachlorobenzene (HCB) and nitrosamines, both known carcinogens. Agent White was a proprietary product of the Dow Chemical Company. Around 1985, Dow Chemical was forced to re-certify Picloram after having greatly reduced the amounts of both contaminants.

Agent White was often used when Agent Orange was not available, including for several months after the use of Agent Orange was halted in April 1970. Approximately 5.4 million US gallons (20,000 m3) of Agent White was used in Vietnam between 1966 and 1971. In addition the US Military tested Agent White, Tordon 101 and Picloram in varying concentrations at test sites in the US and Puerto Rico in the 1960s (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Event: Anthrax
Date: 2012
Source: Wikipedia

Abstract: Anthrax is an acute disease caused by the bacterium Bacillus anthracis. Most forms of the disease are lethal, and it affects both humans and other animals. There are effective vaccines against anthrax, and some forms of the disease respond well to antibiotic treatment.

Like many other members of the genus Bacillus, Bacillus anthracis can form dormant endospores (often referred to as "spores" for short, but not to be confused with fungal spores) that are able to survive in harsh conditions for decades or even centuries. Such spores can be found on all continents, even Antarctica. When spores are inhaled, ingested, or come into contact with a skin lesion on a host they may become reactivate and multiply rapidly.

Anthrax commonly infects wild and domesticated herbivorous mammals that ingest or inhale the spores while grazing. Ingestion is thought to be the most common route by which herbivores contract anthrax. Carnivores living in the same environment may become infected by consuming infected animals. Diseased animals can spread anthrax to humans, either by direct contact (e.g., inoculation of infected blood to broken skin) or by consumption of a diseased animal's flesh.

Anthrax spores can be produced in vitro and used as a biological weapon. Anthrax does not spread directly from one infected animal or person to another; it is spread by spores. These spores can be transported by clothing or shoes. The body of an animal that had active anthrax at the time of death can also be a source of anthrax spores.

Until the twentieth century, anthrax infections killed hundreds of thousands of animals and people each year in Australia, Asia, Africa, North America, and Europe, particularly in the concentration camps during WWII. French scientist Louis Pasteur developed the first effective vaccine for anthrax in 1881. Thanks to over a century of animal vaccination programs, sterilization of raw animal waste materials and anthrax eradication programs in North America, Australia, New Zealand, Russia, Europe, and parts of Africa and Asia, anthrax infection is now relatively rare in domestic animals, with only a few dozen cases reported every year. Anthrax is especially rare in dogs and cats, as is evidenced by a single reported case in the USA in 2001. Anthrax typically does not cause disease in carnivores and scavengers, even when these animals consume anthrax-infected carcasses. Anthrax outbreaks do occur in some wild animal populations with some regularity. The disease is more common in developing countries without widespread veterinary or human public health programs. Bacillus anthracis bacterial spores are soil-borne, and, because of their long lifetime, they are still present globally and at animal burial sites of anthrax-killed animals for many decades; spores have been known to have reinfected animals over 70 years after burial sites of anthrax-infected animals were disturbed.

Signs & Symptoms

Pulmonary

Respiratory infection in humans initially presents with cold or flu-like symptoms for several days, followed by severe (and often fatal) respiratory collapse. Historical mortality was 92%, but, when treated early (seen in the 2001 anthrax attacks), observed mortality was 45%. Distinguishing pulmonary anthrax from more common causes of respiratory illness is essential to avoiding delays in diagnosis and thereby improving outcomes. An algorithm for this purpose has been developed. Illness progressing to the fulminant phase has a 97% mortality regardless of treatment.

A lethal infection is reported to result from inhalation of about 10,000–20,000 spores, though this dose varies among host species. As with all diseases, it is presumed that there is a wide variation to susceptibility with evidence that some people may die from much lower exposures; there is little documented evidence to verify the exact or average number of spores needed for infection. Inhalational anthrax is also known as Woolsorters' or Ragpickers' disease as these professions were more susceptible to the disease due to their exposure to infected animal products. Other practices associated with exposure include the slicing up of animal horns for the manufacture of buttons, the handling of hair bristles used for the manufacturing of brushes, and the handling of animal skins. Whether these animal skins came from animals that died of the disease or from animals that had simply laid on ground that had spores on it is unknown. This mode of infection is used as a bioweapon.

Gastrointestinal

Gastrointestinal infection in humans is most often caused by eating anthrax-infected meat and is characterized by serious gastrointestinal difficulty, vomiting of blood, severe diarrhea, acute inflammation of the intestinal tract, and loss of appetite. Some lesions have been found in the intestines and in the mouth and throat. After the bacterium invades the bowel system, it spreads through the bloodstream throughout the body, making even more toxins on the way. Gastrointestinal infections can be treated but usually result in fatality rates of 25% to 60%, depending upon how soon treatment commences. This form of anthrax is the rarest form. In the United States, there have only been two official cases, the first reported in 1942 by the CDC and the second reported in 2010 that was treated at the Massachusetts General Hospital. It is the only known case of survival from GI anthrax in the U.S.

Cutaneous

Cutaneous (on the skin) anthrax infection in humans shows up as a boil-like skin lesion that eventually forms an ulcer with a black center (eschar). The black eschar often shows up as a large, painless necrotic ulcer (beginning as an irritating and itchy skin lesion or blister that is dark and usually concentrated as a black dot, somewhat resembling bread mold) at the site of infection. In general, cutaneous infections form within the site of spore penetration between 2 and 5 days after exposure. Unlike bruises or most other lesions, cutaneous anthrax infections normally do not cause pain.

Cutaneous anthrax is typically caused when Bacillus anthracis spores enter through cuts on the skin. This form of Anthrax is found most commonly when humans handle infected animals and/or animal products (e.g., the hide of an animal used to make drums).

Cutaneous anthrax is rarely fatal if treated, because the infection area is limited to the skin, preventing the Lethal Factor, Edema Factor, and Protective Antigen from entering and destroying a vital organ. Without treatment, about 20% of cutaneous skin infection cases progress to toxemia and death.

Cause

Bacteria

Bacillus anthracis is a rod-shaped, Gram-positive, aerobic bacterium about 1 by 9 micrometers in length. It was shown to cause disease by Robert Koch in 1876. The bacterium normally rests in endospore form in the soil, and can survive for decades in this state. Herbivores are often infected whilst grazing or browsing, especially when eating rough, irritant, or spiky vegetation: the vegetation has been hypothesized to cause wounds within the gastrointestinal tract permitting entry of the bacterial endo-

spores into the tissues, though this has not been proven. Once ingested or placed in an open wound, the bacterium begins multiplying inside the animal or human and typically kills the host within a few days or weeks. The endo-spores germinate at the site of entry into the tissues and then spread via the circulation to the lymphatics, where the bacteria multiply.

It is the production of two powerful exo-toxins and lethal toxin by the bacteria that causes death. Veterinarians can often tell a possible anthrax-induced death by its sudden occurrence, and by the dark, non-clotting blood that oozes from the body orifices. Most anthrax bacteria inside the body after death are out-competed and destroyed by anaerobic bacteria within minutes to hours postmortem. However, anthrax vegetative bacteria that escape the body via oozing blood or through the opening of the carcass may form hardy spores. One spore forms per one vegetative bacterium. The triggers for spore formation are not yet known, though oxygen tension and lack of nutrients may play roles. Once formed, these spores are very hard to eradicate.

The infection of herbivores (and occasionally humans) via the inhalational route normally proceeds as follows: Once the spores are inhaled, they are transported through the air passages into the tiny air particles sacs (alveoli) in the lungs. The spores are then picked up by scavenger cells (macrophages) in the lungs and are transported through small vessels (lymphatics) to the lymph nodes in the central chest cavity (mediastinum). Damage caused by the anthrax spores and bacilli to the central chest cavity can cause chest pain and difficulty breathing. Once in the lymph nodes, the spores germinate into active bacilli that multiply and eventually burst the macrophages, releasing many more bacilli into the bloodstream to be transferred to the entire body. Once in the blood stream, these bacilli release three proteins named lethal factor, edema factor, and protective antigen. All three are non-toxic by themselves, but the combination is incredibly lethal to humans. Protective antigen combines with these other two factors to form lethal toxin and edema toxin, respectively. These toxins are the primary agents of tissue destruction, bleeding, and death of the host. If antibiotics are administered too late, even if the antibiotics eradicate the bacteria, some hosts will still die of toxemia. This is because the toxins produced by the bacilli remain in their system at lethal dose levels.

The lethality of the anthrax disease owes itself to the bacterium's two principal virulence factors: (i) the poly-D-glutamic acid capsule, which protects the bacterium from phagocytosis by host neutrophils, and (ii) the tripartite protein toxin, called anthrax toxin. Anthrax toxin is a mixture of three protein components: (i) protective antigen (PA), (ii) edema factor (EF), and (iii) lethal factor (LF). PA plus LF produces lethal toxin, and PA plus EF produces edema toxin. These toxins cause death and tissue swelling (edema), respectively.

In order to enter the cells, the edema and lethal factors use another protein produced by B. anthracis called protective antigen. Protective antigen binds to two surface receptors on the host cell. A cell protease then cleaves PA into two fragments: PA20 and PA63. PA20 dissociates into the extracellular medium, playing no further role in the toxic cycle. PA63 then oligomerizes with six other PA63 fragments forming a heptameric ring-shaped structure named a prepore. Once in this shape, the complex can competitively bind up to three EF or LF forming a resistant complex. Receptor-mediated endocytosis occurs next, providing the newly formed toxic complex access to the interior of the host cell. The acidified environment within the endosome triggers the heptamer to release the LF and/or EF into the cytosol. It is unknown how exactly the complex results in the death of the cell.

Edema factor is a calmodulin-dependent adenylate cyclase. Adenylate cyclase catalyzes the conversion of ATP into cyclic AMP (cAMP) and pyrophosphate. The complexation of adenylate cyclase with calmodulin removes calmodulin from stimulating calcium-triggered signaling, thus inhibiting the immune response. To be specific, LF inactivates neutrophils (a type of phagocytic cell) by the process just described so that they cannot phagocytose bacteria. Throughout history, it was believed that lethal factor caused macrophages to make TNF-alpha and interleukin 1, beta (IL1B). TNF-alpha is a cytokine whose primary role is to regulate immune cells as well as to induce inflammation and apoptosis or programmed cell death. Interleukin 1, beta is another cytokine that also regulates inflammation and apoptosis. The over-production of TNF-alpha and IL1B ultimately leads to septic shock and death. However, recent evidence indicates that anthrax also targets endothelial cells (cells that

line serous cavities such as the pericardial cavity, pleural cavity, and the peritoneal cavity, lymph vessels, and blood vessels), causing vascular leakage of fluid and cells, and ultimately hypovolemic shock (low blood volume), and septic shock.

Exposure
Occupational exposure to infected animals or their products (such as skin, wool, and meat) is the usual pathway of exposure for humans. Workers who are exposed to dead animals and animal products are at the highest risk, especially in countries where anthrax is more common. Anthrax in livestock grazing on open range where they mix with wild animals still occasionally occurs in the United States and elsewhere. Many workers who deal with wool and animal hides are routinely exposed to low levels of anthrax spores but most exposures are not sufficient to develop anthrax infections. It is presumed that the body's natural defenses can destroy low levels of exposure. These people usually contract cutaneous anthrax if they catch anything. Throughout history, the most dangerous form of inhalational anthrax was called Woolsorters' disease because it was an occupational hazard for people who sorted wool. Today this form of infection is extremely rare, as almost no infected animals remain. The last fatal case of natural inhalational anthrax in the United States occurred in California in 1976, when a home weaver died after working with infected wool imported from Pakistan. The autopsy was done at UCLA hospital. To minimize the chance of spreading the disease, the deceased was transported to UCLA in a sealed plastic body bag within a sealed metal container.

In November 2008, a drum maker in the United Kingdom who worked with untreated animal skins died from anthrax. Gastrointestinal anthrax is exceedingly rare in the United States, with only one case on record, reported in 1942, according to the Centers for Disease Control and Prevention. In December 2009 an outbreak of anthrax occurred amongst heroin addicts in Glasgow, Scotland, resulting in ten deaths. The source of the anthrax is believed to be dilution of the heroin with bone meal in Afghanistan.

Also during December 2009, The New Hampshire Department of Health and Human Services confirmed a case of gastrointestinal anthrax in an adult female. The CDC investigated the source and the possibility that it was contracted from an African drum recently used by the woman taking part in a drumming circle. The woman apparently inhaled anthrax [in spore form] from the hide of the drum. She became critically ill, but with gastrointestinal anthrax rather than inhaled anthrax, which made her unique in American medical history. The building where the infection took place was cleaned and reopened to the public and the woman recovered. Jodie Dionne-Odom, New Hampshire state epidemiologist, states, "It is a mystery. We really don't know why it happened."

Mode of Infection
Anthrax can enter the human body through the intestines (ingestion), lungs (inhalation), or skin (cutaneous) and causes distinct clinical symptoms based on its site of entry. In general, an infected human will be quarantined. However, anthrax does not usually spread from an infected human to a noninfected human. But, if the disease is fatal to the person's body, its mass of anthrax bacilli becomes a potential source of infection to others and special precautions should be used to prevent further contamination. Inhalational anthrax, if left untreated until obvious symptoms occur, may be fatal.

Anthrax can be contracted in laboratory accidents or by handling infected animals or their wool or hides. It has also been used in biological warfare agents and by terrorists to intentionally infect as exemplified by the 2001 anthrax attacks.

Diagnosis
Other than Gram stain of specimens, there are no specific direct identification techniques for identification of *Bacillus species* in clinical material. These organisms are Gram-positive but with age can be Gram-variable to Gram-negative. A specific feature of *Bacillus species* that makes it unique from other aerobic microorganisms is its ability to produce spores. Although spores are not always evident on a Gram stain of this organism, the presence of spores confirms that the organism is of the genus *Bacillus*.

All *Bacillus species* grow well on 5% Sheep blood agar and other routine culture media. PLET (polymyxin-lysozyme-EDTA-thallous acetate) can be used to isolate *B.anthracis* from contaminated specimens, and bicarbonate agar is used as an identification method to induce capsule formation.

Bacillus sp. will usually grow within 24 hours of incubation at 35 degrees C, in ambient air (room temperature) or in 5% CO_2. If bicarbonate agar is used for identification then the media must be incubated in 5% CO_2.

B.anthracis appears as medium-large, gray, flat, irregular with swirling projections, often referred to as "medusa head" appearance, and is non-hemolytic on 5% sheep blood agar. It is non-motile, is susceptible to penicillin and produces a wide zone of lecithinase on egg yolk agar. Confirmatory testing to identify B.anthracis includes gamma bacteriophage testing, indirect hemagglutination and enzyme linked immunosorbent assay to detect antibodies. Anthrax is also a Biphasic disease

Prevention

Vacsines
There are several vaccines in current use. The Georgian/Russian vaccine (called STI) is a live-attenuated vaccine based on spores from the Stern strain of B. anthracis. The USA vaccine (also known as AVA, manufactured by Emergent BioSolutions under the brand name BioThrax) is adsorbed onto aluminium-hydroxide.

The STI vaccine's serious side-effects restrict use to healthy adults.

BioThrax is licensed by the U.S. Food and Drug Administration (FDA) and was formerly administered in a six-dose primary series at 0, 2, 4 weeks and 6, 12, 18 months, with annual boosters to maintain immunity. On December 11, 2008, the FDA approved omitting the week 2 dose, resulting in the currently recommended five-dose series.

Prophylaxis
If a person is suspected as having died from anthrax, every precaution should be taken to avoid skin contact with the potentially contaminated body and fluids exuded through natural body openings. The body should be put in strict quarantine. A blood sample taken in a sealed container and analyzed in an approved laboratory should be used to ascertain if anthrax is the cause of death. Microscopic visualization of the encapsulated bacilli, usually in very large numbers, in a blood smear stained with polychrome methylene blue (McFadyean stain) is fully diagnostic, though culture of the organism is still the gold standard for diagnosis. Full isolation of the body is important to prevent possible contamination of others. Protective, impermeable clothing and equipment such as rubber gloves, rubber apron, and rubber boots with no perforations should be used when handling the body. No skin, especially if it has any wounds or scratches, should be exposed. Disposable personal protective equipment is preferable, but if not available, decontamination can be achieved by autoclaving. Disposable personal protective equipment and filters should be autoclaved, and/or burned and buried. Bacillus anthracis bacillii range from 0.5–5.0 μm in size. Anyone working with anthrax in a suspected or confirmed victim should wear respiratory equipment capable of filtering this size of particle or smaller. The US National Institute for Occupational Safety and Health (NIOSH) and Mine Safety and Health Administration (MSHA) approved high efficiency-respirator, such as a half-face disposable respirator with a high-efficiency particulate air (HEPA) filter, is recommended. All possibly contaminated bedding or clothing should be isolated in double plastic bags and treated as possible bio-hazard waste. The victim should be sealed in an airtight body bag. Dead victims that are opened and not burned provide an ideal source of anthrax spores. Cremating victims is the preferred way of handling body disposal. No embalming or autopsy should be attempted without a fully equipped biohazard laboratory and trained and knowledgeable personnel.

Delays of only a few days may make the disease untreatable and treatment should be started even without symptoms if possible contamination or exposure is suspected. Animals with anthrax often just die without any apparent symptoms. Initial symptoms may resemble a common cold—sore throat, mild fever,

muscle aches and malaise. After a few days, the symptoms may progress to severe breathing problems and shock and ultimately death. Death can occur from about two days to a month after exposure with deaths apparently peaking at about 8 days after exposure. Antibiotic-resistant strains of anthrax are known.

Early detection of sources of anthrax infection can allow preventive measures to be taken. In response to the anthrax attacks of October 2001 the United States Postal Service (USPS) installed BioDetection Systems (BDS) in their large scale mail cancellation facilities. BDS response plans were formulated by the USPS in conjunction with local responders including fire, police, hospitals and public health. Employees of these facilities have been educated about anthrax, response actions and prophylactic medication. Because of the time delay inherent in getting final verification that anthrax has been used, prophylactic antibiotic treatment of possibly exposed personnel must be started as soon as possible.

Treatment

Anthrax cannot be spread directly from person to person, but a person's clothing and body may be contaminated with anthrax spores. Effective decontamination of people can be accomplished by a thorough wash-down with antimicrobial effective soap and water. Waste water should be treated with bleach or other anti-microbial agent. Effective decontamination of articles can be accomplished by boiling contaminated articles in water for 30 minutes or longer. Chlorine bleach is ineffective in destroying spores and vegetative cells on surfaces, though formaldehyde is effective. Burning clothing is very effective in destroying spores. After decontamination, there is no need to immunize, treat or isolate contacts of persons ill with anthrax unless they were also exposed to the same source of infection.

Antibiotics

Early antibiotic treatment of anthrax is essential—delay significantly lessens chances for survival.

Treatment for anthrax infection and other bacterial infections includes large doses of intravenous and oral antibiotics, such as fluoroquinolones like ciprofloxacin, or doxycycline, erythromycin, vancomycin or penicillin. FDA-approved agents include ciprofloxacin, doxycycline and penicillin.

In possible cases of inhalation anthrax, early antibiotic prophylaxis treatment is crucial to prevent possible death.

In May 2009, Human Genome Sciences submitted a Biologic License Application (BLA, permission to market) for its new drug, raxibacumab (brand name ABthrax) intended for emergency treatment of inhaled anthrax. If death occurs from anthrax the body should be isolated to prevent possible spread of anthrax germs. Burial does not kill anthrax spores.

In recent years there have been many attempts to develop new drugs against anthrax, but existing drugs are effective if treatment is started soon enough.

History

Etymology

The name comes from *anthrax [ἄνθραξ]*, the Greek word for 'coal', because of the black skin lesions developed by victims with a cutaneous anthrax infection.

Discovery

Robert Koch, a German physician and scientist, first identified the bacterium that caused the anthrax disease in 1875. His pioneering work in the late nineteenth century was one of the first demonstrations that diseases could be caused by microbes. In a groundbreaking series of experiments, he uncovered the life cycle and means of transmission of anthrax. His experiments not only helped create an understanding of anthrax, but also helped elucidate the role of microbes in causing illness at a time when debates still took place over spontaneous generation versus cell theory. Koch went on to study the mechanisms of

other diseases and won the 1905 Nobel Prize in Physiology or Medicine for his discovery of the bacterium causing tuberculosis.

First Vaccination
In May 1881 Louis Pasteur performed a public experiment to demonstrate his concept of vaccination. He prepared two groups of 25 sheep, one goat and several cows. The animals of one group were injected with an anthrax vaccine prepared by Pasteur twice, at an interval of 15 days; the control group was left unvaccinated. Thirty days after the first injection, both groups were injected with a culture of live anthrax bacteria. All the animals in the non-vaccinated group died, while all of the animals in the vaccinated group survived. The human vaccine for anthrax became available in 1954. This was a cell-free vaccine instead of the live-cell Pasteur-style vaccine used for veterinary purposes. An improved cell-free vaccine became available in 1970.

Society and Culture
The virulent Ames strain, which was used in the 2001 anthrax attacks in the United States, has received the most news coverage of any anthrax outbreak. The Ames strain contains two virulence plasmids, which separately encode for a three-protein toxin, called anthrax toxin, and a poly-glutamic acid capsule. Nonetheless, the Vollum strain, developed but never used as a biological weapon during the Second World War, is much more dangerous. The Vollum (also incorrectly referred to as Vellum) strain was isolated in 1935 from a cow in Oxfordshire, UK. This is the same strain that was used during the Gruinard bioweapons trials. A variation of Vollum known as "Vollum 1B" was used during the 1960s in the US and UK bioweapon programs. Vollum 1B is widely believed to have been isolated from William A. Boyles, a 46-year-old scientist at the U.S. Army Biological Warfare Laboratories at Camp (later Fort) Detrick (precursor to USAMRIID) who died in 1951 after being accidentally infected with the Vollum strain. The Sterne strain, named after the Trieste-born immunologist Max Sterne, is an attenuated strain used as a vaccine, which contains only the anthrax toxin virulence plasmid and not the poly-glutamic acid capsule expressing plasmid.

Site Cleanup
Anthrax spores can survive for very long periods of time in the environment after release. Methods for cleaning anthrax-contaminated sites commonly use oxidizing agents such as peroxides, ethylene oxide, Sandia Foam, chlorine dioxide (used in the Hart Senate Office Building), and liquid bleach products containing sodium hypochlorite. These agents slowly destroy bacterial spores. A bleach solution for treating hard surfaces has been approved by the EPA. Bleach and vinegar must not be combined together directly, as doing so could produce chlorine gas. Rather some water must first be added to the bleach (e.g., two cups water to one cup of bleach), then vinegar (e.g., one cup), and then the rest of the water (e.g., six cups). The pH of the solution should be tested with a paper test strip; and treated surfaces must remain in contact with the bleach solution for 60 minutes (repeated applications will be necessary to keep the surfaces wet).

Chlorine dioxide has emerged as the preferred biocide against anthrax-contaminated sites, having been employed in the treatment of numerous government buildings over the past decade. Its chief drawback is the need for in situ processes to have the reactant on demand.

To speed the process, trace amounts of a non-toxic catalyst composed of iron and tetro-amido macrocyclic ligands are combined with sodium carbonate and bicarbonate and converted into a spray. The spray formula is applied to an infested area and is followed by another spray containing tert-Butyl hydroperoxide.

Using the catalyst method, a complete destruction of all anthrax spores can be achieved in under 30 minutes. A standard catalyst-free spray destroys fewer than half the spores in the same amount of time. They can be heated, exposed to the harshest chemicals, and they do not easily die.[vague]

Cleanups at a Senate office building, several contaminated postal facilities and other U.S. government and private office buildings showed that decontamination is possible, but it is time-consuming and costly. Clearing the Senate office building of anthrax spores cost $27 million, according to the Government

Accountability Office. Cleaning the Brentwood postal facility outside Washington cost $130 million and took 26 months. Since then newer and less costly methods have been developed.

Clean up of anthrax-contaminated areas on ranches and in the wild is much more problematic. Carcasses may be burned, though it often takes up to three days to burn a large carcass and this is not feasible in areas with little wood. Carcasses may also be buried, though the burying of large animals deeply enough to prevent resurfacing of spores requires much manpower and expensive tools. Carcasses have been soaked in formaldehyde to kill spores, though this has environmental contamination issues. Block burning of vegetation in large areas enclosing an anthrax outbreak has been tried; this, while environmentally destructive, causes healthy animals to move away from an area with carcasses in search of fresh graze and browse. Some wildlife workers have experimented with covering fresh anthrax carcasses with shadecloth and heavy objects. This prevents some scavengers from opening the carcasses, thus allowing the putrefactive bacteria within the carcass to kill the vegetative B. anthracis cells and preventing sporulation. This method also has drawbacks, as scavengers such as hyenas are capable of infiltrating almost any exclosure.

Biological Warfare
Anthrax spores can and have been used as a biological warfare weapon. Its first modern incidence occurred when Scandinavian freedom fighters ("the rebel groups") supplied by the German General Staff used anthrax with unknown results against the Imperial Russian Army in Finland in 1916. Anthrax was first tested as a biological warfare agent by Unit 731 of the Japanese Kwantung Army in Manchuria during the 1930s; some of this testing involved intentional infection of prisoners of war, thousands of whom died. Anthrax, designated at the time as Agent N, was also investigated by the allies in the 1940s.

There is a long history of practical bioweapons research in this area. For example, in 1942 British bioweapons trials severely contaminated Gruinard Island in Scotland with anthrax spores of the Vollum-14578 strain, making it a no-go area until it was decontaminated in 1990. The Gruinard trials involved testing the effectiveness of a submunition of an "N-bomb"—a biological weapon. Additionally, five million "cattle cakes" impregnated with anthrax were prepared and stored at Porton Down for "Operation Vegetarian"—an anti-livestock weapon intended for attacks on Germany by the Royal Air Force.[46] The infected cattle cakes were to be dropped on Germany in 1944. However neither the cakes nor the bomb was used; the cattle cakes were incinerated in late 1945.

Weaponized anthrax was part of the U.S. stockpile prior to 1972, when the United States signed the Biological Weapons Convention. President Nixon ordered the dismantling of US biowarfare programs in 1969 and the destruction of all existing stockpiles of bioweapons. In the period 1978–1979 the Rhodesian government used anthrax against cattle and humans during its war with black nationalists. The Soviet Union created and stored 100 to 200 tons of anthrax spores at Kantubek on Vozrozhdeniya Island. They were abandoned in 1992 and destroyed in 2002.

American military and British Army personnel are routinely vaccinated against anthrax prior to active service in places where biological attacks are considered a threat.

Sverdlovsk Incident (2 April 1979): Main article: Sverdlovsk anthrax leak
Despite signing the 1972 agreement to end bioweapon production the government of the Soviet Union had an active bioweapons program that included the production of hundreds of tons of weapons-grade anthrax after this period. On 2 April 1979, some of the over one million people living in Sverdlovsk (now called Ekaterinburg, Russia), about 850 miles east of Moscow, were exposed to an accidental release of anthrax from a biological weapons complex located near there. At least 94 people were infected, of whom at least 68 died. One victim died four days after the release, ten over an eight-day period at the peak of the deaths, and the last six weeks later. Extensive cleanup, vaccinations and medical interventions managed to save about 30 of the victims. Extensive cover-ups and destruction of records by the KGB continued from 1979 until Russian President Boris Yeltsin admitted this anthrax accident in 1992. Jeanne Guillemin reported in 1999 that a combined Russian and United States team investigated the accident in 1992.

Nearly all of the night shift workers of a ceramics plant directly across the street from the biological facility (compound 19) became infected, and most died. Since most were men, there were suspicions by NATO governments that the Soviet Union had developed a sex-specific weapon. The government blamed the outbreak on the consumption of anthrax-tainted meat and ordered the confiscation of all uninspected meat that entered the city. They also ordered that all stray dogs be shot and that people not have contact with sick animals. There was also a voluntary evacuation and anthrax vaccination program established for people from 18–55.

To support the cover-up story Soviet medical and legal journals published articles about an outbreak in livestock that caused GI anthrax in people having consumed infected meat, and cutaneous anthrax in people having come into contact with the animals. All medical and public health records were confiscated by the KGB. In addition to the medical problems that the outbreak caused, it also prompted Western countries to be more suspicious of a covert Soviet Bioweapons program and to increase their surveillance of suspected sites. In 1986, the US government was allowed to investigate the incident, and concluded that the exposure was from aerosol anthrax from a military weapons facility. In 1992, President Yeltsin admitted that he was "absolutely certain" that "rumors" about the Soviet Union violating the 1972 Bioweapons Treaty were true. The Soviet Union, like the US and UK, had agreed to submit information to the UN about their bioweapons programs but omitted known facilities and never acknowledged their weapons program.

Anthrax Bioterrorism

In theory, anthrax spores can be cultivated with minimal special equipment and a first-year collegiate microbiological education, but in practice the procedure is difficult and dangerous. To make large amounts of an aerosol form of anthrax suitable for biological warfare requires extensive practical knowledge, training, and highly advanced equipment.

Concentrated anthrax spores were used for bioterrorism in the 2001 anthrax attacks in the United States, delivered by mailing postal letters containing the spores. The letters were sent to several news media offices as well as to two Democratic senators: Tom Daschle of South Dakota and Patrick Leahy of Vermont. As a result, 22 were infected and five died. Only a few grams of material were used in these attacks and in August 2008 the US Department of Justice announced they believed that Dr. Bruce Ivins, a senior biodefense researcher employed by the United States government, was responsible These events also spawned many anthrax hoaxes.

Due to these events, the U.S. Postal Service installed biohazard detection systems at its major distribution centers to actively scan for anthrax being transported through the mail.

Decontaminating Mail

In response to the postal anthrax attacks and hoaxes the US Postal Service sterilized some mail using a process of gamma irradiation and treatment with a proprietary enzyme formula supplied by Sipco Industries Ltd.

A scientific experiment performed by a high school student, later published in The Journal of Medical Toxicology, suggested that a domestic electric iron at its hottest setting (at least 400 °F (204 °C)) used for at least 5 minutes should destroy all anthrax spores in a common postal envelope (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Black Death
Date: 2012
Source: Wikipedia

Abstract: The Black Death was one of the most devastating pandemics in human history, peaking in Europe between 1348 and 1350. Although there were several competing theories as to the etiology of the Black Death, it has been conclusively proven via analysis of ancient DNA from plague victims in northern and southern Europe that the pathogen responsible is the Yersinia pestis bacterium. Thought to have started in China, it travelled along the Silk Road and reached the Crimea by 1346.

From there it was probably carried by Oriental rat fleas living on the black rats that were regular passengers on merchant ships. It spread throughout the Mediterranean and Europe. The Black Death is estimated to have killed 30–60 percent of Europe's population, reducing world population from an estimated 450 million to between 350 and 375 million in the 14th century. The aftermath of the plague created a series of religious, social and economic upheavals, which had profound effects on the course of European history. It took 150 years for Europe's population to recover. The plague returned at various times, killing more people, until it left Europe in the 19th century.

Overview

There have been three major outbreaks of plague. The Plague of Justinian in the 6th and 7th centuries is the first known attack on record, and marks the first firmly recorded pattern of bubonic plague. From historical descriptions, as much as 40 percent of the population of Constantinople died from the plague. Modern estimates suggest half of Europe's population was wiped out before the plague disappeared in the 700s. After 750, major epidemic diseases did not appear again in Europe until the Black Death of the 14th century. The Third Pandemic hit China in the 1890s and devastated India but was confined to limited outbreaks in the west.

The Black Death originated in or near China and spread by way of the Silk Road or by ship. It may have reduced world population from an estimated 450 million to between 350 and 375 million in 1400.

The plague is thought to have returned at intervals with varying virulence and mortality until the 18th century. On its return in 1603, for example, the plague killed 38,000 Londoners. Other notable 17th-century outbreaks were the Italian Plague (1629–1631), the Great Plague of Seville (1647–1652), the Great Plague of London (1665–1666),[9] and the Great Plague of Vienna (1679). There is some controversy over the identity of the disease, but in its virulent form, after the Great Plague of Marseille in 1720–1722, the Great Plague of 1738 (which hit Eastern Europe), and the Russian plague of 1770-1772,

it seems to have gradually disappeared from Europe. By the early 19th century, the threat of plague had diminished, but it was quickly replaced by a new disease. The Asiatic cholera was the first of several cholera pandemics to sweep through Asia and Europe during the 19th and 20th centuries.

The 14th century eruption of the Black Death had a drastic effect on Europe's population, irrevocably changing the social structure. It was, arguably, a serious blow to the Catholic Church, and resulted in widespread persecution of minorities such as Jews, foreigners, beggars, and lepers. The uncertainty of daily survival has been seen as creating a general mood of morbidity, influencing people to "live for the moment", as illustrated by Giovanni Boccaccio in The Decameron (1353).

Naming

Medieval people called the catastrophe of the 14th century either the "Great Pestilence"' or the "Great Plague". Writers contemporary to the plague referred to the event as the "Great Mortality". Swedish and Danish chronicles of the 16th century described the events as "black" for the first time, not to describe the late-stage sign of the disease, in which the sufferer's skin would blacken due to subepidermal hemorrhages and the extremities would darken with gangrene, but more likely to refer to black in the sense of glum or dreadful and to denote the terror and gloom of the events. The German physician and medical writer Justus Hecker suggested that a mistranslation of the Latin atra mors (terrible, or black, death) had occurred in Scandinavia when he described the catastrophe in 1832 in his publication "Der schwarze Tod im vierzehnten Jahrhundert". The work was translated into English the following year, and with the cholera epidemic happening at that time, "The Black Death in the 14th century" gained widespread attention and the terms Schwarzer Tod and Black Death became more widely used in the German and English speaking worlds, respectively.

Migration

Populations in Crisis

In Europe, the Medieval Warm Period ended some time towards the end of the 13th century, bringing the "Little Ice Age" and harsher winters with reduced harvests. In northern Europe, new technological innovations such as the heavy plough and the three-field system were not as effective in clearing new fields for harvest as they were in the Mediterranean because the north had poor clay soil. Food shortages and rapidly inflating prices were a fact of life for as much as a century before the plague. Wheat, oats, hay and consequently livestock were all in short supply. Their scarcity resulted in malnutrition, which increases susceptibility to infections due to weakened immunity. Consistently high fertility rates, at five or more children per woman throughout Europe, resulted in high population growth rates and contributed to food shortages. In the autumn of 1314, heavy rains began to fall, followed by several years of cold and wet winters. The already weak harvests of the north suffered and the seven-year famine ensued. In the years 1315 to 1317 a catastrophic famine, known as the Great Famine, struck much of northwest Europe. It was arguably the worst in European history, reducing the population by perhaps more than 10 percent. Infection and migration

The plague disease, generally thought to be caused by Yersinia pestis, is enzootic (commonly present) in populations of fleas carried by ground rodents, including marmots, in various areas including Central Asia, Kurdistan, Western Asia, Northern India and Uganda. Nestorian graves dating to 1338–9 near Lake Issyk Kul in Kyrgizstan have inscriptions referring to plague and are thought by many epidemiologists to mark the outbreak of the epidemic, from which they could easily have spread to China and India. In October 2010, medical geneticists confirmed that the plague originated in Yunnan, province in southwest China.[5] In China, the 13th century Mongol conquest caused a decline in farming and trading. However, economic recovery had been observed in the beginning of the 14th century. In 1330s a high frequency of

natural disasters and plagues led to widespread famine starting in 1331, with a deadly plague arriving soon after.[18]The population dropped from approximately 120 to 60 million. The 14th-century plague killed an estimated 25 million Chinese and other Asians during the 15 years before it entered Constantinople in 1347.

The disease may have travelled along the Silk Road with Mongol armies and traders or it could have come via ship. By the end of 1346 reports of plague had reached the seaports of Europe: "India was depopulated, Tartary, Mesopotamia, Syria, Armenia were covered with dead bodies".

Plague was reportedly first introduced to Europe at the trading city of Caffa in the Crimea in 1347. After a protracted siege, during which the Mongol army under Jani Beg was suffering the disease, they catapulted the infected corpses over thecity walls to infect the inhabitants. The Genoese traders fled, taking the plague by ship into Sicily and the south of Europe, whence it spread north. Whether or not this hypothesis is accurate, it is clear that several existing conditions such as war, famine, and weather contributed to the severity of the Black Death.

European Outbreak
'The seventh year after it began, it came to England and first began in the towns and ports joining on the seacoasts, in Dorsetshire, where, as in other counties, it made the country quite void of inhabitants so that there were almost none left alive.

... But at length it came to Gloucester, yea even to Oxford and to London, and finally it spread over all England and so wasted the people that scarce the tenth person of any sort was left alive.' (Geoffrey the Baker, Chronicon Angliae)

There appear to have been several introductions into Europe. It reached Sicily in October 1347 carried by twelve Genoese galleys, where it rapidly spread all over the island. Galleys from Caffa reached Genoa and Venice in January 1348 but it was the outbreak in Pisa a few weeks later that was the entry point to northern Italy. Towards the end of January one of the galleys expelled from Italy arrived in Marseille.

From Italy the disease spread northwest across Europe, striking France, Spain, Portugal and England by June 1348, then turned and spread east through Germany and Scandinavia from 1348 to 1350. It was introduced in Norway in 1349 when a ship landed at Askøy, then spread to Bjørgvin (modern Bergen) but never reached Iceland. Finally it spread to north-western Russia in 1351. The plague spared some parts of Europe, including the Kingdom of Poland and isolated parts of Belgium and the Netherlands.

Middle Eastern Outbreak
The plague struck various countries in the Middle East during the pandemic, leading to serious depopulation and permanent change in both economic and social structures. As it spread to western Europe, the disease also entered the region from southern Russia. By autumn 1347, the plague reached Alexandria in Egypt, probably through the port's trade with Constantinople, and ports on the Black Sea. During 1347, the disease travelled eastward to Gaza, and north along the eastern coast to cities in Lebanon, Syria and Palestine, including Ashkelon, Acre, Jerusalem, Sidon, Damascus, Homs, and Aleppo. In 1348–49, the disease reached Antioch. The city's residents fled to the north, most of them dying during the journey, but the infection had been spread to the people of Asia Minor.

Mecca became infected in 1349. During the same year, records show the city of Mawsil (Mosul) suffered a massive epidemic, and the city of Baghdad experienced a second round of the disease. In 1351, Yemen experienced an outbreak of the plague. This coincided with the return of King Mujahid of

Yemen from imprisonment in Cairo. His party may have brought the disease with them from Egypt.

Symptoms
Contemporary accounts of the plague are often varied or imprecise. The most commonly noted symptom was the appearance of buboes (or gavocciolos) in the groin, the neck and armpits, which oozed pus and bled when opened. Boccaccio's description is graphic:

"In men and women alike it first betrayed itself by the emergence of certain tumours in the groin or armpits, some of which grew as large as a common apple, others as an egg...From the two said parts of the body this deadly gavocciolo soon began to propagate and spread itself in all directions indifferently; after which the form of the malady began to change, black spots or livid making their appearance in many cases on the arm or the thigh or elsewhere, now few and large, now minute and numerous. As the gavocciolo had been and still was an infallible token of approaching death, such also were these spots on whomsoever they showed themselves."

Ziegler comments that the only medical detail that is questionable is the infallibility of approaching death, as if the bubo discharges, recovery is possible.

This was followed by acute fever and vomiting of blood. Most victims died within two to seven days after infection. David Herlihy identifies another potential sign of the plague: freckle-like spots and rashes which could be the result of flea-bites.

Some accounts, like that of Louis Heyligen, a musician in Avignon who died of the plague in 1348, noted a distinct form of the disease which infected the lungs and led to respiratory problems and which is identified with pneumonic plague.

"It is said that the plague takes three forms. In the first people suffer an infection of the lungs, which leads to breathing difficulties. Whoever has this corruption or contamination to any extent cannot escape but will die within two days. Another form...in which boils erupt under the armpits,...a third form in which people of both sexes are attacked in the groin."

Causes
Medical knowledge had stagnated during the Middle Ages. The most authoritative account at the time came from the medical faculty in Paris in a report to the king of France that blamed the heavens, in the form of a conjunction of three planets in 1345 that caused a "great pestilence in the air".[33] This report became the first and most widely circulated of a series of "plague tracts" that sought to give advice to sufferers. That the plague was caused by bad air became the most widely accepted theory. The word plague had no special significance at this time, and only the recurrence of outbreaks during the Middle Ages gave it the name that has become the medical term.

The importance of hygiene was recognised only in the nineteenth century; until then it was common that the streets were filthy, with live animals of all sorts around and human parasites abounding. A transmissible disease will spread easily in such conditions. One development as a result of the Black Death was the establishment of the idea of quarantine in Dubrovnik in 1377 after continuing outbreaks.

The dominant explanation for the Black Death is the plague theory, which attributes the outbreak to Yersinia pestis, also responsible for an epidemic that began in southern China in 1865, eventually spreading to India. The investigation of the pathogen that caused the 19th-century plague was begun by teams of scientists who visited Hong Kong in 1894, among whom was Alexandre Yersin, after whom the

pathogen was named Yersinia pestis. The mechanism by which Y. pestis was usually transmitted was established in 1898 by Paul-Louis Simond and was found to involve the bites of fleas whose midguts had become obstructed by replicating Y. pestis several days after feeding on an infected host. This blockage results in starvation and aggressive feeding behaviour by the fleas, which repeatedly attempt to clear their blockage by regurgitation, resulting in thousands of plague bacteria being flushed into the feeding site, infecting the host. The bubonic plague mechanism was also dependent on two populations of rodents: one resistant to the disease, which act as hosts, keeping the disease endemic, and a second that lack resistance. When the second population dies, the fleas move on to other hosts, including people, thus creating a human epidemic.

The historian Francis Aidan Gasquet, who had written about the 'Great Pestilence' in 1893 and suggested that "it would appear to be some form of the ordinary Eastern or bubonic plague" was able to adopt the epidemiology of the bubonic plague for the Black Death for the second edition in 1908, implicating rats and fleas in the process, and his interpretation was widely accepted for other ancient and medieval epidemics, such as the Justinian plague that was prevalent in the Eastern Roman Empire from 541 to 700 AD.

More recently other forms of plague have been implicated. The modern bubonic plague has a mortality rate of 30 to 75 percent and symptoms including feverof 38–41 °C (101–105 °F), headaches, painful, aching joints, nausea and vomiting, and a general feeling of malaise. If untreated, of those that contract the bubonic plague, 80 percent die within eight days. Pneumonic plague has mortality rate of 90 to 95 percent. Symptoms include fever, cough, and blood-tinged sputum. As the disease progresses, sputum becomes free flowing and bright red. Septicemic plague is the least common of the three forms, with a mortality rate close to 100 percent. Symptoms are high fevers and purple skin patches (purpura due to disseminated intravascular coagulation). In cases of pneumonic and particularly septicemic plague the progress of the disease is so rapid that there would often be no time for the development of the enlarged lymph nodes that were noted as buboes.

"Many modern scholars accept that the lethality of the Black Death stemmed from the combination of bubonic and pneumonic plague with other diseases and warn that every historical mention of 'pest' was not necessarily bubonic plague...In her study of 15th Century outbreaks, Ann Carmichael states that worms, the pox, fevers and dysentery clearly accompanied bubonic plague."

Alternative Explanations

It is recognised that an epidemiological account of the plague is as important as an identification of symptoms, but researchers are hampered by the lack of reliable statistics from this period. Most work has been done on the spread of the plague in England, and even estimates of overall population at the start vary by over 100% as no census was undertaken between the Domesday Bookand 1377. Estimates of plague victims are usually extrapolated from figures for the clergy.This interpretation was first significantly challenged by the work of British bacteriologist J. F. D. Shrewsbury in 1970, who noted that the reported rates of mortality in rural areas during the 14th century pandemic were inconsistent with the modern bubonic plague, leading him to conclude that contemporary accounts were exaggerations. In 1984 zoologist Graham Twigg produced the first major work to challenge the bubonic plague theory directly, and his doubts about the identity of the Black Death have been taken up by a number of authors, including Samuel K. Cohn, Jr. (2002), David Herlihy (1997), and Susan Scott and Christopher Duncan (2001).

In addition to arguing that the rat population was insufficient to account for a bubonic plague pandemic, sceptics of the bubonic plague theory point out that the symptoms of the Black Death are not unique (and

arguably in some accounts may differ from bubonic plague); that transference via fleas in goods was likely to be of marginal significance and that the DNA results may be flawed and might not have been repeated elsewhere, despite extensive samples from other mass graves. Other arguments include the lack of accounts of the death of rats before outbreaks of plague between the 14th and 17th centuries; temperatures that are too cold in northern Europe for the survival of fleas; that, despite primitive transport systems, the spread of the Black Death was much faster than that of modern bubonic plague; that mortality rates of the Black Death appear to be very high; that, while modern bubonic plague is largely endemic as a rural disease, the Black Death indiscriminately struck urban and rural areas; and that the pattern of the Black Death, with major outbreaks in the same areas separated by five to fifteen years, differs from modern bubonic plague, which often becomes endemic for decades, flaring up on an annual basis.

Walløe complains that all of these authors "take it for granted that Simond's infection model, black rat → rat flea → human, which was developed to explain the spread of plague in India, is the only way an epidemic of Yersinia pestis infection could spread", whilst pointing to several other possibilities.

DNA Evidence

A variety of alternatives to the Y. pestis have been put forward. Twigg suggested that the cause was a form of anthrax and N. F. Cantor (2001) thought it may have been a combination of anthrax and other pandemics. Scott and Duncan have argued that the pandemic was a form of infectious disease that characterise as hemorrhagic plague similar to Ebola. Archaeologist Barney Sloane has argued that there are insufficient evidence of the extinction of large number of rats in the archaeological record of the medieval waterfront in London and that the plague spread too quickly to support the thesis that the Y. pestis was spread from fleas on rats and argues that transmission must have been person to person. However, no single alternative solution has achieved widespread acceptance. Many scholars arguing for the Y. pestis as the major agent of the pandemic, suggest that its extent and symptoms can be explained by a combination of bubonic plague with other diseases, including typhus, smallpox and respiratory infections. In addition to the bubonic infection, others point to additional septicemic (a type of "blood poisoning") and pneumonic (an airborne plague that attacks the lungs before the rest of the body) forms of the plague, which lengthen the duration of outbreaks throughout the seasons and help account for its high mortality rate and additional recorded symptoms.

In October 2010 the open-access scientific journal PLoS Pathogens published a paper by a multinational team who undertook a new investigation into the role of Yersinia pestis in the Black Death following the disputed identification by Drancourt & Raoult in 1998. Their surveys tested for DNA and protein signatures specific for Y. pestis in human skeletons from widely distributed mass graves in northern, central and southern Europe that were associated archaeologically with the Black Death and subsequent resurgences. The authors concluded that this new research, together with prior analyses from the south of France and Germany"...ends the debate about the etiology of the Black Death, and unambiguously demonstrates that Y. pestis was the causative agent of the epidemic plague that devastated Europe during the Middle Ages."

The study also found that there were two previously unknown but related clades (genetic branches) of the Y. pestis genome associated with medieval mass graves. These clades (which are thought to be extinct) were found to be ancestral to modern isolates of the modern Y. pestis strains Orientalis and Medievalis, suggesting that the plague may have entered Europe in two waves. Surveys of plague pit remains in France and England indicate that the first variant entered Europe through the port of Marseille around November 1347 and spread through France over the next two years, eventually reaching England in the spring of 1349, where it spread through the country in three epidemics. Surveys of plague pit remains

from the Dutch town of Bergen op Zoom showed that the Y. pestis genotype responsible for the pandemic that spread through the Low Countries from 1350 differed from that found in Britain and France, implying that Bergen op Zoom (and possibly other parts of the southern Netherlands) was not directly infected from England or France in 1349 and suggesting that a second wave of plague, different from those in Britain and France, may have been carried to the Low Countries from Norway, the Hanseatic cities or another site.

The results of the Haensch study have since been confirmed and amended. Based on genetic evidence derived from Black Death victims in the East Smithfield burial site in England, Schuenemann et al. in 2011 further conclude "that the Black Death in medieval Europe was caused by a variant of Y. pestis that may no longer exist." A study published in Nature in October 2011 sequenced the genome of Y. pestis from plague victims and indicated that the strain that caused the Black Death is ancestral to most modern strains of the disease.

Consequences

Death Toll

Figures for the death toll vary widely by area and from source to source as new research and discoveries come to light. It killed an estimated 75 million–200 million people in the 14th century. According to medieval historian Philip Daileader in 2007:

The trend of recent research is pointing to a figure more like 45 percent to 50 percent of the European population dying during a four-year period. There is a fair amount of geographic variation. In Mediterranean Europe, areas such as Italy, the south of France and Spain, where plague ran for about four years consecutively, it was probably closer to 75 percent to 80 percent of the population. In Germany and England ... it was probably closer to 20 percent.

The most widely accepted estimate for the Middle East, including Iraq, Iran and Syria, during this time, is for a death rate of about a third. The Black Death killed about 40% of Egypt's population. Half of Paris's population of 100,000 people died. In Italy, Florence's population was reduced from 110,000 or 120,000 inhabitants in 1338 to 50,000 in 1351. At least 60 percent of Hamburg's and Bremen's population perished. Before 1350, there were about 170,000 settlements in Germany, and this was reduced by nearly 40,000 by 1450. In 1348, the plague spread so rapidly that before any physicians or government authorities had time to reflect upon its origins, about a third of the European population had already perished. In crowded cities, it was not uncommon for as much as 50 percent of the population to die. Europeans living in isolated areas suffered less, whereas monks and priests were especially hard hit since they cared for the Black Death's victims.

Persecutions

Because 14th century healers were at a loss to explain the cause, Europeans turned to astrological forces, earthquakes, and the poisoning of wells by Jews as possible reasons for the plague's emergence. The governments of Europe had no apparent response to the crisis because no one knew its cause or how it spread. The mechanism of infection and transmission of diseases was little understood in the 14th century; many people believed only God's anger could produce such horrific displays.

There were many attacks against Jewish communities. In August 1349, the Jewish communities of Mainz and Cologne were exterminated. In February of that same year, the citizens of Strasbourg murdered 2,000 Jews. By 1351, 60 major and 150 smaller Jewish communities were destroyed. The Brotherhood of the Flagellants, a movement said to number up to 800,000, reached its peak of popularity.

In culture

Main article: Black Death in medieval culture

They died by the hundreds, both day and night, and all were thrown in ... ditches and covered with earth. And as soon as those ditches were filled, more were dug. And I, Agnolo di Tura ... buried my five children with my own hands ... And so many died that all believed it was the end of the world.The Black Death had a profound impact on art and literature throughout the generation that experienced it. Much of the most useful manifestations of the Black Death in literature, to historians, comes from the accounts of its chroniclers. Some of these chroniclers were famous writers, philosophers and rulers such as Boccaccio and Petrarch. Their writings, however, did not reach the majority of the European population. Petrarch's work was read mainly by wealthy nobles and merchants of Italian city-states. He wrote hundreds of letters and vernacular poetry, and passed on to later generations a revised interpretation of courtly love. There was one troubadour, writing in the lyric style long out of fashion, who was active in 1348. Peire Lunel de Montech composed the sorrowful sirventes "Meravilhar no·s devo pas las gens" during the height of the plague in Toulouse.—The Plague in Siena: An Italian Chronicle

How many valiant men, how many fair ladies, breakfast with their kinfolk and the same night supped with their ancestors in the next world! The condition of the people was pitiable to behold. They sickened by the thousands daily, and died unattended and without help. Many died in the open street, others dying in their houses, made it known by the stench of their rotting bodies. Consecrated churchyards did not suffice for the burial of the vast multitude of bodies, which were heaped by the hundreds in vast trenches, like goods in a ships hold and covered with a little earth. —Giovanni Boccaccio

Recurrence

An epidemic of plague dies out after a few months because it has no host in which the bacteria can survive. However that does not mean that there is not somewhere some surviving infection, in a rodent or flea or warm place, that acts as a reservoir so that sooner or later it breaks out again.

The plague repeatedly returned to haunt Europe and the Mediterranean throughout the 14th to 17th centuries. According to Biraben, plague was present somewhere in Europe in every year between 1346 and 1671. The Second Pandemic was particularly widespread in the following years: 1360–1363; 1374; 1400; 1438–1439; 1456–1457; 1464–1466; 1481–1485; 1500–1503; 1518–1531; 1544–1548; 1563–1566; 1573–1588; 1596–1599; 1602–1611; 1623–1640; 1644–1654; and 1664–1667. According to Geoffrey Parker, "France alone lost almost a million people to plague in the epidemic of 1628–31."

In England, in the absence of census figures, historians propose a range of pre-incident population figures from as high as 7 million to as low as 4 million in 1300, and a post-incident population figure as low as 2 million. By the end of 1350 the Black Death subsided, but it never really died out in England. Over the next few hundred years, there were further outbreaks in 1361–62, 1369, 1379–83, 1389–93, and throughout the first half of the 15th century. An outbreak in 1471 took as much as 10–15 percent of the population, while the death rate of the plague of 1479–80 could have been as high as 20 percent. The most general outbreaks in Tudor and Stuart England seem to have begun in 1498, 1535, 1543, 1563, 1589, 1603, 1625, and 1636, and ended with the Great Plague of London in 1665.

In the first half of the 17th century a plague claimed some 1,730,000 victims in Italy, or about 14% of the population. In 1656 the plague killed about half of Naples' 300,000 inhabitants. More than 1,250,000 deaths resulted from the extreme incidence of plague in 17th century Spain. The plague of 1649 probably reduced the population of Seville by half. In 1709–1713, a plague epidemic that followed the Great

Northern War (1700–1721, Sweden v. Russia and allies) killed about 100,000 in Sweden, and 300,000 in Prussia. The plague killed two-thirds of the inhabitants of Helsinki, and claimed a third of Stockholm's population. Europe's last major epidemic occurred in 1720 in Marseilles In 1466, perhaps 40,000 people died of plague in Paris. During the 16th and 17th centuries, plague visited Paris for almost one year out of three. The Black Death ravaged Europe for three years before it continued on into Russia, where the disease hit somewhere once every five or six years from 1350 to 1490. Plague epidemics ravaged London in 1563, 1593, 1603, 1625, 1636, and 1665, reducing its population by 10 to 30% during those years. Over 10% of Amsterdam's population died in 1623–1625, and again in 1635–1636, 1655, and 1664. There were twenty-two outbreaks of plague in Venice between 1361 and 1528. The plague of 1576–1577 killed 50,000 in Venice, almost a third of the population. Late outbreaks in central Europe included the Italian Plague of 1629–1631, which is associated with troop movements during the Thirty Years' War, and the Great Plague of Vienna in 1679. Over 60 percent of Norway's population died from 1348 to 1350. The last plague outbreak ravaged Oslo in 1654.

Third Plague Pandemic

The Black Death ravaged much of the Islamic world. Plague was present in at least one location in the Islamic world virtually every year between 1500 and 1850. Plague repeatedly struck the cities of North Africa. Algiers lost 30,000–50,000 to plague in 1620–21, and again in 1654–57, 1665, 1691, and 1740–42. Plague remained a major event in Ottoman society until the second quarter of the 19th century. Between 1701 and 1750, 37 larger and smaller plague epidemics were recorded in Constantinople, and 31 between 1751 and 1800. Baghdad has suffered severely from visitations of the plague, and sometimes two-thirds of its population has been wiped out.

Main article: Third plague pandemic

The Third plague pandemic (1855–1959) started in China in the middle of the 19th century, spreading plague to all inhabited continents and killing 10 million people in India alone. There were twelve plague outbreaks in Australia between 1900 and 1925 resulting in well over 1000 deaths, mainly in Sydney. This led to the establishment of a Public Health Department there which undertook some leading edge research on plague transmission from rat fleas to humans via the bacillus

Yersinia Pestis

The first North American plague epidemic was the San Francisco plague of 1900–1904, followed by another outbreak in 1907–1908. From 1944 through 1993, 362 cases of human plague were reported in the United States; approximately 90 percent of these occurred in four western states; Arizona, California, Colorado, and New Mexico. Plague was confirmed in the United States from nine western states during 1995.

The plague bacterium could develop drug-resistance and again become a major health threat. The ability to resist many of the antibiotics used against plague has been found so far in only a single case of the disease in Madagascar, in 1995 (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Bolivian Hemorrhagic Fever
Date: 2012
Source: Wikipedia

Abstract: Bolivian hemorrhagic fever (BHF), also known as black typhus or Ordog Fever, is a hemorrhagic fever and zoonotic infectious disease originating in Bolivia after infection by Machupo virus. BHF was first identified in 1959 by a research group led by Karl Johnson, an ambisense RNA virus of the Arenaviridae family. The mortality rate is estimated at 5 to 30 percent. Due to its pathogenicity, Machupo virus requires Biosafety Level Four conditions, the highest level.

In February and March 2007, some 20 suspected BHF cases (3 fatal) were reported to the El Servicio Departamental de Salud (SEDES) in Beni Department, Bolivia, and in February 2008, at least 200 suspected new cases (12 fatal) were reported to SEDES. In November 2011, a SEDES expert involved in a serosurvey to determine the extent of Machupo virus infections in the Department after the discovery of a second confirmed case near the departmental capital of Trinidad in November, 2011, expressed concern about expansion of the virus' distribution outside the endemic zone in Mamoré and Iténez provinces.

Epidemiology

Vectors
The vector is the vesper mouse *Calomys callosus*, a rodent indigenous to northern Bolivia. Infected animals are asymptomatic and shed the virus in excreta, thereby infecting humans. Evidence of person-to-person transmission of BHF exists but is believed to be rare.

Symptoms
The infection has a slow onset with fever, malaise, headache and muscular pains. Petechiae (blood spots) on the upper body and bleeding from the nose and gums are observed when the disease progresses to the hemorrhagic phase, usually within seven days of onset.

Prevention
Measures to reduce contact between the vesper mouse and humans have effectively limited the number of outbreaks, with no cases identified between 1973 and 1994. Although, there are no cures or immunization for the disease, a vaccine developed for the genetically related Junín virus which causes Argentine hemorrhagic fever has shown evidence of cross-reactivity to Machupo virus and may therefore be an effective prophylactic measure for people at high risk of infection. Post infection (and providing that the person survives the infection), those that have contracted BHF are usually immune to further infection of the disease.

Weaponization
Bolivian hemorrhagic fever was one of three hemorrhagic fevers and one of more than a dozen agents that the United States researched as potential biological weapons before the nation suspended its biological weapons program (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Botulinum Toxin
Date: 2012
Source: Wikipedia

Abstract: Botulinum toxin is a protein produced by the bacterium Clostridium botulinum and is the most powerful neurotoxin yet discovered.[citation needed] Botulinum toxin can cause botulism, a serious and life-threatening illness in humans and animals. When introduced intravenously in monkeys, type A (Botox Cosmetic) of the toxin exhibits an LD50 of 40-56 ng, type C1 around 32 ng, type D 3200 ng, and type E 88 ng, rendering the above types some of the most powerful neurotoxins known. Popularly known by one of its trade names, Botox, it is used for various cosmetic and medical procedures. Botulinum can be absorbed from eyes, mucous membranes, respiratory tract or non-intact skin.

History

Justinus Kerner described botulinum toxin as a "sausage poison" and "fatty poison", because the bacterium that produces the toxin often caused poisoning by growing in improperly handled or prepared meat products. It was Kerner, a physician, who first conceived a possible therapeutic use of botulinum toxin and coined the name botulism (from Latin botulus meaning "sausage"). In 1897, Emile van Ermengem found the producer of the botulin toxin was a bacterium, which he named Clostridium botulinum. In 1928, P. Tessmer Snipe and Hermann Sommer for the first time purified the toxin. In 1949, Arnold Burgen's group discovered, through an elegant experiment, that botulinum toxin blocks neuromuscular transmission through decreased acetylcholine release.

Therapeutic Research

In the late 1960s Alan Scott, M.D., a San Francisco ophthalmologist, and Edward Schantz were the first to work on a standardized botulinum toxin preparation for therapeutic purposes. By 1973, Scott (now at Smith-Kettlewell Institute) used botulinum toxin type A (BTX-A) in monkey experiments, and, in 1980, he officially used BTX-A for the first time in humans to treat strabismus"crossed eyes", a condition in which the eyes are not properly aligned with each other, and "uncontrollable blinking" (blepharospasm). In 1993, Pasricha and colleagues showed that botulinum toxin could be used for the treatment of achalasia, a spasm of the lower esophageal sphincter. In 1994 Bushara showed that botulinum toxin injections inhibit sweating. This was the first demonstration of non-muscular use of BTX-A in humans.

Blepharospasm and Strabismus

In the early 1980s, university-based ophthalmologists in the U.S.A. and Canada further refined the use of botulinum toxin as a therapeutic agent. By 1985, a scientific protocol of injection sites and dosage had been empirically determined for treatment of blepharospasm and strabismus.[12] Side effects were deemed to be rare, mild and treatable. The beneficial effects of the injection lasted only 4–6 months. Thus, blepharospasm patients required re-injection two or three times a year.

In 1986, Scott's micro-manufacturer and distributor of Botox was no longer able to supply the drug because of an inability to obtain product liability insurance. Patients became desperate as supplies of

Botox were gradually consumed, forcing him to abandon patients who would have been due for their next injection. For a period of four months, American blepharospasm patients had to arrange to have their injections performed by participating doctors at Canadian eye centers until the liability issues could be resolved.

In December 1989, Botox, manufactured by Allergan, Inc., was approved by the U.S. Food and Drug Administration (FDA) for the treatment of strabismus, blepharospasm, and hemifacial spasm in patients over 12 years old.

Cosmetic
The cosmetic effect of BTX-A on wrinkles was originally documented by a plastic surgeon from Sacramento, California, Dr. Richard Clark, and published in the journal Plastic and Reconstructive Surgery in 1989. Canadian husband and wife ophthalmologist and dermatologist physicians Carruthers JD and Carruthers JA were the first to publish a study on BTX-A for the treatment of glabellar frown lines in 1992. Similar effects had reportedly been observed by a number of independent groups (Brin, and the Columbia University group). After formal trials, on April 12, 2002, the FDA announced regulatory approval of botulinum toxin type A (Botox Cosmetic) to temporarily improve the appearance of moderate-to-severe frown lines between the eyebrows (glabellar lines). Subsequently, cosmetic use of botulinum toxin type A has become widespread with many celebrities viewing it as less intrusive and/or artificial than other types of plastic surgery. The results of cosmetic procedures vary but can last up to eight months. The U.S. Food and Drug Administration approved an alternative product-safety testing method in response to increasing public concern that LD50 testing was required for each batch sold in the market.

Muscle Spasms
The acceptance of BTX-A use for the treatment of muscle pain disorders is growing, with approvals pending in many European countries. The efficacy of BTX-A in treating a variety of other medical conditions (including prostatic dysfunction,asthma, and others) is an area of continued study.

Upper Motor Neuron Syndrome
BTX-A is now a common treatment for muscles affected by the upper motor neuron syndrome such as cerebral palsy, for muscles with an impaired ability to effectively lengthen. Muscles affected by the Upper Motor Neuron Syndrome frequently are limited by weakness, loss of reciprocal inhibition, decreased movement control and hypertonicity (including spasticity). Joint motion may be restricted by severe muscle imbalance related to the Upper Motor Neuron Syndrome, when some muscles are markedly hypertonic, and lack effective active lengthening. Injecting an overactive muscle to decrease its level of contraction can allow improved reciprocal motion, and so improved ability to move and exercise. In June 2009, its use for treating hypertonic muscles helped an Australian man to walk again. He had required a wheelchair for mobility following a stroke 20 years prior.

Sweating
While treating patients with hemifacial spasm at Southend Hospital in England in 1993, Khalaf Bushara and David Park were the first to show that botulinum toxin injections inhibit sweating. This was the first demonstration of non-muscular use of BTX-A. Bushara further showed the efficacy of botulinum toxin in treating hyperhidrosis (excessive sweating). BTX-A was later approved for the treatment of excessive underarm sweating.

Cervical Dystonia
Botulinum Toxin Type B (BTX-B) received FDA approval for treatment of cervical dystonia on December 21, 2000. Trade names for BTX-B are Myobloc in the United States, and Neurobloc in the European Union.[citation needed]

Chronic Migraine
OnabotulinumtoxinA (trade name Botox) received FDA approval for treatment of chronic migraines on October 15, 2010. The toxin is injected into the head and neck to treat these chronic headaches. Approval followed evidence presented to the agency from two studies funded by Allergan, Inc. showing a very slight improvement in incidence of chronic migraines for migraine sufferers undergoing the Botox

treatment.

Since then, several randomized control trials have shown Botulinum Toxin Type A to improve headache symptoms and quailty of life when used prophylactically for patients with chronic migraine who exhibit headache characteristics consistent with: pressure perceived from outside source, shorter total duration of chronic migraines (<30 years), "detoxification" of patients with co-existing chronic daily headache due to medication overuse, no current history of other preventative headache medications.

Denaturing
Botulinum toxin is denatured at temperatures greater than 80 °C (176 °F).

Sources
Botulism toxins are produced by these bacteria: Clostridium botulinum, C. butyricum, C. baratii and C. argentinense. Foodborne botulism can be transmitted through food that has not been heated correctly prior to being canned or food that was not cooked correctly from a can. Most infant botulism cases cannot be prevented because the bacteria that cause this disease are in soil and dust. The bacteria can be found inside homes on floors, carpet, and countertops even after cleaning. Honey can contain the bacteria that cause infant botulism, so children less than twelve months old should not be fed honey. Honey is safe for persons one year of age and older.

Chemical Overview & Lethality
There are seven serologically distinct toxin types, designated A through G. Additionally, six of the seven toxin types have subtypes with five subtypes of BoNT A having been described. The toxin is a two-chain polypeptide with a 100-kDa heavy chain joined by a disulfide bond to a 50-kDa light chain. This light chain is an enzyme (a protease) that attacks one of the fusion proteins (SNAP-25, syntaxin or synaptobrevin) at a neuromuscular junction, preventing vesicles from anchoring to the membrane to release acetylcholine. By inhibiting acetylcholine release, the toxin interferes with nerve impulses and causes flaccid (sagging) paralysis of muscles in botulism, as opposed to the spastic paralysis seen in tetanus.

There are over 70 structures of this toxin deposited in the PDB which reveal the tertiary structure of this class of toxins, as shown above.

It is the most acutely toxic substance known, with a median lethal dose of about 1 ng/kg when introduced intravenously and 3 ng/kg when inhaled. This means that, depending on the method of introduction into the body, a mere 90–270 nanograms of botulinum toxin could be enough to kill an average 90 kg (200 lb) person, and four kilograms of the toxin, if evenly distributed, would be more than enough to kill the entire human population of the world.

Food-borne botulism usually results from ingestion of food that has become contaminated with spores (such as a perforated can) in an anaerobic environment, allowing the spores to germinate and grow. The growing (vegetative) bacteria produce toxin. It is the ingestion of preformed toxin that causes botulism, not the ingestion of the spores or the vegetative bacteria. Infant and wound botulism both result from infection with spores, which subsequently germinate, resulting in production of toxin and the symptoms of botulism.

Proper refrigeration at temperatures below 3 °C (38 °F) retards the growth of Clostridium botulinum. The organism is also susceptible to high salt and low pH levels. The toxin itself is rapidly destroyed by heat, such as in thorough cooking. On the other hand, the spores that produce the toxin are heat-tolerant and will survive boiling water for an extended period of time. Fortunately, ingestion of the spores is safe, except in infants, as the highly oxygenated and highly acidic environment of an adult human digestive system prevents the spores from growing and producing the botulinum toxin.[citation needed]

Botulinum toxin has been recognized and feared as a potential bioterror weapon.

Medical and Cosmetic Uses
Although botulinum toxin is a lethal, naturally occurring substance, it can be used as an effective and powerful medication. Researchers discovered in the 1950s that injecting overactive muscles with minute quantities of botulinum toxin type-A would result in decreased muscle activity by blocking the release of acetylcholine from the neuron by preventing the vesicle where the acetylcholine is stored from binding to the membrane where the neurotransmitter can be released. This will effectively weaken the muscle for a period of three to four months.

In cosmetic applications, a Botox injection, consisting of a small dose of botulinum toxin, can be used to prevent development of wrinkles by paralyzing facial muscles. As of 2007, it is the most common cosmetic operation, with 4.6 million procedures in the United States, according to the American Society of Plastic Surgeons. Qualifications for Botox injectors vary by county, state and country. Botox cosmetic providers include dermatologists, plastic surgeons, aesthetic spa physicians, dentists, nurse practitioners, nurses and physician assistants. The wrinkle preventing effect of Botox normally lasts for approximately three to four months, but can last up to six months.

In addition to its cosmetic applications, Botox is currently used in the treatment of spasms and dystonias, by weakening involved muscles, for the 60-70 day effective period of the drug. The main conditions treated with botulinum toxin are:

1. Cervical dystonia (spasmodic torticollis) (a neuromuscular disorder involving the head and neck)
2. Blepharospasm (excessive blinking)
3. Severe primary axillary hyperhidrosis (excessive sweating)
4. Strabismus (Squints)
5. Achalasia (failure of the lower oesophageal sphincter to relax)
6. Local intradermal injection of BTX-A is helpful in chronic focal neuropathies. The analgesic effects are not dependent on changes in muscle tone.
7. Migraine and other headache disorders, although the evidence is conflicting in this indication
8. Excessive sweating is a condition for the treatment of which FDA has approved the use of Botox.

Other uses of botulinum toxin type A that are widely known but not specifically approved by the U.S. Food and Drug Administration (off-label uses) include treatment of:

1. Idiopathic and neurogenic detrusor overactivity,
2. Pediatric incontinence, incontinence due to overactive bladder, and incontinence due to neurogenic bladder.
3. Anal fissure
4. vaginismus To reduce the spasm of the vaginal muscles.
5. Movement disorders associated with injury or disease of the central nervous system including trauma, stroke, multiple sclerosis, Parkinson's disease, or cerebral palsy
6. Focal dystonias affecting the limbs, face, jaw, or vocal cords
7. TMJ pain disorders
8. Diabetic neuropathy
9. Wound healing
10. Excessive salivation
11. Vocal cord dysfunction (VCD) including spasmodic dysphonia and tremor
12. Reduction of the Masseter muscle for decreasing the apparent size of the lower jaw
13. Painful bladder syndrome,
14. Detrusor sphincter dyssynergia and benign prostatic hyperplasia,

Treatment and prevention of chronic headache and chronic musculoskeletal pain are emerging uses for botulinum toxin type A. In addition, there is evidence that Botox may aid in weight loss by increasing the

gastric emptying time.

Links to Deaths
In September 2005, a paper published in the Journal of American Academy of Dermatology reported from the FDA saying that use of Botox has resulted in 28 deaths between 1989 and 2003, though none were attributed to cosmetic use.

On February 8, 2008, the FDA announced that Botox has "been linked in some cases to adverse reactions, including respiratory failure and death, following treatment of a variety of conditions using a wide range of doses," due to its ability to spread to areas distant from the site of the injection. In April 2009, the FDA updated its mandatory boxed warning cautioning that the effects of the botulinum toxin may spread from the area of injection to other areas of the body, causing symptoms similar to those of botulism.

In January 2009, the Canadian government warned that botox can have the adverse effect of spreading to other parts of the body, which could cause muscle weakness, swallowing difficulties, pneumonia, speech disorders and breathing problems.

Several cases of death have been linked to the use of other chemicals as substitutes for Botox, one of the causes of death listed on the Spike TV show, 1000 Ways to Die.

Side Effects
Side effects, which are generally minor and temporary, can be predicted from the mode of action (muscle paralysis) and chemical structure (protein) of the molecule, resulting broadly speaking in two major areas of side effects: paralysis of the wrong muscle group and allergic reaction. Bruising at the site of injection is a side effect not of the toxin, but rather the mode of administration. In cosmetic use, this can result in inappropriate facial expression such as drooping eyelid, double vision, uneven smile, or loss of the ability to close eyes. This will wear off in around six weeks. Bruising is prevented by the clinician applying pressure to the injection site, but may still occur, and will last around 7–11 days. When injecting the masseter muscle of the jaw, loss of muscle function will result in a loss or reduction of power to chew solid foods. All cosmetic treatments are of limited duration, and can be as short a period as six weeks, but usually the effective period lasts from two to three months. At the extremely low doses used medicinally, botulinum toxin has a very low degree of human and animal toxicity.

Other adverse events from cosmetic use include headaches, dysphagia, flu-like syndromes, blurred vision, dry mouth, fatigue, allergic reactions and swelling or redness at the injection site.

There has been a petition by Public Citizen to the FDA requesting regulatory action concerning the possible spread of botulinum toxin (Botox, Myobloc) from the site of injection to other parts of the body.

Individuals who are pregnant, have egg allergies or a neuromuscular disorder are advised to avoid Botox.

As published in Forbes and originally published in the journal Social Psychology and Personality Science, Botox takes away or dampens the emotional feelings in a particular situation. That may be due to less interaction between facial muscle movement and brain. According to David Neal, a psychology professor at the University of Southern California, “if muscular signals from the face to the brain are dampened, you’re less able to read emotions.”

One way botox might affect emotional feelings is by dampening the relay of signals from the face to the amygdala and brainstem centers for autonomic arousal.

The mental effects of botox may extend beyond emotional feelings to the ability to understand language about emotions. An experimental study suggests that cosmetic use of botulinum toxin for treatment of glabellar lines affects human cognition. As reported in the L.A. Times, Havas and colleagues (Havas, Glenberg, Gutowski, Lucarelli, & Davidson, 2010) asked subjects to read emotional (angry, sad, happy) sentences before and two weeks after botox injections in the corrugator supercilii muscle used in frowning. Reading times for angry and sad sentences were longer after botox injection than before injection, while reading times for happy sentences were unchanged. This finding suggests that facial muscle paralysis has a selective effect in human cognition, and shows that botox hinders the ability to understand language. According to the lead researcher in this study, "botox causes a kind of mild, temporary, cognitive blindness to information in the world, social information about the emotions of other people."

Biochemical mechanism of toxicity

Target molecules of botulinum (BoNT) and tetanus (TeNT) toxins inside the axon terminal.

The heavy chain of the toxin is particularly important for targeting the toxin to specific types of axon terminals. The toxin must get inside the axon terminals in order to cause paralysis. Following the attachment of the toxin heavy chain to proteins on the surface of axon terminals, the toxin can be taken into neurons by endocytosis. The light chain is able to cleave endocytotic vesicles and reach the cytoplasm. The light chain of the toxin has protease activity. The type A toxin proteolytically degrades the SNAP-25 protein, a type of SNARE protein. The SNAP-25 protein is required for vesicle fusion that releases neurotransmitters from the axon endings (in particular Acetylcholine). Botulinum toxin specifically cleaves these SNAREs, and so prevents neuro-secretory vesicles from docking/fusing with the nerve synapse plasma membrane and releasing their neurotransmitters.

Though it affects the nervous system, common nerve agent treatments (namely the injection of atropine and pralidoxime) will increase mortality by enhancing botulin toxin's mechanism of toxicity. Attacks involving botulinum toxin are distinguishable from those involving nerve agent in that NBC detection equipment (such as M-8 paper or the ICAM) will not indicate a "positive" when a sample of the agent is tested. Furthermore, botulism symptoms develop relatively slowly, over several days compared to nerve agent effects, which can be instantaneous.

Treatment of Botulinum Poisoning

If the symptoms of botulism are diagnosed early, an equine antitoxin, use of enemas, and extracorporeal removal of the gut contents can be used to treat the food-borne illness. Wound infections can be treated surgically. Information regarding methods of safe canning, and public education about the disease are methods of prevention. Tests to detect botulism include a brain scan, nerve conduction test, and a tensilon test for myasthenia gravis in order to differentiate botulism from other diseases that manifest in the same way. Electromyography (EMG) can be utilized to differentiate myasthenia gravis and Guillain-Barré syndrome, diseases that botulism often mimics. Toxicity testing of serum specimens, wound tissue cultures, and toxicity testing, and stool specimen cultures are the best methods for idientifying botulism. Laboratory tests of the patient's serum or stool, which are then injected into mice are also indicative of botulism. But the faster way to detect botulinum toxin in people is using the mass spectrometry technology because it reduces testing time to three or four hours and at the same time it can identify the seven types of the toxin.

The case fatality rate for botulinum poisoning between 1950 and 1996 was 15.5%, down from approximately 60% over the previous 50 years. Death is generally secondary to respiratory failure due to paralysis of the respiratory muscles, so treatment consists of antitoxin administration and artificial ventilation until the neurotoxins are excreted or metabolised. If initiated on time these treatments are quite effective, although antisera can not affect BoNT polypeptides that have already entered cells. Occasionally, functional recovery may take several weeks to months or more.

There are two primary Botulinum Antitoxins available for treatment of botulism.

Trivalent (A,B,E) Botulinum Antitoxin is derived from equine sources utilizing whole antibodies (Fab & Fc portions). This antitoxin is available from the local health department via the CDC in the USA.
The second antitoxin is Heptavalent (A,B,C,D,E,F,G) Botulinum Antitoxin, which is derived from "despeciated" equine IgG antibodies, which have had the Fc portion cleaved off leaving the F(ab')2 portions. This is a less immunogenic antitoxinthat is effective against all known strains of botulism where not contraindicated. This is available from the United States Army. On June 1, 2006 the United States Department of Health and Human Services awarded a $363 million contract with Cangene Corporation for 200,000 doses of Heptavalent Botulinum Antitoxin over five years for delivery into the Strategic National Stockpile beginning in 2007.

Manufacturers
In the United States, Botox is manufactured by Allergan, Inc. for both therapeutic and cosmetic use (100Unit). In the United States, Xeomin (manufactured in Germany by Merz) is available for both therapeutic and cosmetic use.

Dysport, a therapeutic formulation of the type A toxin developed and manufactured in Ireland, is licensed for the treatment of focal dystonias and certain cosmetic uses in the US and worldwide in 100, 300 and 500 Units. Lanzhou Institute (China) manufactures a BTX-A product, producing 50U and 100U type A toxin. Neuronox, a BTX-A product, was introduced by Medy-Tox Inc. of South Korea, in 2009. In America, Neuronox is also known as Siax. Merz manufactures the toxin and sells it under the trade name Xeomin. Solstice Neurosciences, LLC, a wholly owned subsidiary of US WorldMeds, LLC sells their product under the names Myobloc or Neurobloc, although it contains Botulinum Toxin Type B, not the common Type A found in Botox.

Botulinum toxin is a protein produced by the bacterium Clostridium botulinum, and is considered the most powerful neurotoxin ever discovered. Botulinum toxin causes Botulism poisoning, a serious and life-threatening illness in humans and animals. When introduced intravenously in monkeys, type A (Botox Cosmetic) of the toxin exhibits an LD of 40-56 ng, type C1 around 32 ng, type D 3200 ng, and type E 88 ng, rendering the above types some of the most powerful neurotoxins known. Popularly known by one of its trade names, Botox or Dysport or Xeomin, it is used for various cosmetic and medical procedures (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Brucellosis
Date: 2012
Source: Wikipedia

Abstract: Brucellosis, also called Bang's disease, Crimean fever, Gibraltar fever, Malta fever, Maltese fever, Mediterranean fever, rock fever, or undulant fever, is a highly contagious zoonosis caused by ingestion of unsterilized milk or meat from infected animals or close contact with their secretions. Transmission from human to human, through sexual contact or from mother to child, is rare but possible. *Brucella* spp. are small, Gram-negative, non-motile, non-spore-forming, rod shaped (coccobacilli) bacteria. They function as facultative intracellular parasites causing chronic disease, which usually persists for life. Symptoms include profuse sweating and joint and muscle pain. Brucellosis has been recognized in animals including humans since the 20th century.

History and Nomenclature
Under the name *Malta fever*, the disease now called brucellosis first came to the attention of British medical officers in the 1850s in Malta during the Crimean War. The causal relationship between organism and disease was first established in 1887 by Dr. David Bruce.

In 1897, Danish veterinarian Bernhard Bang isolated *Brucella abortus* as the agent; and the additional name Bang's disease was assigned.

Maltese doctor and archaeologist Sir Themistocles Zammit earned a knighthood for identifying unpasteurized milk as the major source of the pathogen in 1905, and it has since become known as Malta Fever. In cattle, this disease is also known as contagious abortion and infectious abortion.

The popular name undulant fever originates from the characteristic undulance (or "wave-like" nature) of the fever, which rises and falls over weeks in untreated patients. In the 20th century, this name, along with *brucellosis* (after *Brucella*, named for Dr. Bruce), gradually replaced the 19th century names Mediterranean fever and *Malta fever*.

In 1989, neurologists in Saudi Arabia discovered neurobrucellosis, a neurological involvement in brucellosis.

The following obsolete names have previously been applied to brucellosis:

1. Brucelliasis
2. Bruce's septicemia
3. Chumble fever
4. continued fever
5. Crimean fever
6. Cyprus fever
7. febris melitensis
8. febris undulans
9. Fist of mercy
10. goat fever
11. melitensis septicemia
12. melitococcosis
13. milk sickness
14. mountain fever
15. Neapolitan fever
16. Satan's fever
17. slow fever
18. Scottish Delight
19. Jones Disease

Brucellosis in Animals
Species infecting domestic livestock are *B. melitensis* (goats and sheep, see Brucella melitensis), *B. suis* (pigs, see Swine brucellosis), *B. abortus* (cattle and bison), *B. ovis* (sheep), and *B. canis* (dogs). *B. abortus* also infects bison and elk in North America and *B. suis* is endemic in caribou. *Brucella* species have also been isolated from several marine mammal species (pinnipeds and cetaceans).

Brucellosis in Cattle
The bacterium *Brucella abortus* is the principal cause of brucellosis in cattle. The bacteria are shed from an infected animal at or around the time of calving or abortion. Once exposed, the likelihood of an animal becoming infected is variable, depending on age, pregnancy status, and other intrinsic factors of the animal, as well as the amount of bacteria to which the animal was exposed. The most common clinical signs of cattle infected with *Brucella abortus* are high incidences of abortions, arthritic joints and retained after-birth. There are two main causes for spontaneous abortion in animals. The first is due to erythritol, which can promote infections in the fetus and placenta. The second is due to the lack of anti-Brucella activity in the amniotic fluid. Males can also harbor the bacteria in their reproductive tracts, namely seminal vesicles, ampullae, testicles, and epididymides.

Brucellosis in Dogs
The causative agent of brucellosis in dogs is *Brucella canis*. It is transmitted to other dogs through breeding and contact with aborted fetuses. Brucellosis can occur in humans that come in contact with infected aborted tissue or semen. The bacteria in dogs normally infect the genitals and lymphatic system, but can also spread to the eye, kidney, and intervertebral disc (causing discospondylitis). Symptoms of brucellosis in dogs include abortion in female dogs and scrotal inflammation and orchitis (inflammation of the testicles) in males. Fever is uncommon. Infection of the eye can cause uveitis, and infection of the intervertebral disc can cause pain or weakness. Blood testing of the dogs prior to breeding can prevent the spread of this disease. It is treated with antibiotics, as with humans, but it is difficult to cure.

Brucellosis in Humans

Symptoms
Granuloma and necrosis in the liver of a guinea pig infected with *Brucella suis*

Brucellosis in humans is usually associated with the consumption of unpasteurized milk and soft cheeses made from the milk of infected animals, primarily goats, infected with *Brucella melitensis* and

with occupational exposure of laboratory workers, veterinarians and slaughterhouse workers. Some vaccines used in livestock, most notably *B. abortus* strain 19, also cause disease in humans if accidentally injected. Brucellosis induces inconstant fevers, sweating, weakness, anaemia, headaches, depression and muscular and bodily pain.

The symptoms are like those associated with many other febrile diseases, but with emphasis on muscular pain and sweating. The duration of the disease can vary from a few weeks to many months or even years. In the first stage of the disease, septicaemia occurs and leads to the classic triad of undulant fevers, sweating (often with characteristic smell, likened to wet hay) and migratory arthralgia and myalgia. Blood tests characteristically reveal leukopenia and anemia, show some elevation of AST and ALT, and demonstrate positive Bengal Rose and Huddleston reactions. This complex is, at least in Portugal, known as the Malta fever. During episodes of Malta fever, melitococcemia (presence of brucellae in blood) can usually be demonstrated by means of blood culture in tryptose medium or Albini medium. If untreated, the disease can give origin to focalizations or become chronic. The focalizations of brucellosis occur usually in bones and joints and spondylodiscitis of lumbar spine accompanied by sacroiliitis is very characteristic of this disease. Orchitis is also frequent in men.

Diagnosis of brucellosis relies on:

1. Demonstration of the agent: blood cultures in tryptose broth, bone marrow cultures. The growth of brucellae is extremely slow (they can take until 2 months to grow) and the culture poses a risk to laboratory personnel due to high infectivity of brucellae.
2. Demonstration of antibodies against the agent either with the classic Huddleson, Wright and/or Bengal Rose reactions, either with ELISA or the 2-mercaptoethanol assay for IgM antibodies associated with chronic disease
3. Histologic evidence of granulomatous hepatitis (hepatic biopsy)
4. Radiologic alterations in infected vertebrae: the Pedro Pons sign (preferential erosion of antero-superior corner of lumbar vertebrae) and marked osteophytosis are suspicious of brucellic spondylitis.

The disease's sequelae are highly variable and may include granulomatous hepatitis, arthritis, spondylitis, anaemia, leukopenia, thrombocytopenia, meningitis, uveitis, optic neuritis, endocarditis and various neurological disorders collectively known as neurobrucellosis.

Treatment and Prevention

Antibiotics like tetracyclines, rifampicin, and the aminoglycosides streptomycin and gentamicin are effective against *Brucella* bacteria. However, the use of more than one antibiotic is needed for several weeks, because the bacteria incubate within cells.

The gold standard treatment for adults is daily intramuscular injections of streptomycin 1 g for 14 days and oral doxycycline 100 mg twice daily for 45 days (concurrently). Gentamicin 5 mg/kg by intramuscular injection once daily for seven days is an acceptable substitute when streptomycin is not available or difficult to obtain. Another widely used regimen is doxycycline plus rifampin twice daily for at least six weeks. This regimen has the advantage of oral administration. A triple therapy of doxycycline, with rifampin and cotrimoxazole, has been used successfully to treat neurobrucellosis. Doxycycline is able to cross the blood–brain barrier, but requires the addition of two other drugs to prevent relapse. Ciprofloxacin and cotrimoxazole therapy is associated with an unacceptably high rate of relapse. In brucellic endocarditis, surgery is required for an optimal outcome. Even with optimal antibrucellic therapy, relapses still occur in 5–10 percent of patients with Malta fever.

The main way of preventing brucellosis is by using fastidious hygiene in producing raw milk products, or by pasteurizing all milk that is to be ingested by human beings, either in its unaltered form or as a derivate, such as cheese. Experiments have shown that cotrimoxazol and rifampin are both safe drugs to use in treatment of pregnant women who have brucellosis.

Biological Warfare
In 1954, *B. suis* became the first agent weaponized by the United States at its Pine Bluff Arsenal in Arkansas. *Brucella* species survive well in aerosols and resist drying. *Brucella* and all other remaining biological weapons in the U.S. arsenal were destroyed in 1971–72 when the U.S. offensive biological weapons (BW) program was discontinued.

The United States BW program focused on three agents of the *Brucella* group:

1. Porcine Brucellosis (Agent US)
2. Bovine Brucellosis (Agent AB)
3. Caprine Brucellosis (Agent AM)

Agent US was in advanced development by the end of World War II. When the U.S. Air Force (USAF) wanted a biological warfare capability, the Chemical Corps offered Agent US in the M114 bomblet, based after the 4-pound bursting bomblet developed for anthrax in World War II. Though the capability was developed, operational testing indicated that the weapon was less than desirable, and the USAF termed it an interim capability until replaced by a more effective biological weapon. The main drawbacks of the M114 with Agent US was that it was incapacitating (the USAF wanted "killer" agents), the storage stability was too low to allow for storing at forward air bases, and the logistical requirements to neutralize a target were far higher than originally anticipated, requiring unreasonable logistical air support.

Agents US and AB had a median infective dose of 500 org/person, and AM was 300 org/person. The rate-of-action was believed to be 2 weeks, with a duration of action of several months. The lethality estimate was based on epidemiological information at 1–2%. AM was always believed to be a more virulent disease, and a 3% fatality rate was expected.

Epidemiology: Control and Eradiation Efforts

United States
Dairy herds in the USA are tested at least once a year with the Brucella Milk Ring Test (BRT).[13] Cows that are confirmed to be infected are often killed. In the United States, veterinarians are required to vaccinate all young stock, thereby further reducing the chance of zoonotic transmission. This vaccination is usually referred to as a "calfhood" vaccination. Most cattle receive a tattoo in their ear serving as proof of their vaccination status. This tattoo also includes the last digit of the year they were born.

The first state–federal cooperative efforts towards eradication of brucellosis caused by *Brucella abortus* in the U.S. began in 1934.

Greater Yellowstone Area
Wild bison and elk in the Greater Yellowstone Area (GYA) are the last remaining reservoir of *Brucella abortus* in the U.S. The recent transmission of brucellosis from elk to cattle in Idaho and Wyoming illustrates how the GYA is the last remaining reservoir in the United States, adversely affecting the livestock industry. Eliminating brucellosis from this area is a challenge, as there are many viewpoints on how to manage diseased wildlife.

Canada
Canada declared their cattle herd brucellosis-free on September 19, 1985. Brucellosis ring testing of milk and cream, as well as testing of slaughter cattle, ended April 1, 1999. Monitoring continues through auction market testing, standard disease reporting mechanisms, and testing of cattle being qualified for export to countries other than the USA.

Europe

Malta
Until the early 20th century the disease was endemic in Malta to the point of it being referred to as "the Maltese fever". The link between the illness and unpasteurised milk was established by Temi

Zammit. Today thanks to a strict regime of certification of milk animals and widespread use of pasturisation the illness has been eradicated from Malta.

Republic of Ireland
Ireland was declared free of brucellosis on 1 July 2009. The disease had troubled the country's farmers and veterinarians for several decades. The Irish government submitted an application to the European Commission, which verified that Ireland had been liberated.[18] Brendan Smith, Ireland's then Minister for Agriculture, Food and the Marine, said the elimination of brucellosis was "a landmark in the history of disease eradication in Ireland".[17][18] Ireland's Department of Agriculture, Food and the Marine intends to reduce its brucellosis eradication programme now that eradication has been confirmed.

Oceania

Australia
Australia is at present free of cattle brucelosis, although it occurred in the past. Brucellosis of sheep or goats has never been reported. Brucellosis of pigs does occur. Feral pigs are the typical source of human infections.

New Zealand
Brucellosis in New Zealand is limited to sheep (*Brucella ovis*). The country is free of all other species of *Brucella* (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: If and when a full-scale bio-terror attack occurs, the live pathogens or agents responsible for the pandemic will likely be dispersed via A) chemtrails by government airplanes or drones, B) by the U.S. Postal Service via Tide detergent samples, C) by the government and medical establishment via tainted vaccines, or by D) the portable petri dish commonly known as a Trojan condom.

Recent news and events related to airplanes and drones suggests that it is possible that aerial spraying vehicle could be used in a biological attack on an unsuspecting public, especially if they refuse to line up and take the deadly vaccines. Chemtrails, the name given to toxins emitted from aerial machines such as drones, planes and rockets, is a cocktail of deadly toxins which could be further laced with a bio-terror pathogen.

Title: Chemtrails Conspiracy Theory
Date: 2012
Source: Wikipedia

Abstract: The chemtrail conspiracy theory holds that some trails left by aircraft are actually chemical or biological agents deliberately sprayed at high altitudes for purposes undisclosed to the general public in clandestine programs directed by government officials. This theory is not accepted by the scientific community, which states that they are just normal contrails, and that there is no scientific evidence supporting the chemtrail theory.

As a result of the popularity of the conspiracy theory, official agencies have received thousands of complaints from people who have demanded an explanation. The existence of chemtrails has been repeatedly denied by scientists around the world, who say the trails are normal contrails.[3] The United States Air Force states that the theory is a hoax which "has been investigated and refuted by many established and accredited universities, scientific organizations, and major media publications". The United Kingdom's Department for Environment, Food and Rural Affairs has stated that chemtrails are not scientifically recognized phenomena. The Canadian Leader of the Government in the House of Commons has rejected the idea of chemtrails as being a "popularised expression", adding that "there is no scientific evidence to support their existence."

The term chemtrail is derived from "chemical trail", in the similar fashion that contrail is a portmanteau of condensation trail. It does not refer to other forms of aerial spraying such as crop dusting, cloud seeding, skywriting, or aerial firefighting. The term specifically refers to aerial trails allegedly caused by the systematic high-altitude release of chemical substances not found in ordinary contrails, resulting in the appearance of characteristic sky tracks. Supporters of this conspiracy theory speculate that the purpose of the chemical release may be for solar radiation management, population control, weather control, or biological warfare/chemical warfare and claim that these trails are causing respiratory illnesses and other health problems (Wikipedia, 2012).

Title: Denying Chemtrails Is Dangerous For Your Health
Date: March 17, 2012
Source: Natural News

Abstract: Statistical evidence shows that lung issues such as asthma and COPD have risen considerably over the past two decades. While there may be a few factors behind this, hardly anyone includes chemtrails as one of them.

Scientists and governments have allowed some "limited hangouts" (partial disclosures) on chemtrails or stratospheric geo-engineering, framing it as "experimental." They openly discuss geo-engineering as "potential" solutions for weather control and protection against global warming.

Apparently, they've been doing a lot of open "experimenting" since the early 1990s. They don't really have to deny much. There's plenty of denial from those on the ground who don't look up to see anything different. Or upon noticing chemtrails, they will argue that they are contrails.

There are even internet pages devoted to "scientifically" debunking chemtrails as erroneous conspiracy theories, similar to "Quackwatch" sites that go after medical practitioners who successfully treat disease without drugs.

The Obvious differences between Chemtrails and Contrails
Contrails appear from aircraft propulsion systems of all types at stratospheric altitudes, 30,000 to 40,000 feet up. They are exhaust vapors that become ice crystals in high altitude, low pressure frigid air.

Contrails are harmless and dissipate quickly. They don't linger. They usually extend from 20 to 50 plane lengths behind the aircraft. They are very white and somewhat thinly textured. Sometimes high altitude planes can be seen as silver specks without any trail at all. Chemtrails, however, are very different.

Chemtrails often extend from one horizon to the other. They tend to be thicker and wider than contrails, and their white plumes can be tainted with slight discolorations. **Chemtrails linger for hours or whole days.**

They tend to fan out and mingle with themselves or actual clouds, forming larger clouds or a haze that covers the sky. At higher ground levels, they can be observed drifting downward to earth.

Their paths do not correspond with normal commercial airline flight paths. They often turn around and continue their smoky plumes. Sometimes they will create grid patterns or Xs. See examples here (http://youtu.be/eEFITGpXwZk).

Do you recall meeting other aircraft while on a commercial flight, and deviating from the prescribed route to doodle in the sky with the other planes? Of course not. Chemtrails are usually emitted by non-commercial planes.

Back on the Ground
Several sky watchers throughout the world have had residue samples analyzed after collecting them in water containers, air traps, and on shrubbery twigs. **They have all come up with two common elements: barium and aluminum.**

Barium is very toxic. Reportedly, it was sprayed from aircraft during Gulf War I to weaken the enemy on the ground. Some consider barium salts more toxic than lead. It affects the lungs directly.

Aluminum is a toxin that leads to dementia and neurological diseases. The nasal passages and lungs enable aluminum to have easy entry into our blood streams and affect tissues, including the heart and brain.

Even if not breathed in to cause immediate respiratory and other long term health problems, these two metals are absorbed into drinking water and crop soils. Interestingly, Monsanto has recently genetically engineered an aluminum resistant gene that can be inserted into crop seeds.

A pathogen has been found in some chemtrail analyses. *Mycoplasma Fermetens Incognitus,* which was observed to be in half the Gulf War Syndrome victims by Dr.Garth Nicholson.

The first thing to do is **take time to observe and recognize the differences in aircraft trails**. Research more, starting with source links below, while detoxing metals regularly. Then get involved on some level to help curb chemtrail activities (Natural News, 2012).

Title: What In The World Are They Spraying?
Date: December 20, 2010
Source: YouTube

Title: Aerosol Crimes
Date: December 17, 2010
Source: YouTube

Title: Government Admits Secretly Spraying Poison On Us!!!
Date: December 10, 2011
Source: News 12

Title: Spraying San Francisco, Exposing The Geo-Engineers.
Date: January 13, 2012
Source: YouTube

Title: US-Military Weather Warfare Chemtrails Aerosol Crimes Explained
Date: November 14, 2011
Source: Massachusetts School Of Law

Title: US-Military Weather Warfare Chemtrails Aerosol Crimes Explained
Date: March 19, 2008
Source: YouTube

The following U.S. patents are in respect to chemtrail related technologies.

United States Patent and Trademark Office: Click here in order to execute a number search.

1338343 – April 27, 1920 – Process And Apparatus For The Production of Intense Artificial Clouds, Fogs, or Mists

1619183 – March 1, 1927 – Process of Producing Smoke Clouds From Moving Aircraft

1631753 – June 7, 1927 – Electric Heater – Referenced in 3990987

1665267 – April 10, 1928 – Process of Producing Artificial Fogs

1892132 – December 27, 1932 – Atomizing Attachment For Airplane Engine Exhausts

1928963 – October 3, 1933 – Electrical System And Method

1957075 – May 1, 1934 – Airplane Spray Equipment

2097581 – November 2, 1937 – Electric Stream Generator – Referenced in 3990987

2409201 – October 15, 1946 – Smoke Producing Mixture

2476171 – July 18, 1945 – Smoke Screen Generator

2480967 – September 6, 1949 – Aerial Discharge Device

2550324 – April 24, 1951 – Process For Controlling Weather

2510867 – October 9, 1951 – Method of Crystal Formation and Precipitation

2582678 – June 15, 1952 – Material Disseminating Apparatus For Airplanes

2591988 – April 8, 1952 – Production of TiO2 Pigments – Referenced in 3899144

2614083 – October 14, 1952 – Metal Chloride Screening Smoke Mixture

2633455 – March 31, 1953 – Smoke Generator

2688069 – August 31, 1954 – Steam Generator – Referenced in 3990987

2721495 – October 25, 1955 – Method And Apparatus For Detecting Minute Crystal Forming Particles Suspended in a Gaseous Atmosphere

2730402 – January 10, 1956 – Controllable Dispersal Device

2801322 – July 30, 1957 – Decomposition Chamber for Monopropellant Fuel – Referenced in 3990987

2881335 – April 7, 1959 – Generation of Electrical Fields

2908442 – October 13, 1959 – Method For Dispersing Natural Atmospheric Fogs And Clouds

2986360 – May 30, 1962 – Aerial Insecticide Dusting Device

2963975 – December 13, 1960 – Cloud Seeding Carbon Dioxide Bullet

3126155 – March 24, 1964 – Silver Iodide Cloud Seeding Generator – Referenced in 3990987

3127107 – March 31, 1964 – Generation of Ice-Nucleating Crystals

3131131 – April 28, 1964 – Electrostatic Mixing in Microbial Conversions

3174150 – March 16, 1965 – Self-Focusing Antenna System

3234357 – February 8, 1966 – Electrically Heated Smoke Producing Device

3274035 – September 20, 1966 – Metallic Composition For Production of Hydroscopic Smoke

3300721 – January 24, 1967 – Means For Communication Through a Layer of Ionized Gases

3313487 – April 11, 1967 – Cloud Seeding Apparatus

3338476 – August 29, 1967 – Heating Device For Use With Aerosol Containers – Referenced in 3990987

3410489 – November 12, 1968 – Automatically Adjustable Airfoil Spray System With Pump

3429507 – February 25, 1969 – Rainmaker

3432208 – November 7, 1967 – Fluidized Particle Dispenser

3441214 – April 29, 1969 – Method And Apparatus For Seeding Clouds

3445844 – May 20, 1969 – Trapped Electromagnetic Radiation Communications System

3456880 – July 22, 1969 – Method Of Producing Precipitation From The Atmosphere

3518670 – June 30, 1970 – Artificial Ion Cloud

3534906 – October 20, 1970 – Control of Atmospheric Particles

3545677 – December 8, 1970 – Method of Cloud Seeding

3564253 – February 16, 1971 – System And Method For Irradiation Of Planet Surface Areas

3587966 – June 28, 1971 – Freezing Nucleation

3601312 – August 24, 1971 – Methods of Increasing The Likelihood oF Precipatation By The Artificial Introduction Of Sea Water Vapor Into The Atmosphere Winward Of An Air Lift Region

3608810 – September 28, 1971 – Methods of Treating Atmospheric Conditions

3608820 – September 20, 1971 – Treatment of Atmospheric Conditions by Intermittent Dispensing of Materials Therein

3613992 – October 19, 1971 – Weather Modification Method

3630950 – December 28, 1971 – Combustible Compositions For Generating Aerosols, Particularly Suitable For Cloud Modification And Weather Control And Aerosolization Process

USRE29142 – This patent is a reissue of patent US3630950 – Combustible compositions for generating aerosols, particularly suitable for cloud modification and weather control and aerosolization process

3659785 – December 8, 1971 – Weather Modification Utilizing Microencapsulated Material

3666176 – March 3, 1972 – Solar Temperature Inversion Device

3677840 – July 18, 1972 – Pyrotechnics Comprising Oxide of Silver For Weather Modification Use

3722183 – March 27, 1973 – Device For Clearing Impurities From The Atmosphere

3769107 – October 30, 1973 – Pyrotechnic Composition For Generating Lead Based Smoke

3784099 – January 8, 1974 – Air Pollution Control Method

3785557 – January 15, 1974 – Cloud Seeding System

3795626 – March 5, 1974 – Weather Modification Process

3808595 – April 30, 1974 – Chaff Dispensing System

3813875 – June 4, 1974 – Rocket Having Barium Release System to Create Ion Clouds In The Upper Atmopsphere

3835059 – September 10, 1974 – Methods of Generating Ice Nuclei Smoke Particles For Weather Modification And Apparatus Therefore

3835293 – September 10, 1974 – Electrical Heating Aparatus For Generating Super Heated Vapors – Referenced in 3990987

3877642 – April 15, 1975 – Freezing Nucleant

3882393 – May 6, 1975 – Communications System Utilizing Modulation of The Characteristic Polarization of The Ionosphere

3896993 – July 29, 1975 – Process For Local Modification of Fog And Clouds For Triggering Their Precipitation And For Hindering The Development of Hail Producing Clouds

3899129 – August 12, 1975 – Apparatus for generating ice nuclei smoke particles for weather modification

3899144 – August 12, 1975 – Powder contrail generation

3940059 – February 24, 1976 – Method For Fog Dispersion

3940060 – February 24, 1976 – Vortex Ring Generator

3990987 – November 9, 1976 – Smoke generator

3992628 – November 16, 1976 – Countermeasure system for laser radiation

3994437 – November 30, 1976 – Broadcast dissemination of trace quantities of biologically active chemicals

4042196 – August 16, 1977 – Method and apparatus for triggering a substantial change in earth characteristics and measuring earth changes

RE29,142 – February 22, 1977 – Reissue of: 03630950 – Combustible compositions for generating aerosols, particularly suitable for cloud modification and weather control and aerosolization process

4035726 – July 12, 1977 – Method of controlling and/or improving high-latitude and other communications or radio wave surveillance systems by partial control of radio wave et al

4096005 – June 20, 1978 – Pyrotechnic Cloud Seeding Composition

4129252 – December 12, 1978 – Method and apparatus for production of seeding materials

4141274 – February 27, 1979 – Weather modification automatic cartridge dispenser

4167008 – September 4, 1979 – Fluid bed chaff dispenser

4347284 – August 31, 1982 – White cover sheet material capable of reflecting ultraviolet rays

4362271 – December 7, 1982 – Procedure for the artificial modification of atmospheric precipitation as well as compounds with a dimethyl sulfoxide base for use in carrying out said procedure

4402480 – September 6, 1983 – Atmosphere modification satellite

4412654 – November 1, 1983 – Laminar microjet atomizer and method of aerial spraying of liquids

4415265 – November 15, 1983 – Method and apparatus for aerosol particle absorption spectroscopy

4470544 – September 11, 1984 – Method of and Means for weather modification

4475927 – October 9, 1984 – Bipolar Fog Abatement System

4600147 – July 15, 1986 – Liquid propane generator for cloud seeding apparatus

4633714 – January 6, 1987 – Aerosol particle charge and size analyzer

4643355 – February 17, 1987 – Method and apparatus for modification of climatic conditions

4653690 – March 31, 1987 – Method of producing cumulus clouds

4684063 – August 4, 1987 – Particulates generation and removal

4686605 – August 11, 1987 – Method and apparatus for altering a region in the earth's atmosphere, ionosphere, and/or magnetosphere

4704942 – November 10, 1987 – Charged Aerosol

4712155 – December 8, 1987 – Method and apparatus for creating an artificial electron cyclotron heating region of plasma

4744919 – May 17, 1988 – Method of dispersing particulate aerosol tracer

4766725 – August 30, 1988 – Method of suppressing formation of contrails and solution therefor

4829838 – May 16, 1989 – Method and apparatus for the measurement of the size of particles entrained in a gas

4836086 – June 6, 1989 – Apparatus and method for the mixing and diffusion of warm and cold air for dissolving fog

4873928 – October 17, 1989 – Nuclear-sized explosions without radiation

4948257 – August 14, 1990 – Laser optical measuring device and method for stabilizing fringe pattern spacing

48050 – August 14, 1990 – Liquid atomizing a94pparatus for aerial spraying

4999637 – March 12, 1991 – Creation of artificial ionization clouds above the earth

5003186 – March 26, 1991 – Stratospheric Welsbach seeding for reduction of global warming

5005355 – April 9, 1991 – Method of suppressing formation of contrails and solution therefor

5038664 – August 13, 1991 – Method for producing a shell of relativistic particles at an altitude above the earths surface

5041760 – August 20, 1991 – Method and apparatus for generating and utilizing a compound plasma configuration

5041834 – August 20, 1991 – Artificial ionospheric mirror composed of a plasma layer which can be tilted

5056357 – October 15, 1991- Acoustic method for measuring properties of a mobile medium

5059909 – October 22, 1991 – Determination of particle size and electrical charge

5104069 – April 14, 1992 – Apparatus and method for ejecting matter from an aircraft

5110502 – May 5, 1992 – Method of suppressing formation of contrails and solution therefor

5156802 – October 20, 1992 – Inspection of fuel particles with acoustics

5174498 – December 29, 1992 – Cloud Seeding

5148173 – September 15, 1992 – Millimeter wave screening cloud and method

5245290 – September 14, 1993 – Device for determining the size and charge of colloidal particles by measuring electroacoustic effect

5286979 – February 15, 1994 – Process for absorbing ultraviolet radiation using dispersed melanin

5296910 – March 22, 1994 – Method and apparatus for particle analysis

5327222 – July 5, 1994 – Displacement information detecting apparatus

5357865 – October 25, 1994 – Method of cloud seeding

5360162 – November 1, 1994 – Method and composition for precipitation of atmospheric water

5383024 – January 17, 1995 – Optical wet steam monitor

5425413 – June 20, 1995 – Method to hinder the formation and to break-up overhead atmospheric inversions, enhance ground level air circulation and improve urban air quality

5434667 – July 18, 1995 – Characterization of particles by modulated dynamic light scattering

5441200 – August 15, 1995 – Tropical cyclone disruption

5486900 – January 23, 1996 – Measuring device for amount of charge of toner and image forming apparatus having the measuring device

5556029 – September 17, 1996 – Method of hydrometeor dissipation (clouds)

5628455 – May 13, 1997 – Method and apparatus for modification of supercooled fog

5631414 – May 20, 1997 – Method and device for remote diagnostics of ocean-atmosphere system state

5639441 – June 17, 1997 – Methods for fine particle formation

5762298 – June 9, 1998 – Use of artificial satellites in earth orbits adaptively to modify the effect that solar radiation would otherwise have on earth's weather

5912396 – June 15, 1999 – System and method for remediation of selected atmospheric conditions

5922976 – July 13, 1999 – Method of measuring aerosol particles using automated mobility-classified aerosol detector

5949001 – September 7, 1999 – Method for aerodynamic particle size analysis

5984239 – November 16, 1999 – Weather modification by artificial satellite

6025402 – February 15, 2000 – Chemical composition for effectuating a reduction of visibility obscuration, and a detoxifixation of fumes and chemical fogs in spaces of fire origin

6030506 – February 29, 2000 – Preparation of independently generated highly reactive chemical species

6034073 – March 7, 2000 – Solvent detergent emulsions having antiviral activity

6045089 – April 4, 2000 – Solar-powered airplane

6056203 – May 2, 2000 – Method and apparatus for modifying supercooled clouds

6110590 – August 29, 2000 – Synthetically spun silk nanofibers and a process for making the same

6263744 – July 24, 2001 – Automated mobility-classified-aerosol detector

6281972 – August 28, 2001 – Method and apparatus for measuring particle-size distribution

6315213 – November 13, 2001 – Method of modifying weather

6382526 – May 7, 2002 – Process and apparatus for the production of nanofibers

6408704 – June 25, 2002 – Aerodynamic particle size analysis method and apparatus

6412416 – July 2, 2002 – Propellant-based aerosol generation devices and method

6520425 – February 18, 2003 – Process and apparatus for the production of nanofibers

6539812 – April 1, 2003 – System for measuring the flow-rate of a gas by means of ultrasound

6553849 – April 29, 2003 – Electrodynamic particle size analyzer

6569393 – May 27, 2003 – Method and device for cleaning the atmosphere

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Chlorine
Date: 2012
Source: Wikipedia

Abstract: Chlorine is the chemical element with atomic number 17 and symbol Cl. It is the second lightest halogen, with fluorine being the lightest. Chlorine is found in the periodic table in group 17. The element forms diatomic molecules under standard conditions, called dichlorine. It has the highest electron affinity and the third highest electronegativity of all the elements; for this reason, chlorine is a strong oxidizing agent.

The most common compound of chlorine, sodium chloride, has been known since ancient times; however, around 1630, chlorine gas was obtained by the Belgian chemist and physician Jan Baptist van Helmont. The synthesis and characterization of elemental chlorine occurred in 1774 by Swedish chemist Carl Wilhelm Scheele, who called it "dephlogisticated muriatic acid air," having thought he synthesized the oxide obtained from the hydrochloric acid. Because acids were thought at the time to necessarily contain oxygen, a number of chemists, including Claude Berthollet, suggested that Scheele's dephlogisticated muriatic acid air must be a combination of oxygen and the yet undiscovered element, and Scheele named the supposed new element within this oxide as muriaticum. The suggestion that this newly discovered gas was a simple element was made in 1809 by Joseph Louis Gay-Lussac and Louis-Jacques. This was confirmed by Sir Humphry Davy in 1810, who named it chlorine, from the Greek word χλωρος (chlōros), meaning "green-yellow."

Chlorine is a component of various compounds, including table salt. It is the second most abundant halogen and 21st most abundant chemical element in Earth's crust. The great oxidizing potential of chlorine led it to its bleaching and disinfectant uses, as well as uses of an essential reagent in the chemical industry. As a common disinfectant, chlorine compounds are used inswimming pools to keep them clean and sanitary. In the upper atmosphere, chlorine-containing molecules such as chlorofluorocarbons have been implicated in ozone depletion. Elemental chlorine is extremely dangerous and poisonous for all lifeforms; however, chlorine is necessary to most forms of life, including humans, in form of chloride ions.Use as a Weapon

World War I: Main article: Poison gas in World War I

Chlorine gas, also known as bertholite, was first used as a weapon in World War I by Germany on April 22, 1915 in the Second Battle of Ypres. As described by the soldiers it had a distinctive smell of a mixture between pepper and pineapple. It also tasted metallic and stung the back of the throat and chest. Chlorine can react with water in the mucosa of the lungs to form hydrochloric acid, an irritant that can be lethal. The damage done by chlorine gas can be prevented by a gas mask, or other filtration method, which makes the overall chance of death by chlorine gas much lower than those of other chemical weapons. It was pioneered by a German scientist later to be a Nobel laureate, Fritz Haber of the Kaiser Wilhelm Institute in Berlin, in collaboration with the German chemical conglomerate IG Farben, who

developed methods for discharging chlorine gas against an entrenched enemy. It is alleged that Haber's role in the use of chlorine as a deadly weapon drove his wife, Clara Immerwahr, to suicide. After its first use, chlorine was utilized by both sides as a chemical weapon, but it was soon replaced by the more deadly phosgene and mustard gas.

Iraq War: Main article: 2007 chlorine bombings in Iraq

Chlorine Cracking
Chlorine gas has also been used by insurgents against the local population and coalition forces in the Iraq War in the form of chlorine bombs. On March 17, 2007, for example, three chlorine filled trucks were detonated in the Anbar province killing two and sickening over 350. Other chlorine bomb attacks resulted in higher death tolls, with more than 30 deaths on two separate occasions. Most of the deaths were caused by the force of the explosions rather than the effects of chlorine, since the toxic gas is readily dispersed and diluted in the atmosphere by the blast. The Iraqi authorities have tightened up security for chlorine, which is essential for providing safe drinking water for the population.

The element is widely used for purifying water owing to its powerful oxidizing properties, especially potable water supplies and water used in swimming pools. Several catastrophic collapses of swimming pool ceilings have occurred owing to stress corrosion cracking of stainless steel rods used to suspend them.[52] Some polymers are also sensitive to attack, including acetal resin andpolybutene. Both materials were used in hot and cold water domestic supplies, and stress corrosion cracking caused widespread failures in the USA in the 1980s and 1990s. One example shows an acetal joint in a water supply system, which, when it fractured, caused substantial physical damage to computers in the labs below the supply. The cracks started at injection moldingdefects in the joint and grew slowly until finally triggered. The fracture surface shows iron and calcium salts that were deposited in the leaking joint from the water supply before failure.

Health Effects
Chlorine is a toxic gas that irritates the respiratory system. Because it is heavier than air, it tends to accumulate at the bottom of poorly ventilated spaces. Chlorine gas is a strong oxidizer, which may react with flammable materials.

Chlorine is detectable with measuring devices in concentrations of as low as 0.2 parts per million (ppm), and by smell at 3 ppm. Coughing and vomiting may occur at 30 ppm and lung damage at 60 ppm. About 1000 ppm can be fatal after a few deep breaths of the gas. Breathing lower concentrations can aggravate the respiratory system, and exposure to the gas can irritate the eyes. The toxicity of chlorine comes from its oxidizing power. When chlorine is inhaled at concentrations above 30 ppm, it begins to react with water and cells, which change it into hydrochloric acid (HCl) and hypochlorous acid (HClO).

When used at specified levels for water disinfection, the reaction of chlorine with water is not a major concern for human health. However, other materials present in the water may generate disinfection by-products that can damage human health (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Cholera
Date: 2012
Source: Wikipedia

Abstract: Cholera is an infection of the small intestine caused by the bacterium *Vibrio cholerae*. The main symptoms are profuse, watery diarrhea and vomiting. Transmission occurs primarily by drinking water or eating food that has been contaminated by the feces of an infected person (even an asymptomatic one). The severity of the diarrhea and vomiting can lead to rapid dehydration and electrolyte imbalance, and death in some cases. The primary treatment is with oral rehydration solution (ORS) to replace water and electrolytes; if this is not tolerated or does not provide quick enough treatment, intravenous fluids can also be used. Antibiotics are beneficial in those with severe disease to shorten its duration and severity. Worldwide, it affects 3–5 million people and causes 100,000–130,000 deaths a year as of 2010. Cholera was one of the earliest infections to be studied by epidemiological methods.

Signs & Symptoms

A person with severe dehydration due to cholera - note the sunken eyes and decreased skin turgor which produces wrinkled hands.

The primary symptoms of cholera are profuse, painless diarrhea and vomiting of clear fluid. These symptoms usually start suddenly, one to five days after ingestion of the bacteria. The diarrhea is frequently described as "rice water" in nature and may have a fishy odor. An untreated person with cholera may produce 10–20 litres of diarrhea a day with fatal results. For every symptomatic person, three to 100 people get the infection but remain asymptomatic. Cholera has been nicknamed the "blue death" due to a patient's skin turning a bluish-gray hue from extreme loss of fluids.

If the severe diarrhea and vomiting are not aggressively treated, they can, within hours, result in life-threatening dehydration and electrolyte imbalances. The typical symptoms of dehydration include low blood pressure, poor skin turgor (wrinkled hands), sunken eyes, and a rapid pulse.

Cause

Main article: Vibrio cholerae

Transmission is primarily by the fecal contamination of food and water caused by poor sanitation. This bacterium can, however, live naturally in any environment.

Susceptibility

About one hundred million bacteria must typically be ingested to cause cholera in a normal healthy adult. This dose, however, is less in those with lower gastric acidity (for instance those using proton pump inhibitors). Children are also more susceptible, with two- to four-year-olds having the highest rates of infection. Individuals' susceptibility to cholera is also affected by their blood type, with those with type O blood being the most susceptible. Persons with lower immunity, such as persons with AIDS or children who are malnourished, are more likely to experience a severe case if they become infected. However, it should be noted that any individual, even a healthy adult in middle age, can

experience a severe case, and each person's case should be measured by the loss of fluids, preferably in consultation with a doctor or other health worker.

The cystic fibrosis genetic mutation in humans has been said to maintain a selective advantage: heterozygous carriers of the mutation (who are thus not affected by cystic fibrosis) are more resistant to *V. cholerae* infections. In this model, the genetic deficiency in the cystic fibrosis transmembrane conductance regulator channel proteins interferes with bacteria binding to the gastrointestinal epithelium, thus reducing the effects of an infection.

Transmission

Cholera is typically transmitted by either contaminated food or water. In the developed world, seafood is the usual cause, while in the developing world it is more often water. Cholera has been found in only two other animal populations: shellfish and plankton.

People infected with cholera often have diarrhea, and if this highly liquid stool, colloquially referred to as "rice-water" or "faucet butt", contaminates water used by others, disease transmission may occur. The source of the contamination is typically other cholera sufferers when their untreated diarrheal discharge is allowed to get into waterways, groundwater or drinking water supplies. Drinking any infected water and eating any foods washed in the water, as well as shellfish living in the affected waterway, can cause a person to contract an infection. Cholera is rarely spread directly from person to person. Both toxic and nontoxic strains exist. Nontoxic strains can acquire toxicity through a temperate bacteriophage. Coastal cholera outbreaks typically follow zooplankton blooms, thus making cholera a zoonotic disease.

Mechanism

Most bacteria, when consumed, do not survive the acidic conditions of the human stomach. The few surviving bacteria conserve their energy and stored nutrients during the passage through the stomach by shutting down much protein production. When the surviving bacteria exit the stomach and reach the small intestine, they need to propel themselves through the thick mucus that lines the small intestine to get to the intestinal walls, where they can thrive. *V. cholerae* bacteria start up production of the hollow cylindrical protein flagellin to make flagella, the cork-screw helical fibers they rotate to propel themselves through the mucus of the small intestine.

Once the cholera bacteria reach the intestinal wall, they no longer need the flagella to move. The bacteria stop producing the protein flagellin, thus again conserving energy and nutrients by changing the mix of proteins which they manufacture in response to the changed chemical surroundings. On reaching the intestinal wall, *V. cholerae* start producing the toxic proteins that give the infected person a watery diarrhea. This carries the multiplying new generations of *V. cholerae* bacteria out into the drinking water of the next host if proper sanitation measures are not in place.

The cholera toxin (CTX or CT) is an oligomeric complex made up of six protein subunits: a single copy of the A subunit (part A), and five copies of the B subunit (part B), connected by a disulfide bond. The five B subunits form a five-membered ring that binds to GM1 gangliosides on the surface of the intestinal epithelium cells. The A1 portion of the A subunit is an enzyme that ADP-ribosylates G proteins, while the A2 chain fits into the central pore of the B subunit ring. Upon binding, the complex is taken into the cell via receptor-mediated endocytosis. Once inside the cell, the disulfide bond is reduced, and the A1 subunit is freed to bind with a human partner protein called ADP-ribosylation factor 6 (Arf6). Binding exposes its active site, allowing it to permanently ribosylate the Gs alpha subunit of the heterotrimeric G protein. This results in constitutive cAMP production, which in turn leads to secretion of H_2O, Na^+, K^+, Cl^-, and HCO_3^- into the lumen of the small intestine and rapid dehydration. The gene encoding the cholera toxin is introduced into *V. cholerae* by horizontal gene transfer. Virulent strains of *V. cholerae* carry a variant of temperate bacteriophage called CTXf or CTXφ.

Microbiologists have studied the genetic mechanisms by which the *V. cholerae* bacteria turn off the production of some proteins and turn on the production of other proteins as they respond to the series of chemical environments they encounter, passing through the stomach, through the mucous layer of the small intestine, and on to the intestinal wall. Of particular interest have been the genetic mechanisms by which cholera bacteria turn on the protein production of the toxins that interact with

host cell mechanisms to pump chloride ions into the small intestine, creating an ionic pressure which prevents sodium ions from entering the cell. The chloride and sodium ions create a salt-water environment in the small intestines, which through osmosis can pull up to six litres of water per day through the intestinal cells, creating the massive amounts of diarrhea. The host can become rapidly dehydrated if an appropriate mixture of dilute salt water and sugar is not taken to replace the blood's water and salts lost in the diarrhea.

By inserting separate, successive sections of *V. cholerae* DNA into the DNA of other bacteria, such as *E. coli* that would not naturally produce the protein toxins, researchers have investigated the mechanisms by which *V. cholerae* responds to the changing chemical environments of the stomach, mucous layers, and intestinal wall. Researchers have discovered a complex cascade of regulatory proteins controls expression of *V. cholerae* virulence determinants. In responding to the chemical environment at the intestinal wall, the *V. cholerae* bacteria produce the TcpP/TcpH proteins, which, together with the ToxR/ToxS proteins, activate the expression of the ToxT regulatory protein. ToxT then directly activates expression of virulence genes that produce the toxins, causing diarrhea in the infected person and allowing the bacteria to colonize the intestine. Current research aims at discovering "the signal that makes the cholera bacteria stop swimming and start to colonize (that is, adhere to the cells of) the small intestine."

Genetic Structure
Amplified fragment length polymorphism fingerprinting of the pandemic isolates of *V. cholerae* has revealed variation in the genetic structure. Two clusters have been identified: Cluster I and Cluster II. For the most part, Cluster I consists of strains from the 1960s and 1970s, while Cluster II largely contains strains from the 1980s and 1990s, based on the change in the clone structure. This grouping of strains is best seen in the strains from the African continent.

Diagnosis
A rapid dip-stick test is available to determine the presence of *V. cholerae*. In those samples that test positive, further testing should be done to determine antibiotic resistance. In epidemic situations, a clinical diagnosis may be made by taking a patient history and doing a brief examination. Treatment is usually started without or before confirmation by laboratory analysis.

Stool and swab samples collected in the acute stage of the disease, before antibiotics have been administered, are the most useful specimens for laboratory diagnosis. If an epidemic of cholera is suspected, the most common causative agent is *V. cholerae* O1. If *V. cholerae* serogroup O1 is not isolated, the laboratory should test for *V. cholerae* O139. However, if neither of these organisms is isolated, it is necessary to send stool specimens to a reference laboratory. Infection with *V. cholerae* O139 should be reported and handled in the same manner as that caused by *V. cholerae* O1. The associated diarrheal illness should be referred to as cholera and must be reported in the United States.

A number of special media have been employed for the cultivation for cholera vibrios. They are classified as follows:

Enrichment Media
1. Alkaline peptone water at pH 8.6
2. Monsur's taurocholate tellurite peptone water at pH 9.2

Plating Media
1. Alkaline bile salt agar (BSA): The colonies are very similar to those on nutrient agar.
2. Monsur's gelatin Tauro cholate trypticase tellurite agar (GTTA) medium: Cholera vibrios produce small, translucent colonies with a greyish-black center.
3. TCBS medium: This is the mostly widely used medium; it contains thiosulphate, citrate, bile salts and sucrose. Cholera vibrios produce flat, 2–3 mm in diameter, yellow-nucleated colonies.

Direct microscopy of stool is not recommended, as it is unreliable. Microscopy is preferred only after enrichment, as this process reveals the characteristic motility of *Vibrio* and its inhibition by appropriate antisera. Diagnosis can be confirmed, as well, as serotyping done by agglutination with specific sera.

Prevention
Although cholera may be life-threatening, prevention of the disease is normally straightforward if proper sanitation practices are followed. In developed countries, due to nearly universal advanced water treatment and sanitation practices, cholera is no longer a major health threat. The last major outbreak of cholera in the United States occurred in 1910–1911. Effective sanitation practices, if instituted and adhered to in time, are usually sufficient to stop an epidemic. There are several points along the cholera transmission path at which its spread may be halted:

1. Sterilization: Proper disposal and treatment of infected fecal waste water produced by cholera victims and all contaminated materials (e.g. clothing, bedding, etc.) are essential. All materials that come in contact with cholera patients should be sanitized by washing in hot water, using chlorine bleach if possible. Hands that touch cholera patients or their clothing, bedding, etc., should be thoroughly cleaned and disinfected with chlorinated water or other effective antimicrobial agents.

2. Sewage: antibacterial treatment of general sewage by chlorine, ozone, ultraviolet light or other effective treatment before it enters the waterways or underground water supplies helps prevent undiagnosed patients from inadvertently spreading the disease.

3. Sources: Warnings about possible cholera contamination should be posted around contaminated water sources with directions on how to decontaminate the water (boiling, chlorination etc.) for possible use.

4. Water purification: All water used for drinking, washing, or cooking should be sterilized by either boiling, chlorination, ozone water treatment, ultraviolet light sterilization (e.g. by solar water disinfection), or antimicrobial filtration in any area where cholera may be present. Chlorination and boiling are often the least expensive and most effective means of halting transmission. Cloth filters, though very basic, have significantly reduced the occurrence of cholera when used in poor villages in Bangladesh that rely on untreated surface water. Better antimicrobial filters, like those present in advanced individual water treatment hiking kits, are most effective. Public health education and adherence to appropriate sanitation practices are of primary importance to help prevent and control transmission of cholera and other diseases.

Surveillance
Surveillance and prompt reporting allow for containing cholera epidemics rapidly. Cholera exists as a seasonal disease in many endemic countries, occurring annually mostly during rainy seasons. Surveillance systems can provide early alerts to outbreaks, therefore leading to coordinated response and assist in preparation of preparedness plans. Efficient surveillance systems can also improve the risk assessment for potential cholera outbreaks. Understanding the seasonality and location of outbreaks provide guidance for improving cholera control activities for the most vulnerable. For prevention to be effective, it is important that cases are reported to national health authorities.

Vaccine
Main article: Cholera vaccine

A number of safe and effective oral vaccines for cholera are available. Dukoral, an orally administered, inactivated whole cell vaccine, has an overall efficacy of about 52% during the first year after being given and 62% in the second year, with minimal side effects. It is available in over 60 countries. However, it is not currently recommended by the Centers for Disease Control and Prevention (CDC) for most people traveling from the United States to endemic countries. One injectable vaccine was found to be effective for two to three years. The protective efficacy was 28% lower in children less than 5 years old. However, as of 2010, it has limited availability. Work is under way to investigate the role of mass vaccination. The World Health Organization (WHO) recommends immunization of high risk groups, such as children and people with HIV, in countries where this

disease is endemic. If people are immunized broadly, herd immunity results, with a decrease in the amount of contamination in the environment.

Treatment
Continued eating speeds the recovery of normal intestinal function. The World Health Organization recommends this generally for cases of diarrhea from whatever cause. A CDC training manual specifically for cholera states: “Continue to breastfeed your baby if the baby has watery diarrhea, even when traveling to get treatment. Adults and older children should continue to eat frequently.”

Fluids
In most cases, cholera can be successfully treated with oral rehydration therapy (ORT), which is highly effective, safe, and simple to administer. Rice-based solutions are preferred to glucose-based ones due to greater efficiency. In severe cases with significant dehydration, intravenous rehydration may be necessary. Ringer's lactate is the preferred solution, often with added potassium. Large volumes and continued replacement until diarrhea has subsided may be needed. Ten percent of a person's body weight in fluid may need to be given in the first two to four hours. This method was first tried on a mass scale during the Bangladesh Liberation War, and was found to have much success.

If commercially produced oral rehydration solutions are too expensive or difficult to obtain, solutions can be made. One such recipe calls for 1 litre of boiled water, 1/2 teaspoon of salt, 6 teaspoons of sugar, and added mashed banana for potassium and to improve taste.

Electrolytes
As there frequently is initially acidosis, the potassium level may be normal, even though large losses have occurred. As the dehydration is corrected, potassium levels may decrease rapidly, and thus need to be replaced.

Antibiotics
Antibiotic treatments for one to three days shorten the course of the disease and reduce the severity of the symptoms. People will recover without them, however, if sufficient hydration is maintained. Doxycycline is typically used first line, although some strains of *V. cholerae* have shown resistance. Testing for resistance during an outbreak can help determine appropriate future choices. Other antibiotics proven to be effective include cotrimoxazole, erythromycin, tetracycline, chloramphenicol, and furazolidone. Fluoroquinolones, such as norfloxacin, also may be used, but resistance has been reported.

In many areas of the world, antibiotic resistance is increasing. In Bangladesh, for example, most cases are resistant to tetracycline, trimethoprim-sulfamethoxazole, and erythromycin. Rapid diagnostic assay methods are available for the identification of multiple drug-resistant cases. New generation antimicrobials have been discovered which are effective against in *in vitro* studies.

Sari Filtration
An effective and relatively cheap method to prevent transmission of *V. cholera* is the practice of folding a sari multiple times to create a simple filter for drinking water. Folding saris four to eight times may create a simple filter to reduce the amount of active *V. cholera* in the filtered water. The education of proper sari filter use is imperative, as there is a positive correlation between sari misuse and the incidence of childhood diarrhea; soiled saris worn by women are vectors of transmission of enteric pathogens to young children. Educating at-risk populations about the proper use of the sari filter method may decrease *V. cholera*-associated disease.

Prognosis
If people with cholera are treated quickly and properly, the mortality rate is less than 1%; however, with untreated cholera, the mortality rate rises to 50–60%. For certain genetic strains of cholera, such as the one present during the 2010 epidemic in Haiti and the 2004 outbreak in India, death can occur within two hours of the first sign of symptoms.

Epidemiology
See also: Cholera outbreaks and pandemics

Hand bill from the New York City Board of Health, 1832 - the outdated public health advice demonstrates the lack of understanding of the disease and its actual causative factors.

Cholera affects an estimated 3-5 million people worldwide, and causes 100,000-130,000 deaths a year as of 2010. This occurs mainly in the developing world. In the early 1980s, death rates are believed to have been greater than 3 million a year. It is difficult to calculate exact numbers of cases, as many go unreported due to concerns that an outbreak may have a negative impact on the tourism of a country. Cholera remains both epidemic and endemic in many areas of the world.

Although much is known about the mechanisms behind the spread of cholera, this has not led to a full understanding of what makes cholera outbreaks happen some places and not others. Lack of treatment of human feces and lack of treatment of drinking water greatly facilitate its spread, but bodies of water can serve as a reservoir, and seafood shipped long distances can spread the disease. Cholera was not known in the Americas for most of the 20th century, but it reappeared towards the end of that century and seems likely to persist.

History
The word cholera is from Greek: χολέρα *kholera* from χολή *kholē* "bile". Cholera likely has its origins in the Indian Subcontinent; it has been prevalent in the Ganges delta since ancient times. The disease first spread by trade routes (land and sea) to Russia in 1817, then to Western Europe, and from Europe to North America. Seven cholera pandemics have occurred in the past 200 years, with the seventh originating in Indonesia in 1961

The first cholera pandemic occurred in the Bengal region of India starting in 1817 through 1824. The disease dispersed from India to Southeast Asia, China, Japan, the Middle East, and southern Russia. The second pandemic lasted from 1827 to 1835 and affected the United States and Europe. The third pandemic erupted in 1839, persisted until 1856, extended to North Africa, and reached South America, for the first time specifically infringing upon Brazil. Cholera hit the sub-Saharan African region during the fourth pandemic from 1863 to 1875. The fifth and sixth pandemics raged from 1881–1896 and 1899-1923. These epidemics were less fatal due to a greater understanding of the cholera bacteria. Egypt, the Arabian peninsula, Persia, India, and the Philippines were hit hardest during these epidemics, while other areas, like Germany in 1892 and Naples from 1910–1911, experienced severe outbreaks. The final pandemic originated in 1961 in Indonesia and is marked by the emergence of a new strain, nicknamed El Tor, which still persists today in developing countries.

From a local disease, cholera became one of the most widespread and deadly diseases of the 19th century, killing an estimated tens of millions of people. In Russia alone, between 1847 and 1851, more than one million people perished of the disease. It killed 150,000 Americans during the second pandemic. Between 1900 and 1920, perhaps eight million people died of cholera in India.

Cholera became the first reportable disease in the United States due to the significant effects it had on health John Snow, in England, was the first to identify the importance of contaminated water in its cause in 1854.[1] Cholera is now no longer considered a pressing health threat in Europe and North America due to filtering and chlorination of water supplies, but still heavily affects populations in developing countries.

In the past, people traveling in ships would hang a yellow quarantine flag if one or more of the crew members suffered from cholera. Passengers from boats with a yellow flag hung would not be allowed to disembark at any harbor for an extended period, typically 30 to 40 days. In modern international maritime signal flags, the quarantine flag is yellow and black.

Cholera Morbus
The term *cholera morbus* was used in the 19th and early 20th centuries to describe both nonepidemic cholera and other gastrointestinal diseases (sometimes epidemic) that resembled cholera. The term is not in current use, but is found in many older references. The other diseases are now known collectively as gastroenteritis.

Research
The Russian-born bacteriologist Waldemar Haffkine developed the first cholera vaccine around 1900. The bacterium had been originally isolated 45 years earlier (1855) by Italian anatomist Filippo Pacini, but its exact nature and his results were not widely known.

One of the major contributions to fighting cholera was made by the physician and pioneer medical scientist John Snow (1813–1858), who in 1854 found a link between cholera and contaminated drinking water. Dr. Snow proposed a microbial origin for epidemic cholera in 1849. In his major "state of the art" review of 1855, he proposed a substantially complete and correct model for the etiology of the disease. In two pioneering epidemiological field studies, he was able to demonstrate human sewage contamination was the most probable disease vector in two major epidemics in London in 1854. His model was not immediately accepted, but it was seen to be the more plausible, as medical microbiology developed over the next 30 years or so.

Cities in developed nations made massive investment in clean water supply and well-separated sewage treatment infrastructures between the mid-1850s and the 1900s. This eliminated the threat of cholera epidemics from the major developed cities in the world. In 1883, Robert Koch identified *V. cholerae* with a microscope as the bacillus causing the disease.

Cholera has been a laboratory for the study of evolution of virulence. The province of Bengal in British India was partitioned into West Bengal and East Pakistan in 1947. Prior to partition, both regions had cholera pathogens with similar characteristics. After 1947, India made more progress on public health than East Pakistan (now Bangladesh). As a consequence,[*clarification needed*] the strains of the pathogen that succeeded in India had a greater incentive in the longevity of the host. They have become less virulent than the strains prevailing in Bangladesh. These draw upon the resources of the host population and rapidly kill many victims.

More recently, in 2002, Alam, *et al.*, studied stool samples from patients at the International Centre for Diarrhoeal Disease in Dhaka, Bangladesh. From the various experiments they conducted, the researchers found a correlation between the passage of *V. cholerae* through the human digestive system and an increased infectivity state. Furthermore, the researchers found the bacterium creates a hyperinfected state where genes that control biosynthesis of amino acids, iron uptake systems, and formation of periplasmic nitrate reductase complexes were induced just before defecation. These induced characteristics allow the cholera vibrios to survive in the "rice water" stools, an environment of limited oxygen and iron, of patients with a cholera infection.

Notable Cases
Tchaikovsky's death has traditionally been attributed to cholera, most probably contracted through drinking contaminated water several days earlier. Since the water was not boiled and cholera was affecting St. Petersburg, such a connection is quite plausible ...." Tchaikovsky's mother died of cholera, and his father became sick with cholera at this time but made a full recovery. Some scholars, however, including English musicologist and Tchaikovsky authority David Brown and biographer Anthony Holden, have theorized that his death was a suicide.

After the 2011 earthquake, a severe outbreak of cholera swept over Haiti. The number of deaths have been difficult to verify due to the fact that most people do not contain enough money to go to the hospital and are dying at home.an estimated 470,00 cases of this infection has been reported in this third world country.

“After one year, this marks the worst cholera outbreak in recent history, as well as the best documented cholera outbreak in modern public health.(center for disease control and prevention (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Coccidioidomycosis
Date: 2012
Source: Wikipedia

Abstract: Coccidioidomycosis [pronounced: kok-siddee-oydo-my-cohssiss](commonly known as "Valley fever", as well as "California fever", "Desert rheumatism", and "San Joaquin Valley fever") is a fungal disease caused by *Coccidioides immitis* or *C. posadasii*. It is endemic in certain parts of Arizona, California, Nevada, New Mexico, Texas, Utah and northwestern Mexico.

C. immitis resides in the soil in certain parts of the southwestern United States, northern Mexico, and parts of Central and South America. It is dormant during long dry spells, then develops as a mold with long filaments that break off into airborne spores when the rains come. The spores, known as arthroconidia, are swept into the air by disruption of the soil, such as during construction, farming, or an earthquake. Infection is caused by inhalation of the particles. The disease is not transmitted from person to person. *C. immitis* is a dimorphic saprophytic organism that grows as a mycelium in the soil and produces a spherule form in the host organism.

Presentation
The disease is usually mild, with flu-like symptoms and rashes. The Mayo Clinic estimates that half the population in some affected areas have suffered from the disease. On occasion, those particularly susceptible may develop a serious or even fatal illness. Serious complications include severe pneumonia, lung nodules, and disseminated disease, where the fungus spreads throughout the body. The disseminated form of valley fever can devastate the body, causing skin ulcers, abscesses, bone lesions, severe joint pain, heart inflammation, urinary tract problems, meningitis, and often death. In order of decreasing risk, people of Filipino, African, Native American, Hispanic, and Asian descent are susceptible to the disseminated form of the disease. Men and pregnant women, and people with weakened immune systems (as from AIDS) are more susceptible than non-pregnant women.

It has been known to infect humans, cattle, deer, dogs, elk, fish, mules, livestock, apes, kangaroos, wallabies, tigers, bears, badgers, otters and marine mammals.

Symptomatic infection (40% of cases) usually presents as an influenza-like illness with fever, cough, headaches, rash, and myalgia (muscle pain). Some patients fail to recover and develop chronic pulmonary infection or widespread disseminated infection (affecting meninges, soft tissues, joints, and bone). Severe pulmonary disease may develop in HIV-infected persons.

An additional risk is that health care providers who are unfamiliar with it or are unaware that the patient has been exposed to it may misdiagnose it as cancer and subject the patient to unnecessary surgery.

Types
Coccidioidomycosis may be divided into the following types:

1. Primary pulmonary coccidioidomycosis
2. Disseminated coccidioidomycosis
3. Primary cutaneous coccidioidomycosis

Incidence (North America)
California state prisons, as far back as 1919, have been particularly affected by Coccidioidomycosis. In 2005 and 2006, the Pleasant Valley State Prison near Coalinga and Avenal State Prison near Avenal on the western side of the San Joaquin Valley had the highest incidence in 2005, of at least 3,000 per 100,000.

Incidence varies widely across the west and southwest. In Arizona, for instance, in 2007, there were 3,450 cases in Maricopa County, which in 2007 had an estimated population of 3,880,181 for an incidence of approximately 1 in 1,125. In contrast, though southern New Mexico is considered an endemic region, there were 35 cases in the entire state in 2008, and 23 in 2007, in a region that had an estimated 2008 population of 1,984,356 for an incidence of approximately 1 in 56,695. Infection rates vary greatly by county, and although population density is important, so are other factors that have not been proven yet. Greater construction activity may disturb spores in the soil. In addition, the effect of altitude on fungi growth and morphology has not been studied, and altitude can range from sea level to 10,000 feet or higher across California, Arizona, Texas and New Mexico.

In California from 2000 to 2007, there were 16,970 reported cases (5.9 per 100,000 people) and 752 deaths (0.26 per 100,000 people) with the highest incidence in the San Joaquin Valley (44.1 per 100,000).

Biological Warfare
C. immitis was investigated by the United States during the 1950s and 1960s as a potential biological weapon.[*citation needed*] The Cash strain received the military symbol OC, and original hopes were for its use as an incapacitant. As medical epidemiology later made clear, OC would have lethal effects on several segments of the population, so it was later considered a lethal agent. It was never standardized, and beyond a few field trials, it was never weaponized. Most military work on OC was on vaccines by the mid-1960s. It is still on the CDC's list of select agents however.

Diagnostic Test
The fungal infection can be demonstrated by microscopic detection of diagnostic cells in body fluids, exudates, sputum and biopsy-tissue. With specific nucleotide primers *C.immitis* DNA can be amplified by PCR. It can also be detected in culture by morphological identification or by using molecular probes that hybridize with *C.immitis* RNA. An indirect demonstration of fungal infection can be achieved also by serologic analysis detecting fungal antigen or host antibody produced against the fungus.

Treatment
There are no published prospective studies that examine optimal antifungal therapy for coccidioidomycosis. Mild cases often do not require treatment.
Oral Fluconazole and intravenous Amphotericin B are used in progressive or disseminated disease, or in which patients are immunocompromised. Alternatively, itraconazole or ketoconazole may be used. Posaconazole and voriconazole have also been used (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Ebola Virus Disease
Date: 2012
Source: Wikipedia

Abstract: Ebola virus disease (EVD) (or more commonly, Ebola hemorrhagic fever (EHF)) is the name for the human disease which may be caused by any of the five known ebolaviruses. These five viruses are: Bundibugyo Ebolavirus (BEBOV or BDBV), Zaire Ebolavirus (ZEBOV or ambiguously, EBOV), Sudan Ebolavirus (SEBOV or SUDV), Reston Ebolavirus (REBOV) and Taï Forest virus (TAFV, formerly and more commonly Cote d'Ivoire Ebolavirus (Ivory Coast Ebolavirus, CIEBOV)). EVD is a viral hemorrhagic fever (VHF), and is clinically nearly indistinguishable from Marburg virus disease (MVD).

Classification

The genera *Ebolavirus* and *Marburgvirus* were originally classified as the species of the now-obsolete *Filovirus* genus. In March 1998, the Vertebrate Virus Subcommittee proposed in the International Committee on Taxonomy of Viruses (ICTV) to change the *Filovirus* genus to the *Filoviridae* family with two specific genera: *Ebola-like viruses* and *Marburg-like viruses*. This proposal was implemented in Washington, D.C., as of April 2001 and in Paris as of July 2002. In 2000 another proposal was made in Washington, D.C., to change the "-like viruses" to "-virus" resulting in today's *Ebolavirus* and *Marburgvirus*

Rates of genetic change are one hundred times slower than influenza A in humans, but on the same magnitude as those of hepatitis B. Extrapolating backwards using these rates indicates that Ebolavirus and Marburgvirus diverged several thousand years ago. However, paleoviruses (genomic fossils) of filoviruses (Filoviridae) found in mammals indicate that the family itself is at least tens of millions of years old. Viral fossils that are closely related to ebolaviruses have been found in the genome of the Chinese hamster.

The Five Characterised Ebola Species Are:

Zaire Ebolavirus (ZEBOV)
Also known simply as the *Zaire virus*, ZEBOV has the highest case-fatality rate, up to 90% in some epidemics, with an average case fatality rate of approximately 83% over 27 years. There have been more outbreaks of *Zaire ebolavirus* than of any other species. The first outbreak took place on 26 August, 1976 in Yambuku. Mabalo Lokela, a 44-year-old schoolteacher, became the first recorded case. The symptoms resembled malaria, and subsequent patients received quinine. Transmission has been attributed to reuse of unsterilized needles and close personal contact.

Sudan Ebolavirus (SEBOV)
Like the *Zaire virus*, SEBOV emerged in 1976; it was at first assumed to be identical with the Zaire species. SEBOV is believed to have broken out first amongst cotton factory workers in Nzara, Sudan, with the first case reported as a worker exposed to a potential natural reservoir. Scientists tested local animals and insects in response to this; however, none tested positive for the virus. The carrier is still unknown. The lack of barrier nursing (or "bedside isolation") facilitated the spread of the disease. The

most recent outbreak occurred in May, 2004. 20 confirmed cases were reported in Yambio County, Sudan, with five deaths resulting. The average fatality rates for SEBOV were 54% in 1976, 68% in 1979, and 53% in 2000 and 2001.

Reston Ebolavirus (REBOV)
Discovered during an outbreak of simian hemorrhagic fever virus (SHFV) in crab-eating macaques from Hazleton Laboratories (now Covance) in 1989. Since the initial outbreak in Reston, Virginia, it has since been found in non-human primates in Pennsylvania, Texas and Siena, Italy. In each case, the affected animals had been imported from a facility in the Philippines, where the virus has also infected pigs. Despite its status as a Level-4 organism and its apparent pathogenicity in monkeys, REBOV did not cause disease in exposed human laboratory workers.

Côte D'Ivoire Ebolavirus (CIEBOV)
Also referred to as *Taï Forest ebolavirus* and by the English place name, "Ivory Coast", it was first discovered among chimpanzees from the Taï Forest in Côte d'Ivoire, Africa, in 1994. Necropsies showed blood within the heart to be brown; no obvious marks were seen on the organs; and one necropsy displayed lungs filled with blood. Studies of tissues taken from the chimpanzees showed results similar to human cases during the 1976 Ebola outbreaks in Zaire and Sudan. As more dead chimpanzees were discovered, many tested positive for Ebola using molecular techniques. The source of the virus was believed to be the meat of infected Western Red Colobus monkeys, upon which the chimpanzees preyed. One of the scientists performing the necropsies on the infected chimpanzees contracted Ebola. She developed symptoms similar to those of dengue fever approximately a week after the necropsy, and was transported to Switzerland for treatment. She was discharged from the hospital after two weeks and had fully recovered six weeks after the infection.

Bundibugyo Ebolavirus
On November 24, 2007, the Uganda Ministry of Health confirmed an outbreak of Ebolavirus in the Bundibugyo District. After confirmation of samples tested by the United States National Reference Laboratories and the CDC, the World Health Organization confirmed the presence of the new species. On 20 February, 2008, the Uganda Ministry officially announced the end of the epidemic in Bundibugyo, with the last infected person discharged on 8 January, 2008. An epidemiological study conducted by WHO and Uganda Ministry of Health scientists determined there were 116 confirmed and probable cases the new Ebola species, and that the outbreak had a mortality rate of 34% (39 deaths).

Signs & Symptoms
EVD/EHF is clinically indistinguishable from Marburg virus disease (MVD), and it can also easily be confused with many other diseases prevalent in Equatorial Africa, such as other viral hemorrhagic fevers, falciparum malaria, typhoid fever, shigellosis, rickettsial diseases, cholera, gram-negative septicemia or EHEC enteritis. The most detailed studies on the frequency, onset, and duration of EVD clinical signs and symptoms were performed during the 1995 outbreak in Kikwit, Zaire (EBOV) and the 2007-2008 outbreak in Bundibugyo, Uganda (BDBV). The mean incubation period, best calculated currently for EVD outbreaks due to EBOV infection, is 12.7 days (standard deviation = 4.3 days), but can be as long as 25 days. EVD begins with a sudden onset of an influenza-like stage characterized by general malaise, fever with chills, arthralgia and myalgia, and chest pain. Nausea is accompanied by abdominal pain, anorexia, diarrhea, and vomiting. Respiratory tract involvement is characterized by pharyngitis with sore throat, cough, dyspnea, and hiccups.

The central nervous system is affected as judged by the development of severe headaches, agitation, confusion, fatigue, depression, seizures, and sometimes coma. The circulatory system is also frequently involved, with the most prominent signs being edema and conjunctivitis. Hemorrhagic symptoms are infrequent (fewer than 10% of cases for most serotypes), (the reason why Ebola hemorrhagic fever (EHF) is a misnomer) and include hematemesis, hemoptysis, melena, and bleeding from mucous membranes (gastroinestinal tract, nose, vagina and gingiva).

Cutaneous presentation may include: maculopapular rash, petechiae, purpura, ecchymoses, and hematomas (especially around needle injection sites). Development of hemorrhagic symptoms is generally indicative of a negative prognosis. However, contrary to popular belief, hemorrhage does not lead to hypovolemia and is not the cause of death (total blood loss is low except during labor). Instead, death occurs due to multiple organ dysfunction syndrome (MODS) due to fluid redistribution, hypotension, disseminated intravascular coagulation, and focal tissue necroses.

Causes
Main article: Ebolavirus

EVD is caused by four of five viruses classified in the genus *Ebolavirus*, family *Filoviridae*, order *Mononegavirales*: Bundibugyo virus (BDBV), Ebola virus (EBOV), Sudan virus (SUDV), and Taï Forest virus (TAFV). The fifth virus, Reston virus (RESTV), is thought to be apathogenic for humans and therefore not discussed here.

Genus Ebolavirus: species and their EVD-causing viruses

Species Name / Virus Name

1. Bundibugyo ebolavirus / Bundibugyo virus (BDBV; previously BEBOV)
2. Sudan ebolavirus / Sudan virus (SUDV; previously SEBOV)
3. Taï Forest ebolavirus / Taï Forest virus (TAFV; previously CIEBOV)
4. Zaire ebolavirus / Ebola virus (EBOV; previously ZEBOV)

Risk Factors
Between 1976 and 1998, from 30,000 mammals, birds, reptiles, amphibians, and arthropods sampled from outbreak regions, no *ebolavirus* was detected apart from some genetic traces found in six rodents (*Mus setulosus* and *Praomys*) and one shrew (*Sylvisorex ollula*) collected from the Central African Republic. Traces of EBOV were detected in the carcasses of gorillas and chimpanzees during outbreaks in 2001 and 2003, which later became the source of human infections. However, the high lethality from infection in these species makes them unlikely as a natural reservoir.

Plants, arthropods, and birds have also been considered as possible reservoirs; however, bats are considered the most likely candidate. Bats were known to reside in the cotton factory in which the index cases for the 1976 and 1979 outbreaks were employed, and they have also been implicated in Marburg virus infections in 1975 and 1980. Of 24 plant species and 19 vertebrate species experimentally inoculated with EBOV, only bats became infected. The absence of clinical signs in these bats is characteristic of a reservoir species. In a 2002–2003 survey of 1,030 animals which included 679 bats from Gabon and the Republic of the Congo, 13 fruit bats were found to contain EBOV RNA fragments. As of 2005, three types of fruit bats (*Hypsignathus monstrosus*, *Epomops franqueti*, and *Myonycteris torquata*) have been identified as being in contact with EBOV. They are now suspected to represent the EBOV reservoir hosts.

The existence of integrated genes of filoviruses in some genomes of small rodents, insectivorous bats, shrews, tenrecs, and marsupials indicates a history of infection with filoviruses in these groups as well. However, it has to be stressed that infectious ebolaviruses have not yet been isolated from any nonhuman animal.

Bats drop partially eaten fruits and pulp, then terrestrial mammals such as gorillas and duikers feed on these fallen fruits. This chain of events forms a possible indirect means of transmission from the natural host to animal populations, which have led to research towards viral shedding in the saliva of bats. Fruit production, animal behavior, and other factors vary at different times and places which may trigger outbreaks among animal populations. Transmission between natural reservoirs and humans are rare, and outbreaks are usually traceable to a single index case where an individual has handled the carcass of gorilla, chimpanzee, or duiker. The virus then spreads person-to-person, especially within families, hospitals, and during some mortuary rituals where contact among individuals becomes more likely.

The virus has been confirmed to be transmitted through body fluids. Transmission through oral exposure and through conjunctiva exposure is likely and has been confirmed in non-human primates. Filoviruses are not naturally transmitted by aerosol. They are, however, highly infectious as breathable 0.8–1.2 micrometre droplets in laboratory conditions; because of this potential route of infection, these viruses have been classified as Category A biological weapons.

All epidemics of Ebola have occurred in sub-optimal hospital conditions, where practices of basic hygiene and sanitation are often either luxuries or unknown to caretakers and where disposable needles and autoclaves are unavailable or too expensive. In modern hospitals with disposable needles and knowledge of basic hygiene and barrier nursing techniques, Ebola has never spread on a large scale. In isolated settings such as a quarantined hospital or a remote village, most victims are infected shortly after the first case of infection is present. The quick onset of symptoms from the time the disease becomes contagious in an individual makes it easy to identify sick individuals and limits an individual's ability to spread the disease by traveling. Because bodies of the deceased are still infectious, some doctors had to take measures to properly dispose dead bodies in a safe manner despite local traditional burial rituals.

Virology

Main article: Ebola virus

Genome
Like all mononegaviruses, ebolavirions contain linear nonsegmented, single-stranded, non-infectious RNA genomes of negative polarity that possesses inverse-complementary 3' and 5' termini, do not possess a 5' cap, are not polyadenylated, and are not covalently linked to a protein. Ebolavirus genomes are approximately 19 kilobase pairs long and contain seven genes in the order 3'-UTR-*NP-VP35-VP40-GP-VP30-VP24-L*-5'-UTR. The genomes of the five different ebolaviruses (BDBV, EBOV, RESTV, SUDV, and TAFV) differ in sequence and the number and location of gene overlaps.

Structure
Like all filoviruses, ebolavirions are filamentous particles that may appear in the shape of a shepherd's crook or in the shape of a "U" or a "6", and they may be coiled, toroid, or branched. Ebolavirions are generally 80 nm in width, but vary somewhat in length. In general, the median particle length of ebolaviruses ranges from 974–1,086 nm (in contrast to marburgvirions, whose median particle length was measured to be 795–828 nm), but particles as long as 14,000 nm have been detected in tissue culture. Ebolavirions consist of seven structural proteins. At the center is the helical ribonucleocapsid, which consists of the genomic RNA wrapped around a polymer of nucleoproteins (NP). Associated with the ribonucleoprotein is the RNA-dependent RNA polymerase (L) with the polymerase cofactor (VP35) and a transcription activator (VP30). The ribonucleoprotein is embedded in a matrix, formed by the major (VP40) and minor (VP24) matrix proteins. These particles are surrounded by a lipid membrane derived from the host cell membrane. The membrane anchors a glycoprotein ($GP_{1,2}$) that projects 7 to 10 nm spikes away from its surface. While nearly identical to marburgvirions in structure, ebolavirions are antigenically distinct.

Replication
The ebolavirus life cycle begins with virion attachment to specific cell-surface receptors, followed by fusion of the virion envelope with cellular membranes and the concomitant release of the virus nucleocapsid into the cytosol. The virus RdRp partially uncoats the nucleocapsid and transcribes the genes into positive-stranded mRNAs, which are then translated into structural and nonstructural proteins. Ebolavirus L binds to a single promoter located at the 3' end of the genome. Transcription either terminates after a gene or continues to the next gene downstream. This means that genes close to the 3' end of the genome are transcribed in the greatest abundance, whereas those toward the 5' end are least likely to be transcribed. The gene order is therefore a simple but effective form of transcriptional regulation. The most abundant protein produced is the nucleoprotein, whose concentration in the cell determines when L switches from gene transcription to genome replication. Replication results in full-length, positive-stranded antigenomes that are in turn transcribed into negative-stranded virus progeny genome copies. Newly synthesized structural proteins and genomes self-assemble and accumulate near the inside of the cell membrane. Virions bud off from

the cell, gaining their envelopes from the cellular membrane they bud from. The mature progeny particles then infect other cells to repeat the cycle.

Pathophysiology
Endothelial cells, mononuclear phagocytes, and hepatocytes are the main targets of infection. After infection, in a secreted glycoprotein (sGP) the Ebola virus glycoprotein (GP) is synthesized. Ebola replication overwhelms protein synthesis of infected cells and host immune defenses. The GP forms a trimeric complex, which binds the virus to the endothelial cells lining the interior surface of blood vessels. The sGP forms a dimeric protein which interferes with the signaling of neutrophils, a type of white blood cell, which allows the virus to evade the immune system by inhibiting early steps of neutrophil activation. These white blood cells also serve as carriers to transport the virus throughout the entire body to places such as the lymph nodes, liver, lungs, and spleen. The presence of viral particles and cell damage resulting from budding causes the release of cytokines (specifically TNF-α, IL-6, IL-8, etc.), which are the signaling molecules for fever and inflammation. The cytopathic effect, from infection in the endothelial cells, results in a loss of vascular integrity. This loss in vascular integrity is furthered with synthesis of GP, which reduces specific integrins responsible for cell adhesion to the inter-cellular structure, and damage to the liver, which leads to coagulopathy.

Diagnosis
EVD is clinically indistinguishable from Marburg virus disease (MVD), and it can also easily be confused with many other diseases prevalent in Equatorial Africa, such as other viral hemorrhagic fevers, falciparum malaria, typhoid fever, shigellosis, rickettsial diseases such as typhus, cholera, gram-negative septicemia, borreliosis such as relapsing fever or EHEC enteritis. Other infectious diseases that ought to be included in the differential diagnosis include leptospirosis, scrub typhus, plague, Q fever, candidiasis, histoplasmosis, trypanosomiasis, visceral leishmaniasis, hemorrhagic smallpox, measles, and fulminant viral hepatitis. Non-infectious diseases that can be confused with EVD are acute promyelocytic leukemia, hemolytic uremic syndrome, snake envenomation, clotting factor deficiencies/platelet disorders, thrombotic thrombocytopenic purpura, hereditary hemorrhagic telangiectasia, Kawasaki disease, and even warfarin intoxication.

The most important indicator that may lead to the suspicion of EVD at clinical examination is the medical history of the patient, in particular the travel and occupational history (which countries were visited?) and the patient's exposure to wildlife (exposure to bats, bat excrement, nonhuman primates?). EVD can be confirmed by isolation of ebolaviruses from or by detection of ebolavirus antigen or genomic or subgenomic RNAs in patient blood or serum samples during the acute phase of EVD. Ebolavirus isolation is usually performed by inoculation of grivet kidney epithelial Vero E6 or MA-104 cell cultures or by inoculation of human adrenal carcinoma SW-13 cells, all of which react to infection with characteristic cytopathic effects. Filovirions can easily be visualized and identified in cell culture by electron microscopy due to their unique filamentous shapes, but electron microscopy cannot differentiate the various filoviruses alone despite some overall length differences. Immunofluorescence assays are used to confirm ebolavirus presence in cell cultures. During an outbreak, virus isolation and electron microscopy are most often not feasible options. The most common diagnostic methods are therefore RT-PCR in conjunction with antigen-capture ELISA which can be performed in field or mobile hospitals and laboratories. Indirect immunofluorescence assays (IFAs) are not used for diagnosis of EVD in the field anymore.

Prevention
A researcher working with the Ebola virus while wearing a biosafety level 4 positive pressure suit to avoid infection

Ebolaviruses are highly infectious as well as contagious.

As an outbreak of ebola progresses, bodily fluids from diarrhea, vomiting, and bleeding represent a hazard. Due to lack of proper equipment and hygienic practices, large-scale epidemics occur mostly in poor, isolated areas without modern hospitals or well-educated medical staff. Many areas where the infectious reservoir exists have just these characteristics. In such environments, all that can be done is to immediately cease all needle-sharing or use without adequate sterilization procedures,

isolate patients, and observe strict barrier nursing procedures with the use of a medical-rated disposable face mask, gloves, goggles, and a gown at all times, strictly enforced for all medical personnel and visitors. The aim of all of these techniques is to avoid any person's contact with the blood or secretions of any patient, including those who are deceased.

Vaccines have successfully protected nonhuman primates; however, the six months needed to complete immunization made it impractical in an epidemic. To resolve this, in 2003, a vaccine using an adenoviral (ADV) vector carrying the Ebola spike protein was tested on crab-eating macaques. The monkeys were challenged with the virus 28 days later, and remained resistant. In 2005, a vaccine based on attenuated recombinant vesicular stomatitis virus (VSV) vector carrying either the Ebola glycoprotein or Marburg glycoprotein successfully protected nonhuman primates, opening clinical trials in humans. By October, the study completed the first human trial; giving three vaccinations over three months showing capability of safely inducing an immune response. Individuals were followed for a year, and in 2006, a study testing a faster-acting, single-shot vaccine began. This study was completed in 2008.

Vaccines
There are currently no Food and Drug Administration-approved vaccines for the prevention of EVD. Many candidate vaccines have been developed and tested in various animal models. Of those, the most promising ones are DNA vaccines or are based on adenoviruses, vesicular stomatitis Indiana virus (VSIV)[or filovirus-like particles (VLPs) as all of these candidates could protect nonhuman primates from ebolavirus-induced disease. DNA vaccines, adenovirus-based vaccines, and VSIV-based vaccines have entered clinical trials.

Contrary to popular belief, ebolaviruses are not transmitted by aerosol during natural EVD outbreaks. Due to the absence of an approved vaccine, prevention of EVD therefore relies predominantly on behavior modification, proper personal protective equipment, and sterilization/disinfection.

In 6 December 2011 the development of a successful vaccine against Ebola for mice were reported. Unlike the predecessors it can be freeze-dried and thus stored for long periods in wait for an outbreak. The research will be presented in Proceedings of National Academy of Sciences.

In Endemic Zones
The natural maintenance hosts of ebolaviruses remain to be identified. This means that primary infection cannot necessarily be prevented in nature. The avoidance of EVD risk factors, such as contact with nonhuman primates or bats, is highly recommended, but may not be possible for inhabitants of tropical forests or people dependent on nonhuman primates as a food source.

During outbreaks
Since ebolaviruses do not spread via aerosol, the most straightforward prevention method during EVD outbreaks is to avoid direct (skin-to-skin) contact with patients, their excretions and body fluids, or possibly contaminated materials and utensils. Patients ought to be isolated but still have the right to be visited by family members. Medical staff should be trained and apply strict barrier nursing techniques (disposable face mask, gloves, goggles, and a gown at all times). Traditional burial rituals, especially those requiring embalming of bodies, ought to be discouraged or modified, ideally with the help of local traditional healers.

In the Laboratory
Ebolaviruses are World Health Organization Risk Group 4 Pathogens, requiring Biosafety Level 4-equivalent containment. Laboratory researchers have to be properly trained in BSL-4 practices and wear proper personal protective equipment.

Treatment
There is currently no Food and Drug Administration-approved ebolavirus-specific therapy for EVD. Treatment is primarily supportive in nature and includes minimizing invasive procedures, balancing fluids and electrolytes to counter dehydration, administration of anticoagulants early in infection to prevent or control disseminated intravascular coagulation, administration of procoagulants late in infection to control hemorrhaging, maintaining oxygen levels, pain management, and administration of antibiotics or antimycotics to treat secondary infections. Hyperimmune equine

immunoglobulin raised against EBOV has been used in Russia to treat a laboratory worker who accidentally infected herself with EBOV—but the patient died anyway. Experimentally, recombinant vesicular stomatitis Indiana virus (VSIV) expressing the glycoprotein of EBOV or SUDV has been used successfully in nonhuman primate models as post-exposure prophylaxis. Such a recombinant post-exposure vaccine was also used to treat a German researcher who accidentally pricked herself with a possibly EBOV-contaminated needle. Treatment might have been successful as she survived. However, actual EBOV infection could never be demonstrated without a doubt. Novel, very promising, experimental therapeutic regimens rely on antisense technology. Both small interfering RNAs (siRNAs) and phosphorodiamidate morpholino oligomers (PMOs) targeting the EBOV genome could prevent disease in nonhuman primates.

Prognosis
Prognosis is generally poor (average case-fatality rate of all EVD outbreaks to date = 68%). If a patient survives, recovery may be prompt and complete, or protracted with sequelae, such as orchitis, arthralgia, myalgia, desquamation or alopecia. Ocular manifestations, such as photophobia, hyperlacrimation, iritis, iridocyclitis, choroiditis and blindness have also been described. Importantly, EBOV and SUDV are known to be able to persist in the sperm of some survivors, which could give rise to secondary infections and disease via sexual intercourse.

Epidemiology
Distribution of Ebola and Marburg virus in Africa (note that integrated genes from filoviruses have been detected in mammals from the New World as well). (A) Known points of filovirus disease. Projected distribution of ecological niche of: (B) all filoviruses, (C) ebolaviruses, (D) marburgviruses.

For more about specific outbreaks and their descriptions, see List of Ebola outbreaks.

Outbreaks of EVD have mainly been restricted to Africa. The virus often consumes the population. Governments and individuals quickly respond to quarantine the area while the lack of roads and transportation helps to contain the outbreak. EVD was first described after almost simultaneous viral hemorrhagic fever outbreaks occurred in Zaire and Sudan in 1976. EVD is believed to occur after an ebolavirus is transmitted to a human index case via contact with an infected animal host. Human-to-human transmission occurs via direct contact with blood or bodily fluids from an infected person (including embalming of a deceased victim) or by contact with contaminated medical equipment such as needles. In the past, explosive nosocomial transmission has occurred in underequipped African hospitals due to the reuse of needles and/or absence of proper barrier nursing. Aerosol transmission has not been observed during natural EVD outbreaks. The potential for widespread EVD epidemics is considered low due to the high case-fatality rate, the rapidity of demise of patients, and the often remote areas where infections occur.

Ebola Virus Disease (EVD) Outbreaks:

Year-Virus-Geographic Location-Human Cases/Deaths (Case-Fatality Rate)

1. 1976: SUDV: Juba, Maridi, Nzara, and Tembura, Sudan: **284/151 (53%)**
2. 1976: EBOV: Yambuku, Zaire: **318/280 (88%)**
3. 1977: EBOV: Bonduni, Zaire: **1/1 (100%)**
4. 1979: SUDV: Nzara, Sudan: **34/22 (65%)**
5. 1988: EBOV: Porton Down, United Kingdom **1/0 (0%) [laboratory accident]**
6. 1994: TAFV: Taï National Park, Côte d'Ivoire; Switzerland: **1/0 (0%)**
7. 1994–1995: EBOV Woleu-Ntem and Ogooué-Ivindo Provinces, Gabon: **52/32 (62%)**
8. 1995: EBOV: Kikwit, Zaire: **317/245 (77%)**

9. 1996: EBOV: Mayibout 2, Gabon: **31/21 (68%)**

10. 1996: EBOV: Sergiyev Posad, Russia: **1/1 (100%) [laboratory accident]**

11. 1996–1997: EBOV: Ogooué-Ivindo Province, Gabon; Cuvette-Ouest Department, Republic of the Congo: **62/46 (74%)**

12. 2000–2001: SUDV: Gulu, Mbarara, and Masindi Districts, Uganda: **425/224 (53%)**

13. 2001–2002: EBOV: Ogooué-Ivindo Province, Gabon; Cuvette-Ouest Department, Republic of the Congo: **124/97 (78%)**

14. 2002: EBOV: Ogooué-Ivindo Province, Gabon; Cuvette-Ouest Department, Republic of the Congo: **11/10 (91%)**

15. 2002–2003: EBOV: Cuvette-Ouest Department, Republic of the Congo; Ogooué-Ivindo Province, Gabon: **143/128 (90%)**

16. 2003–2004: EBOV: Cuvette-Ouest Department, Republic of the Congo: **35/29 (83%)**

17. 2004: EBOV: Koltsovo, Russia: **1/1 (100%) [laboratory accident]**

18. 2004: SUDV: Yambio County, Sudan: **17/7 (41%)**

19. 2005: EBOV: Cuvette-Ouest Department, Republic of the Congo: **11/9 (82%)**

20. 2007: EBOV: Kasai Occidental Province, Democratic Republic of the Congo: **264/186 (71%)**

21. 2007–2008: BDBV: Bundibugyo District, Uganda: **116/39 (34%)**

22. 2008–2009: EBOV: Kasai Occidental Province, Democratic Republic of the Congo: **32/15 (47%)**

23. 2011: SUDV Luweero District, Uganda: **1/1 (100%)**

While investigating an outbreak of Simian hemorrhagic fever virus (SHFV) in November 1989, an electron microscopist from USAMRIID discovered filoviruses similar in appearance to Ebola in tissue samples taken from Crab-eating Macaque imported from the Philippines to Hazleton Laboratories Reston, Virginia. Due to the lethality of the suspected and previously obscure virus, the investigation quickly attracted attention.[*citation needed*] Blood samples were taken from 178 animal handlers during the incident. Of those, six animal handlers eventually seroconverted. When the handlers failed to become ill, the CDC concluded that the virus had a very low pathogenicity to humans.

The Philippines and the United States had no previous cases of infection, and upon further isolation it was concluded to be another strain of Ebola or a new filovirus of Asian origin, and named *Reston ebolavirus* (REBOV) after the location of the incident. Because of the virus's high mortality, it is a potential agent for biological warfare. In 1992, members of Japan's Aum Shinrikyo cult considered using Ebola as a terror weapon. Their leader, Shoko Asahara, led about 40 members to Zaire under the guise of offering medical aid to Ebola victims in a presumed attempt to acquire a virus sample.[106]

Given the lethal nature of Ebola, and since no approved vaccine or treatment is available, it is classified as a biosafety level 4 agent, as well as a Category A bioterrorism agent by the Centers for Disease Control and Prevention. It has the potential to be weaponized for use in biological warfare. The effectiveness as a biological weapon is compromised by its rapid lethality as patients quickly die off before they are capable of effectively spreading the contagion. The attention gathered from the outbreak in Reston prompted an increase in public interest, leading to the publication of numerous fictional works and a non-fiction work authored by Richard Preston known as *The Hot Zone*.

The BBC reports in a study that frequent outbreaks of Ebola may have resulted in the deaths of 5,000 gorillas.

Recent Cases
As of August 30, 2007, 103 people (100 adults and three children) were infected by a suspected hemorrhagic fever outbreak in the village of Kampungu, Democratic Republic of the Congo. The outbreak started after the funerals of two village chiefs, and 217 people in four villages fell ill. The World Health Organization sent a team to take blood samples for analysis and confirmed that many of the cases are the result of *Ebolavirus*. The Congo's last major Ebola epidemic killed 245 people in 1995 in Kikwit, about 200 miles (320 km) from the source of the August 2007 outbreak.

On November 30, 2007, the Uganda Ministry of Health confirmed an outbreak of Ebola in the Bundibugyo District. After confirmation of samples tested by the United States National Reference Laboratories and the Centers for Disease Control, the World Health Organization confirmed the presence of a new species of *Ebolavirus* which is now tentatively named Bundibugyo. The epidemic came to an official end on February 20, 2008. While it lasted, 149 cases of this new strain were reported, and 37 of those led to deaths.

An International Symposium to explore the environment and filovirus, cell system and filovirus interaction, and filovirus treatment and prevention was held at Centre Culturel Français, Libreville, Gabon, during March 2008. The virus appeared in southern Kasai Occidental on November 27, 2008, and blood and stool samples were sent to laboratories in Gabon and South Africa for identification.

On December 25, 2008, a mysterious disease that had killed 11 and infected 21 people in southern Democratic Republic of Congo was identified as the Ebola virus. Doctors Without Borders reported 11 deaths as of Monday 29 December 2008 in the Western Kasai province of the Democratic Republic of Congo, stating that a further 24 cases were being treated. In January 2009, Angola closed down part of its border with DRC to prevent the spread of the outbreak.

On March 12, 2009, an unidentified 45-year-old scientist from Germany accidentally pricked her finger with a needle used to inject Ebola into lab mice. She was given an experimental vaccine never before used on humans. Since the peak period for an outbreak during the 21-day Ebola incubation period has passed as of April 2, 2009, she has been declared healthy and safe. It remains unclear whether or not she was ever actually infected with the virus.

In May 2011, a 12-year-old girl in Uganda died from Ebola (Sudan subspecies). No further cases were recorded.

In December 2011, an unidentified woman presented at a Nairobi hospital with "Ebola-like symptoms" and subsequently expired. The pathogen has yet to be identified.

History
For more about the outbreak in Virginia, see Reston ebolavirus.

Ebolavirus first emerged in 1976 in outbreaks of Ebola hemorrhagic fever in Zaire and Sudan. The strain of Ebola that broke out in Zaire has one of the highest case fatality rates of any human pathogenic virus, roughly 90%, with case-fatality rates at 88% in 1976, 59% in 1994, 81% in 1995, 73% in 1996, 80% in 2001–2002, and 90% in 2003. The strain that broke out later in Sudan has a case fatality rate of around 50%. The virus is believed to be transmitted to humans via contact with an infected animal host. The virus is then transmitted to other people that come into contact with blood and bodily fluids of the infected person, and by human contact with contaminated medical equipment such as needles. Both of these infectious mechanisms will occur in clinical (nosocomial) and non-clinical situations. Due to the high fatality rate, the rapidity of demise, and the often remote areas where infections occur, the potential for widespread epidemic outbreaks is considered low.

Proceedings of an International Colloquium on Ebola Virus Infection and Other Hemorrhagic Fevers were held in Antwerp, Belgium, on December 6 through December 8 in 1977.

While investigating an outbreak of Simian hemorrhagic fever virus (SHFV) in November 1989, an electron microscopist from USAMRIID discovered filoviruses similar in appearance to Ebola in tissue samples taken from Crab-eating Macaque imported from the Philippines to Hazleton Laboratories Reston, Virginia. Due to the lethality of the suspected and previously obscure virus, the investigation quickly attracted attention.[*citation needed*]

Blood samples were taken from 178 animal handlers during the incident. Of those, six animal handlers eventually seroconverted. When the handlers failed to become ill, the CDC concluded that the virus had a very low pathogenicity to humans.

The Philippines and the United States had no previous cases of infection, and upon further isolation it was concluded to be another strain of Ebola or a new filovirus of Asian origin, and named *Reston ebolavirus* (REBOV) after the location of the incident.

In other Animals
Outbreaks of EVD among human populations generally result from handling infected wild animal carcasses. Declines in animal populations generally precede outbreaks among human populations. Since 2003, such declines have been monitored through surveillance of animal populations with the aim of predicting and preventing EVD outbreaks in humans. Recovered carcasses from gorillas contain multiple Ebola virus strains, which suggest multiple introductions of the virus. Bodies decompose quickly and carcasses are not infectious after three to four days. Contact between gorilla groups is rare, suggesting transmission among gorilla groups is unlikely, and that outbreaks result from transmission between viral reservoir and animal populations.

Outbreaks of EVD have been responsible for an 88% decline in observed chimpanzee populations since 2003. Transmission among chimpanzees through meat consumption constitutes a significant 5.2 (1.3–21.1 with 95% confidence) relative risk factor, while contact between individuals, such as touching dead bodies and grooming, do not (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Glanders
Date: 2012
Source: Wikipedia

Abstract: Glanders is an infectious disease that occurs primarily in horses, mules, and donkeys. It can be contracted by other animals such as dogs, cats and goats. It is caused by infection with the bacterium *Burkholderia mallei*, usually by ingestion of contaminated food or water. Symptoms of glanders include the formation of nodular lesions in the lungs and ulceration of the mucous membranes in the upper respiratory tract. The acute form results in coughing, fever and the release of an infectious nasal discharge, followed by septicaemia and death within days. In the chronic form, nasal and subcutaneous nodules develop, eventually ulcerating. Death can occur within months, while survivors act as carriers.

Glanders is endemic in Africa, Asia, the Middle East, Central and South America. It has been eradicated from North America, Australia and most of Europe through surveillance and destruction of affected animals, and import restrictions.

Burkholderia mallei is able to infect humans and is therefore classed as a zoonotic agent. Transmission occurs by direct contact with infected animals and entry is through skin abrasions, nasal and oral mucosal surfaces, or by inhalation.

The mallein test is a sensitive and specific clinical test for glanders. Mallein (ATCvet code: QI05AR01), a protein fraction of the glanders organism (*Burkholderia mallei*), is injected intradermo-palpebrally or given by eye-drop. In infected animals, the eyelid swells markedly in 1 or 2 days.

Glanders has not been reported in the United States since 1945.

Biological Warfare Use
Due to the high mortality rate in humans and the small number of organisms required to establish infection, *Burkholderia mallei* is regarded as a potential biological warfare (BW) or bioterrorism agent, as is the closely related organism, *Burkholderia pseudomallei*, the causative agent of melioidosis. During World War I, Glanders was believed to have been spread deliberately by German agents to infect large numbers of Russian horses and mules on the Eastern Front. Other agents attempted to introduce the disease in the United States and Argentina. This had an effect on troop and supply convoys as well as on artillery movement, which were dependent on horses and mules. Human cases in Russia increased with the infections during and after WWI. The Japanese deliberately infected horses, civilians, and prisoners of war with *B. mallei* at the Pinfang (China) Institute during World War

The U.S. studied this agent as a possible BW weapon in 1943–44 but did not weaponize it. U.S. interest in Glanders (Agent LA) continued through the 1950s, except it had an inexplicable tendency to lose virulence in the lab, making it difficult to weaponize. The Soviet Union is also believed to have been interested in *B. mallei* as a potential BW agent after World War II (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Influenza A Virus Subtype H1N1
Date: 2012
Source: Wikipedia

Abstract: 'Influenza' A (H1N1) virus is a subtype of influenza A virus and was the most common cause of human influenza (flu) in 2009. Some strains of H1N1 are endemic in humans and cause a small fraction of all influenza-like illness and a small fraction of all seasonal influenza. H1N1 strains caused a few percent of all human flu infections in 2004–2005.[1] Other strains of H1N1 are endemic in pigs (swine influenza) and in birds (avian influenza).

In June 2009, the World Health Organization declared the new strain of swine-origin H1N1 as a pandemic. This strain is often called swine flu by the public media. This novel virus spread worldwide and had caused about 17,000 deaths by the start of 2010. On August 10, 2010, the World Health Organization declared the H1N1 influenza pandemic over, saying worldwide flu activity had returned to typical seasonal patterns.

As of 26 April 2011, an H1N1 pandemic preparedness alert has been issued by the World Health Organisation (WHO) for the Americas. The affected areas have included the Chihuahua region of Mexico where its severity and work load have been high. It is reported by the aforementioned Recombinomics source that the current vaccine (California/7/2009) for H1N1 influenza might be losing its effectiveness in 2011. This point is all the more significant since it is the current virus target for the northern hemisphere's flu vaccine, and is the intended choice for the southern hemisphere.

Swine Influenza
Swine influenza (also called swine flu, or pig flu) is an infection by any one of several types of swine influenza virus. Swine influenza virus (SIV) is any strain of the influenza family of viruses that is endemic in pigs. As of 2009, the known SIV strains include influenza C and the subtypes of influenza A known as H1N1, H1N2, H3N1, H3N2, and H2N3.

Swine influenza virus is common throughout pig populations worldwide. Transmission of the virus from pigs to humans is not common and does not always lead to human influenza, often resulting only in the production of antibodies in the blood. If transmission does cause human influenza, it is called zoonotic swine flu. People with regular exposure to pigs are at increased risk of swine flu infection. The meat of an infected animal poses no risk of infection when properly cooked.

Pigs experimentally infected with the strain of swine flu that is causing the current human pandemic showed clinical signs of flu within four days, and the virus spread to other uninfected pigs housed with the infected ones.

During the mid-20th century, identification of influenza subtypes became possible, allowing accurate diagnosis of transmission to humans. Since then, only 50 such transmissions have been confirmed. These strains of swine flu rarely pass from human to human. Symptoms of zoonotic swine flu in humans are similar to those of influenza and of influenza-like illness in general, namely chills, fever, sore throat, muscle pains, severe headache, coughing, weakness, and general discomfort. The recommended time of isolation is about five days.

Notable Incidents

Spanish Flu: Main article: 1918 flu pandemic

The Spanish flu, also known as la grippe, La Gripe Española, or La Pesadilla, was an unusually severe and deadly strain of avian influenza, a viral infectious disease, that killed some 50 to 100 million people worldwide over about a year in 1918 and 1919. It is thought to be one of the most deadly pandemics in human history.

The 1918 flu caused an unusual number of deaths, possibly due to it causing a cytokine storm in the body. (The current H5N1 bird flu, also an Influenza A virus, has a similar effect.)[7] The Spanish flu virus infected lung cells, leading to overstimulation of the immune system via release of cytokines into the lung tissue. This leads to extensive leukocyte migration towards the lungs, causing destruction of lung tissue and secretion of liquid into the organ. This makes it difficult for the patient to breathe. In contrast to other pandemics, which mostly kill the old and the very young, the 1918 pandemic killed unusual numbers of young adults, which may have been due to their healthy immune systems mounting a too-strong and damaging response to the infection.

The term "Spanish" flu was coined because Spain was at the time the only European country where the press were printing reports of the outbreak, which had killed thousands in the armies fighting World War I. Other countries suppressed the news in order to protect morale.

Fort Dix Outbreak: Main article: 1976 swine flu outbreak

In 1976, a novel swine influenza A (H1N1) caused severe respiratory illness in 13 soldiers with 1 death at Fort Dix, New Jersey. The virus was detected only from January 19 to February 9 and did not spread beyond Fort Dix. Retrospective serologic testing subsequently demonstrated that up to 230 soldiers had been infected with the novel virus, which was a H1N1 strain. The cause of the outbreak is still unknown and no exposure to pigs was identified.

Russian Flu
The 1977–1978 Russian flu epidemic was caused by strain Influenza A/USSR/90/77 (H1N1). It infected mostly children and young adults under 23 because a similar strain was prevalent in 1947–57, causing most adults to have substantial immunity. Because of a striking similarity in the viral RNA of both strains – one which is unlikely to appear in nature due to antigenic drift – it is being speculated that the later outbreak was due to a laboratory incident in Russia or Northern China, though this is being denied by scientists in those countries. The virus was included in the 1978–1979 influenza vaccine. See also Influenza A virus subtype H2N2#Russian flu for the 1889–1890 Russian flu

2009 A(H1N1) Pandemic
In the 2009 flu pandemic, the virus isolated from patients in the United States was found to be made up of genetic elements from four different flu viruses – North American swine influenza, North American avian influenza, human influenza, and swine influenza virus typically found in Asia and Europe – "an unusually mongrelised mix of genetic sequences." This new strain appears to be a result of reassortment of human influenza and swine influenza viruses, in all four different strains of subtype H1N1.Main article: Pandemic H1N1/09 virus

Preliminary genetic characterization found that the hemagglutinin (HA) gene was similar to that of swine flu viruses present in U.S. pigs since 1999, but the neuraminidase (NA) and matrix protein (M) genes resembled versions present in European swine flu isolates. The six genes from American swine flu are themselves mixtures of swine flu, bird flu, and human flu viruses. While viruses with this genetic makeup had not previously been found to be circulating in humans or pigs, there is no formal national surveillance system to determine what viruses are circulating in pigs in the U.S.

In April 2009, an outbreak of Influenza-like illness occurred in Mexico and the USA; the CDC reported seven cases of novel A/H1N1 influenza. By April 24 it became clear that the outbreak of ILI in Mexico and the confirmed cases of novel influenza A in the southwest US were related and WHO issued a health advisory on the outbreak of "influenza like illness in the United States and Mexico". The disease then spread very rapidly, with the number of confirmed cases rising to 2,099 by May 7, despite aggressive measures taken by the Mexican government to curb the spread of the disease.

On June 11, 2009, the WHO declared an H1N1 pandemic, moving the alert level to phase 6, marking the first global pandemic since the 1968 Hong Kong flu.

On October 25, 2009 U.S. President Barack Obama officially declared H1N1 a national emergency[25] Despite President Obama's concern, a Fairleigh Dickinson University PublicMind poll found in October 2009 that an overwhelming majority of New Jerseyans (74%) were not very worried or not at all worried about contracting the H1N1 flu virus. Though the President's declaration caused many U.S. employers to take actions to help stem the spread of the swine flu and to accommodate employees and / or workflow which may be impacted by an outbreak.

A study conducted in coordination with the University of Michigan Health Service is scheduled for publication in the December 2009 American Journal of Roentgenology warning that H1N1 flu can cause pulmonary embolism, surmised as a leading cause of death in this current pandemic. The study authors suggest physician evaluation via contrast enhanced CT scans for the presence of pulmonary emboli when caring for patients diagnosed with respiratory complications from a "severe" case of the H1N1 flu.

March 21, 2010 worldwide update by the U.N.'s World Health Organization (WHO) states that "213 countries and overseas territories/communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 16,931 deaths."

As of May 30, 2010 worldwide update by World Health Organization(WHO) more than 214 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including over 18,138 deaths.

The research team of Andrew Miller MD showed pregnant patients are at increased risk. It has been suggested that pregnant women and certain populations such as native North Americans have a greater likelihood of developing a T helpertype 2 response to H1N1 influenza which may be responsible for the systemic inflammatory response syndrome that causes pulmonary edema and death (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Pandemic H1N1/09 Virus
Date: 2012
Source: Wikipedia

Abstract: The Pandemic H1N1/09 virus is a swine origin Influenza A virus subtype H1N1 virus strain responsible for the 2009 flu pandemic. For other names see the Nomenclature section below.

Virus Characteristics
The virus is a novel strain of influenza. Existing vaccines against seasonal flu provide no protection. A study at the U.S. Centers for Disease Control and Prevention (CDC) published in May 2009 found that children had no preexisting immunity to the new strain but that adults, particularly those over 60, had some degree of immunity. Children showed no cross-reactive antibody reaction to the new strain, adults aged 18 to 64 had 6-9%, and older adults 33%. Much reporting of early analysis repeated that the strain contained genes from five different flu viruses: North American swine influenza, North American avian influenza, human influenza, and two swine influenza viruses typically found in Asia and Europe. Further analysis showed that several of the proteins of the virus are most similar to strains that cause mild symptoms in humans, leading virologist Wendy Barclay to suggest on May 1, 2009 that the initial indications are that the virus was unlikely to cause severe symptoms for most people. Other leading researchers indicated that all segments of the virus were in fact swine in origin, despite it being a multiple reassortment. The first complete genome sequence of the pandemic strain was deposited in public databases on April 27, 2009, by scientists from the U.S. Centers for Disease Control and Prevention in Atlanta. Scientists in Winnipeg later completed the full genetic sequencing of viruses from Mexico and Canada on May 6, 2009.

Virus Origins
On June 23, 2009 The New York Times reported that U.S. federal agriculture officials, "contrary to the popular assumption that the new swine flu pandemic arose on factory farms in Mexico," now believe that it "most likely emerged in pigs in Asia, but then traveled to North America in a human." They emphasized that there was no way to prove their hypothesis, but stated that there is no evidence that this new virus, which combines Eurasian and North American genes, has ever circulated in North American pigs, "while there is tantalizing evidence that a closely related 'sister virus' has circulated in Asia."

In early June 2009, using computational methods developed over the last ten years, an international team of researchers attempted to reconstruct the origins and timescale of the 2009 flu pandemic. Dr Oliver Pybus of Oxford University's Department of Zoology, and part of the research team, claims "Our results show that this strain has been circulating among pigs, possibly among multiple continents, for many years prior to its transmission to humans." The research team that worked on this report also believe that it was "derived from several viruses circulating in swine," and that the initial transmission to humans occurred several months before recognition of the outbreak. The team concluded that "despite widespread influenza surveillance in humans, the lack of systematic swine surveillance allowed for the undetected persistence and evolution of this potentially pandemic strain for many years."Structure of the influenza virion.

The hemagglutinin (HA) and neuraminidase (NA) proteins are shown on the surface of the particle. The viral RNAs that make up the genome are shown as red coils inside the particle and bound to ribonucleoproteins (RNPs).

According to the researchers, movement of live pigs between Eurasia and North America "seems to have facilitated the mixing of diverse swine influenza viruses, leading to the multiple reassortment events associated with the genesis of the (new H1N1) strain." They also stated that this new pandemic "provides further evidence of the role of domestic pigs in the ecosystem of influenza A."

In November 2009, a study was published in Virology Journal in which it was suggested that the virus may be the product of three strains from three continents that swapped genes in a lab or a vaccine-making plant, and subsequently "escaped". The study, published in a free, online journal reviewed by other scientists, follows debate among researchers in May 2009, when the authors asked the World Health Organization to consider the hypothesis. After reviewing the initial paper, WHO and other organizations concluded the pandemic strain was a naturally occurring virus and not laboratory-derived.

Contagiousness
The virus is contagious and is believed to spread from human to human in much the same way as seasonal flu. The most common mechanisms by which it spreads are by droplets from coughs and sneezes of infected people, and also potentially touching a surface or the hand of a person contaminated with the virus and then touching one's eyes, nose or mouth. In 2009 the WHO reported that H1N1/09 seemed to be more contagious than seasonal flu. However, a New England Journal of Medicine report stated that the transmissibility of the 2009 H1N1 influenza virus in households was lower than that seen in past pandemics. The US CDC had recommended that people should wait at least a day after their fever subsides (usually 3–4 days after the onset of symptoms) before resuming normal activities, but it has been found that they can continue to shed virus for several days after that

Virulence
The virulence of swine flu virus is mild and the mortality rates are very low. In mid-2009 the US Centers for Disease Control and Prevention (CDC) noted that most infections were mild, similar to seasonal flu, and that recovery tended to be fairly quick.The number of deaths as of September 2009 is sometimes misleadingly said to be a tiny fraction of the annual number of deaths from seasonal flu, but comparisons of human fatality figures with seasonal influenza are prone to underestimate impact of the pandemic and the pandemic H1N1/09 virus was in fact the dominant strain of influenza causing illness in the 2009/10 flu season.

Research carried out at Imperial College London has shown that, unlike seasonal flu, H1N1/09 can infect cells deep in the lungs. Seasonal flu can only infect cells with receptor type a2-6 which are typically located in the nose and throat but H1N1/09 can also infect cells with receptor type a2-3. This may explain why some patients experience severe respiratory symptoms. (The H5N1 virus is also able to infect cells deep in the lungs with receptor type a2-3 but cannot infect cells with receptor type a2-6 making it less contagious than H1N1/09.)

As of September 2009 most people infected by this flu suffer a mild illness, but the small minority hospitalized are often severely ill. Arand Kumar, intensive care expert at the University of Manitoba, Winnipeg, Canada, said "this pandemic is like two diseases; either you're off work for a few days or you go to hospital, often to the intensive-care unit (ICU). There's no middle ground." In the southern hemisphere 15 to 33% of hospitalized cases went to the ICU in July and August 2009.
Unlike H5N1 avian flu and SARS which provoke a runaway body-wide immune response, H1N1/09 destroys the lungs' alveoli, often causing acute respiratory distress syndrome, which kills in half of all cases. Preliminary research suggests that severity is linked to a genetic variation in immune systems. From April 2009 to November 2009, in the US, 3,900 people died of the H1N1 pandemic virus, sometimes compared to 36,000 people per year die from the "common flu", mostly in winter, although the former figure is for confirmed cases, whereas the latter is an estimate. The death rate of H1N1 in the US could be calculated as less than 0.02% from November 2009 figures from the CDC, and has been explicitly calculated as 0.026% in England.

Vaccines
Existing vaccines against seasonal flu provide no protection. Vaccines were released in North America in late October. Production may be 3 billion doses per year rather than the earlier estimate of 5 billion

Evolutionary Potential
On May 22, 2009, World Health Organization (WHO) Director-General Dr. Margaret Chan said that the virus must be closely monitored in the southern hemisphere, as it could mix with ordinary seasonal influenza and change in unpredictable ways. Experts writing in the July issue of The New England Journal of Medicine note that historically, pandemic viruses have evolved between seasons, and the current strain may become more severe or transmissible in the coming months. They therefore stress the importance of international cooperation to engage in proper surveillance to help monitor changes in the virus's behavior, which will aid in both "vaccine targeting" and interpreting illness patterns in the fall of 2009.

Other experts are also concerned that the new virus strain could mutate over the coming months. Guan Yi, a leading virologist from the University of Hong Kong, for instance, described the new H1N1 influenza virus as "very unstable", meaning it could mix and swap genetic material (reassortment) when exposed to other viruses. During an interview he said "Both H1N1 and H5N1 are unstable so the chances of them exchanging genetic material are higher, whereas a stable (seasonal flu) virus is less likely to take on genetic material." The H5N1 virus is mostly limited to birds, but in rare cases when it infects humans it has a mortality rate of between 60% to 70%. Experts worry about the emergence of a hybrid of the more virulent Asian-lineage HPAI (highly pathogenic avian influenza) A/H5N1 strain (media labeled "bird flu") with more human-transmissible Influenza A strains such as this novel 2009 swine-origin A/H1N1 strain (media labeled "swine flu"), especially since the H5N1 strain is endemic among birds in countries like China, Indonesia, Vietnam and Egypt. (See the suite of H5N1 articles for details.)

Other studies conclude that the virus is likely well adapted to humans, has a clear biological advantage over seasonal flu strains and that reassortment is unlikely at this time due to its current ease in replication and transmission.

However, Federal health officials in the U.S. noted that the horrific 1918 flu epidemic, which killed hundreds of thousands in the United States alone, was preceded by a mild "herald" wave of cases in the spring, followed by devastating waves of illness in the autumn.

As of late July 2009, U.S. health officials said that the swine flu isn't yet mutating to become more dangerous, but they are closely tracking that as the virus continues to circle the globe.

As of October 2009, research done by Taubenberger showed that the evolution of A (H1N1) is relatively slow since the structure of the 2009 H1N1 virus is similar to the strain of H1N1 implicated in the 1918 flu pandemic. A study from Hokkaido University found a homology between the Hemagglutinin antigen amino acid residues found in the earlier 1918 strain and the 2009 H1N1 strain. This may have played a role in individuals who had been infected with the 1918 strain and its early descendants in showing stronger specific immunity to the 2009 H1N1 virus. This finding provides insight into future monitoring of the H1N1 virus and its evolution within the human population.

Mutation
On November 20, 2009 the Norwegian Institute of Public Health released a statement saying that they had discovered a potentially significant mutation in the H1N1 influenza strain that could be responsible for causing the severest symptoms among those infected. In the statement they said "The mutation could be affecting the virus' ability to go deeper into the respiratory system, thus causing more serious illness".

The World Health Organization said that the mutation did not appear to be widespread in Norway and the virus in its mutated form remained sensitive to antivirals and pandemic vaccines. A similar mutation had been detected in H1N1 viruses circulating in several other countries, including China and the United States, in severe as well as in some mild cases. "Although further investigation is under way, no evidence currently suggests that these mutations are leading to an unusual increase in

the number of H1N1 infections or a greater number of severe or fatal cases."

On December 2, 2009 the WHO announced that they have been informed of two recent clusters of patients infected with oseltamivir-resistant H1N1 viruses. Both clusters, detected in Wales, UK and North Carolina, USA, occurred in a single ward in a hospital, and both involved patients whose immune systems were severely compromised or suppressed. Transmission of resistant virus from one patient to another is suspected in both outbreaks.

Resistance
As of December 2010, the World Health Organization (WHO) reported 314 samples of 2009 pandemic H1N1 flu tested worldwide have shown resistance to oseltamivir (Tamiflu). This is not totally unexpected as 99.6% of the seasonal H1N1 flu strains tested have developed resistance to oseltamivir. No circulating flu has yet shown any resistance to zanamivir (Relenza), the other available anti-viral.

Species Affected

Swine
Before being transmitted to humans, an H1N1 type virus is known to have circulated in swine. In August 2007, about 25 people and 160 pigs developed flu at a county fair in Ohio. Analysis showed they were infected with the same strain—an H1N1 type containing genes of human, bird and swine origin. A 2004 study found that in Iowa, 20 percent of swine veterinarians and 3 percent of meatpackers, but no university workers, had antibodies in their blood indicating they had been infected with swine flu. Another study, of 804 rural Iowans, found that pig farmers were 50 times more likely, and their spouses about 30 times more likely, than university workers to carry swine flu antibodies. Pigs are also known to have been infected by humans.

Humans
Humans have been affected since early 2009. The November 27, 2009 worldwide update by the U.N.'s World Health Organization (WHO) states that "more than 207 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including over 7,820 deaths". The WHO has also tracked more than 622,482 laboratory-confirmed cases of H1N1. The symptoms of this virus are identical to that of seasonal influenza.

Birds
In late August 2009, the government of Chile discovered that the human H1N1/09 virus had jumped, unmutated, to birds, "opening a new chapter in the global epidemic." Top flu and animal-health experts with the WHO and the CDC were monitoring the situation closely. They said the infected turkeys have suffered only mild effects, easing concern about a potentially dangerous development. Chile's turkey meat remains safe to eat, they said, and so far there have been no signs of a potentially dangerous mutation. Virus experts are concerned that a more dangerous and easily transmitted strain could emerge if H1N1/09 combines again with avian flu, which at present is far more virulent but much less contagious to humans. By October 2009, another outbreak at a turkey breeder was identified in Ontario, Canada.

Other animals
In October 2009, a ferret exhibiting flu symptoms was confirmed to have contracted the H1N1 virus from its owner in Oregon, USA. In November 2009, a case of novel H1N1 was confirmed in a household cat. The Oregon Veterinary Medical Association has confirmed the first cat fatality in the U.S. from the H1N1 virus. The association recommends that cat owners with flu symptoms avoid touching cat's eyes, nose, and mouth while sick. Thoroughly wash your hands after handling a sick pet since it may be possible for cats to transmit the virus to humans. This is the third confirmed case of H1N1 in a cat in the U.S.; other cases have occurred in Utah and Iowa. The first case of a dog with H1N1 was reported in December 2009. On July 22, 2011 the Norwegian Veterinary Institute reported the first occurrence of 2009-H1N1 influenza virus in minks.

Nomenclature
The initial outbreak of a novel swine-origin H1N1 flu pandemic strain in 2009 was called by many names. In July 2009, WHO experts named it "pandemic H1N1/09 virus" to distinguish it from both various seasonal H1N1 virus strains and the 1918 flu pandemic H1N1 strain.

Some authorities object to calling the flu outbreak "swine flu". U.S. Agriculture Secretary Tom Vilsack expressed concerns that this would lead to the misconception that pork is unsafe for consumption. The CDC began referring to it as "Novel influenza A (H1N1)"; "A/H1N1" is sometimes used. The CDC stopped using the nomenclature "novel H1N1" and updated various web pages to reflect the change to "2009 H1N1 Flu". In the Netherlands it was originally called "pig flu" but is now called "Mexican flu" by the national health institute and in the media. South Korea and Israel briefly considered calling it the "Mexican virus". Later the South Korean press used "SI", short for "swine influenza". Taiwan suggested the names "H1N1 flu" or "new flu", which most local media adopted. The World Organization for Animal Health proposed the name "North American influenza". The European Commission adopted the term "novel flu virus".

Genetics

On April 24, 2009, the U.S. Centers for Disease Control and Prevention (CDC) determined that seven samples from suspected cases in Mexico matched the strain that had infected patients in Texas and California with no known linkages to animals or one another; the strain appeared to be spreading from human to human. The CDC determined that the strain contained genes from four different flu viruses – North American swine influenza, North American avian influenza, human influenza, and swine influenza virus typically found in Asia and Europe – "an unusually mongrelised mix of genetic sequences." A CDC investigative team arrived in Mexico City on April 25, 2009 to work with Mexican counterparts to study the virus.

Pigs are susceptible to influenza viruses that can also infect both humans and birds, so they may act as a "mixing vessel" in which reassortment can occur between flu viruses of several species. Reassortment is a process that happens if two different types of influenza virus infect a single cell and it can produce a new strain of influenza. This is because the virus genome is split between eight independent pieces of RNA, which allows pieces of RNA from different viruses to mix and form a novel type of virus as new virus particles are being assembled. This new strain appears to be a result of the reassortment of two swine influenza viruses, one from North America and one from Europe. But the North American pig strain was itself the product of previous reassortments, and has carried an avian PB2 gene for at least ten years and a human PB1 gene since 1993. These genes were passed on to the new virus.

Gene sequences for every viral gene were made available through the Global Initiative on Sharing Avian Influenza Data (GISAID). A preliminary analysis found that thehemagglutinin (HA) gene was similar to that of swine flu viruses present in U.S. pigs since 1999, but the neuraminidase (NA) and matrix protein (M) genes resembled versions present in European swine flu isolates. While viruses with this genetic makeup had not previously been found to be circulating in humans or pigs, there is no formal national surveillance system to determine what viruses are circulating in pigs in the U.S. So far, little is known about the spread of the virus in any pig population. A preliminary analysis has also shown that several of the proteins involved in the pathophysiology of the virus are most similar to strains that cause mild symptoms in humans. This suggests that the virus is unlikely to cause severe infections similar to those caused by the 1918 pandemic flu virus or the H5N1 avian influenza.

Late on May 6, 2009, Canada's National Microbiology Laboratory first completed the sequencing of Mexican samples of the virus, publishing the result to GenBank as A/Mexico/InDRE4487/2009(H1N1). This was later shown to be nearly identical to A/California/07/2009 (H1N1), the strain from California sequenced and published by the CDC on 27 April. Samples from Mexico, Nova Scotia and Ontario had the same sequence, ruling out genetic explanations for the greater severity of the Mexican cases.

The genetic divergence of the virus in samples from different cases has been analysed by Mike Worobey at the University of Arizona at Tucson, USA, who found that the virus jumped to humans in 2008 probably after June, and not later than the end of November. Worobey's research also indicated the virus had been latent in pigs for several months prior to the outbreak, suggesting a need to increase agricultural surveillance to prevent future outbreaks (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Influenza A Virus Subtype H5N1
Date: 2012
Source: Wikipedia

Abstract: Influenza A virus subtype H5N1, also known as "bird flu", A(H5N1) or simply H5N1, is a subtype of the influenza A virus which can cause illness in humans and many other animal species. A bird-adapted strain of H5N1, called HPAI A(H5N1) for "highly pathogenic avian influenza virus of type A of subtype H5N1", is the causative agent of H5N1 flu, commonly known as "avian influenza" or "bird flu". It is enzootic in many bird populations, especially in Southeast Asia. One strain of HPAI A(H5N1) is spreading globally after first appearing in Asia. It is epizootic (an epidemic in nonhumans) and panzootic (affecting animals of many species, especially over a wide area), killing tens of millions of birds and spurring the culling of hundreds of millions of others to stem its spread. Most references to "bird flu" and H5N1 in the popular media refer to this strain.

According to the FAO Avian Influenza Disease Emergency Situation Update, H5N1 pathogenicity is continuing to gradually rise in endemic areas, but the avian influenza disease situation in farmed birds is being held in check by vaccination. Eleven outbreaks of H5N1 were reported worldwide in June 2008 in five countries (China, Egypt, Indonesia, Pakistan and Vietnam) compared to 65 outbreaks in June 2006 and 55 in June 2007. The "global HPAI situation can be said to have improved markedly in the first half of 2008 [but] cases of HPAI are still underestimated and underreported in many countries because of limitations in country disease surveillance systems". On October 10, 2011 the WHO announced a total of 566 human cases which resulted in the deaths of 332 people since 2003.

A filtered and purified influenza A vaccine for humans is being developed, and many countries have recommended it be stockpiled so, if an avian influenza pandemic starts jumping to humans, the vaccine can quickly be administered to avoid loss of life. Avian influenza is sometimes called avian flu, and commonly bird flu.

A novel, highly contagious strain of H5N1 was created by Ron Fouchier of the Erasmus Medical Centre in Rotterdam, the Netherlands, who first presented his work to the public at an influenza conference in Malta in September 2011. Five mutations were introduced into the H5N1 genome, and the virus was then bred by passing it from the noses of infected ferrets to the noses of uninfected ones, which was repeated 10 times. Fouchier described the result as "probably one of the most dangerous viruses you can make".

Overview
HPAI A(H5N1) is considered an avian disease, although there is some evidence of limited human-to-human transmission of the virus. A risk factor for contracting the virus is handling of infected poultry, but transmission of the virus from infected birds to humans is inefficient. Still, around 60% of humans known to have been infected with the current Asian strain of HPAI A(H5N1) have died from it, and H5N1 may mutate or reassort into a strain capable of efficient human-to-human transmission. In 2003, world-renowned virologist Robert G. Webster published an article titled "The world is teetering on the edge of a pandemic that could kill a large fraction of the human population" in American Scientist. He called for adequate resources to fight what he sees as a major world threat to possibly billions of lives. On September 29, 2005, David Nabarro, the newly appointed Senior United Nations

System Coordinator for Avian and Human Influenza, warned the world that an outbreak of avian influenza could kill anywhere between 5 million and 150 million people. Experts have identified key events (creating new clades, infecting new species, spreading to new areas) marking the progression of an avian flu virus towards becoming pandemic, and many of those key events have occurred more rapidly than expected.

Due to the high lethality and virulence of HPAI A(H5N1), its endemic presence, its increasingly large host reservoir, and its significant ongoing mutations, the H5N1 virus is the world's largest current pandemic threat, and billions of dollars are being spent researching H5N1 and preparing for a potential influenza pandemic. At least 12 companies and 17 governments are developing prepandemicinfluenza vaccines in 28 different clinical trials that, if successful, could turn a deadly pandemic infection into a nondeadly one. Full-scale production of a vaccine that could prevent any illness at all from the strain would require at least three months after the virus's emergence to begin, but it is hoped that vaccine production could increase until one billion doses were produced by one year after the initial identification of the virus.

H5N1 may cause more than one influenza pandemic, as it is expected to continue mutating in birds regardless of whether humans develop herd immunity to a future pandemic strain. Influenza pandemics from its genetic offspring may include influenza A virus subtypes other than H5N1. While genetic analysis of the H5N1 virus shows that influenza pandemics from its genetic offspring can easily be far more lethal than the Spanish flu pandemic, planning for a future influenza pandemic is based on what can be done and there is no higher Pandemic Severity Index level than a Category 5 pandemic which, roughly speaking, is any pandemic as bad as the Spanish flu or worse; and for which all intervention measures are to be used.

Signs & Symptoms

The avian influenza hemagglutinin binds alpha 2-3 sialic acid receptors, while human influenza hemagglutinins bind alpha 2-6 sialic acid receptors. This means when the H5N1 strain infects humans, it will replicate in the lower respiratory tract, and consequently will cause viral pneumonia. There is as yet no human form of H5N1, so all humans who have caught it so far have caught avian H5N1. In general, humans who catch a humanized influenza A virus (a human flu virus of type A) usually have symptoms that include fever, cough, sore throat, muscle aches,conjunctivitis, and, in severe cases, breathing problems and pneumonia that may be fatal. The severity of the infection depends in large part on the state of the infected persons' immune systemsand whether they had been exposed to the strain before (in which case they would be partially immune). No one knows if these or other symptoms will be the symptoms of a humanized H5N1 flu.

The reported mortality rate of highly pathogenic H5N1 avian influenza in a human is high; WHO data indicate 60% of cases classified as H5N1 resulted in death. However, there is some evidence the actual mortality rate of avian flu could be much lower, as there may be many people with milder symptoms who do not seek treatment and are not counted.

In one case, a boy with H5N1 experienced diarrhea followed rapidly by a coma without developing respiratory or flu-like symptoms. There have been studies of the levels of cytokines in humans infected by the H5N1 flu virus. Of particular concern is elevated levels of tumor necrosis factor-alpha, a protein associated with tissue destruction at sites of infection and increased production of other cytokines. Flu virus-induced increases in the level of cytokines is also associated with flu symptoms, including fever, chills, vomiting and headache. Tissue damage associated with pathogenic flu virus infection can ultimately result in death. The inflammatory cascade triggered by H5N1 has been called a 'cytokine storm' by some, because of what seems to be a positive feedback process of damage to the body resulting from immune system stimulation. H5N1 induces higher levels of cytokines than the more common flu virus types.

Genetics

Further information: Influenzavirus A and H5N1 genetic structure

The first known strain of HPAI A(H5N1) (called A/chicken/Scotland/59) killed two flocks of chickens in Scotland in 1959, but that strain was very different from the current highly pathogenic strain of H5N1. The dominant strain of HPAI A(H5N1) in 2004 evolved from 1999 to 2002 creating the Z genotype. It

has also been called "Asian lineage HPAI A(H5N1)".

Asian lineage HPAI A(H5N1) is divided into two antigenic clades. "Clade 1 includes human and bird isolates from Vietnam, Thailand, and Cambodia and bird isolates from Laos and Malaysia. Clade 2 viruses were first identified in bird isolates from China, Indonesia, Japan, and South Korea before spreading westward to the Middle East, Europe, and Africa. The clade 2 viruses have been primarily responsible for human H5N1 infections that have occurred during late 2005 and 2006, according to WHO.

Genetic analysis has identified six subclades of clade 2, three of which have a distinct geographic distribution and have been implicated in human infections: Map

1. Subclade 1, Indonesia
2. Subclade 2, Europe, Middle East, and Africa (called EMA)
3. Subclade 3, China"

A 2007 study focused on the EMA subclade has shed further light on the EMA mutations. "The 36 new isolates reported here greatly expand the amount of whole-genome sequence data available from recent avian influenza (H5N1) isolates. Before our project, GenBank contained only 5 other complete genomes from Europe for the 2004–2006 period, and it contained no whole genomes from the Middle East or northern Africa. Our analysis showed several new findings. First, all European, Middle Eastern, and African samples fall into a clade that is distinct from other contemporary Asian clades, all of which share common ancestry with the original 1997 Hong Kong strain. Phylogenetic trees built on each of the 8 segments show a consistent picture of 3 lineages, as illustrated by the HA tree shown in Figure 1. Two of the clades contain exclusively Vietnamese isolates; the smaller of these, with 5 isolates, we label V1; the larger clade, with 9 isolates, is V2. The remaining 22 isolates all fall into a third, clearly distinct clade, labeled EMA, which comprises samples from Europe, the Middle East, and Africa. Trees for the other 7 segments display a similar topology, with clades V1, V2, and EMA clearly separated in each case. Analyses of all available complete influenza (H5N1) genomes and of 589 HA sequences placed the EMA clade as distinct from the major clades circulating in People's Republic of China, Indonesia, and Southeast Asia."

Terminology
H5N1 isolates are identified like this actual HPAI A(H5N1) example, A/chicken/Nakorn-Patom/Thailand/CU-K2/04(H5N1):

1. A stands for the species of influenza (A, B or C).
2. Chicken is the species the isolate was found in
3. Nakorn-Patom/Thailand is the place this specific virus was isolated
4. CU-K2 identifies it from other influenza viruses isolated at the same place
5. 04 represents the year 2004
6. H5 stands for the fifth of several known types of the protein hemagglutinin.
7. N1 stands for the first of several known types of the protein neuraminidase.

Other examples include: A/duck/Hong Kong/308/78(H5N3), A/avian/NY/01(H5N2), A/chicken/Mexico/31381-3/94(H5N2), and A/shoveler/Egypt/03(H5N2).

As with other avian flu viruses, H5N1 has strains called "highly pathogenic" (HP) and "low-pathogenic" (LP). Avian influenza viruses that cause HPAI are highly virulent, and mortality rates in infected flocks often approach 100%. LPAI viruses have negligible virulence, but these viruses can serve as progenitors to HPAI viruses. The current strain of H5N1 responsible for the deaths of birds across the world is an HPAI strain; all other current strains of H5N1, including a North American strain that causes no disease at all in any species, are LPAI strains. All HPAI strains identified to date have involved H5 and H7 subtypes. The distinction concerns pathogenicity in poultry, not humans. Normally, a highly pathogenic avian virus is not highly pathogenic to either humans or nonpoultry birds. This current deadly strain of H5N1 is unusual in being deadly to so many species, including some, like domestic cats, never previously susceptible to any influenza virus.

Genetic Structure and Related Subtypes
H5N1 is a subtype of the species Influenza A virus of the Influenzavirus A genus of the Orthomyxoviridae family. Like all other influenza A subtypes, the H5N1 subtype is an RNA virus. It has a segmentedgenome of eight negative sense, single-strands of RNA, abbreviated as PB2, PB1, PA, HA, NP, NA, MP and NS.

HA codes for hemagglutinin, an antigenic glycoprotein found on the surface of the influenza viruses and is responsible for binding the virus to the cell that is being infected. NA codes for neuraminidase, an antigenic glycosylated enzyme found on the surface of the influenza viruses. It facilitates the release of progeny viruses from infected cells. The hemagglutinin (HA) and neuraminidase (NA) RNA strands specify the structure of proteins that are most medically relevant as targets for antiviral drugs and antibodies. HA and NA are also used as the basis for the naming of the different subtypes of influenza A viruses. This is where the H and N come from in H5N1.

Influenza A viruses are significant for their potential for disease and death in humans and other animals. Influenza A virus subtypes that have been confirmed in humans, in order of the number of known human pandemic deaths that they have caused, include:

1. H1N1, which caused the 1918 flu pandemic ("Spanish flu") and currently is causing seasonal human flu and the 2009 flu pandemic ("swine flu")
2. H2N2, which caused "Asian flu"
3. H3N2, which caused "Hong Kong flu" and currently causes seasonal human flu
4. H5N1, ("bird flu"), which is noted for having a strain (Asian-linage HPAI H5N1) that kills over half the humans it infects, infecting and killing species that were never known to suffer from influenza viruses before (e.g. cats), being unable to be stopped by culling all involved poultry - some think due to being endemic in wild birds, and causing billions of dollars to be spent in flu pandemic preparation and preventiveness
5. H7N7, which has unusual zoonotic potential and killed one person
6. H1N2, which is currently endemic in humans and pigs and causes seasonal human flu
7. H9N2, which has infected three people
8. H7N2, which has infected two people
9. H7N3, which has infected two people
10. H10N7, which has infected two people

Low Pathogenic H5N1
Low pathogenic avian influenza H5N1 (LPAI H5N1) also called "North American" H5N1 commonly occurs in wild birds. In most cases, it causes minor sickness or no noticeable signs of disease in birds. It is not known to affect humans at all. The only concern about it is that it is possible for it to be transmitted to poultry and in poultry mutate into a highly pathogenic strain.

1. 1975 – LPAI H5N1 was detected in a wild mallard duck and a wild blue goose in Wisconsin.
2. 1981 and 1985 – LPAI H5N1 was detected in ducks by the University of Minnesota conducting a sampling procedure in which sentinel ducks were monitored in cages placed in the wild for a short period of time.
3. 1983 – LPAI H5N1 was detected in ring-billed gulls in Pennsylvania.
4. 1986 - LPAI H5N1 was detected in a wild mallard duck in Ohio.
5. 2005 - LPAI H5N1 was detected in ducks in Manitoba, Canada.
6. 2008 - LPAI H5N1 was detected in ducks in New Zealand.
7. 2009 - LPAI H5N1 was detected in commercial poultry in British Columbia.

"In the past, there was no requirement for reporting or tracking LPAI H5 or H7 detections in wild birds so states and universities tested wild bird samples independently of USDA. Because of this, the above list of previous detections might not be all inclusive of past LPAI H5N1 detections. However, the World Organization for Animal Health (OIE) recently changed its requirement of reporting detections of avian influenza. Effective in 2006, all confirmed LPAI H5 and H7 AI subtypes must be reported to the OIE because of their potential to mutate into highly pathogenic strains. Therefore, USDA now tracks these detections in wild birds, backyard flocks, commercial flocks and live bird markets."

High Mutation Rate
Influenza viruses have a relatively high mutation rate that is characteristic of RNA viruses. The segmentation of its genome facilitates genetic recombination by segment reassortment in hosts infected with two different influenza viruses at the same time. A previously uncontagious strain may then be able to pass between humans, one of several possible paths to a pandemic.

The ability of various influenza strains to show species-selectivity is largely due to variation in the hemagglutinin genes. Genetic mutations in the hemagglutinin gene that cause single amino acid substitutions can significantly alter the ability of viral hemagglutinin proteins to bind to receptors on the surface of host cells. Such mutations in avian H5N1 viruses can change virus strains from being inefficient at infecting human cells to being as efficient in causing human infections as more common human influenza virus types. This doesn't mean that one amino acid substitution can cause a pandemic, but it does mean that one amino acid substitution can cause an avian flu virus that is not pathogenic in humans to become pathogenic in humans.

Influenza A virus subtype H3N2 is endemic in pigs in China, and has been detected in pigs in Vietnam, increasing fears of the emergence of new variant strains. The dominant strain of annual flu virus in January 2006 was H3N2, which is now resistant to the standard antiviral drugs amantadine and rimantadine. The possibility of H5N1 and H3N2 exchanging genes through reassortment is a major concern. If a reassortment in H5N1 occurs, it might remain an H5N1 subtype, or it could shift subtypes, as H2N2 did when it evolved into the Hong Kong Flu strain of H3N2.

Both the H2N2 and H3N2 pandemic strains contained avian influenza virus RNA segments. "While the pandemic human influenza viruses of 1957 (H2N2) and 1968 (H3N2) clearly arose through reassortment between human and avian viruses, the influenza virus causing the 'Spanish flu' in 1918 appears to be entirely derived from an avian source".

Prevention
There are several H5N1 vaccines for several of the avian H5N1 varieties, but the continual mutation of H5N1 renders them of limited use to date: while vaccines can sometimes provide cross-protection against related flu strains, the best protection would be from a vaccine specifically produced for any future pandemic flu virus strain. Dr. Daniel Lucey, co-director of the Biohazardous Threats and Emerging Diseases graduate program at Georgetown University has made this point, "There is no H5N1 pandemic so there can be no pandemic vaccine". However, "pre-pandemic vaccines" have been created; are being refined and tested; and do have some promise both in furthering research and preparedness for the next pandemic. Vaccine manufacturing companies are being encouraged to increase capacity so that if a pandemic vaccine is needed, facilities will be available for rapid production of large amounts of a vaccine specific to a new pandemic strain.

Public Health

Further information: Influenza pandemic

"The United States is collaborating closely with eight international organizations, including the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and 88 foreign governments to address the situation through planning, greater monitoring, and full transparency in reporting and investigating avian influenza occurrences. The United States and these international partners have led global efforts to encourage countries to heighten surveillance for outbreaks in poultry and significant numbers of deaths in migratory birds and to rapidly introduce containment measures. The U.S. Agency for International Development (USAID) and the U.S. Department of State, the U.S. Department of Health and Human Services (HHS), and Agriculture (USDA) are coordinating future international response measures on behalf of the White House with departments and agencies across the federal government".

Together steps are being taken to "minimize the risk of further spread in animal populations", "reduce the risk of human infections", and "further support pandemic planning and preparedness".

Ongoing detailed mutually coordinated onsite surveillance and analysis of human and animal H5N1 avian flu outbreaks are being conducted and reported by the USGS National Wildlife Health Center,

the Centers for Disease Control and Prevention, the World Health Organization, the European Commission, and others.

Treatment

Further information: Flu research

There is no highly effective treatment for H5N1 flu, but oseltamivir (commercially marketed by Roche as Tamiflu), can sometimes inhibit the influenza virus from spreading inside the user's body. This drug has become a focus for some governments and organizations trying to prepare for a possible H5N1 pandemic. On April 20, 2006, Roche AG announced that a stockpile of three million treatment courses of Tamiflu are waiting at the disposal of the World Health Organizationto be used in case of a flu pandemic; separately Roche donated two million courses to the WHO for use in developing nations that may be affected by such a pandemic but lack the ability to purchase large quantities of the drug.

However, WHO expert Hassan al-Bushra has said:"Even now, we remain unsure about Tamiflu's real effectiveness. As for a vaccine, work cannot start on it until the emergence of a new virus, and we predict it would take six to nine months to develop it. For the moment, we cannot by any means count on a potential vaccine to prevent the spread of a contagious influenza virus, whose various precedents in the past 90 years have been highly pathogenic".

Animal and lab studies suggest that Relenza (zanamivir), which is in the same class of drugs as Tamiflu, may also be effective against H5N1. In a study performed on mice in 2000, "zanamivir was shown to be efficacious in treating avian influenza viruses H9N2, H6N1, and H5N1 transmissible to mammals". In addition, mice studies suggest the combination of zanamivir, celecoxib and mesalazine looks promising producing a 50% survival rate compared to no survival in the placebo arm. While no one knows if zanamivir will be useful or not on a yet to exist pandemic strain of H5N1, it might be useful to stockpile zanamivir as well as oseltamivir in the event of an H5N1 influenza pandemic. Neither oseltamivir nor zanamivir can currently be manufactured in quantities that would be meaningful once efficient human transmission starts. In September, 2006, a WHO scientist announced that studies had confirmed cases of H5N1 strains resistant to Tamiflu and Amantadine. Tamiflu-resistant strains have also appeared in the EU, which remain sensitive to Relenza.

Epidemiology

Further information: Transmission and infection of H5N1 and Global spread of H5N1

The earliest infections of humans by H5N1 coincided with an epizootic (an epidemic in nonhumans) of H5N1 influenza in Hong Kong's poultry population. This panzootic (a disease affecting animals of many species, especially over a wide area) outbreak was stopped by the killing of the entire domestic poultry population within the territory. However, the disease has continued to spread. On December 21, 2009 the WHO announced a total of 447 cases which resulted in the deaths of 263.

Contagiousness

H5N1 is mainly spread by domestic poultry, both through the movements of infected birds and poultry products and through the use of infected poultry manure as fertilizer or feed. Humans with H5N1 have typically caught it from chickens, which were in turn infected by other poultry or waterfowl. Migrating waterfowl (wild ducks, geese and swans) carry H5N1, often without becoming sick. Many species of birds and mammals can be infected with HPAI A(H5N1), but the role of animals other than poultry and waterfowl as disease-spreading hosts is unknown. H5N1 is easily transmissible between birds facilitating a potential global spread of H5N1. While H5N1 undergoes mutation and reassortment, creating variations which can infect species not previously known to carry the virus, not all of these variant forms can infect humans. H5N1 as an avian virus preferentially binds to a type of galactose receptors that populate the avian respiratory tract from the nose to the lungs and are virtually absent in humans, occurring only in and around the alveoli, structures deep in the lungs where oxygen is passed to the blood. Therefore, the virus is not easily expelled by coughing and sneezing, the usual route of transmission.

According to a report by the World Health Organization, H5N1 may be spread indirectly. The report stated that the virus may sometimes stick to surfaces or get kicked up in fertilizer dust to infect people.

Virulence
H5N1 has mutated into a variety of strains with differing pathogenic profiles, some pathogenic to one species but not others, some pathogenic to multiple species. Each specific known genetic variation is traceable to a virus isolate of a specific case of infection. Through antigenic drift, H5N1 has mutated into dozens of highly pathogenic varieties divided into genetic clades which are known from specific isolates, but all currently belonging to genotype Z of avian influenza virus H5N1, now the dominant genotype. H5N1 isolates found in Hong Kong in 1997 and 2001 were not consistently transmitted efficiently among birds and did not cause significant disease in these animals. In 2002 new isolates of H5N1 were appearing within the bird population of Hong Kong. These new isolates caused acute disease, including severe neurological dysfunction and death in ducks. This was the first reported case of lethal influenza virus infection in wild aquatic birds since 1961. Genotype Z emerged in 2002 through reassortment from earlier highly pathogenic genotypes of H5N1 that first infected birds in China in 1996, and first infected humans in Hong Kong in 1997. Genotype Z is endemic in birds in Southeast Asia, has created at least two clades that can infect humans, and is spreading across the globe in bird populations. Mutations are occurring within this genotype that are increasing their pathogenicity. Birds are also able to shed the virus for longer periods of time before their death, increasing the transmissibility of the virus.

Transmission and Host Range
Because migratory birds are among the carriers of the highly pathogenic H5N1 virus, it is spreading to all parts of the world. H5N1 is different from all previously known highly pathogenic avian flu viruses in its ability to be spread by animals other than poultry.Infected birds transmit H5N1 through their saliva, nasal secretions, feces and blood. Other animals may become infected with the virus through direct contact with these bodily fluids or through contact with surfaces contaminated with them. H5N1 remains infectious after over 30 days at 0 °C (32.0 °F) (over one month at freezing temperature) or 6 days at 37 °C (98.6 °F) (one week at human body temperature) at ordinary temperatures it lasts in the environment for weeks. In Arctic temperatures, it doesn't degrade at all.

In October 2004, researchers discovered that H5N1 is far more dangerous than was previously believed. Waterfowl were revealed to be directly spreading the highly pathogenic strain of H5N1 to chickens, crows, pigeons, and other birds, and the virus was increasing its ability to infect mammals as well. From this point on, avian flu experts increasingly referred to containment as a strategy that can delay, but not ultimately prevent, a future avian flu pandemic.

"Since 1997, studies of influenza A (H5N1) indicate that these viruses continue to evolve, with changes in antigenicity and internal gene constellations; an expanded host range in avian species and the ability to infect felids; enhanced pathogenicity in experimentally infected mice and ferrets, in which they cause systemic infections; and increased environmental stability."

The New York Times, in an article on transmission of H5N1 through smuggled birds, reports Wade Hagemeijer of Wetlands International stating, "We believe it is spread by both bird migration and trade, but that trade, particularly illegal trade, is more important".

On September 27, 2007 researchers reported that the H5N1 bird flu virus can also pass through a pregnant woman's placenta to infect the fetus. They also found evidence of what doctors had long suspected—that the virus not only affects the lungs, but also passes throughout the body into the gastrointestinal tract, the brain, liver, and blood cells.

Society & Culture: Main article: Social impact of H5N1

H5N1 has had a significant effect on human society, especially the financial, political, social, and personal responses to both actual and predicted deaths in birds, humans, and other animals. Billions of U.S. dollars are being raised and spent to research H5N1 and prepare for a potential avian influenza pandemic. Over ten billion dollars have been spent and over two hundred million birds killed to try to contain H5N1.

People have reacted by buying less chicken causing poultry sales and prices to fall. Many individuals have stockpiled supplies for a possible flu pandemic. International health officials and other experts have pointed out that many unknown questions still hover around the disease.

Dr. David Nabarro, Chief Avian Flu Coordinator for the United Nations, and former Chief of Crisis Response for the World Health Organization has described himself as "quite scared" about H5N1's potential impact on humans. Nabarro has been accused of being alarmist before and on his first day in his role for the United Nations he proclaimed the avian flu could kill 150 million people. In an interview with the International Herald Tribune, Nabarro compares avian flu to AIDS in Africa, warning that underestimations led to inappropriate focus for research and intervention (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Hemolytic-Uremic Syndrome (HUS)
Date: 2012
Source: Wikipedia

Abstract: Hemolytic-uremic syndrome (or haemolytic-uraemic syndrome), abbreviated HUS, is a disease characterized by hemolytic anemia, acute renal failure (uremia) and a low platelet count (thrombocytopenia). It predominantly, but not exclusively, affects children. Most cases are preceded by an episode of diarrhea caused by E. coli O157:H7, which is acquired as a foodborne illness. It is a medical emergency and carries a 5–10% mortality; of the remainder, the majority recover without major consequences but a small proportion develop chronic kidney disease and become reliant on renal replacement therapy. HUS was first defined as a syndrome in 1955.

Signs & Symptoms

In Children

The classic childhood case of HUS occurs after ingestion of a strain of bacteria, usually types of E. coli, that expresses verotoxin (also called shiga-like toxin). Bloody diarrhea typically follows. HUS develops about 5-10 days after onset of diarrhea, with decreased urine output (oliguria), blood in the urine (hematuria), kidney failure, low platelet counts (thrombocytopenia) and destruction of red blood cells (microangiopathic hemolytic anemia). Hypertension is common. In some cases, there are prominent neurologic changes.

In Adults

Adult HUS has similar symptoms and pathology, but is an uncommon outcome of the following: HIV; antiphospholipid syndrome (associated with lupus erythematosus and generalized hypercoagulability); postpartum renal failure; malignant hypertension; scleroderma; and certain drugs, including some chemotherapy drugs and other immunosuppressive agents (mitomycin, ciclosporin, cisplatin and bleomycin).

Atypical Cases

A third category is referred to as familial HUS or atypical HUS (aHUS).

It represents 5-10% of HUS cases and is largely due to mutations in the complement proteins factor H, membrane cofactor protein and factor leading to uncontrolled complement system activation.

Recurrent thromboses result in a high mortality rate.

Most reported HUS cases during the 2011 Escherichia coli O104:H4 outbreak were atypical cases.

Pathogenesis

HUS is one of the thrombotic microangiopathies, a category of disorders that includes thrombotic thrombocytopenic purpura (TTP).

In the classical form (90% of cases), the STEC toxin enters the bloodstream and causes damage to the body's vascular endothelium. This is especially damaging to the kidney, where the toxin attaches to the glomerular endothelium and initiates a noninflammatory reaction leading to acute renal failure. Moreover, the generalized endothelial damage leads to platelet activation that causes thrombocytopenia (low platelet count). The renal glomerular endothelial cells express a receptor for the toxin.

The consumption of platelets as they adhere to the thrombi lodged in the small vessels typically leads to mild or moderate thrombocytopaenia with a platelet count of less than 60,000 per mL. The typical pathophysiology involves the shiga-toxin binding to proteins on the surface of glomerular endothelium and inactivating a metalloproteinase called ADAMTS13, which is also involved in the closely related thrombotic thrombocytopenic purpura (TTP). Once the ADAMTS13 is disabled, multimers of von Willebrand Factor (vWF) form and initiate platelet activation and cause microthrombi formation. Inhibition of ADAMTS13 causes activated platelets because the large multimers of uncleaved vWF are hyperactive. The arterioles and capillaries of the body become obstructed by the resulting complexes of activated platelets which have adhered to endothelium via large multimeric vWF. The growing thrombi lodged in smaller vessels destroyred blood cells (RBCs) as they squeeze through the narrowed blood vessels, forming schistocytes, or fragments of sheared RBCs. This mechanism, known as microangiopathic hemolysis, has been likened to the effect of a cheesewire or garotte across the vessel lumen. The presence of schistocytes is a key finding that helps to diagnose HUS. Typically, this haemolysis results in a haemoglobin level of less than 80 mg/L.

As in the related condition TTP, reduced blood flow through the narrowed blood vessels of the microvasculature leads to reduced blood flow to vital organs, and ischemia may develop. The kidneys and the central nervous system (brain and spinal cord) are the parts of the body most critically dependent on high blood flow, thus they are the most likely organs to be affected. However, in comparison to TTP, the kidneys tend to be more severely affected in HUS, and the central nervous system is less commonly affected.

In contrast with typical disseminated intravascular coagulation seen with other causes of septicemia and occasionally with advanced cancer, coagulation factors are not consumed in HUS (or TTP) and the coagulation screen, fibrinogen level, and assays for fibrin degradation products such as "D-Dimers", are generally normal despite the low platelet count (thrombocytopenia).

HUS occurs after 2-7% of all E. coli O157:H7 infections. Children and adolescents are commonly affected. Grossly, the kidneys may show patchy or diffuse renal cortical necrosis. Histologically, the glomeruli show thickened and sometimes split capillary walls due largely to endothelial swelling. Large deposits of fibrin-related materials in the capillary lumens, subendothelially, and in the mesangium are also found along with mesangiolysis. Interlobular and afferent arterioles show fibrinoid necrosis and intimal hyperplasia and are often occluded by thrombi.

A somewhat less common form of HUS (~10% of cases) does not follow STEC infection and is thought to result from factor H deficiency (a complement regulatory protein) that results in uncontrolled complement activation after minor endothelialinjury resulting in thrombosis
Diagosis
Clinically, HUS can be very hard to distinguish from thrombotic thrombocytopenic purpura.
The laboratory features are almost identical, and not every case of HUS is preceded by diarrhea. HUS is characterized by the triad of hemolytic anemia,thrombocytopenia, and acute renal failure. The only distinguishing feature is that in TTP, fever and neurological symptoms are often present; but this is not always the case. A pericardial friction rub can also sometimes be heard on auscultation (uremic pericarditis). The two conditions are sometimes treated as a single entity called TTP/HUS. However,

some dispute this grouping, and TTP is now known to be caused by an acquired defect in the protein ADAMTS13.

Treatment

The effect of antibiotics in E. coli O157:H7 colitis is controversial. Certain antibiotic may stimulate further verotoxin production and thereby increase the risk of HUS.
However there is also tentative evidence that some antibiotics likequinolones may decrease the risk of haemolytic uraemic syndrome.

Treatment is generally supportive, with dialysis as needed. Untreated HUS in adults, however, may progress to end-stage organ damage. Platelet transfusion may actually worsen the outcome.

In most children with postdiarrheal HUS, there is a good chance of spontaneous resolution, so observation in a hospital is often all that is necessary, with supportive care such as hemodialysis where indicated. In children with neurological or other nonrenal involvement, and in adult cases, particularly when there is diagnostic uncertainty between HUS and TTP, plasmapheresis (plasma exchange) is the treatment of choice. This is generally performed daily until the platelet count is normal, using fresh frozen plasma as the replacement fluid for the patient's plasma which is removed. Plasmapheresis may reverse the ongoing platelet consumption.

There are case reports of experimental treatments with eculizumab, a monoclonal antibody that blocks part of the complement system, being used to treat congenital atypical hemolytic uremic syndrome, as well as severe shiga-toxin associated hemolytic uremic syndrome. These have shown promising results.

Prognosis

With aggressive treatment, more than 90% survive the acute phase. About 9% may develop end stage renal disease. About one-third of persons with HUS have abnormal kidney function many years later, and a few require long-term dialysis. Another 8% of persons with HUS have other lifelong complications, such as high blood pressure, seizures, blindness, paralysis, and the effects of having part of their colon removed. The overall mortality rate from HUS is 5-15%. Children and the elderly have a worse prognosis.

Epidemiology & Notable Outbreaks

HUS has a peak incidence between six months and four years of age.

HUS and the E. coli infections which caused it have been the source of much negative publicity for the Food and Drug Administration (FDA), meat industries, and fast-food restaurants since the 1990s, especially in the Jack in the Boxcontaminations. It was also featured in the Robin Cook novel Toxin. In 2006, an epidemic of harmful E. coli emerged in the United States due to contaminated spinach. The known cases have been reported at 183, including 29 cases of HUS. In June, 2009, Nestle Toll House cookie dough was linked to an outbreak of E. coli 0157:H7 in the United States, which sickened 70 people in 30 states.

In May, 2011 an epidemic of bloody diarrhea caused by E. coli O104:H4 contaminated fenugreek seeds hit Germany. Tracing the epidemic revealed more than 4000 cases, with hemolytic-uremic syndrome developing in more than 800 of the cases, with 50 of them resulting in death. Over 90% of the cases were in adults (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Japanese Encephalitis
Date: 2012
Source: Wikipedia

Abstract: Japanese encephalitis, previously known as Japanese B encephalitis to distinguish it from von Economo's A encephalitis—is a disease caused by the mosquito-borne Japanese encephalitis virus. The Japanese encephalitis virus is a virus from the family Flaviviridae. Domestic pigs and wild birds (herons) are reservoirs of the virus; transmission to humans may cause severe symptoms. Amongst the most important vectors of this disease are the mosquitoes Culex tritaeniorhynchus and *Culex vishnui*. This disease is most prevalent in Southeast Asia and the Far East.

Signs and Symptoms
Japanese encephalitis has an incubation period of 5 to 15 days and the vast majority of infections are asymptomatic: only 1 in 250 infections develop into encephalitis.

Severe rigors mark the onset of this disease in humans. Fever, headache and malaise are other non-specific symptoms of this disease which may last for a period of between 1 and 6 days. Signs which develop during the acute encephalitic stage include neck rigidity, cachexia, hemiparesis, convulsions and a raised body temperature between 38 and 41 degrees Celsius. Mental retardation developed from this disease usually leads to coma. Mortality of this disease varies but is generally much higher in children. Transplacental spread has been noted. Life-long neurological defects such as deafness, emotional lability and hemiparesis may occur in those who have had central nervous system involvement. In known cases some effects also include nausea, headache, fever, vomiting and sometimes swelling of the testicles.

Increased microglial activation following JEV infection has been found to influence the outcome of viral pathogenesis. Microglia are the resident immune cells of the central nervous system (CNS) and have a critical role in host defense against invading microorganisms. Activated microglia secrete cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF-α), which can cause toxic effects in the brain. Additionally, other soluble factors such as neurotoxins, excitatory neurotransmitters, prostaglandin, reactive oxygen, and nitrogen species are secreted by activated microglia.

In a murine model of JE, it was found that in the hippocampus and the striatum, the number of activated microglia was more than anywhere else in the brain closely followed by that in the thalamus. In the cortex, number of activated microglia was significantly less when compared with other regions of the mouse brain. An overall induction of differential expression of proinflammatory cytokines and chemokines from different brain regions during a progressive JEV infection was also observed.

Although the net effect of the proinflammatory mediators is to kill infectious organisms and infected cells as well as to stimulate the production of molecules that amplify the mounting response to damage, it is also evident that in a nonregenerating organ such as brain, a dysregulated innate immune response would be deleterious. In JE the tight regulation of microglial activation appears to

be disturbed, resulting in an autotoxic loop of microglial activation that possibly leads to bystander neuronal damage.

In animals, key signs include infertility and abortion in pigs, neurological disease in horses and systemic signs including fever, lethargy and anorexia.

Evolution
The virus appears to have originated from its ancestral virus in the mid 1500s in the Indonesia-Malaysia region and evolved there into five different genotypes and spread across Asia. The mean evolutionary rate has been estimated to be 4.35×10(-4) (range: 3.4906×10(-4) to 5.303×10(-4)) nucleotides substitutions per site per year.

Virology
The causative agent Japanese encephalitis virus is an enveloped virus of the genus flavivirus and is closely related to the West Nile virus and St. Louis encephalitis virus. The positive sense single stranded RNA genome is packaged in the capsid which is formed by the capsid protein. The outer envelope is formed by envelope (E) protein and is the protective antigen. It aids in entry of the virus to the inside of the cell. The genome also encodes several nonstructural proteins also (NS1,NS2a,NS2b,NS3,N4a,NS4b,NS5). NS1 is produced as secretory form also. NS3 is a putative helicase, and NS5 is the viral polymerase. It has been noted that the Japanese encephalitis virus (JEV) infects the lumen of the endoplasmic reticulum (ER)[4][5] and rapidly accumulates substantial amounts of viral proteins for the JEV.

Japanese Encephalitis is diagnosed by detection of antibodies in serum and CSF (cerebrospinal fluid) by IgM capture ELISA.

Viral antigen can also be shown in tissues by indirect fluorescent antibody staining.

Based on the envelope gene (E) there are five genotypes (I - V). The Muar strain, isolated from patient in Malaya in 1952, is the prototype strain of genotype V. Genotype IV appears to be the ancestral strain and the virus appears to have evolved in the Indonesian-Malayasian region. The first clinical reports date from 1870 but the virus appears to have evolved in the mid 1500s.

Over 60 complete genomes of this virus have been sequenced as of 2010.

Prevention
Infection with JEV confers life-long immunity. All current vaccines are based on the genotype III virus. A formalin-inactivated mouse-brain derived vaccine was first produced in Japan in the 1930s and was validated for use in Taiwan in the 1960s and in Thailand in the 1980s. The widespread use of vaccine and urbanisation has led to control of the disease in Japan, Korea, Taiwan and Singapore. The high cost of the vaccine, which is grown in live mice, means that poorer countries have not been able to afford to give it as part of a routine immunisation programme.

In the UK, the three vaccines used (two of which are unlicensed) which are JE-Vax, Green Cross and IXIARO (licensed). JE-Vax however has subsequentally been removed from market. JE-Vax and Green Cross require three doses given at 0, 7–14 and 28–30 days. The dose is 1ml for children and adult, and 0.5ml for infants under 36 months of age. IXIARO the new vaccine has been produced by Intercell Biomedical Ltd and requires only 2 doses, and is currently licensed in the U.S., Europe (inc UK), Canada and Australia.

The most common adverse effects are redness and pain at the injection site. Uncommonly, an urticarial reaction can develop about four days after injection. Because the vaccine is produced from mouse brain, there is a risk of autoimmune neurological complications of around 1 per million vaccinations. However in the case of IXIARO where the vaccine is not produced in mouse brains but in vitro using cell culture there is little adverse effects compared to the Placebo, the main side effects are headache and myalgia.

Neutralising antibody persists in the circulation for at least two to three years, and perhaps longer. The total duration of protection is unknown, but because there is no firm evidence for protection beyond three years, boosters are recommended every three years for people who remain at risk. Furthermore there is also no data available regarding the interchangeability of other JE vaccines and IXIARO and recommended those previously immunised with other JE vaccines receive Green Cross or JE-Vax or a primary course of IXIARO.

There are a number of new vaccines under development. The mouse-brain derived vaccine is likely to be replaced by a cell-culture derived vaccine that is both safer and cheaper to produce. China licensed a live attenuated vaccine in 1988 and more than 200 million doses have been given; this vaccine is available in Nepal, Sri Lanka, South Korea and India. There is also a new chimeric vaccine based on the yellow fever 17D vaccine that is currently under development.

Treatment

There is no specific treatment for Japanese encephalitis and treatment is supportive; with assistance given for feeding, breathing or seizure control as required. Raised intracranial pressure may be managed with mannitol.[12] There is no transmission from person to person and therefore patients do not need to be isolated.

A breakthrough in the field of Japanese encephalitis therapeutics is the identification of macrophage receptor involvement in the disease severity. A recent report of an Indian group demonstrates the involvement of monocyte and macrophage receptor CLEC5A in severe inflammatory response in JEV infection of brain. This transcriptomic study provides a hypothesis of neuroinflammation and a new lead in development of appropriate therapeutic against Japanese encephalitis.

Epidemiology

Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia, with 30,000–50,000 cases reported annually. Case-fatality rates range from 0.3% to 60% and depends on the population and on age. Rare outbreaks in U.S. territories in Western Pacific have occurred. Residents of rural areas in endemic locations are at highest risk; Japanese encephalitis does not usually occur in urban areas. Countries which have had major epidemics in the past, but which have controlled the disease primarily by vaccination, include China, Korea, Japan, Taiwan and Thailand. Other countries that still have periodic epidemics include Vietnam, Cambodia, Myanmar, India, Nepal, and Malaysia. Japanese encephalitis has been reported on the Torres Strait Islands and two fatal cases were reported in mainland northern Australia in 1998. The spread of the virus in Australia is of particular concern to Australian health officials due to the unplanned introduction of *Culex gelidus*, a potential vector of the virus, from Asia. However, the current presence on mainland Australia is minimal. Human, cattle and horses are dead-end hosts and disease manifests as fatal encephalitis. Swine acts as amplifying host and has very important role in epidemiology of the disease. Infection in swine is asymptomatic, except in pregnant sows, when abortion and fetal abnormalities are common sequelae. The most important vector is *Culex tritaeniorhynchus*, which feeds on cattle in preference to humans, it has been proposed that moving swine away from human habitation can divert the mosquito away from humans and swine. The natural host of the Japanese encephalitis virus is bird, not human, and many believe the virus will therefore never be completely eliminated. In November 2011, Japanese encephalitis virus was reported in *Culex bitaeniorhynchus* in the Republic of Korea.

Recently whole genome microarray research of neuron in JE virus infection has shown that neurons play an important role in their own defense against Japanese encephalitis viral infection. Although this challenges the long-held belief that neurons are immunologically quiescent,an improved understanding of the proinflammatory effects responsible for immune-mediated control of viral infection and neuronal injury during JEV infection is an essential step for developing strategies for limiting the severity of CNS disease.

A number of drugs have been investigated to either reduce viral replication or provide neuroprotection in cell lines or studies upon mice. None are currently advocated in treating human patients.

The use of rosmarinic acid, and arctigenin, have been shown to be effective in a mouse model of Japanese encephalitis

Curcumin has been shown to impart neuroprotection against JEV infection in an in vitro study. Curcumin possibly acts by decreasing cellular reactive oxygen species level, restoration of cellular membrane integrity, decreasing pro-apoptotic signaling molecules, and modulating cellular levels of stress-related proteins. It has also been shown that the production of infective viral particles from previously infected neuroblastoma cells are reduced, which is achieved by the inhibition of ubiquitin-proteasome system.

Minocycline in mice resulted in marked decreases in the levels of several markers, viral titer, and the level of proinflammatory mediators and also prevents blood brain barrier damage (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Listeria
Date: 2012
Source: Wikipedia

Abstract: Listeria is a bacterial genus that contains seven species. Named after the English pioneer of sterile surgery Joseph Lister, the genus received its current name in 1940. Listeria species are Gram-positive bacilli. The major human pathogen in the Listeria genus is L. monocytogenes. It is usually the causative agent of the relatively rare bacterial disease, listeriosis, a serious infection caused by eating food contaminated with the bacteria. The disease affects primarily pregnant women, newborns, adults with weakened immune systems, and the elderly.

Listeriosis is a serious disease for humans; the overt form of the disease has a mortality rate of about 20 percent. The two main clinical manifestations are sepsis and meningitis. Meningitis is often complicated by encephalitis, a pathology that is unusual for bacterial infections. Listeria ivanovii is a pathogen of mammals, specifically ruminants, and has rarely caused listeriosis in humans.

Background
The first documented case of Listeria was in 1924. In the late 1920s, two researchers independently identified Listeria monocyctogenes from animal outbreaks. They proposed the genusListerella in honor of surgeon and early antiseptic advocate Joseph Lister; however, that name was already in use for a slime mold and a protozoan. Eventually, the genus Listeria was proposed and accepted. All species within the Listeria genus are Gram-positive, nonsporeforming, catalase-positive rods. The genus Listeria was classified in the family Corynebacteriaceae through the seventh edition of Bergey's Manual of Systematic Bacteriology. The 16S rRNA cataloging studies of Stackebrandt, et al. demonstrated that L. monocytogenes is a distinct taxon within the Lactobacillus-Bacillus branch of the bacterial phylogeny constructed by Woese. In 2001, the genus was placed in the newly created Family Listeriaceae. The only other genus in the family is Brochothrix.

The genus Listeria currently contains seven species: L. grayi, L. innocua, L. ivanovii, L. monocytogenes, L. murrayi, L. seeligeri, and L. welshimeri. Listeria dinitrificans, previously thought to be part of the Listeria genus, was reclassified into the new genus Jonesia. Under the microscope, Listeria species appear as small, Gram-positive rods, which are sometimes arranged in short chains. In direct smears, they may be coccoid, so they can be mistaken for streptococci. Longer cells may resemble corynebacteria. Flagella are produced at room temperature, but not at 37 °C. Hemolytic activity on blood agar has been used as a marker to distinguish L. monocytogenes among other Listeria species, but it is not an absolutely definitive criterion. Further biochemical characterization may be necessary to distinguish between the different species of Listeria.

Listeria can be found in soil, which can lead to vegetable contamination. Animals can also be carriers. Listeria has been found in uncooked meats, uncooked vegetables, fruit such as cantaloupes pasteurized or unpasteurized milk, foods made from milk, and processed foods. Pasteurization and sufficient cooking

kill Listeria; however, contamination may occur after cooking and before packaging. For example, meat-processing plants producing ready-to-eat foods, such as hot dogs and deli meats, must follow extensive sanitation policies and procedures to prevent Listeria contamination. Listeria monocytogenes is commonly found in soil, stream water, sewage, plants, and food. Listeria is responsible for listeriosis, a rare but potentially lethal food-borne infection. The case fatality rate for those with a severe form of infection may approach 25%. (Salmonella, in comparison, has a mortality rate estimated at less than 1%.) Although Listeria monocytogenes has low infectivity, it is hardy and can grow in temperatures from 4 °C (39.2 °F) (the temperature of a refrigerator), to 37 °C (98.6 °F), (the body's internal temperature). Listeriosis is a serious illness, and the disease may manifest as meningitis, or affect newborns due to its ability to penetrate the endothelial layer of the placenta.

Pathogenesis: Main article: Listeria monocytogenes

Listeria uses the cellular machinery to move around inside the host cell: It induces directed polymerization of actin by the ActA transmembrane protein, thus pushing the bacterial cell around.

Listeria monocytogenes, for example, encodes virulence genes that are thermoregulated. The expression of virulence factor is optimal at 37°C, and is controlled by a transcriptional activator, PrfA, whose expression is thermoregulated by thePrfA thermoregulator UTR element. At low temperatures, the PrfA transcript is not translated due to structural elements near the ribosome binding site. As the bacteria infect the host, the temperature of the host melts the structure and allows translation initiation for the virulent genes.

The majority of Listeria bacteria are targeted by the immune system before they are able to cause infection. Those that escape the immune system's initial response, however, spread through intracellular mechanisms and are, therefore, guarded against circulating immune factors (AMI).

To invade, Listeria induces macrophage phagocytic uptake by displaying D-galactose in their teichoic acids that are then bound by the macrophage's polysaccharide receptors. Other important adhesins are the internalins. Once phagocytosed, the bacterium is encapsulated by the host cell's acidic phagolysosome organelle. Listeria, however, escapes the phagolysosome by lysing the vacuole's entire membrane with secreted hemolysin,[10] now characterized as the exotoxinlisteriolysin O. The bacteria then replicate inside the host cell's cytoplasm.

Listeria must then navigate to the cell's periphery to spread the infection to other cells. Outside the body, Listeria has flagellar-driven motility, sometimes described as a "tumbling motility". However, at 37 °C, flagella cease to develop and the bacterium instead usurps the host cell's cytoskeleton to move. Listeria, inventively, polymerizes an actin tail or "comet", from actin monomers in the host's cytoplasm with the promotion of virulence factor ActA. The comet forms in a polar manner and aids the bacteria's migration to the host cell's outer membrane. Gelsolin, an actin filament severing protein, localizes at the tail of Listeria and accelerates the bacterium's motility. Once at the cell surface, the actin-propelled Listeria pushes against the cell's membrane to form protrusions called filopods or "rockets". The protrusions are guided by the cell's leading edge to contact adjacent cells, which then engulf the listeria rocket and the process is repeated, perpetuating the infection. Once phagocytosed, the bacterium is never again extracellular: it is an intracytoplasmic parasite like Shigella flexneri and Rickettsia.

Epidemiology

The Center for Science in the Public Interest has published a list of foods that have sometimes caused outbreaks of Listeria: hot dogs, deli meats, pasteurized or unpasteurized milk, cheeses (particularly soft-ripened cheeses like feta, Brie, Camembert, blue-veined, or Mexican-style queso blanco), raw and cooked poultry, raw meats, ice cream, raw vegetables, and raw and smoked fish.[13] Cantaloupe has been implicated in an outbreak of listeriosis from a farm in Colorado, and the Australian company GMI Food Wholesalers were fined AU$236,000 for providing Listeria monocytogenes-contaminated chicken wraps to the airline Virgin Blue.

Prevention
Preventing listeriosis as a food illness requires effective sanitation of food contact surfaces. Alcohol is an effective topical sanitizer against Listeria. Quaternary ammonium can be used in conjunction with alcohol as a food contact safe sanitizer with increased duration of the sanitizing action. Refrigerated foods in the home should be kept below 4 °C (39.2 °F) to discourage bacterial growth. Preventing listeriosis also can be done by carrying out an effective sanitation of food contact surfaces.

Treatment
Antibiotics effective against Listeria species include ampicillin, vancomycin (unclear effectiveness), ciprofloxacin, linezolid, and azithromycin.

Research
Listeria is an opportunistic pathogen: It is most prevalent in the elderly, pregnant mothers, and AIDS patients. With improved healthcare leading to a growing elderly population and extended life expectancies for AIDS patients, physicians are more likely to encounter this otherwise-rare infection (only 7 per 1,000,000 healthy people are infected with virulent Listeria each year). Better understanding the cell biology of Listeria infections, including relevant virulence factors, may lead to better treatments for listeriosis and other intracytoplasmic parasite infections. Researchers are now investigating the use of Listeria as a cancer vaccine, taking advantage of its "ability to induce potent innate and adaptive immunity" (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Marburg Virus
Date: 2012
Source: Wikipedia

Abstract: The Marburg virus in the Filoviridae family was first noticed and described during a small epidemic in the city of Marburg, Germany. Workers were accidentally exposed to infected green monkey tissue at the city's former main industrial plant, the Behring-Werke, then part of Hoechst, and today of CSL Behring. The plant was founded by Marburg citizen and first Nobel Prize in Physiology or Medicine winner, Emil Adolf von Behring. During the outbreak, 31 people became infected and seven of them died. "Marburg virus" is named after the city, consistent with the custom of naming hemorrhagic fever viruses after the location of their first recorded outbreak.

Marburg virus (MARV) causes severe disease in humans and nonhuman primates in the form of viral hemorrhagic fever. MARV is a select agent,[1] WHO risk group 4 pathogen (requiring biosafety level 4-equivalent containment), NIH/National Institute of Allergy and Infectious Diseases category A priority pathogen, Centers for Disease Control and Prevention Category A Bioterrorism Agent, and is listed as a biological agent for export control by the Australia Group.

Use of Term

Marburg virus was first described in 1967. Today, the virus is one of two members of the species *Marburg marburgvirus*, which is included into the genus *Marburgvirus*, family *Filoviridae*, order *Mononegavirales*. The name Marburg virus is derived from Marburg (the city in Hesse, West Germany, where the virus was first discovered) and the taxonomic suffix *virus*.

Note

Marburg virus is pronounced ˌmɑrbərg vɑɪrəs (IPA) or mahr-berg vahy-ruhs in English phonetic notation. According to the rules for taxon naming established by the International Committee on Taxonomy of Viruses (ICTV), the name Marburg virus is always to be capitalized, but is never italicized, and may be abbreviated (with MARV being the official abbreviation).

Previous Designations

Marburg virus was first introduced under this name in 1967. In 2005, the virus name was changed to Lake Victoria marburgvirus, which unfortunately was the same spelling as the species *Lake Victoria marburgvirus*. However, most scientific articles continued to refer to Marburg virus. Consequently, in 2010, the name Marburg virus was reinstated. A previous abbreviation for the virus was MBGV.

Virus Inclusion Criteria

A virus that fulfills the criteria for being a member of the species Marburg marburgvirus is a Marburg virus if its genome diverges from that of the prototype Marburg marburgvirus, Marburg virus variant Musoke (MARV/Mus), by <10% at the nucleotide level.

Disease
Main article: Marburg virus disease

MARV is one of two marburgviruses that causes Marburg virus disease (MVD) in humans (in the literature also often referred to as Marburg hemorrhagic fever, MHF). In the past, MARV has caused the following MVD outbreaks:

Marburg Virus Disease (MVD) Outbreaks Due to Marburg Virus (MARV) Infection

Year-Location-Human/DeathsCases (case-fatality rate)

1. 1967: Marburg and Frankfurt, West Germany, and Belgrade, Yugoslavia: 7/31 (23%)
2. 1975: Rhodesia and Johannesburg, South Africa: 1/3 (33%)
3. 1980: Kenya: 1/2 (50%)
4. 1987: Kenya: 1/1 (100%)
5. 1988: Koltsovo, Soviet Union: 1/1 (100%) [Laboratory Accident]
6. 1990: Koltsovo, Soviet Union: 0/1 (0%) [Laboratory Accident]
7. 1998: Durba and Watsa, Democratic Republic of the Congo: ? (A total of 154 cases and 128 deaths of marburgvirus infection were recorded during this outbreak. The case fatality was 83%. Two different marburgviruses, MARV and Ravn virus (RAVV), cocirculated and caused disease. It has never been published how many cases and deaths were due to MARV or RAVV infection)
8. 2004-2005: Angola: 227/252 (90%)
9. 2007: Uganda: 1/3 (33%)
10. 2008: Uganda: 1/1 (100%)

Virology

Genome
Like all mononegaviruses, marburgvirions contain non-infectious, linear nonsegmented, single-stranded RNA genomes of negative polarity that possesses inverse-complementary 3' and 5' termini, do not possess a 5' cap, are not polyadenylated, and are not covalently linked to a protein. Marburgvirus genomes are approximately 19 kb long and contain seven genes in the order 3'-UTR-*NP-VP35-VP40-GP-VP30-VP24-L*-5'-UTR. The genomes of the two different marburgviruses (MARV and RAVV) differ in sequence.

Structure

Like all filoviruses, marburgvirions are filamentous particles that may appear in the shape of a shepherd's crook or in the shape of a "U" or a "6", and they may be coiled, toroid, or branched. Marburgvirions are generally 80 nm in width, but vary somewhat in length. In general, the median particle length of marburgviruses ranges from 795–828 nm (in contrast to ebolavirions, whose median particle length was measured to be 974–1,086 nm), but particles as long as 14,000 nm have been detected in tissue culture. Marburgvirions consist of seven structural proteins. At the center is the helical ribonucleocapsid, which consists of the genomic RNA wrapped around a polymer of nucleoproteins (NP). Associated with the ribonucleoprotein is the RNA-dependent RNA polymerase (L) with the polymerase cofactor (VP35) and a transcription activator (VP30). The ribonucleoprotein is embedded in a matrix, formed by the major (VP40) and minor (VP24) matrix proteins. These particles are surrounded by a lipid membrane derived from the host cell membrane. The membrane anchors a glycoprotein ($GP_{1,2}$) that projects 7 to 10 nm spikes away from its surface. While nearly identical to ebolavirions in structure, marburgvirions are antigenically distinct.

Replication
The marburgvirus life cycle begins with virion attachment to specific cell-surface receptors, followed by fusion of the virion envelope with cellular membranes and the concomitant release of the virus nucleocapsid into the cytosol. The virus RdRp partially uncoats the nucleocapsid and transcribes the genes into positive-stranded mRNAs, which are then translated into structural and nonstructural proteins. Marburgvirus L binds to a single promoter located at the 3' end of the genome. Transcription either terminates after a gene or continues to the next gene downstream. This means

that genes close to the 3' end of the genome are transcribed in the greatest abundance, whereas those toward the 5' end are least likely to be transcribed. The gene order is therefore a simple but effective form of transcriptional regulation. The most abundant protein produced is the nucleoprotein, whose concentration in the cell determines when L switches from gene transcription to genome replication. Replication results in full-length, positive-stranded antigenomes that are in turn transcribed into negative-stranded virus progeny genome copies. Newly synthesized structural proteins and genomes self-assemble and accumulate near the inside of the cell membrane. Virions bud off from the cell, gaining their envelopes from the cellular membrane they bud from. The mature progeny particles then infect other cells to repeat the cycle.

Ecology
In 2009, the successful isolation of infectious MARV was reported from caught healthy Egyptian rousettes (*Rousettus aegyptiacus*). This isolation, together with the isolation of infectious RAVV, strongly suggests that Old World fruit bats are involved in the natural maintenance of marburgviruses. Further studies are necessary to establish whether Egyptian rousettes are the actual hosts of MARV and RAVV or whether they get infected via contact with another animal and therefore serve only as intermediate hosts.

Weaponization
The Soviet Union had an extensive offensive and defensive biological weapons program that included MARV. At least three Soviet research institutes had MARV research programs during offensive times: the Virology Center of the Scientific-Research Institute for Microbiology in Zagorsk (today Sergiev Posad), the Scientific-Production Association "Vektor" (today the State Research Center of Virology and Biotechnology "Vektor") in Koltsovo, and the Irkutsk Scientific-Research Anti-Plague Institute of Siberia and the Far East in Irkutsk. As most performed research was highly classified, it remains unclear how successful the MARV program was. However, Soviet defector Ken Alibek claimed that a weapon filled with MARV was tested at the Stepnogorsk Scientific Experimental and Production Base in Stepnogorsk, Kazakh Soviet Socialist Republic (today Kazakhstan),[41] suggesting that the development of a MARV biological weapon had reached advanced stages. Independent confirmation for this claim is lacking. At least one laboratory accident with MARV, resulting in the death of Koltsovo researcher Nikolai Ustinov, occurred during offensive times in the Soviet Union and was first described in detail by Alibek. After the collapse of the Soviet Union, MARV research continued in all three institutes, but judging from published material this research has been defensive in nature.

Popular Culture

In the non-fiction thriller, *The Hot Zone,* Richard Preston describes several MARV infections

In the TV series *Millennium*, at the end of Season 2, a "prion version" of MARV causes a disease outbreak in Seattle, killing (amongst others) Frank Black's wife, Catherine. In the Season 3 episode *Collateral Damage*, Peter Watt's daughter is infected with MARV by a Gulf War veteran who claims that the Millennium Group did the same to American soldiers during the first Gulf War

In the crossover event of the TV series *Medical Investigation*, episode 17, and *Third Watch*, season 6 episode 16, Marburg virus disease breaks out in New York City, killing 5 of 6 infected people

In the Sarah Jane Smith series (Series Two), MARV is used as a weapon by a doomsday cult

In the short story *Hell Hath Enlarged Herself* by Michael Marshall Smith, one of the original scientists is infected with MARV in an attempt to test ImmunityWorks ver. 1.0

In the novel *Microserfs* by Douglas Coupland, MARV is mentioned several times as a metaphor for the spread of information through the internet

In the novel *Resident Evil: Caliban Cove* an insane scientist and former professor named Nicolas Griffith is referred to by Rebecca Chambers as having infected three men with MARV after they had been led to believe it was a harmless common cold virus

In the novel *Pandora's Legion* by Harold Coyle and Barrett Tillman, an Al-Qaeda cell in Pakistan injects volunteers with MARV, who then board flights to major international airports in the western world where the large flow of people would facilitate the spreading of the virus into a pandemic (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Melioidosi
Date: 2012
Source: Wikipedia

Abstract: Melioidosis is an infectious disease caused by a Gram-negative bacterium, *Burkholderia pseudomallei*, found in soil and water. It is of public health importance in endemic areas, particularly in Thailand and northern Australia. It exists in acute and chronic forms. Symptoms may include pain in chest, bones, or joints; cough; skin infections, lung nodules and pneumonia.

B. pseudomallei was previously classed as part of the *Pseudomonas* genus and until 1992, it was known as *Pseudomonas pseudomallei*. It is phylogenetically related closely to *Burkholderia mallei* which causes glanders, an infection primarily of horses, donkeys and mules. The name Melioidosis is derived from the Greek *melis* (μηλις) meaning "a distemper of asses" with the suffixes -oid meaning "similar to" and -osis meaning "a condition", that is, a condition similar to glanders.

Epidemiology
Melioidosis is endemic in parts of southeast Asia (including Thailand, Laos and southern China, Singapore,Malaysia, Burma and Vietnam), Taiwan and northern Australia. Multiple cases have also been described in Hong Kong and Brunei India, and sporadic cases in Central and South America, the Middle East, the Pacific and several African countries. Although only one case of melioidosis has ever been reported in Bangladesh, at least five cases have been imported to the UK from that country, which suggests that melioidosis is endemic to that country and that there is a serious problem of underdiagnosis or under-reporting, most likely due to a lack of adequate laboratory facilities.

Northeast Thailand has the highest incidence of melioidosis recorded in the world (21.3 cases of melioidosis per 100,000 people per year). In Northeast Thailand, 80% of children are positive for antibodies against *B. pseudomallei* by the age of 4; the figures are lower in other parts of the world.

Melioidosis is a recognised disease in animals, including cats, goats, sheep, and horses. Cattle, water buffalo, and crocodiles are considered to be relatively resistant to melioidosis despite their constant exposure to mud. An outbreak at the Paris Zoo in the 1970s ("*L'affaire du jardin des plantes*") was thought to have originated from an imported panda.

Burkholderia pseudomallei is normally found in soil and surface water; a history of contact with soil or surface water is therefore almost invariable in patients with melioidosis; that said, the majority of patients who do have contact with infected soil suffer no ill effects. Even within an area, the distribution of *B. pseudomallei* within the soil can be extremely patchy, and competition with other *Burkholderia* species has been suggested as a possible reason. Contaminated ground water was implicated in one outbreak in northern Australia. Severe weather events such as floodingtsunamis and typhoons.

It has been suggested, on the basis of whole genome sequencing, that humans may play a role in moving *B. pseudomallei* from place to place.

The single most important risk factor for developing severe melioidosis is diabetes mellitus. Other risk factors include thalassaemia, kidney disease, occupation (rice paddy farmers), and cystic fibrosis. The mode of infection is believed to be either through a break in the skin, or through the inhalation of aerosolized *B. pseudomallei*. Person-to-person spread has been described but is extremely unusual.

There is a clear association with increased rainfall: with the number (and severity) of cases increasing following increased precipitation.

Clinical Features

Acute Melioidosis
In the subgroup of patients where an inoculating event was noted, the mean incubation period of acute melioidosis was 9 days (range 1–21 days). Patients with latent melioidosis may be symptom free for decades; the longest period between presumed exposure and clinical presentation is 62 years. The potential for prolonged incubation was recognized in US servicemen involved in the Vietnam War, and was referred to as the "Vietnam time-bomb". There is a wide spectrum of severity; in chronic presentations, symptoms may last months, but fulminant infection, particularly associated with near-drowning, may present with severe symptoms over hours.

A patient with active melioidosis usually presents with fever. Pain or other symptoms may be suggestive of a clinical focus, which is found in around 75% of patients. Such symptoms include cough or pleuritic chest pain suggestive of pneumonia, bone or joint pain suggestive of osteomyelitis or septic arthritis, or cellulitis. Intra-abdominal infection (including liver and/or splenic abscesses, or prostatic abscesses) do not usually present with focal pain, and imaging of these organs using ultrasound or CT should be performed routinely. In one series of 214 patients, 27.6% had abscesses in the liver or spleen (95% confidence interval, 22.0% to 33.9%). It has been suggested that *B. pseudomallei* abscesses have a characteristic "honeycomb" or "swiss cheese" architecture (hypoechoic, multi-septate, multiloculate) on CT.

There are regional variations in disease presentation: parotid abscesses characteristically occur in Thai children but this presentation has only been described once in Australia. Conversely, prostatic abscesses are found in up to 20% of Australian males but are rarely described elsewhere. An encephalomyelitis syndrome is recognised in northern Australia.

Patients with melioidosis usually have risk factors for disease, such as diabetes, thalassemia, hazardous alcohol use or renal disease, and frequently give a history of occupational or recreational exposure to mud or pooled surface water. However, otherwise healthy patients, including children, may also get melioidosis.

In up to 25% of patients, no focus of infection is found and the diagnosis is usually made on blood cultures or throat swab. Melioidosis is said to be able to affect any organ in the body except the heart valves (endocarditis). Although meningitis has been described secondary to ruptured brain abscesses, primary meningitis has not been described. Less common manifestations include intravascular infection, lymph node abscesses (1.2–2.2%), pyopericardium and myocarditis, mediastinal infection, and thyroid and scrotal abscesses and ocular infection.

Chronic Melioidosis
Chronic melioidosis is usually defined by a duration of symptoms greater than 2 months and occurs in approximately 10% of patients. The clinical presentation of chronic melioidosis is protean and includes such presentations as chronic skin infection, skin ulcers and lung nodules or chronic pneumonia, closely mimicking tuberculosis, sometimes being called "Vietnamese tuberculosis". Chronic melioidosis can mimic tuberculous pericarditis.

Diagnosis
A definitive diagnosis is made by culturing the organism from any clinical sample, because the organism is never part of the normal human flora.

A definite history of contact with soil may not be elicited as melioidosis can be dormant for many years before manifesting. Attention should be paid to a history of travel to endemic areas in returned travellers. Some authors recommend considering possibility of melioidosis in every febrile patient with a history of traveling to and/or staying at endemic areas.

A complete screen (blood culture, sputum culture, urine culture, throat swab and culture of any aspirated pus) should be performed on all patients with suspected melioidosis (culture on blood agar as well as Ashdown's medium). A definitive diagnosis is made by growing *B. pseudomallei* from any site. A throat swab is not sensitive but is 100% specific if positive, and compares favourably with sputum culture. The sensitivity of urine culture is increased if a centrifuged specimen is cultured, and any bacterial growth should be reported (not just growth above 10^4 organisms/ml which is the usual cut off). Very occasionally, bone marrow culture may be positive in patients who have negative blood cultures for B. pseudomallei, but these are not usually recommended. A common error made by clinicians unfamiliar with melioidosis is to only send a specimen from the affected site (which is the usual procedure for most other infections) instead of sending a full screen.

Ashdown's medium, a selective medium containing gentamicin, may be required for cultures taken from non-sterile sites. *Burkholderia cepacia* medium may be a useful alternative selective medium in non-endemic areas, where Ashdown's is not available. A new medium derived from Ashdown known as Francis medium may help differentiate *B. pseudomallei* from *B. cepacia* and may help in the early diagnosis of melioidosis, but has not yet been extensively clinically validated.

Many commercial kits for identifying bacteria may mis-identify *B. pseudomallei* (*see* Burkholderia pseudomallei for a more detailed discussion of these issues).

There is also a serological test for melioidosis (indirect haemagglutination), but this is not commercially available in most countries. A high background titre may reduce the positive predictive value of serological tests in endemic countries. A specific direct immunofluorescent test and latex agglutination, based on monoclonal antibodies, are used widely in Thailand but are not available elsewhere. There is almost complete cross-reactivity with *B. thailandensis*. There exists a commercial ELISA kit for melioidosis which appears to perform well. but no ELISA test has yet been clinically validated as a diagnostic tool.

It is not possible to make the diagnosis on imaging studies alone (X-rays and scans), but imaging is routinely performed to assess the full extent of disease. Imaging of the abdomen using CT scans or ultrasound is recommended routinely, as abscesses may not be clinically apparent and may coexist with disease elsewhere. Australian authorities suggest imaging of the prostate specifically due to the high incidence of prostatic abscesses in northern Australian patients. A chest x-ray is also considered routine, with other investigations as clinically indicated. The presence of honeycomb abscesses in the liver are considered characteristic, but are not diagnostic.

The differential diagnosis is extensive; melioidosis may mimic many other infections, including tuberculosis.

Treatment

Current Treatment
The treatment of melioidosis is divided into two stages, an intravenous high intensity phase and an eradication phase to prevent recurrence.

Intravenous Intensive Phase.
Intravenous ceftazidime is the current drug of choice for treatment of acute melioidosis. Meropenem, imipenem and the cefoperazone-sulbactam combination (Sulperazone) are also active. Intravenous amoxicillin-clavulanate (co-amoxiclav) may be used if none of the above four

drugs are available, but it produces inferior outcomes. Intravenous antibiotics are given for a minimum of 10 to 14 days, and are not usually stopped until the patient's temperature has returned to normal for more than 48 hours. Even with appropriate antibiotic therapy, fevers often persist for weeks or months, and patients may continue to develop new lesions even while on appropriate treatment. The median fever clearance time in melioidosis is 10 days: and failure of the fever to clear is not a reason to alter treatment. It is not uncommon for patients to require parenteral treatment continuously for a month or more.

Intravenous meropenem is routinely used in Australia: outcomes appear to be good and meropenem is currently being tested with ceftazidime in a Thai clinical trial (ATOM).

There are theoretical reasons for believing that mortality might be lower in patients treated with imipenem: first, there is less endotoxin released by dying bacteria during imimipenem treatment, and the minimum inhibitory concentration for imipenem is lower than for ceftazidime. However, no clinically relevant difference was found in mortality between imipenem and ceftazidime treatment. The MIC of meropenem is higher for *B. pseudomallei* than for many other organisms, and patients being haemofiltered will need more frequent or higher doses.

Moxifloxacin, cefepime, tigecycline and ertapenem do not appear to be effective *in vitro*.[75][76] Piperacillin-sulbactam, doripenem and biapenem appear to be effective *in vitro,* but there is no clinical experience on which to recommend their use.

Adjunctive treatment with GCSF or co-trimoxazole were not associated with decreased fatality rates in trials in Thailand.

Eradication Phase
Following the treatment of the acute disease, it is recommended that eradication (or maintenance) treatment with co-trimoxazole and doxycycline be used for 12 to 20 weeks to reduce the rate of recurrence.[81] Chloramphenicol is no longer routinely recommended for this purpose. Co-amoxiclav is an alternative for those patients who are unable to take co-trimoxazole and doxycycline (e.g., pregnant women and children under the age of 12), but is not as effective. Single agent treatment with a fluoroquinolone (e.g., ciprofloxacin) or doxycyclinefor the oral maintenance phase is ineffective.

In Australia, co-trimoxazole is used on its own for eradication therapy, with relapse rates that are lower than those seen in Thailand; there is also *in vitro* evidence to suggest that co-trimoxazole and doxycycline are antagonistic, and that co-trimoxazole on its own may be preferable. A randomised controlled trial (MERTH) to compare this with the current standard of co-trimoxazole and doxycycline started in 2006 and is due for completion in 2008. Studies reinforce the need for adequate follow up and good adherence to the eradication phase of therapy. Dosing for co-trimoxazole is based on weight: (<40 kg: 160/800 mg every 12 hours; 40–60kg: 240/1200 mg every 12 hours, >60 kg: 320/1600 mg every 12 hours).

Surgical Treatment
Surgical drainage is usually indicated for prostatic abscesses and septic arthritis, may be indicated for parotid abscesses and not usually indicated for hepatosplenic abscesses. In bacteraemic melioidosis unresponsive to intravenous antibiotic therapy, splenectomy has been attempted, but there is only anecdotal evidence to support this practice.

Historical Treatment
Prior to 1989, the standard treatment for acute melioidosis was a three-drug combination of chloramphenicol, co-trimoxazole and doxycycline; this regimen is associated with a mortality rate of 80% and should no longer be used unless no other alternatives are available. All four drugs are bacteriostatic (they stop the bacterium from growing but do not kill it) and the action of co-trimoxazole antagonizes both chloramphenicol and doxycycline.

Prognosis
Without access to appropriate antibiotics (principally ceftazidime or meropenem), the septicemic form of melioidosis has a mortality rate that exceeds 90%. With appropriate antibiotics, the mortality rate is

about 10% for uncomplicated cases but up to 80% for cases with bacteraemia or severe sepsis. It seems certain that access to intensive care facilities is also important, and probably at least partially explains why total mortality is 20% in Northern Australia but 40% in Northeast Thailand. Response to appropriate antibiotic treatment is slow with the average duration of fever following treatment being 5–9 days.

Recurrence occurs in 10 to 20% of patients. While molecular studies have established that the majority of recurrences are due to the original infecting strain, a significant proportion of recurrences (perhaps up to a quarter) in endemic areas may be due to reinfection, particularly after 2 years. Risk factors include severity of disease (patients with positive blood cultures or multifocal disease have a higher risk of relapse), choice of antibiotic for eradication therapy (doxycycline monotherapy and fluoroquinolone therapy are not as effective), poor compliance with eradication therapy and duration of eradication therapy less than 8 weeks.

Prevention
Person-to-person transmission is exceedingly unusual; and patients with melioidosis should not be considered contagious. Lab workers should handle *Burkholderia pseudomallei* under BSL-3 isolation conditions, as laboratory acquired melioidosis has been described.

In endemic areas, people (rice-paddy farmers in particular) are warned to avoid contact with soil, mud and surface water where possible. Case clusters have been described following flooding and cyclones and probably relate to exposure. Other case clusters have related to contamination of drinking water supplies. Populations at risk include patients with diabetes mellitus, chronic renal failure, chronic lung disease or patients with an immune deficiency of any kind. The effectiveness of measures to reduce exposure to the causative organism have not been established. A vaccine is not yet available.

Post-Exposure prophylaxis
After exposure to *B. pseudomallei* (particularly following a laboratory accident) combined treatment with co-trimoxazole and doxycycline is recommended. Trovafloxacin and grepafloxacin have been shown to be effective in animal models.

Vaccination
Further information: Burkholderia_pseudomallei#Vaccine_candidates

There are no vaccines currently licensed for the prevention of melioidosis.

Biological Warfare Potential
There has been interest in melioidosis because it has the potential to be developed as a biological weapon. It is classed by the US Centers for Disease Control (CDC) as a Category B agent. *B. pseudomallei*, like its relative *B. mallei* which causes Glanders, was studied by the U.S. as a potential biological warfare agent, but was never weaponized. It has been reported that the Soviet Union was also experimenting with *B. pseudomallei* as a biological warfare agent.

Synonyms

1. **Pseudoglanders**
2. **Whitmore's Disease** (after Captain Alfred Whitmore, who first described the disease)
3. **Nightcliff Gardener's Disease** (Nightcliff is a suburb of Darwin, Australia where melioidosis is endemic)
4. **Paddy-Field Dsease**
5. **Morphia Injector's Septicaemia** (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Monkeypox
Date: 2012
Source: Wikipedia

Abstract: Monkeypox is an exotic infectious disease caused by the monkeypox virus. The disease was first identified in laboratory monkeys, hence its name, but in its natural state it seems to infectrodents more often than primates. The disease is most prevalent in Central and West Africa, but an outbreak occurred also in the United States in 2003.

Human monkeypox is a zoonotic viral disease that occurs primarily in remote villages of Central and West Africa in proximity to tropical rainforests where there is more frequent contact with infected animals. Monkeypox is usually transmitted to humans from rodents, pets, and primates through contact with the animal's blood or through a bite. Human monkeypox can be difficult to distinguish clinically from smallpox (to which it is closely related) and chickenpox (to which it is not).

Epidemiology
In addition to monkeys, giant pouched rats (Cricetomys sp.), dormice (Graphiurus sp.) and African squirrels (Heliosciurus, Funisciurus) have all been implicated as reservoirs of the virus. The use of these animals as food may be an important source of transmission to humans.[citation needed]

Monkeypox as a disease in humans was first associated with an illness in the Democratic Republic of the Congo (formerly Zaire), in the town of Basankusu, Équateur Province, in 1970. A second outbreak of human illness was identified inDRC/Zaire in 1996–1997. In 2003, a small outbreak of human monkeypox in the United States occurred among owners of pet prairie dogs.[4] The outbreak originated from Villa Park, Illinois, outside of Chicago, when a exotic animal dealer kept young prairie dogs in close proximity to an infected Gambian pouched rat (Cricetomys gambianus) recently imported from West Africa. Seventy-three people were reportedly infected, of which there were no fatalities.

A second African focus of infection has been discovered in Sudan. No infected patients died.

Monkeypox Disease in Animals
The symptoms of a sick animal include: listlessness, ocular and nasal discharges, frequent vomiting, coughing, hair loss sometimes accompanied by painful scabs, and pneumonia. Look for nodules similar to mosquito bites and inflammation of the lymph glands.

Monkeypox Disease in Humans

Symptoms and Course
In humans, monkeypox is similar to smallpox, although it is often milder. Vaccination against smallpox is assumed to provide protection against human monkeypox infection considering they are closely related viruses and the vaccine protects animals from experimental lethal monkeypox challenge. This has not

been conclusively demonstrated in humans because routine smallpox vaccination was discontinued following the apparent eradication of smallpox and due to safety concerns with the vaccine. Limited person-to-person spread of infection has been reported in disease-endemic areas in Africa. Case-fatality ratios in Africa have ranged from 1% to 10%.

Prevention and Treatment
Currently, there is no proven, safe treatment for monkeypox. Smallpox vaccine has been reported to reduce the risk of monkeypox among previously vaccinated persons in Africa. The United States Centers for Disease Control and Prevention(CDC) recommends that persons investigating monkeypox outbreaks and involved in caring for infected individuals or animals should receive a smallpox vaccination to protect against monkeypox. Persons who have had close or intimate contact with individuals or animals confirmed to have monkeypox should also be vaccinated. The people who have been infected can be vaccinated up to 14 days after exposure. CDC does not recommend preexposure vaccination for unexposedveterinarians, veterinary staff, or animal control officers, unless such persons are involved in field investigations.

This film, produced by INCEF for distribution in communities prone to infection, describes the nature of the illness and how best to confront it.

2003 U.S. Outbreak
Through June 18, 2003, 93 cases of monkeypox in the United States occurred in Wisconsin (44 cases), Indiana (24), Illinois (19), Ohio (4), Kansas (1), Missouri (1), and New Jersey (1). Analysis of the first 53 cases showed 50 had contact withprairie dogs that were purchased from Phil's Pocket Pets of Villa Park, Illinois.[8] Electron microscopy and serologic studies were used to confirm that the disease was human monkeypox.

The onset of the illness among the patients in the United States began in early May 2003. Patients typically experienced a prodrome consisting of fever, headaches, myalgias, chills, and drenching sweats. Roughly one-third of patients had nonproductive coughs. This prodromal phase was followed 1–10 days later by the development of a papular rash that typically progressed through stages of vesiculation, pustulation, umbilication, and crusting. In some patients, early lesions had become ulcerated. Rash distribution and lesions occurred on head, trunk, and extremities; many of the patients had initial and satellite lesions on palms, soles, and extremities. Rashes were generalized in some patients. After onset of the rash, patients generally manifested rash lesions in different stages. All patients reported direct or close contact with prairie dogs, most of which were sick. Illness in prairie dogs was frequently reported as beginning with a blepharoconjunctivitis, progressing to presence of nodular lesions in some cases. Some prairie dogs died from the illness, while others reportedly recovered (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Morgellons
Date: January 10, 2012
Source: Wikipedia

Abstract: Morgellons (also called Morgellons disease or Morgellons syndrome) is a name that was given in 2002 by stay-at-home-mom Mary Leitao to a proposed condition characterized by a range of cutaneous (skin) symptoms including crawling, biting, and stinging sensations (formication); finding fibers on or under the skin; and persistent skin lesions (e.g., rashes or sores). Doctors, including dermatologists and psychiatrists, regard Morgellons as delusional infestation (also called delusional parasitosis), the belief that there is a pathogenic infestation that remains despite contrary medical evidence.

Despite the lack of evidence that Morgellons is a novel or distinct condition and the absence of any agreed set of diagnostic symptoms, the Morgellons Research Foundation and self-diagnosed Morgellons patients successfully lobbied members of Congress and the U.S. government's Centers for Disease Control and Prevention (CDC) to investigate the proposed condition. The CDC researchers issued the results of their multi-year study in January 2012, indicating that there were no disease organisms present in Morgellons patients, the fibers found were normal clothing fibers, and suggested that patients' sensations were manifestations of "delusional infestation."

History

Mary Leitao and the MRF

In 2001, according to Mary Leitao, her then two-year-old son developed sores under his lip and began to complain of "bugs." Leitao, who graduated with a Bachelor of Science in Biology and worked for five years at Boston hospitals as a lab technician before becoming a stay-at-home mother, says she examined the sores with her son's toy microscope and discovered red, blue, black, and white fibers. She states that she took her son to see at least eight different doctors who were unable to find any disease, allergy, or anything unusual about her son's described symptoms. Fred Heldrich, a Johns Hopkins pediatrician with a reputation "for solving mystery cases," examined Leitao's son. Heldrich found nothing abnormal about the boy's skin, wrote to the referring physician that "Leitao would benefit from a psychiatric evaluation and support," and registered his worry about Leitao's "use" of her son. Psychology Today reports that Leitao last consulted an unnamed Johns Hopkins infectious disease specialist who after reviewing her son's records refused to see him, suggesting Leitao herself might suffer from "Munchausen's by proxy, a psychiatric syndrome in which a parent pretends a child is sick or makes him sick to get attention from the medical system." This opinion of a potential psychological disorder, according to Leitao, was shared by several medical professionals she sought out:

(Leitao) said she long ago grew accustomed to being doubted by doctors whenever she sought help for her son, who is now 7 and still suffering from recurring lesions. "They suggested that maybe I was

neurotic," Leitao said, "They said they were not interested in seeing him because I had Munchausen Syndrome by Proxy."

Leitao says that her son developed more sores, and more fibers continued to poke out of them. She and her husband, Edward Leitao, an internist with South Allegheny Internal Medicine in Pennsylvania, felt their son suffered from "something unknown." She chose the name Morgellons disease (with a hard g) from a description of an illness in the monograph A Letter to a Friend by Sir Thomas Browne, in 1690, wherein Browne describes several medical conditions in his experience, including "that endemial distemper of children in Languedoc, called the morgellons, wherein they critically break out with harsh hairs on their backs." There is no suggestion that the symptoms described by Browne are linked to the alleged modern cases.

Leitao started the Morgellons Research Foundation (MRF) in 2002 (informally) and as an official non-profit in 2004. The MRF states on its website that its purpose is to raise awareness and funding for research into the proposed condition, described by the organization as a "poorly understood illness, which can be disfiguring and disabling." Leitao stated that she initially hoped to receive information from scientists or physicians who might understand the problem, but instead, thousands of others contacted her describing their sores and fibers, as well as neurological symptoms, fatigue, muscle and joint pain, and other symptoms. The MRF claims to have received self-identified reports of Morgellons from all 50 US states and 15 other countries, including Canada, the UK, Australia, and the Netherlands, and states that it has been contacted by over 12,000 families.

In 2012 the Morgellons Research Foundation closed down, and directed future inquires to Oklahoma State University

Media Coverage
In May 2006, a CBS news segment on Morgellons aired in Southern California. The same day the Los Angeles County Department of Health services issued a statement saying, "No credible medical or public health association has verified the existence or diagnosis of 'Morgellons Disease'," and "at this time there is no reason for individuals to panic over unsubstantiated reports of this disease." In June and July 2006 there were segments on CNN, ABC's Good Morning America, and NBC's The Today Show. In August 2006, a segment of the ABC show Medical Mysteries was devoted to the subject. The disease was featured on ABC's Nightline on January 16, 2008, and as the cover story of the January 20, 2008 issue of the Washington Post Magazine.

The first article to propose Morgellons as a new disease in a scientific journal was a review article co-authored by members of the MRF and published in 2006 by the American Journal of Clinical Dermatology. An article in the San Francisco Chronicle reported, "There have been no clinical studies" (of Morgellons disease). A New Scientist article in 2007 also covered the phenomenon noting that people are reporting similar symptoms in Europe and Australia.

In an article published in The Los Angeles Times on April 22, 2010, singer-songwriter Joni Mitchell claimed to be a sufferer of the condition, stating:
"I have this weird, incurable disease that seems like it's from outer space, but my health's the best it's been in a while, Two nights ago, I went out for the first time since Dec. 23: I don't look so bad under incandescent light, but I look scary under daylight. Garbo and Dietrich hid away just because people became so upset watching them age, but this is worse. Fibers in a variety of colors protrude out of my skin like mushrooms after a rainstorm: they cannot be forensically identified as animal, vegetable or mineral. Morgellons is a slow, unpredictable killer — a terrorist disease: it will blow up one of your organs, leaving you in bed for a year. But I have a tremendous will to live: I've been through another pandemic — I'm a polio survivor, so I know how conservative the medical body can be. In America, the Morgellons is always diagnosed as "delusion of parasites," and they send you to a psychiatrist. I'm actually trying to get out of the music business to battle for Morgellons sufferers to receive the credibility that's owed to them."

On 13 June 2011, the Australian Broadcasting Corporation's 'Radio National' broadcast The mystery of Morgellons with guests including the Mayo clinic's Professor Mark Davis.

On February 3, 2012, the Russian Channel One popular Let Them Talk show hosted by Andrey Malakhov, in the programme entitled "The Curse of The World's End" featured several alleged victims of the disease in the studio some of whom provided home-made footage. According to one of the guests, Valentina Serova, in Rostov oblast where she came from, the spread of Morgellons has gained epidemic proportions and is totally ignored by the state. Among theories and hypothesis aired, one dealt with the possible result of bacteriological weapons testing (Salsk Steppes, in particular, were rumoured to have served as sites for such testings in the USSR). One of the invited experts, Irina Ermakova, head of the National Genetic Security Association of Russia, linked the possible origins of Morgellons directly to the production of GMO, claiming that of the 15 thousand families afflicted by the disease around the world, the majority live nearby fields wheretransgenic plants are being produced.

Former Major League Baseball pitcher Billy Koch and his entire immediate family have been noted in the media to be sufferers.

CDC Investigation

Following a mailing campaign coordinated by the Morgellons Research Foundation in which self-described sufferers clicked on the foundation Web site and sent thousands of form letters to members of Congress, a Centers for Disease Control and Prevention (CDC) task force first met in June 2006. In July 2006, Dan Rutz, MPH, a communications specialist for the CDC, said, "We're not ready to concede there's a new disease, but the volume of concern has stepped up because a lot of people are writing or calling their congressmen about it." By August 2006, the task force consisted of 12 people, including two pathologists, a toxicologist, an ethicist, a mental health expert and specialists in infectious, parasitic, environmental and chronic diseases. In May 2007, KGW-TV Newschannel 8's Laural Porter asked Rutz if he had any information about the nature of the fibers. At that time Rutz said, "None. We don't know. We haven't studied them in a lab yet. There is nothing to imply there is [an infectious process], but our mind is open to everything, including that remote possibility."

In June 2007, the CDC opened a website on "Unexplained Dermopathy (aka 'Morgellons')". By November 2007, the CDC had announced an investigation process, stating that, "The primary goals of the investigation are to better describe the clinical and epidemiologic features of this condition and to generate hypotheses about possible risk factors." Kaiser Permanente in Northern California was chosen to assist with the investigation, which began after the scientific protocols and review board structure had been prepared and approved. Investigators planned to report on the geographic distribution of the illness, and estimate rates of illness in affected communities. The investigation involved skin biopsies from affected patients, and characterization of foreign material such as fibers or threads obtained from patients to determine their potential source. In January 2008 it was reported that the CDC was enlisting the aid of the U.S. Armed Forces Institute of Pathology and the American Academy of Dermatology "to conduct 'immediate' and 'rigorous' research."

On 4 November 2009, the CDC issued a preliminary report based on an external peer review of the project. As of 24 March 2011 the CDC said "We recently completed the data analysis. A final report has been submitted for publication in a peer-reviewed scientific journal."

On 25 January 2012 the CDC released the results of the study finding no infectious or environmental links. The study consisted of skin biopsies, blood tests, and interviews of over 100 Morgellons patients, and yielded no evidence of an infection (bacterial, fungal, or otherwise) or common environmental factor causing the problems. Laboratory analysis of the threads found by participants revealed nothing unusual, but consisted of cotton and other materials likely to be found in clothing. The researchers could not find any explanation for sensations participants reported under their skin and suggested these could be “delusional infestation,” wherein people falsely believe their bodies are being invaded by small organisms. Various Morgellons groups responded to the results of the studies by saying it confirmed their expectations that the government-run study is trying to cover up larger issues. Jan Smith, owner and operator of "Morgellons Exposed", a site which hosts her theories on the cause of Morgellons (including alien nano-technology implants), believed the problem was more than a medical condition and responded, “There’s something being hidden.”

Mayo Clinic Study
A study conducted of 108 patients at the Mayo Clinic was published in Archives of Dermatology on May 16, 2011. The study failed to find evidence of skin infestation despite doing skin biopsies and examining specimens provided by the patients. The study, which was conducted between 2001 and 2007, concluded that the feeling of skin infestation was a delusion, delusional parasitosis.

Symptoms & Diagnosis
Morgellons is not recognized as a unique disorder, so there is currently no list of symptoms or differential diagnosis for Morgellons that is generally accepted by the medical community. Patients usually self-diagnose based on media reports and the internet.

The 2007 Atlas of Human Parasitology covers the proposed condition in its section on "Pseudoparasites and Artifacts":

Many dermatologists refute the suggestion that this is an actual disease but instead indicate that many of these patients have psychological problems or other common skin disorders. Given the large numbers of individuals who feel that they have this affliction, it will be most helpful over the coming years to have a valid scientific assessment of Morgellons disease and its possible etiology (or etiologies). One of the chief criticisms by many patients has been that they feel the medical community and other scientists consulted have not been open to the idea that there is possibly an as yet unidentified infectious or physiologic causation for the disease. However it is certainly true that many expert parasitologists, medical entomologists and other microbiologists have in fact carefully examined fibers and other materials expressed or extracted from such patients and found that biological organisms are not present. Although an apparent association of the condition with the presence of Lyme disease has been reported (Savely et al., 2006, Am J Clin Dermatol, 7:1–6), further research will be needed to help resolve the validity of Morgellons disease. Until then, whether Morgellons disease is another name for delusional parasitosis or a real disease entity with a biologic or physiologic basis will remain up in the air.

The main purported symptom of Morgellons is "a fixed belief" that fibers are embedded in or extruding from the skin. The Morgellons Research Foundation claims patients have reported additional—though unsubstantiated—symptoms, including:

1. Formication, the sensation of insects "moving, stinging or biting" beneath the skin
2. Skin lesions, both spontaneous and self-inflicted
3. Musculoskeletal effects and pain, including joints, muscles, tendons and connective tissue
4. Disabling fatigue
5. Cognitive and emotional effects

William T. Harvey, director of the MRF medical advisory board, claimed in 2007 that Morgellons patients exhibit laboratory findings including increased levels of inflammatory cytokines, increased insulin, and antibodies to three bacterial pathogens, but did not provide evidence for these claims. Many Morgellons patients have symptoms that are also consistent with chronic fatigue syndrome, depression, obsessive–compulsive disorder, and attention deficit disorder. Rhonda Casey, chief of pediatrics at OSU Medical Center, while working with the OSU-CHS for the Investigation of Morgellons Disease, stated that her Morgellons patients looked ill with neurological symptoms, which included confusion, difficulty walking and controlling their feet (foot drop), and a sagging mouth when speaking. The OSU-CHS has issued a list of symptoms similar to that of the MRF.

Causes & Pathophysiology

Delusional Parasitosis and other Neuropsychological Disorders
Most dermatologists, psychiatrists, and other medical professionals view Morgellons as a new name for a well established condition, delusional parasitosis, also known as "delusions of parasitosis" (DP or DOP) and Ekbom's Syndrome: Morgellons is "a pattern of dermatologic symptoms very similar, if not identical, to those of delusions of parasitosis," and "the vast majority" (elsewhere, 95%) of Morgellons patients are

diagnosed with delusional parasitosis or another psychosomatic illness. This explanation is, however, "unpopular among individuals identifying themselves as having Morgellons disease."

In delusional parasitosis, patients hold a delusional belief that they are infested with parasites. They may experience formication, a sensation similar to that of insects crawling on or under the skin. Individuals suffering from this condition may develop elaborate rituals of inspection and cleansing to locate and remove "parasites" and fibers, resulting in a form of self-mutilation; they injure themselves in attempts to be rid of the "parasites" by picking at the skin, causing lesions, and then pick at the lesions, preventing them from healing. Patients with delusional parasitosis often present at the doctor's office with what MDs term the "matchbox sign" -- a medical sign characterized by the patient making collections of fibers and other foreign objects supposedly retrieved from the skin -- and, because of "unshakeable delusional ideation", strongly reject diagnoses that do not involve parasites. A significant minority of DP cases occur in groups of two, three, or more individuals in close proximity, even families, known by the French terms folie à deux, folie à trois, and folie à famille. Delusional parasitosis, with symptoms that have "extraordinary similarities" to Morgellons, has been described in the medical literature for over 75 years. Dr. Noah Craft, a dermatologist at the Harbor-UCLA Medical Center, Torrance, CA, has seen a handful of Morgellons patients and biopsied their skin lesions, but found only normal skin and inflammation, as one would find in a bump that has been picked at.

Some cases of delusional parasitosis have organic causes other than those associated with neurological/psychological conditions of unknown etiology. For example, formication, the sensation that bugs are crawling under one's skin, can be caused by allergies, diabetic neuropathy, menopause, skin cancer, demodex mites, stimulant drug abuse or herpes zoster. Both dementia and mental retardation have been reported in association with DP.^Symptoms associated with delusional parasitosis, including urticaria (hives), paresthesia (unexplained tingling sensations in the skin), and pruritus are common side-effects of many prescription drugs or drug abuse. The sensations are real, but the attribution of the sensations to unknown parasites and the collection of fibers is part of the delusion.

The MRF's William Harvey has written that non-healing "Morgellons lesions" have been found on infants' bodies in locations that the infants cannot themselves reach to scratch.

Some cases of Morgellons have been diagnosed as "cutaneous dysaesthesia".

Role of the Internet

Morgellons patients usually self-diagnose with the Internet and find support and confirmation in on-line communities of people with similar illness beliefs. In 2006, Waddell and Burke reported the influence of the Internet on their self-diagnosed Morgellons patients: "physicians are becoming more and more challenged by the many persons who attempt self-diagnosis on-line. In many cases, these attempts are well-intentioned, yet wrong, and a patient's belief in some of these oftentimes unscientific sites online may preclude their trust in the evidence-based approaches and treatment recommendations of their physician." Dermatologist Caroline Koblenzer specifically faults the MRF website for misleading patients: "Clearly, as more and more of our patients discover this site (MRF), there will be an ever greater waste of valuable time and resources on fruitless research into fibers, fluffs, irrelevant bacteria, and innocuous worms and insects." Vila-Rodriguez and MacEwan said in the American Journal of Psychiatry that the Internet is important in spreading and supporting "bizarre" disease beliefs, because "a belief is not considered delusional if it is accepted by other members of an individual's culture or subculture."

The LA Times, in an article on Morgellons, notes that "(t)he recent upsurge in symptoms can be traced directly to the Internet, following the naming of the disease by Mary Leitao, a Pennsylvania mother." Robert Bartholomew, a sociologist who has studied the Morgellons phenomenon, states that the "World Wide Web has become the incubator for mass delusion and it (Morgellons) seems to be a socially transmitted disease over the Internet." According to this hypothesis, patients with delusions of parasitosis and other psychological disorders become convinced they have "Morgellons" after reading internet accounts of others with similar symptoms. A 2005 Popular Mechanics article stated that Morgellons symptoms are well-known and characterized in the context of other disorders, and that "widespread reports of the strange fibers date back" only a few years to when the MRF first described them on the

Internet.

The Dallas Observer writes that Morgellons may be spread via the Internet and mass media, and "(i)f this is the case, then Morgellons is one in a long line of weird diseases that have swept through populations, only to disappear without a trace once public concern subsides." The article draws parallels to several mass media-spread mass delusions. An article in the journal Psychosomatics in 2009 similarly asserts that Morgellons is an Internet meme.

In 2008 the Washington Post Magazine reported that Internet discussions about Morgellons include many conspiracy theories about the cause, including biological warfare, nanotechnology, chemtrails and extraterrestrial life.

Known Skin Conditions

Some cases of self-diagnosed Morgellons disease are actually other recognized skin disorders, including allergic dermatitis, contact dermatitis, idiopathic urticaria and infestation with the parasite scabies. There are also case reports of patients submitting self-dissected superficial nerves.

Hypotheses about the Fibers

Randy Wymore, a former research director of the MRF and presently director of the Oklahoma State University Center for Health Sciences' Center for the Investigation of Morgellons Disease, claims that Morgellons patients have submitted masses of dark fibers visible at 60x magnification under the unbroken skin, while unaffected individuals do not. Wymore sent samples of fibers, none of which was collected by biopsy, to the Police Crime Lab in Tulsa, Oklahoma, for analysis. A forensic scientist at the Tulsa Police Crime Lab in Oklahoma searched the FBI's national database, but the Morgellons sample did not match any known fiber in the database. Lab director Mark Boese said the fibers were "consistent with something that the body may be producing," adding, "These fibers cannot be manmade and do not come from a plant. This could be a byproduct of a biological organism."

Dermatologists say many fibers are from clothing embedded in self-imposed sores and the fibers patients bring in bags are textile in nature. The fibers may also be peripheral nerve endings.

One sufferer, who happened to be a general practitioner in England, was able to extract tropical rat mites from his skin. "What these mites do is go in through the hair follicles and find a blood vessel at the bottom. That's where they sit and that's what the 'fibres' are – their legs folded back."

Bacterial Hypothesis

Three members of the Morgellons Research Foundation, including Raphael Stricker, Director and former President of the International Lyme and Associated Diseases Society (ILADS), and Ginger Savely, also an ILADS member, authored an article about Morgellons published by the American Journal of Clinical Dermatology in early 2006. The authors wrote that "Morgellons disease may be linked to an undefined infectious process," and reported that many patients with Morgellons disease have positive Western blots for Borrelia burgdorferi, the causative agent of Lyme disease, and treatment with anti-bacterials appropriate for Lyme disease leads to remission of Morgellons symptoms in most patients; however, no methodology or clinical data are provided in support of any of these claims. Stricker, along with Citovsky, MRF board member from the State University of New York at Stony Brook, claimed that Morgellons skin fibers could come fromAgrobacterium, a plant-infecting organism known to induce cellulose fibers at infected sites within plant tissues. Agrobacterium is already known to be responsible for opportunistic infections in humans with weakened immune systems, but has not been shown to be a primary pathogen in otherwise healthy individuals.

Environmental Toxins

Richard Fagerlund, an entomologist who has a column titled "Ask the Bugman" in the San Francisco Chronicle and Albuquerque Journal, stated that he takes Morgellons disease seriously, and he receives letters from people with Morgellons symptoms daily. Twenty years ago, he got three to four letters like this a year. He believes the condition is reaching epidemic proportions and speculates only a small

percentage of cases are delusional parasitosis, while the rest may be caused by something else, such as pollutants, especially pesticides.

Treatment

Treatment for Delusional Parasitosis
Many dermatologists treat Morgellons as delusional parasitosis. After a thorough medical examination to rule out known organic causes for the symptoms, delusional parasitosis patients are typically prescribed one of several typical antipsychoticdrugs. In the past, pimozide was the drug of choice; in addition to antipsychotic activity, it also has antipruritic activity, meaning it inhibits the sensation of itching. However, pimozide requires frequent electrocardiographic monitoring. Currently, atypical antipsychotics such as olanzapine or risperidone are used as first line treatment. Antipsychotics are effective at treating delusional parasitosis at doses as low as one-fifth to one-tenth the dose typically prescribed for schizophrenia. It is common for patients who believe they have Morgellons to reject a physician's diagnosis of delusional parasitosis. It has been suggested that the term Morgellons should be adopted by dermatologists to enhance theirrapport with their patients, allowing them to overcome this resistance.

Treatment for Infectious Disease
People who say they have Morgellons frequently reject the diagnosis of delusional parasitosis, "report that their symptoms are not taken seriously," and refuse psychotropic medicine. Randy Wymore, a former MRF director, has claimed on his website that some Morgellons patients who test positive for Lyme disease obtain symptom relief using aggressive, long-term antibiotic treatment similar to what is used by some doctors to treat "chronic" Lyme disease, another proposed but medically disputed condition. Virginia Savely, a nurse with the MRF and member of the International Lyme and Associated Diseases Society (ILADS), claims to have similar unpublished results. The antibiotic treatment is not curative, because when it is discontinued, the symptoms return. Dermatologists say that these positive effects of antibiotic use for some patients are likely the result of a placebo effect or anti-inflammatory actions of the drugs. They advise against prescribing antibiotics, which may reinforce the patients' delusions instead of addressing what these doctors consider the core problem: delusional parasitosis. In addition, long-term antibiotic use can have serious side effects.

Self-Treatment
Persons with Morgellons symptoms may turn to alternative remedies described on web sites and discussion groups. Some treatments are dangerous, however, and have included the use of bleach, veterinary medicines intended for deworming horses, and industrial insecticides (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Ectromelia Virus
Date: 2012
Source: Wikipedia

Abstract: Ectromelia virus (ECTV) is a virus of the family Poxviridae and the genus Orthopoxvirus that causes mousepox, a disease of mice. It has only been seen in mouse colonies kept for research purposes. Mousepox causes skin lesions and generalized disease, which can be fatal. It is the only poxvirus to cause disease naturally in mice (Wikipedia, 2012).

Title: Mousepox As Bioweapons
Date: February 2001
Source: Free Republic

Abstract:

Introduction
Periodic mouse plagues that occur in rural areas can eat their way through thousands of hectares of crops. Combating these plagues usually involves air drops of poisoned baits. Whilst this is sometimes effective, a more reliable and specific method of controlling mouse populations is needed.

So scientists at Canberra's Co-operative Research Centre (CRC) for the Biological Control of Pest Animals teamed up with the John Curtin School of Medical Research at the Australian National University in Canberra to create a strain of the mousepox virus that would cause sterility in female mice.

The Poxviridae
Mousepox is a virus that belongs to a family of viruses known as the Poxviridae. They are double-stranded DNA viruses. The pox viruses take their name from the pustules (pocks) that erupt on the skin of infected organisms. These pustules contain fluid teaming with newly made virus particles. Physical contact is the primary mode of transmission of the virus. They are a significant family of viruses in that there is a pox virus for just about every mammal you can think of - foulpox, camelpox, mousepox, cowpox, monkeypox, chickenpox, swinepox, foxpox, sealpox, dolphinpox kangaroopox and many many more. There are also pox viruses for invertebrates. Most pox viruses are specific for their host, although there are examples of pox viruses that can infect multiple species. There are around 20 pox viruses that can infect humans. The most common and well known is chickenpox. The name is misleading in that it is not a chicken virus, it is a human virus known as the Varicella Zoster virus.

For the most part, pox viruses cause relatively minor infections that leave the organism immune to future infections. There are some notable exceptions to this generalisation. The Varicella Zoster virus can cause chickenpox (mostly in childhood) but can recur later in life and cause the painful condition known as Shingles. The biggest exception is a virus known as the Variola virus. This causes an infection known as smallpox, one of history's deadliest diseases. Smallpox was one of the most contagious and virulent

diseases ever known. It killed countless millions across the world, especially in Europe, India and China. The Pharaoh Ramses V died of smallpox in 1157 BC. The disease reached Europe in 710 AD and was transferred to America by Hernando Cortez in 1520. 3.5 million Aztecs died in the next 2 years. In the cities of 18th century Europe, smallpox reached plague proportions and was a feared scourge. Five reigning European monarchs died from smallpox during the 18th century. In Europe, nearly everyone caught it at some stage in their lives. About 10-20% of infected people died as a result. Of the survivors, around 15% were permanently disfigured by the scars left from the pustules that covered the body. The English physician Edward Jenner developed the first smallpox vaccine 1798 by discovering that inoculating people with cowpox stimulated immunity to both cowpox and smallpox. Jenner coined the terms "vaccination" and "vaccine" from the name for the cowpox virus (the Vaccinia virus), which in turn comes from the Latin for cow (vacca). Since then better smallpox vaccines have been developed. The World Health Organization's world-wide smallpox vaccination campaign has resulted in the eradication of the disease. The last recorded case was in Somalia in 1977. Samples of the smallpox virus are kept in various high-security laboratories in the USA and Russia.

The Experiment

The scientists genetically engineered a mousepox virus to carry the mouse egg shell protein ZP3, or zona pellucida 3, as a mouse contraceptive. The reasoning was that by infecting mice with the engineered virus, the mice would contract a mild mousepox infection and launch an immune response to the virus. But the virus expresses the mouse egg protein, so infected mice would not only make antibodies against the virus, but also against the egg protein. In females, these anti-ZP3 antibodies would then attack their own eggs in their ovaries and cause sterility whilst leaving the mice healthy (once they recovered from the mild mousepox disease) and free to mate with males. Thus, these sterile females would "dilute out" the effectiveness of breeding males in a population. This was the theory and it seemed to work quite well in one laboratory strain of mouse, but in other strains it was ineffective. If the virus is to be useful in the wild then it will have to be able to work across different strains of mice.

In order to try and make the engineered virus more effective across different strains, the scientists inserted another gene into the virus - the interleukin-4 gene (IL-4). This gene codes for a cytokine (or hormone) that is one of the many that regulate the functioning of the immune system. There was previous work that suggested a virus expressing IL-4 would increase the antibody-producing response in mice and tone down the effectiveness of virus-clearing cells of the immune system (called "killer T-cells"). It was hoped that this would increase the immune response to the ZP3 protein and make the virus an effective contraceptive across multiple strains of mice.

The results from the newly engineered mousepox virus were very unexpected. They expected only to strengthen the antibody response in resistant strains, but instead the virus overwhelmed the mice, proliferating out of control and destroying their livers. Even mice that had been vaccinated against mousepox (which is normally extremely effective at conferring resistance) fared poorly, with half dying immediately and the remainder developing a chronic abscess at the site of infection.

The Implications

On a virology and immunology level, this is a very interesting result. But the implications go far beyond that. The goal of the research was certainly benign, but the study provided the first evidence to suggest that all it takes to transform an innocuous virus into a deadly virus is the insertion of a single gene. Something that was thought to be hard - increasing the pathogenicity of a virus - appears, in this case, to be easy. This has some alarming implications for the development of biological weapons. Up until now the concerns regarding biological weapons centred on the use of existing pathogens. A terrorist's ultimate aim would be to obtain a sample of smallpox. It has been 23 years since anyone's immune system has seen the smallpox virus. Smallpox vaccination is no longer included in the standard course of childhood vaccinations, and stocks of the vaccine are low. But smallpox is very difficult to obtain, so the next best options are bacterial pathogens - Bacillus anthracis(which causes Anthrax) and Yersinia pestis (which causes The Plague). However, when it comes to the large scale production of these pathogens, biological weapons inspectors know what to look for. The specific facilities and reagents needed are a dead give-away. The mousepox result, however, may indicate that commonly used technology found in any biotechnology laboratory in the world could be used to create new viruses that overwhelm resistance and

render vaccination useless. The close relationship between the pox viruses raises the question as to whether it would be possible to transform other members of the family, including those that infect humans. By inserting IL-4 into chickenpox, would it be possible to transform chickenpox into a virus that is more deadly than smallpox?

The team spent 18 months confirming the data and debating whether to go public with them. In the end, disclosure won out over concerns about educating future bioterrorists and alarming the public. In an interesting twist, on publication of the results it was not environmentalists or media commentators that were sounding the warning, but the scientists themselves. On 16 January the CRC issued a press release timed to accompany the article that pleaded for stronger measures to combat the threat of biowarfare arising from such good intentions. Not surprisingly, the press release triggered sensational warnings in the Australian media and elsewhere. The scientists said that it should serve as a warning to the community to be more aware of the potentially harmful consequences of their work. "We need the public to trust us if we are going to seek their approval to release pest-control viruses down the track," says CRC director Bob Seamark, who led the research. But any intentional release, he hastens to add, won't involve viruses carrying the IL-4 gene. "These are confined to the high-security lab."

Despite the warnings, it's not clear whether the unexpected result, which turned a vector into a potent killer, could be duplicated in viruses that affect humans. Such fears may be overrated, says Ron Jackson, the CRC virologist who carried out much of the work. Jackson suspects that the findings may be peculiar to the mousepox virus, which naturally carries other proteins that weaken the antiviral response. He notes that the same result did not occur with the vaccinia virus (cowpox) in other experiments.

Deterring Bioweapons Development
The implications of this finding are of intense interest to organizations such as the Federation of American Scientists, which has formed a working group to develop a protocol that would add verification powers to the currently toothless international convention on biological weapons - the 1975 Biological and Toxin Weapons Convention (BTWC).

The emerging fields of genomics and proteomics holds great potential for the development of new useful biological reagents, but many of these will also have utility as biological weapons, or will suggest ways of creating such weapons. The treaty does not prohibit research, but it does prohibit the development, production, or stockpiling of biological or toxic agents and of devices to deliver such agents for other than peaceful purposes. However, with no provisions for verification, the treaty has proved to be a weak deterrent to nations committed to biological weapons development.

For this reason, an addendum to the BTWC has been negotiated over the past five years. The addendum calls for:

1. Annual declarations of facilities with the potential for use in a biological weapons program.
2. Random visits to such facilities by teams of international inspectors.
3. Establishing a mechanism for investigation of suspicions of violation of the BTWC.

Its adoption would significantly improve international security and reduce the risk of bioterrorism by inhibiting bioweapons development. The United States, however, has consistently delayed progress and pressed for a weakening of the new provisions, and now might completely derail the negotiations by stalling past the deadline imposed for completion of the addendum (Free Republic, 2001).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Methicillin-Resistant Staphylococcus Aureus
Date: 2012
Source: Wikipedia

Abstract: Methicillin-resistant Staphylococcus aureus (MRSA) is a bacterium responsible for several difficult-to-treat infections in humans. It is also called multidrug-resistant Staphylococcus aureus and oxacillin-resistant Staphylococcus aureus (ORSA). MRSA is any strain of Staphylococcus aureus that has developed resistance to beta-lactam antibiotics, which include the penicillins (methicillin, dicloxacillin, nafcillin, oxacillin, etc.) and the cephalosporins. The development of such resistance does not cause the organism to be more intrinsically virulent than strains of Staphylococcus aureus that have no antibiotic resistance, but resistance does make MRSA infection more difficult to treat with standard types of antibiotics and thus more dangerous. MRSA is especially troublesome in hospitals and nursing homes, where patients with open wounds, invasive devices, and weakened immune systems are at greater risk of infection than the general public

Signs & Symptoms
S. aureus most commonly colonizes the anterior nares (the nostrils). The rest of the respiratory tract, open wounds, intravenous catheters, and the urinary tract are also potential sites for infection. Healthy individuals may carry MRSA asymptomatically for periods ranging from a few weeks to many years. Patients with compromised immune systems are at a significantly greater risk of symptomatic secondary infection.

In most patients, MRSA can be detected by swabbing the nostrils and isolating the bacteria found inside. Combined with extra sanitary measures for those in contact with infected patients, screening patients admitted to hospitals has been found to be effective in minimizing the spread of MRSA in hospitals in the United States, Denmark, Finland, and the Netherlands.

MRSA may progress substantially within 24–48 hours of initial topical symptoms. After 72 hours, MRSA can take hold in human tissues and eventually become resistant to treatment. The initial presentation of MRSA is small red bumps that resemble pimples, spider bites, or boils; they may be accompanied by fever and, occasionally, rashes. Within a few days, the bumps become larger and more painful; they eventually open into deep, pus-filled boils. About 75 percent of community-associated (CA-) MRSA infections are localized to skin and soft tissue and usually can be treated effectively. But some CA-MRSA strains display enhanced virulence, spreading more rapidly and causing illness much more severe than traditional healthcare-associated (HA-) MRSA infections, and they can affect vital organs and lead to widespread infection (sepsis), toxic shock syndrome, and necrotizing ("flesh-eating") pneumonia. This is thought to be due to toxins carried by CA-MRSA strains, such as PVL and PSM, though PVL was recently found to not be a factor in a study by the National Institute of Allergy and Infectious Diseases (NIAID) at the NIH. It is not known why some healthy people develop CA-MRSA skin infections that are treatable while others infected with the same strain develop severe infections or die.

The most common manifestations of CA-MRSA are skin infections, such as necrotizing fasciitis and pyomyositis (most commonly found in the tropics), necrotizing pneumonia, infective endocarditis (which affects the valves of the heart), and bone and joint infections. CA-MRSA often results in abscess formation that requires incision and drainage. Before the spread of MRSA into the community, abscesses were not considered contagious, because it was assumed that infection required violation of skin integrity and the introduction of staphylococci from normal skin colonization. However, newly emerging CA-MRSA is transmissible (similar, but with very important differences) from Hospital-Associated MRSA. CA-MRSA is less likely than other forms of MRSA to cause cellulitis.

Risk Factors

Some of the populations at risk:

1. People with weak immune systems (people living with HIV/AIDS, people living with lupus, cancer patients, transplant recipients, severe asthmatics, etc.)
2. Diabetics
3. Intravenous drug users
4. Users of quinolone antibiotics
5. Young children
6. The elderly
7. College students living in dormitories
8. People staying or working in a health care facility for an extended period of time
9. People who spend time in coastal waters where MRSA is present, such as some beaches in Florida and the west coast of the United States
10. People who spend time in confined spaces with other people, including occupants of homeless shelters and warming centers, prison inmates, military recruits in basic training, and individuals who spend considerable time in change roomsor gyms.

Hospital Patients
Many MRSA infections occur in hospitals and healthcare facilities, with a higher incidence rate in nursing homes or long-term care facilities. When infections occur in this manner it is known as healthcare acquired MRSA or HA-MRSA. These Rates of MRSA infection are also increased in hospitalized patients who are treated with quinolones. Healthcare provider-to-patient transfer is common, especially when healthcare providers move from patient to patient without performing necessary hand-washing techniques between patients.

Prison Inmates
In confined environments such as prisons, with continual admission of new members who may typically be in poor health and adopt poor hygiene practices, there have been a number of challenges reported first in the U.S. and then in Canada. The earliest reports were made by the CDC in state prisons. Subsequently reports of a massive rise in skin and soft tissue infections were reported by the CDC in the Los Angeles County Jail system in 2001, and this has continued. Pan et al. reported on the changing epidemiology of MRSA skin infection in the San Francisco County Jail, noting the MRSA accounted for more than 70% of S. aureus infection in the jail by 2002. Lowy and colleagues reported on frequent MRSA skin infections in New York State Prisons. Two reports on inmates in Maryland have demonstrated frequent colonization with MRSA.

In the news media hundreds of reports of MRSA outbreaks in prisons appeared between 2000 and 2008. For example, in February 2008, The Tulsa County Jail in the U.S. State of Oklahoma started treating an average of twelve Staphylococcus cases per month. A report on skin and soft tissue infections in the Cook County Jail in Chicago in 2004–05 demonstrated that MRSA was the most common cause of these infections among cultured lesions and furthermore that few risk factors were more strongly associated with MRSA infections than infections caused by methicillin-susceptible S. aureus. In response to these and many other reports on MRSA infections among incarcerated and recently incarcerated persons, the Federal Bureau of Prisons has released guidelines for the management and control of the infections

although few studies provide an evidence base for these guidelines.

People in Contact with Live Food-Producing Animals
Cases of MRSA have increased in livestock animals. CC398 is a new clone of MRSA that has emerged in animals and is found in intensively reared production animals (primarily pigs, but also cattle and poultry), where it can be transmitted to humans. Though dangerous to humans, CC398 is often asymptomatic in food-producing animals.

A 2011 study reported 47% of the meat and poultry sold in surveyed U.S. grocery stores was contaminated with S. aureus and, of those, 52%—or 24.4% of the total—were resistant to at least three classes of antibiotics. "Now we need to determine what this means in terms of risk to the consumer," said Dr. Keim, a co-author of the paper. Some samples of commercially sold meat products in Japan were also found to harbor MRSA strains.

Athletes
In the United States, there have been increasing numbers of reports of outbreaks of MRSA colonization and infection through skin contact in locker rooms and gyms, even among healthy populations. A study published in the New England Journal of Medicine linked MRSA to the abrasions caused by artificial turf. Three studies by the Texas State Department of Health found that the infection rate among football players was 16 times the national average. In October 2006, a high school football player was temporarily paralyzed from MRSA-infected turf burns. His infection returned in January 2007 and required three surgeries to remove infected tissue, as well as three weeks of hospital stay.

Children
MRSA is also becoming a problem in pediatric settings, including hospital nurseries. A 2007 study found that 4.6% of patients in U.S. health care facilities were infected or colonized with MRSA.

Diagnosis
Diagnostic microbiology laboratories and reference laboratories are key for identifying outbreaks of MRSA. New rapid techniques for the identification and characterization of MRSA have been developed. This notwithstanding, the bacterium generally must be cultured via blood, urine, sputum, santorum, or other body fluid cultures, and grown up in the lab in sufficient numbers to perform these confirmatory tests first, so there is no quick and easy method to diagnose a MRSA infection. Therefore, initial treatment is often based upon 'strong suspicion' by the treating physician, since any delay in treating this type of infection can have fatal consequences. These techniques include Real-time PCR and Quantitative PCR and are increasingly being employed in clinical laboratories for the rapid detection and identification of MRSA strains.

Another common laboratory test is a rapid latex agglutination test that detects the PBP2a protein. PBP2a is a variant penicillin-binding protein that imparts the ability of S. aureus to be resistant to oxacillin.

Genetics
Antimicrobial resistance is genetically based; resistance is mediated by the acquisition of extrachromosomal genetic elements containing resistance genes. Exemplary are plasmids, transposable genetic elements, and genomic islands, which are transferred between bacteria via horizontal gene transfer. A defining characteristic of MRSA is its ability to thrive in the presence ofpenicillin-like antibiotics, which normally prevent bacterial growth by inhibiting synthesis of cell wall material. This is due to a resistance gene, mecA, which stops β-lactam antibiotics from inactivating the enzymes (transpeptidases) that are critical for cell wall synthesis.

SCCmec
Staphylococcal cassete chromosome mec (SCCmec) is a genomic island of unknown origin containing the antibiotic resistance gene mecA. SCCmec contains additional genes beyond mecA, including the cytolysin gene psm-mec, which may suppress virulence in hospital-acquired MRSA strains. SCCmec also contains ccrA and ccrB; both genes encode recombinases that mediate the site-specific integration and excision of the SCCmec element from the S. aureuschromosome. Currently, six unique SCCmec

types ranging in size from 21-67 kb have been identified; they are designated types I-VI and are distinguished by variation in mec and ccr gene complexes. Owing to the size of the SCCmec element and the constraints of horizontal gene transfer, a limited number of clones is thought to be responsible for the spread of MRSA infections.

Different SCCmec genotypes confer different microbiological characteristics, such as different antimicrobial resistance rates. Different genotypes are also associated with different types of infections. Types I-III SCCmec are large elements that typically contain additional resistance genes and are characteristically isolated from HA-MRSA strains. Conversely, CA-MRSA is associated with types IV and V, which are smaller and lack resistance genes other than mecA.

mecA

mecA is responsible for resistance to methicillin and other β-lactam antibiotics. After acquisition of mecA, the gene must be integrated and localized in the S. aureus chromosome. mecA encodes penicillin-binding protein 2a (PBP2a), which differs from other penicillin-binding proteins as its active site does not bind methicillin or other β-lactam antibiotics. As such, PBP2a can continue to catalyze the transpeptidation reaction required for peptidoglycan cross-linking, enabling cell wall synthesis in the presence of antibiotics. As a consequence of the inability of PBP2a to interact with β-lactam moieties, acquisition of mecA confers resistance to all β-lactam antibiotics in addition to methicillin.

mecA is under the control of two regulatory genes, mecI and mecR1. MecI is usually bound to the mecA promoter and functions as a repressor. In the presence of a β-lactam antibiotic, MecR1 initiates a signal transduction cascade that leads to transcriptional activation of mecA. This is achieved by MecR1-mediated cleavage of MecI, which alleviates MecI repression. mecA is further controlled by two co-repressors, BlaI and BlaR1. blaI and blaR1 are homologous tomecI and mecR1, respectively, and normally function as regulators of blaZ, which is responsible for penicillin resistance. The DNA sequences bound by MecI and BlaI are identical; therefore, BlaI can also bind the mecA operator to repress transcription of mecA.

Strains

Diagram depicting antibiotic resistance through alteration of the antibiotic's target site, modeled after MRSA's resistance to penicillin. Beta-lactam antibiotics permanently inactivate PBP enzymes, which are essential for bacterial life, by permanently binding to their active sites. Some forms ofMRSA, however, expresses a PBP that will not allow the antibiotic into its active site.

Acquisition of SCCmec in methicillin-sensitive staphylococcus aureus (MSSA) gives rise to a number of genetically different MRSA lineages. These genetic variations within different MRSA strains possibly explain the variability in virulence and associated MRSA infections. The first MRSA strain, ST250 MRSA-1 originated from SCCmec and ST250-MSSA integration.Historically, major MRSA clones: ST2470-MRSA-I, ST239-MRSA-III, ST5-MRSA-II, and ST5-MRSA-IV were responsible for causing hospital-acquired MRSA (HA-MRSA) infections. ST239-MRSA-III, known as the Brazilian clone, was highly transmissible compared to others and distributed in Argentina, Czech Republic, and Portugal.

In the UK, where MRSA is commonly called "Golden Staph", the most common strains of MRSA are EMRSA15 and EMRSA16. EMRSA16 is the best described epidemiologically: it originated inKettering, England, and the full genomic sequence of this strain has been published. EMRSA16 has been found to be identical to the ST36:USA200 strain, which circulates in the United States, and to carry the SCCmec type II, enterotoxin A and toxic shock syndrome toxin 1 genes. Under the new international typing system, this strain is now called MRSA252. EMRSA 15 is also found to be one of the common MRSA strains in Asia. Other common strains include ST5:USA100 and EMRSA 1. These strains are genetic characteristics of HA-MRSA.

It is not entirely certain why some strains are highly transmissible and persistent in healthcare facilities. One explanation is the characteristic pattern of antibiotic susceptibility. Both the EMRSA15 and EMRSA16 strains are resistant to erythromycin and ciprofloxacin. It is known that Staphylococcus aureus can survive intracellularly, for example in the nasal mucosa and in the tonsil tissue. Erythromycin and

Ciprofloxacin are precisely the antibiotics that best penetrate intracellularly; it may be that these strains of S. aureus are therefore able to exploit an intracellular niche.

Community-acquired MRSA (CA-MRSA) strains emerged in late 1990 to 2000, infecting healthy people; who have not been in contact with health care facilities. Researchers suggests that CA-MRSA did not evolved from the HA-MRSA. This is further proven by molecular typing of CA-MRSA strains and genome comparison between CA-MRSA and HA-MRSA, which indicate that novel MRSA strains integrated SCCmec into MSSA separately on its own. By mid 2000, CA-MRSA is introduced into the health care systems and distinguishing between CA-MRSA from HA-MRSA became a difficult process. Community-acquired MRSA (CA-MRSA) is more easily treated and more virulent, than hospital-acquired MRSA (HA-MRSA). The genetic mechanism for the enhanced virulence in CA-MRSA remains as an active area of research. Especially, the Panton-Valentine leukocidin (PVL) genes are of interest because they are a unique feature of CA-MRSA.

In the United States, most cases of CA-MRSA are caused by a CC8 strain designated ST8:USA300, which carries SCCmec type IV, Panton-Valentine leukocidin, PSM-alpha and enterotoxins Q and K, and ST1:USA400. ST8:USA300 strain results in skin infections, necrotizing fasciitis, toxic shock syndrome. Whereas, ST1:USA400 strain results in necrotizing pneumonia and pulmonary sepsis. Other community-acquired strains of MRSA are ST8:USA500 and ST59:USA1000. In many nations of the world, MRSA strains with different predominant genetic background types have come to predominate among CA-MRSA strains; USA300 easily tops the list in the U. S. and is becoming more common in Canada after its first appearance there in 2004. For example, in Australia ST93 strains are common, while in continental Europe ST80 strains predominate (Tristan et al., Emerging Infectious Diseases, 2006), which carries SCCmec type IV. In Taiwan, ST59 strains, some of which are resistant to many non-beta-lactam antibiotics, have arisen as common causes of skin and soft tissue infections in the community. In a remote region of Alaska, unlike most of the continental U. S., USA300 was found rarely in a study of MRSA strains from outbreaks in 1996 and 2000 as well as in surveillance from 2004–06 (David et al., Emerg Infect Dis 2008).

In June 2011, the discovery of a new strain of MRSA was announced by two separate teams of researchers in the UK. Its genetic make-up was reportedly more similar to strains found in animals, and testing kits designed to detect MRSA were unable to identify it. This MRSA strain, Clonal Complex 398 (CC398), is responsible for Livestock-associated MRSA (LA-MRSA) infections. Although it is known to be more persistent in colonizing pigs and calves, there has been cases of LA-MRSA carriers with pneumonia, endocarditis, and necrotising fasciitis.

Prevention

Screening Programs
Patient screening upon hospital admission, with nasal cultures, prevents the cohabitation of MRSA carriers with non-carriers, and exposure to infected surfaces. The test used (whether a rapid molecular method or traditional culture) is not as important as the implementation of active screening. n the United States and Canada, the Centers for Disease Control and Prevention issued guidelines on October 19, 2006, citing the need for additional research, but declined to recommend such screening.

In some UK hospitals screening for MRSA is performed in every patient and all NHS surgical patients, except for minor surgeries, are previously checked for MRSA. There is no community screening in the UK however screening of individuals is offered by some private companies.

In a US cohort of 1300 healthy children, 2.4% carried MRSA in their nose.

Surface Sanitizing
Alcohol has been proven to be an effective surface sanitizer against MRSA. Quaternary ammonium can be used in conjunction with alcohol to extend the longevity of the sanitizing action. The prevention of nosocomial infections involves routine and terminal cleaning. Non-flammable Alcohol Vapor in Carbon Dioxide systems (NAV-CO2) do not corrode metals or plastics used in medical environments and do not

contribute to antibacterial resistance.

In healthcare environments, MRSA can survive on surfaces and fabrics, including privacy curtains or garments worn by care providers. Complete surface sanitation is necessary to eliminate MRSA in areas where patients are recovering from invasive procedures. Testing patients for MRSA upon admission, isolating MRSA-positive patients, decolonization of MRSA-positive patients, and terminal cleaning of patients' rooms and all other clinical areas they occupy is the current best practice protocol for nosocomial MRSA.

Studies published from 2004-2007 reported hydrogen peroxide vapor could be used to decontaminate busy hospital rooms, despite taking significantly longer than traditional cleaning. One study noted rapid recontamination by MRSA following the hydrogen peroxide application.

Also tested, in 2006, was a new type of surface cleaner, incorporating accelerated hydrogen peroxide, which was pronounced "a potential candidate" for use against the targeted microorganisms.

Hand Washing
In September 2004, after a successful pilot scheme to tackle MRSA, the UK National Health Service announced its Clean Your Hands campaign. Wards were required to ensure that alcohol-based hand rubs are placed near all beds so that staff can hand wash more regularly. It is thought that even if this cuts infection by no more than 1%, the plan will pay for itself many times over.

As with some other bacteria, MRSA is acquiring more resistance to some disinfectants and antiseptics. Although alcohol-based rubs remain somewhat effective, a more effective strategy is to wash hands with running water and an anti-microbial cleanser with persistent killing action, such as Chlorhexidine.

A June 2008 report, centered on a survey by the Association for Professionals in Infection Control and Epidemiology, concluded that poor hygiene habits remain the principal barrier to significant reductions in the spread of MRSA.

Use of Surgical Respirator
The U.S. Food and Drug Administration (FDA) announced on 8 April 2011 that it had cleared a novel type of N95 Surgical Respirator, the SpectraShield 9500, that kills methicillin-resistant Staphylococcus aureus, Streptococcus pyogenes andHaemophilus influenzae. This mask is manufactured by Nexera Medical Ltd. of Richmond, British Columbia The mask blocks at least 95% of small particles in a standardized test. The FDA clearance also included evaluation by the National Institute of Occupational Safety and Health.

Proper Disposal of Hospital Gowns
Used paper hospital gowns are associated with MRSA hospital infections, which could be avoided by proper disposal.

Isolation
Current US guidance does not require workers in the general workplace (excluding medical facilities) with MRSA infections to be routinely excluded from going to work. Therefore, unless directed by a health care provider, exclusion from work should be reserved for those with wound drainage that cannot be covered and contained with a clean, dry bandage and for those who cannot maintain good hygiene practices. Workers with active infections should be excluded from activities where skin-to-skin contact is likely to occur until their infections are healed. Health care workers should follow the Centers for Disease Control and Prevention's Guidelines for Infection Control in Health Care Personnel.

To prevent the spread of staph or MRSA in the workplace, employers should ensure the availability of adequate facilities and supplies that encourage workers to practice good hygiene; that surface sanitizing in the workplace is followed; and that contaminated equipment are sanitized with Environmental Protection Agency (EPA)-registered disinfectants.

Restricting Antibiotic Use
Glycopeptides, cephalosporins and in particular quinolones are associated with an increased risk of colonisation of MRSA. Reducing use of antibiotic classes that promote MRSA colonisation, especially fluoroquinolones, is recommended in current guidelines.

Public Health Considerations
Mathematical models describe one way in which a loss of infection control can occur after measures for screening and isolation seem to be effective for years, as happened in the UK. In the "search and destroy" strategy that was employed by all UK hospitals until the mid-1990s, all patients with MRSA were immediately isolated, and all staff were screened for MRSA and were prevented from working until they had completed a course of eradication therapy that was proven to work. Loss of control occurs because colonised patients are discharged back into the community and then readmitted; when the number of colonised patients in the community reaches a certain threshold, the "search and destroy" strategy is overwhelmed. One of the few countries not to have been overwhelmed by MRSA is the Netherlands: An important part of the success of the Dutch strategy may have been to attempt eradication of carriage upon discharge from hospital.

The Centers for Disease Control and Prevention (CDC) estimated that about 1.7 million nosocomial infections occurred in the United States in 2002, with 99,000 associated deaths. The estimated incidence is 4.5 nosocomial infections per 100 admissions, with direct costs (at 2004 prices) ranging from $10,500 (£5300, €8000 at 2006 rates) per case (for bloodstream, urinary tract, or respiratory infections in immunocompetent patients) to $111,000 (£57,000, €85,000) per case for antibiotic-resistant infections in the bloodstream in patients with transplants. With these numbers, conservative estimates of the total direct costs of nosocomial infections are above $17 billion. The reduction of such infections forms an important component of efforts to improve healthcare safety. (BMJ 2007) MRSA alone was associated with 8% of nosocomial infections reported to the CDC National Healthcare Safety Network from January 2006 to October 2007.

This problem is not unique to one country; the British National Audit Office estimated that the incidence of nosocomial infections in Europe ranges from 4% to 10% of all hospital admissions. As of early 2005, the number of deaths in the United Kingdom attributed to MRSA has been estimated by various sources to lie in the area of 3,000 per year. Staphylococcus bacteria account for almost half of all UK hospital infections. The issue of MRSA infections in hospitals has recently been a major political issue in the UK, playing a significant role in the debates over health policy in the United Kingdom general election held in 2005.

On January 6, 2008, half of 64 non-Chinese cases of MRSA infections in Hong Kong in 2007 were Filipino domestic helpers. Ho Pak-leung, professor of microbiology at the University of Hong Kong, traced the cause to high use of antibiotics. In 2007, there were 166 community cases in Hong Kong compared with 8,000 hospital-acquired MRSA case (155 recorded cases—91 involved Chinese locals, 33 Filipinos, 5 each for Americans and Indians, and 2 each from Nepal, Australia, Denmark and England).

Worldwide, an estimated 2 billion people carry some form of S. aureus; of these, up to 53 million (2.7% of carriers) are thought to carry MRSA. In the United States, 95 million carry S. aureus in their noses; of these, 2.5 million (2.6% of carriers) carry MRSA. A population review conducted in three U.S. communities showed the annual incidence of CA-MRSA during 2001–2002 to be 18–25.7/100,000; most CA-MRSA isolates were associated with clinically relevant infections, and 23% of patients required hospitalization.

One possible contribution to the increased spread of MRSA infections comes from the use of antibiotics in intensive pig farming. A 2008 study in Canada found MRSA in 10% of tested pork chops and ground pork; a U.S. study in the same year found MRSA in the noses of 70% of the tested farm pigs and in 45% of the tested pig farm workers. There have also been anecdotal reports of increased MRSA infection rates in rural communities with pig farms.

Healthcare facilities with high bed occupancy rates, high levels of temporary nursing staff, or low

cleanliness scores no longer have significantly higher MRSA rates. Simple tabular evidence helps provide a clear picture of these changes, showing, for instance, that hospitals with occupancy over 90% had, in 2006–2007, MRSA rates little above those in hospitals with occupancy below 85%, in contrast to the period 2001–2004. In one sense, the disappearance of these relationships is puzzling. Reporters now blame IV cannula and catheters for spreading MRSA in hospitals. (Hospital organisation and speciality mix, 2008).

Decolonization

Care should be taken when trying to drain boils, as disruption of surrounding tissue can lead to larger infections, or even infection of the blood stream (often with fatal consequences). Any drainage should be disposed of very carefully. After the drainage of boils or other treatment for MRSA, patients can shower at home using chlorhexidine (Hibiclens) or hexachlorophene (Phisohex) antiseptic soap (available over-the-counter at many pharmacies) from head to toe. Alternatively, a dilute bleach bath can be taken at a concentration of 1/2 cup bleach per 1/4-full bathtub of water. Care should be taken to use a clean towel, and to ensure that nasal discharge (i.e. snot) doesn't infect the towel (see below).

All infectious lesions should be kept covered with a dressing (band-aids etc.). Mupirocin (Bactroban) 2% ointment can be effective at reducing the size of lesions. A secondary covering of clothing is preferred.

The nose is a common refuge for MRSA, however a test swab can be taken of the nose to indicate whether MRSA is present. Mupirocin (Bactroban) 2% ointment can be applied inside each nostril twice daily for 7 days, using a cotton-tipped swab. However, care should be taken so that the swab doesn't penetrate into the sinus. Household members are recommended to follow the same decolonization protocol. After treatment, the nose should be swabbed again to ensure that the treatment was effective. If not, the process should be repeated.

Toilet seats are a common vector for infection, therefore the seat can be wiped clean before and/or after each use. Door handles, faucets, light switches (with care!), etc. can be disinfected daily (or regularly; use of disinfectant wipes is recommended). Spray disinfectants can be used on upholstery. Carpets can be washed with disinfectant, and hardwood floors can be scrubbed with diluted tea tree oil (e.g. Melaleuca). Laundry soap containing tea tree oil may be effective at decontaminating clothing and bedding, especially if hot water and heavy soil cycles are used, however tea tree oil may cause a rash which MRSA can re-colonize. Alcohol-based sanitizers can be placed near bedsides, near sitting areas, in vehicles etc. to encourage their use.

Doctors may also prescribe antibiotics such as clindamycin, doxycycline or trimethoprim/sulfamethoxazole. Although very few studies have shown that using more antibiotics actually has the effect of preventing recurrent MRSA skin infections, anecdotal evidence and common sense demonstrate that antibiotics reduce the size of any infections and therefore reduce the ability of MRSA to spread.

Treatment

Both CA-MRSA and HA-MRSA are resistant to traditional anti-staphylococcal beta-lactam antibiotics, such as cephalexin. CA-MRSA has a greater spectrum of antimicrobial susceptibility, including to sulfa drugs (like co-trimoxazole/trimethoprim-sulfamethoxazole), tetracyclines (like doxycycline and minocycline) and clindamycin, but the drug of choice for treating CA-MRSA is now believed to be vancomycin, according to a Henry Ford Hospital Study. Linezolid is now felt to be the best drug for treating patients with MRSA pneumonia. HA-MRSA is resistant even to these antibiotics and often is susceptible only to vancomycin. Newer drugs, such as linezolid (belonging to the newer oxazolidinones class) and daptomycin, are effective against both CA-MRSA and HA-MRSA. Ceftaroline and ceftabiparole, a new fifth generation cephalosporins, are the first beta-lactam antibiotics approved in the US to treat MRSA infections (skin and soft tissue only).

Vancomycin and teicoplanin are glycopeptide antibiotics used to treat MRSA infections. Teicoplanin is a structural congener of vancomycin that has a similar activity spectrum but a longer half-life. Because the oral absorption of vancomycin and teicoplanin is very low, these agents must be administered

intravenously to control systemic infections. Drugs are administered via a peripherally inserted central catheter, or a Picc Line, which is inserted by radiologists, doctors, physician assistants (in the U.S.), radiologist assistants (in the U.S.), or specially trained certified registered nurses. Treatment of MRSA infection with vancomycin can be complicated, due to its inconvenient route of administration. Moreover, many clinicians believe that the efficacy of vancomycin against MRSA is inferior to that of anti-staphylococcal beta-lactam antibiotics against methicillin-susceptible Staphylococcus aureus (MSSA).

Several newly discovered strains of MRSA show antibiotic resistance even to vancomycin and teicoplanin. These new evolutions of the MRSA bacterium have been dubbed Vancomycin intermediate-resistant Staphylococcus aureus(VISA). Linezolid, quinupristin/dalfopristin(synercid), daptomycin, and tigecycline are used to treat more severe infections that do not respond to glycopeptides such as vancomycin.

There have been claims that bacteriophage can be used to cure MRSA.

The psychedelic mushroom Psilocybe semilanceata has been shown to strongly inhibit the growth of Staphylococcus aureus.

Initial studies at the University of East London have demonstrated that allicin (a compound found in garlic) exhibits a strong antimicrobial response to the bacteria, indicating that it may one day lead to more effective treatments.

A report released in 2010 details the efficacy of the active ingredients of a new composite dressing (hydrogen peroxide, tobramycin, chlorhexidine digluconate, chlorhexidine gluconate, levofloxacin, and silver) against MRSA.

A 1990 study tested MRSA isolates obtained from veterans and found they could be killed by several substances, including bacitracin, nitrofurantoin, hydrogen peroxide, novobiocin, netilmicin and vancomycin. The study went on to conclude that netilmicin might be useful as an alternative to intravenous vancomycin, and suggested that topical applications of hydrogen peroxide may be useful to reduce MRSA on skin and some mucous membranes.

History

US & UK

In 1959 methicillin was licensed in England to treat penicillin-resistant S. aureus infections. Just as bacterial evolution had allowed microbes to develop resistance to penicillin, strains of S. aureusevolved to become resistant to methicillin. In 1961 the first MRSA isolates were reported in a British study, and between 1961-1967 there were infrequent hospital outbreaks in Western Europe and Australia. The first United States hospital outbreak of MRSA occurred at the Boston City Hospital in 1968. Between 1968-mid 1990s the percent of S. aureus infections that were caused by MRSA increased steadily, and MRSA became recognized as an endemic pathogen. In 1997 2% of hospital-acquired S. aureus infections could be attributed to MRSA. The rate had increased to 22% by 1995, and by 1997 the percent of hospital S. aureus infections attributable to MRSA had reached 50%.

The first report of CA-MRSA occurred in 1981, and in 1982 there was a large outbreak of CA-MRSA among intravenous drug users in Detroit, Michigan. Additional outbreaks of CA-MRSA were reported through the 1980s and 1990s, including outbreaks among Australian Aboriginal populations that had never been exposed to hospitals. In the mid 1990s there were scattered reports of CA-MRSA outbreaks among US children. While HA-MRSA rates stabilized between 1998-2008, CA-MRSA rates continued to rise. A report released by The University of Chicago Children's Hospital comparing two time periods (1993-1995 and 1995-1997) found a 25-fold increase in the rate of hospitalizations due to MRSA among children in the United States. In 1999 The University of Chicago reported the first deaths from invasive MRSA among otherwise healthy children in the United States. By 2004 MRSA accounted for 64% of hospital-acquiredS. aureus infections in the United States.

The Office for National Statistics reported 1,629 MRSA-related deaths in England and Wales during 2005, indicating a MRSA-related mortality rate half the rate of that in the United States for 2005, even though the figures from the British source were explained to be high because of "improved levels of reporting, possibly brought about by the continued high public profile of the disease" during the time of the 2005 United Kingdom General Election. MRSA is thought to have caused 1,652 deaths in 2006 in UK up from 51 in 1993.

It has been argued that the observed increased mortality among MRSA-infected patients may be the result of the increased underlying morbidity of these patients. Several studies, however, including one by Blot and colleagues, that have adjusted for underlying disease still found MRSA bacteremia to have a higher attributable mortality than methicillin-susceptible S. aureus (MSSA) bacteremia.

A population-based study of the incidence of MRSA infections in San Francisco during 2004–05 demonstrated that nearly 1 in 300 residents suffered from such an infection in the course of a year and that greater than 85% of these infections occurred outside of the healthcare setting. A 2004 study showed that patients in the United States with S. aureus infection had, on average, three times the length of hospital stay (14.3 vs. 4.5 days), incurred three times the total cost ($48,824 vs $14,141), and experienced five times the risk of in-hospital death (11.2% vs 2.3%) than patients without this infection. In a meta-analysis of 31 studies, Cosgrove et al., concluded that MRSA bacteremia is associated with increased mortality as compared with MSSA bacteremia (odds ratio = 1.93; 95% CI = 1.93±0.39). In addition, Wyllie et al. report a death rate of 34% within 30 days among patients infected with MRSA, a rate similar to the death rate of 27% seen among MSSA-infected patients.

According to the CDC, the most recent estimates of the incidence of healthcare-associated infections that are attributable to MRSA in the United States indicate a decline in such infection rates. Incidence of MRSA central line-associated blood stream infections as reported by hundreds of intensive care units decreased 50-70% from 2001-2007. A separate system tracking all hospital MRSA bloodstream infections found an overall 34% decrease between 2005-2008.

MRSA is sometimes sub-categorised as community-acquired MRSA (CA-MRSA) or healthcare-associated MRSA (HA-MRSA), although the distinction is complex. Some researchers have defined CA-MRSA by the characteristics of patients whom it infects, while others define it by the genetic characteristics of the bacteria themselves. By 2005, identified CA-MRSA risk factors included athletes, military recruits, incarcerated people, emergency room patients, urban children, HIV-positive individuals, men who have sex with men, and indigenous populations.

Worldwide
The first reported cases of CA-MRSA began to appear in the mid-1990s in Australia, New Zealand, the United States, the United Kingdom, France, Finland, Canada and Samoa, and were notable because they involved people who had not been exposed to a healthcare setting.

Because measurement and reporting varies, it is difficult to compare rates of MRSA in different countries. An international comparison of 2004 MRSA-attributable S. arueus rates in middle and high income countries released by the Center For Disease Dynamics, Economics, and Policy in showed that Iceland had the lowest rate of infection, and Romania had the highest at over 70%.

Research

Clinical
It has been reported that maggot therapy to clean out necrotic tissue of MRSA infection has been successful. Studies in diabetic patients reported significantly shorter treatment times than those achieved with standard treatments.

Many antibiotics against MRSA are in phase II and phase III clinical trials. e.g.:

1. Phase III : Ceftobiprole, Ceftaroline, Dalbavancin, Telavancin, Aurograb, Torezolid, Iclaprim
2. Phase II : Nemonoxacin.

Pre-Clinical
An entirely different and promising approach is phage therapy (e.g., at the Eliava Institute in Georgia), which in mice had a reported efficacy against up to 95% of tested Staphylococcus isolates.

On May 18, 2006, a report in Nature identified a new antibiotic, called platensimycin, that had demonstrated successful use against MRSA.

A 2010 study noted significant antimicrobial action of Ulmo 90 and manuka UMF 25+ honey against several microorganisms, including MRSA. The investigators noted the superior antimicrobial action of Ulmo 90 honey, and suggested it be investigated further. A separate 2010 study examined the use of medical-grade honey against several antibiotic-resistant strains of bacteria, including MRSA. The study concluded that the antimicrobial action of the honey studied was due to the activity of hydrogen peroxide, methylglyoxal, and a novel compound named bee defensin-1.

Ocean-dwelling living sponges produce compounds that may make MRSA more susceptible to antibiotics.

Some semi-toxic fungi/mushrooms excrete broad spectrum antibiotics, not all of which have been fully identified.

Cannabinoids (components of Cannabis sativa),
including cannabidiol (CBD), cannabinol (CBN), cannabichromene (CBC), Δ9-tetrahydrocannabinol (THC) and cannabigerol (CBG), show activity against a variety of MRSA strains (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Psittacosis
Date: 2012
Source: Wikipedia

Abstract: In medicine (pulmonology), psittacosis — also known as parrot disease, parrot fever, and ornithosis — is a zoonotic infectious disease caused by a bacterium called *Chlamydophila psittaci* (formerly *Chlamydia psittaci*) and contracted from parrots, such as macaws, cockatiels and budgerigars, and pigeons, sparrows, ducks, hens, gulls and many other species of bird. The incidence of infection in canaries and finches is believed to be lower than in psittacine birds.

In certain contexts, the word "psittacosis" is used when the disease is carried by any species of bird belonging to the Psittacidae family, whereas "ornithosis" is used when other birds carry the disease.

In Birds

In birds, *Chlamydophila psittaci* infection is referred to as avian chlamydiosis (AC). Infected birds shed the bacteria through feces and nasal discharges, which can remain infectious for several months. Many strains remain quiescent in birds until activated under stress. Birds are excellent, highly mobile vectors for the distribution of chlamydial infection because they feed on, and have access to, the detritus of infected animals of all sorts.

Signs

C. psittaci in birds is often systemic and infections can be inapparent, severe, acute or chronic with intermittent shedding. Signs in birds include "inflamed eyes, difficulty in breathing, watery droppings and green urates."

Diagnosis

Initial diagnosis may be via symptoms, but is usually confirmed via an antigen and antibody test. A PCR-based test is also available. Although any of these tests can confirm psittacosis, false negatives are possible and so a combination of clinical and lab tests is recommended before giving the bird a clean bill of health. It may die within 3 weeks.

Epidemiology

Infection is usually via the droppings of another infected bird, though it can also be transmitted via feathers and eggs, and is typically either inhaled or ingested.

C. psittaci strains in birds infect mucosal epithelial cells and macrophages of the respiratory tract. Septicaemia eventually develops and the bacteria become localized in epithelial cells and macrophages of most organs, conjunctiva, and gastrointestinal tract. It can also be passed in the eggs. Stress will commonly trigger onset of severe symptoms, resulting in rapid deterioration and death. *C. psittaci* strains are similar in virulence, grow readily in cell culture, have 16S-rRNA genes that differ by <0.8%, and belong to eight known serovars. All should be considered to be readily transmissible to humans.

C. psittaci serovar A is endemic among psittacine birds and has caused sporadic zoonotic disease in humans, other mammals, and tortoises. Serovar B is endemic among pigeons, has been isolated from turkeys, and has also been identified as the cause of abortion in a dairy herd. Serovars C and D are occupational hazards for slaughterhouse workers and for people in contact with birds. Serovar E isolates (known as Cal-10, MP or MN) have been obtained from a variety of avian hosts worldwide and, although they were associated with the 1920s–1930s outbreak in humans, a specific reservoir for serovar E has not been identified. The M56 and WC serovars were isolated during outbreaks in mammals.

Treatment
Treatment is usually via antibiotics, such as doxycycline or tetracycline, and can be administered via drops in the water, or injections. Many strains of *C. psittaci* are susceptible to bacteriophage.

In Humans

Symptoms
In humans, after an incubation period of 5–14 days, the symptoms of the disease range from inapparent illness to systemic illness with severe pneumonia. It presents chiefly as an atypical pneumonia. In the first week of psittacosis the symptoms mimic typhoid fever: prostrating high fevers, arthralgias, diarrhea, conjunctivitis, epistaxis and leukopenia. Rose spots can appear and these are called Horder's spots.[4] Splenomegaly is frequent toward the end of first week. Diagnosis can be suspected in case of respiratory infection associated with splenomegaly and/or epistaxis. Headache can be so severe that suggests meningitis and some nuchal rigidity is not unusual. Towards the end of first week stupor or even coma can result in severe cases.

The second week is more akin to acute bacteraemic pneumococcal pneumonia with continuous high fevers, cough and dyspnoea. X rays show patchy infiltrates or a diffuse whiteout of lung fields.

Bloodwork shows leukopenia, thrombocytopenia and moderately elevated liver enzymes.

Differential diagnosis must be made with typhus, typhoid and atypical pneumonia by Mycoplasma, Legionella or Q fever. Exposure history is paramount to diagnosis.

Complications in the form of endocarditis, hepatitis, myocarditis, arthritis, keratoconjunctivitis, and neurologic complications (encephalitis) may occasionally occur. Severe pneumonia requiring intensive-care support may also occur. Fatal cases have been reported (less than 1% of cases).

Diagnosis
Diagnosis involves microbiological cultures from respiratory secretions of patients or serologically with a fourfold or greater increase in antibody titers against *C. psittaci* in blood samples combined with the probable course of the disease. Typical inclusions called "Leventhal-Cole-Lillie bodies" can be seen within macrophages in BAL (Bronchial Alveolar Lavage) fluid. Culture of Chlamydia psittaci is hazardous and should only be carried out in biosafety laboratories.

Epidemiology
Psittacosis was first reported in Europe in 1879.

In 1929, a highly publicized outbreak of psittacosis hit the United States. Although not the first report of psittacosis in the United States, it was the largest up to that time. It led to greater controls on the import of pet parrots. The aftermath of the outbreak and how it was handled led to the establishment of the National Institutes of Health.

From 2002 through 2009, 66 human cases of psittacosis were reported to the Centers for Disease Control and most resulted from exposure to infected pet birds, usually cockatiels, parakeets, parrots, and macaws. Many more cases may occur that are not correctly diagnosed or reported.

Bird owners, pet shop employees, zookeepers and veterinarians are at risk of the infection. Some outbreaks of psittacosis in poultry processing plants have been reported.

Treatment
The infection is treated with antibiotics. Tetracyclines and chloramphenicol are the drugs of choice for treating patients with psittacosis. Most persons respond to oral therapy doxycycline, tetracycline hydrochloride, or chloramphenicol palmitate. For initial treatment of severely ill patients, doxycycline hyclate may be administered intravenously. Remission of symptoms usually is evident within 48–72 hours. However, relapse can occur, and treatment must continue for at least 10–14 days after fever abates. Although its in vivo efficacy has not been determined, erythromycin probably is the best alternative agent for persons for whom tetracycline is contraindicated (*e.g.*, children aged less than 9 years and pregnant women).

Use as a Biological Weapon
Psittacosis was one of more than a dozen agents that the United States researched as potential biological weapons before the nation suspended its biological weapons program.

Notable Casualties
The most high-profile death caused by Parrot Fever is that of Thea Selway, mother of singer Philip Selway, of Familial fame and part-time drummer for Radiohead along with band-founder Clive Deamer (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Q Fever
Date: 2012
Source: Wikipedia

Abstract: Q fever is a disease caused by infection with Coxiella burnetii, a bacterium that affects humans and other animals. This organism is uncommon, but may be found in cattle, sheep, goats and other domestic mammals, including cats and dogs. The infection results from inhalation of a spore-like small cell variant, and from contact with the milk, urine, feces, vaginal mucus, or semen of infected animals. Rarely, the disease is tick borne. The incubation period is 9–40 days. A human being can be infected by a single bacterium. The bacterium is an obligate intracellular pathogen.

History
It was first described by Edward Holbrook Derrick in abattoir workers in Brisbane, Queensland, Australia. The "Q" stands for "query" and was applied at a time when the causative agent was unknown; it was chosen over suggestions of "abattoir fever" and "Queensland rickettsial fever", to avoid directing negative connotations at either the cattle industry or the state of Queensland.

The pathogen of Q fever was discovered in 1937, when Frank Macfarlane Burnet and Mavis Freeman isolated the bacterium from one of Derrick’s patients. It was originally identified as a species of *Rickettsia*. H.R. Cox and Gordon Davis isolated it from ticks in Montana, USA in 1938. It is a zoonotic disease whose most common animal reservoirs are cattle, sheep and goats. *Coxiella burnetii* is no longer regarded as closely related to Rickettsiae, but as similar to *Legionella* and *Francisella*, and is a proteobacterium.

Manifestations
Incubation period is usually two to three weeks. The most common manifestation is mild flu-like symptoms with abrupt onset of fever, malaise, profuse perspiration, severe headache, myalgia (muscle pain), joint pain, loss of appetite, upper respiratory problems, dry cough, pleuritic pain, chills, confusion and gastrointestinal symptoms, such as nausea, vomiting and diarrhea. The fever lasts approximately seven to 14 days.

Approximately half of infected individuals exhibit no symptoms.

During the course, the disease can progress to an atypical pneumonia, which can result in a life-threatening acute respiratory distress syndrome (ARDS), whereby such symptoms usually occur during the first four to five days of infection.

Less often, Q fever causes (granulomatous) hepatitis, which may be asymptomatic or becomes symptomatic with malaise, fever, liver enlargement (hepatomegaly) and pain in the right upper quadrant of the abdomen. Whereas transaminase values are often elevated, jaundice is uncommon. Retinal vasculitis is a rare manifestation of Q fever.

The chronic form of Q fever is virtually identical to inflammation of the inner lining of the heart (endocarditis), which can occur months or decades following the infection. It is usually fatal if untreated. However, with appropriate treatment, the mortality falls to around 10%.

Clinical Signs in Animals
Cattle, goats and sheep are most commonly infected, and can serve as a reservoir for the bacteria. Infected animals may show respiratory signs such as pneumonia, but also abortion and infertility. Severe systemic signs, such as anorexia and fever, may occur concurrently.

Appearance and Incidence
The pathogenic agent is to be found everywhere except New Zealand. The bacterium is extremely sustainable and virulent: a single organism is able to cause an infection. The common way of infection is inhalation of contaminated dust, contact with contaminated milk, meat, wool and particularly birthing products. Ticks can transfer the pathogenic agent to other animals. Transfer between humans seems extremely rare and has so far been described in very few cases.

Some studies have shown more men to be affected than women, which may be attributed to different employment rates in typical professions.

"At risk" occupations include, but are not limited to:

1. Veterinary personnel
2. Stockyard workers
3. Farmers
4. Shearers
5. Animal transporters
6. Laboratory workers handling potentially infected veterinary samples or visiting abattoirs
7. People who cull and process kangaroos
8. Hide (tannery) workers

Diagnosis
Diagnosis is usually based on serology (looking for an antibody response) rather than looking for the organism itself. Serology allows to detect chronic infection as high antibody levels are found against the virulent form of the bacterium. Molecular detection of bacterial DNA is increasingly used. Culture is technically difficult and not routinely available in most microbiology laboratories.

Q fever can cause endocarditis (infection of the heart valves) which may require transoesophageal echocardiography to diagnose. Q fever hepatitis manifests as an elevation of ALT and AST, but a definitive diagnosis is only possible on liver biopsy, which shows the characteristic fibrin ring granulomas.

Treatment
Treatment of the acute Q fever with antibiotics is very effective[citation needed] and should take place in consultation with an infectious diseases specialist.[citation needed] Commonly used are doxycycline, tetracycline, chloramphenicol, ciprofloxacin, ofloxacin, and hydroxychloroquine. The chronic form is more difficult to treat and can require up to four years of treatment with doxycycline and quinolones or doxycycline with hydroxychloroquine.

Q fever in pregnancy is especially difficult to treat because doxycycline and ciprofloxacin are contraindicated in pregnancy. The preferred treatment is five weeks of co-trimoxazole.

Prevention
Protection is offered by Q-Vax, a whole-cell, inactivated vaccine developed by an Australian vaccine manufacturing company CSL. The intradermal vaccination is composed of killed *Coxiella burnetii* organisms. Skin and blood tests should be done before vaccination to identify pre-existing immunity, because vaccinating subjects who already have an immunity can result in a severe local reaction. After a single dose of vaccine, protective immunity lasts for many years. Revaccination is not generally required. Annual screening is typically recommended.

In 2001, Australia introduced a national Q fever vaccination program for people working in "at risk" occupations.

The Soviet Union had earlier developed a killed vaccine, but its side effects prevented its licensing abroad.

Vaccination of animals is not a current method of control.

Biological warfare
Q fever has been described as a possible biological weapon.

The United States investigated Q fever as a potential biological warfare agent in the 1950s, with eventual standardization as agent OU. At Fort Detrick and Dugway Proving Ground, human trials were conducted on Whitecoat volunteers to determine the median infective dose (18 $MICLD_{50}$/person i.h.) and course of infection. As a standardized biological, it was manufactured in large quantities at Pine Bluff Arsenal, with 5,098 gallons in the arsenal in bulk at the time of demilitarization in 1970.

Q fever is a category "B" agent. It can be contagious, and is very stable in aerosols in a wide range of temperatures. Q fever microorganisms may survive on surfaces up to 60 days.

It is considered a good agent in part because its ID50 (number of bacilli needed to infect 50% of individuals) is considered to be 1, making it the lowest known to man (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Ricin
Date: 2012
Source: Wikipedia

Abstract: Ricin from the castor oil plant Ricinus communis, is a highly toxic, naturally occurring protein. A dose as small as a few grains of salt can kill an adult. The LD of ricin is around 22 micrograms per kilogram (1.76 mg for an average adult, around 1/228 of a standard aspirin tablet (0.4 g gross)) in humans if exposure is from injection or inhalation. Oral exposure to ricin is far less toxic and lethal dose can be up to 20–30 milligrams per kilogram.

Ricin is poisonous if inhaled, injected, or ingested, acting as a toxin by the inhibition of protein synthesis. It is resistant, but not impervious, to digestion by peptidases. By ingestion, the pathology of ricin is largely restricted to the gastrointestinal tract where it may cause mucosal injuries; with appropriate treatment, most patients will make a full recovery. Because the symptoms are caused by failure to make protein, they emerge only after a variable delay from a few hours to a full day after exposure. An antidote not yet tested on humans has been developed by the UK military, and a vaccine has been developed by the US military, and has had some human testing, and so far shown to be safe, and effective when lab mice were injected with ricin-antibody rich blood mixed with ricin. Symptomatic and supportive treatment is available. Long term organ damage is likely in survivors. Ricin causes severe diarrhea and victims can die of shock. Death typically occurs within 3–5 days of the initial exposure. Abrin is a similar toxin, found in the highly ornamental rosary pea.

Deaths caused by ingestion of castor plant seeds are rare, partly because of the indigestible capsule, and partly because ricin can be digested (although it is resistant). The pulp from eight beans is considered toxic for an adult. A solution of saline and glucose has been used to treat ricin overdose. Rauber and Heard have written that close examination of early 20th century case reports indicates that public and professional perceptions of ricin toxicity "do not accurately reflect the capabilities of modern medical management".

Overdosage

Most acute poisoning episodes in humans are the result of oral ingestion of castor beans, 5-20 of which could prove fatal to an adult. Victims often manifest nausea, diarrhea, tachycardia, hypotension and seizures persisting for up to a week. Blood, plasma or urine ricin concentrations may be measured to confirm diagnosis.

Biochemistry

Ricin is classified as a type 2 ribosome inactivating protein (RIP). Whereas Type 1 RIPs consist of a single enzymatic protein chain, Type 2 RIPs, also known as holotoxins, are heterodimeric glycoproteins. Type 2 RIPs consist of an A chain that is functionally equivalent to a Type 1 RIP, covalently connected by a single disulfide bond to a B chain that is catalytically inactive, but serves to mediate entry of the A-B protein complex into the cytosol. Both Type 1 and Type 2 RIPs are functionally active against ribosomes

in vitro, however only Type 2 RIPs display cytoxicity due to the lectin properties of the B chain. In order to display its ribosome inactivating function, the ricin disulfide bond must be reductively cleaved.

Structure
The tertiary structure of ricin was shown to be a globular, glycosylated heterodimer of approximately 60-65 kDA. Ricin toxin A chain and ricin toxin B chain are of similar molecular weight, approximately 32 kDA and 34 kDA respectively.

1. Ricin A Chain (RTA) is an N-glycoside hydrolase composed of 267 amino acids. It has three structural domains with approximately 50% of the polypeptide arranged into alpha-helices andbeta-sheets. The three domains form a pronounced cleft that is the active site of RTA.

2. Ricin B Chain (RTB) is a lectin composed of 262 amino acids that is able to bind terminal galactose residues on cell surfaces. RTB form a bilobal, barbell-like structure lacking alpha-helicesor beta-sheets where individual lobes contain three subdomains. At least one of these three subdomains in each homologous lobe possesses a sugar-binding pocket that gives RTB its functional character.

Many plants such as barley have the A chain but not the B chain. People do not get sick from eating large amounts of such products, as ricin A is of extremely low toxicity as long as the B chain is not present.
Entry into the cytosol

The ability of ricin to enter the cytosol depends on hydrogen bonding interactions between RTB amino acid residues and complex carbohydrates on the surface of eukaryotic cells containing either terminal N-acetyl galactosamine or beta-1,4-linked galactose residues. Additionally, the mannose-type glycans of ricin are able to bind cells that express mannose receptors. Experimentally, RTB has been shown to bind to the cell surface on the order of 106-108 ricin molecules per cell surface.

The profuse binding of ricin to surface membranes allows internalization with all types of membrane invaginations. Experimental evidence points to ricin uptake in both clathrin-coated pits, as well as clathrin-independent pathways including caveolae and macropinocytosis. Vesicles shuttle ricin to endosomes that are delivered to the Golgi apparatus. The active acidification of endosomes are thought to have little effect on the functional properties of ricin. Because ricin is stable over a wide pH range, degradation in endosomes or lysosomes offer little or no protection against ricin. Ricin molecules are thought to follow retrograde transport via early endosomes, the trans-Golgi network, and the Golgi to enter the lumen of the endoplasmic reticulum (ER).

For ricin to function cytotoxically, RTA must be reductively cleaved from RTB in order to release a steric block of the RTA active site. This process is catalysed by the protein PDI (protein disulphide isomerase) that resides in the lumen of the ER. Free RTA in the ER lumen then partially unfolds and partially buries into the ER membrane, where it is thought to mimic a misfolded membrane-associated protein. Roles for the ER chaperones GRP94 and EDEM have been proposed prior to the 'dislocation' of RTA from the ER lumen to the cytosol in a manner that utilizes components of the endoplasmic reticulum-associated protein degradation (ERAD) pathway. ERAD normally removes misfolded ER proteins to the cytosol for their destruction by cytosolic proteasomes. Dislocation of RTA requires ER membrane-integral E3 ubiquitin ligase complexes, but RTA avoids the ubiquitination that usually occurs with ERAD substrates because of its low content of lysine residues, which are the usual attachment sites for ubiquitin. Thus RTA avoids the usual fate of dislocated proteins (destruction that is mediated by targeting ubiquitinylated proteins to the cytosolic proteasomes). In the mammalian cell cytosol, RTA then undergoes triage by cytosolic molecular chaperones that results in its folding to a catalytic conformation that de-purinates ribosomes, thus halting protein synthesis.

Ribosome Inactivation
Study of the N-glycosidase activity of ricin was pioneered by Endo and Tsurugi who showed that RTA cleaves a glycosidic bond within the large rRNA of the 60S subunit of eukaryotic ribosomes. They subsequently showed RTA specifically and irreversibly hydrolyses the N-glycosidic bond of

the adenine residue at position 4324 (A4324) within the 28S rRNA, but leaves the phosphodiester backbone of the RNA intact. The ricin targets A4324 that is contained in a highly conserved sequence of 12 nucleotides universally found in eukaryotic ribosomes. The sequence, 5'-AGUACGAGAGGA-3', termed the sarcin-ricin loop, is important in binding elongation factors during protein synthesis. The depurination event rapidly and completely inactivates the ribosome, resulting in toxicity from inhibited protein synthesis. A single RTA molecule in the cytosol is capable of depurinating approximately 1500 ribosomes per minute.

Depurination Reaction

Within the active site of RTA, there exist several invariant amino acid residues involved in the depurination of ribosomal RNA. Although the exact mechanism of the event is unknown, key amino acid residues identified include tyrosine at positions 80 and 123, glutamic acid at position 177, and arginine at position 180. In particular, Arg180 and Glu177 have been shown to be involved in thecatalytic mechanism, and not substrate binding, with enzyme kinetic studies involving RTA mutants.

The model proposed by Mozingo and Robertus, based x-ray structures, is as follows:

1. Sarcin-ricin loop substrate binds RTA active site with target adenine stacking against tyr80 and tyr123.
2. Arg180 is positioned such that it can protonate N-3 of adenine and break the bond between N-9 of the adenine ring and C-1' of the ribose.
3. Bond cleavage results in an oxycarbonium ion on the ribose, stabilized by Glu177.
4. N-3 protonation of adenine by Arg180 allows deprotonation of a nearby water molecule.
5. Resulting hydroxyl attacks ribose carbonium ion.
6. Depurination of adenine results in a neutral ribose on an intact phosphodiester RNA backbone.

Manufacture

Ricin is easily purified from castor oil manufacturing waste. The aqueous phase left over from the oil extraction process is called waste mash. It would contain about 5–10% ricin by weight, but heating during the oil extraction process denatures the protein, making the resultant seed cake safe for use as animal feed. From fresh seed, separation requires chromatographic techniques similar to other plant proteins.

Patented Extraction Process

A process for extracting ricin has been described in a patent. The described extraction method is very similar to that used for the preparation of soy protein isolates.

The patent was removed from the United States Patent and Trademark Office (USPTO) database sometime in 2004. Modern theories of protein chemistry cast doubt on the effectiveness of the methods disclosed in the patent.

Potential Medicinal Use

Some researchers have speculated about using ricins in the treatment of cancer, as a so-called "magic bullet" to destroy targeted cells. Because ricin is a protein, it can be genetically linked to a monoclonal antibody to target malignant cells recognized by the antibody. The major problem with ricin is that its native internalization sequences are distributed throughout the protein. If any of these native internalization sequences are present in a therapeutic, then the drug will be internalized by, and kill, untargeted epithelial cells as well as targeted cancer cells.

Some researchers hope that modifying ricin will sufficiently lessen the likelihood that the ricin component of these immunotoxins will cause the wrong cells to internalize it, while still retaining its cell-killing activity when it is internalized by the targeted cells. Generally, however, ricin has been superseded for medical purposes by more practical fragments of bacterial toxins, such as diphtheria toxin, which is used in denileukin diftitox, an FDA-approved treatment for leukemia and lymphoma.

No approved therapeutics contain ricin.

A promising approach is also to use the non-toxic B subunit as a vehicle for delivering antigens into cells thus greatly increasing their immunogenicity. Use of ricin as an adjuvant has potential implications for developing mucosal vaccines.

Ricinine has some insecticidal effects on three insect pests as well as a hepatoprotective activity. Ricinine, when administered to mice at low doses has memory-improving effects. The signs of intoxication caused by ricinine can be used as chemical model of epilepsy in the screening of anticonvulsant drugs.

Incidents Involving Ricin: Main article: Incidents involving ricin

Ricin has been involved in a number of incidents, including the high-profile assassination of Georgi Markov using a weapon disguised as an umbrella.

The ingestion of Ricinus communis cake is responsible for fatal ricin poisoning in animals.

Use as a Chemical/Biological Warfare Agent

The United States investigated ricin for its military potential during the First World War. At that time it was being considered for use either as a toxic dust or as a coating for bullets and shrapnel. The dust cloud concept could not be adequately developed, and the coated bullet/shrapnel concept would violate the Hague Convention of 1899 (adopted in U.S. law at 32 Stat. 1903), specifically Annex § 2, Ch.1, Article 23, stating "...it is especially prohibited...[t]o employ poison or poisoned arms". The First World War ended before the U.S. weaponized ricin.

During the Second World War the United States and Canada undertook studying ricin in cluster bombs. Though there were plans for mass production and several field trials with different bomblet concepts, the end conclusion was that it was no more economical than using phosgene. This conclusion was based on comparison of the final weapons rather than ricin's toxicity (LCt50 ~40 mg·min/m3). Ricin was given the military symbol W or later WA. Interest in it continued for a short period after the Second World War, but soon subsided when the U.S. Army Chemical Corps began a program to weaponize sarin.

The Soviet Union also possessed weaponized ricin. There were speculations that the KGB even used it outside of the Soviet bloc; however, this was never proven. In 1978, the Bulgarian dissident Georgi Markov was assassinated by Bulgariansecret police who surreptitiously 'shot' him on a London street with a modified umbrella using compressed gas to fire a tiny pellet contaminated with ricin into his leg. He died in a hospital a few days later; his body was passed to a special poison branch of the British Ministry of Defence (MOD) that discovered the pellet during an autopsy. The prime suspects were the Bulgarian secret police: Georgi Markov had defected from Bulgaria some years previously and had subsequently written books and made radio broadcasts which were highly critical of the Bulgarian communist regime. However, it was believed at the time that Bulgaria would not have been able to produce the pellet, and it was also believed that the KGB had supplied it. The KGB denied any involvement although high-profile KGB defectors Oleg Kalugin and Oleg Gordievsky have since confirmed the KGB's involvement. Earlier, Soviet dissident Aleksandr Solzhenitsyn also suffered (but survived) ricin-like symptoms after a 1971 encounter with KGB agents.

Despite ricin's extreme toxicity and utility as an agent of chemical/biological warfare, it is extremely difficult to limit the production of the toxin. The castor bean plant from which ricin is derived is a

common ornamental and can be grown at home without any special care, and the major reason ricin is a public health threat is that it is easy to obtain.

Under both the 1972 Biological Weapons Convention and the 1997 Chemical Weapons Convention, ricin is listed as a schedule 1 controlled substance. Despite this, more than 1 million tonnes of castor beans are processed each year, and approximately 5% of the total is rendered into a waste containing negligible concentrations of undenatured ricin toxin.

Ricin is several orders of magnitude less toxic than botulinum or tetanus toxin, but the latter are harder to come by. Compared to botulinum or anthrax as biological weapons or chemical weapons, the quantity of ricin required to achieve LD50 over a large geographic area is significantly more than an agent such as anthrax (tons of ricin vs. only kilogram quantities of anthrax). Ricin is easy to produce, but is not as practical nor likely to cause as many casualties as other agents. Ricin is inactivated (the protein changes structure and becomes less dangerous) much more readily than anthrax spores, which may remain lethal for decades. Jan van Aken, a Dutch expert on biological weapons, explained in a report for The Sunshine Project that Al Qaeda's experiments with ricin suggest their inability to produce botulinum or anthrax.

Ian Davison, a British white supremacist and neo-Nazi, was arrested in 2009 for planning terrorist attacks involving ricin.

In 2011 the United States government discovered information that terrorist groups were attempting to obtain large amounts of castor beans for weaponized ricin use.

On November 1, 2011 the FBI arrested 4 North Georgia men and charged them in plots to purchase explosives, a silencer and to manufacture the biological toxin ricin from castor beans (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Rocky Mountain Spotted Fever
Date: 2012
Source: Wikipedia

Abstract: Rocky Mountain spotted fever is the most lethal and most frequently reported rickettsial illness in the United States. It has been diagnosed throughout the Americas. Some synonyms for Rocky Mountain spotted fever in other countries include "tick typhus," "Tobia fever" (Colombia), "São Paulo fever" or "*febre maculosa*" (Brazil), and "*fiebre manchada*" (Mexico). It is distinct from the viral tick-borne infection, Colorado tick fever. The disease is caused by *Rickettsia rickettsii*, a species of bacterium that is spread to humans by *Dermacentor* ticks. Initial signs and symptoms of the disease include sudden onset of fever, headache, and muscle pain, followed by development of rash. The disease can be difficult to diagnose in the early stages, and without prompt and appropriate treatment it can be fatal.

The name "Rocky Mountain spotted fever" is somewhat of a misnomer. Beginning in the 1930s, it became clear that this disease occurred in many areas of the United States other than the Rocky Mountain region. It is now recognized that this disease is broadly distributed throughout the continental United States, and occurs as far north as Canada and as far south as Central America and parts of South America. Between 1981 and 1996, this disease was reported from every U.S. state except Hawaii, Vermont, Maine, and Alaska.

Rocky Mountain spotted fever remains a serious and potentially life-threatening infectious disease today. Despite the availability of effective treatment and advances in medical care, approximately 3% to 5% of individuals who become ill with Rocky Mountain spotted fever still die from the infection. However, effective antibiotic therapy has dramatically reduced the number of deaths caused by Rocky Mountain spotted fever; before the discovery of tetracycline and chloramphenicol in the late 1940s, as many as 30% of persons infected with *R. rickettsii* died.

Natural History
Rocky Mountain spotted fever, like all rickettsial infections, is classified as a zoonosis. Zoonoses are diseases of animals that can be transmitted to humans. Some zoonotic diseases require a vector (e.g., a mosquito, tick, or mite) to be transmitted from the animal host to the human host. In the case of Rocky Mountain spotted fever, ticks are the natural hosts, serving as both reservoirs and vectors of *R. rickettsii*. Ticks transmit the organism to vertebrates primarily by their bites. Less commonly, infections may occur following exposure to crushed tick tissues, fluids, or tick feces.

The life cycle of *Dermacentor variabilis* and *Dermacentor andersoni* ticks (Family Ixodidae)

A female tick can transmit *R. rickettsii* to her eggs in a process called transovarial transmission. Ticks can also become infected with *R. rickettsii* while feeding on blood from the host in either the larval or nymphal stage. After the tick develops into the next stage, the *R. rickettsii* may be transmitted to the second host during the feeding process. Furthermore, male ticks may transfer *R. rickettsii* to female ticks through body fluids or spermatozoa during the mating process. These types of transmission

represent how generations or life stages of infected ticks are maintained. Once infected, the tick can carry the pathogen for life.

Rickettsiae are transmitted to a vertebrate host through saliva while a tick is feeding. It usually takes about 24 hours of attachment and feeding before the rickettsiae are transmitted to the host. The risk of exposure to a tick carrying *R. rickettsii* is low. In general, about 1%-3% of the tick population carries *R. rickettsii*, even in areas where the majority of human cases are reported.

Vectors include *Dermacentor variabilis*, *Dermacentor andersoni*, *Rhipicephalus sanguineus*, and *Amblyomma cajennense*. However, not all of these are of equal importance, and most are restricted to certain geographic areas.

There are two major vectors of *R. rickettsii* in the United States: the American dog tick and the Rocky Mountain wood tick. American dog ticks (*Dermacentor variabilis*) are widely distributed east of the Rocky Mountains and also occur in limited areas on the Pacific Coast. Dogs and medium-sized mammals are the preferred hosts of adult *D. variabilis*, although it feeds readily on other large mammals, including humans. This tick is the most commonly identified species responsible for transmitting *R. rickettsii* to humans. Rocky Mountain wood ticks (*Dermacentor andersoni*) are found in the Rocky Mountain states and in southwestern Canada. The life cycle of this tick may require up to 2 to 3 years for completion. Adult ticks feed primarily on large mammals. Larvae and nymphs feed on small rodents.

Other tick species have been shown to be naturally infected with *R. rickettsii* or serve as experimental vectors in the laboratory. However, these species are likely to play only a minor role in the ecology of *R. rickettsii*.

There are only 800 cases reported in the U.S. a year and only 20% find the tick.

Diagnosis and Symptoms
Spotted fever can be very difficult to diagnose in its early stages, even among experienced physicians who are familiar with the disease.

People infected with *R. rickettsii* usually notice symptoms following an incubation period of one to two weeks after a tick bite. The early clinical presentation of Rocky Mountain spotted fever is nonspecific and may resemble a variety of other infectious and non-infectious diseases

Initial Symptoms Include:

1. Fever
2. Nausea
3. Emesis (vomiting)
4. Severe headache
5. Muscle pain
6. Lack of appetite
7. Parotitis in some cases (somewhat rare).

Later Signs and Symptoms Include:

1. Maculopapular rash
2. Petechial rash
3. Abdominal pain
4. Joint pain

The classic triad of findings for this disease are fever, rash and history of tick bite. However, this combination is often not identified when the patient initially presents for care. The rash has a centripetal, or "inward" pattern of spread, meaning it begins at the extremities and courses towards the trunk.

The rash first appears 2–5 days after the onset of fever and is often very subtle. Younger patients usually develop the rash earlier than older patients. Most often it begins as small, flat, pink, non-itchy spots (macules) on the wrists, forearms, and ankles. These spots turn pale when pressure is applied and eventually become raised on the skin. The characteristic red, spotted (petechial) rash of Rocky Mountain spotted fever is usually not seen until the sixth day or later after onset of symptoms, but this type of rash occurs in only 35% to 60% of patients with Rocky Mountain spotted fever. The rash involves the palms or soles in as many as 50% to 80% of patients; however, this distribution may not occur until later in the course of the disease. As many as 10% to 15% of patients may never develop a rash.

Abnormal laboratory findings seen in patients with Rocky Mountain spotted fever may include thrombocytopenia, hyponatremia, or elevated liver enzyme levels.

Rocky Mountain spotted fever can be a very severe illness and patients often require hospitalization. Because *R. rickettsii* infects the cells lining blood vessels throughout the body, severe manifestations of this disease may involve the respiratory system, central nervous system, gastrointestinal system, or renal system. Host factors associated with severe or fatal Rocky Mountain spotted fever include advanced age, male sex, African-Caribbean race, chronic alcohol abuse, and glucose-6-phosphate dehydrogenase (G6PD) deficiency. Deficiency of G6PD is a sex-linked genetic condition affecting approximately 12% of the U.S. African-American male population; deficiency of this enzyme is associated with a high proportion of severe cases of Rocky Mountain spotted fever. This is a rare clinical course that is often fatal within 5 days of onset of illness.

Long-term health problems following acute Rocky Mountain spotted fever infection include partial paralysis of the lower extremities, gangrene requiring amputation of fingers, toes, or arms or legs, hearing loss, loss of bowel or bladder control, movement disorders and language disorders. These complications are most frequent in persons recovering from severe, life-threatening disease, often following lengthy hospitalizations.

Treatment

Appropriate antibiotic treatment is initiated *immediately* when there is a suspicion of Rocky Mountain spotted fever on the basis of clinical and epidemiological findings. Treatment should *not* be delayed until laboratory confirmation is obtained. In fact, failure to respond to a tetracycline antibiotic argues against a diagnosis of Rocky Mountain spotted fever. Severely ill patients may require longer periods before their fever resolves, especially if they have experienced damage to multiple organ systems. Preventive therapy in healthy patients who have had recent tick bites is not recommended and may, in fact, only delay the onset of disease.

Doxycycline (for adults at 100 mg every 12 hours or for children under 45 kg (99 lb) at 4 mg/kg body weight per day in two divided doses) is the drug of choice for patients with Rocky Mountain spotted fever. Therapy is continued for at least 3 days after fever subsides and until there is unequivocal evidence of clinical improvement, generally for a minimum total course of 5 to 10 days. Severe or complicated disease may require longer treatment courses. Doxycycline is also the preferred drug for patients with ehrlichiosis, another tick-transmitted infection with signs and symptoms that may resemble Rocky Mountain spotted fever.

Chloramphenicol is an alternative drug that can be used to treat Rocky Mountain spotted fever; however, this drug may be associated with a wide range of side effects and may require careful monitoring of blood levels (as it can cause aplastic anemia).

History

Rocky Mountain spotted fever was first recognized in 1896 in the Snake River Valley of Idaho and was originally called “black measles” because of the characteristic rash. It was a dreaded and frequently fatal disease that affected hundreds of people in this area. By the early 1900s, the recognized geographic distribution of this disease grew to encompass parts of the United States as far north as Washington and Montana and as far south as California, Arizona, and New Mexico.

Howard T. Ricketts was the first to establish the identity of the infectious organism that causes this disease. He and others characterized the basic epidemiological features of the disease, including the role of tick vectors. Their studies found that Rocky Mountain spotted fever is caused by *Rickettsia rickettsii*. This species is maintained in nature by a complex cycle involving ticks and mammals; humans are considered to be accidental hosts and are not involved in the natural transmission cycle of this pathogen. Tragically—and ironically—Dr. Ricketts died of typhus (another rickettsial disease) in Mexico in 1910, shortly after completing his remarkable studies on Rocky Mountain spotted fever.

Prior to 1922, Drs. McCray and McClintic both died doing research on the fever; so did an aide of Noguchi at the Rockefeller Institute. Drs. McCalla and Brerton also did early fever research.

Research began in 1922 in western Montana — in the Bitterroot Valley; Hamilton, Montana — after the governor's daughter and son-in-law died of the fever. Past Assistant Surgeon R.R. Spencer of the Hygienic Laboratory of the US Public Health Service was ordered to the region and led a research team at an abandoned local schoolhouse through at least 1924. Spencer's fateful day was May 19, 1924 when he ultimately put a large dose of mushed wood ticks — from lot 2351B — and weak carbolic acid into his arm by inoculation. The vaccine worked.Spencer was aided by R. R. Parker, Bill Gettinger, Henry Cowan, Henry Greenup, Elmer Greenup, Salsbury and Kerlee, et al. Gettinger, Cowan and Kerlee would all die from the fever during the research efforts.

Much of the early research was conducted at Rocky Mountain Laboratories (part of the National Institute of Allergy and Infectious Diseases), which is the source of the name of the condition (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Rift Valley Fever
Date: 2012
Source: Wikipedia

Abstract: Rift Valley Fever (RVF) is a viral zoonosis (affects primarily domestic livestock, but can be passed to humans) causing fever. It is spread by the bite of infected mosquitoes, typically the Aedes or Culex genera. The disease is caused by the RVF virus, a member of the genus Phlebovirus (family Bunyaviridae). The disease was first reported among livestock in Kenya around 1915, but the virus was not isolated until 1931.

RVF outbreaks occur across sub-Saharan Africa, with outbreaks occurring elsewhere infrequently, but sometimes severely. In Egypt in 1977-78, several million people were infected and thousands died during a violent epidemic. In Kenya in 1998, the virus claimed the lives of over 400 Kenyans. In September 2000, an outbreak was confirmed in Saudi Arabia and Yemen). On 19 Oct 2011, the first confirmed human case of Rift Valley fever contracted in Zimbabwe was reported in a Caucasian female traveler who returned to France after a 26-day stay in Marondera, Mashonaland East Province during July and August, 2011.

Clinical Signs and Diagnosis

In humans, the virus can cause several syndromes. Usually, sufferers have either no symptoms or only a mild illness with fever, headache, myalgia and liver abnormalities. In a small percentage of cases (< 2%), the illness can progress to hemorrhagic fever syndrome, meningoencephalitis (inflammation of the brain), or affecting the eye. Patients who become ill usually experience fever, generalized weakness, back pain, dizziness, and weight loss at the onset of the illness. Typically, patients recover within two to seven days after onset.

About 1% of human sufferers die of the disease. In livestock, the fatality level is significantly higher. Pregnant livestock infected with RVF abort virtually 100% of fetuses. An epizootic (animal disease epidemic) of RVF is usually first indicated by a wave of unexplained abortions. Other signs in livestock include vomiting and diarrhoea, respiratory disease, fever, lethargy, anorexia and sudden death in young animals. Diagnosis relies on viral isolation from tissues, or serological testing with an ELISA.

Animal Vaccination

Several animal vaccines have been made to protect against RVF infection. The first one to be developed was a live vaccine. When administered to mice, the results were promising; this vaccine provided immunity for three years. However, a problem was encountered: administration to pregnant ewes on many occasions led to abortion. Since then, attenuated vaccines have been developed. Although they are protective and do not cause adverse effects, these results are only achieved after multiple inoculations. The fact that multiple doses are required may prove problematic, especially in areas where RVF is endemic.

2006/07 Outbreak in Kenya and Somalia

1. In November 2006, a Rift Valley fever outbreak occurred in Kenya. The victims are from the North Eastern Province and Coast Province of Kenya, which had received heavy rain in recent months, causing floods and creating breeding grounds for mosquitoes, which spread the virus of the fever from infected livestock to humans.

2. By 7 January 2007, about 75 people had died and another 183 were infected.[3] The outbreak has forced the closure of livestock markets in the North Eastern Province, affecting the economy of the region.The outbreak was subsequently reported to have moved into Maragua and Kirinyaga districts of Central Province of Kenya.

3. On 20 January 2007, the outbreak was reported to have crossed into Somalia from Kenya and killed 14 people in the Lower Jubba region.

4. As of 23 January 2007, cases had started to crop up at the Kenyan capital, Nairobi. An estimated large number of businesses were supposedly suffering large losses as customers were shunning the common meat joints for the popular nyama choma (roast meat), as it was believed to be spreading the fever.

5. In December 2006 and again in January 2007, Taiwan International Health Action (TaiwanIHA) began operating missions in Kenya consisting of medical experts assisting in training laboratory and health facility personnel, and included donations of supplies, such as mosquito sprays. The United States Centers for Disease Control has also set up an assistance mission and laboratory in Kenya.

6. By the end of January, 2007, some 148 people had died since the outbreak began in December.

7. As at 14 March 2007, the Kenyan government declared RVF as having diminished drastically after spending an estimated 2.5 million in vaccine and deployment costs. It also lifted the ban on cattle movement in the affected areas.

8. As of 2 November 2007, 125 cases, including 60 deaths, had been reported from more than 10 localities of White Nile, Sinnar, and Gezira states in Sudan. Young adult males are predominantly affected. More than 25 human samples have been found positive for RVF by PCR or ELISA.

2010 South Africa Outbreak

As of 8 April 2010, the Ministry of Health South Africa had reported 87 human cases infected with Rift Valley fever (RVF), including two deaths in Free State, Eastern Cape and Northern Cape provinces. Most of these cases reported direct contact with RVFV-infected livestock and or were linked to farms with confirmed animal cases of RVF. The human cases are: farmers, veterinarians and farm workers. All cases were confirmed with RVF by test conducted at the National Institute of Communicable Diseases (NICD) in Johannesburg, South Africa.

An ongoing outbreak of Rift Valley fever virus (RVFV) infection is affecting sheep, goats, cattle and wildlife on farms within Free State, Eastern Cape, Northern Cape, Western Cape, Mpumalanga, North West, and Gauteng provinces. As of 29 March 2010, about 78 farms reported laboratory-confirmed animal cases, with extensive livestock deaths.

Outbreak investigations by the Department of Health and the Department of Agriculture, Forestry and Fisheries are ongoing, and are being supported by the South African Field Epidemiology and Training Programme and NICD. The Department of Health and the Department of Agriculture are taking measures to enhance disease surveillance among cattle and in managing the control of the disease outbreak.

Sporadic cases of RVFV infection in animals have been documented in South Africa in recent years. The last major outbreak of the disease in humans occurred between 1974 and 1976, where an estimated 10,000 to 20,000 cases were recorded.

Use as a Biological Weapon

Rift Valley fever was one of more than a dozen agents that the United States researched as potential biological weapons before the nation suspended its biological weapons program in 1969 (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Shigella
Date: 2012
Source: Wikipedia

Abstract: *Shigella* is a genus of Gram-negative, nonspore forming, non-motile, rod-shaped bacteria closely related to *Escherichia coli* and *Salmonella*. The causative agent of human shigellosis, *Shigella* causes disease in primates, but not in other mammals. It is only naturally found in humans and apes. During infection, it typically causes dysentery. The genus is named after Kiyoshi Shiga, who first discovered it in 1898.

Phylogenetic studies indicate that *Shigella* is more appropriately treated as subgenus of *Escherichia*, and that certain strains generally considered *E. coli* – such as *E. coli* O157:H7 – are better placed in *Shigella* (see *Escherichia coli#Diversity* for details).

Classification
Shigella species are classified by four serogroups:

1. Serogroup *A*: *S. dysenteriae* (12 serotypes)
2. Serogroup *B*: *S. flexneri* (6 serotypes
3. Serogroup *C*: *S. boydii* (18 serotypes)
4. Serogroup *D*: *S. sonnei* (1 serotype)

Groups *A–C* are physiologically similar; *S. sonnei* (group *D*) can be differentiated on the basis of biochemical metabolism assays. Three *Shigella* groups are the major disease-causing species: *S. flexneri* is the most frequently isolated species worldwide, and accounts for 60% of cases in the developing world; *S. sonnei* causes 77% of cases in the developed world, compared to only 15% of cases in the developing world; and *S. dysenteriae* is usually the cause of epidemics of dysentery, particularly in confined populations such as refugee camps.

Pathogenesis
Shigella infection is typically via ingestion (fecal–oral contamination); depending on age and condition of the host, less than 100 bacterial cells can be enough to cause an infection. *Shigella* causes dysentery that results in the destruction of the epithelial cells of the intestinal mucosa in the cecum and rectum. Some strains produce enterotoxin and shiga toxin, similar to the verotoxin of *E. coli* O157:H7 and other verotoxin-producing Escherichia coli. Both shiga toxin and verotoxin are associated with causing hemolytic uremic syndrome. As noted above, these supposed *E. coli* strains are at least in part actually more closely related to *Shigella* than to the "typical" *E. coli*.

Shigella invade the host through the M-cells in the gut epithelia of the large intestine, as they cannot enter directly through the epithelial cells. Using a Type III secretion system acting as a biological syringe, the bacterium injects IpaD protein into cells, triggering bacterial invasion and the subsequent lysis of vacuolar membranes using IpaB and IpaC proteins. It uses a mechanism for its

motility by which its IcsA protein triggers actin polymerization in the host cell (via N-WASP recruitment of Arp2/3 complexes) in a "rocket" propulsion fashion for cell-to-cell spread. The most common symptoms are diarrhea, fever, nausea, vomiting, stomach cramps and flatulence. The stool may contain blood, mucus, or pus. In rare cases, young children may have seizures. Symptoms can take as long as a week to show up, but most often begin two to four days after ingestion. Symptoms usually last for several days, but can last for weeks. *Shigella* is implicated as one of the pathogenic causes of reactive arthritis worldwide.

Each of the *Shigella* genomes includes a virulence plasmid that encodes conserved primary virulence determinants. The *Shigella* chromosomes share most of their genes with those of *E. coli* K12 strain MG1655.

Diagnosis
Shigella species are negative for motility and are not lactose fermenters. (However, *S. sonnei* can ferment lactose). They typically do not produce gas from carbohydrates (with the exception of certain strains of *S. flexneri*) and tend to be overall biochemically inert. *Shigella* should also be urea hydrolysis negative . When inoculated to a triple sugar iron (TSI) slant, they react as follows: K/A, gas -, H2S -. Indole reactions are mixed, positive and negative, with the exception of *S. sonnei*, which is always indole negative. Growth on *Hektoen enteric agar* will produce bluish-green colonies for Shigella and bluish-green colonies with black centers for *Salmonella*.

Treatment
Severe dysentery can be treated with ampicillin, TMP-SMX, or fluoroquinolones, such as ciprofloxacin, and of course rehydration. Medical treatment should only be used in severe cases. Antibiotics are usually avoided in mild cases because some Shigella are resistant to antibiotics, and their use may make the germ even more resistant. Antidiarrheal agents may worsen the sickness, and should be avoided. For *Shigella*-associated diarrhea, antibiotics shorten the length of infection (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Smallpox
Date: 2012
Source: Wikipedia

Abstract: Smallpox was an infectious disease unique to humans, caused by either of two virus variants, Variola major and Variola minor. The disease is also known by the Latin names Variola orVariola vera, which is a derivative of the Latin varius, meaning "spotted", or varus, meaning "pimple". The term "smallpox" was first used in Europe in the 15th century to distinguish variola from the "great pox" (syphilis). The last naturally occurring case of smallpox (Variola minor) was diagnosed on 26 October 1977.

Smallpox localizes in small blood vessels of the skin and in the mouth and throat. In the skin, this results in a characteristic maculopapular rash, and later, raised fluid-filled blisters. V. majorproduces a more serious disease and has an overall mortality rate of 30–35%. V. minor causes a milder form of disease (also known as alastrim, cottonpox, milkpox, whitepox, andCuban itch) which kills about 1% of its victims. Long-term complications of V. major infection include characteristic scars, commonly on the face, which occur in 65–85% of survivors. Blindness resulting from corneal ulceration and scarring, and limb deformities due to arthritis and osteomyelitis are less common complications, seen in about 2–5% of cases.

Smallpox is believed to have emerged in human populations about 10,000 BC. The earliest physical evidence of smallpox is probably the pustular rash on the mummified body of PharaohRamses V of Egypt. The disease killed an estimated 400,000 Europeans per year during the closing years of the 18th century (including five reigning monarchs), and was responsible for a third of all blindness. Of all those infected, 20–60%—and over 80% of infected children—died from the disease. Smallpox was responsible for an estimated 300–500 million deaths during the 20th century. As recently as 1967, the World Health Organization (WHO) estimated that 15 million people contracted the disease and that two million died in that year.

After vaccination campaigns throughout the 19th and 20th centuries, the WHO certified the eradication of smallpox in 1979. Smallpox is one of the two infectious diseases to have been eradicated, the other being rinderpest, which was declared eradicated in 2011.

Classification

There are two clinical forms of smallpox. Variola major is the severe and most common form, with a more extensive rash and higher fever. Variola minor is a less common presentation, and a much less severe disease, with historical death rates of 1% or less. Subclinical (asymptomatic) infections with variola virus have been noted, but are not common. In addition, a form called variola sine eruptione (smallpox without rash) is seen generally in vaccinated persons. This form is marked by a fever that occurs after the usual incubation period and can be confirmed only by antibody studies or, rarely, by virus isolation.

Signs & Symptoms
The incubation period between contraction and the first obvious symptoms of the disease is around 12 days. Once inhaled, variola major virus invades the oropharyngeal (mouth and throat) or the respiratory mucosa, migrates to regional lymph nodes, and begins to multiply. In the initial growth phase the virus seems to move from cell to cell, but around the 12th day, lysis of many infected cells occurs and the virus is found in the bloodstream in large numbers (this is called viremia), and a second wave of multiplication occurs in the spleen, bone marrow, and lymph nodes. The initial or prodromal symptoms are similar to other viral diseases such as influenza and the common cold: fever of at least 38.5 °C (101 °F), muscle pain, malaise, headache and prostration. As the digestive tract is commonly involved, nausea and vomiting and backache often occur. The prodrome, or preeruptive stage, usually lasts 2–4 days. By days 12–15 the first visible lesions—small reddish spots called enanthem—appear on mucous membranes of the mouth, tongue, palate, and throat, and temperature falls to near normal. These lesions rapidly enlarge and rupture, releasing large amounts of virus into the saliva.

Smallpox virus preferentially attacks skin cells, causing the characteristic pimples (called macules) associated with the disease. A rash develops on the skin 24 to 48 hours after lesions on the mucous membranes appear. Typically the macules first appear on the forehead, then rapidly spread to the whole face, proximal portions of extremities, the trunk, and lastly to distal portions of extremities. The process takes no more than 24 to 36 hours, after which no new lesions appear. At this point variola major infection can take several very different courses, resulting in four types of smallpox disease based on the Rao classification: ordinary, modified, malignant (or flat), and hemorrhagic. Historically, smallpox has an overall fatality rate of about 30%; however, the malignant and hemorrhagic forms are usually fatal.

Ordinary
Ninety percent or more of smallpox cases among unvaccinated persons are of the ordinary type. In this form of the disease, by the second day of the rash, the macules become raised papules. By the third or fourth day the papules fill with an opalescent fluid to become vesicles. This fluid becomes opaque and turbid within 24–48 hours, giving them the appearance of pustules; however, the so-called pustules are filled with tissue debris, not pus.

By the sixth or seventh day, all the skin lesions have become pustules. Between 7 and 10 days the pustules mature and reach their maximum size. The pustules are sharply raised, typically round, tense, and firm to the touch. The pustules are deeply embedded in the dermis, giving them the feel of a small bead in the skin. Fluid slowly leaks from the pustules, and by the end of the second week the pustules deflate, and start to dry up, forming crusts (or scabs). By day 16–20 scabs have formed over all the lesions, which have started to flake off, leaving depigmented scars.

Ordinary smallpox generally produces a discrete rash, in which the pustules stand out on the skin separately. The distribution of the rash is densest on the face; denser on the extremities than on the trunk; and on the extremities, denser on the distal parts than on the proximal. The palms of the hands and soles of the feet are involved in the majority of cases. Sometimes, the blisters merge together into sheets, forming a confluent rash, which begin to detach the outer layers of skin from the underlying flesh. Patients with confluent smallpox often remain ill even after scabs have formed over all the lesions. In one case series, the case-fatality rate in confluent smallpox was 62%.

Modified
Referring to the character of the eruption and the rapidity of its development, modified smallpox occurs mostly in previously vaccinated people. In this form the prodromal illness still occurs but may be less severe than in the ordinary type. There is usually no fever during evolution of the rash. The skin lesions tend to be fewer and evolve more quickly, are more superficial, and may not show the uniform characteristic of more typical smallpox. Modified smallpox is rarely, if ever, fatal. This form of variola major is more easily confused with chickenpox.

Malignant
In malignant-type smallpox (also called flat smallpox) the lesions remain almost flush with the skin at the time when raised vesicles form in the ordinary type. It is unknown why some people develop this type.

Historically, it accounted for 5%–10% of cases, and the majority (72%) were children. Malignant smallpox is accompanied by a severe prodromal phase that lasts 3–4 days, prolonged high fever, and severe symptoms of toxemia. The rash on the tongue and palate is extensive. Skin lesions mature slowly and by the seventh or eighth day they are flat and appear to be buried in the skin. Unlike ordinary-type smallpox, the vesicles contain little fluid, are soft and velvety to the touch, and may contain hemorrhages. Malignant smallpox is nearly always fatal.

Hemorrhagic

Hemorrhagic smallpox is a severe form that is accompanied by extensive bleeding into the skin, mucous membranes, and gastrointestinal tract. This form develops in approximately 2% of infections and occurred mostly in adults. In hemorrhagic smallpox the skin does not blister, but remains smooth. Instead, bleeding occurs under the skin, making it look charred and black, hence this form of the disease is also known as black pox.

In the early, or fulminating form, hemorrhaging appears on the second or third day as sub-conjunctival bleeding turns the whites of the eyes deep red. Hemorrhagic smallpox also produces a dusky erythema, petechiae, and hemorrhages in the spleen, kidney, serosa, muscle, and, rarely, the epicardium, liver, testes, ovaries and bladder. Death often occurs suddenly between the fifth and seventh days of illness, when only a few insignificant skin lesions are present. A later form of the disease occurs in patients who survive for 8–10 days. The hemorrhages appear in the early eruptive period, and the rash is flat and does not progress beyond the vesicular stage. Patients in the early stage of disease show a decrease in coagulation factors (e.g. platelets,prothrombin, and globulin) and an increase in circulating antithrombin. Patients in the late stage have significant thrombocytopenia; however, deficiency of coagulation factors is less severe. Some in the late stage also show increased antithrombin. This form of smallpox occurs in anywhere from 3 to 25% of fatal cases depending on the virulence of the smallpox strain. Hemorrhagic smallpox is usually fatal.

Cause

Smallpox is caused by infection with variola virus, which belongs to the genus Orthopoxvirus, the family Poxviridae and subfamily chordopoxvirinae. Variola is a large brick-shaped virus measuring approximately 302 to 350 nanometers by 244 to 270 nm, with a single linear double stranded DNA genome 186 kilobase pairs(kbp) in size and containing a hairpin loop at each end. The two classic varieties of smallpox are variola major and variola minor.

Four orthopoxviruses cause infection in humans: variola, vaccinia, cowpox, and monkeypox. Variola virus infects only humans in nature, although primates and other animals have been infected in a laboratory setting. Vaccinia, cowpox, and monkeypox viruses can infect both humans and other animals in nature.

The lifecycle of poxviruses is complicated by having multiple infectious forms, with differing mechanisms of cell entry. Poxviruses are unique among DNA viruses in that they replicate in thecytoplasm of the cell rather than in the nucleus. In order to replicate, poxviruses produce a variety of specialized proteins not produced by other DNA viruses, the most important of which is a viral-associated DNA-dependent RNA polymerase.

Both enveloped and unenveloped virions are infectious. The viral envelope is made of modified Golgi membranes containing viral-specific polypeptides, including hemagglutinin. Infection with either variola major or variola minor confers immunity against the other.

Transmission

Transmission occurs through inhalation of airborne variola virus, usually droplets expressed from the oral, nasal, or pharyngeal mucosa of an infected person. It is transmitted from one person to another primarily through prolonged face-to-face contact with an infected person, usually within a distance of 6 feet (1.8 m), but can also be spread through direct contact with infected bodily fluids or contaminated objects (fomites) such as bedding or clothing. Rarely, smallpox has been spread by virus carried in the air in enclosed settings such as buildings, buses, and trains. The virus can cross the placenta, but the incidence of congenital smallpox is relatively low. Smallpox is not notably infectious in the prodromal period and

viral shedding is usually delayed until the appearance of the rash, which is often accompanied by lesions in the mouth and pharynx. The virus can be transmitted throughout the course of the illness, but is most frequent during the first week of the rash, when most of the skin lesions are intact. Infectivity wanes in 7 to 10 days when scabs form over the lesions, but the infected person is contagious until the last smallpox scab falls off.

Smallpox is highly contagious, but generally spreads more slowly and less widely than some other viral diseases, perhaps because transmission requires close contact and occurs after the onset of the rash. The overall rate of infection is also affected by the short duration of the infectious stage.
In temperate areas, the number of smallpox infections were highest during the winter and spring. In tropical areas, seasonal variation was less evident and the disease was present throughout the year. Age distribution of smallpox infections depends on acquired immunity.Vaccination immunity declines over time and is probably lost in all but the most recently vaccinated populations. Smallpox is not known to be transmitted by insects or animals and there is noasymptomatic carrier state.

Diagnosis
The clinical definition of smallpox is an illness with acute onset of fever greater than 101 °F (38.3 °C) followed by a rash characterized by firm, deep seated vesicles or pustules in the same stage of development without other apparent cause. If a clinical case is observed, smallpox is confirmed using laboratory tests.

Microscopically, poxviruses produce characteristic cytoplasmic inclusions, the most important of which are known as Guarnieri bodies, and are the sites of viral replication. Guarnieri bodies are readily identified in skin biopsies stained with hematoxylin and eosin, and appear as pink blobs. They are found in virtually all poxvirus infections but the absence of Guarnieri bodies cannot be used to rule out smallpox. The diagnosis of an orthopoxvirus infection can also be made rapidly by electron microscopic examination of pustular fluid or scabs. However, all orthopoxviruses exhibit identical brick-shaped virions by electron microscopy.

Definitive laboratory identification of variola virus involves growing the virus on chorioallantoic membrane (part of a chicken embryo) and examining the resulting pock lesions under defined temperature conditions. Strains may be characterized by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis. Serologic tests and enzyme linked immunosorbent assays (ELISA), which measure variola virus-specific immunoglobulin and antigen have also been developed to assist in the diagnosis of infection.

Chickenpox was commonly confused with smallpox in the immediate post-eradication era. Chickenpox and smallpox can be distinguished by several methods. Unlike smallpox, chickenpox does not usually affect the palms and soles. Additionally, chickenpox pustules are of varying size due to variations in the timing of pustule eruption: smallpox pustules are all very nearly the same size since the viral effect progresses more uniformly. A variety of laboratory methods are available for detecting chickenpox in evaluation of suspected smallpox cases.

Prevention

Main article: Smallpox vaccine

Vial containing Variolation Material (India)
The earliest procedure used to prevent smallpox was inoculation (also known as variolation). Inoculation was possibly practiced in India as early as 1000 BC, and involved either nasalinsufflation of powdered smallpox scabs, or scratching material from a smallpox lesion into the skin. However, the idea that inoculation originated in India has been challenged as few of the ancient Sanskrit medical texts described the process of inoculation. Accounts of inoculation against smallpox in China can be found as early as the late 10th century, and the procedure was widely practiced by the 16th century, during the Ming Dynasty. If successful, inoculation produced lasting immunity to smallpox. However, because the person was infected with variola virus, a severe infection could result, and the person could transmit smallpox to

others. Variolation had a 0.5–2% mortality rate, considerably less than the 20–30% mortality rate of the disease itself.

Lady Mary Wortley Montagu observed smallpox inoculation during her stay in the Ottoman Empire, writing detailed accounts of the practice in her letters, and enthusiastically promoted the procedure in England upon her return in 1718. In 1721, Cotton Mather and colleagues provoked controversy in Boston by inoculating hundreds. In 1796, Edward Jenner, a doctor in Berkeley, Gloucestershire, rural England, discovered that immunity to smallpox could be produced by inoculating a person with material from a cowpox lesion. Cowpox is a poxvirus in the same family as variola. Jenner called the material used for inoculation vaccine, from the root word vacca, which is Latin for cow. The procedure was much safer than variolation, and did not involve a risk of smallpox transmission. Vaccination to prevent smallpox was soon practiced all over the world. During the 19th century, the cowpox virus used for smallpox vaccination was replaced byvaccinia virus. Vaccinia is in the same family as cowpox and variola but is genetically distinct from both. The origin of vaccinia virus and how it came to be in the vaccine are not known.

Components of a modern smallpoxvaccination kit including the diluent, a vial of Dryvax vaccinia vaccine, and a bifurcated needle.

The current formulation of smallpox vaccine is a live virus preparation of infectious vaccinia virus. The vaccine is given using a bifurcated (two-pronged) needle that is dipped into the vaccine solution. The needle is used to prick the skin (usually the upper arm) a number of times in a few seconds. If successful, a red and itchy bump develops at the vaccine site in three or four days. In the first week, the bump becomes a large blister (called a “Jennerian vesicle”) which fills with pus, and begins to drain. During the second week, the blister begins to dry up and a scab forms. The scab falls off in the third week, leaving a small scar.

The antibodies induced by vaccinia vaccine are cross-protective for other orthopoxviruses, such as monkeypox, cowpox, and variola (smallpox) viruses. Neutralizing antibodies are detectable 10 days after first-time vaccination, and seven days after revaccination. Historically, the vaccine has been effective in preventing smallpox infection in 95% of those vaccinated. Smallpox vaccination provides a high level of immunity for three to five years and decreasing immunity thereafter. If a person is vaccinated again later, immunity lasts even longer. Studies of smallpox cases in Europe in the 1950s and 1960s demonstrated that the fatality rate among persons vaccinated less than 10 years before exposure was 1.3%; it was 7% among those vaccinated 11 to 20 years prior, and 11% among those vaccinated 20 or more years prior to infection. By contrast, 52% of unvaccinated persons died.

There are side effects and risks associated with the smallpox vaccine. In the past, about 1 out of 1,000 people vaccinated for the first time experienced serious, but non-life-threatening, reactions including toxic or allergic reaction at the site of the vaccination (erythema multiforme), spread of the vaccinia virus to other parts of the body, and to other individuals. Potentially life-threatening reactions occurred in 14 to 500 people out of every 1 million people vaccinated for the first time. Based on past experience, it is estimated that 1 or 2 people in 1 million (0.000198%) who receive the vaccine may die as a result, most often the result of postvaccinial encephalitis or severe necrosis in the area of vaccination (called progressive vaccinia).

Given these risks, as smallpox became effectively eradicated and the number of naturally occurring cases fell below the number of vaccine-induced illnesses and deaths, routine childhood vaccination was discontinued in the United States in 1972, and was abandoned in most European countries in the early 1970s. Routine vaccination of health care workers was discontinued in the U.S. in 1976, and among military recruits in 1990 (although military personnel deploying to the Middle East and Korea still receive the vaccination.) By 1986, routine vaccination had ceased in all countries. It is now primarily recommended for laboratory workers at risk for occupational exposure.

Treatment

Smallpox vaccination within three days of exposure will prevent or significantly lessen the severity of smallpox symptoms in the vast majority of people. Vaccination four to seven days after exposure can

offer some protection from disease or may modify the severity of disease. Other than vaccination, treatment of smallpox is primarily supportive, such as wound care and infection control, fluid therapy, and possible ventilator assistance. Flat and hemorrhagic types of smallpox are treated with the same therapies used to treat shock, such as fluid resuscitation. People with semi-confluent and confluent types of smallpox may have therapeutic issues similar to patients with extensive skin burns.

No drug is currently approved for the treatment of smallpox. However, antiviral treatments have improved since the last large smallpox epidemics, and studies suggest that the antiviral drug cidofovir might be useful as a therapeutic agent. The drug must be administered intravenously, however, and may cause serious kidney toxicity.

Prognosis

The overall case-fatality rate for ordinary-type smallpox is about 30%, but varies by pock distribution: ordinary type-confluent is fatal about 50–75% of the time, ordinary-type semi-confluent about 25–50% of the time, in cases where the rash is discrete the case-fatality rate is less than 10%. The overall fatality rate for children younger than 1 year of age is 40%–50%. Hemorrhagic and flat types have the highest fatality rates. The fatality rate for flat-type is 90% or greater and nearly 100% is observed in cases of hemorrhagic smallpox. The case-fatality rate for variola minor is 1% or less. There is no evidence of chronic or recurrent infection with variola virus.

In fatal cases of ordinary smallpox, death usually occurs between the tenth and sixteenth days of the illness. The cause of death from smallpox is not clear, but the infection is now known to involve multiple organs. Circulating immune complexes, overwhelming viremia, or an uncontrolled immune response may be contributing factors. In early hemorrhagic smallpox, death occurs suddenly about six days after the fever develops. Cause of death in hemorrhagic cases involved heart failure, sometimes accompanied by pulmonary edema. In late hemorrhagic cases, high and sustained viremia, severe platelet loss and poor immune response were often cited as causes of death. In flat smallpox modes of death are similar to those in burns, with loss of fluid, protein and electrolytes beyond the capacity of the body to replace or acquire, and fulminating sepsis.

Complications

Complications of smallpox arise most commonly in the respiratory system and range from simple bronchitis to fatal pneumonia. Respiratory complications tend to develop on about the eighth day of the illness and can be either viral or bacterial in origin. Secondary bacterial infection of the skin is a relatively uncommon complication of smallpox. When this occurs, the fever usually remains elevated.

Other complications include encephalitis (1 in 500 patients), which is more common in adults and may cause temporary disability; permanent pitted scars, most notably on the face; and complications involving the eyes (2% of all cases). Pustules can form on the eyelid, conjunctiva, and cornea, leading to complications such as conjunctivitis, keratitis, corneal ulcer, iritis, iridocyclitis, and optic atrophy. Blindness results in approximately 35% to 40% of eyes affected with keratitis and corneal ulcer. Hemorrhagic smallpox can cause subconjunctival and retinal hemorrhages. In 2% to 5% of young children with smallpox, virions reach the joints and bone, causing osteomyelitis variolosa. Lesions are symmetrical, most common in the elbows, tibia, and fibula, and characteristically cause separation of an epiphysis and marked periosteal reactions. Swollen joints limit movement, and arthritis may lead to limb deformities, ankylosis, malformed bones, flail joints, and stubby fingers.

History: Main article: History of smallpox

Viral Evolution

Drawing accompanying text in Book XII of the 16th-century Florentine Codex (compiled 1540–1585), showing Nahuas of conquest-era central Mexico suffering from smallpox.

The date of the appearance of smallpox is not settled. It most likely evolved from a rodent virus between 68,000 and 16,000 years ago. The wide range of dates is due to the different records used to calibrate

the molecular clock. One clade was the variola major strains (the more clinically severe form of smallpox) which spread from Asia between 400 and 1,600 years ago. A second clade included both alastrim minor (a phenotypically mild smallpox) described from the American continents and isolates from West Africa which diverged from an ancestral strain between 1,400 and 6,300 years before present. This clade further diverged into two subclades at least 800 years ago.

A second estimate has placed the separation of variola from Taterapox at 3000–4000 years ago. This is consistent with archaeological and historical evidence regarding the appearance of smallpox as a human disease which suggests a relatively recent origin. However if the mutation rate is assumed to be similar to that of the herpesviruses the divergence date between variola from Taterapox has been estimated to be 50,000 years ago. While this is consistent with the other published estimates it suggests that the archaeological and historical evidence is very incomplete. Better estimates of mutation rates in these viruses are needed.

It seems to have emerged in its endemic form in India 2500–3000 years ago. The variola virus was transferred from West Africa to South America in the 19th century.

Human History

The earliest credible clinical evidence of smallpox is found in the Egyptian mummy of Ramses V who died over 3000 years ago (1145 BCE). Historical records from Asia describe evidence of smallpox-like disease in medical writings from ancient India (as early as 1500 BCE) and China (1122 BCE). It has been speculated that Egyptian traders brought smallpox to India during the 1st millennium BC, where it remained as an endemic human disease for at least 2000 years. Smallpox was probably introduced in China during the 1st century AD from the southwest, and in the 6th century was carried from China to Japan. In Japan, the epidemic of 735–737 is believed to have killed up to one-third of the population. At least seven religious deities have been specifically dedicated to smallpox, such as the god Sopona in the Yoruba religion. In India, the Hindu goddess of smallpox, Sitala Mata, was worshiped in temples throughout the country.

The arrival of smallpox in Europe and south-western Asia is less clear. Smallpox is not described in either the Old or New Testaments of the Bible, or in literature of the Greeks and Romans. Scholars agree it is very unlikely such a serious disease as variola major would have escaped a description by Hippocrates if it existed in the Mediterranean region. While the Antonine Plague that swept through the Roman Empire in 165–180 AD may have been caused by smallpox, other historians speculate that Arab armies first carried smallpox out of Africa to Southwestern Europe during the 7th and 8th centuries AD. In the 9th century the Persian physician, Rhazes, provided one of the most definitive observations of smallpox and was the first to differentiate smallpox from measles and chickenpox in his Kitab fi al-jadari wa-al-hasbah (The Book of Smallpox and Measles). During the Middle Ages, smallpox made periodic incursions into Europe but did not become established there until the population increased and population movement became more active during the time of the Crusades. By the 16th century smallpox was well established over most of Europe. With its introduction in populated areas in India, China and Europe, smallpox affected mainly children, with periodic epidemics that killed up to 30% of those infected. The appearance of smallpox in Europe is of particular importance, as successive waves of European exploration and colonization served to spread the disease to other parts of the world. By the 16th century it had become an important cause of morbidity and mortality in the known world.

There are no credible descriptions of smallpox-like disease in the Americas before the westward exploration by Europeans in the 15th century AD. In 1507 smallpox was introduced into the Caribbean island of Hispaniola and to the mainland in 1520, when Spanish settlers from Hispaniola arriving in Mexico brought smallpox with them. Smallpox devastated the native Amerindianpopulation and was an important factor in the conquest of the Aztecs and the Incas by the Spaniards. Settlement of the east coast of North America in 1633 in Plymouth, Massachusetts was also accompanied by devastating outbreaks of smallpox among Native American populations, and subsequently among the native-born colonists. Some estimates indicate case fatality rates of 80–90% in Native American populations during smallpox epidemics. Smallpox was introduced into Australia in 1789 and again in 1829. Although the disease was never endemic on the continent, it was the principal cause of death in Aboriginal populations

between 1780 and 1870.

By the mid-18th century smallpox was a major endemic disease everywhere in the world except in Australia and in several small islands. In Europe smallpox was a leading cause of death in the 18th century, killing an estimated 400,000 Europeans each year. Through the century smallpox resulted in the deaths of perhaps 10% of all the infants of Sweden every year, and the death rate of infants in Russia may have been even higher. The widespread use of variolation in a few countries, notably Great Britain, its North American colonies, and China, somewhat reduced the impact of smallpox among the wealthy classes during the latter part of the 18th century, but a real reduction in its incidence did not occur until vaccination became a common practice toward the end of the 19th century. Improved vaccines and the practice of re-vaccination led to a substantial reduction in cases in Europe and North America, but smallpox remained almost unchecked everywhere else in the world. In the United States and South Africa a much milder form of smallpox, variola minor, was recognized just before the close of the 19th century. By the mid-20th century variola minor occurred along with variola major, in varying proportions, in many parts of Africa. Patients with variola minor experience only a mild systemic illness, are often ambulantthroughout the course of the disease, and are therefore able to more easily spread disease. Infection with v. minor induces immunity against the more deadly variola major form. Thus as v. minorspread all over the USA, into Canada, the South American countries and Great Britain it became the dominant form of smallpox, further reducing mortality rates.

Eradication

Since Jenner demonstrated the effectiveness of cowpox to protect humans from smallpox in 1796, various attempts were made to eliminate smallpox on a regional scale. As early as 1803, the Spanish Crown organized a mission (the Balmis expedition) to transport the vaccine to the Spanish colonies in the Americas and the Philippines, and establish mass vaccination programs there. The US Congress passed the Vaccine Act of 1813 to ensure that safe smallpox vaccine would be available to the American public. By about 1817, a very solid state vaccination program existed in the Dutch East Indies. In British India a program was launched to propagate smallpox vaccination, through Indian vaccinators, under the supervision of European officials. Nevertheless, British vaccination efforts in India, and in Burma in particular, were hampered by stubborn indigenous preference for inoculation and distrust of vaccination, despite tough legislation, improvements in the local efficacy of the vaccine and vaccine preservative, and education efforts. By 1832, the federal government of the United States established a smallpox vaccination program for Native Americans. In 1842, the United Kingdom banned inoculation, later progressing to mandatory vaccination. The British government introduced compulsory smallpox vaccination by an Act of Parliament in 1853. In the United States, from 1843 to 1855 first Massachusetts, and then other states required smallpox vaccination. Although some disliked these measures, coordinated efforts against smallpox went on, and the disease continued to diminish in the wealthy countries. By 1897, smallpox had largely been eliminated from the United States. In Northern Europe a number of countries had eliminated smallpox by 1900, and by 1914, the incidence in most industrialized countries had decreased to comparatively low levels. Vaccination continued in industrialized countries, until the mid to late 1970s as protection against reintroduction. Australia and New Zealand are two notable exceptions; neither experienced endemic smallpox and never vaccinated widely, relying instead on protection by distance and strict quarantines.

The first hemisphere-wide effort to eradicate smallpox was made in 1950 by the Pan American Health Organization. The campaign was successful in eliminating smallpox from all American countries except Argentina, Brazil, Colombia, and Ecuador. In 1958 Professor Viktor Zhdanov, Deputy Minister of Health for the USSR, called on the World Health Assembly to undertake a global initiative toeradicate smallpox. The proposal (Resolution WHA11.54) was accepted in 1959. At this point, 2 million people were dying from smallpox every year. Overall, however, the progress towards eradication was disappointing, especially in Africa and in the Indian subcontinent. In 1966 an international team, the Smallpox Eradication Unit, was formed under the leadership of an American, Donald Henderson. In 1967, the World Health Organization intensified the global smallpox eradication by contributing $2.4 million annually to the effort, and adopted the new disease surveillance method promoted by Czech epidemiologist Karel Raška.

In the early 1950s an estimated 50 million cases of smallpox occurred in the world each year. To eradicate smallpox, each outbreak had to be stopped from spreading, by isolation of cases and vaccination of everyone who lived close by. This process is known as "ring vaccination". The key to this strategy was monitoring of cases in a community (known as surveillance) and containment. The initial problem the WHO team faced was inadequate reporting of smallpox cases, as many cases did not come to the attention of the authorities. The fact that humans are the only reservoir for smallpox infection, and that carriers did not exist, played a significant role in the eradication of smallpox. The WHO established a network of consultants who assisted countries in setting up surveillance and containment activities. Early on donations of vaccine were provided primarily by the Soviet Union and the United States, but by 1973, more than 80% of all vaccine was produced in developing countries.

The last major European outbreak of smallpox was in 1972 in Yugoslavia, after a pilgrim from Kosovo returned from the Middle East, where he had contracted the virus. The epidemic infected 175 people, causing 35 deaths. Authorities declared martial law, enforced quarantine, and undertook widespread re-vaccination of the population, enlisting the help of the WHO. In two months, the outbreak was over. Prior to this, there had been a smallpox outbreak in May–July 1963 in Stockholm, Sweden, brought from the Far East by a Swedish sailor; this had been dealt with by quarantine measures and vaccination of the local population.

By the end of 1975, smallpox persisted only in the Horn of Africa. Conditions were very difficult in Ethiopia and Somalia, where there were few roads. Civil war, famine, and refugees made the task even more difficult. An intensive surveillance and containment and vaccination program was undertaken in these countries in early and mid-1977, under the direction of Australian microbiologist Frank Fenner. As the campaign neared its goal, Fenner and his team played an important role in verifying eradication. The last naturally occurring case of indigenous smallpox (Variola minor) was diagnosed in Ali Maow Maalin, a hospital cook in Merca, Somalia, on 26 October 1977. The last naturally occurring case of the more deadly Variola major had been detected in October 1975 in a two-year-old Bangladeshi girl, Rahima Banu.

The global eradication of smallpox was certified, based on intense verification activities in countries, by a commission of eminent scientists on 9 December 1979 and subsequently endorsed by the World Health Assembly on 8 May 1980.

The first two sentences of the resolution read:

“Having considered the development and results of the global program on smallpox eradication initiated by WHO in 1958 and intensified since 1967 … Declares solemnly that the world and its peoples have won freedom from smallpox, which was a most devastating disease sweeping in epidemic form through many countries since earliest time, leaving death, blindness and disfigurement in its wake and which only a decade ago was rampant in Africa, Asia and South America." —World Health Organization, Resolution WHA33.3

Post-Eradication
Three former directors of the Global Smallpox Eradication Program read the news that smallpox had been globally eradicated, 1980

The last cases of smallpox in the world occurred in an outbreak of two cases (one of which was fatal) in Birmingham, UK in 1978. A medical photographer, Janet Parker, contracted the disease at the University of Birmingham Medical School and died on September 11, 1978, after which the scientist responsible for smallpox research at the university, Professor Henry Bedson, committed suicide. In light of this incident, all known stocks of smallpox were destroyed or transferred to one of two WHO reference laboratories which had BSL-4 facilities; the Centers for Disease Control and Prevention (CDC) in the United States and the State Research Center of Virology and Biotechnology VECTOR inKoltsovo, Russia.

In 1986, the World Health Organization first recommended destruction of the virus, and later set the date of destruction to be 30 December 1993. This was postponed to 30 June 1999. Due to resistance from the US and Russia, in 2002 the World Health Assembly agreed to permit the temporary retention of the virus stocks for specific research purposes. Destroying existing stocks would reduce the risk involved with ongoing smallpox research; the stocks are not needed to respond to a smallpox outbreak. Some scientists have argued that the stocks may be useful in developing new vaccines, antiviral drugs, and diagnostic tests, however, a 2010 review by a team of public health experts appointed by the World Health Organization concluded that no essential public health purpose is served by the US and Russia continuing to retain virus stocks. The latter view is frequently supported in the scientific community, particularly among veterans of the WHO Smallpox Eradication Program.

In March 2004 smallpox scabs were found tucked inside an envelope in a book on Civil War medicine in Santa Fe, New Mexico. The envelope was labeled as containing scabs from a vaccination and gave scientists at the Centers for Disease Control and Prevention an opportunity to study the history of smallpox vaccination in the US.

Society & Culture

Biological Warfare

The British at least considered using smallpox as a biological warfare agent at the Siege of Fort Pitt during the French and Indian Wars (1754–63) against France and its Native American allies. Although it is not clear whether the actual use of smallpox had official sanction, on June 24, 1763, William Trent, a local trader, wrote, "Out of our regard for them [sc. representatives of the besieging Delawares], we gave them two Blankets and an Handkerchief out of the Small Pox Hospital. I hope it will have the desired effect." Historians do not agree on whether this effort to broadcast the disease was successful. It has also been alleged that smallpox was used as a weapon during the American Revolutionary War (1775–83).

During World War II, scientists from the United Kingdom, United States and Japan were involved in research into producing a biological weapon from smallpox. Plans of large scale production were never carried through as they considered that the weapon would not be very effective due to the wide-scale availability of a vaccine.

In 1947 the Soviet Union established a smallpox weapons factory in the city of Zagorsk, 75 km to the northeast of Moscow. An outbreak of weaponized smallpox possibly occurred during testing at the factory in the 1970s. General Prof. Peter Burgasov, former Chief Sanitary Physician of the Soviet Army and a senior researcher within the Soviet program of biological weapons, described the incident:

“On Vozrozhdeniya Island in the Aral Sea, the strongest recipes of smallpox were tested. Suddenly I was informed that there were mysterious cases of mortalities in Aralsk. A research ship of the Aral fleet came to within 15 km of the island (it was forbidden to come any closer than 40 km). The lab technician of this ship took samples of plankton twice a day from the top deck. The smallpox formulation—400 gr. of which was exploded on the island—”got her” and she became infected. After returning home to Aralsk, she infected several people including children. All of them died. I suspected the reason for this and called the Chief of General Staff of Ministry of Defense and requested to forbid the stop of the Alma-Ata—Moscow train in Aralsk. As a result, the epidemic around the country was prevented. I called Andropov, who at that time was Chief of KGB, and informed him of the exclusive recipe of smallpox obtained on Vozrazhdenie Island.”

Others contend that the first patient may have contracted the disease while visiting Uyaly or Komsomolsk-on-Ustyurt, two cities where the boat docked.

Responding to international pressures, in 1991 the Soviet government allowed a joint US-British inspection team to tour four of its main weapons facilities at Biopreparat. The inspectors were met with evasion and denials from the Soviet scientists, and were eventually ordered out of the facility. In 1992 Soviet defector Ken Alibek alleged that the Soviet bioweapons program at Zagorsk had produced a large stockpile—as much as twenty tons—of weaponized smallpox (possibly engineered to resist vaccines,

Alibek further alleged), along with refrigerated warheads to deliver it. Alibek's stories about the former Soviet program's smallpox activities have never been independently verified.

In 1997, the Russian government announced that all of its remaining smallpox samples would be moved to the Vector Institute in Koltsovo. With the breakup of the Soviet Union and unemployment of many of the weapons program's scientists, US government officials have expressed concern that smallpox and the expertise to weaponize it may have become available to other governments or terrorist groups who might wish to use virus as means of biological warfare. Specific allegations made against Iraq in this respect, however, proved to be false.

Concern has been expressed by some that artificial gene synthesis could be used to recreate the virus from existing digital genomes, for use in biological warfare. Insertion of the synthesized smallpox DNA into existing related pox virusescould theoretically be used to recreate the virus. The first step to mitigating this risk, it has been suggested, should be to destroy the remaining virus stocks so as to enable unequivocal criminalization of any possession of the virus.

Notable Cases
Famous historical figures who contracted smallpox include Lakota Chief Sitting Bull, Ramses V of Egypt, the Kangxi Emperor (survived), Shunzhi Emperor and Tongzhi Emperor (refer to the official history) of China, Date Masamune of Japan (who lost an eye to the disease). Cuitláhuac, the 10th tlatoani (ruler) of the Aztec city of Tenochtitlan, died of smallpox in 1520, shortly after its introduction to the Americas, and the Incan emperor Huayna Capac died of it in 1527. More recent public figures include Guru Har Krishan, 8th Guru of the Sikhs, in 1664, Peter II of Russia in 1730 (died), George Washington (survived), king Louis XV in 1774 (died) and Maximilian III Joseph, Elector of Bavaria in 1777.

Prominent families throughout the world often had several people infected by and/or perish from the disease. For example, several relatives of Henry VIII survived the disease but were scarred by it. These include his sister Margaret, Queen of Scotland, his fourth wife, Anne of Cleves, and his two daughters: Mary I of England in 1527 and Elizabeth I of England in 1562 (as an adult she would often try to disguise the pockmarks with heavy makeup). His great-niece, Mary, Queen of Scots, contracted the disease as a child but had no visible scarring.

In Europe, deaths from smallpox often changed dynastic succession. The only surviving son of Henry VIII, Edward VI, died from complications shortly after apparently recovering from the disease, thereby rendering his sire's infamous efforts to provide England with a male heir moot. (His immediate successors were all females.) Louis XV of France succeeded his great-grandfather Louis XIV through a series of deaths of smallpox or measles among those earlier in the succession line. He himself died of the disease in 1774. William III lost his mother to the disease when he was only ten years old in 1660, and named his uncle Charles as legal guardian: her death from smallpox would indirectly spark a chain of events that would eventually lead to the permanent ousting of the Stuart line from the British throne. William III's wife, Mary II of England, died from smallpox as well.

In China, the Qing Dynasty had extensive protocols to protect Manchus from the Peking's endemic smallpox. Most notably, the Kangxi Emperor was promoted to the throne because he had survived the disease, ahead of older brothers who had not yet had it.

U.S. Presidents George Washington, Andrew Jackson, and Abraham Lincoln all contracted and recovered from the disease. Washington became infected with smallpox on a visit to Barbados in 1751. Jackson developed the illness after being taken prisoner by the British during the American Revolution, and though he recovered, his brother Robert did not. Lincoln contracted the disease during his Presidency, possibly from his son Tad, and was quarantined shortly after giving the Gettysburg address in 1863.

Famous theologian Jonathan Edwards died of smallpox in 1758 following an inoculation.

U.S.S.R. leader Joseph Stalin fell ill with smallpox at the age of seven. His face was badly scarred by the disease. He later had photographs retouched to make his pockmarks less apparent.

Hungarian poet Ferenc Kölcsey, who wrote the Hungarian national anthem, lost his right eye to smallpox.

Gods & Goddesses

As a reaction to the devastation of smallpox, smallpox gods and goddesses were invented as a mechanism to cope with the disease. Two examples of this occurred in China and India. In China, the smallpox goddess was referred to as T'ou-Shen Niang-Niang. The Chinese actively worked to please the goddess and thus keep the disease at bay. For example, the Chinese referred to the smallpox pustules as "beautiful flowers"; this was an attempt to not offend the goddess and keep her happy. The Chinese also took great measure to protect children from the dangers of smallpox by tricking their smallpox goddess. It was believed that the goddess enjoyed passing the disease to attractive children. This transmission was most likely to occur on the last night of the year, so children wore ugly masks to bed to trick the goddess into passing over them. If infection of smallpox did occur, shrines were set up in the homes of the victims. These shrines were worshipped and made offerings too while the victim was sick. If the victim recovered, the shrines were taken away from the home in a special handmade paper chair or boat and burned. If the patient did not recover, the shrine was destroyed and curses were used to remove the goddess from the house. India's first records of smallpox can be found in a medical book that dates back to A.D. 400. This book describes a disease that sounds exceptionally like smallpox. India, like China, created a goddess in response to its exposure to smallpox. Shitala Mata was both worshipped and feared during her reign. It was believed that this goddess was both evil and kind and had the ability to inflict victims when angered, as well as calm the fevers of the already afflicted. Portraits of the goddess show her holding a broom in her right hand to continue to move the disease and a pot of cool water in the other hand in an attempt to soothe victims. Shrines were created where many India natives, both healthy and not, went to worship and attempt to protect themselves from this disease. Some Indian women, in an attempt to ward off Shitala Mata, placed plates of cooling foods and pots of water on the roofs of their homes (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Tularemia
Date: 2012
Source: Wikipedia

Abstract: Tularemia (also known as Pahvant Valley plague, rabbit fever, deer fly fever, and Ohara's fever:286) is a serious infectious disease caused by the bacterium Francisella tularensis. A Gram-negative, nonmotile coccobacillus, the bacterium has several subspecies with varying degrees of virulence. The most important of those is F. tularensis tularensis (Type A), which is found in lagomorphs in North America, and is highly virulent in humans and domestic rabbits. F. tularensis palaearctica (Type B) occurs mainly in aquatic rodents (beavers, muskrats) in North America and in hares and small rodents in northern Eurasia. It is less virulent for humans and rabbits. The primary vectors are ticks and deer flies, but the disease can also be spread through other arthropods. The disease is named after Tulare County, California.

History

Ancient

F. tularensis has been identified as the cause of human outbreaks in ancient Canaan in about 1715 BC and in 1075 BC. A long-lasting epidemic that plagued the eastern Mediterranean in the 14th century BC was also traced back to a focus in Canaan along the Arwad-Euphrates trading route. According to Siro I. Trevisanato, this epidemic contaminated an area stretching from Cyprus to Iraq, and from Israel to Syria, sparing Egypt (due to a quarantine) and Anatolia (owing to effective political boundaries). Subsequently, wars are believed to have spread the same disease into central Anatolia, from whence it was deliberately introduced into western Anatolia, in acts constituting the first known record of biological warfare.[6]. Finally, Aegean soldiers fighting in western Anatolia returned home to their Greek islands, further spreading the same epidemic.

Modern

The tularemia bacterium was first isolated by G.W. McCoy of the U.S. Public Health Service plague lab and reported in 1912. Scientists determined tularemia could be dangerous to humans; a human being may catch the infection after contacting an infected animal. The ailment soon became frequent with hunters, cooks and agricultural workers.

Epidemiology

The disease is endemic in North America, and parts of Europe and Asia. The most common mode of transmission is via arthropod vectors. Ticks involved include Amblyomma, Dermacentor, Haemaphysalis, and Ixodes.[10] Rodents, rabbits, and hares often serve as reservoir hosts, but waterborne infection accounts for 5 to 10% of all tularemia in the US. Tularemia can also be transmitted by biting flies, particularly the deer fly Chrysops discalis. Individual flies can remain infective for 14 days and ticks for over two years. Tularemia may also be spread by direct contact with contaminated animals or material, by ingestion of poorly cooked flesh of infected animals or contaminated water, or by inhalation.

In the United States, although records show that tularemia was never particularly common, incidence rates continued to drop over the course of the 20th century, so between 1990 and 2000, the rate was less than 1 per 1,000,000, meaning the disease is extremely rare in the US today.[13]
Clinical manifestations and microbiological diagnosis

Clinical Manifestations & Microbiological Diagnosis
Depending on the site of infection, tularemia has six characteristic clinical syndromes: ulceroglandular (the most common type representing 75% of all forms), glandular, oropharyngeal, pneumonic, oculoglandular, and typhoidal.

The incubation period for tularemia is one to 14 days; most human infections become apparent after three to five days.In most susceptible mammals, the clinical signs include fever, lethargy, anorexia, signs of septicemia, and possibly death. Nonhuman mammals rarely develop the skin lesions seen in people. Subclinical infections are common, and animals often develop specific antibodies to the organism. Fever is moderate or very high, and tularemia bacilli can be isolated from blood cultures at this stage. The face and eyes redden and become inflamed. Inflammation spreads to the lymph nodes, which enlarge and may suppurate (mimicking bubonic plague). Lymph node involvement is accompanied by a high fever. Death occurs in less than 1% if therapy is initiated promptly.

The microbiologist must be informed when tularemia is suspected because F. tularensis requires special media for cultivation such as buffered charcoal and yeast extract (BCYE). It cannot be isolated in the routine culture media because of the need for sulfhydryl group donors (such as cysteine). Serological tests (detection of antibodies in the serum of the patients) are available and widely used. Cross reactivity with Brucella can confuse interpretation of the results, so diagnosis should not rely only on serology. Molecular methods such as PCR are available in reference laboratories. The bacteria can penetrate into the body through damaged skin and mucous membranes, or through inhalation. Humans are most often infected by tick bite or through handling an infected animal. Ingesting infected water, soil, or food can also cause infection. Tularemia can also be acquired by inhalation; hunters are at a higher risk for this disease because of the potential of inhaling the bacteria during the skinning process. It has been contracted from inhaling particles from an infected rabbit ground up in a lawnmower (see below). Tularemia is not spread directly from person to person.

Francisella tularensis is an intracellular bacterium, meaning it is able to live as a parasite within host cells. It primarily infects macrophages, a type of white blood cell, thus is able to evade the immune system. The course of disease involves the spread of the organism to multiple organ systems, including the lungs, liver, spleen, and lymphatic system. The course of disease is different depending on the route of exposure. Mortality in untreated (before the antibiotic era) patients has been as high as 50% in the pneumoniac and typhoidal forms of the disease, which however account for less than 10% of cases.[16] Overall mortality was 7% for untreated cases, and the disease responds well to antibiotics, with a fatality rate of about 1%. The exact cause of death is unclear, but it is thought to be a combination of multiple organ system failures.

Treatment & Prevention
The drug of choice is streptomycin. Tularemia may also be treated with gentamicin for ten days, tetracycline-class drugs such as doxycycline for two to three weeks, chloramphenicol or fluoroquinolones. An attenuated, live vaccine is available, but its use is only for high risk groups. Its use as postexposure prophylaxis is not recommended.

Tularemia as a Biological Weapon
The Centers for Disease Control and Prevention (CDC) regard F. tularensis as a viable biological warfare agent, and it has been included in the biological warfare programs of the United States, Soviet Union and Japan at various times. A former Soviet biological weapons scientist, Kenneth Alibek, has alleged that an outbreak of tularemia among German soldiers shortly before the siege of Stalingrad was due to the release of F. tularensis by Soviet forces. Others who have studied the pathogen "propose that an outbreak resulting from natural causes is more likely". In the US, practical research into using rabbit

fever as a biological warfare agent took place in 1954 at Pine Bluff Arsenal, Arkansas, an extension of the Camp Detrick program.

It was viewed as an attractive agent because:

1. It is easy to aerosolize,
2. It is highly infective; 10-50 bacteria are required to infect,
3. It is nonpersistent and easy to decontaminate (unlike anthrax),
4. It is highly incapacitating to infected persons,
5. It has comparatively low lethality, which is useful where enemy soldiers are in proximity to noncombatants, e.g. civilians.

The Schu S4 strain was standardized as "Agent UL" for use in the United States M143 bursting spherical bomblet. It was a lethal biological warfare agent with an anticipated fatality rate of 40 – 60%. The rate-of-action was around three days, with a duration-of-action of one to three weeks (treated) and two to three months (untreated), with frequent relapses. UL was streptomycin resistant. The aerobiological stability of UL was a major concern, being sensitive to sunlight, and losing virulence over time after release. When the 425 strain was standardized as "agent JT" (an incapacitant rather than lethal agent), the Schu S4 strain's symbol was changed again to SR.

Both wet and dry types of F. tularensis (identified by the codes TT and ZZ) were examined during the "Red Cloud" tests, which took place from November 1966 to February 1967 in the Tanana Valley, Alaska.

No vaccine is available to the general public. The best way to prevent tularemia infection is to wear rubber gloves when handling or skinning wild lagomorphs and rodents, avoid ingesting uncooked wild game and untreated water sources, wear long-sleeved clothes, and use an insect repellent to prevent tick bites.

Documented Outbreaks
From May to October 2000, an outbreak of tularemia in Martha's Vineyard resulted in one fatality, and brought the interest of the CDC as a potential investigative ground for aerosolized Francisella tularensis. Over the following summers, Martha's Vineyard was identified as the only place in the world where documented cases of tularemia resulted from lawn mowing.

An outbreak of tularemia occurred in Kosovo in 1999-2000.

In 2004, three researchers at Boston University Medical Center were accidentally infected with F. tularensis, after apparently failing to follow safety procedures.

In 2005, small amounts of F. tularensis were detected in the Mall area of Washington, DC the morning after an antiwar demonstration on September 24, 2005. Biohazard sensors were triggered at six locations surrounding the Mall. While thousands of people were potentially exposed, no infections were reported. The detected bacteria likely originated from a natural source, not from a bioterror attempt.

Tularemia is endemic in the Gori region of the Eurasian country of Georgia. The last outbreak was in 2006.

In July 2007, an outbreak was reported in the Spanish autonomous region of Castile and León and traced to the plague of voles infesting the region. Another outbreak had taken place ten years before in the same area.

In August 2009, a Swedish tourist was bitten by an unidentified insect at Point Grey, Vancouver, BC, Canada. It was not until after return to Sweden that he was diagnosed with tularemia, despite seeking medical treatment in Vancouver.[citation needed]

In Jan 2011, researchers searching for brucellosis among feral hog populations in Texas discovered widespread tularemia infection or evidence of past infection in feral hog populations of at least 2 Texas counties, even though tularemia is not normally associated with pigs at all. Precautions were recommended for those who hunt, dress, or prepare feral hogs. Since feral hogs roam over large distances, there is concern that tularemia may spread or already be present in feral hogs over a very wide geographic area.

In June 2011, in Armenia, Mrgahovit village of Lori Marz two people were infected.[citation needed]

In November 2011, it was found in Tasmania, Australia. Reports claimed it to be the first in the southern hemisphere. However, the causative organism was documented to have been isolated from a foot wound in the Northern Territory, Australia in 2003 (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Epidemic Typhus
Date: 2012
Source: Wikipedia

Abstract: Epidemic typhus (also called "camp fever", "jail fever", "hospital fever", "ship fever", "famine fever", "putrid fever", "petechial fever", "Epidemic louse-borne typhus," and "louse-borne typhus" is a form of typhus so named because the disease often causes epidemics following wars and natural disasters. The causative organism is *Rickettsia prowazekii*, transmitted by the human body louse (*Pediculus humanus corporis*). Feeding on a human who carries the bacillus infects the louse. *R. prowazekii* grows in the louse's gut and is excreted in its feces. The disease is then transmitted to an uninfected human who scratches the louse bite (which itches) and rubs the feces into the wound. The incubation period is one to two weeks. *R. prowazekii* can remain viable and virulent in the dried louse feces for many days. Typhus will eventually kill the louse, though the disease will remain viable for many weeks in the dead louse.

Signs and Symptoms
Symptoms include severe headache, a sustained high fever, cough, rash, severe muscle pain, chills, falling blood pressure, stupor, sensitivity to light, and delirium. A rash begins on the chest about five days after the fever appears, and spreads to the trunk and extremities. A symptom common to all forms of typhus is a fever which may reach 39 °C (102°F).

Brill-Zinsser disease, first described by Nathan Brill in 1913 at Mount Sinai Hospital in New York City, is a mild form of epidemic typhus which recurs in someone after a long period of latency (similar to the relationship between chickenpox and shingles). This recurrence often occurs in times of relative immunosuppression, which is often in the context of malnutrition and other illnesses. In combination with poor sanitation and hygiene which leads to a greater density of lice, this reactivation is why typhus forms epidemics in times of social chaos and upheaval.

Transmission
Epidemic typhus is thus found most frequently during times of war and deprivation. For example, typhus killed hundreds of thousands of prisoners in Nazi concentration camps during World War II. The deteriorating quality of hygiene in camps such as Theresienstadt and Bergen-Belsen created conditions where diseases such as typhus flourished. Situations in the twenty-first century with potential for a typhus epidemic would include refugee camps during a major famine or natural disaster.

Henrique da Rocha Lima in 1916 then proved that the bacterium *Rickettsia prowazekii* was the agent responsible for typhus; he named it after H. T. Ricketts and Stanislaus von Prowazek, two zoologists who had died from typhus while investigating epidemics. Once these crucial facts were recognized, Rudolf Weigl in 1930 was able to fashion a practical and effective vaccine production method by grinding up the insides of infected lice that had been drinking blood. It was, however, very dangerous to produce, and carried a high likelihood of infection to those who were working on it.

A safer mass-production-ready method using egg yolks was developed by Herald R. Cox in 1938.This vaccine was widely available and used extensively by 1943.

Treatment
The infection is treated with antibiotics. Intravenous fluids and oxygen may be needed to stabilize the patient. The mortality rate is 10% to 60%, but is vastly lower (close to zero) if intracellular antibiotics such as tetracycline are used before 8 days. Infection can also be prevented by vaccination.

History
Civilian Public Service worker distributes rat poison for typhus control in Gulfport, Mississippi, ca. 1945.

The first description of typhus was probably given in 1083 at a convent near Salerno, Italy.[7] In 1546, Girolamo Fracastoro, a Florentine physician, described typhus in his famous treatise on viruses and contagion, *De Contagione et Contagiosis Morbis*.

Before a vaccine was developed in World War II, typhus was a devastating disease for humans and has been responsible for a number of epidemics throughout history. These epidemics tend to follow wars, famine, and other conditions that result in mass casualties.

During the second year of the Peloponnesian War (430 BC), the city-state of Athens in ancient Greece was hit by a devastating epidemic, known as the Plague of Athens, which killed, among others, Pericles and his two elder sons. The plague returned twice more, in 429 BC and in the winter of 427/6 BC. Epidemic typhus is a strong candidate for the cause of this disease outbreak, supported by both medical and scholarly opinions.

Typhus also arrived in Europe with soldiers who had been fighting on Cyprus. The first reliable description of the disease appears during the Spanish siege of Moorish Granada in 1489. These accounts include descriptions of fever and red spots over arms, back and chest, progressing to delirium, gangrenous sores, and the stench of rotting flesh. During the siege, the Spaniards lost 3,000 men to enemy action but an additional 17,000 died of typhus.

Typhus was also common in prisons (and in crowded conditions where lice spread easily), where it was known as *Gaol fever* or *Jail fever*. Gaol fever often occurs when prisoners are frequently huddled together in dark, filthy rooms. Imprisonment until the next term of court was often equivalent to a death sentence. It was so infectious that prisoners brought before the court sometimes infected the court itself. Following the Assize held at Oxford in 1577, later deemed the Black Assize, over 300 died from Epidemic typhus, including Sir Robert Bell Lord Chief Baron of the Exchequer. The outbreak that followed, between 1577 to 1579, killed about 10% of the English population. During the Lent Assize Court held at Taunton (1730) typhus caused the death of the Lord Chief Baron, as well as the High Sheriff, the sergeant, and hundreds of others. During a time when there were 241 capital offences, more prisoners died from 'gaol fever' than were put to death by all the public executioners in the realm. In 1759 an English authority estimated that each year a quarter of the prisoners had died from gaol fever. In London, typhus frequently broke out among the ill-kept prisoners of Newgate Gaol and then moved into the general city population.

Epidemics occurred throughout Europe and occurred during the English Civil War, the Thirty Years' War and the Napoleonic Wars. During Napoleon's retreat from Moscow in 1812, more French soldiers died of typhus than were killed by the Russians. A major epidemic occurred in Ireland between 1816–19, and again in the late 1830s, and yet another major typhus epidemic occurred during the Great Irish Famine between 1846 and 1849. The Irish typhus spread to England, where it was sometimes called "Irish fever" and was noted for its virulence. It killed people of all social classes, since lice were endemic and inescapable, but it hit particularly hard in the lower or "unwashed" social strata. In Canada, the typhus epidemic of 1847 killed more than 20 000 people died from 1847 to 1848, mainly Irish immigrants in fever sheds and other forms of quarantine, who had contracted the disease aboard coffin ships.

In America, a typhus epidemic killed the son of Franklin Pierce in Concord, New Hampshire in 1843 and struck in Philadelphia in 1837. Several epidemics occurred in Baltimore, Memphis and Washington DC between 1865 and 1873. Typhus fever was also a significant killer during the US Civil War, although typhoid fever was the more prevalent cause of US Civil War "camp fever". Typhoid is a completely different disease from typhus.

During World War I typhus caused three million deaths in Russia and more in Poland and Romania. Delousing stations were established for troops on the Western front but the disease ravaged the armies of the Eastern front, with over 150,000 dying in Serbia alone. Fatalities were generally between 10 to 40 percent of those infected, and the disease was a major cause of death for those nursing the sick. Between 1918 and 1922 typhus caused at least 3 million deaths out of 20–30 million cases. In Russia after World War I, during a civil war between the White and Red armies, typhus killed three million, largely civilians. During World War II typhus struck the German army as it invaded Russia in 1941. In 1942 and 1943 typhus hit French North Africa, Egypt and Iran particularly hard. Typhus epidemics killed inmates in the Nazi Germany concentration camps; infamous pictures of typhus victims' mass graves can be seen in footage shot at Bergen-Belsen concentration camp. Thousands of prisoners held in appalling conditions in Nazi concentration camps such Theresienstadt and Bergen-Belsen also died of typhus during World War II, including Anne Frank at the age of 15 and her sister Margot. Even larger epidemics in the post-war chaos of Europe were only averted by the widespread use of the newly discovered DDT to kill the lice on millions of refugees and displaced persons.

Following the development of a vaccine during World War II, epidemics have usually occurred in Eastern Europe, the Middle East and parts of Africa.

Biological Weapon

Typhus was one of more than a dozen agents that the United States researched as potential biological weapons before President Richard Nixon suspended all non-defensive aspects of the U.S. biological weapons program in 1969 (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only “threats” the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Scrub Typhus
Date: 2012
Source: Wikipedia

Abstract: Scrub typhus or Bush typhus is a form of typhus caused by *Orientia tsutsugamushi* first isolated and identified in 1930 in Japan.

Although it is similar in presentation to other forms of typhus, it is caused by an agent in a different genus, and is frequently classified separately from the other typhi.

Causes and Geographical Distribution
Scrub typhus is transmitted by some species of trombiculid mites ("chiggers"), particularly *Leptotrombidium deliense*), which are found in areas of heavy scrub vegetation. The bite of this mite leaves a characteristic black eschar that is useful to the doctor for making the diagnosis.

Scrub typhus is endemic to a part of the world known as the "tsutsugamushi triangle" (after the name "Orientia tsutsugamushi" (formerly "Rickettsia tsutsugamushi"), the obligate intracellular gram-negative bacterium causing same), which extends from northern Japan and far-eastern Russia in the north, to the territories around the Solomon Sea into northern Australia in the south, and to Pakistan and Afghanistan in the west.

The precise incidence of the disease is unknown, as diagnostic facilities are not available in much of its large native range which spans vast regions of equatorial jungle to the sub-tropics. In rural Thailand and in Laos, murine and scrub typhus accounts for around a quarter of all adults presenting to hospital with fever and negative blood cultures. The incidence in Japan has fallen over the past few decades, probably due to land development driven decreasing exposure, and many prefectures report fewer than 50 cases per year. It affects females more than males in Korea, but not in Japan, and this is conjectured to be because sex-differentiated cultural roles have women tending garden plots more often, thus being exposed to plant tissues inhabited by chiggers.

Symptoms and Signs
Symptoms include fever, headache, muscle pain, cough, and gastrointestinal symptoms. More virulent strains of *O. tsutsugamushi* can cause hemorrhaging and intravascular coagulation.

Signs
Maculopapular rash, eschar, splenomegaly and lymphadenopathies are typical signs.

Laboratory Findings
Leukopenia and abnormal liver function tests are commonly seen in the early phase of the illness.

Complications
Pneumonitis, encephalitis, and myocarditis occur in the late phase of illness.

Acute scrub typhus appears to improve viral loads in patients with HIV. This interaction is refused by an in vitro study.

Diagnosis
In endemic areas, diagnosis is generally made on clinical grounds alone. Where there is doubt, the diagnosis may be confirmed by a laboratory test such as serology.

The choice of laboratory test is not straightforward, and all currently available tests have their limitations. The cheapest and most easily available serological test is the Weil-Felix test, but this is notoriously unreliable. The gold standard is indirect immunofluorescence,[14] but the main limitation of this method is the availability of fluorescent microscopes, which are not often available in resource-poor settings where scrub typhus is endemic. Indirect immunoperoxidase (IIP) is a modification of the standard IFA method that can be used with a light microscope, and the results of these tests are comparable to those from IFA.[13][16] Rapid bedside kits have been described that produce a result within one hour, but the availability of these tests are severely limited by their cost. Serological methods are most reliable when a fourfold-rise in antibody titre is looked for. If the patient is from a non-endemic area, then diagnosis can be made from a single acute serum sample. In patients from endemic areas, this is not possible because antibodies may be found in up to 18% of healthy individuals.

Other methods include culture and PCR, but these are not routinely available and the results do not always correlate with serological testing, and are affected by prior antibiotic treatment. The currently available diagnostic methods have been summarized.

Treatment
Without treatment, the disease is often fatal. Since the use of antibiotics, case fatalities have decreased from 4%–40% to less than 2%.

The drug most commonly used is doxycycline; but chloramphenicol is an alternative. Strains that are resistant to doxycycline and to chloramphenicol are common in northern Thailand. Rifampin and azithromycin are alternatives. Azithromycin is an alternative in children and pregnant women with scrub typhus, and when doxycycline-resistance is suspected. Ciprofloxacin cannot be used safely in pregnancy and is associated with stillbirths and miscarriage. Combination therapy with doxycycline and rifampicin is not recommended due to possible antagonism.

Other drugs that may be effective are clarithromycin, roxithromycin, and the fluoroquinolones, but there is no clinical evidence on which to recommend their use. Azithromycin or chloramphenicol is useful for infection in children or pregnant women.

Vaccine
There are currently no licensed vaccines available.

An early attempt to create a scrub typhus vaccine occurred in the United Kingdom in 1937 (with the Wellcome Foundation infecting around 300,000 cotton rats in a classified project called "Operation Tyburn"), but the vaccine was not used. The first known batch of scrub typhus vaccine actually used to inoculate human subjects was despatched to India for use by Allied Land Forces, South-East Asia Command (A.L.F.S.E.A.) in June 1945. By December 1945, 268,000 cc. had been despatched. The vaccine was produced at Wellcomes laboratory at Ely Grange, Frant, Sussex. An attempt to verify the efficacy of the vaccine by using a placebo group for comparison was vetoed by the military commanders, who objected to the experiment.

It is now known that there is enormous antigenic variation in *Orientia tsutsugamushi* strains, and immunity to one strain does not confer immunity to another. Any scrub typhus vaccine should give protection to all the strains present locally, in order to give an acceptable level of protection. A vaccine

developed for one locality may not be protective in another locality, because of antigenic variation. This complexity continues to hamper efforts to produce a viable vaccine.

History
An Australian soldier, Private George "Dick" Whittington, is aided by Papuan orderly Raphael Oimbari, near Buna on 25 December 1942. Whittington died in February 1943 from the effects of 'bush typhus'. (Picture by *Life* photographer George Silk)

Severe epidemics of the disease occurred among troops in Burma and Ceylon during World War II (WWII). Several members of the U.S. Army's 5307th Composite Unit (Merrill's Marauders) died of the disease; and before 1944, there were no effective antibiotics or vaccines available.

World war II provides some indicators that the disease is endemic to undeveloped areas in all of Oceania in the Pacific Theater, although war records frequently lack assured diagnoses to desired by Epidemiological statics—and many records of "high fever" evacuations were also likely to be other tropical illnesses. In the chapter entitled "The Green War", General MacArthur's biographer William Manchester identifies that the disease was one of a number debilitating afflictions affecting both sides on New Guinea in the running bloody Kokoda battles over unbelievably harsh terrains under incredible hardships— fought during a six month span all along the Kokoda Track in 1942-43, and mentions that to be hospital evacuated, Allied soldiers (who cycled forces) had to run a fever of 102°F—and that sickness casualties outnumbered weapons inflicted casualties 5:1. Similarly, the illness was a casualty producer in all the jungle fighting of the land battles of New Guinea campaign and Guadalcanal campaign. Where the allies had bases, they could remove and cut back vegetation or use DDT as a prophylaxis area barrier treatment, so tick induced sickness rates in forces off the front lines was diminished.

The disease was also a problem for US troops stationed in Japan after WWII, and was variously known as "Shichitō fever" (by troops stationed in the Izu Seven Islands) or "Hatsuka fever" (Chiba prefecture) (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Vaccinia
Date: 2012
Source: Wikipedia

Abstract: Vaccinia virus (VACV or VV) is a large, complex, enveloped virus belonging to the poxvirus family. It has a linear, double-stranded DNA genome approximately 190 kbp in length, and which encodes for approximately 250 genes. The dimensions of the virion are roughly 360 × 270 × 250 nm, with a mass of approximately 5-10 fg. Vaccinia virus is well known for its role as a vaccine (its namesake) that eradicated the smallpox disease, making it the first human disease to be successfully eradicated by science. This endeavour was carried out by the World Health Organization under the Smallpox Eradication Program. Post eradication of smallpox, scientists study Vaccinia virus to use as a tool for delivering genes into biological tissues (gene therapy and genetic engineering).

In the early 21st century, due to concerns about smallpox being used as an agent for bioterrorism, there was renewed interest in studying the Vaccinia virus.

Classification

Vaccinia infections may be divided into the following types:

1. Generalized vaccinia
2. Eczema vaccinatum
3. Progressive vaccinia (Vaccinia gangrenosum, Vaccinia necrosum)
4. Roseola vaccinia

Origin

Vaccinia virus is closely related to the virus that causes cowpox; historically the two were often considered to be one and the same. The precise origin of vaccinia virus is unknown, however, due to the lack of record-keeping as the virus was repeatedly cultivated and passaged in research laboratories for many decades. The most common notion is that vaccinia virus, cowpox virus, and variola virus (the causative agent of smallpox) were all derived from a common ancestral virus. There is also speculation that vaccinia virus was originally isolated from horses.

Basic Biology

Poxviruses are unique among DNA viruses because they replicate only in the cytoplasm of the host cell, outside of the nucleus. Therefore, the large genome is required for encoding various enzymes and proteins involved in viral DNA replication and gene transcription. During its replication cycle, VV produces four infectious forms which differ in their outer membranes: intracellular mature virion (IMV), the intracellular enveloped virion (IEV), the cell-associated enveloped virion (CEV) and the extracellular enveloped virion (EEV).[7] Although the issue remains contentious, the prevailing view is that the IMV consists of a single lipoprotein membrane, while the CEV and EEV are both surrounded by two

membrane layers and the IEV has three envelopes. The IMV is the most abundant infectious form and is thought to be responsible for spread between hosts. On the other hand, the CEV is believed to play a role in cell-to-cell spread and the EEV is thought to be important for long range dissemination within the host organism.

Host Resistance
Vaccinia contains within its genome several proteins that give the virus resistance to interferons. K3L is a protein with homology to the protein eukaryotic initiation factor 2 (eIF-2alpha). K3L protein inhibits the action of PKR, an activator of interferons. E3L is another protein encoded by Vaccinia. E3L also inhibits PKR activation; and is also able to bind to double stranded RNA.

Use as a Vaccine
A Vaccinia virus infection is very mild and is typically asymptomatic in healthy individuals, but it may cause a mild rash and fever. Immune responses generated from a Vaccinia virus infection protects the person against a lethal smallpox infection. For this reason, Vaccinia virus was, and is still being used as a live-virus vaccine against smallpox. Unlike vaccines that use weakened forms of the virus being vaccinated against, the Vaccinia virus vaccine cannot cause a smallpox infection because it does not contain the smallpox virus. However, certain complications and/or vaccine adverse effects occasionally arise. The chance of this happening is significantly increased in people who are immunocompromised. Approximately one in one million individuals will develop a fatal response to the vaccination. Currently, the vaccine is only administered to health care workers or research personnel who have a high risk of contracting the varioloa virus, and to the military personnel of the United States of America. Due to the present threat of smallpox-related bioterrorism, there is a possibility the vaccine may have to be widely administered again in the future. Therefore, scientists are currently developing novel vaccine strategies against smallpox which are safer and much faster to deploy during a bioterrorism event.

On September 1, 2007, the U.S. Food and Drug Administration (FDA) licensed a new vaccine ACAM2000 against smallpox which can be produced quickly upon need. Manufactured by Acambis ofCambridge, England, and Cambridge, Massachusetts, the U.S. Centers for Disease Control and Prevention stockpiled 192.5 million doses of the new vaccine (see list of common strains below).

History
The original vaccine for smallpox, and the origin of the idea of vaccination, was Cowpox, reported on by Edward Jenner in 1796. The Latin term used for Cowpox was variola vaccina, essentially a direct translation of "cow-related pox". That term lent its name to the whole idea of vaccination. When it was realized that the virus used in smallpox vaccination was not, or was no longer, the same as the Cowpox virus, the name 'vaccinia' stayed with the vaccine-related virus. (See OED.) Vaccine potency and efficacy prior to the invention of refrigerated methods of transportation was unreliable. The vaccine would be rendered impotent by heat and sunlight, and the method of drying samples on quills and shipping them to countries in need often resulted in an inactive vaccine. Another method employed was the "arm to arm" method. This involved vaccinating an individual then transferring it to another as soon as the infectious pustule forms, then to another, etc. This method was used as a form of living transportation of the vaccine, and usually employed orphans as carriers. However, this method was problematic due to the possibility of spreading other blood diseases, such as hepatitis and syphilis. 41 Italian children contracted syphilis after being vaccinated by the arm to arm method in 1861.

In 1913, E. Steinhardt, C. Israeli, and R. A. Lambert grew vaccinia virus in fragments of guinea pig corneal tissue culture.

In 1939 Alan Downie showed that the smallpox vaccines being used in the 20th century and cowpox virus were not the same, but some sorts of cousins.

Recent Cases
In March 2007, a 2-year-old Indiana boy and his mother contracted a life-threatening vaccinia infection from the boy's father. The boy developed the telltale rash over 80 percent of his body after coming into close contact with his father, who was vaccinated for smallpox before being deployed overseas by

the United States Army. The United States military resumed smallpox vaccinations in 2002. The child acquired the infection due to eczema, which is a known risk factor for vaccinia infection. The boy was treated with intravenous immunoglobulin, cidofovir, and an experimental drug being developed by SIGA Technologies. On April 19, 2007, he was sent home with no after effects except for possible scarring of the skin.

In 2010, the Centers for Disease Control and Prevention (CDC) reported that a woman in Washington had contracted vaccinia virus infection after digital vaginal contact with her boyfriend, a military member who had recently been vaccinated for smallpox. The woman had a history of childhood eczema, but she had not been symptomatic as an adult. The CDC indicated that it was aware of four similar cases in the preceding 12 months of vaccinia infection after sexual contact with a recent military vaccinee.

Common Strains

This is a list of some of the well-characterized vaccinia strains used in research and immunizations.

1. Western Reserve
2. Copenhagen
3. Dryvax (also known as "Wyeth"): the vaccine strain previously used in the United States, produced by Wyeth. It was replaced in 2008 [17] by ACAM2000 (see below), produced by Acambis. It was produced as preparations of calf lymphwhich was freeze-dried and treated with antibiotics.
4. ACAM2000: The current strain in use in the USA, produced by Acambis. ACAM2000 was derived from a clone of a Dryvax virus by plaque purification. It is produced in cultures of Vero cells.
5. Modified vaccinia Ankara: a highly attenuated (not virulent) strain created by passaging vaccinia virus several hundred times in chicken embryo fibroblasts. Unlike some other vaccinia strains it does not make immunodeficient mice sick and therefore may be safer to use in humans who have weaker immune systems due to being very young, very old, having HIV/AIDS, etc (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: West Nile Virus
Date: 2012
Source: Wikipedia

Abstract: West Nile virus (WNV) is a virus of the family Flaviviridae. Part of the Japanese encephalitis (JE) antigenic complex of viruses, it is found in both tropical and temperate regions. It mainly infects birds, but is known to infect humans, horses, dogs, cats, bats, chipmunks, skunks, squirrels, domestic rabbits, crows, robins, crocodiles and alligators. The main route of human infection is through the bite of an infected mosquito. Approximately 90% of West Nile Virus infections in humans are without any symptoms.

Image reconstructions and cryoelectron microscopy reveal a 45–50 nm virion covered with a relatively smooth protein surface. This structure is similar to the dengue fever virus; both belong to the genus Flavivirus within the family Flaviviridae. The genetic material of WNV is a positive-sense, single strand of RNA, which is between 11,000 and 12,000 nucleotides long; these genes encode seven non-structural proteins and three structural proteins. The RNA strand is held within a nucleocapsid formed from 12 kDa protein blocks; the capsid is contained within a host-derived membrane altered by two viral glycoproteins.

Symptoms
The West Nile Virus produces one of three different outcomes in humans. The first is an asymptomatic infection; the second is a mild febrile syndrome termed West Nile Fever; the third is a neuroinvasive disease termed West Nile meningitis or encephalitis. The population proportion of these three states is roughly 110:30:1.

The second, febrile stage has an incubation period of 2 to 8 days followed by fever, headache, chills, diaphoresis (excessive sweating), weakness, lymphadenopathy (swollen lymph nodes), drowsiness, pain in the joints and symptoms like those of influenza or the flu. Occasionally there is a short-lived truncal rash and some patients experience gastrointestinal symptoms including nausea, vomiting, loss of appetite, or diarrhea. Symptoms are generally resolved within 7 to 10 days, although fatigue can persist for some weeks and lymphadenopathy up to two months.

The more dangerous encephalitis is characterized by similar early symptoms but also a decreased level of consciousness, sometimes approaching near-coma. Deep tendon reflexes are hyperactive at first, later diminished. There are also extrapyramidal disorders. Recovery is marked by a long convalescence with fatigue.

More recent outbreaks have resulted in a deeper study of the disease and other, rarer, outcomes have been identified. The spinal cord may be infected, marked by anterior myelitis with or without encephalitis. WNV-associated Guillain-Barré syndrome has been identified and other rare effects include multifocal chorioretinitis (which has 100% specificity for identifying WNV infection in patients with possible WNV encephalitis), hepatitis, myocarditis, nephritis, pancreatitis, and splenomegaly.

Mortality Rate
There is no way to accurately measure the number of worldwide cases at this time. However, the United States keeps records of West Nile infection cases. In 2009, there were 663 cases. Three hundred and thirty-five of these cases were encephalitis or meningitis infections, a reaction to the virus that approximately 1 in 150 people who get the virus will show. Three hundred two cases were filed for West Nile fever, the most likely symptom of the virus. Twenty six cases were unspecified. The state of Texas had the most cases, with 104 total. The total mortality rate for 2009 was 30 deaths of the 663 reported serious cases. That is a 4.5% casualty rate, but only of the severe infections. Approximately 80% of cases have no symptoms, and therefore the total casualty rate would be less than 1% of total infections in the U.S. This data and earlier years data is available from the Centers for Disease Control and Prevention (CDC).

Transmission & Susceptibility

Transmission
The proboscis of an Aedes albopictus mosquito feeding on human blood. Under experimental conditions, the Aedes albopictus mosquito (also known as the Asian Tiger Mosquito) has been found to be a vector of West Nile Virus.

The virus is transmitted through mosquito vectors, which bite and infect birds. The birds are amplifying hosts, developing sufficient viral levels to transmit the infection to other biting mosquitoes which go on to infect other birds (in the Western hemisphere the American robin and the American crow are the most common carriers) and also humans. The infected mosquito species vary according to geographical area; in the US Culex pipiens (Eastern US), Culex tarsalis (Midwest and West), and Culex quinquefasciatus (Southeast) are the main sources.

In mammals the virus does not multiply as readily (i.e. does not develop high viremia during infection), and it is believed that mosquitoes biting infected mammals do not ingest sufficient virus to become infected, making mammals so-called dead-end infections.

A 2004 paper in Science found that Culex pipiens mosquitoes existed in two populations in Europe, one which bites birds and one which bites humans. In North America 40% of Culex pipiens were found to be hybrids of the two types which bite both birds and humans, providing a vector for WNV. This is argued to provide an explanation of why the West Nile disease has spread more quickly in North America than Europe. However, these conclusions have been disputed. In 2010 it was verified by the Greek Center for Disease Control and Prevention that Culex pipiens was responsible for an outbreak of the virus in northern Greece.

Susceptibility
It was initially believed that direct human-to-human transmission was only caused by occupational exposure, or conjunctival exposure to infected blood. The US outbreak revealed novel transmission methods, through blood transfusion, organ transplant, intrauterine exposure, and breast feeding. Since 2003, blood banks in the US routinely screen for the virus amongst their donors. As a precautionary measure, the UK's National Blood Service initially ran a test for this disease in donors who donate within 28 days of a visit to the United States, Canada or the North Eastern provinces of Italy. Currently (September 2011) the policy of the National Blood Service is as follows:

"In the last year there have been significant outbreaks in mainland Greece, Romania, Albania, Israel and in the south west of the Russian Federation just north of the Black and Caspian seas. In recent years North Eastern Italy in the provincial districts of Ferrara, Rovigo, Mantua, Modena, Bologna and Reggio Emilia (an area north of Rimini and east of Parma) have also been affected. Donors who have visited a WNV endemic area between April 1st and November 30th may donate blood four weeks after their return, as long as they have had neither symptoms nor evidence of infection. If the donor was diagnosed with WNV, or had a history of symptoms suggestive of WNV, whilst in the endemic area or following their return then they must wait 6 months before donating."

The Scottish National Blood Transfusion Service is to ask prospective donors to wait 28 days after returning from North America or the North Eastern provinces of Italy before donating.

The more severe outcomes of WNV infection are clearly associated with advancing age and a patient history of organ transplantation and diabetes. A genetic factor also appears to increase susceptibility to West Nile disease. A mutation of the gene CCR5 gives some protection against HIV but leads to more serious complications of WNV infection. Carriers of two mutated copies of CCR5 made up 4 to 4.5% of a sample of West Nile disease sufferers while the incidence of the gene in the general population is only 1%.

Recently, the potential for mosquito saliva to impact the course of WNV disease was demonstrated. Mosquitoes inoculate their saliva into the skin while obtaining blood. Mosquito saliva is a pharmacologic cocktail of secreted molecules, principally proteins, that can affect vascular constriction, blood coagulation, platelet aggregation, inflammation, and immunity. It has become clear that mosquito saliva alters the immune response in a manner that may be advantageous to a virus. Studies have shown that it can specifically modulate the immune response during early virus infection, and mosquito feeding can exacerbate WNV infection leading to higher viremia and more severe forms of disease. It is unknown what benefit, if any, the mosquito receives by assisting the virus in this manner, so it is likely that the virus is simply exploiting the preexisting qualities of mosquito saliva developed for other purposes.

There is no vaccine for humans. A vaccine for horses (ATCvet code: QI05AA10) based on killed viruses exists; some zoos have given this vaccine to their birds, although its effectiveness there is unknown. Dogs and cats show few if any signs of infection. There have been no known cases of direct canine-human or feline-human transmission; although these pets can become infected, it is unlikely that they are in turn capable of infecting native mosquitoes and thus continuing the disease cycle.

Avoiding mosquito bites is the most straightforward means to avoid infection—remaining indoors (while preventing mosquitoes from entering) at dawn and dusk, wear light-colored clothing that covers arms and legs as well as trunk, use insect repellents on both skin and clothing (such as DEET, picaradin, or oil of lemon eucalyptus for skin and permethrin for clothes). If one becomes infected, generally, treatment is purely supportive: analgesia for the pain of neurologic diseases; rehydration for nausea, vomiting, or diarrhea; encephalitis may also require airway protection and seizure management.

Reported cases in the U.S. in 2005 exceeded those in 2004, and cases in 2006 exceeded 2005's totals. On August 19, 2006, the LA Times reported that the expected incidence rate of WNV was dropping as the local population becomes exposed to the virus. "In countries like Egypt and Uganda, where West Nile was first detected, people became fully immune to the virus by the time they reached adulthood", federal health officials said. However, just days later, the CDC said that WNV cases could reach a three-year high because hot temperatures had allowed a larger brood of mosquitoes. Although currently there is no West Nile Virus vaccine available for humans, many scientists are working on this issue, and there is hope that a vaccine will become available in the next few years.

History

Studies of phylogenetic lineages have determined that WNV emerged as a distinct virus around 1000 years ago. This initial virus developed into two distinct lineages, Lineage 1 and its multiple profiles is the source of the epidemic transmission in Africa and throughout the world. Lineage 2 was considered an Africa zoonose. However, in 2008, lineage 2, previously only seen in horses in sub-Saharan Africa and Madagascar, began to appear in horses in Europe, where the first known outbreak affected 18 animals in Hungary in 2008. Lineage 1 West Nile virus was detected in South Africa in 2010 in a mare and her aborted fetus; previously, only lineage 2 West Nile virus had been detected in horses and humans in South Africa. A 2007 fatal case in a killer whale in Texas broadened the known host range of West Nile virus to include cetaceans.

WNV has been posited as one of the possible causes of Alexander the Great's early death based on reports of avian deaths before his illness period.[49]

WNV was first isolated from a feverish 37 year old woman at Omogo in the West Nile District of Uganda in 1937 during research on yellow fever virus.[50] A series of serosurveys in 1939 in central Africa found anti-WNV positive results ranging from 1.4% (Congo) to 46.4% (White Nile region, Sudan). It was subsequently identified in Egypt (1942) and India (1953), a 1950 serosurvey in

Egypt found 90% of those over 40 years in age had WNV antibodies. The ecology was characterized in 1953 with studies in Egypt and Israel. The virus became recognized as a cause of severe human meningoencephalitis in elderly patients during an outbreak in Israel in 1957. The disease was first noted in horses in Egypt and France in the early 1960s and found to be widespread in southern Europe, southwest Asia and Australia.

The first appearance of WNV in the Western hemisphere was in 1999 with encephalitis reported in humans, dogs, cats, and horses, and the subsequent spread in the United States may be an important milestone in the evolving history of this virus. The American outbreak began in the New York City area (specifically, College Point, Queens) and was later seen in New Jersey and Connecticut; the virus is believed to have entered in an infected bird or mosquito, although there is no clear evidence. The US virus was very closely related to a lineage 1 strain found in Israel in 1998. Since the first North American cases in 1999, the virus has been reported throughout the United States, Canada, Mexico, the Caribbean and Central America. There have been human cases and equine cases, and many birds are infected. The Barbary Macaque, Macaca sylvanus, was the first non-human primate to contract WNV. Both the US and Israeli strains are marked by high mortality rates in infected avian populations; the presence of dead birds—especially corvidae—can be an early indicator of the arrival of the virus.

A high level of media coverage through 2001/2002 raised public awareness of WNV. This coverage was most likely the result of successive appearances of the virus in new areas, and had the unintended effect of increasing funding for research on this virus and related arthropod-borne viruses. Such research has expanded our understanding of viruses transmitted by mosquitoes.

Overwintering Mechanism

Vertical transmission of West Nile Virus from female *Culex pipiens* mosquitoes to their progeny has been demonstrated in the laboratory. It has not been suggested that vertically infected *Culex* could survive the winter to initiate a WNV amplification cycle the following spring. *Culex* mosquitoes spend the winter hibernating in protected structures such as root cellars, bank barns, caves, abandoned tunnels and other subterranean locations. The first overwintering adult mosquitoes to test positive for WNV were collected in New York, 2000. Since then, positive samples have been identified in New Jersey, 2003 and in Pennsylvania, 2003, 2004 and 2005.

Geographic Distribution

West Nile virus has been described in Africa, Europe, the Middle East, west and central Asia, Oceania (subtype Kunjin), and most recently, North America. Recent outbreaks of West Nile virus encephalitis in humans have occurred in Algeria (1994), Romania (1996 to 1997), the Czech Republic (1997), Congo (1998), Russia (1999), the United States (1999 to 2009), Canada (1999–2007), Israel (2000) and Greece (2010). Epizootics of disease in horses occurred in Morocco (1996), Italy (1998), the United States (1999 to 2001), and France (2000). In 2003, West Nile virus was found in horses in Mexico. In 2011, West Nile Virus was found in horses in Sardinia (Italy). In the US in 2008, West Nile virus was reported in animals in 47 states, D.C. and Puerto Rico. 45 states and D.C. reported human cases in 2008 with only Maine, Alaska and Hawaii having never had a human case. (Maine has had occasional animal cases.)

Recent outbreaks

United States: From 1999 through 2001, the CDC confirmed 149 West Nile virus infections, including 18 deaths. In 2002, a total of 4,156 cases were reported, including 284 fatalities. 13 cases in 2002 were contracted through blood transfusion. The cost of WNV-related health care in 2002 was estimated at $200 million. The first human West Nile disease in 2003 occurred in June and one West Nile-infected blood transfusion was also identified that month. In the 2003 outbreak, 9,862 cases and 264 deaths were reported by the CDC. At least 30% of those cases were considered severe involving meningitis or encephalitis. In 2004, there were only 2,539 reported cases and 100 deaths. In 2005, there was a slight increase in the number of cases, with 3,000 cases and 119 deaths reported. 2006 saw another increase, with 4,269 cases and 177 deaths. In 2007, the number of cases reported decreased to 3,623 and the number of deaths dropped to 124. In 2007, 1,227 cases of wnv neuroinvasion disease and 117 deaths occurred. In 2008, West Nile surveillance data reported to CDC, a total of 28 states have reported 236 cases of human WNV illness. A total of 137 cases for which such data were available occurred in males, median age patients was 48 years. Dates of illness onset ranged from January 17 to August 14: Two cases were fatal.

Canada
One human death occurred in 1999. In 2002, ten human deaths out of 416 confirmed and probable cases were reported by Canadian health officials. In 2003, 14 deaths and 1,494 confirmed and probable cases were reported. Cases were reported in 2003 in Nova Scotia, Quebec, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia, and the Yukon. In 2004, only 26 cases were reported and two deaths; however, 2005 saw 239 cases and 12 deaths. By October 28, 2006, 127 cases and no deaths had been reported. One case was asymptomatic and only discovered through a blood donation. In 2007, 445 Manitobans had confirmed cases of WNV and two people died with a third unconfirmed but suspected. 17 people have either tested positive or are suspected of having the virus in Saskatchewan, and only one person has tested positive in Alberta. Saskatchewan has reported 826 cases of WNV plus three deaths. The spread of West Nile Virus infected mosquitoes to British Columbia for the first time was reported in 2009.

Israel: In the year 2000, the CDC found that there were 417 confirmed cases with 326 hospitalizations. 33 of these people died. The main clinical presentations were encephalitis (57.9%), febrile disease (24.4%), and meningitis (15.9%).

Romania: In 1996–1997 about 500 cases occurred in Romania with a fatality rate of nearly 10%. In 2010 there were 34 confirmed cases and 3 fatalities.

Greece: In the summer of 2010 several cases were reported in northern Greece. In total there were 261 diagnosed cases and 34 fatalities.

Surveillance Methods
West Nile virus can be sampled from the environment by the pooling of trapped mosquitoes, testing avian blood samples drawn from wild birds and dogs and sentinel monkeys, as well as testing brains of dead birds found by various animal control agencies and the public. Testing of the mosquito samples requires the use of RT-PCR to directly amplify and show the presence of virus in the submitted samples. When using the blood sera of wild bird and sentinel chickens, samples must be tested for the presence of WNV antibodies by use of immunohistochemistry (IHC) or Enzyme-Linked Immunosorbent Assay (ELISA). Dead birds, after necropsy, have their various tissues tested for virus by either RT-PCR or immunohistochemistry, where virus shows up as brown stained tissue because of a substrate-enzyme reaction.

Control
West Nile control is achieved through mosquito control, by elimination of mosquito breeding sites, larviciding active breeding areas and encouraging personal use of mosquito repellents. The public is also encouraged to spend less time outdoors, wear long covering clothing, apply bug repellant that contains DEET and ensure that mosquitoes cannot enter buildings. Environmentalists have condemned attempts to control the transmitting mosquitoes by spraying pesticide, saying that the detrimental health effects of spraying outweigh the relatively few lives which may be saved, and that there are more environmentally friendly ways of controlling mosquitoes. They also question the effectiveness of insecticide spraying, as they believe mosquitoes that are resting or flying above the level of spraying will not be killed; the most common vector in the northeastern U.S., Culex pipiens, is a canopy feeder.

The first effective horse vaccine, West Nile-INNOVATOR was introduced by Fort Dodge Animal Health (Wyeth). Shortly thereafter, a second, one-annual-dose vaccine called Prevenile was introduced by Intervet/Schering-Plough Animal Health (Merck), followed by a DNA-based vaccine, called Recombitek (Merial). In 2009, a new killed virus vaccine was introduced by Boehringer-Ingelheim, a privately held pharmaceutical company, incorporating an equine origin WNV strain (E159), representative of the more recent WNV strains impacting horses.

Treatment Research
AMD3100, which had been proposed as an antiretroviral drug for HIV, has shown promise against West Nile encephalitis. Morpholino antisense oligos conjugated to cell penetrating peptides have been shown to partially protect mice from WNV disease. There have also been attempts to treat infections using ribavirin, intravenous immunoglobulin, or alpha interferon. GenoMed, a U.S. biotech

company, has found that blocking angiotensin II can treat the "cytokine storm" of West Nile virus encephalitis as well as other viruses.

In 2007 the World Community Grid launched the Discovering Dengue Drugs – Together project. This uses a distributed network of volunteers' computers via the Berkeley Open Infrastructure for Network Computing (BOINC) to perform computer simulations of interacting molecules. Thousands of small molecules are screened for potential anti-viral properties with respect to West Nile and related viruses (Wikipedia, 2012).

Bio Terror Bible

EXPOSING THE COMING BIO-TERROR PANDEMIC

BIOTERRORBIBLE.COM: There is an ever expanding list of potential bio-terror agents that could be used in a bio-terror attack, but anthrax, smallpox and flu are the only "threats" the government appears worried about. These 3 agents will likely be used the same way that they were used in the U.S. government bio-terror war-games entitled Dark Winter and Atlantic Storm.

Title: Yellow Fever
Date: 2012
Source: Wikipedia

Abstract: Yellow fever (slang term "Yellow Jack") is an acute viral hemorrhagic disease. The virus is a 40 to 50 nm enveloped RNA virus with positive sense of the Flaviviridae family.

The yellow fever virus is transmitted by the bite of female mosquitoes (the yellow fever mosquito, Aedes aegypti, and other species) and is found in tropical and subtropical areas in South America and Africa, but not in Asia. The only known hosts of the virus are primates and several species of mosquito. The origin of the disease is most likely to be Africa, from where it was introduced to South America through the slave trade in the 16th century. Since the 17th century, several major epidemics of the disease have been recorded in the Americas, Africa and Europe. In the 19th century, yellow fever was deemed one of the most dangerous infectious diseases.

Yellow fever presents in most cases with fever, nausea, and pain and it generally subsides after several days. In some patients, a toxic phase follows, in which liver damage with jaundice (giving the name of the disease) can occur and lead to death. Because of the increased bleeding tendency (bleeding diathesis), yellow fever belongs to the group of hemorrhagic fevers. The WHO estimates that yellow fever causes 200,000 illnesses and 30,000 deaths every year in unvaccinated populations; around 90% of the infections occur in Africa.

A safe and effective vaccine against yellow fever has existed since the middle of the 20th century, and some countries require vaccinations for travelers. Since no therapy is known, vaccination programs are of great importance in affected areas, along with measures to prevent bites and reduce the population of the transmitting mosquito. Since the 1980s, the number of cases of yellow fever has been increasing, making it a reemerging disease. This is likely due to warfare and social disruption in several African nations.

Signs & Symptoms
Yellow fever begins after an incubation period of three to six days. Most cases only cause a mild infection with fever, headache, chills, back pain, loss of appetite, nausea, and vomiting. In these cases the infection lasts only three to four days. In fifteen percent of cases, however, sufferers enter a second, toxic phase of the disease with recurring fever, this time accompanied by jaundice due to liver damage, as well as abdominal pain. Bleeding in the mouth, the eyes and in thegastrointestinal tract will cause vomitus containing blood (giving the name black vomit). The toxic phase is fatal in approximately 20% of cases, making the overall fatality rate for the disease 3% (15% * 20%).

Surviving the infection causes life-long immunity and normally there is no permanent organ damage.

Cause
Yellow fever is caused by the yellow fever virus, a 40 to 50 nm wide enveloped RNA virus belonging to the family Flaviviridae. The positive sense single-stranded RNA is approximately 11,000nucleotides long and has a single open reading frame encoding a polyprotein. Host proteases cut this polyprotein into three structural (C, prM, E) and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5); the enumeration corresponds to the arrangement of the protein coding genes in the genome. The viruses infect amongst others monocytes, macrophages and dendritic cells. They attach to the cell surface via specific receptors and are taken up by an endosomal vesicle. Inside the endosome, the decreased pH induces the fusion of the endosomal membrane with thevirus envelope. Thus, the capsid reaches the cytosol, decays and releases the genome. Receptor binding as well as membrane fusion are catalyzed by the protein E, which changes its conformation at low pH, which causes a rearrangement of the 90 homodimers to 60 homotrimers.

After entering the host cells, the viral genome is replicated in the rough endoplasmic reticulum (ER) and in the so-called vesicle packets. At first, an immature form of the virus particle is produced inside the ER, whose M-protein is not yet cleaved to its mature form and is therefore denoted as prM (precursor M) and forms a complex with protein E. The immature particles are processed in the Golgi apparatus by the host protein furin, which cleaves prM to M. This releases E from the complex which can now take its place in the mature, infectious virion.

Transmission
The yellow fever virus is mainly transmitted through the bite of the yellow fever mosquito Aedes aegypti, but other mosquitoes such as the "tiger mosquito" (Aedes albopictus) can also serve as a vector for the virus. Like other Arboviruses which are transmitted via mosquitoes, the yellow fever virus is taken up by a female mosquito which sucks the blood of an infected person. Viruses reach the stomach of the mosquito, and if the virus concentration is high enough, the virions can infect epithelial cells and replicate there. From there they reach the haemocoel (the blood system of mosquitoes) and from there the salivary glands. When the mosquito sucks blood the next time, it injects its saliva into the wound, and thus the virus reaches the blood of the bitten person. There are also indications for transovarial and transstadial transmission of the yellow fever virus within A. aegypti, i.e., the transmission from a female mosquito to her eggs and then larvae. This infection of vectors without a previous blood meal seems to play a role in single, sudden breakouts of the disease.

There are three epidemiologically different infectious cycles, in which the virus is transmitted from mosquitoes to humans or other primates. In the urban cycle, only the yellow fever mosquitoAedes aegypti is involved, which is well adapted to urban centres and can also transmit other diseases including Dengue and Chikungunya. The urban cycle is responsible for the major outbreaks of yellow fever that occur in Africa. Except in an outbreak in 1999 in Bolivia, this urban cycle no longer exists in South America and is only present in Africa.

Besides the urban cycle there is, both in Africa and South America, a sylvatic cycle (Forest cycle or Jungle cycle), where Aedes africanus (in Africa) or mosquitoes of the genus Haemagogusand Sabethes (in South America) serve as a vector. In the jungle, mainly non-human primates get infected; the disease is mostly asymptomatic in African primates. In South America, the sylvatic cycle is currently the only way humans can infect themselves, which explains the low incidence of yellow fever cases on this continent. People who become infected in the jungle can carry the virus to urban centres, where Aedes aegypti acts as a vector. It is because of this sylvatic cycle that yellow fever cannot be eradicated.

In Africa there is a third infectious cycle, also known as savannah cycle or intermediate cycle, which occurs between the jungle and urban cycle. Different mosquitoes of the genus Aedes are involved. In recent years this is the most common form of yellow fever seen in Africa.

Pathogenesis
After transmission of the virus from a mosquito the viruses replicate in the lymph nodes and infect dendritic cells in particular. From there they reach the liver and infect hepatocytes (probably

indirectly via Kupffer cells), which leads to eosinophilic degradation of these cells and to the release of cytokines. Necrotic masses (Councilman bodies) appear in the cytoplasm of hepatocytes.

When the disease takes a deadly course, a cardiovascular shock and multi organ failure with strongly increased cytokine levels (cytokine storm) follow.

Diagnosis
Yellow fever is a clinical diagnosis, which often relies on the whereabouts of the diseased person during the incubation time. Mild courses of the disease can only be confirmed virologically. Since also mild courses of yellow fever can significantly contribute to regional outbreaks, every suspected yellow fever has to be treated seriously (six to ten days after leaving the affected area symptoms of fever, pain, nausea and vomiting).

If yellow fever is suspected, the virus cannot be confirmed until six to ten days after the illness. A direct confirmation can be obtained by Reverse transcription polymerase chain reaction where the genome of the virus is amplified. Another direct approach is the isolation of the virus and its growth in cell culture using blood plasma; this can take one to four weeks.

Serologically an enzyme linked immunosorbent assay during the acute phase of the disease using specific IgM against yellow fever or an increase in specific IgG-titer (compared to an earlier sample) can confirm yellow fever. Together with clinical symptoms, the detection of IgM or a fourfold increase in IgG-titer is considered sufficient indication for yellow fever. Since these tests can cross-react with other Flaviviruses, like Dengue virus, these indirect methods can never prove yellow fever infection.
Liver biopsy can verify inflammation and necrosis of hepatocytes and detect viral antigens. Because of the bleeding tendency of yellow fever patients, a biopsy is only advisable post mortem to confirm the cause of death.

In a differential diagnosis, infections with yellow fever have to be distinguished from other feverish illnesses like malaria. Other viral hemorrhagic fever, such as Ebola virus, Lassa virus, Marburg virus or Junin virus have to be excluded as cause.

Prevention
Personal prevention of yellow fever includes vaccination as well as avoidance of mosquito bites in areas where yellow fever is endemic. Institutional measures for prevention of yellow fever include vaccination programmes and measures of controlling mosquitoes.

Vaccination: Main article: Yellow fever vaccine

For journeys into affected areas, vaccination is highly recommended since mostly non-native people are affected by severe cases of yellow fever. The protective effect is established 10 days after vaccination in 95% of the vaccinated people and lasts for at least 10 years (even 30 years later, 81% of patients retained the immunity). The attenuated live vaccine (stem 17D) was developed in 1937 by Max Theiler from a diseased patient in Ghana and is produced in chicken eggs. WHO recommends routine vaccinations for people living in endemic areas between the 9th and 12th month after birth.

In about 20% of all cases, mild, flu-like symptoms may develop. In rare cases (less than one in 200,000 to 300,000), the vaccination can cause YEL-AVD (yellow fever vaccine-associated viscerotropic disease), which is fatal in 60% of all cases. It is probably due to a genetic defect in the immune system. But in some vaccination campaigns, a 20 fold higher incidence rate has been reported. Age is an important risk factor; in children the complication rate is less than one case per 10 million vaccinations. Another possible side effect is an infection of the nervous system that occurs in one in 200,000 to 300,000 of all cases, causing YEL-AND (yellow fever vaccine-associated neurotropic disease), which can cause meningoencephalitis and is less than 5% of all cases fatal.

In 2009, the largest mass vaccination against yellow fever commenced in West Africa, specifically Benin, Liberia and Sierra Leone. When it is completed in 2015, more than 12 million people

will have been vaccinated against the disease. According to the World Health Organization, the mass vaccination cannot eliminate yellow fever because of the massive number of infected mosquitoes in urban areas of the target countries, but it will significantly reduce the number of people infected. However, the WHO plans to continue the vaccination campaign in another five African countries—Central African Republic, Ghana, Guinea, Ivory Coast and Nigeria—and stated that approximately 160 million people in the continent could be at risk unless the organization acquires additional funding.

Compulsory Vaccination
Some countries in Asia are theoretically in danger of yellow fever epidemics (mosquitoes with the capability to transmit yellow fever and susceptible monkeys are present), even though the disease does not yet occur there. To prevent introduction of the virus, some countries demand previous vaccination of foreign visitors, if they have passed through yellow fever areas. Vaccination has to be proven in a vaccination certificate which is valid 10 days after the vaccination and lasts for 10 years. A list of the countries which require yellow fever vaccination is published by the WHO. If the vaccination cannot be conducted for some reasons, dispensation is possible. In this case an exemption certificate issued by a WHO approved vaccination center is required.

Even though 32 of 44 countries where yellow fever occurs endemically do have vaccination programmes, in many of these countries fewer than 50% of their population is vaccinated.

Vector Control
Besides vaccination, control of the yellow fever mosquito Aedes aegypti is of major importance, especially because the same mosquito can also transmit Dengue and Chikungunya disease. Aedes aegypti breeds preferentially in water, for example in installations by inhabitants of areas with precarious drinking water supply, or in domestic waste; especially tires, cans and plastic bottles. Especially in proximity to urban centres of developing countries these conditions are very common and make a perfect habitat for Aedes aegypti. Two strategies are employed to fight the mosquito:

One approach is to kill the developing larva. Measures are taken to reduce water build-up (the habitat of the larva), and larvicides are used as well as larva-eating fish and copepods, which reduce the number of larva and thus indirectly the number of disease-transmitting mosquitoes. For many years, copepods of the genus Mesocyclops have been used in Vietnam for fighting Dengue fever (yellow fever does not occur in Asia), with the effect that in the affected areas no cases of Dengue fever have occurred since 2001. Similar mechanisms are probably also effective against yellow fever. Pyriproxyfen is recommended as a chemical larvicide, mainly because it is safe for humans and effective even in small doses.

Besides larva, the adult yellow fever mosquitoes are also targeted. The curtains and lids of water tanks are sprayed with insecticides. Spraying insecticides inside houses is another measure, although it is not recommended by the WHO. Similar to the malaria carrier, the Anopheles mosquito, insecticide treated mosquito nets are used successfully against Aedes aegypti.

Treatment
For yellow fever there is, like for all diseases caused by Flaviviruses, no causative cure. Hospitalization is advisable and intensive care may be necessary because of rapid deterioration in some cases. Different methods for acute treatment of the disease have been shown to not be very successful; passive immunisation after emergence of symptoms is probably without effect. Ribavirin and other antiviral drugs as well as treatment with interferons do not have a positive effect in patients. A symptomatic treatment includes rehydration and pain relief with drugs like paracetamol (known as acetaminophen in the United States). Acetylsalicylic acid (for example Aspirin) should not be given because of its anticoagulant effect, which can be devastating in the case of inner bleeding that can occur with yellow fever.

Epidemiology
Yellow fever is endemic in tropical and subtropical areas of South America and Africa. Even though the main vector Aedes aegypti also occurs in Asia, in the Pacific and the Middle East, yellow fever does not occur in these areas; the reason for this is unknown. Worldwide there are about 600 million people living

in endemic areas and the official estimations of the WHO amount to 200,000 cases of disease and 30,000 deaths a year; the number of officially reported cases is far lower. An estimated 90% of the infections occur on the African continent. In 2008, the largest number of cases was recorded in Togo.

Phylogenetic analysis identified seven genotypes of yellow fever viruses, and it is assumed that they are differently adapted to humans and to the vectorAedes aegypti. Five genotypes occur solely in Africa, and is assumed that the West Africa–genotype I is especially virulent or infectious, because this type is often associated with major outbreaks of yellow fever. In South America two genotypes have been identified.

History

Main articles: History of yellow fever and Yellow Fever Epidemic of 1793

The evolutionary origins of yellow fever most likely lie in Africa. It is thought that the virus originated in East or Central Africa and spread from there to West Africa. When an outbreak of yellow fever would occur in an African village with colonists, it would wipe out nearly all the Europeans, while leaving the native population with usually nonlethal symptoms resembling influenza. The virus as well as the vector A. aegypti were probably transferred to South America by ship. The first recorded outbreak of the disease was in 1648 in Yucatan, where the illness was termed xekik (black vomit). At least 25 major outbreaks followed. In colonial times and during the Napoleonic wars, the West Indies was a particularly dangerous posting, and both the English and French forces posted there were decimated by the "Yellow Jack". Napoleon had his eye on conquering the New World, and sent his brother-in-law in command of an army to seize control of Haiti, but over 27,000 of his troops perished of the "Yellow Jack", including their commander. An outbreak as far north as Philadelphia in 1793 resulted in the deaths of several thousand people and forced the administration to flee the city, including president George Washington. Yellow fever epidemics in North America have caused some 100,000-150,000 deaths. Major outbreaks have also occurred in southern Europe. Barcelona suffered the loss of several thousand citizens during an outbreak in 1821. St. Matthew's German Evangelical Lutheran Church in Charleston, South Carolina suffered 308 yellow fever deaths in 1858, reducing the congregation by half. In 1873, Shreveport, Louisiana lost almost a quarter of its population to yellow fever, and in 1878, about 20,000 people died in an epidemic in the Mississippi River Valley. The last major U.S. outbreak was in 1905 in New Orleans. In 1878 Memphis was hit with an unusually large amount of rain, which led to an increase in the mosquito population. The result was a huge outbreak of yellow fever. The steamship John D. Porter took people fleeing Memphis northward in hopes of escaping the disease, but the ship was not allowed to disembark due to concerns of spreading yellow fever. The ship roamed the Mississippi for the next two months before unloading her passengers.

Carlos Finlay, a Cuban doctor and scientist, first proposed in 1881 that yellow fever might be transmitted by mosquitoes rather than direct human contact. Since the losses from yellow fever in the Spanish–American War in the 1890s were thirteenfold higher than the losses due to military operations, further experiments were conducted by a team under Walter Reed, composed of doctors James Carroll, Aristides Agramonte, and Jesse William Lazear, that successfully proved the ″Mosquito Hypothesis″. Yellow fever was thus the first virus shown to be transmitted by mosquitoes. The physician William Gorgas then applied these insights and eradicated yellow fever from Havana, and fought yellow fever during the construction of the Panama Canal after a previous effort on the part of the French failed in part due to the high incidence of yellow fever and malaria.

Although Dr. Reed received much of the credit in history books for "beating" yellow fever, Reed himself credited Dr. Finlay with the discovery of the yellow fever vector, and thus how it might be controlled. Dr. Reed often cited Finlay's papers in his own articles and gave him credit for the discovery in his personal correspondence. The acceptance of Finlay's work was one of the most important and far-reaching effects of the Walter Reed Commission of 1900. Applying methods first suggested by Finlay, yellow fever was eradicated in Cuba and later in Panama, allowing completion of the Panama Canal.

In 1927, the yellow fever virus was isolated in West Africa, which led to the development of two vaccines in the 1930s. The vaccine 17D was developed by the South African microbiologist Max Theiler at

theRockefeller Institute. Following the work of Ernest Goodpasture, he used chicken eggs to culture the virus and won a Nobel Prize for this achievement in 1951. A French team developed the vaccine FNV (French neurotropic vaccine), which was extracted from mouse brain tissue – but since it was associated with a higher incidence of encephalitis, FNV was not recommended after 1961. 17D on the other hand is still in use and over 400 million doses have been distributed. Little has been invested in the development of new vaccines, and the 60-year-old technology might be too slow to stop a yellow fever epidemic. Newer vaccines based on vero cells are in development and should replace 17D at some point.

Using vector control and strict vaccination programs, the urban cycle of yellow fever was nearly eradicated from South America. Since 1943 only a single urban outbreak in Santa Cruz de la Sierra, Bolivia has occurred. Since the 1980s, the number of yellow fever cases have been increasing again and A. aegypti has returned to the urban centers of South America. This is partly due to limitations on insecticides available, and partly because the vector control program was simply abandoned. Even though no new urban cycle has yet been established, it is feared that this could happen again at any point. An outbreak in Paraguay in 2008 was first feared to be urban in nature, but this ultimately proved not to be the case.

In Africa virus eradication programs have mostly relied upon vaccination. These programs have largely been unsuccessful, since they were unable to break the sylvatic cycle. With few countries establishing regular vaccination programs, measures to fight yellow fever have been neglected, making the virus a dangerous threat to spread again.

Research

In the hamster model of yellow fever, early administration of the antiviral ribavirin is an effective early treatment of many pathological features of the disease. Ribavirin treatment during the first five days after virus infection improved survival rates, reduced tissue damage in target organs (liver and spleen), prevented hepatocellular steatosis, and normalised alanine aminotransferase (a liver damage marker) levels. The results of this study suggest that ribavirin may be effective in the early treatment of yellow fever, and that its mechanism of action in reducing liver pathology in yellow fever virus infection may be similar to that observed with ribavirin in the treatment of hepatitis C, a virus related to yellow fever. Because ribavirin had failed to improve survival in a virulent primate (rhesus) model of yellow fever infection, it had been previously discounted as a possible therapy.

In the past, yellow fever has been researched by several countries as a potential biological weapon (Wikipedia, 2012).