

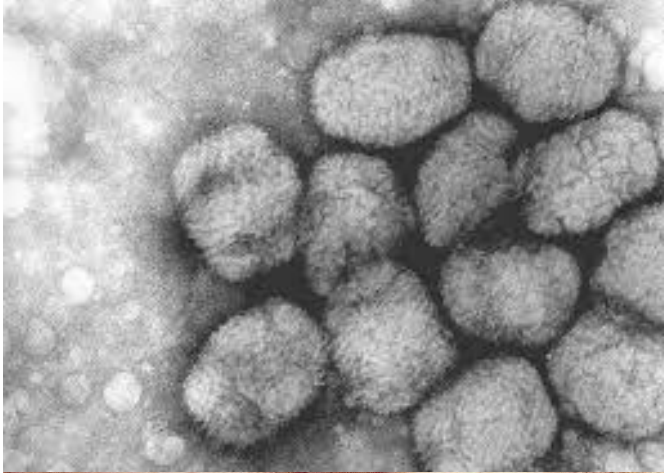
PART 2 - Presentation by Dave Kreps

This is a continuation of a presentation on vaccination that I produced dealing with vaccination. The first slide is a repeat of the last slide from the first presentation.

An Introduction to Immunization Against Infection

Smallpox-Our First Example Of Immunization

The Virus



Skin Pustules



The smallpox virus is a highly infectious organism that has been with us for thousands of years. It is picked up via the respiratory tract or by direct contact with infected individuals. The virus is spread throughout the body by the circulatory system, but we typically see pustules developing on the skin. The typical form of the disease had a mortality rate of 30% which was due to damage done to multiple organs of the body. Hemorrhagic smallpox, a more lethal form of the disease had a much higher mortality rate. Those who survived the infection had significant scarring after the pustules, opened, drained, and crusted over.

It is estimated that millions of people died because of smallpox epidemics. Entire civilizations in the Americas were decimated after the poxvirus was introduced by the Spanish Conquistadores, starting in the 1500's. It is not surprising that there were attempts early on to reduce the destructive powers of this disease agent

Protection Against Smallpox (Variolation)



A process known as variolation was practiced by the Chinese and Turks starting in the 15th century. Scabs from infected individuals were dried and inhaled by a noninfected person. The treated individual would develop a mild form of the disease but would recover and be immune to a natural infection. Complications with variolation were not uncommon.



LADY MARY WORTLEY MONTAGU.

Lady Mary Wortley Montagu, whose husband was stationed in Turkey, observed the process of variolation and informed friends back in England about the virtues of the process. She had her own children variolated in 1718 and 1721. This type of immunization against smallpox became widespread in Europe and was used to protect British troops being sent to the colonies. George Washington, not wanting to be outdone, had his soldiers variolated.



Complete Eradication of Smallpox



In 1798, Dr. Edward Jenner coined the term “vaccination” since he had correctly deduced that cowpox (vacca-cow), caused by a virus that we now know is related to the human poxvirus, could be picked up by the “milkmaids.” He believed the pus from the pustules on their hands could be used to protect humans from the lethal effects of the human form of the disease. On May 14, 1796, pus taken from the hand of Sarah Nelms (lower right corner of the picture) and injected it into the arm of 8 year old James Phipps, who then developed immunity to smallpox infection when later exposed to the smallpox virus. A strain of the cowpox virus was used until 1972 when smallpox was declared eradicated. The vaccine, in this case, was made up of an organism that still capable of replicating in the body.



In the three previous slides, we looked at the development of a treatment for smallpox. It involved the use of a virus that was similar but was a weaker form of a highly virulent virus that had caused millions of deaths and the disfigurement of millions more for hundreds of years. In the next section of this presentation on the production of immunity against disease, we will look at how we were able to immunize humans against the presence of poisons or toxins produced by bacteria. Specifically we will be dealing with tetanus, whooping cough, and diphtheria.

Tetanus: Caused by *Clostridium tetani* – Our Second Example of Immunization

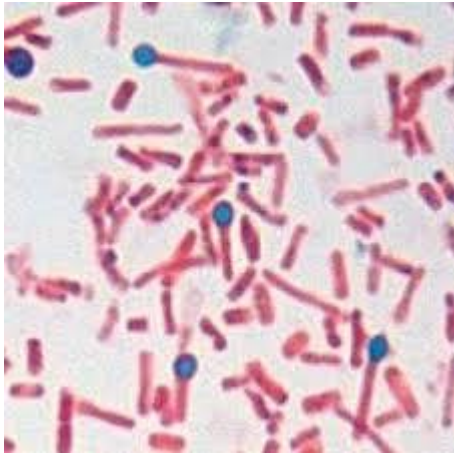
Wherever there is dirt contaminated with fecal material you will find the tetanus bacterium. It will be found on rusty nails, wood splinters, jagged pieces of metal, etc. When punctures of the skin occurs when encountering these objects, bacterial spores, the dormant form of the bacterium, can be introduced into the wound. The spore becomes active and releases a bacterium which can now reproduce and eventually produce a toxic protein which will inhibit the normal flow of nervous impulses resulting in uncontrollable muscle spasms as shown below.



Soldier dying of the “grinning death” painted by Sr. Charles Bell in 1809.

Child with advanced stage of tetanus





***Clostridium tetani*,**
dormant spores are in
blue



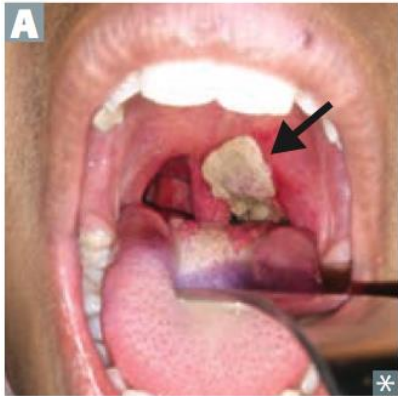
Kitasato Shibasaburo discovered the cause of tetanus in 1891. He also co-discovered the cause of bubonic plague.

The protein toxin responsible for tetanus was isolated in 1924 and converted to a “toxoid.” A *toxoid* is defined as a toxic substance that has been neutralized in some manner so that it has lost its toxicity but can still stimulate the human body to make antibodies which will neutralize the toxic properties of the toxin. Currently, the tetanus toxoid is given in conjunction two other vaccines which I will say more about later. Typically five doses are given between 2 months and 15 years; after that, a booster shot is recommended every 10 years.

Immunization Against Whooping Cough and Diphtheria

Whooping cough and diphtheria are viewed together at this time because immunization to these two diseases has been closely linked to protection against tetanus, plus all three are associated with the exposure to bacteria.

Diphtheria: The name diphtheria comes from the Greek word for leather which describes the leathery deposit located in the back of the throats of those with active symptoms associated with the disease caused by the bacterium *Corynebacterium diphtheriae*.



(Pseudomembrane indicated by arrow)

Diphtheria, first describe by Hippocrates in the 5th century BC, appears in the literature under a variety of names. In 1613, Spain experienced a serious epidemic which gave rise to the term “The year of the strangulation” which reflects the affected individual’s inability to breath and swallow because of the leathery “pseudomembrane” that forms in the back of the throat.

The disease, typically seen in young children, starts out with a sore throat but progresses to a blockage of the airways. A toxin produced by *C. diphtheriae* is released may give rise to heart damage.

(Diphtheria Continued)

Before the advent of immunization, *C. diphtheriae* was associated with millions of cases on diphtheria worldwide per year with 5-10 % of the illnesses resulting in death of the infected, usually children. In 1897, it was observed the serum from individuals who had recovered from the disease could protect those who had an active form of the disease, thus the birth of an anti-toxin. Antitoxin was produced commercially in horses and made available to doctors for treating active cases. The annual Iditarod dog sled race in Alaska commemorates the historic race to Nome Alaska where a serious outbreak of diphtheria occurred in 1925. It took 20 mushers and 150 dogs to make the 674 mile trip to carry the necessary antitoxin to those in Nome who were suffering the toxic affects of diphtheria. If you go to Central Park in NYC, you can see the statue of “Balto” the lead dog in the final leg of the race to Nome.

In the 1920's, there were 13,00-15,000 deaths in the U.S. due to diphtheria. When the cause of diphtheria was discovered in 1928, a vaccine soon followed resulting in a 90% drop in mortality. Today, sporadic outbreaks still occur. In 2017 there were 300 cases in Venezuela and 600 in Indonesia. Because many parents in the U.S. refuse to vaccinate their children, we see a few cases of diphtheria in the states.



Whooping Cough – Infections Due to *Bordetella pertussis*

Like tetanus and diphtheria, whooping cough is due to bacterium; tetanus is picked from the soil while diphtheria and whooping cough are highly infectious organisms that are passed by human to human contact. Whooping cough starts out with symptoms similar to a common cold but progresses to uncontrollable coughing fits that sound like “whoops”. The violent coughing often progresses to spasms, vomiting, and fatigue. Whooping cough is found worldwide with 16.3 million cases in 2015 with a mortality rate of approximately 0.5%. There was an increase in the number of cases in the U.S. in the last ten years with 10 infant deaths in California in 2010 and 20,000 in country wide in 2015. Statistics would suggest that whooping cough is the most vaccine-preventable disease in the U.S.

A vaccine containing whole cell bacteria was produced in the 1930’s which helped to reduce the number of worldwide cases per year. Unfortunately the immunity drops in 5-10 years and a number of people develop a reaction to the whole cell vaccine. In 1981, the Japanese developed an acellular preparation of the pertussis vaccine which reduced the risk of developing inflammatory reaction but the level of immunity fades more rapidly than the whole cell vaccine. Currently, tetanus, diphtheria, and pertussis immunization is carried out by administering the tetanus toxin, diphtheria toxin, and acellular pertussis in a single infection known as DTaP which stands for Diphtheria, Tetanus, and acellular Pertussis.

The next installment will cover polio, measles, mumps, and rubella.



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