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Vaccines--How and Why?

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History

Long before the causes of disease were known and long before the processes of recovery were understood, an interesting thing was observed: if people recovered from a disease, rather than succumbing to it, they appeared to be immune from a second bout with the same illness. Perhaps it was these types of observations that led the Chinese to try to prevent smallpox--a deadly disease characterized by pus-filled blisters--by exposing uninfected individuals to matter from smallpox lesions. This process, known as "variolation," took a variety of forms. One form consisted of removing pus and fluid from a smallpox lesion and using a needle to place it under the skin of the person to be protected. Another method involved peeling scabs from lesions, drying and grinding them to a powder, and letting an uninfected person inhale this powder. The third method involved picking up a small amount of the scab powder with a needle and then using the needle to place the powder directly into the individual's veins. Lady Mary Wortley Montagu, wife of the British Ambassador to Turkey, observed this third method in the early 1700s and brought it back to England. Although the effects of variolation varied, ranging from causing a mild illness in most individuals to causing death in a few, the mortality and morbidity rates due to smallpox were certainly lower in populations that used variolation than in those that did not.

One person who experienced variolation as a child in the late 1700s was Edward Jenner, a young boy who survived the process and grew up to become a country doctor in England. As a country doctor, Jenner noticed a relationship between the equine disease known as "grease" and a bovine disease known as "cow pox." He saw that farmers who treated horses with grease lesions often saw the development of cowpox in their cows, complete with blisters similar to those seen in smallpox infection. Unlike lethal smallpox, however, the cowpox blisters eventually disappeared, leaving only a small scar at the site of each blister.

At the same time, Jenner was interested when a milkmaid told him that she could not catch smallpox because she had had cowpox. Jenner noted that there were many people like the milkmaid - people who milked cows and who did not get smallpox even when exposed repeatedly. With this in mind, Jenner undertook a daring experiment in 1796: he infected a young boy with cowpox in hopes of preventing subsequent smallpox infection. After allowing the boy to recover fully from cowpox, Jenner - in an experiment that would be considered unethical by today's scientific community - intentionally infected the boy with smallpox by injecting pus from a smallpox lesion directly under his skin. As Jenner had predicted, the boy did not contract smallpox.

Although Jenner wanted to report his first case study in the Transactions of the Royal Society of London, his study was rejected. Despite this, Jenner went on to collect 23 case histories over the next months and published his own book detailing his observations. The book was called "An inquiry into the causes and
effects of the variolae vaccinae, a disease discovered in some of the western counties of England, particularly Gloucestershire, and known by the name of The Cow Pox." It soon became clear that Jenner's experiments had paid off, and that intentional infection with cowpox protected people from much more serious infection with smallpox. As a result, within a few years thousands of people protected themselves from the deadly smallpox disease by intentionally infecting themselves with cowpox.

Jenner's process came to be called "vaccination," after "vacca," the Latin word for cow, and the substance used to vaccinate was called a "vaccine." Now, some 200 years later, we have progressed from a time when vaccination was a rare event, and Jenner's theories about vaccination were not widely accepted, to the late 1900s when vaccines are so commonplace that most children receive multiple vaccinations before they reach their first birthdays. The result of such widespread vaccination has been a marked decrease in diseases which once ravaged the world's population. An example of this is smallpox: once a major cause of death world-wide, the smallpox virus is now found only in freezers in high-containment laboratories at the Centers for Disease Control and Prevention (CDC) in Atlanta and the Institute for Viral Preparations in Moscow.

**How Vaccines Work**

Disease causing organisms have at least two distinct effects on the body. The first effect is very obvious: we feel sick, exhibiting symptoms such as fever, nausea, vomiting, diarrhea, rash, and many others. Although the second effect is less obvious, it is this effect that generally leads to eventual recovery from the infection: the disease causing organism induces an immune response in the infected host. As the response increases in strength over time, the infectious agents are slowly reduced in number until symptoms disappear and recovery is complete.

How does induction of the immune response occur? The disease causing organisms contain proteins called "antigens" which stimulate the immune response. The resulting immune response is multi-fold and includes the synthesis of proteins called "antibodies." These proteins bind to the disease causing organisms and lead to their eventual destruction. In addition, "memory cells" are produced in an immune response. These are cells which remain in the blood stream, sometimes for the life span of the host, ready to mount a quick protective immune response against subsequent infections with the particular disease causing agent which induced their production. If such an infection were to occur, the memory cells would respond so quickly that the resulting immune response could inactivate the disease causing agents, and symptoms would be prevented. This response is often so rapid that infection doesn't develop - you are immune from infection.

**How to Make Vaccines**

Obviously, a live, virulent organism cannot be used as a vaccine because it would induce the very disease it should prevent. Therefore, the first step in making a vaccine is to separate the two effects of disease causing organisms. In practice, this means isolating or creating an organism, or part of one, that is unable to cause full blown disease, but that still retains the antigens responsible for inducing the host's immune response. This can be done in many ways. One way is to kill the organism using formalin; vaccines produced in this way are called "inactivated" or "killed" vaccines. Examples of killed vaccines in common use today are the typhoid vaccine and the Salk poliomyelitis vaccine.

Another way to produce a vaccine is to use only the antigenic part of the disease causing organism, for example the capsule, the flagella, or part of the protein cell wall; these types of vaccines are called "acellular vaccines." An example of an acellular vaccine is the Haemophilus influenzae B (HIB) vaccine. Acellular vaccines exhibit some similarities to killed vaccines: neither killed nor acellular vaccines generally induce the strongest immune responses and may therefore require a "booster" every few years.
to insure their continued effectiveness. In addition, neither killed nor acellular vaccines can cause disease and are therefore considered to be safe for use in immunocompromised patients.

A third way of making a vaccine is to "attenuate" or weaken a live microorganism by aging it or altering its growth conditions. Vaccines made in this way are often the most successful vaccines, probably because they multiply in the body thereby causing a large immune response. However, these live, attenuated vaccines also carry the greatest risk because they can mutate back to the virulent form at any time. Such mutation would result in induction of the disease rather than in protection against it. For this reason, attenuated vaccines are not recommended for use in immunocompromised patients. Examples of attenuated vaccines are those that protect against measles, mumps, and rubella. Immunity is often lifelong with attenuated vaccines and does not require booster shots.

Some vaccines are made from toxins. In these cases, the toxin is often treated with aluminum or adsorbed onto aluminum salts to decrease it's harmful effects; after such treatment the toxin is called a "toxoid." Examples of toxoids are the diphtheria and the tetanus vaccines. Vaccines made from toxoids often induce low level immune responses and are therefore sometimes administered with an "adjuvant" - an agent which increases the immune response. For example, the diphtheria and tetanus vaccines are often combined with the pertussis vaccine and administered together as a DPT immunization. The pertussis acts as an adjuvant in this vaccine. When more than one vaccine is administered together it is called a "conjugated vaccine." Toxoid vaccines often require a booster every ten years.

Another way of making a vaccine is to use an organism which is similar to the virulent organism but that does not cause serious disease, such as Jenner did with his use of the relatively mild cowpox virus to protect against the similar, but often lethal, smallpox virus. A more recent example of this type of vaccine is the BCG vaccine used to protect against Mycobacterium tuberculosis. The BCG vaccine currently in use is an attenuated strain of Mycobacterium bovis and requires boosters every 3 - 4 years.

In addition, biotechnology and genetic engineering techniques have been used to produce "subunit vaccines" - vaccines which use only the parts of an organism yet which stimulate a strong immune response. To create a subunit vaccine, researchers isolate the gene or genes which code for appropriate subunits from the genome of the infectious agent. This genetic material is placed into bacteria or yeast host cells which then produce large quantities of subunit molecules by transcribing and translating the inserted foreign DNA. It is important to note that these subunit molecules are encoded by genetic material from the infectious agent, not from the host cell's genetic material. These "foreign" molecules can be isolated, purified, and used as a vaccine. Hepatitis B vaccine is an example of this type of vaccine. Subunit vaccines are safe for immunocompromised patients because they cannot cause the disease.

Vaccines are effective in preventing disease not only in individuals, but also in communities. This type of protection is called "herd immunity." When a disease spreads from one human to another, it requires both an infected individual to spread it and a susceptible individual to catch it. Herd immunity works by decreasing the numbers of susceptible people. When the number of susceptible people drops low enough, the disease will disappear from the community because there are not enough people to carry on the catch-and-infect cycle. The greater the proportion of vaccinated members of the community, the more rapidly the disease will disappear. This is the reason that school children are often required to be vaccinated before attending school. This required vaccination has resulted in the marked decrease of many once-common diseases including pertussis (whooping cough), polio, smallpox, and others. Look for the story of the Polio Vaccine in a future Classic Collection chapter. Viva la Vaccine!

For further information please see: