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Vaccines, a health need and a public asset

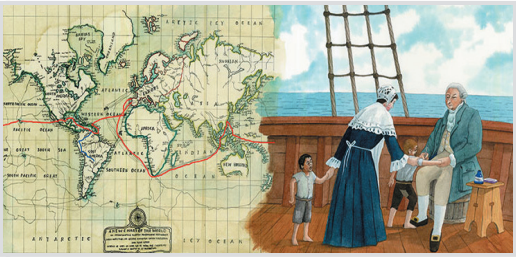

Illustration of the journey of the Royal Philanthropic Expedition of Vaccination by Carles Puche (*Mètode*)

Introduction

Vaccination is one of the greatest contributions to health and has led to the eradication of a deadly disease—smallpox—and the almost total elimination of poliomyelitis and measles. Each vaccine gives us immunity to the specific disease for which it was prepared. When a sufficiently large proportion of the population has been vaccinated, they act as a barrier to the transmission of the disease. However, if the number of people not vaccinated increases, the likelihood of the disease spreading among susceptible people also increases. All countries of the European Union have made a commitment to the World Health Organization to eliminate measles no later than 2015 but, according to recent epidemiological studies, this goal may not be achieved. Measles has resurfaced recently in the European Union, owing to sub-optimal levels of immunization of the population. In fact, there was a downward trend until 2009, but the number of cases quadrupled in the period 2010-2011. According to vaccination coverage data gathered by the World Health Organization, in the European Union between 2000 and 2010 nearly 5 million children between the ages of 2 and 12 were not vaccinated.

A little history

From the Palaeolithic until well into the 20th century, infectious diseases were the main scourge of mankind. The plague, tuberculosis, typhoid, measles, poliomyelitis and many others came close to exterminating our species many times. In the 17th century smallpox displaced the plague as the infectious disease that caused most deaths. During the 18th century several European royal families were hit by smallpox: it caused the death of Emperor Joseph I of Austria, King Louis I of Spain, Tsar Peter II of Russia and King Louis XV of France. The sudden death of the young Joseph I (1678-1711), the Austrian Holy Roman Emperor, marked the fate of such distant nations from Austria as Catalonia and Valencia. When Joseph died, his brother Charles (1685-1740) was appointed emperor. To occupy the vacant throne, he gave up the fight for the Spanish crown, fostered the Treaty of Utrecht and left the fate of those two small and insignificant Mediterranean nations to the will of the great powers (England, France, Holland, Austria and Spain).

In 1796, the English physician Edward Jenner (1749-1823) inoculated liquid from pustules on a cow udder into the arm of a child and then, as the pustules appeared, transferred them to other children. These pustules were harmless and life-saving because, though the cow virus is slightly different from that of humans, it has the same coverage and can induce immunity to the human smallpox virus. The news spread like wildfire, often leading to fears that people would "become cows". Anti-vaccination campaigns were immediately organized. Their arguments were different from those of the current campaigns, but equally unfounded.

On the other hand, movements in favour of vaccination arose in the early nineteenth century in Spain, which was then suffering a period of moral and economic decay (real and royal).

Key Ideas

- Vaccines are the main tool for preventing many infectious diseases, both viral and bacterial.
- People who have been vaccinated or immunized against a particular disease indirectly protect those who have not been vaccinated.
- People who have not been vaccinated against a disease are at risk of contracting it and transmitting it to family, friends and other susceptible people in their environment.
- Like any medical procedure, vaccination may have undesirable effects in a very small number of cases. Therefore, the greatest precaution should be taken in its preparation and administration.
- The problems (side effects) associated with vaccination tend to involve a lower risk to the patient receiving it than the bacterial or viral disease against which they have been vaccinated.
- There is no proven scientific evidence that vaccines cause autism or sterility.

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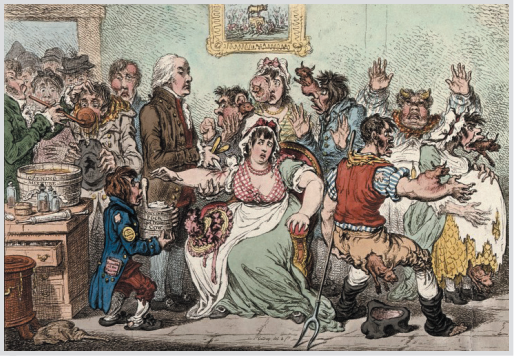

1802 poster of the Anti-Vaccination League, "demonstrating" the harmful effects in recipients of Dr. Jenner's vaccine (Source: Wellcome Library Images)

Especially worth mentioning is Francesc Xavier Balmis i Berenguer (1753-1819), a military doctor from Alicante who organized the Royal Philanthropic Vaccination Expedition, which extended smallpox vaccination to all territories of the Spanish crown in both America and the Philippines.

Some general concepts of immunology

According to the dictionary, to vaccinate means "to inoculate with a vaccine in order to produce immunity to an infectious disease such as diphtheria or typhus". Immunity is the human body's ability to distinguish itself (the body and its symbiotic microbiota) from what is foreign to it. This discriminatory capacity provides protection against infectious diseases, because the immune system identifies microbes as foreign. The immune system develops a defence against antigens (molecules of a specific microbe or group of related microbes). This defence is known as the *immune response* and, in general, it involves the production of blood molecules known as *antibodies* (or immunoglobulins) and the production of specific cells that destroy microbes.

There are two basic mechanisms for acquiring immunity: passive and active immunity. Passive immunity consists in receiving antibodies produced by humans (e.g. in blood transfusions, in which, in addition to blood cells, immunoglobulins can also be transmitted) or from other sources. This type of immunity provides protection against some infections, but it is temporary. Antibodies degrade over a period of weeks or months, and the recipient is no longer protected. The most common form of passive immunity is that which a child receives from its mother. The antibodies are transported through the placenta during the last one or two months of pregnancy and through breast milk. As a result, during the first few months of independent life children have the same type of antibodies as their mothers, and are therefore protected against diseases until they are about one year old.

Active immunity is the stimulation of the immune system to produce a specific humoral response (against an antigen) and a cellular response. Unlike passive immunity, which is temporary, active immunity lasts many years, and in some cases for life. A natural way to acquire active immunity is to overcome an infectious disease, because the body will have produced specific antibodies to the disease. The persistence of the protection years after the infection is known as *immunological memory*. After the immune system has been exposed to an antigen, cells called memory B cells are formed, and they either continue to circulate in the blood or remain in the bone marrow for many years. After a new exposure of the body to the antigen, the memory B cells begin to multiply and quickly produce antibodies to restore the protection. Another way to produce active immunity is through vaccination. Vaccines produce an immune response similar to that produced by the natural infection, but the recipient does not suffer from the disease or any of its complications.

Some general concepts of vaccines

Each vaccine immunizes specifically against a particular disease. However, there are combination vaccines that protect against more than one disease because they contain several vaccines together in a single preparation. In this type, there are preparations such as the DTP vaccine (against diphtheria, tetanus and whooping cough) and the MMR vaccine (against measles, mumps and rubella).

Vaccines may be composed of attenuated live microbes, killed microbes (whole inactivated vaccines), or only some parts or products of the microbe (split inactivated vaccines and toxoid vaccines). Live attenuated vaccines are obtained by modifying a virus or a bacteria that was originally a pathogen through a series of laboratory cultures. The organism contained in the resulting vaccine retains the ability to multiply and induce the production of antibodies in the host, but does not cause disease. To produce an immune response, the microbes in live attenuated vaccines must multiply in the vaccinated person. The immune response to a live attenuated vaccine is virtually identical to that produced in the case of a natural infection. The immune system does not distinguish whether the "invader" is the original pathogen or the attenuated vaccine.

In whole inactivated vaccines, the inactivation is performed by heat treatment or by chemical agents. Inactivated vaccines do not contain live bacteria, so the microbes they contain cannot multiply. This makes them suitable for people with immune problems, but they always require multiple doses. The first dose does not protect in the same way as attenuated vaccines, and the recipients need two to three subsequent exposures to acquire immunity. The vaccines against whooping cough and tetanus are of this type.

Vaccine antigens can also be obtained by genetic engineering. These vaccines are called *recombinant vaccines* and an example is the vaccine for human papilloma virus (HPV).

Photographs of the last woman who suffered smallpox and of the virus that causes the disease (Sources: *Quo* / Mind-Body Institute Vancouver, British Columbia)

The safety of vaccines

Like other drugs or therapies, vaccines are not free of side effects, although these rarely affect the health of the recipients. The side effects may be real adverse reactions or merely accidental events. Therefore, all side effects should be carefully investigated in order to determine their origin. Adverse reactions to vaccines are divided into three general categories: local, systemic and allergic. Local reactions are usually less severe and are the most frequent. They involve pain, swelling and redness at the injection site. Systemic reactions are more generalized and include fever, malaise, muscle pain, headache and loss of appetite. The proven cases of systemic side effects are associated with live attenuated vaccines. They usually occur seven to twenty-one days after the vaccination. Allergic reactions (anaphylaxis) are less common but more serious. They can be caused by the antigen or by some other component of the vaccine, such as a stabilizer or preservative.

Self-diagnosis and self-medication (or self-discontinuation) are currently very common. On the Internet we have access to great amounts of information related to health and medicine. Some information is correct, but some is not. Information does not automatically imply knowledge. There is a false sense of "wisdom", which encourages therapeutic practices whose effectiveness is based on myths and has no scientific basis. One of these myths is the rejection of vaccines.

We should not confuse the emotional rejection of vaccines by some groups of opinion with the necessary vigilance to avoid administering them when they are contraindicated. A contraindication is a condition in which the possibility of a serious adverse reaction in a recipient is very high. It is a condition that depends on the characteristics of the person vaccinated rather than on the vaccine itself. As stated above, the administration of preparations with immunoglobulins would interfere with the immune response of attenuated vaccines. Therefore, during the two or three weeks after vaccination with attenuated vaccines, immunoglobulins may not be administered. Attenuated vaccines are also totally contraindicated for individuals who are immunocompromised or receiving immunosuppressive treatment. In these cases, only inactivated or toxoid vaccines can be administered. Although none have been demonstrated, the possibility of adverse effects of live attenuated vaccines cannot be ruled out, so doctors are advised not to administer them to pregnant women as a preventive measure. On the other hand, there would be no problem with inactivated vaccines. Furthermore no contraindications have been observed in vaccines administered to nursing mothers.

The perception of risk

Europe is experiencing what is called *the vaccine paradox*, in which vaccines are somehow victims of their own success. In fact, the introduction of a safe, effective vaccine and the implementation of a good vaccine coverage in the population lead to a dramatic decrease in the incidence of the disease, followed by a dangerous decrease in the perception of risk of the disease and its complications. Risk perception is highly influenced by the appearance of a relatively small but active number of movements that oppose vaccination with the argument that vaccines have side effects. These movements tend to make effective use of emotional communication to create fear, uncertainty and doubt regarding vaccines. They claim that they are not "against vaccination" but rather "in favour of safe vaccination", arguing that vaccines are toxic or unnatural and that vaccination campaigns are promoted by pharmaceutical companies in their desire to get rich.

In the past various pathological conditions such as autism and developmental disorders have been attributed to vaccines, but there is no evidence to support these claims. In 1998, an article by Andrew J. Wakefield in the journal *The Lancet* caused public alarm by suggesting a possible association between the MMR vaccine and autism. As a result, many parents stopped vaccinating their children. In 2004 *The Lancet* withdrew Wakefield's article because it had been found to be a fraud. The authors of the article retracted and admitted the damage they had done with their unproven claims. However, the publication of these new results has not had the same impact on the population as the fraudulent article, and many people still believe in the great dangers of vaccination.

The health authorities of each country must investigate promptly and reliably any possible adverse effects of vaccination and publicize the results quickly and effectively in order to respond transparently to the concerns of society and allay fears about the lack of vaccine safety. The authorities should provide access to information about the benefits of vaccination, the safety of vaccines and the severity of the illnesses they prevent.

Vaccines in the eye of the storm: the vaccines against human papilloma virus and influenza

Human papilloma virus (HPV) is the most common sexually transmitted disease. Epidemiological studies done in the 1990s showed a link between HPV infection and cervical cancer. More than 130 types of HPV have been identified and are differentiated by the genetic sequence of the outer capsid protein L1. Of the more than 130 types, type 16 causes approximately 50% of cervical cancers worldwide and types 16 and 18

together account for about 70%. Infection with a high-risk HPV type is considered necessary for the development of cervical cancer, but alone it is not sufficient to cause the disease because the vast majority of women with HPV infection do not develop it. In fact, although the incidence of infection is high, in most it resolves spontaneously. In a small proportion of infected women, however, the infection persists. This chronic nature of the infection is a risk factor for the development of precursor lesions of cervical cancer. The most common clinical manifestation of genital HPV infection is persistent cervical intraepithelial neoplasia. In addition to cervical cancer, it is believed that HPV is responsible for 90% of anal cancers, 40% of cancers of the vulva, vagina and penis, and 12% of oral and pharyngeal cancers. It has been observed that HPV infection often occurs shortly after the start of sexual activity.

Ideally, HPV vaccine should be administered before possible exposure to the virus through sexual contact. However, the vaccine is also beneficial to sexually active people who have not been infected with the virus. In principle, the protection is lower in people who are already infected, but it has also been found to cause cellular immunity and to stimulate the production of cytokines (molecules that modulate the immune response), which can control the progression of the virus. The most frequent adverse reactions reported during clinical trials of HPV vaccines were local reactions in 20%-90% of recipients at the site of injection. The symptoms were pain, redness or swelling, and slight fever (about 37.7 °C) in 10%-13% of recipients during the fifteen days following administration. In some cases, syncope (brief loss of consciousness) has also been observed in other types of vaccines. For this reason, the person who receives the vaccine must be seated when it is administered. Medical staff must monitor vaccine recipients for 15 to 20 minutes after vaccination. Please note that these vaccines are not a substitute for regular gynaecologic examinations (Pap tests).

Influenza (flu) is a highly contagious viral disease that has caused major epidemics in the last few centuries. The “Spanish flu” pandemic of 1918-1919 caused 21 million deaths worldwide. The first pandemic of the 21st century occurred in 2009-2010. In April 2009 the influenza virus A-H1N1 appeared and quickly spread across North America. By May 2009, the virus had spread to many areas of the world.

At irregular intervals of 10 to 40 years, significant differences occur in the antigens of the influenza virus and, because the population does not have protective antibodies against these new antigens, a pandemic occurs. There are three types of influenza virus: A, B and C. Type A infects humans and other animals (especially birds). In humans it causes a moderate to severe disease affecting all ages. Type B is uniquely human and the symptoms are more moderate than in type A; it most commonly affects children. Type C does not seem to affect humans, probably because many cases do not involve clinical symptoms and the disease has not been associated with any epidemic episode.

There are inactivated and attenuated flu vaccines. The inactivated vaccine is trivalent and is administered by intramuscular or intradermal injection. It contains three viruses: type A-H1N1, type A-H3N2 and a type B variant, which is the one expected to circulate during the winter season. The attenuated vaccine contains the same viruses as the inactivated one. For practical purposes, immunity after vaccination with inactivated vaccine lasts less than a year because of the decrease in antibodies and the antigenic drift of circulating viruses. The effectiveness of the vaccine in preventing influenza among people over 65 years is only 30%-40%, but it is very effective at preventing complications and reducing the number of deaths. The immunity acquired through the attenuated vaccine remains up to two years, with an efficiency of 87%, though in the second year the virus antigens have changed.

Conclusions

Vaccination is one of the main weapons that humans have against death. From Jenner to the present, vaccination has controlled twelve major diseases: smallpox, diphtheria, tetanus, yellow fever, whooping cough, infections due to *Haemophilus influenzae B*, poliomyelitis, measles, mumps, rubella, typhoid and rabies. The success of vaccination has been demonstrated in the eradication of smallpox and 99% of poliomyelitis worldwide. Vaccination is a tool for prevention, a public health strategy and a supportive action. It is an expression of our desire to defend the society in which we live, because the group immunity achieved when a population is vaccinated is a barrier to the circulation of infectious agents. Vaccination, which is still individually voluntary, is also a collective obligation.

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