Vaccine

A **vaccine** is a biological preparation that provides active acquired immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins, or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as a threat, destroy it, and to further recognize and destroy any of the microorganisms associated with that agent that it may encounter in the future. Vaccines can be prophylactic (example: to prevent or ameliorate the effects of a future infection by a natural or "wild" pathogen), or therapeutic (e.g., vaccines against cancer are being investigated). The effectiveness of vaccination has been widely studied and verified; for example, the influenza vaccine the HPV vaccine,and the chicken pox vaccine.[7] The World Health Organization (WHO) reports that licensed vaccines are currently available for twenty-five different preventable infections.

The administration of vaccines is called vaccination. Vaccination is the most effective method of preventing infectious diseases; widespread immunity due to vaccination is largely responsible for the worldwide eradication of smallpox and the restriction of diseases such as polio, measles, and tetanus from much of the world.

The terms *vaccine* and *vaccination* are derived from *Variolae vaccinae* (smallpox of the cow), the term devised by Edward Jenner to denote cowpox. He used it in 1798 in the long title of his *Inquiry into the Variolae vaccinae known as the Cow Pox*, in which he described the protective effect of cowpox against smallpox.[10] In 1881, to honor Jenner, Louis Pasteur proposed that the terms should be extended to cover the new protective inoculations then being developed.

The efficacy or performance of the vaccine is dependent on a number of factors:

- the disease itself (for some diseases vaccination performs better than for others)
- the strain of vaccine (some vaccines are specific to, or at least most effective against, particular strains of the disease)[15]
- whether the vaccination schedule has been properly observed.
- idiosyncratic response to vaccination; some individuals are "non-responders" to certain vaccines, meaning that they do not generate antibodies even after being vaccinated correctly.
- assorted factors such as ethnicity, age, or genetic predisposition.

If a vaccinated individual does develop the disease vaccinated against (breakthrough infection), the disease is likely to be less virulent than in unvaccinated victims.[16]

The following are important considerations in the effectiveness of a vaccination program:[*citation needed*]

1. careful modeling to anticipate the impact that an immunization campaign will have on the epidemiology of the disease in the medium to long term
2. ongoing surveillance for the relevant disease following introduction of a new vaccine
3. maintenance of high immunization rates, even when a disease has become rare.

Vaccines have contributed to the eradication of smallpox, one of the most contagious and deadly diseases in humans. Other diseases such as rubella, polio, measles, mumps, chickenpox, and typhoid are nowhere near as common as they were a hundred years ago. As long as the vast majority of people are vaccinated, it is much more difficult for an outbreak of disease to occur, let alone spread. This effect is called herd immunity. Polio, which is transmitted only between humans, is targeted by an extensive eradication campaignthat has seen endemic polio restricted to only parts of three countries (Afghanistan, Nigeria, and Pakistan).[19] However, the difficulty of reaching all children as well as cultural misunderstandings have caused the anticipated eradication date to be missed several times.

Vaccines also help prevent the development of antibiotic resistance. For example, by greatly reducing the incidence of pneumonia caused by *Streptococcus pneumoniae*, vaccine programs have greatly reduced the prevalence of infections resistant to penicillin or other first-line antibiotics.[20]

Types

Vaccines are dead or inactivated organisms or purified products derived from them.

There are several types of vaccines in use. These represent different strategies used to try to reduce the risk of illness while retaining the ability to induce a beneficial immune response.

Inactivated

Some vaccines contain inactivated, but previously virulent, micro-organisms that have been destroyed with chemicals, heat, or radiation.Examples include the polio vaccine, hepatitis A vaccine, rabies vaccine and some influenza vaccines.

Attenuated

Some vaccines contain live, attenuated microorganisms. Many of these are active viruses that have been cultivated under conditions that disable their virulent properties, or that use closely related but less dangerous organisms to produce a broad immune response. Although most attenuated vaccines are viral, some are bacterial in nature. Examples include the viral diseases yellow fever, measles, mumps, and rubella, and the bacterial disease typhoid. The live *Mycobacterium tuberculosis* vaccine developed by Calmette and Guérin is not made of a contagious strain but contains a virulently modified strain called "BCG" used to elicit an immune response to the vaccine. The live attenuated vaccine containing strain *Yersinia pestis* EV is used for plague immunization. Attenuated vaccines have some advantages and disadvantages. They typically provoke more durable immunological responses and are the preferred type for healthy adults. But they may not be safe for use in immunocompromised individuals, and may rarely mutate to a virulent form and cause disease.[26]

Toxoid

Toxoid vaccines are made from inactivated toxic compounds that cause illness rather than the micro-organism.Examples of toxoid-based vaccines include tetanus and diphtheria. Toxoid vaccines are known for their efficacy.Not all toxoids are for micro-organisms; for example, *Crotalus atrox* toxoid is used to vaccinate dogs against rattlesnakebites.

Subunit

Protein subunit – rather than introducing an inactivated or attenuated micro-organism to an immune system (which would constitute a "whole-agent" vaccine), a fragment of it can create an immune response.Examples include the subunit vaccine against Hepatitis B virus that is composed of only the surface proteins of the virus (previously extracted from the blood serum of chronically infected patients, but now produced by recombination of the viral genes into yeast)the virus-like particle (VLP) vaccine against human papillomavirus (HPV) that is composed of the viral major capsidprotein. and the hemagglutinin and neuraminidase subunits of the influenza virus.Subunit vaccine is being used for plague immunization.

Conjugate

Conjugate – certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g., toxins), the immune system can be led to recognize the polysaccharide as if it were a protein antigen.[*citation needed*] This approach is used in the *Haemophilus influenzae* type B vaccine.[*citation needed*]

innovative vaccines

A number of innovative vaccines are also in development and in use:

- Dendritic cell vaccines combine dendritic cells with antigens in order to present the antigens to the body's white blood cells, thus stimulating an immune reaction. These vaccines have shown some positive preliminary results for treating brain tumors [27] and are also tested in malignant melanoma.[28]
- Recombinant Vector – by combining the physiology of one micro-organism and the DNA of the other, immunity can be created against diseases that have complex infection processes
- DNA vaccination – an alternative, experimental approach to vaccination called *DNA vaccination*, created from an infectious agent's DNA, is under development. The proposed mechanism is the insertion (and expression, enhanced by the use of electroporation, triggering immune system recognition) of viral or bacterial DNA into human or animal cells. Some cells of the immune system that recognize the proteins expressed will mount an attack against these proteins and cells expressing them. Because these cells live for a very long time, if the pathogen that normally expresses these proteins is encountered at a later time, they will be attacked instantly by the immune system. One potential advantage of DNA vaccines is that they are very easy to produce and store. As of 2015, DNA vaccination is still experimental and is not approved for human use.
- T-cell receptor peptide vaccines are under development for several diseases using models of Valley Fever, stomatitis, and atopic dermatitis. These peptides have been shown to modulate cytokine production and improve cell-mediated immunity.
- Targeting of identified bacterial proteins that are involved in complement inhibition would neutralize the key bacterial virulence mechanism.[29]

While most vaccines are created using inactivated or attenuated compounds from micro-organisms, synthetic vaccines are composed mainly or wholly of synthetic peptides, carbohydrates, or antigens.

Valence

Vaccines may be *monovalent* (also called *univalent*) or *multivalent* (also called *polyvalent*). A monovalent vaccine is designed to immunize against a single antigen or single microorganism.[30] A multivalent or polyvalent vaccine is designed to immunize against two or more strains of the same microorganism, or against two or more microorganisms.[31]The valency of a multivalent vaccine may be denoted with a Greek or Latin prefix (e.g., *tetravalent* or *quadrivalent*). In certain cases, a monovalent vaccine may be preferable for rapidly developing a strong immune response.[32]

Heterotypic

Also known as heterologous or "Jennerian" vaccines, these are vaccines that are pathogens of other animals that either do not cause disease or cause mild disease in the organism being treated. The classic example is Jenner's use of cowpox to protect against smallpox. A current example is the use of BCG vaccine made from Mycobacterium bovis to protect against human tuberculosis.[33]

Nomenclature

Various fairly standardized abbreviations for vaccine names have developed, although the standardization is by no means centralized or global. For example, the vaccine names used in the United States have well-established abbreviations that are also widely known and used elsewhere. An extensive list of them provided in a sortable table and freely accessible, is available at a US Centers for Disease Control and Prevention web page.[34] The page explains that "The abbreviations [in] this table (Column 3) were standardized jointly by staff of the Centers for Disease Control and Prevention, ACIP Work Groups, the editor of the *Morbidity and Mortality Weekly Report* (MMWR), the editor of *Epidemiology and Prevention of Vaccine-Preventable Diseases* (the Pink Book), ACIP members, and liaison organizations to the ACIP."[34] Some examples are "DTaP" for diphtheria and tetanus toxoids and acellular pertussis vaccine, "DT" for diphtheria and tetanus toxoids, and "Td" for tetanus and diphtheria toxoids. At its page on tetanus vaccination,[35] the CDC further explains that "Upper-case letters in these abbreviations denote full-strength doses of diphtheria (D) and tetanus (T) toxoids and pertussis (P) vaccine.

Lower-case 'd' and 'p' denote reduced doses of diphtheria and pertussis used in the adolescent/adult-formulations. The 'a' in DTaP and Tdap stands for 'acellular,' meaning that the pertussis component contains only a part of the pertussis organism."[35] Another list of established vaccine abbreviations is at the CDC's page called "Vaccine Acronyms and Abbreviations", with abbreviations used on U.S. immunization records.[36] The United States Adopted Name system has some conventions for the word order of vaccine names, placing head nouns first and adjectives postpositively. This is why the USAN for "OPV" is "poliovirus vaccine live oral" rather than "oral poliovirus vaccine".

Developing immunity

The immune system recognizes vaccine agents as foreign, destroys them, and "remembers" them. When the virulent version of an agent is encountered, the body recognizes the protein coat on the virus, and thus is prepared to respond, by (1) neutralizing the target agent before it can enter cells, and (2) recognizing and destroying infected cells before that agent can multiply to vast numbers.

When two or more vaccines are mixed together in the same formulation, the two vaccines can interfere. This most frequently occurs with live attenuated vaccines, where one of the vaccine components is more robust than the others and suppresses the growth and immune response to the other components. This phenomenon was first noted in the trivalent Sabin polio vaccine, where the amount of serotype 2 virus in the vaccine had to be reduced to stop it from interfering with the "take" of the serotype 1 and 3 viruses in the vaccine.[37]This phenomenon has also been found to be a problem with the dengue vaccines currently being researched,[*when?*] where the DEN-3 serotype was found to predominate and suppress the response to DEN-1, −2 and −4 serotypes.[38]

Adjuvants and preservatives

Vaccines typically contain one or more adjuvants, used to boost the immune response. Tetanus toxoid, for instance, is usually adsorbed onto alum. This presents the antigen in such a way as to produce a greater action than the simple aqueous tetanus toxoid. People who have an adverse reaction to adsorbed tetanus toxoid may be given the simple vaccine when the time comes for a booster.[*citation needed*]

In the preparation for the 1990 Persian Gulf campaign, whole cell pertussis vaccine was used as an adjuvant for anthrax vaccine. This produces a more rapid immune response than giving only the anthrax vaccine, which is of some benefit if exposure might be imminent.[*citation needed*]

Vaccines may also contain preservatives to prevent contamination with bacteria or fungi. Until recent years, the preservative thimerosal was used in many vaccines that did not contain live virus. As of 2005, the only childhood vaccine in the U.S. that contains thimerosal in greater than trace amounts is the influenza vaccine,[39] which is currently recommended only for children with certain risk factors.[40] Single-dose influenza vaccines supplied in the UK do not list thiomersal (its UK name) in the ingredients. Preservatives may be used at various stages of production of vaccines, and the most sophisticated methods of measurement might detect traces of them in the finished product, as they may in the environment and population as a whole.[41]

Schedule

Main article: Vaccination schedule

> *For country-specific information on vaccination policies and practices, see: Vaccination policy*

In order to provide the best protection, children are recommended to receive vaccinations as soon as their immune systems are sufficiently developed to respond to particular vaccines, with additional "booster" shots often required to achieve "full immunity". This has led to the development of complex vaccination schedules. In the United States, the Advisory Committee on Immunization Practices, which recommends schedule additions for

the Centers for Disease Control and Prevention, recommends routine vaccination of children against: hepatitis A, hepatitis B, polio, mumps, measles, rubella, diphtheria, pertussis, tetanus, HiB, chickenpox, rotavirus, influenza, meningococcal disease and pneumonia.[43] A large number of vaccines and boosters recommended (up to 24 injections by age two) has led to problems with achieving full compliance. In order to combat declining compliance rates, various notification systems have been instituted and a number of combination injections are now marketed (e.g., Pneumococcal conjugate vaccine and MMRV vaccine), which provide protection against multiple diseases.

Besides recommendations for infant vaccinations and boosters, many specific vaccines are recommended for other ages or for repeated injections throughout life—most commonly for measles, tetanus, influenza, and pneumonia. Pregnant women are often screened for continued resistance to rubella. The human papillomavirus vaccine is recommended in the U.S. (as of 2011)[44] and UK (as of 2009).[45] Vaccine recommendations for the elderly concentrate on pneumonia and influenza, which are more deadly to that group. In 2006, a vaccine was introduced against shingles, a disease caused by the chickenpox virus, which usually affects the elderly.

History

Edward Jenner

Prior to the introduction of vaccination with material from cases of cowpox (heterotypic immunisation), smallpox could be prevented by deliberate inoculation of smallpox virus, later referred to as variolation to distinguish it from smallpox vaccination. The earliest hints of the practice of inoculation for smallpox in China come during the 10th century. The Chinese also practiced the oldest documented use of variolation, dating back to the fifteenth century. They implemented a method of "nasal insufflation" administered by blowing powdered smallpox material, usually scabs, up the nostrils. Various insufflation techniques have been recorded throughout the sixteenth and seventeenth centuries within China.Two reports on the Chinese practice of inoculation were received by the Royal Society in London in 1700; one by Dr. Martin Lister who received a report by an employee of the East India Company stationed in China and another by Clopton Havers. Sometime during the late 1760s whilst serving his apprenticeship as a surgeon/apothecary Edward Jenner learned of the story, common in rural areas, that dairy workers would never have the often-fatal or disfiguring disease smallpox, because they had already had cowpox, which has a very mild effect in humans. In 1796, Jenner took pus from the hand of a milkmaid with cowpox, scratched it into the arm of an 8-year-old boy, and six weeks later inoculated (variolated) the boy with smallpox, afterwards observing that he did not catch smallpox.[49][50] Jenner extended his studies and in 1798 reported that his vaccine was safe in children and adults and could be transferred from arm-to-arm reducing reliance on uncertain supplies from infected cows.[10]Since vaccination with cowpox was much safer than smallpox inoculation,[51] the latter, though still widely practised in England, was banned in 1840.[52]

The second generation of vaccines was introduced in the 1880s by Louis Pasteur who developed vaccines for chicken cholera and anthrax,[11] and from the late nineteenth century vaccines were considered a matter of national prestige, and compulsory vaccination laws were passed.[49]

The twentieth century saw the introduction of several successful vaccines, including those against diphtheria, measles, mumps, and rubella. Major achievements included the development of the polio vaccine in the 1950s and the eradication of smallpox during the 1960s and 1970s. Maurice Hilleman was the most prolific of the developers of the vaccines in the twentieth century. As vaccines became more common, many people began taking them for granted. However, vaccines remain elusive for many important diseases, including herpes simplex, malaria, gonorrhea and HIV.[49][53]