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Immunization against diseases of public health importance

The benefits of immunization

Vaccines — which protect against disease by inducing immunity — are widely and routinely administered around the world based on the common-sense principle that it is better to keep people from falling ill than to treat them once they are ill. Suffering, disability, and death are avoided. Immunization averted about two million deaths in 2002. In addition, contagion is reduced, strain on health-care systems is eased, and money is frequently saved that can be used for other health services.

Immunization is a proven tool for controlling and even eradicating disease. An immunization campaign carried out by the World Health Organization (WHO) from 1967 to 1977 eradicated the natural occurrence of smallpox. When the programme began, the disease still threatened 60% of the world's population and killed every fourth victim. Eradication of poliomyelitis is within reach. Since the launch by WHO and its partners of the Global Polio Eradication Initiative in 1988, infections have fallen by 99%, and some five million people have escaped paralysis. Between 1999 and 2003, measles deaths dropped worldwide by almost 40%, and some regions have set a target of eliminating the disease. Maternal and neonatal tetanus will soon be eliminated in 14 of 57 high-risk countries.

New vaccines also have been introduced with significant results, including the first vaccine to help prevent liver cancer, hepatitis B vaccine, which is now routinely given to infants in 77% of WHO's Member States. Rapid progress in the development of new vaccines means protection will be available in the near future against a wider range of serious infectious diseases.

History

Introducing a small amount of smallpox virus by inhaling through the nose or by making a number of small pricks through the skin (variolation) to create resistance to the disease appears to have begun in the 10th or 11th century in Central Asia. The practice spread; in Asia and Africa, the method was nasal, while in Europe it involved skin punctures. Variolation was introduced into England in 1721. There, in 1798, Edward Jenner, having studied the success of variolation with cowpox — a mild

illness — in protecting against smallpox, began to carry out inoculations against smallpox, the first systematic effort to control a disease through immunization.

In 1885, Louis Pasteur developed the first vaccine to protect humans against rabies. Toxoids against diphtheria and tetanus were introduced in the early 1900s; the bacillus Calmette-Guérin vaccine (against tuberculosis) in 1927; the Salk polio vaccine in 1955; and vaccines against measles and mumps in the 1960s.

Commonly used vaccines

Routine vaccination is now provided in all developing countries against measles, polio, diphtheria, tetanus, pertussis, and tuberculosis. To this basic package of vaccines, which served as the standard for years, have come new additions. Immunization against hepatitis B is now recommended by WHO for all nations, and currently is offered to infants in 147 of 192 WHO Member States. Immunization against Haemophilus influenzae type b (Hib) is recommended where resources permit its use and the burden of disease is established; it is provided in 89 countries (only in selected parts of two of those countries). Yellow fever vaccine is offered in about two-thirds of the nations at risk for yellow fever outbreaks. Routine immunization against rubella is provided in 111 countries.

In industrialized countries a wider span of protection is typically provided than in developing countries, often including vaccines against influenza, predominant strains of pneumococcal disease, and mumps (usually in combination with measles and rubella vaccine). Immunization programmes may be aimed at adolescents or adults — depending on the disease concerned — as well as at infants and children.

Global immunization coverage

Coverage has greatly increased since WHO's Expanded Programme on Immunization began in 1974. In 2003, global DTP3 (three doses of the diphtheria-tetanus-pertussis combination vaccine) coverage was 78% — up from 20% in 1980. However, 27 million children worldwide were not reached by DTP3 in 2003, including 9.9 million in South Asia and 9.6 million in sub-Saharan Africa. Those who miss out on routine vaccination programmes tend to be people living in remote locations, urban slums and border areas. They also include indigenous groups, displaced populations, those lacking access to vaccination because of various social barriers, those lacking awareness or motivation to be vaccinated and those who refuse.

An estimated 2.1 million people around the world died in 2002 of diseases preventable by widely used vaccines. This toll included 1.4 million children under the age of five. Among these childhood deaths, over 500 000 were caused by measles; nearly 400 000 by Hib; nearly 300 000 by pertussis; and 180 000 by neonatal tetanus.

Vaccines under development

Numerous new vaccines with major potential for improving health in developing countries are in the research and development pipeline. They include vaccines for rotavirus diarrhoea, which kills 300 000 to 600 000 children under age five every year; human papillomavirus, a leading cause of cervical cancer, which afflicts some

500 000 women each year, 80% of them in developing countries; and pneumococcal disease, which causes a large fraction of the world's approximately two million annual deaths from childhood pneumonia. In addition, a conjugate vaccine now in development should be much more effective against Group A meningococcal disease (Men A), a frequently fatal form of meningitis that causes recurring epidemics in a number of countries in sub-Saharan Africa. Several of these vaccines ─ those against rotavirus, pneumococcal disease, and Men A ─ may be available in developing countries by 2008-2009.

How vaccines work

Vaccines typically provide the immune system with harmless copies of an antigen: a portion of the surface of a bacterium or virus that the immune system recognizes as "foreign." (An antigen often plays a role in causing disease — for example by enabling a virus or bacterium to attach to cells.) A vaccine may also provide a non-active version of a toxin — a poison produced by a bacterium — so that the body can devise a defence against it.

Once an antigen is detected by the immune system, white blood cells called B-lymphocytes create a protein called an antibody that is precisely designed to attach to that antigen. Many copies of this antibody are produced. If a true infection of the same disease occurs, still more antibodies are created, and as they attach to their targets they may block the activity of the virus or bacterial strain directly, thus combating infection. In addition, once in place, the antibodies make it much easier for other components of the immune system (particularly phagocytes) to recognize and destroy the invading agent.

Immune systems are designed to "remember" — once exposed to a particular bacterium or virus, they retain immunity against it for years, decades, or even a lifetime — and so are prepared to defeat a later infection, and to do so quickly. This ability, and the speed with which it occurs, is a huge benefit: a body encountering a germ for the first time may need from seven to 12 days to mount an effective defence, and by then serious illness and even death may occur.

Types of vaccines

Vaccines come in different forms. The injected polio vaccine is a killed, intact virus; the oral polio vaccine is a live, weakened virus. The vaccine for typhoid is a killed, intact bacteria. Vaccines for measles and the other standard "childhood" diseases — mumps, chickenpox, and rubella — are live, attenuated (or weakened) viruses. Vaccines for diphtheria and tetanus consist of toxins that have been "inactivated." Influenza vaccines often consist of killed, "disrupted" viruses (that is, the proteins on the coat of the virus have been released into a solution by solvents). Vaccines against Hib, pneumococcal disease, and meningococcal disease consist of highly purified complex sugars taken from bacterial coats or capsules.

Vaccines are frequently administered as combinations of antigens. The most widely used combinations are diphtheria-tetanus-pertussis (DTP); diphtheria-tetanus-pertussis-hepatitis B (DTP-HepB); pentavalent vaccine: diphtheria-tetanus-pertussis-hepatitis B-Hib; and measles-mumps-and rubella (MMR).

Effectiveness and safety

All vaccines used for routine immunization are very effective in preventing disease, although no vaccine attains 100% effectiveness. More than one dose of a vaccine is generally given to increase the chance of developing immunity.

Vaccines are very safe, and side effects are minor ─ especially when compared to the diseases they are designed to prevent. Serious complications occur rarely. For example, severe allergic reactions result at a rate of one for every 100 000 doses of measles vaccine. Two to four cases of vaccine-associated paralytic polio have been reported for every one million children receiving oral polio vaccine.

The cost-effectiveness of immunization

Immunization is considered among the most cost-effective of health investments. There is a well-defined target group; contact with the health system is only needed at the time of delivery; and vaccination does not require any major change of lifestyle.

A recent study estimated that a one-week "supplemental immunization activity" against measles carried out in Kenya in 2002 ─ in which 12.8 million children were vaccinated — would result in a net saving in health costs of US$ 12 million over the following ten years; during that time it would prevent 3 850 000 cases of measles and 125 000 deaths. In the United States, cost-benefit analysis indicate that every dollar invested in a vaccine dose saves US$ 2 to US$ 27 in health expenses.

The cost of immunizing a child

In mid-1990s, vaccines to provide "basic" coverage for tuberculosis, polio, diphtheria, tetanus, pertussis, and measles cost about US$ 1 per child. Inclusion of vaccines for hepatitis B and Hib, raises the vaccine cost alone to US$ 7-13 per child (not including administration and injection equipment) in the developing world. When vaccine administration is included, the costs amount to between US$ 20-40 per child. It has become a significant challenge for low-income countries and international health agencies to find ways to introduce more highly-priced vaccines such as those for hepatitis B and Hib, which can greatly increase the costs of national immunization programmes. With many new vaccines expected to be available in the near future, issues of financing and financial sustainability will become ever more important.

Financing immunization

Many developing countries have difficulties affording vaccines. International initiatives such as the Expanded Programme on Immunization and the Global Alliance for Vaccines and Immunization (GAVI) have provided impetus, funding, and technical support that have helped increase immunization coverage and the number of vaccines provided. The proposed WHO-UNICEF Global Immunization Vision and Strategies, intended to run from 2006-2015, would further this existing coordination, aim to expand vaccination coverage, and enable the logistical systems set up for that purpose to provide other health care services as well.

The economics of vaccine development have tended to run against the interests of the world's poorer countries. Vaccines are much less profitable than medicines, and pharmaceutical firms understandably have been reluctant to make the high investments necessary to research and develop vaccines against infectious diseases, realizing that the largest pool of potential customers are governments that likely could not afford to pay enough for these products to ensure a profit. For the same reason, when new vaccines have been developed, limited quantities often have been manufactured, increasing the cost per dose. Part of the difficulty for manufacturers is in forecasting demand and in accounting for various market uncertainties.

Steps have been taken to deal with these challenges. For example, since 1977, the Region of the Americas Revolving Fund for Vaccine Procurement has acted as a bulk purchaser for countries that join the programme. The Fund assures manufacturers of a large and predictable market for vaccines, and over 30 participating countries of prices up to 80% below those offered to individual countries. The UNICEF Vaccine Independence Initiative, established in 1991, sets up a revolving fund for each participating country, allows these countries to buy vaccines through UNICEF's procurement system using local currencies, and enables them to pay for the vaccines only after delivery. A more recent approach is to guarantee a large market and a reasonable price in advance to pharmaceutical firms which develop vaccines that will have great health benefits for poor nations. This "push-pull" approach is being financed and progressively fine-tuned by a coalition of international donors, bilateral aid programmes, private philanthropists, and some governments.

WHO immunization work

In the field of immunization WHO works with partners including governments, United Nations agencies and other international organizations, bilateral government health and development agencies, non-governmental organizations, professional groups and the private sector. WHO's specific responsibilities include:

- Supporting and facilitating research and development;
- Ensuring the quality and safety of vaccines;
- Developing policies and strategies for maximizing the use of vaccines;
- Reducing financial and technical barriers to the introduction of vaccines and technologies; and
- Supporting countries in acquiring the skills and infrastructure needed to achieve disease control and eradication.

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