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The History of Vaccination

Introduction

The two public health interventions that have had the greatest impact on the world's health clean water and vaccines. Thanks to such pioneers as Jenner and Pasteur, a handful of vaccines prevent illness or death for millions of individuals every year. But there is still a long way to go. Immunization, the most cost-effective public health intervention, continues to be under-used.. It is profoundly tragic that almost two million children still die each year from diseases for which are available at low cost . And over 90 000 fall victim to paralytic polio, which could also have been prevented by immunization. Indeed, many years elapsed between the invention of current vaccines and their widespread use in immunization programmes. The reasons for these delays are many and complex. If history is to serve any useful purpose, it should help us to find ways to avoid such delays in future.

The invention era

The closing years of the 19th century and the early years of the 20th century were marked by the achievements of great vaccine scientists such as Pasteur. Since the introduction of *vaccinia* by Jenner 200 years ago ("vaccination" in its true sense), nine major diseases of man have been controlled to a greater or lesser extent through the use of vaccines (Table 1.). Several other vaccines have been used in individuals at risk from disease of such as rabies and plague, but have not been systematically applied on a

global scale. While BCG has been widely administered to newborns, thus successfully preventing complications such as meningitis and miliary tuberculosis, administration of the vaccine has not resulted in control of the disease.

Table 1. The date of introduction of first generation of vaccines for use in humans*

- 1798 Smallpox
- 1885 Rabies
- 1897 Plague
- 1923 Diphtheria
- 1926 Pertussis
- 1927 Tuberculosis (BCG)
- 1927 Tetanus
- 1935 Yellow Fever

After World War II

- 1955 Injectable Polio Vaccine (IPV)
- 1962 Oral Polio Vaccine (OPV)
- 1964 Measles
- 1967 Mumps
- 1970 Rubella
- 1981 Hepatitis B

****This list is not exhaustive. After Plotkin SA and Mortimer EA , 1994 (ref 1)***

Although the first vaccines were, in some respects, crude, they have proved to be robust and efficient, and continue to be the workhorses of global immunization programmes. They have dramatically reduced the burden of death and disease from these nine infections, and have given credibility to the entire preventive health movement. During the 1920s, diphtheria and tetanus toxoids, whole cell pertussis vaccine and BCG were introduced. Thanks to the development of the chorioallantoic membrane for culturing viruses, a yellow fever vaccine was available by 1935. After the Second World War, there followed an explosion of technology, resulting in the emergence of other vaccines still in use today. These included the killed and oral polio vaccines, and the measles, mumps and rubella vaccines.

Early national immunization programmes 1900-1973

During this period, the use of available vaccines was largely confined to industrialized countries. For instance, smallpox vaccine was offered to all age groups, but only those at risk - health care workers and travellers - were specially targeted. As a result, coverage was patchy and outbreaks continued to occur throughout the world. When this happened, massive vaccination efforts were mounted by health authorities, often very successfully, to contain the infection through vaccination and isolation or quarantine of infected individuals or suspected cases.

Other vaccines such as BCG were gradually introduced in the West, (Table 2) as they became available. Better-off families who could afford vaccination benefited most - the poor benefited the least. Because of low, irregular coverage, communities continued to be devastated intermittently by outbreaks of these vaccine-preventable diseases throughout the 1930s and 1940s.

An injectable form of killed polio vaccine (IPV) became available in 1955, resulting in widespread administration in schools and clinics in industrialized countries across a broad age range resulting in a marked drop in cases in these countries. In 1962, the oral polio vaccine (OPV) replaced IPV and continues to be the vaccine of choice for eradication of the virus. Despite initial low coverage, the vaccine showed itself capable of dramatically reducing the number of polio cases when administered to a wide age range over a short period of time.

Table 2. Vaccines used in national immunization programmes up to 1974

- Smallpox
- BCG
- Diphtheria toxoid
- Tetanus toxoid
- Pertussis
- IPV then OPV
- Measles

In terms of strategy, the early programmes offered routine immunization through regular maternal and

child health services. While efforts were made to encourage acceptance, no major effort was made to achieve total coverage. The implied target was to raise coverage, but there was no disease reduction target specified.

The eradication era

The early years of the 19th century saw widespread but haphazard use of Jenner's vaccine. However, application of smallpox vaccine was systematic in Mexico and Guatemala around 1805 (ref 2). The first attempt to use it on a global scale began in 1956 when the World Health Organization and others selected smallpox for eradication from the globe.

It was not the first time disease eradication had been mooted. Already the scientific community had considered the possibility of eradicating bovine contagious pleuropneumonia (a highly fatal disease of cattle), hookworm, yellow fever, malaria and yaws. Now with a clear strategy and a highly effective, affordable vaccine, it was possible to unite all countries in a mighty effort to rid themselves of this disease and the tremendous annual cost it incurred. To meet this special circumstance, very high population coverage with the smallpox vaccine was used. Finally in the late 1960s, an additional strategy was developed whereby cases were identified through intensive surveillance and confined ("containment"), and possible contacts within a given radius were vaccinated. Details of this effort are chronicled elsewhere (ref 3).

The next notable attempt at large-scale control was undertaken in Gambia in 1967-1970 when Foege and his team administered measles vaccine in a mass country-wide campaign. As a result, indigenous measles was entirely absent from the Gambia until 1972. However, due to the inability to sustain immunization coverage, the situation soon reverted to pre-campaign levels (ref 4).

The Expanded Programme on Immunization (EPI)

Following the impressive success of the smallpox eradication programme, the World Health Organization looked for other activities that could

build on what had already been achieved. In 1974 the Expanded Programme on Immunization was created. "Expanded" because most programmes until then had only used smallpox, BCG and diphtheria, tetanus and pertussis (DTP) vaccines. EPI would include two new diseases. The six diseases chosen were tuberculosis, diphtheria, neonatal tetanus, whooping cough, poliomyelitis and measles. Selection was made on the basis of a high burden of disease and the availability of a well-tried vaccines at an affordable price. "Expanded" also meant increased coverage - incredibly, less than 5% of children in developing countries were being reached at that time by immunization services.

Gradually, global coverage for the six vaccines rose (Fig.1), although success was not uniform. Regions and countries with the greatest resources, infrastructure and political will were able to raise coverage faster and higher (Fig. 2). Many organizations such as UNICEF and Rotary International became partners in the programme. Between 1974 and 1980, the programme developed training materials and disseminated them widely. In those busy years, almost every country in the world adopted the principle of a national immunization programme. (Many used and continue to use the name "EPI" which has become a trade mark). Hundreds of training courses in dozens of languages were conducted resulting in a huge mobilizations of human resources. Personnel were trained in the management of the programme so that every community was reached (at least in theory) by some form of immunization service. The number of doses administered and the number of target diseases occurring were recorded and reported.

Table 3. Vaccines used by the Expanded Programme on Immunization from 1974 onwards

- BCG
- Polio
- DTP
- Measles*

Added later

- Yellow Fever (in endemic countries)
- Hepatitis B

- Many industrialized countries now use measles, mumps and rubella combined vaccine (MMR)

Disease control era

Although coverage for all EPI target diseases climbed steadily in all regions throughout the 1980s disease incidence was not always proportionate decreasing. It became clear that pockets of low coverage in most if not all countries could perpetuate disease transmission. In the mid-1980s, more effort was placed on developing surveillance systems. As the programme moved into the 1990s with a mandate for eradication of polio, it became imperative that all countries should be able to mount effective surveillance of all target diseases. Now countries were able to focus attention on areas of low coverage and high disease incidence. Special strategies such as house-to-house visits were developed in the Americas and elsewhere, enabling pockets of low coverage and high disease incidence to be reached.

i) Polio eradication by the year 2000

In 1988, the World Health Assembly responded to the remarkable successes of the Americas in controlling poliomyelitis by selecting this disease as the next disease to be targeted for global eradication. Strong commitment at global, regional and national levels has led to wide implementation of WHO's recommended strategies with consequent reduction in virus transmission. Globally, as of September 1995, 78% of children had received at least three doses of polio vaccine by 12 months of age by routine immunization, and supplementary immunization has now been conducted as national or sub-national immunization days in 63 countries.

The key to polio eradication lies in effective surveillance for all cases of acute flaccid paralysis in children. One hundred and seven countries are now conducting surveillance specifically for cases of acute flaccid paralysis. Six specialized reference laboratories, 16 regional and 60 national laboratories are now providing virological confirmation of diagnosis in suspected cases. In addition, they are able to identify the source of the virus by molecular studies.

All countries embarking on polio eradication have undertaken mass campaigns using OPV, followed by "mopping-up" (house-to-house visits) in locations where cases persist. The incidence of polio has continued downward and, more importantly, increasing areas of the world are becoming free of the disease. In 1994, the Americas were declared polio-free. Polio-free zones also exist in Western Europe and in the Pacific basin, with emerging low incidence zones in the countries of the Maghreb Union, the Gulf countries and in Southern Africa. Dramatic reductions in incidence have been recorded in countries such as China and Egypt. As of September 1995, 146 countries reported zero polio cases. While success is in sight, zones and countries where there is currently armed conflict remain difficult locations in which to implement effective and comprehensive immunization programmes. Here the problems have been partly overcome by "Days of tranquillity" when conflicts cease and immunization of women and children is carried out.

ii) Neonatal Tetanus elimination

Since the early 1980s, major progress has been made towards neonatal tetanus elimination. In 1989, the World Health Assembly declared its commitment to the global elimination of neonatal tetanus by the year 1995. In 1994, an estimated 733 000 deaths due to neonatal tetanus were **prevented**, and immunization coverage of pregnant women with at least two doses of tetanus toxoid was 48%. EPI has promoted the administration of tetanus toxoid (TT) to either pregnant women, or to all women of child-bearing age. Five doses of TT given to a mother provide full, life-long protection, but even two doses given in pregnancy provide impressive protection for the newborn against neonatal tetanus.

Unfortunately, mothers have not been vaccinated as successfully as their babies, and coverage has remained unacceptably low in many countries. As a complementary strategy, clean delivery practices have improved in recent years, but most babies in developing countries are still delivered at home without the assistance of a trained attendant. The reduction in neonatal tetanus deaths is the result of impressive progress in certain high-risk countries.

However, as of September 1995, the estimated global number of neonatal tetanus deaths still occurring annually was 489 000. Eighty percent of these deaths occur in only 12 countries, but 13 other countries have an estimated neonatal tetanus mortality rate of more than 5 per **thousand**.

iii) Measles Control

In 1990, the World Health Assembly set another global goal, this time for a "Reduction by 95% in measles **deaths** and reduction by 90 per cent of measles **cases** compared to pre-immunization levels by 1995, as a major step towards the global eradication of measles in the longer run". As of September 1995, estimated global coverage for measles vaccine had reached 78%, and is expected to rise still further. Many countries, especially those mounting mass campaigns, have already achieved the reduction goals.

For many countries, however, the disease reduction goal will be hard to reach. Many of them did not introduce the use of measles vaccine until 1985, thirty years it had become available. Since then however the global number of reported cases of measles has **fallen**, but thousands of measles cases continue to occur every year in many of the larger developing countries, especially in Africa. High transmission rates for measles virus in densely populated areas means that very high, uniform measles vaccine coverage is needed to control the disease in this environment if a one-dose schedule is followed.

Mass campaigns in the Americas have resulted in the virtual disappearance of measles from that hemisphere. One after another, countries have undertaken **mass campaigns** targeting 9 months to 14 year olds, regardless of previous immunization history. There is clearly a role for this strategy to be expanded to other areas of the globe.

iv) Hepatitis B

The vaccine became available in the early 1980s, although the unit price was so high, only a few countries could afford it. The price of the vaccine has fallen dramatically since then and the vaccine had been introduced into 28 countries by September 1995

as part of the routine immunization programme, with three doses provided in the first year of life. Many countries in Africa need protection that most have, until now, been unable to afford this vaccine. Prospects are now improving though with the commitment of UNICEF to purchase the vaccine in bulk.

v) Yellow fever

Although a vaccine has been available since 1935, this disease has not yet been adequately controlled. While the global burden of disease is not as high as some other vaccine-preventable diseases, outbreaks still occur in endemic countries with great loss of life. Indeed, statistics indicate the disease is currently on the upswing.

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