WHO in Action

Protecting the world’s children: the story of WHO’s immunization programme

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Systematic immunization on a worldwide scale was not officially recognized as a practical possibility until 1974, when WHO launched its Expanded Programme on Immunization. Today, 80% of the world’s children receive this form of protection against childhood diseases during their first year of life. Coverage can reach 90% by the year 2000, the effectiveness of the vaccines used is improving, and vaccines against additional diseases are being added to the programme.

The true founding father of the Expanded Programme on Immunization was the English country doctor Edward Jenner, who in 1796 showed that scratching cowpox virus onto the skin produced immunity against the killer disease of smallpox. Thanks to his scientific demonstration of the efficacy of this procedure, the practice of vaccination gradually became widespread during the 19th century, and began to be applied to other infections (see table).

Medical scientists recognized that a great many diseases could be prevented if people, especially children, could be given timely injections of killed or attenuated agents of those diseases. But the use of vaccines was largely confined to industrialized countries. Smallpox vaccine was available to all age groups, but only those at risk, such as health care workers and travellers, were advised to use it. As a result, coverage was patchy and outbreaks continued to occur, mass vaccination being used only in an effort to bring them under control.

In the early years of the World Health Organization, immunization as such played no great role in the organization’s activities. In The first ten years of WHO, published in 1958, the chapter on Maternal and Child Health focused almost entirely on childbirth-related deaths and training in paediatrics. A single sentence suggested that laboratory tests of a pertussis vaccine could “provide a reliable indication of whether the vaccine tested is likely to protect children effectively.”
The date of introduction of some first generation vaccines for use in humans

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccine</th>
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<tr>
<td>After 1796</td>
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<tr>
<td>1798</td>
<td>Smallpox</td>
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<td>1885</td>
<td>Rabies</td>
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<td>1897</td>
<td>Plague</td>
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<td>1923</td>
<td>Diphtheria</td>
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<td>1926</td>
<td>Pertussis (whooping cough)</td>
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<td>1927</td>
<td>Tuberculosis (BCG)</td>
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<td>1927</td>
<td>Tetanus</td>
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<td>1935</td>
<td>Yellow fever</td>
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<tr>
<td>After 1945</td>
<td></td>
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<tr>
<td>1955</td>
<td>Injectable Polio Vaccine (IPV)</td>
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<tr>
<td>1952</td>
<td>Oral polio Vaccine (OPV)</td>
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<tr>
<td>1963</td>
<td>Measles</td>
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<tr>
<td>1967</td>
<td>Mumps</td>
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<td>1969</td>
<td>Rubella (German measles)</td>
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<tr>
<td>1981</td>
<td>Hepatitis B</td>
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“WHO has assisted several countries – particularly in the South-East Asia and Western Pacific Regions – in developing campaigns for mass immunization of children against diphtheria, pertussis and tetanus ... In order to improve the coverage and reduce the cost of mass immunization, campaigns have been combined with BCG, smallpox and other vaccination programmes in many countries.”

Referring to the development of new vaccines, such as those for measles and mumps, the authors suggested that “it would be advisable for countries with high death rates from measles to consider the establishment of programmes for the routine vaccination of children as they reach nine to twelve months of age.” There was no apparent trend towards combining these immunizations into one package.

**Launch of EPI**

Only six years later, however, in 1974, WHO launched its Expanded Programme on Immunization (EPI). The aim was to take vaccination against the six target diseases – diphtheria, pertussis, tetanus, measles, poliomyelitis, and tuberculosis – to the children of the world. At that time, fewer than 5% of them had been immunized against these diseases. The word “expanded” referred to the addition of measles and poliomyelitis to the vaccines then being used in the immunization programme. In practice, many developing countries did not include measles vaccine in their routine immunization programmes.
until 1985, partly because of the tendency of this vaccine to be heat labile, causing difficulties of transport and storage.

What swung world opinion in favour of this tremendous initiative in international public health? Much of the credit goes to the success of the Smallpox Eradication Programme. This was launched in 1958 but only began to gain ground in the late 1960s after efforts were intensified and the Soviet Union donated 75 million doses of freeze-dried vaccine over a three-year period. By the early 1970s it was clear that smallpox eradication was in sight. It was also clear that an immensely valuable worldwide technical and logistic network had been built up in order to achieve this, and it would have been a pity to let it go to waste when vaccination against smallpox ceased. It made much more sense to fit other vaccine-preventable diseases into the network.

Vaccination of children was already commonplace before 1974, but coverage varied widely from country to country and there was no coordinated effort on a global scale to provide protection against childhood diseases. The six target diseases were chosen on the basis of their high incidence and the availability of well-tested vaccines for them at affordable prices. Organizations such as UNICEF and Rotary International became partners of WHO in the programme.

By 1994, immunization services that were virtually non-existent in developing countries in the mid-1970s had reached almost 80% of children before their first birthday, preventing over three million needless deaths a year (see Fig. 1). Today the possibility of vaccinating at least 90% of the world’s children aged under one is recognized, and it is anticipated that this will drastically reduce the two million deaths a year still caused by vaccine-preventable diseases.

As well as increasing coverage and expanding the number of diseases targeted, one of the key goals of EPI is to reduce the number of contacts needed to immunize a child fully, particularly by finding ways to combine both the initial dose of vaccine and the booster doses in a single dose. Another goal is to develop vaccines that can be given at an earlier age. This will help to reduce child deaths in two ways: by avoiding the higher drop-out rates that occur when vaccines are given later in life, and by protecting children at a more vulnerable age. Another priority is the development of a more effective vaccine against tuberculosis – a re-emerging disease which kills three million people a year.

So far, only two new vaccines, hepatitis B and yellow fever, have been recommended for inclusion in EPI globally since its launch 22 years ago. The countries at highest risk for these diseases are also among the poorest in the world and therefore the ones with the least developed immunization programmes. Yellow fever vaccine is relatively inexpensive, but three doses of the hepatitis B vaccine cost as
much again as all six of the original EPI vaccines.

**Poliomyelitis**

During 1996, almost half of the world’s children aged under five – a record 450 million children – were immunized against polio as part of the push to eradicate the disease globally by the year 2000. On national immunization days (see Fig. 2), particularly in January 1996, over 126 million children received the oral vaccine. In that month, in India alone, 82 million children aged under three years were protected. Reported cases in China dropped from 5000 in 1990 to zero in 1995 following national days of massive immunization in December 1993 and January 1994. In Sri Lanka, a one-day truce called a “Day of Tranquillity” was agreed between the warring sides, when many thousands of children were immunized. Since then such truces have been duplicated in other countries.

In Africa, which has the lowest coverage rates in the world, WHO, with Rotary International and other partners, launched a three-year mass immunization campaign called “Kick polio out of Africa!” Inaugurated by President Nelson Mandela, who

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is the Chairman of the Committee for a Polio-free Africa, this campaign relies heavily on national immunization days, with maximum publicity being given to the advantages of having every child protected against this potentially paralysing disease. Helping the campaign as a WHO goodwill ambassador is the Ghanaian footballer Abedi Ayew Pele.
Fig. 2
Countries conducting National and Subnational Immunization Days (NIDs and SNIDs), December 1997

Legend:
- No NIDs
- NIDs needed
- SNIDs
- NIDs conducted
- NIDs planned for before Jan. 1998
Polio has already been eradicated in the Americas, and an increasing number of countries elsewhere are reporting zero incidence of the disease. From 31,000 reported cases in the world (and 350,000 estimated cases) in 1988 when the eradication effort was launched, the numbers have fallen to fewer than 4000 (and under 40,000 estimated cases), while several major areas are rapidly becoming polio-free.

Polio is a viral infection of the nervous system which mainly affects children and can cause lifelong paralysis, breathing incapacity and sometimes death. The oral polio vaccine is the one favoured by EPI because it is five times cheaper than the inactivated injectable vaccine and – since it requires no needles or syringes – is easier and safer to administer. Oral polio vaccine also induces immunity in the gut, the key site where wild poliovirus multiplies.

While the managers of the programme remain highly optimistic, it is still too early to guarantee that the eradication target will be attained by the year 2000. Reaching children in the poorest countries is growing harder rather than easier, especially where because of war or other disastrous events basic health services have been destroyed, vaccine supply lines have been cut and immunization programmes suspended. Other threats arise from donor fatigue and the competing need for funds to combat other diseases, as well as the false sense of security that health officials and mothers tend to acquire as the numbers of cases fall and the risk of infection recedes. The poor quality of surveillance, or its absence, in many countries may make it difficult for them in three years' time to supply proof that polio has indeed been eradicated.

In a more general way, there is no doubt that polio eradication and basic immunization services can go hand-in-hand to strengthen the general health infrastructure. EPI in fact provides the world's mothers and children with the best possi-

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ble access gate to the health services. It brings the vertical and horizontal approaches to health care together: the power focused on a highly specific target provides the impetus and involvement needed for all the health services.

Measles

WHO estimates that in 1996 one million children died from measles, more than the total child deaths from all the other EPI vaccine-preventable diseases combined. Most of these deaths occur in developing countries, and globally measles accounts for over 10% of deaths occurring in the 0-5 year age group, half of them in children under one year old. Indeed, the measles virus may be responsible for more child deaths than any other single pathogen, mainly through the complications of pneumonia, diarrhoea and malnutrition. Measles can also lead to lifelong disabilities, including brain damage, blindness and deafness.

Although it is estimated that some 36.5 million cases of measles occur each year, fewer than 5% of them are reported. It thrives in cities, especially where overcrowding, poor sanitation and pockets of low immunization ensure its continued
transmission. Population movements then carry the disease to other towns and villages.

Before the launch of EPI in 1974 the annual death toll from measles stood at about eight million, and there were an estimated 130 million cases. By 1990, global immunization coverage had reached 80% but it has since declined to about 78%, where it has remained. Coverage is still very uneven. In some developing countries it remains stubbornly below 50% while in others it has reached over 90%. In the Americas, hopes are high of eliminating the disease by the year 2000, and transmission has been interrupted in Chile, Cuba and the English-speaking countries of the Caribbean. In the South-East Asia Region, on the other hand, only two countries have succeeded in reducing the number of cases by 90%, and in the African Region only five. Globally, there has been a dramatic reduction in the numbers of measles cases and deaths. By December 1996, just over one-third of all countries had achieved a 90% reduction in cases and over half had cut the number of deaths by at least 95%. It is reasonable to hope that early in the next century measles will join the list of diseases that have been eradicated from the planet.

Diphtheria

Before the age of vaccines, diphtheria was a widely dreaded childhood disease. Children who contracted it in the industrialized world were often confined to special isolation hospitals because the contagion, affecting the tonsils, upper respiratory tract and the heart, tended to spread very rapidly among playmates and schoolfellows. Even with appropriate treatment, up to 10% of cases are fatal. Since the universal deployment of the combined diphtheria, tetanus and pertussis (DTP) vaccine, this disease has become so rare that doctors often do not recognize it when it does occur.

The threat of diphtheria remains, despite the invention of a successful vaccine. Over time, vaccine-induced immunity wanes and groups of non-immune individuals may build up, creating ideal conditions for an epidemic. In Algeria, this happened in 1993 after a period of high immunization coverage. There were 163 confirmed cases of diphtheria, causing 31 deaths. Much more serious is the situation in the former Soviet Union, where a dramatic fall in immunization coverage, mass movements of population and serious economic problems helped to spark off a major epidemic in 1990. The number of cases soared from under 2000 in 1990 to over 47,000 by 1994. More than 2500 people have died from diphtheria in this region during the past five years. WHO and UNICEF declared the epidemic an international health emergency in 1994.

WHO recommends that all countries should give priority to ensuring that at least 90% of children aged under one year are immunized with three doses of the DTP vaccine. In developing countries where the reservoir of diphtheria organisms is large and people are therefore frequently exposed to the disease, the primary immunization may be enough to secure long-lasting immunity. But in countries which enjoy sustained high levels of immunization coverage, and
where exposure is rarer, a series of booster doses may also be needed.

**Pertussis (whooping cough)**

Every year nearly five million children suffer from respiratory complications as a result of pertussis infection, and 50,000 suffer long-term neurological complications, including permanent brain damage. In developing countries the death rate can exceed 15%, but it is much lower in the industrialized world, with four deaths out of every 10,000 infected children. In 1994, there were an estimated 40 million cases of the disease worldwide and 360,000 deaths.

Pertussis vaccine has been on the market for almost half a century. By 1994, 80% of the world’s infants had received three doses of DTP vaccine before their first birthday and consequently an estimated 70 million cases of pertussis and 610,000 deaths were prevented. Although the global coverage rates are high, in some countries fewer than one-third of children receive this protection. The figures for July 1997, for instance, showed that in Afghanistan only 12% of children under one year of age had received it, in Chad 20%, in the Democratic Republic of the Congo 36% and in Cameroon 46%. The EPI schedule includes three doses of DTP vaccine within the first six months of life, but in the developing world immunizations are often delayed and there are high drop-out rates between the first and third doses.

**Tetanus**

Neonatal tetanus is caused by the introduction of tetanus spores from soil through poor hygiene or the use of unsterile instruments or dressings during childbirth. The disease is thus commonly associated with poverty, lack of education, poor living conditions and home births supervised by untrained birth attendants. Immunization programmes are supplemented by training for birth attendants in safe delivery practices which emphasize the importance of cleanliness. Information campaigns stress the hazards of some traditional childbirth practices, such as using cattle dung to “heal” the umbilical stump.

In 1994, more than 50% of babies were born unprotected against tetanus because their mothers were not given the tetanus toxoid. Almost half a million of those babies died during their first three weeks of life because their mothers had no protective antibodies to pass on during pregnancy. Each year an estimated 30,000–60,000 mothers also die of tetanus infection. Since 1989 an effort has been under way to eliminate tetanus as a public health problem (less than one case for every 1000 live births), and almost 60 developing countries have achieved this. About 80% of the remaining reported cases now occur in only 12 countries: Bangladesh, China, Democratic Republic of the Congo, Ethiopia, Ghana, India, Indonesia, Nepal, Nigeria, Pakistan, Somalia and Sudan.

**Tuberculosis**

Tuberculosis is the world’s most lethal infectious disease and is responsible for some three million deaths a year, most of which occur in adults. Each day there are
over 7000 deaths and over 24,000 new cases. A third of the world’s population, two billion people, are already infected with *Mycobacterium tuberculosis*, and over the next decade it is feared there will be an additional 300 million. Only 10% of those infected go on to develop an active form of this disease, but if they are also infected with HIV they are 30 times more likely to develop active tuberculosis than those who are not. Conversely, tuberculosis infection can further suppress the immune system of an HIV-infected person and accelerate the onset of opportunistic infections. By the year 2000, tuberculosis is expected to be the leading cause of death among HIV-positive people.

Although drug treatment for tuberculosis is effective, it has to be rigorously followed for six months. Patients who stop taking the prescribed drugs before they are cured continue to infect others and risk spreading drug-resistant strains of the bacteria. Already more than 50 million people are believed to be infected with these drug-resistant strains.

The Bacille Calmette-Guérin (BCG) vaccine currently used to immunize children was developed in 1921 and is still the most widely used vaccine in EPI. In 1994, almost 90% of the children in the world under one year of age were immunized with it, but it is only 50–80% effective in protecting them against the most severe forms of childhood tuberculosis, and provides little or no protection against the adult form. BCG is still needed in child health programmes, and also confers some degree of protection against leprosy, but is unlikely to have much impact on the current tuberculosis epidemic.

**EPI Plus**

In 1993, the World Bank maintained that, in developing countries, an EPI package which also incorporates vaccines against hepatitis B and yellow fever, together with supplements of vitamin A and iodine, would have “the highest cost-effectiveness of any health measure available today.” This package, known as EPI Plus, is widely accepted as an idea, but neither hepatitis B nor yellow fever vaccine is available today in many of the countries that need them most, and nor are the micronutrient supplements.

More than 2000 million people alive today have at some time in their lives been infected with the hepatitis B virus. Of these, about 350 million remain chronically infected carriers who can transmit the disease for many years and themselves develop liver cancer or cirrhosis of the liver. Every year there are more than four million acute clinical cases of hepatitis B and about a million deaths. In 1991 hepatitis B vaccine became the seventh EPI antigen when WHO recommended that all children receive it as part of the regular immunization schedule in all countries. By 1998, 90 countries had added it to their routine immunization schedules. Safe and effective hepatitis B vaccines have been available since 1982 and are now known to be more than 90% effective in preventing the development of clinical hepatitis and the carrier state. There has been a reduction in liver cancer in immunized children.

In most countries of sub-Saharan Africa and the former Soviet Union hepatitis B immunization has not yet begun, mainly
for economic reasons. The price of the vaccine in developing countries has fallen dramatically with increased competition from a number of new producers. Although it is still more expensive than the other EPI vaccines, an increasing number of developing countries are able to afford it. Unfortunately, donors have not made hepatitis B vaccine available to the countries in greatest need, although in many of them the prevalence of this disease is high.

Yellow fever, an untreatable viral haemorrhagic disease with a high fatality rate, is re-emerging with the potential for explosive epidemics. Transmitted by mosquitoes, the disease was kept at bay from the 1950s to the 1970s by vaccination and vector control. Now, however, urban poverty, overcrowding and massive population movements, coupled with poor immunization coverage and the abandonment or failure of programmes to control mosquitoes, have created ideal conditions for outbreaks. In the latest outbreak in Peru in 1995, there were 440 cases and 169 deaths over a six-month period. Further outbreaks are feared in South America and Africa. A safe and highly effective vaccine has been available since 1937, but the cost of supplying it to the 21 million children born in those countries each year would be an estimated $4.6 million, and so far donors have not been willing to supply more expensive vaccine.

**Outlook for the future**

The future of immunization depends on three main factors: research and the development of new vaccines, the supply and quality of vaccines, and the logistics of delivery.

The impetus for research and development in the past has been the existence of a ready market in the industrialized world, and at present this is not the case for some of the vaccines most badly needed. Nevertheless, progress is being made in some quarters, and possibilities now being studied include the following: a non-injectable thermostable measles vaccine, a DNA vaccine for tuberculosis, a more effective oral vaccine for cholera, and more affordable versions of other vaccines now in use or being developed. No “magic bullet” vaccine against malaria is yet in sight. Indeed no effective vaccine has yet been developed against a human parasite, and the ability of both the parasite and the mosquito to develop resistance to drugs and chemicals suggests that any vaccine will need to be used alongside other control activities. The world is still waiting for news of a breakthrough in the quest for a vaccine against HIV/AIDS.

WHO’s Vaccine Supply and Quality Unit works with the pharmaceutical industry to encourage research on new vaccines and efforts to make existing ones more readily available and affordable. At the same time, if national immunization programmes are to be maintained and expanded, governments have to take on as much of the financial and managerial responsibility for them as they can. A strategy for self-sufficiency, which sets appropriate targets for governments and uses limited donor support to fill the gaps, was developed in 1994. The strategy provides a mechanism to set targets for each country based on its financial capacity, and to prioritize donor support to the neediest. Developing countries are assuming a greater share of the cost of their vaccines. The poorest countries have increased their share of vaccine purchase from 2% in 1990 to 25% in 1996, and the middle-income countries have increased their share from 40% to over 90%. UNICEF is the traditional
main supplier of vaccine to developing countries and has launched a global targeting system to ensure the sustainability of vaccine financing in individual countries.

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The aim is to make sure that all countries that can afford to pay for their own vaccines do so.

At present, not all the vaccines in use meet WHO minimum requirements for safety and efficacy. The Vaccine Supply and Quality Unit issues warnings regularly that compromising on vaccine standards not only endangers children's lives but can also destroy public confidence in immunization, thus putting even more lives at risk. Matters are improving, however, and a Global Training Network has been established in five countries to increase the number of high quality staff who are trained in ensuring vaccine quality.

In addition, heat-sensitive labels called “vaccine vial monitors” have been in use since 1996. These labels are attached to vials of oral polo vaccine at the time of manufacture. They warn storekeepers and health workers when a vaccine has been excessively exposed to heat and should not be used. The label shows an inner square surrounded by a reference colour; when the inner square is as dark as the outer colour or darker than it, the vaccine should not be used. These monitors are a great help in ensuring that potent vaccine is delivered during outreach and mass campaigns in remote and tropical areas. They are now on all oral polio vaccine vials supplied by UNICEF and WHO.

Logistics of delivery

The cold chain is a network of refrigerators, freezers, cold boxes and other equipment, and continues to be the backbone of the EPI. Its function is to ensure that vaccines are kept at the correct temperature from the point of manufacture, through shipping and storage, to the time and place of use. A major setback has been the international commitment to phase out – for the best of ecological reasons – ozone-depleting chlorofluorocarbons (CFCs) commonly used in refrigerators. CFC-free refrigerators are steadily replacing the older models but they are less efficient, and this can compromise the validity of stored vaccines. WHO and UNICEF are working with manufacturers to meet this challenge.

In 1994, WHO reported that surveys carried out in four of its six regions indicated that up to a third of immunization injections were unsterile. Unsafe injection practices can put the lives of both children and health workers at risk, for instance, of cross-infection with bloodborne diseases such as hepatitis B and AIDS. WHO and UNICEF now recommend the use of auto-destruct syringes wherever possible instead of disposable, single-use syringes, in order to avoid those hazards. The new ones cannot be reused or recycled for sale, but they are as yet more expensive and still require safe disposal.

Mass immunization campaigns to reduce measles and control large-scale epidemics are placing increasing pressure on WHO to find a safe multi-dose needle-free injector. It is hoped that safety problems inherent in current models will be solved.
during 1998. In addition, the Vaccine Research and Development Unit is requestng research groups to supply preliminary data on how vaccines may be dried and injected directly, without reconstitution.

The targets for EPI for the immediate future include the following.

- **1998.** The development of new vaccines for meningococcal meningitis and pneumococcal pneumonia will be completed, and new cholera vaccines will be ready for use in refugee camps.

- **1999.** A quarter of the countries in the world will report zero indigenous measles cases. All countries will have maintained the elimination of neonatal tetanus. New, simpler-to-administer vaccines (single-dose tetanus toxoid, aerosol and oral vaccines) will have been evaluated in advanced clinical trials. Polio eradication will have been certified in the Western Pacific and European Regions. Circulation of wild virus will have been interrupted in the South-East Asia Region and most of the African Region.

- **2000.** Global immunization coverage will be 90%. All vaccines (100%) used within the EPI will be of known good quality. Circulation of wild poliovirus will be interrupted throughout the world.

A challenge for the immunization programmes of the future will be to adapt their activities to health sector reform. EPI will develop guidelines for promoting and ensuring high immunization coverage in countries where the health system is being reorganized.

Immunization has long been the most accessible, the most used and the most cost-effective public health measure.

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WHO’s Expanded Programme on Immunization is arguably the most successful preventive health programme that exists in the world today. Victory over polio would alone suffice to make this case. Working directly with mothers and their children in their homes or at the health post, the programme offers chances of survival and health from which no child should be excluded. If WHO, UNICEF and their partners can give the world a better understanding of the value of vaccines and immunization, the success of the past 20 years in saving millions of children’s lives will be dwarfed by the successes of the next two decades.