Mass Vaccination: Global Aspects - Progress and Obstacles

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Mass Vaccination: When and Why

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Abstract With increased demand for smallpox vaccination during the nineteenth century, vaccination days—early mass vaccination campaigns—were conducted over time-limited periods to rapidly and efficiently protect maximum numbers of susceptible persons. Two centuries later, the challenge to rapidly and efficiently protect populations by mass vaccination continues, despite the strengthening of routine immunization services in many countries through the Expanded Programme on Immunization strategies and GAVI support. Perhaps the most widely accepted reason for mass vaccination is to rapidly increase population (herd) immunity in the setting of an existing or potential outbreak, thereby limiting the morbidity and mortality that might result, especially when there has been no routine vaccination, or because populations have been displaced and routine immunization services disrupted. A second important use of mass vaccination is to accelerate disease control to rapidly increase coverage with a new
vaccine at the time of its introduction into routine immunization programmes, and to attain the herd immunity levels required to meet international targets for eradication and mortality reduction. In the twenty-first century, mass vaccination and routine immunization remain a necessary alliance for attaining both national and international goals in the control of vaccine preventable disease.

1 The Concept of Mass Vaccination

Ever since the practice of variolation was used to prevent serious smallpox infection in China and India sometime about A.D. 1000 [1], vaccination of populations at risk of infectious diseases has remained a challenge. In 1796, Edward Jenner took smallpox vaccination a step further by inoculating humans with material from lesions of cowpox from milkmaids, rather than from smallpox lesions, thus pre-empting the requirement of direct vaccination from a person with smallpox. By the beginning of the nineteenth century still further advances were made, when the practice of vaccination used material from cowpox lesions dried on threads as a vaccine that could then be sent throughout the United Kingdom and to other parts of the world [2]. Vaccination thus became portable—it no longer required direct person-to-person inoculation, and vaccines could be easily transported to vaccinate persons at risk.

Vaccination against smallpox soon became compulsory in Europe with Bavaria, Denmark and Sweden adopting vaccination laws between 1807 and 1816. The Vaccination Acts in Great Britain later in the nineteenth century made vaccine universal, free and mandatory in that country, and vaccination officers enforced them. Those who refused vaccination for any reason were fined. Mandatory smallpox vaccination was soon accepted by many other countries, either through school entry laws or legislation pertaining to young children and families [3].

With increased demand for vaccination, general vaccination days were held in Europe and many other parts of the world where person-to-person vaccination, and vaccination using impregnated threads, was replaced by vaccination directly from cowpox lesions on cows. These vaccination days were early mass vaccination campaigns—vaccination over time-limited periods to provide protection rapidly and efficiently to maximum numbers of susceptible persons. By 1820, Sweden had been able to decrease smallpox by over a hundredfold by mass vaccination [4], and it soon became evident that vaccination not only offered individual protection—it could also be used to prevent infection among those not vaccinated because of an overall decrease in the number of infected persons, reducing the net rate of transmission of the smallpox virus. This principal of herd immunity has become an important benefit
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Mass vaccination—susceptible persons can either gain protection directly by being vaccinated, or indirectly by having their risk of infection reduced as transmission of the infectious agent decreases among those vaccinated.

Since Jenner’s time, mass vaccination campaigns have become a common, and frequently controversial, element of communicable disease control programmes in developing as well as industrialized countries worldwide. This chapter briefly reviews the recent evolution of mass vaccination and the sometimes-uneasy alliance that has emerged between mass vaccination and routine immunization services. Based on this experience, the subsequent sections propose a broad framework for policy makers in evaluating the potential role of mass vaccination in their efforts to control vaccine-preventable diseases.

2
Mass vaccination in the Twentieth Century—Smallpox Eradication

By the twentieth century it was understood that achieving herd immunity could in itself be an important goal of mass vaccination programmes as it could stop person-to-person transmission of an infectious agent. It was further understood that if the infectious agent had no reservoir other than humans, zero transmission among humans worldwide could be equated with eradication of the disease it caused.

In 1967, the member states of the World Health Organization (WHO) resolved to intensify smallpox eradication efforts throughout the world [5], and countries that had not yet interrupted smallpox transmission agreed to supplement routine immunization programmes with mass vaccination campaigns. Smallpox vaccination was not without its complications however. Complications associated with primary smallpox vaccination ranged from vaccinial eruption at sites of the body that are or have previously been eczematous, to generalized vaccinia infection and post-vaccinal encephalitis leading to permanent neurological disability or death. With a case fatality rate for post-vaccinal encephalitis of approximately 30%, the risk of fatal complication from smallpox vaccine was approximately one per million doses of vaccine administered, complications being most severe in children under the age of 2 years [6].

Despite the risks from primary smallpox vaccination the benefits of eradication were clear: 31 countries still had endemic smallpox in 1967 at the time of the resolution to intensify eradication efforts, an estimated two to three million persons in those countries would die from smallpox that year, and uncounted others would be left with severe facial scarring, corneal scarring
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There was no doubt that smallpox eradication would save lives and that the death and disability prevented would be considerable, as would the financial savings associated with foregone medical treatment costs and the cessation of smallpox vaccination [8, 9].

In 1977, after 10 years of intensified country activities to eradicate smallpox, the last naturally occurring chain of human-to-human smallpox transmission had occurred. Three years later, in 1980, an independent global commission certified that smallpox had been eradicated from the world. The smallpox eradication programme became the first public health programme to achieve worldwide equity in the benefits of a vaccine. That equity was achieved in large part through mass vaccination.

3 Routine Immunization and Mass Vaccination Today——
A Necessary Alliance

The fundamental reason that mass vaccination was required to eradicate smallpox was that routine vaccination services in many developing countries lacked the infrastructure needed to vaccinate a sufficient number of their population to attain the herd immunity required to interrupt transmission of the smallpox virus. During the 1970s, as the smallpox eradication programme continued, there was increasing dialogue in WHO expert advisory groups about ensuring equitable distribution of other vaccines in developing countries, such as the DPT vaccine and the newly developed measles and rubella vaccines. These discussions focused on the intensity of the effort required for mass vaccination, the cost of sustaining mass vaccination efforts, and the potential for better sustainability if immunizations were routinely made available along with other maternal and child health services. The outcome of these discussions was the development of the WHO Expanded Programme on Immunizations (EPI) in 1974, the goal of which is to establish and/or strengthen routine immunization programmes in developing countries [10–12].

The overall strategy of the EPI was to increase and sustain the percentage of children who were protected against selected diseases for which vaccines existed. It established common strategies for planning, implementation and evaluation of the effectiveness of national immunization programmes, and introduced these strategies in developing countries through standardized training programmes. In 1977 the World Health Assembly resolved to provide four vaccines (multi-antigen, diphtheria, pertussis and tetanus vaccine; trivalent oral polio vaccine; measles; and BCG) to children throughout the world. By 1990, 16 years after EPI was first established, it was estimated that nearly...
80% of children in the world had been vaccinated, some countries having achieved this goal through supplementary mass vaccination campaigns that had received substantial support from bilateral, multilateral, nongovernmental and international organizations [13, 14].

Sustainability of this extraordinary achievement began to wane in many developing countries soon after 1990, due to non-sustained external support, and internal factors such as civil disturbance and war. By 2003 it was estimated that vaccination coverage globally was 75%, ranging from 80% or more in industrialized countries to less than 56% in much of sub-Saharan Africa. Seventeen of the poorest countries in the world were reaching fewer than 50% of children. Obstacles to vaccinating children through routine immunization programmes included poor quality planning, inadequate funding of peripheral staff and operational costs (resulting in low quality and unreliable services), and inadequate monitoring and supervision of immunization activities [15].

In an effort to help countries overcome these obstacles and strengthen immunization services in 75 of the poorest countries with low coverage, the Global Alliance for Vaccines and Immunization (GAVI) was established in 2000 [16]. GAVI provides incremental funding for immunization services, with continuity in funding linked to improvements in the percentage of children immunized. It also provides finances for the introduction of new vaccines into routine immunization programmes in most of these countries. Despite strengthening routine immunization services in many countries through EPI strategies and GAVI support, the need for mass vaccination remains, both for preventing emerging outbreaks, and for accelerating disease control programmes.

In all mass vaccination activities, except for those involving oral polio vaccine, auto-disable syringes are the method of choice for vaccinating. Puncture-resistant containers for collecting disabled needles and syringes must also be available. Multiple-use jet injectors are only used when public health authorities determine that the benefit outweighs the slight, but real risk of transmission of blood-borne infections [17].

4 Preventing Emerging Outbreaks

Perhaps the most widely accepted reason for using mass vaccination is to rapidly increase population (herd) immunity in the setting of an existing or potential infectious disease outbreak, thereby limiting the morbidity and mortality that might result. The rationale for using a mass vaccination approach is particularly strong when the incidence of an epidemic prone disease
Table 1  Mass vaccination to prevent emerging outbreaks

<table>
<thead>
<tr>
<th>Mass vaccination category</th>
<th>Objective of mass vaccination</th>
<th>Examples</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to an emerging epidemic</td>
<td>Rapidly limit the morbidity and mortality due to the documented presence of a vaccine-preventable disease</td>
<td>Meningitis campaigns in sub-Saharan Africa, annual influenza campaigns in industrialized countries, yellow fever campaigns in sub-Saharan Africa and Latin America</td>
<td>Particularly important when the antigen is not delivered through routine immunization programmes</td>
</tr>
<tr>
<td>Displaced persons</td>
<td>Rapidly establish population immunity when risk occurs</td>
<td>Measles immunization in refugee camps</td>
<td>Compensate for lack of routine services</td>
</tr>
<tr>
<td>Threat of deliberately caused outbreaks</td>
<td>Rapidly establish population immunity when risk is perceived</td>
<td>Smallpox vaccination in response to a real or perceived threat.</td>
<td>May serve as event deterrent</td>
</tr>
</tbody>
</table>

is beginning to rise and when there has been no routine vaccination because the vaccines are unsuitable for routine use, or because populations have been displaced and routine immunization services disrupted (Table 1).

4.1 Meningitis

Meningococcal meningitis is one of a number of diseases for which mass vaccination is a standard, proven element of epidemic control. Although meningococcal meningitis occurs throughout the world the largest epidemics occur in the semi-arid areas of 12 sub-Saharan African countries, designated the African meningitis belt [18]. Most countries within the meningitis belt experience increased transmission each year during the dry period, with large epidemics occurring every 8–12 years during the past 50 years, particularly in regions with extensive communication and mixing of populations.

Meningitis epidemics in sub-Saharan Africa are generally caused by serogroup A organisms, although W135 serogroups have been recently shown to also play a role. Meningococcal vaccines are based on capsular polysaccharide antigens. They are not routinely used in early childhood because of their general lack of efficacy in infants and young children, those at greatest risk of infection and disease [19].
When increased transmission of meningitis occurs in sub-Saharan Africa, epidemiological surveillance is important to determine when the threshold of transmission that generally leads to epidemics has been reached. Once reached, mass vaccination is begun and targeted at a broad age range, sometimes the whole population. Rapidly organized and conducted mass vaccination campaigns effectively protect susceptible individuals and can often interrupt epidemic transmission within 2 or 3 weeks. Mass vaccinations are usually provided by mobile vaccination teams or fixed vaccination stations at health centres or other community facilities [20]. If newly developed meningococcal conjugate vaccines are shown to be protective in infants and young children, meningococcal vaccination could eventually be included in national immunization programmes in areas at high risk of meningococcal disease [21].

4.2 Influenza

Influenza vaccines are not included in routine immunization programmes because of the need to alter the vaccine's composition each year, making it necessary to rapidly vaccinate populations at risk before the epidemic season for influenza begins. Each year seasonal influenza occurs during the winter months in both the northern and southern hemisphere. It is estimated that up to 500 000 persons die each year from seasonal influenza, mainly those over the age of 60 years (WHO). The influenza virus is highly unstable and regularly mutates through a process called antigenic drift. Because antigenic drift decreases the efficacy of the influenza vaccine, the recommended antigenic composition of vaccines is altered each year based on prevalent virus strains. The composition is altered once in February, for the influenza season that will begin 11 months later, and again in August for the influenza season in the southern hemisphere.

As soon as altered influenza vaccines become available each year, they are provided to the population at risk (usually the elderly, and in some countries to health workers as well) prior to the epidemic season and by mass vaccination at fixed health facilities, mainly in industrialized countries [22, 23]. Recently the provincial government of Ontario in Canada recommended vaccination of populations of all ages with influenza vaccine prior to the influenza season. This experience will provide a comparative evaluation of the approach being used in most other countries. Although it is known that seasonal influenza occurs in developing countries, further study is needed to understand the target population and vaccination strategy required to optimize the impact of mass vaccination.
At times, an antigenic shift occurs when a new pandemic influenza virus enters human populations, usually from an avian source. The new virus strain must then be used to develop a new vaccine because little, if any cross immunity is anticipated from existing influenza vaccines. New vaccines for pandemic influenza are targeted at the entire population, and are provided in mass campaigns.

4.3
Yellow Fever

Yellow fever occurs sporadically in 33 countries in Africa and 11 countries in South America. A severe epidemic of human-to-human transmission is most likely to occur when conditions allow the density of mosquito vector populations to substantially increase, as often happens during the rainy season. Epidemiological surveillance is a key strategy for limiting yellow fever epidemics by rapidly identifying human infections when they occur. Mosquito control is also an effective supplemental prevention strategy. However, the most effective means of preventing yellow fever epidemics is through vaccination at 9 months of age using the vaccine as part of routine immunization programmes [24], and yellow fever vaccine is integrated into routine immunization programmes in some, but not all countries at risk.

If routine immunization at 9 months of age does not reach the level needed for herd immunity in the general population, epidemic transmission is a risk and mass vaccination is required to fill the gap in immunity. The target population for mass vaccination, once yellow fever has been identified in human populations, is the entire population living or working in the area from which the infection has been identified. In the event of limited financial resources or vaccine supply, the primary target population is usually children aged from 9 months to 14 years after which adults at risk are also vaccinated. Vaccinations are generally provided through house-to-house campaigns, during which there is active questioning to determine whether additional human infections are occurring. As with any epidemic, planning and implementation of mass vaccination must begin as soon as possible after an outbreak is confirmed, and emergency supplies of 17D yellow fever vaccine ordered immediately.

4.4
Displaced Persons

Sudden and massive influxes of people with varied backgrounds and immunization status can occur during civil disturbance, war and natural disasters.
In such situations routine immunization activities are often not available and, where displaced populations live in close proximity, and where sanitation and water supplies may be compromised, they create a particularly rife environment for epidemics of vaccine preventable diseases. Major vaccines used in mass campaigns among displaced persons are measles, meningococcal meningitis, and yellow fever vaccines. Mass vaccination for measles is usually conducted immediately after displaced persons congregate, particularly if vaccine coverage rates are estimated to be less than 80%. The target population is often extended, to a lower age limit of 6 months and an upper limit of 14 years, with revaccination of infants when they reach 12 months of age. Mass vaccination for meningitis and yellow fever is conducted if risk factors for epidemics are present, while studies of the applicability of the new cholera and typhoid vaccines in displaced populations are currently underway in several geographic areas to evaluate their usefulness in mass campaigns among displaced persons [25].

4.5 Threat of Deliberately Caused Outbreaks

There is a variety of circumstances under which public health authorities gauge the risk of a deliberately-caused epidemic or biologic threat to be sufficient to warrant preventive action. Mass vaccination campaigns are then sometimes conducted as a deterrent, and/or to prevent a deliberately caused outbreak should one be planned or occur. Some countries perceive a particular threat from disease such as smallpox and/or anthrax, and have begun to stockpile vaccines against these perceived threats that would be used for mass vaccination of entire populations should such a threat materialize [26].

Strategies for the use of these vaccines vary, but most countries state as the first priority mass vaccination of primary responders such as health workers, followed by mass vaccination of the general population if the deliberately-used infectious agent has the potential to spread from person to person. The strategies for mass vaccination may, however, be much more complex than for other indications due to the deterrent nature and thus the need to be as safe as possible. For example, because infection with HIV has been associated with generalized vaccinia and death after smallpox vaccination, strategies of preventive mass vaccination using smallpox vaccine need to incorporate the ability to avoid vaccination of HIV infected persons, and to provide them protection by other means such as passive immunization with vaccinia immune globulin [27].
5 Mass Vaccination to Accelerate Disease Control

A second important use of mass vaccination strategies is to accelerate disease control to rapidly increase coverage with a new vaccine at the time of its introduction into routine immunization programmes, or to attain the herd immunity levels required to meet international targets for eradication and mortality reduction. Since the late 1980s, international accelerated disease control targets have been established for eradication, for mortality reduction, and for heightened control of infectious diseases. Reaching these targets requires rapidly increasing population immunity, usually with the goal of interrupting human-to-human transmission of the causative infectious agent. Mass vaccination campaigns are a particularly important element of these efforts as the vaccination coverage levels required to achieve herd immunity, especially in densely populated areas, often exceed the coverage rates from routine immunization programmes (Table 2).

Table 2 Mass vaccination to accelerate disease control

<table>
<thead>
<tr>
<th>Mass vaccination category</th>
<th>Objective of mass vaccination</th>
<th>Examples</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>New vaccine introduction</td>
<td>Rapidly optimize the impact of a new antigen and/or minimize potential side effects associated with its introduction</td>
<td>Rubella campaigns (e.g. targeting children and women &lt; 45 years)</td>
<td>One-time supplement at time of initiation of routine childhood immunization with a new vaccine</td>
</tr>
<tr>
<td>Disease eradication</td>
<td>Achieve population immunity needed during time-limited period to interrupt transmission</td>
<td>National Immunization Days (NIDs) for polio eradication</td>
<td>Essential if coverage required for herd immunity exceeds that of routine immunization coverage or goals</td>
</tr>
<tr>
<td>Mortality reduction</td>
<td>Accelerate achievement of specific national or international disease control goals</td>
<td>Measles morbidity and mortality reduction campaigns, neonatal tetanus elimination campaigns</td>
<td>Sometimes continued as a transition or temporary strategy while routine immunization is strengthened</td>
</tr>
</tbody>
</table>
5.1 New Vaccine Introduction

During the past 60 years more than 20 new vaccines have become available. Mass vaccination can be a key element of new vaccine introduction, the goal being to quickly reduce the proportion of susceptible persons at risk at the time the new vaccine is introduced into the routine immunization programme. The impact of the mass campaign is to equalize population immunity levels, thus preventing a potential exacerbation of the disease that is targeted because of a sudden change in its transmission patterns or other epidemiological characteristic that might occur by vaccinating only a portion of the susceptible population through routine immunization programmes.

At the time of new vaccine introduction, persons considered susceptible and at risk of infection are vaccinated in mass vaccination campaigns to ‘mop up’ or protect all those who were susceptible. Mass vaccination is then ended, and the vaccines remain incorporated in routine immunization programmes to vaccinate susceptible persons as they enter the cohort of susceptibility (usually at birth).

A clear example of this strategy first occurred in the 1950s when the Salk inactivated polio vaccine was first licensed. Initially it was offered in mass campaigns to all populations considered at risk of polio, then incorporated into routine childhood immunization programmes to ensure that children entering the birth cohort were fully protected.

Although routine childhood immunization against rubella is now a standard component of vaccination programmes in industrialized countries, the vaccine has until recently seen limited uptake in developing countries. Decision-making on whether or not to introduce rubella vaccine was complicated by concern that routine childhood immunization against the disease could shift the average age of infection to older girls, inadvertently increasing, at least transiently, the risk of disease in pregnant women and thus the incidence of congenital rubella syndrome. Consequently, the introduction of routine childhood immunization against rubella is accompanied by a one-time mass campaign, targeting all girls less than 15 years of age, and in some countries all women of childbearing age [28].

It is likewise recommended standard practice to accompany the introduction of yellow fever vaccine into routine childhood immunization programmes with a one-time mass vaccination campaign. In these campaigns children aged less than 15 years are targeted to prevent yellow fever epidemics that could continue because of the immunization gap that would occur until immunized childhood cohorts reach adulthood [29].
5.2 Eradication

Polio vaccination has been included in routine immunization programmes since the licensing of the Salk and Sabin vaccines. In 1988, when the target to eradicate polio was set, an increasing number of countries had already interrupted human-to-human transmission of wild poliovirus by using oral poliovirus vaccine (OPV) in routine immunization programmes. In many countries in Latin America, where routine immunization programmes had not ever achieved high level control it was demonstrated that by supplementing routine immunization with mass vaccination these tropical and semi-tropical developing countries could rapidly interrupt transmission.

The mass vaccination strategy currently used in polio eradication targets all children under the age of 5 years, during National Immunization Days or Weeks in which OPV is administered to children through fixed sites with house-to-house mop-up campaigns that sometimes target a broader age group if required to interrupt the final chains of transmission. In some densely populated areas, interrupting poliovirus transmission has required well over 90% coverage in up to seven mass vaccination campaigns each year. Areas with low standards of sanitation and high population densities have required the most campaigns.

Prior to conducting mass vaccination, district level micro-planning is used to identify areas where children under the age of 5 years may be living and to prepare maps that are used by social mobilizers and vaccinators as they pass from community to community and house to house. The oral route of OPV administration allows the widespread use of health workers, school teachers and community volunteers trained in short courses to administer polio vaccine during the campaigns. Worldwide interruption of human-to-human transmission of wild poliovirus is presently targeted for 2005. At the time this chapter was written mass vaccination was being further intensified in the six countries that remained polio-endemic, in six countries that had re-established polio transmission due to imported virus, and in other countries to control outbreaks following polio importation [30].

Despite the impact of the global polio eradication initiative to date, the use of mass vaccination strategies with the endpoint of eradication remains an uneasy alliance with routine immunization programmes, largely due to the massive marginal and opportunity costs associated with eliminating the final chains of human-to-human transmission. This debate has led to the establishment of careful and comprehensive criteria for considering future eradication programmes, particularly the need for explicit and appropriate cost–benefit analysis in advance, as well as the capacity to sustain sufficient societal and political support throughout [31, 32].
5.3 Mortality Reduction

5.3.1 Measles

Although measles vaccine is universally included in routine immunization programmes in developing countries, targeting children between the ages of 9 and 12 months, there is frequent failure of children to seroconvert to measles vaccine because of the presence of maternal antibody to measles. Once maternal antibody disappears the window of opportunity to effectively vaccinate children before natural infection is short and operationally difficult to exploit. Mass vaccination campaigns are a frequently used strategy to overcome this problem [33].

Based on the age profile of measles susceptibility, a one-time nationwide catch-up campaign is conducted in Latin American countries to reduce population susceptibility and interrupt transmission. Usually all children aged less than 15 years are targeted, regardless of prior measles immunization status. Follow-up mass vaccination campaigns, targeting children aged less than 5 years, are then conducted every 3–5 years thereafter, giving those who have not previously seroconverted a second opportunity. Countries that are achieving very high coverage through their routine immunization programmes generally provide the ‘second opportunity’ prior to school entry.

5.3.2 Maternal and Neonatal Tetanus

To prevent maternal and neonatal tetanus, mass vaccination campaigns with tetanus toxoid are conducted in high-risk areas that are delineated using surveillance data and the prevalence of clean birth and delivery practices. In most countries with an explicit maternal and neonatal tetanus elimination goal, districts are now ranked from highest to lowest risk of the diseases. Multiple rounds of mass vaccination are often required, targeting young girls and women of childbearing age, to rapidly boost immunity against tetanus [34].

6 Mass Vaccination in the Twenty-First Century

In the 200 years since Edward Jenner first opened the door to disease control through mass vaccination, much attention has been given to establishing
and strengthening primary health services through which childhood immunizations can be delivered on a routine, ongoing basis. At the same time, mass vaccination campaigns, conducted over short time periods, continue to play an important role in the control of vaccine preventable diseases, in both industrialized and developing country settings. Mass vaccination is particularly important for preventing emerging outbreaks of vaccine-preventable diseases, rapidly boosting population immunity in emergency settings, optimizing the impact of a new vaccine, achieving very high herd immunity levels to achieve international disease control goals (especially eradication), and, in some settings, to efficiently supplement routine immunization of young children. Mass vaccination and routine immunization are a necessary alliance for attaining both national and international goals in the control of vaccine preventable diseases.

References

5. World Health Organization, 1966. World Health Assembly 19.16
17. World Health Organization. “First, do no harm”. Introducing auto-disable syringes and ensuring injection safety in immunization systems of developing countries. WHO/V&B/02.26
28. World Health Organization. Control of rubella and congenital rubella syndrome in developing countries. WHO/V&B/00.03