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Debate

Following in the footsteps of smallpox: can we achieve the global eradication of measles?

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Abstract

Background: Although an effective measles vaccine has been available for almost 40 years, in 2000 there were about 30 million measles infections worldwide and 777,000 measles-related deaths. The history of smallpox suggests that achieving measles eradication depends on several factors; the biological characteristics of the organism; vaccine technology; surveillance and laboratory identification; effective delivery of vaccination programmes and international commitment to eradication.

Discussion: Like smallpox, measles virus has several biological characteristics that favour eradication. Humans are the only reservoir for the virus, which causes a visible illness and infection leading to life-long immunity. As the measles virus has only one genetic serotype which is relatively stable over time, the same basic vaccine can be used world-wide. Vaccination provides protection against measles infection for at least 15 years, although efficacy may be reduced due to host factors such as nutritional status. Measles vaccination may also confer other non-specific health benefits leading to reduced mortality. Accurate laboratory identification of measles cases enables enhanced surveillance to support elimination programmes. The "catch-up, keep-up, follow-up" vaccination programme implemented in the Americas has shown that measles elimination is possible using existing technologies. On 17th October 2003 the "Cape Town Measles Declaration" by the World Health Organisation and the United Nations Childrens Fund called on governments to intensify efforts to reduce measles mortality by supporting universal vaccination coverage and the development of more effective vaccination.

Summary: Although more difficult than for smallpox, recent experience in the Americas suggests that measles eradication is technically feasible. Growing international support to deliver these programmes means that measles, like smallpox, may very well become a curiosity of history.

Background

On the 26th October 1977, the last known case of naturally acquired smallpox occurred in Somalia [1]. This promised a new era in which many infectious diseases would be eradicated. However, nearly a quarter of a century later, 1.7 million children die each year from vaccine preventable diseases, nearly half due to measles (Figure. 1). Although an effective measles vaccine has been available for almost 40 years [2], in 2000 there were about 30 million measles infectious worldwide and 777,000 measles-related deaths [3]; measles is the 5th leading cause of

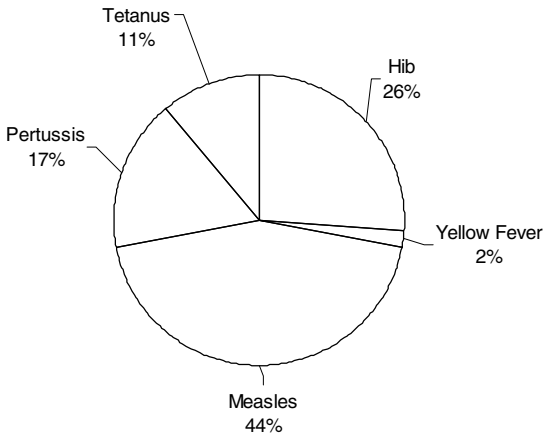

Figure 1
Proportional mortality (1.7 million worldwide) due to vaccine preventable diseases among children (2000) Source: WHO (2002) [31]

death in children under the age of five [4]. One might therefore wonder why have we not eradicated measles?

The history of smallpox has shown us that several factors must be considered in order to eradicate an infectious disease [5-7]; the biological characteristics of the organism; vaccine technology; surveillance and laboratory identification; effective delivery of vaccination programmes and international commitment to eradication. I will consider each of these elements, their implications for measles eradication and draw on lessons from smallpox eradication.

Discussion

Biological characteristics of the measles virus

Measles virus is a spherical single-stranded RNA virus belonging to the paramyxoviridae family [2]. It is spread by airborne droplets causing rash, cough and fever which lasts for several days [8]. Although there is no treatment, most infected individuals recover by themselves. However, complications due to pneumonia occur in 2–27% of cases causing 56–86% of all measles deaths [2]. Less commonly, measles infection can cause serious neurological complications [2]. Compared to smallpox, the measles virus is considerably more contagious, capable of causing large outbreaks even in populations with high vaccine coverage [9]. Nevertheless, measles shares several biological characteristics with smallpox which favour eradication [2,7,10]: humans are the only reservoir for the virus (i.e. animals are not infected); measles causes a visible illness; infection leads to life-long immunity; cases often occur at regular intervals enabling the targeting of interventions; measles virus has only one genetic serotype which is relatively stable over time [2]; an effective vaccine is available and accurate laboratory identification is possible.

Vaccine technology

The limited variability of the measles genome means that the same basic vaccine can be used worldwide [2]. A single dose of the vaccine provides about 90% protection, which is increased to about 99% with a second dose [11]. However vaccination programmes in developing countries may not achieve such high levels of protection, either because of cold chain failures [12] or host factors such as poor nutritional status [13,14]. Antibody titres following vaccination are lower than following infection with wild measles virus [2] and decrease over time. Nevertheless, vaccination can provide immunological memory against wild measles virus for at least 15 years [15]. However, in contrast to immunity following infection by wild measles virus, protection may not be life-long [15]. Infection due to wild virus amongst individuals with reduced vaccine-induced protection may be subclinical or cause milder illness than for individuals who are unvaccinated or did not seroconvert following vaccination [2].

Because of the highly infectious nature of the virus, between 90–95% vaccination coverage is needed to halt measles transmission [10]. An additional difficulty is that maternal antibodies interfere with the vaccine, reducing seroconversion in infants between 6–9 months old [16]. Despite concerns in some industrialised countries about the safety of the measles vaccine, adverse vaccine-associated events are rare [9,17]. A study of 20 million children and adolescents receiving measles vaccination in the UK, Canada, Australia, South Korea, Costa Rica, Romania and New Zealand identified no vaccine-related deaths [9]. The risk of encephalitis was estimated to be 1 per 1 million doses and acute anaphylaxis less than 1 per 1 million doses [9].

Epidemiological research further suggests that measles vaccination (and mild measles illness) may actually confer non-specific health benefits leading to reduced childhood mortality rates [18,19]. The reduction in non-measles mortality following vaccination is greater in girls than boys [20]. Although there is currently no biological explanation for this, greater protection against other infections may be caused by immunological stimulation due to the measles virus or vaccine [18]. If this is indeed the case, the implications would be that continued measles vaccination may be beneficial even after wild measles virus is eradicated [18].

Measles vaccination is currently given by injection, which requires skilled personnel to administer, thereby making widespread coverage more difficult. Injections are also associated with an increased risk of blood borne disease (e.g. HIV, hepatitis), risk of infection at the injection site and they lead to large amounts of medical waste [12,21]. As efforts to eradicate smallpox were transformed by the

Table 1: Number of deaths, vaccination coverage and deaths prevented by WHO region (2000)

Region	No of deaths	Vaccination coverage (%)	Deaths prevented
African	453,000	65	384,960
American	0	91	148,852
Eastern Mediterranean	81,000	79	129,769
European	7,000	92	28,692
Southeast Asia	202,000	83	256,633
Western Pacific	34,000	86	126,132
Total	**777,000**	**80**	**1,071,938**

Source: Adapted from Henao-Restrepo (2003) [4]

development of better vaccine delivery techniques [5,7], a new aerosolised measles vaccine promises to transform the battle against the measles vaccine [21]. The new approach, which is non-invasive and requires only minimal training to administer, has been successfully trailed in Mexico and is hoped to be in widespread use by 2009 [21]. Further research using a wide range of vaccine technologies such as DNA vaccines, bacterial vectors and viral vectors is also being undertaken to develop effective vaccines for infants younger than 6 months old [21].

Surveillance and laboratory identification

A strong measles surveillance network is vital to ensure that vaccine efficacy and coverage are maintained and that outbreaks or reservoirs of disease are identified [22,23]. Identification of measles infection can be made on clinical grounds by experienced clinicians. However, experience with smallpox has shown that as the incidence of disease decreases it becomes increasingly important to investigate every suspected case (case-based surveillance) and provide laboratory confirmation. In order to achieve this, the World Health Organisation is establishing a Global Measles Laboratory Network, which will develop local reference laboratories and train staff [24]. Laboratory identification of measles can be performed using relatively simple methods to test for the presence of measles-specific antibodies in the blood [25]. Where more complex genetic techniques are available, identification of different virus strains can show whether infections are due to local transmission or importation [24,25]. However, many poorer countries currently still lack sufficient resources to develop enhanced measles surveillance and laboratory diagnosis.

Effective delivery of vaccination programmes

In 2000, vaccination programmes worldwide achieved about 80% coverage with one dose of measles vaccine (Table 1). This was lowest in the African region (65%) and highest in the American (91%) and European (92%) regions. Only 74 countries (35%) achieved greater than 90% coverage while sixteen countries achieved coverage below 50% [4]. Since 2001 81% of countries have been offering a second opportunity for measles vaccination [4]. These efforts have had a significant impact on measles morbidity, preventing an estimated 1 million measles-related deaths per year compared to pre-vaccination levels (Table 1) [4].

However, the Americas is the only region that has made significant progress towards measles eradication; no known indigenous measles transmission has occurred since November 2002 [22]. This has been achieved by implementing a "catch-up, keep-up, follow-up" programme [10,22]. The programme begins with a one-time "catch-up" mass-vaccination campaign aimed at all children aged 1–14 years old (individuals over 15 years are considered to have acquired natural immunity and infants are not included). Routine vaccination is given to all individuals at 12 months of age to "keep-up" coverage and periodic mass-vaccination campaigns provide a second "follow-up" opportunity. The universal second opportunity is important because children who miss their first vaccination and those individuals not protected by the first vaccination gradually build-up a population of susceptible individuals able to sustain transmission if the virus is re-introduced. Epidemiological studies suggest that these 'cycles of abundance' occur about every four years [5,22]. However, the need to achieve almost universal coverage of large geographical areas to halt measles transmission has meant that follow-up vaccinations programmes targeted at urban centres or limited geographical areas have sometimes been unsuccessful [26].

Implementing "catch-up, keep-up, follow-up" programmes present several challenges; the high cost can not be met by many countries while donor dependency may create unsustainable programmes in the longer term; poor healthcare infrastructure, limited access to rural areas and vaccine management are likely to reduce vaccination coverage; competing national and international interests may

divert necessary financial and technical resources; campaigns may interrupt or divert resources away from routine vaccination programmes thereby reducing their efficiency; adopting a second opportunity for measles vaccination for all children will almost double the demand for measles vaccine and without adequate demand forecasting, sufficient quantities of vaccine may not be available; political and social upheaval such as armed conflict or natural disasters may interrupt on-going programmes [9,12,27].

International commitment to eradication

In 2001 the World Health Organisation (WHO) and United Nations Children's Fund (UNICEF) published a joint strategic plan for 2001–2005 [23]. The strategy aims to reduce measles mortality in 2005 by 50% compared to 1999 levels and to maintain interruption of indigenous measles transmission in large geographic areas. The strategy was endorsed in 2003 by the World Health Assembly, which includes 192 member states. On 17th October 2003, a meeting of WHO and UNICEF produced the "Cape Town Measles Declaration" calling on governments to intensify efforts to meet the Strategy's goal of mortality reduction [28]. Other initiatives, such as the Global Alliance for Vaccines and Immunisations (GAVI) and the Measles Initiative, are helping to ensure adequate vaccine provision [29,30]. At the end of the strategic plan in 2005, WHO and UNICEF will review progress and assess the feasibility of global measles eradication.

Conclusions

Global eradication of measles is more difficult than for smallpox, mostly due to the greater virulence of the virus, needing almost universal vaccine coverage. However, success in the Americas has shown that measles eradication is technically feasible using existing vaccines and vaccination programmes. Growing international support, to deliver these programmes means that measles, like smallpox, can very well become a curiosity of history.

Summary

▪ Although an effective vaccine has been available for almost 40 years, in 2000 there were about 30 million measles infections and 777,000 measles-related deaths worldwide.

▪ The history of smallpox highlights several important factors for disease eradication; the biological characteristics of the organism; vaccine technology; surveillance and laboratory identification; effective delivery of vaccination programmes and international commitment to eradication.

▪ Although more difficult than for smallpox, consideration of these factors and recent experience in the Americas suggests that measles eradication is technically feasible.

▪ There is growing international support to deliver effective measles vaccination programmes leading to the eradication of measles in our lifetime.

Competing interests

None declared.

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