Assessing Global Progress in the Eradication of Measles

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Introduction

As a disease preventable by a cost-effective and safe vaccine, measles was believed to be on its way to eradication.[1] However, globally there are still 20 million cases reported every year with 450 deaths a day. Most of these deaths occur in those under five making it one of the leading causes of death in children.

Ninety five per cent of deaths occur in countries with low family incomes impeding vaccine purchase and weak infrastructures impeding administration by national health services.[1]

With measles now re-emerging in many countries and a perpetual burden in others, there is a need to reconsider the global threat measles poses and how best to eliminate it.

Transmission and Natural History

Measles is caused by a highly contagious paramyxovirus.[1] Ninety per cent of unimmunized contacts will contract the virus.[2]

It is spread via aerosol droplets and once inhaled replicates in throat and lung cells,[1] for an 8-14 day incubation period.[3] A 2-5 day pre-eruptive stage follows with fever, anorexia and the four 'C's: cough, coryza, conjunctivitis and Koplik's spots.[4] The next stage is the maculopapular rash lasting up to 7 days.[3] Patients are contagious for four days before and four days after this rash develops.

Most healthy people experience a mild self-limit-ing illness with infection giving lifelong immunity.[4] However, complications and, ultimately, mortalities can occur.[2]

Neurological conditions are the most common direct complication with acute encephalitis occurring in 1/1000 cases. This is fatal in 30%, and causes permanent neurological defects in many survivors.[3]

Secondary complications occur as a result of measles weakening the immune system.[2] The most common and the leading cause of measles related fatalities is measles pneumonia.[4] Diarrhoea is the sec-ond most common complication.[4]

Severe vomiting can also occur and secondary bacterial infections affecting the ear and respiratory tract.[1]

The likelihood of complications and mortalities increases with risk factors more common in the economically disadvantaged world such as poor nutrition, in particular low vitamin A. Other risk factors are concurrent infections such as tuberculosis, HIV infection, or inadequate clinical care.[1]

Diagnosis

Clinical diagnosis and a history of exposure usually make the need for a laboratory diagnosis unnecessary. However serology, microscopy, immunofluorescence or virus isolation can confirm diagnosis and allow accurate epidemiological studies.[3]

Treatment

Supportive treatment can prevent complications such as providing adequate fluid replacement for any loss-es through diarrhoea or vomiting.[1,3] Vitamin A reduces mortality by 50% in economically disadvantaged countries and is given in two doses 24 hours following diagnosis.[1,3] Other symptoms or conditions are treated as they occur, for instance, broad-spectrum antibiotics to treat secondary bacterial pneumonia or otitis media.[3]

Global advances towards elimination of measles through vaccination

Historically, measles was accepted as unavoidable. However, in the 1950's, a live attenuated vaccine against measles was developed. The UK introduced this in 1968 and experienced an enormous drop in measles incidence.[5]

Following this and with the success of smallpox eradication, the World Health Organization intro-duced the 'Expanded Programme of Immunization' in 1974. [1,3] The goal was to provide universal access to selected vaccines for all at risk. And these included measles.[1]

It was thought that implementation costs for surveillance; research, education and immunisation programmes would eventually be recovered through prevention of expensive epidemics.

The aim of these vaccination programmes was to limit disease spread, protect non-immunised individ-uals and prevent epidemics. For 'eradication' it was estimated 95% of the population must be immunised -described as 'herd immunity'.[6]

However, herd immunity does not include other factors that can affect success of vaccination programmes. These include:

- Duration of vaccination programme
- Population density influencing disease spread
- Distribution of unimmunized individuals within that population
- Average age at which measles is occurring related
- to when vaccination is administered
- Measles vaccine efficacy (under 100%)[7]

Vaccine efficacy is one of the most significant issues. A child is susceptible to measles between the loss of maternally transmitted measles antibodies and the child gaining immunity from vaccination. If the average age of measles infection in a child's community is low, it is more likely to fall within this susceptible period and the child is more likely to become infected. Lowering vaccination age combats this but risks primary vaccine failure due to residual maternal antibodies. Unrelated secondary vaccine failure can also occur when an infant does not retain long-lasting immunity.[7]

For these reason the World Health Organization estimates 9 months as optimum for vaccination, and suggests a second dose later in childhood.[7]

In 1988 the UK introduced the combined Measles/Mumps/Rubella (MMR) vaccine.[7] It aimed to cover these additional diseases and required fewer vaccinations.

Vaccination successes

With the success of vaccination, formal eradication targets were set. In 1994, elimination of measles from the Americas was proposed.[1] In this context, elimination was defined as the interruption of transmission between individuals as a result of herd immunity, not the total absence of cases.[1,7] This was achieved in 2002.

Targets were also set worldwide to help meet the fourth millennium development goal (MDG4): a two-thirds reduction in mortality of children under five between the years 1990 and 2015.[1] Measles vaccination was considered a key part of this as both a cheap and effective way of reducing mortality, and a good indicator of access to child health services.

In 2001, to aid this target, the WHO, UNICEF, the American Red Cross, the United Nations Foundation and the United States Centres for Disease Co2ntrol and Prevention launched the Measles Initiative To date the Initiative has successfully provided technical and financial support to many governments and communities. There have been mass vaccination campaigns globally ('Supplemented Immunisation Activities'), improved routine immunisation, treatment, and on-going disease surveillance.[2]

Vaccination successes summary

1 Between 2000 and 2008, worldwide measles deaths dropped by 78%.[2]
2 Over 600 million people have been vaccinated through supplemented immunisation activities.[2]
3 Elimination of measles from the Americas
4 Implementation of surveillance laboratories in 95% of member states by 2008, compared to only 37% in 2000. This helps to document success of vaccine activities, lapses in campaigns, and origins of outbreaks.[1]
5 83 % of children worldwide now receive one measles vaccine before their first birthday, an increase of 11% since 2000. This can be seen illustrated by region in Figure 1 below.[1]
6

Vaccine issues in the economically advanced world

In 1998 a Lancet article suggested a link between the MMR, the development of gastrointestinal disease and developmental regression in previously normal children.[9]

Other specialists criticised this research. It was suggested that the study was biased towards children with these conditions instead of representative of the whole population. For example, symptoms were noticed around the time autism would usually develop regardless of MMR presence and it could have been coincidence.[9]

However, public confidence in the vaccine decreased and parents became distrustful of government policies. Vaccine uptake fell throughout Europe.[5]

Uptake was also low for reasons including:

- Perception that measles is not a serious disease
- Belief that if a child is healthy he/she does not require the vaccine to fight infection.
- Organisational failures in inviting children for vaccination
- Lack of information on vaccination given to parents
- Socio-demographic factors: children from parents of ethnic minorities are less likely to be immunised.[6]

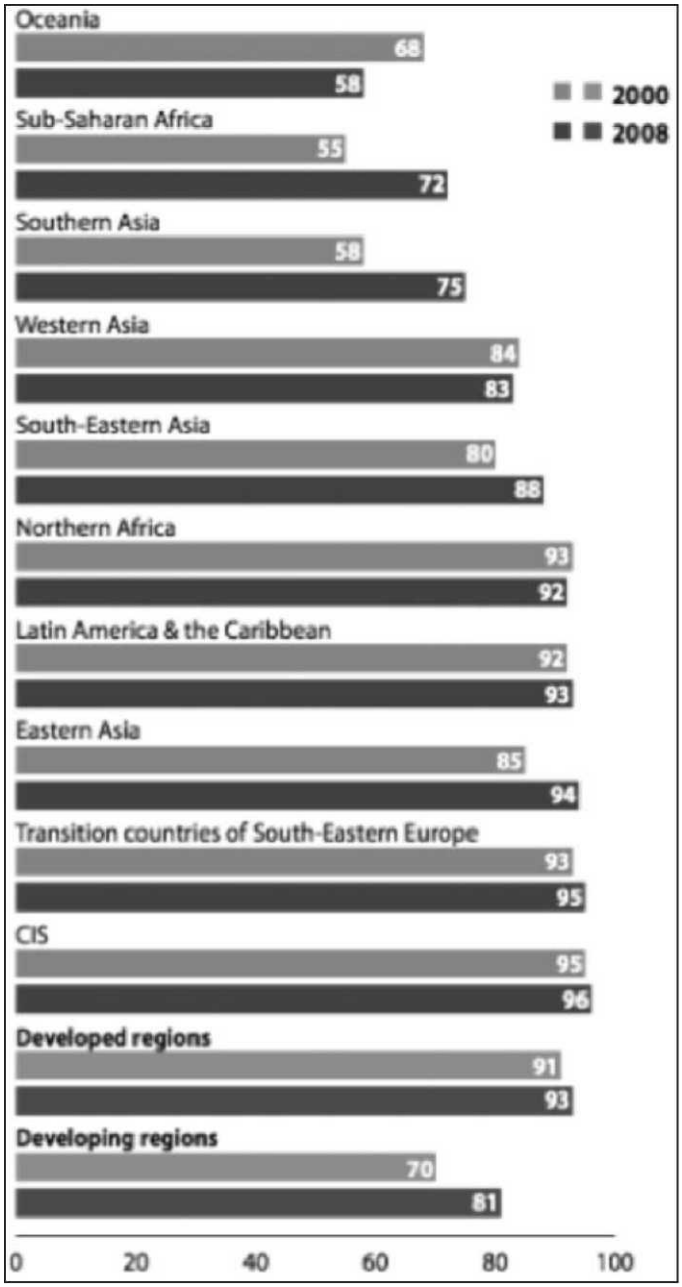

Figure 1:
Proportion of children aged 12-13 months who received at least one dose of measles vaccine, 2000 and 2008 (percentage)[6]

Immunity remained below 95% for a decade and consequently measles has risen throughout Europe. During the first quarter of 2011 there were over 10,000 measles cases and five deaths within 32 European countries.[10] In particular, France accounted for 78% of cases, with a nine-fold increase in the number of cases relative to the same quarter of 2010. Four of the five deaths in France occurred in people between 18 and 30 years.[10] In measles cases where vaccination status was known, 84% were unvaccinated.[10]

Targets:

- Improve vaccination opportunities[6]
- Invitation to vaccinations with accurate recording of the administration
- Opportunistic parent targeting
- Catch up vaccination schemes to immunize the unvaccinated
- Promotion of MMR with media and campaigns[6]
- Inform parents about vaccine, the science behind it, and the consequences of non-vaccination
- Target socio-demographic groups that are less likely to immunise children
- Continue to subsidise vaccination programmes in countries with high measles incidence particularly where increased travel is seen as a route for disease spread.

Vaccine issues in the economically disadvantaged World

Global immunisation percentages are a poor judge of vaccination success in the economically disadvan-taged world. Discrepancies between countries and within countries can be masked by good figures.

Despite vaccinations, 20 million people are still affected by measles every year, with the majority in the economically disadvantaged world.[1] The pie chart (Figure 3) shows the number of deaths measles causes

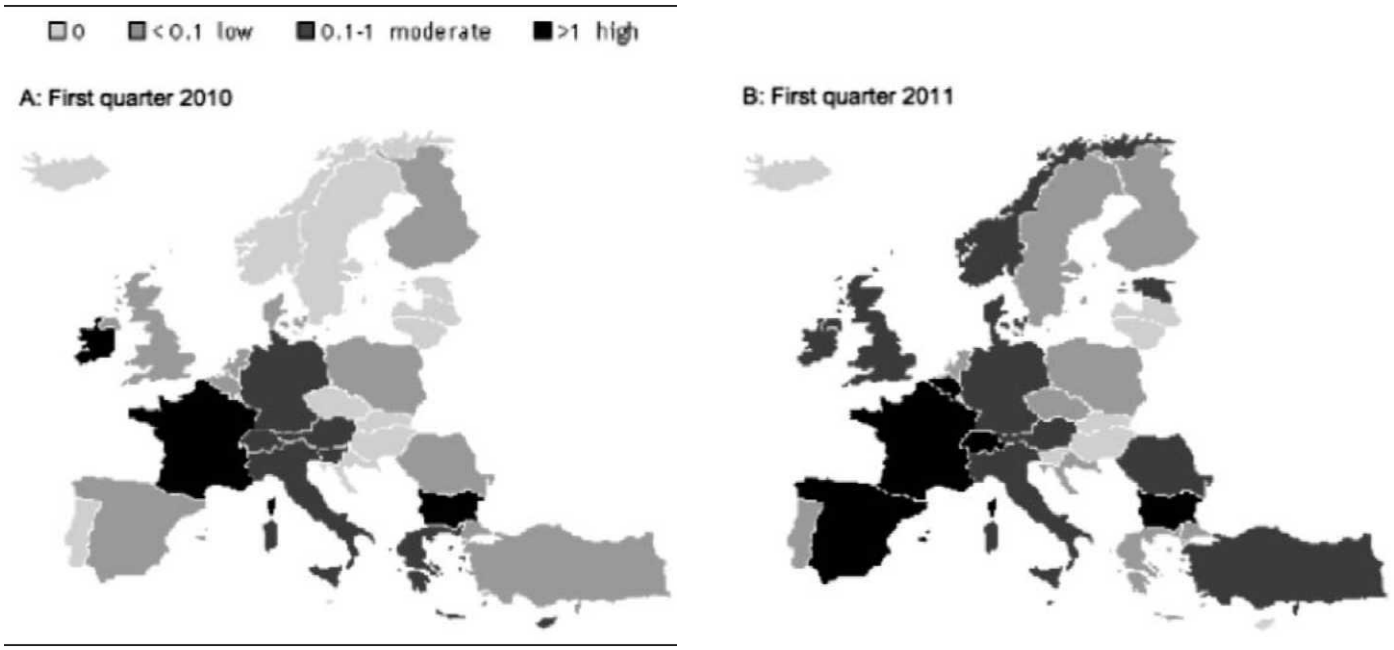

Figure 2:
Geographical crude incidence of measles, first quarter 2010 (A) and first quarter 2011 (B)[1]

Combating measles in economically advanced world

In 2010 the WHO member states set a target for eradication of measles from Europe by 2015. With increased immunisation coverage and surveillance this could be achievable.[1] in children under five relative to other causes. As a disease listed for which there is a cost effective and safe vaccine this figure should be far lower.

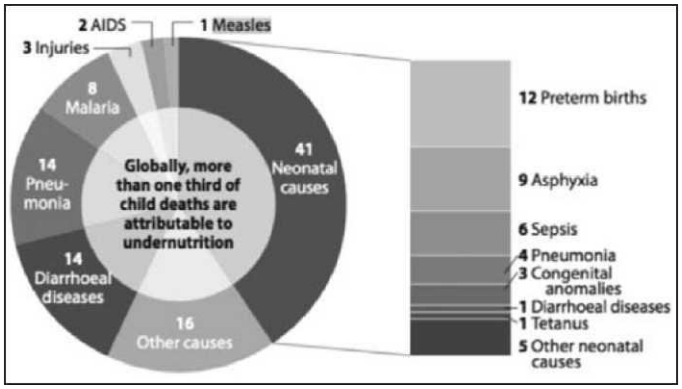

Figure 3:
Causes of deaths among children under age five[6]

Many of these countries suffer from poverty, economic and political instability, and poorly equipped, organized and available health services. Natural dis-asters and conflict that occur more frequently in these countries can disrupt what few services are already available. These factors all decrease vaccine availability and uptake.

Economically disadvantaged countries have a higher proportion of youngsters in the population. Combined with easier spread through overcrowding, the average age of infection can be very low. This decreases the window of opportunity between loss of maternal antibodies and measles infection and reduces the 'time window' in which a vaccine can be delivered to prevent infection.[2,4]

Lowered age of infection also increases complications, especially if combined with inadequate nutri-tion and poor clinical management of infection.

The WHO believes there are two primary obstacles to continued progress in the achievement of MDG4. The first is India's failure to implement measles mortality reduction strategies despite bearing 2/3 of global measles deaths. In part, India's difficulties have been attributed to fear over vaccine safety and concerns that implementing Supplementary Immunisation Activities would interfere with vaccinations schemes already in place.[2]

The second is a lack of funds and political commitment delaying vaccination campaigns in Africa. Projections show that without Supplementary Immunisation Activities in these countries, mortality will quickly rebound, resulting in approximately 1.7 million measles-related deaths between 2010 and 2013.[2]

Combating Measles in the Economically Disadvantaged World

In order to reach MDG4 by 2015 issues in vaccine delivery in these regions must be combated.

First, financial sustainability must increase to bridge the funding gap. Focused targeting of businesses and governments will aim to increase long term funding. Emphasis should be put on risk of resurgence and the positive impact of interventions.

High quality 'Supplementary Immunization Activities' should continue in areas with a high proportion of unimmunized children. Improved labo-ratory based surveillance, will increase awareness of outbreaks, their origin, and thus help identify unimmunized pockets in populations.

Routine immunisation uptakes should be improved, with second doses implemented in all countries, to combat secondary vaccine failure. India in particular should be targeted.

Linking of Measles vaccination with other initiatives such as distribution of malaria nets could also increase vaccination uptake.

Summary

"So much has been achieved [in measles control] in the past several years thanks to the hard work and commitment of national governments and donors. But ... there are signs of stalling momentum. This is a highly contagious disease that will quickly take advantage of any lapse in effort."

This quote from Doctor Margaret Chan, director General of the WHO, embodies our progress so far, and the risks we run globally in underestimating the challenge and the consequences of measles infection. However with effective interventions, surveillance, and education we can eliminate measles and confine it to the history books.[2]

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