IMPACT OF A MEASLES ELIMINATION STRATEGY ON MEASLES INCIDENCE IN MALAYSIA

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Abstract. In Malaysia, the two dose measles - mumps - rubella (MMR) vaccine was introduced in the Expanded Program on Immunization in 2002. The Ministry of Health then initiated a measles elimination strategy which included enhanced case-based surveillance with laboratory testing of all suspected cases. The objective of our study was to analyse national measles laboratory data from 2004 to 2008 to study the impact of the nationwide strategy on measles case incidence. Blood samples collected from suspected measles cases during the acute stage of the illness were investigated for measles specific IgM. The estimated incidence of measles ranged from 22.3 cases (in 2004) to 2.27 cases (in 2006) per 100,000 population. During this time, the measles vaccination coverage was above 85%. Laboratory confirmed measles cases dropped from 42.2% in 2004, when sporadic outbreaks were reported, to 3.9% in 2007. Screening for measles IgG levels in 2008 showed that 82.8% of those > 7 years old had adequate immunity. The measles control strategy appears to have been successful in reducing the incidence of measles. Continuing high vaccination coverage rates and ongoing measles surveillance are necessary to achieve our goal of measles elimination.

INTRODUCTION

Measles is a highly contagious acute viral disease characterized by high fever, cough, coryza, conjunctivitis and the appearance of a maculopapular rash. Serious complications, such as otitis media, bronchopneumonia and encephalitis, sometimes occur, especially in poorly nourished young children. Despite the availability of a safe and effective vaccine since 1963, more than 20 million measles cases occur worldwide every year and measles continues to be a leading cause of vaccine preventable child mortality (CDC, 2008).

In Malaysia, measles was endemic in the pre-vaccine era until a single dose of monovalent measles vaccine was included in the Expanded Program of Immunization (EPI) in 1982. The incidence rate of measles cases in 1982 was 65.2 cases per 100,000 population. With increased vaccination coverage, measles occurence decreased dramatically. From 1989 to 1998 the measles incidence rates were between 1.51 and 5.87 cases per 100,000 population (MOH, 2006). Scattered outbreaks have occurred throughout the country in both rural and urban areas, and higher measles incidence rates have been reported despite increased vaccination coverage. In 2002, measles elimination strategies were implemented by the Ministry of Health (MOH). The

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same year, the measles vaccination strategy was revised and a two dose measles - mumps - rubella (MMR) vaccine was given to children age 12 months and 7 years. In 2003, the WHO Western Pacific Region Member States resolved to eliminate measles, and committed the region to achieving measles elimination by 2012 (WHO, 2003). Effective surveillance of measles by the MOH included establishing case-based surveillance with laboratory testing of all suspected cases and designation of the National Public Health Laboratory (NPHL) as the National Measles Laboratory in 2004 (MOH, 2006).

The objective of our study was to analyse measles laboratory data from 2004 to 2008 to gain insight into the patterns of measles incidence in Malaysia since the addition of the two dose MMR vaccination schedule to the national EPI. The source of the laboratory data in this study was the NPHL and the Institute for Medical Research (IMR) in Kuala Lumpur. Case based laboratory investigations of all suspected measles cases were carried out by the NPHL from all health facilities and outbreak areas, since 2004. Prior to the setting up of the National Measles Laboratory at NPHL, measles laboratory investigations were carried out by the IMR, which is the Virology Reference Laboratory for the MOH. The IMR continues to receive samples from some government hospitals for measles specific IgM and IgG investigations and complements the national laboratory data for measles by close cooperation with the NPHL and the Surveillance Unit of the MOH. In this study, the laboratory confirmed measles cases were determined by the presence of measles specific IgM antibodies in the study population.

MATERIALS AND METHODS

Patients and samples

Blood samples from patients suspected of having meales were collected during the acute stage of their illness. The cases included: all cases from health facilities where the attending physician suspected measles infection; cases where the clinical presentation was fever, maculopapular rash, conjunctivitis, cough and/or coryza; measles or rubella suspected outbreaks. All samples were accompanied by a request form, with patient details and clinical history (MOH, 2006).

Measles IgM and IgG assay protocol

At the NPHL and IMR, all serum samples were tested using the Enzygnost Anti-Measles-Virus/IgM enzyme immunoassays (Dade Behring, Marburg, Germany). For specific measles IgG, sera were tested using the Enzygnost Anti-Measles-Virus IgG enzyme immunoassay (Dade Behring, Marburg, Germany). The test procedure, interpretation and validation of test results followed the manufacturer's instructions. Equivocal samples were retested and reclassified as positive or negative, where indicated.

Controls

For validation of test results, kit controls, as well as in-house positive and negative controls from our laboratories were tested on each plate.

Proficiency of laboratory performance

The NPHL annually sends samples to the WHO Measles Reference Laboratory at the Victorian Infectious Disease Reference laboratory (VIDRL), in Melbourne, Australia for re-testing. The IMR participates annually in Royal College of Pathologists of Australia (RCPA) Serology Quality Assurance Program.

Measles vaccine coverage and measles incidence data

The national data for measles vaccine coverage and the measles incidence rate per 100,000 population were obtained from the Surveillance Unit, Disease Control Division,

Table 1
Laboratory data from suspected measles cases, 2004-2008.

Year	Measles vaccine coverage[a]	Measles incidence per 100,000[a]	Total samples received (% reported cases)	Total IgM positive (%)
2004	100%	22.3	2,791 (43.1%)	1,014 (36.3%)[b]
2005	96%	5.39	1,393 (97.2%)	185 (13.3%)[c]
2006	86.0%	2.27	616 (100%)	27 (4.3 %)
2007	87.3%	3.6	1,340 (100%)	52 (3.8 %)
Until May 2008		3.7	1,524 (100%)	29 (1.9%)
2004 to 2008			7,342	1,313 (17.9%)

[a]Data from the Surveillance Unit, Disease Control Division, Ministry of Health.
[b]Outbreak of measles in Melaka and Selangor states.
[c]Outbreak of measles in Sarawak and Negeri Sembilan states.

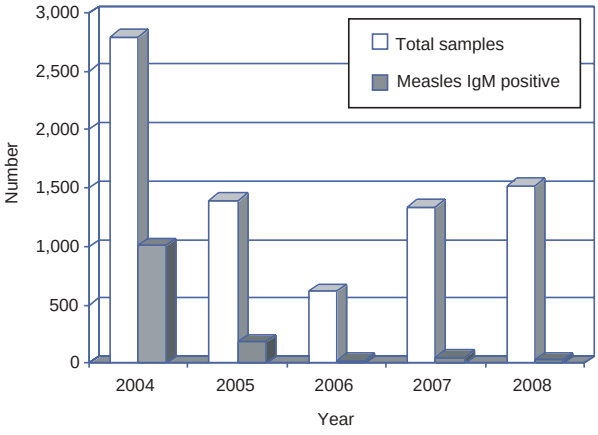
Ministry of Health Malaysia.

RESULTS

Between 2004 and 2008, a total of 7,342 serum samples were detremined for laboratory confirmation of suspected measles cases. The number of samples received for each year and the percentage of IgM positive cases are shown in Table 1 and Fig 1. The years 2004 and 2005 had higher positive rates because of outbreaks of measles among adolescents in educational institutions in the states of Melaka, Selangor, Sarawak and Negeri Sembilan.

During the study period, the estimated incidences of measles ranged from 22.3 cases (in 2004) to 2.27 cases (in 2006) per 100,000 population. The incidence rates are estimates based on notification of clinical cases. During this time, the measles vaccination coverage was above 85%.

In 2008, samples received from hospital cases for investigation of measles at the Virology Unit, Institute for Medical Research were tested for measles specific IgG. The ages of the subjects were available for the case samples but the vaccination history was not available. The cases determined for measles specific IgG in 2008 were stratified into 3 age groups: less than 12 months, 1-7 years old and > 7 years old (Table 2). Equivocal samples were not included in the data analysis. Forty-one out of 51 infants below 12 months of age were IgG negative. Eighteen out of 22 individuals who were between 12 and 20 years of age were IgG negative.



(Source of data: from NPHL and IMR)

Fig 1–Measles laboratory data 2004-2008.

Table 2
Age stratified samples results at the Institute for Medical Research, 2008.

Age group	Number of samples	Number measles IgG positive	Percent measles IgG positive	Number measles IgG negative	Percent measles IgG negative
<1	51	7	13.7%	41	80.3%
1-7	38	29	76.3%	7	18.4%
>7	460	381	82.8%	22	4.8%

DISCUSSION

Measles is a notifiable disease in Malaysia. The age of measles reported cases before 2002 ranged from less than 1 year of age to 84 years old with a mean age of 11.8 years (Rosemawati, 2005). A large proportion (26%) of cases were found in children < 4 years old and in children < 2 years old (15%). Fifty-six percent of cases were in children 5-19 years old. Based on local data, measles outbreaks occurred in all parts of Malaysia, both urban and rural areas. In the surveillance strategy for measles elimination introduced in 2003, physicians have to report all suspected cases of measles and laboratory diagnostic testing of blood, saliva and urine specimens is recommended for all sporadic cases. Outbreaks of suspected measles are investigated by the National Public Health Laboratories with collection of specimens from suspected cases for confirmation and characterization of the viral strain.

A review of national data in our study showed the number of suspected measles cases reported to the Epidemiology and Surveillance Unit, Ministry of Health ranged from 5,798 cases in 2004 to 604 cases in 2006. Samples for laboratory investigation from these suspected cases increased from 43.1% in 2004 to almost 100% in 2006 and 2007. Measles case incidence in our study was highest in 2004, when sporadic outbreaks were reported, especially among adolescents in residential educational institutions (Table 1, Fig 1). Before 2002, monovalent measles vaccine was administered to infants at 9 months of age, but this appeared inadequate. In order to protect susceptible children from measles, catch-up campaigns or mass measles campaigns were planned and implemented in 2004 (Rosemawati, 2005). Since then, the number of reported measles cases in Malaysia has decreased.

Previous serosurveys indicated infants below 12 months age were at risk for measles (Saraswathy *et al*, 1994; Zainah *et al*, 2003) Based on our present study, IgG data from hospital cases for the year 2008 also showed that infants below 12 months remain the susceptible group. Young adults may also be at risk for measles as was seen in outbreaks among adolescents age 12-20 years old in 2004. It is thought they may have had inadequately low levels of measles immunity since they were too old to have been part of the 2-dose measles-mumps-rubella (MMR) vaccination program (introduced in 2002) but had grown up in a period when exposure to wild measles virus was declining. Data from 2008 showed 82.8% of individuals > 7 years old had adequate immunity as seen with serum samples positive for measles IgG.

All suspected cases of measles with an IgM-positive test result were considered to be measles. Prompt rapid investigation by

the Ministry of Health and control measures, such as mass vaccination campaigns, were initiated to prevent further transmission of measles virus. The measles IgM assay is simple, sensitive and easy to perform with results available within 24 hours. It is the recommended assay by the WHO for Measles National Laboratories (WHO, 2007). However, as progress is made towards elimination of measles, there is an increased likelihood of being confronted with false-positive IgM results (Dietz *et al*, 2004). This highlights the need to improve laboratory surveillance and obtain specimens for virus isolation. Isolation of measles virus confirms the serological diagnosis. Molecular characterization by the polymerase chain reaction technique (PCR) also needs to be strengthened since it will become necessary to determine the epidemiology of wild virus transmission.

Measles has been eradicated from several countries in the world and the World Health Organization Regional Office for the Western Pacific (WPRO) aims to eradicate measles by 2012. Good progress has been made in Malaysia since the implementation of the strategy, as shown by the introduction of routine 2 dose MMR vaccination at 12 months and 7 years of age in 2002, and by the immunization coverage of above 85% (100% in 2003 and 2004). Surveillance and laboratory confirmation have improved with the setting up of a National Measles laboratory. Fewer outbreaks were reported in 2007 and 2008, however sporadic cases indicate that much still needs to be done, since viral transmission has not been effectively interrupted. Prompt recognition, reporting, and investigation of measles are important to limit the spread of the disease with early case identification and vaccination of susceptible contacts.

The greatest challenge for future years will be to strive to achieve higher vaccine coverage rates of 95% or more, since virus transmission still persists in the population. As measles reported cases decrease with improved vaccination coverage and decrease in wild type virus circulation, sporadic cases of imported measles will continue to occur. The presence of a sporadic confirmed case that does not result in further disease transmission implies that the population immunity resulting from a high vaccination coverage rate has prevented or limited secondary disease transmission and should be considered a national measles elimination program success (Wolfson *et al*, 2007; De Quadros *et al*, 2008).

The strategy for measles elimination, implemented by the Ministry of Health has been successfull in dramatically reducing measles case incidence in Malaysia. High vaccination coverage rates and active ongoing case based measles surveillance is vital to achieve the goal of measles elimination until global elimination of the disease has been achieved.

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