Outbreak of measles in primary school students with high first dose MMR vaccination coverage

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ABSTRACT

Introduction: Indigenous cases of measles continue to occur in Singapore despite the implementation of a two-dose mumps, measles and rubella (MMR) vaccination policy in 1998. We investigated a measles outbreak that took place in a primary school from April 17 to May 6, 2004 to identify all cases, evaluate vaccine efficacy (VE) and implement outbreak control measures.

Methods: A case of measles was defined as anyone having generalised rash and fever with or without cough, coryza or conjunctivitis during the outbreak period, and who had either laboratory-confirmed acute measles infection or was epidemiologically linked to a patient with laboratory-confirmed measles infection. Vaccination status was obtained from the student's health booklet and confirmed with the National Immunisation Registry. Attack rates in unvaccinated (ARU) and vaccinated (ARV) students were calculated and VE was evaluated using the formula: VE (percent) = [(ARU-ARV) ÷ ARU] × 100 percent.

Results: Nine students, aged between eight and 14 years, from five classes in primary three and primary six, were epidemiologically linked to have measles. None of them had received the second dose of the MMR vaccine. 93 percent of students in the affected classes (n = 184) had prior documented evidence of receiving at least one dose of MMR vaccination, as compared to 96.5 percent for the entire school enrolment (n = 1,309). The attack rate was 1.2 percent in the vaccinated group and 53.8 percent in the unvaccinated group. The VE for the primary dose of MMR in the affected classes was 97.8 percent.

Conclusion: It is important to achieve a high coverage for the primary dose of MMR vaccine in order to prevent any potential outbreaks prior to receiving the booster dose.

Keywords: measles, measles outbreak, vaccine efficacy, vaccination coverage

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INTRODUCTION

Indigenous cases of measles continue to occur in Singapore despite the implementation of a two-dose mumps, measles and rubella (MMR) vaccination policy in 1998. As part of the Singapore National Childhood Immunisation Programme, the primary dose of MMR is given between 12 and 15 months of age, while the booster dose is given prior to leaving primary school at 11–12 years old.[1] Under the Infectious Diseases Act, measles is a notifiable infectious disease, and all doctors are required to notify the National Immunisation Registry (NIR) whenever they have vaccinated anyone against measles.[2] Measles was one of the common infectious diseases in Singapore during the 1970s. A ten-year retrospective analysis of 49,401 children admitted to the Singapore General Hospital between 1969 and 1978 revealed that 1.58% of the children had measles. The case fatality was 1.28% and measles was responsible for 0.76% of all deaths.[3]

Measles vaccination was introduced into the Singapore National Childhood Immunisation Programme in October 1976 and was made compulsory by law for children aged 12–24 months in August 1985, as cyclical epidemics of measles continued to occur. This was due to the poor vaccination acceptance by parents for reasons such as ignorance, superstition or preference to have their children develop natural immunity.[2,4-8] A sharp rise in the incidence of measles cases in 1997 led to the implementation of a "catch-up vaccination" from July to November 1997, where children aged 12–18 years were immunised for measles, regardless of their measles vaccination status or past history of measles. Subsequently, the Expert Committee on the Immunisation recommended that a booster dose

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Table I. Demographical profile of nine cases of measles in a primary school from April 17 to May 6, 2004.

Case no.	Age (years)	Race	Gender	Class	Date of onset	Clinical history*	MMR vaccination history	Anti-measles IgM antibodies
1	11	Malay	M	6B	17/04/04	F, C1, C2, R	Yes (21/12/93)	Positive
2	12	Chinese	M	6B	18/04/04	F, R	No	Positive
3	11	Chinese	M	6B	19/04/04	F, C1, C2, C3, R	No	Positive
4	11	Chinese	M	6E	19/04/04	F, C2, R	No	Positive
5	9	Malay	M	3D	02/05/04	F, R	No	Positive
6	8	Malay	M	3D	02/05/04	F, R	No	Positive
7	14	Malay	M	6G	02/05/04	F, R	No	Positive
8	8	Malay	F	3D	05/05/04	F, C1, R	No	Positive
9	8	Malay	F	3C	06/05/04	F, R	Yes (19/08/97)	Not done

* F: fever; C1: cough; C2: coryza; C3: conjunctivitis; R: maculopapular rash.

of measles vaccination (as part of the MMR vaccination) be introduced into the childhood immunisation programme in January 1998 for all primary school children aged 11–12 years (Primary 6).[1,2]

The incidence of measles has remained low since the introduction of the booster dose of measles vaccination. The number of laboratory confirmed cases of measles was 65 cases in 1999 and 141 cases in 2000. Thereafter, it decreased to 61 cases in 2001, 57 cases in 2002 and 33 cases in 2003. The number of cases then increased to 96 cases in 2004, but decreased again to 33 cases in 2005. Following the introduction of the measles booster, the age-distribution of reported cases was observed to have shifted from those aged 15 years or more to children under the age of one year who have yet to be immunised.[9] We investigated a measles outbreak that took place from April to May 2004 in a primary school to identify all cases, evaluate vaccine efficacy (VE) and implement outbreak control measures.[10]

METHODS

The Ministry was first informed of four laboratory-confirmed cases of measles on May 4, 2004, from which two of the cases were primary six students studying in the same school. We informed the school administrator regarding the two confirmed cases and conducted an epidemiological investigation for the duration of the outbreak. Active case detection was carried out throughout the school to identify recent absentees who had been clinically diagnosed for measles or were displaying symptoms and signs characterised by generalised maculopapular rash and fever, with or without cough, coryza or conjunctivitis.[11] Cases were subsequently serologically tested to confirm that they were having an acute measles infection. A sample of 3–5 ml of plain blood was collected from the cases to detect the presence of anti-measles IgM antibodies by the immunofluorescence method. We defined a case as a person who had signs or symptoms during the outbreak period that were compatible with the case definition as described above, and who had either laboratory-confirmed acute measles infection or was epidemiologically linked to a patient with laboratory-confirmed measles infection.

An interview using a standard questionnaire was conducted in order to obtain epidemological data on their demographical details (age, gender, ethnic group), illness onset, clinical presentation, vaccination history, class and residential address. The vaccination status of the cases and their classmates was obtained from their individual health booklets and confirmed with the NIR. Attack rates in unvaccinated students (ARU) and vaccinated students (ARV) was calculated. The efficacy of the MMR vaccine, VE, was calculated using the formula: $VE\ (\%) = [(ARU\text{-}ARV) \div ARU] \times 100\%$.[12]

RESULTS

The setting of the outbreak of measles was in a primary school with a school enrolment of 1,309 students in the eastern part of Singapore. The demographical profile of the school was predominantly Malay, with 54.6% of students being Malay, 30% being Chinese, 13.1% being Indian and 2.3% from other races. A total of nine students, aged between eight and 14 years, were epidemiologically linked to have measles from April 17, to May 6, 2004. Eight of them tested positive for anti-measles IgM antibodies, while the immune status of the last case, which presented with fever and generalised maculopapular rash and epidemiologically linked to another student with laboratory-confirmed

measles, was not done due to parental refusal. The majority (78%) of cases was male and approximately 67% of them were of Malay ethnicity (Table I). As the school concerned was a neighbourhood school, 89% of the case-patients stayed in the same vicinity, with 55.6% living on the same street. The time distribution of the cases is shown in the epidemiological curve in Fig. 1.

An initial cluster of four primary six students, of which three were from the same class (primary 6B), and another from primary 6E, with disease onset between April 17 and 19, 2004 was identified. The incubation period of measles ranges from 8 to 14 days. It is quite likely that this initial cluster was set off by a primary case within the school in the preceding 8–14 day period. However, investigations did not identify such a case. Thereafter, the disease spread to another student in primary six (primary 6G) and four students in primary three, of which three were from the same class (primary 3D), between May 2 and 6, 2004. The student from primary 6G and two of the students from primary 3D were siblings. The other two of their siblings who were studying in primary one and five in the same school were reported to be well. Another five of their siblings staying in the same residence were also well and did not show any symptoms of measles.

The population of the five affected classes in primary three and primary six was 184 out of the school enrolment of 1,309 students. The demographical profile of the affected classes had a higher proportion of Malay students than that for the school population, with 65.3% of students being Malay, 30.4% being Chinese, 3.8% being Indian and 0.5% from other races. The MMR booster dose, in accordance to the National Childhood Immunisation Programme administered for primary six students, had been scheduled sometime in the later part of 2004. As such, none of these 184 students received the MMR booster dose yet. Approximately 96.5% (1,263 students) of the entire school enrolment had documented evidence of at least one dose of MMR vaccination. However, only 93.0% (171 students) of students in the five affected class had prior documented evidence of MMR vaccination.

It was initially found from the NIR's computerised records that 110 students from the school's total enrolment had not received vaccination against measles. Further verification during our epidemiological investigation revealed that 64 of them had in fact been vaccinated against measles, but their healthcare providers had not notified the NIR regarding their vaccination. Of the 46 students who were not vaccinated, seven were infected with measles, 13 were subsequently given the MMR vaccination by the School Health Services (SHS), seven students claimed that they had prior natural measles, two students were unable to produce proof of previous measles vaccination and refused re-vaccination, two students had already left Singapore and 15 students defaulted their follow-up appointment. The 15 students who defaulted were mainly foreign students who went home during the school holidays. The attack rate was two of 171 (1.2%) students in the vaccinated group and 7 of 13 (53.8%) students in the unvaccinated group. The calculated VE for the MMR primary dose in the affected classes was 97.8%.

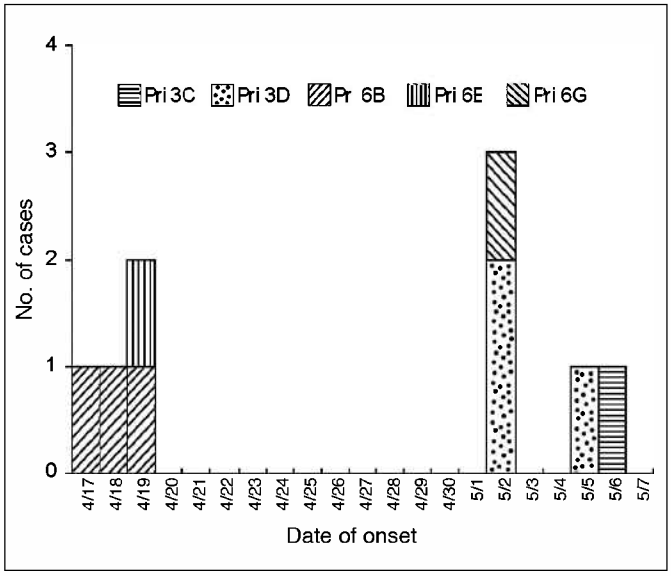

Fig. 1 Epidemiological distribution of nine cases of measles in a primary school, from April 17, 2004 to May 6, 2004.

DISCUSSION

The primary case which set off the measles outbreak in the school could not be identified, despite school-wide active case investigation. The case definition used for active case detection was "recent absentees who had been clinically diagnosed as measles or who had displayed symptoms and signs characterised by generalised maculopapular rash and fever, with or without cough, coryza or conjunctivitis". There are two possible reasons for not identifying the primary case. First, the rash may not have been highlighted by the affected student. This could be due to the rash not been quite apparent in students who are dark-skinned, e.g. some Malays and Indians. The second possibility is that the student had not been absent and therefore was not investigated further.

This primary case had also not been notified to the Ministry of Health, despite notification of measles being mandatory under the Infectious Diseases Act.

A likely reason for this is that the case may have been misdiagnosed as a non-specific viral illness. Measles has become relatively uncommon in Singapore with two decades of widespread measles vaccination, and especially after the second dose policy was implemented in 1998. Many primary care doctors may not even see a single case of measles in a year. This makes diagnosis more difficult.

Despite the high overall MMR primary dose vaccination coverage of the entire school and the relatively high vaccination coverage and VE of the measles primary dose vaccination for students in the affected classes, a small outbreak of measles still occurred. This illustrates that the grouping of susceptible individuals in a population with high MMR primary dose vaccination coverage may still spark off a small outbreak of measles. Institutional outbreaks of measles have also been recorded in similar settings abroad.[13-15] Hence, it is important to achieve the highest possible vaccination coverage for the MMR primary dose vaccination, in order to prevent any potential outbreaks prior to receiving the booster dose.

Furthermore, two of the nine cases had prior history of measles vaccination. These two children had not seroconverted following the primary dose of measles vaccine seroconvert, and as such a booster dose of MMR vaccination had to be administered. Achieving a two-dose measles vaccination coverage of more than 95%, tightening our MMR vaccine delivery system and strengthening surveillance of measles, are essential components which must be addressed in order to halt measles transmission in Singapore, as part of our efforts towards the World Health Organisation (WHO) Western Pacific Regional Plan of Action for Measles Elimination.[16,17] However, implementing enhanced measles surveillance, which involves collection of blood samples from patients with clinically diagnosed measles, would result in substantially increased cost. Our priority now is to focus on ensuring that vaccination coverage for measles is consistently more than or equal to 95%, and to tighten of our MMR vaccine delivery system.

It is agreed that a two-dose strategy is required for the elimination of indigenous measles transmission. The primary dose is generally recommended early in the second year of life.[18,19] However, the age of administration of the booster dose varies among different countries.[20-22] Many industrialised countries now administer the MMR booster dose prior to or at school entry, in order to shorten the duration of accumulation of children who may have failed to seroconvert following the primary dose, and hence are susceptible to measles. Despite our relatively high vaccination coverage for the MMR primary dose, and the majority of those infected with measles being those aged one year or less, or who have not received their measles vaccination, Singapore has nevertheless decided to lower the age of the booster dose of MMR to 6–7 years (primary one) starting from year 2008, so as to further tighten the control of measles.

Our coverage for the two doses of measles vaccination has met the target of 95% set by WHO in years 2004 and 2005. Mathematical modelling shows that this level of coverage is required for the effective interruption of measles transmission.[16,23,24] Our experience since 1998 showed that the primary dose vaccination coverage for measles occasionally fell to 93% in certain years. In order to further improve the maintenance of overall measles vaccination coverage and herd immunity level of the childhood population, the current practice of MMR immunisation requirement for new entrants (local and foreigners) into kindergartens, preschools and primary schools should be strictly adhered to. Since April 2005, the Ministry has worked with the NIR and PAP Community Foundation (PCF) Education Centres to ensure that children aged 2–5 years admitted into their preschools were vaccinated against measles. Children without proper documentation of MMR vaccination were recommended to have their MMR vaccination repeated if there were no contraindications to the vaccination. In the event that there was strong parental objection to revaccination with MMR, serological testing for measles antibodies was offered to determine if repeat immunisation was required.

During the annual primary one registration exercise, the Ministry of Education distributes information on the requirements of various childhood immunisations (i.e. BCG, MMR) before entry to schools. Parents are advised to ensure that their children are immunised before starting primary 1. Although the schools check the immunisation documents of all school entrants before entry,[6] advice is only given when the children have incomplete or no immunisation records. There is no active follow-up to ensure that the children are immunised until the annual health visit by the SHS during the school year.

The SHS provides health screening to all school entrants and school leavers at primary schools. SHS also provides diphtheria/tetanus (second booster) and oral Sabin (second booster) at primary one and diphtheria/tetanus (third booster), oral Sabin (third booster) and MMR (booster dose) at primary six. All students, including foreign students admitted into local schools, who are found to have missed their primary dose of MMR, are referred to the Student Health Centre for immunisation. Reminder letters are sent to students who do not turn up after two weeks. The nurses also remind the students and their parents

through telephone calls. Unfortunately, there are some who choose to default their appointments.

It was observed from the NIR's electronic records that approximately 10% of children in the PCF aged 2–5 years had yet to be vaccinated against measles. Manual checks against the childrens' health booklets revealed that 66% of children whose records were reflected as being not vaccinated against measles had, in fact, already received their measles vaccination. This was because the healthcare provider who vaccinated the child had not notified the Registry of the vaccination. The NIR has started tracking this omission via the doctors, and has identified specific doctors who failed to notify NIR of vaccinations done and sent them reminders to do so. General practitioners comprised 34.2% of the healthcare providers who failed to notify the registry of the notification, hospital institutions and polyclinics comprised 20.5%, while the remaining 45.3% comprised vaccinations given overseas. The NIR also tracks children who, for various reasons, have yet to complete their MMR vaccination and sends their parents/guardians regular reminder letters. In addition, the Health Promotion Board has produced a new pamphlet on MMR vaccination as part of the intensification of community outreach health education messages on the benefits of MMR vaccination. During the annual school visits, the SHS routinely reviews the immunisation status of all primary and secondary school students, to ensure that they were up-to-date with their MMR vaccination. In September 2006, the NIR commenced requesting a copy of the vaccination certificates from foreign children who were staying for more than six months in Singapore.

With the change in the lowering of the age of the booster dose of MMR, the Ministry of Health will be sending out a professional circular to inform all registered medical practitioners of this change and also to remind them to ensure that children under their care have been vaccinated against measles and other relevant vaccinations under the Singapore National Childhood Immunisation Programme. The doctors will also be encouraged to provide the necessary counselling to parents who have misconceptions that measles is a benign childhood infectious disease, and to correct any misconception that there is an association between MMR vaccination and the development of autistic disorders.[25-30] Doctors have also been reminded periodically to notify the NIR when they vaccinate a child, in accordance with the National Childhood Immunisation Programme.

As only approximately 7% of the clinically-diagnosed cases of measles reported locally turned out to be measles by laboratory testing, there is a need for laboratory confirmation of measles to avoid misidentification of cases and improve disease surveillance.[2] The Ministry of Health will continue to work with the WHO Regional Office for the Western Pacific to achieve measles elimination in the Western Pacific Region, including improving the protocols for enhanced measles surveillance.[31,32]

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