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MEASLES EPIDEMICS IN KERMAN, IRAN

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ABSTRACT

In early 1990, an outbreak of measles occurred in Kerman, (population 257, 284) Iran. Overall, 475 cases were identified and four died (case fatality ratio 5.4 per thousand). Illness was limited primarily to children below 15 years of age; 166 (22.3%) were in children under five, 573 (77%) between 5-14 and six (0.8%) above 15 years of age. The age of the cases ranged from five months to 35 years. The age-specific attack rates were 3.9, 1.8, 7.3 and 2.8 per 1,000 for children under 1, 1-4, 5-9, and 10-14 years of age, respectively. Overall, 14 (1.9%) children with measles were hospitalized for severe complications which consisted mainly of pneumonia, otitis and gastroenteritis. Based on 745 cases with an immunization record vaccine efficacy was calculated at 88%, indicating a slight problem with the cold chain or the vaccine.

The outbreak has been primarily related to low immunization coverage during the last 10 years. This outbreak again indicates the need to improve vaccine coverage with the AIK-Cexisting vaccine, and also the advisability of a revaccination programme at school age will need to be considered.

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INTRODUCTION

Measles is an acute communicable disease, frequently complicated by pneumonia, otitis media, gastroenteritis and encephalitis.[1,2] In children, it is the third most important cause of death after acute respiratory infection and diarrhea and is responsible for 10% of all deaths in the 1-4 year age group.[2] Among the vaccine preventable diseases, measles is one of the most important causes of morbidity and mortality.[3,4]

Despite the advent of a measles vaccine in 1959, measles epidemics with high mortality and morbidity continue to occur across the world.[4-6] In many countries, these outbreaks have been effectively brought under control through immunization of susceptible or high-risk populations.

A live attenuated measles virus vaccine is now freely available in the Islamic Republic of Iran for control/prevention of disease and measles immunization at 9 months with a second dose at 15 months of age with the AIK-C human diploid cell strain is a part of the expanded programme on immunization since early 1983.[7] The currently available live vaccine has been shown to produce high seroconversion rates in children of eight months of age or older.[8-10]

In certain population groups where measles occurs in even younger children, the first dose of vaccine is given at six months of age.[11,12]

As there is no known reservoir of infection for measles other than man, there is every possibility that effective immunization and good coverage are likely to control the disease or even lead to its eventual eradication, as was the

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case for smallpox. Thus, measles is one of the diseases in the Islamic Republic of Iran targetted for elimination or eradication. In order to progress toward the goal of measles elimination in Iran, a study of the epidemiology of measles with increasing levels of immunization coverage with high vaccine efficacy are essential.

We report a study conducted during the 1990 measles outbreak in the city of Kerman, Iran. This report discusses the possible reasons for the outbreak and identified the continued need for an effective single dose measles vaccine for children less than nine months of age.

Background

The outbreak occurred primarily in Kerman, the capital of Kerman province, in the south-east of Iran. The city has an area of 49,797 Sq. km. and a population of 257,284 (1987 census).

The health services are provided by private physicians, District Health Center (DHC) and government and university hospitals and clinics. A live attenuated measles virus vaccine is freely available in the area and immunization coverage was 49.2% for those under one year of age and 78% for older children.[7]

The Local Office of the Ministry of Health and Medical Education were first notified of the outbreak in early January 1990, and an investigation was initiated.

SUBJECTS AND METHODS

During the study, we reviewed the DHC and district governmental and private clinics and hospital records to identify measles cases and deaths. Measles diagnosis was based on clinical symptoms and a case of measles defined as a generalized rash of three or more days' duration, with a high fever and any one of the following: cough, coryza or conjunctivitis.[13,14] Cases must meet all three criteria or have a typical pathognomonic enanthema (Koplic spots) to be classified as measles.

A standardized report form was completed for each case presenting to medical facilities with measles symptoms. The following information was collected: name, age, date of birth (if available), gender, measles symptoms and date of onset, immunization status, presence or absence of complications and the need for hospitalization. The information on vaccine history was taken from immunization cards (if available) which are normally issued to mothers for every child during their first immunization. Once a child was identified, upon confirmation of measles diagnosis, the immunization status of the child was recorded from the immunization card and in case of its absence, by asking the mother. If immunization card was not available, a community health worker was referred to the patient's home for confirmation of immunization status or asked the patient's relatives to bring their immunization card at next visit and was carefully checked by the physician. At the same time, the DHC records were reviewed. The DHC recorded 979 cases but we were able to find 745 (76.1%) cases. The rest of the cases occurred outside of the city boundaries or had not presented themselves to medical facilities and we were not able to find them. The 1987 population census was used to calculate attack rates of measles.

Immunization Coverage: The estimated percentage of children aged 12-23 months who have been immunized against tuberculosis, diphtheria, pertussis, tetanus, polio and measles was determined by Nasseri, et al.[7] Children aged 23 months are expected to have completed their immunization. In analysis of immunization coverage, eight children who were vaccinated at nine months of age and received no dose later were classified as unimmunized. All children vaccinated after 12 months of age were classified as immunized.

Immunization Efficacy: Immunization efficacy was estimated for children under one year and older by determining the proportion of cases vaccinated (PCV) for particular age groups. Since the percentage of population vaccinated (PPV) was known,[7] the vaccine efficacy (VE) could be calculated as: $VE = PPV - PCV/PPV(1-PCV) \times 100$.[12,15]

RESULTS

A total of 979 measles cases were reported to have occurred from January 6 to June 1, 1990 by DHC. Of these, 745 cases (76.1%) were reviewed.

Figure 1 shows measles occurrence from January to June 1990. Apparent peaks/epidemics occurred in early March. The number of reported cases began to decline after the first half of March and no cases were reported during the first half of June.

The age and gender distribution of cases are shown in Table I. Of the total patients, 378 (50.54%) were male and 367 (49.5%) were female. Of the total patients, 58 (7.8%) were less than 12 months of age, of whom 38 (65.5%) were less than eight months, 11 (19%) were less than six months and nine (15.5%) were between eight to 12 months of age, and 166 (22.3%) were pre-school aged (less than five), 441 (59.2%) five to nine and 132 (17.7%) 10 to 14 and six (0.8%) above 15 years of age. The youngest child with measles was a five month old infant and the oldest was a 35 year old woman. 739 (99%) patients were under 15, of whom 573 (77%) of cases were school-aged (between 5-14 years). Only four cases died with overall case fatality ratio of 5.4 per thousand.

The overall attack rate was estimated at 4.1 per 1,000 (745/182, 540) subjects under the age of 15 years, with a

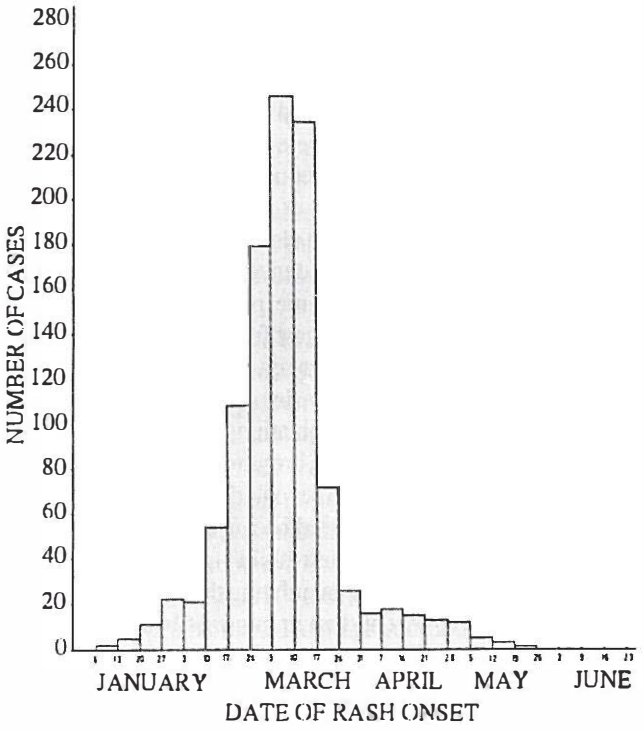

Fig. 1. Reported cases of measles by date of rash onset, Kerman Iran, January-June 1990.

range from 1.7 to 7.7 per 1,000 (Table II). Similar to many outbreaks in other parts of the world on recent years, the highest age-specific attack rate occurred among school-aged children (aged 5-14). Attack rates by age were similar for males and females. In infants less than 12 months, the attack rate was 3.9 per 1,000 while among adults (>15 years) the rate was negligible.

Table III shows that 520 (69.8%) of measles cases had never been immunized and 217 (29.1%) had been correctly immunized and eight cases (1.1%) were only immunized once at nine months of age. Of the total correctly immunized cases, only 20 (9.2%) were vaccinated at nine and at 15 months and 197 (90.1%) were immunized only once at 15 months of age.

14 patients (1.9%) were hospitalized, mostly with pneumonia. In developed countries the percentage of hospitalized patients is estimated at 1%. One patient developed staphylococcal pneumonia and during the hospitalization period, contracted subcutaneous emphysema. Another hospitalized case developed hepatitis. Most of the cases with complications were not immunized. The age of complicated cases ranged from seven months to 35 years. The most frequent complication was pneumonia, followed by otitis and other complications (for example, gastroenteritis). Encephalitis was not seen in these cases.

Immunization Efficacy: The estimated measles immunization coverage at 12 months of age in urban areas of Iran was about 49.2% and for all ages, 78%,[7] indicating that as few as 50% of children have been immunized against measles by their first birthday. The immunization efficacy for cases less than one year was 83.5% and for older cases, 88% (Table IV).

Table I. Age-gender distribution of measles cases, Kerman Iran, January-June 1990

Age		Male		Female		Total	
		No.	%	No.	%	No.	%
<6	Months	5	1.3	6	1.6	11	1.5
6-11	Months	27	7.1	20	5.4	47	6.3
1-1.9	Years	21	5.5	20	5.4	41	5.5
2-2.9	Years	15	4.0	13	3.5	28	3.7
3-3.9	Years	14	3.7	10	2.7	24	3.2
4-4.9	Years	6	1.6	9	2.4	15	2.0
5-5.9	Years	19	5.0	13	3.5	32	4.3
6-6.9	Years	44	11.6	47	12.8	91	12.2
7-7.9	Years	52	13.7	41	11.2	93	12.5
8-8.9	Years	56	14.8	84	22.9	140	18.8
9-9.9	Years	39	10.3	46	12.5	85	11.4
10-14	Years	77	20.4	55	15.0	132	17.7
>15	Years	3	0.8	3	0.8	6	0.8
Total		378	100.0	367	100.0	745	100.0

DISCUSSION

Even though vaccine efficacy was estimated to be 88%, 29.1% of cases had a history of appropriate immunization, indicating some problems with the cold chain, vaccine failure, improper vaccine handling or storage or inadequate immune responses. This problem was expected, however, due to social unrest which resulted from the Iraq-Iran war of 1979 and significant changes and complications that follow it. The complications of war such as irregular and unforeseeable electrical shortages due to alarm signal of bombardments and extreme situations could be responsible for some problems with the cold chain, vaccine storage and administration. However, the relatively high immunization efficacy estimates confirm

Table II. Measles age, gender-specific attack rate during measles outbreak, Kerman Iran, January-June 1990.

Age (Year)	Population Surveyed		No. of cases		Attact rate per 1,000 Population		
	Male	Female	Male	Female	Male	Female	total
<1	7666	7275	32	26	4.2	3.6	3.9
1-4	30885	29731	56	52	1.8	1.7	1.8
5-9	30610	29888	210	231	6.9	7.7	7.3
10-14	24101	22384	77	55	3.2	2.4	2.8
Total	93262	89278	375	364	4.0	4.1	4.0

Six cases were more than 15 years of age.

Table III. Measles immunization status in measles cases, Kerman Iran, January-June 1990

Immunization Status	Male		Female		Total	
	No.	%	No.	%	No.	%
Correctly immunized	104	27.5	113	30.6	217	29.1
Inappropriately immunized	7	1.8	1	0.3	8	1.1
Never immunized	267	70.8	253	68.9	520	69.8
Total	378	100.0	367	100.0	745	100.0

Table IV. Measles immunization efficacy for children under 1 year and above 1 year of age, Kerman Iran, January-June 1990

	<1 Year	>1 Year
Percentage population vaccinated (PPV)	49.2%	78%
Percentage cases vaccinated (PCV)	13.8%	29.1%
Vaccine efficacy (VE)	83.5%	88%

VE= PPV - PCV/ PPV (1-PCV) × 100

that this outbreak resulted chiefly from inadequate immunization coverage, and not from immunization failure. Achieving high coverage with existing vaccine remains the first priority in all countries, but even with high coverage, identifying and reducing pockets of unimmunized children is also important.[16,17]

This outbreak has involved predominantly unimmunized school-aged children and represents the failure of current immunization strategies to achieve high immunization coverage level among school-aged children in urban areas.

However, even high immunization coverage rate can not ensure measles elimination (outbreaks have been documented even when coverage has been greater than 95%[18,20]). Indeed, it is anticipated that even if current measles control policies are effectively implemented, outbreaks will continue to occur, especially among urban poor.

The Global Advisory Group (GAG) of the Expanded Programme on Immunization (EPI) recognized this problem at its October 1989 meeting and recommended action which should be taken to help reduce the impact made by measles in urban settings.[21] The GAG advised EPI programme managers: (1) to define the target populations at greatest risk, (2) to provide for coordination among the many agencies which are frequently engaged in the provision of health and other social services in an attempt to reduce missed opportunities for immunization, (3) to provide outbreak services in order to increase access to immunization services, (4) to support the development of training materials adapted to the urban realities, and (5) to support the development of monitoring systems which measure both immunization coverage and measles incidence among the urban poor in order to be able to make the most appropriate programme and policy decisions.

A total of 58 (7.8%) cases were less than one year of age which is probably related to frequent contact among relatives in this community. Most of these children acquired measles from older siblings or close relatives.

In this study, there is evidence of inefficacy of the present immunization programme, particularly in children under one year of age and suggest further study for evaluation of this programme. However, immunization during the incubation period of measles occurs frequently in outbreaks where mass immunization is occurring and is not a cause for concern. But, immunization at less than nine months of age without a second dose at 15 months of age is of concern. This occurred because of poor information from mothers about their child's date of birth and difficulties in subsequently calculating the age of the child.

On the other hand, children immunized before the first birthday are more likely to have a lower seroconversion rate due to persisting maternal antibodies. In several previous outbreaks, children who received vaccines even at age of 12-14 months have been found to be at increased risk of acquiring measles compared to those immunized at age of 15 months or over.[22] This study also shows that the infection rate in children vaccinated at less than 12 months of age was not much lower than that noted in unimmunized children.[23-26]

This outbreak like other evidence[27] suggests that, for measles, the rate of infection increases from infancy through childhood, peaks during school-aged years, and subsequently drops off during adulthood.

This outbreak illustrates that despite the widely and freely available immunization programme a large percentage of children still are not immune against measles probably due to: a) vaccine misopportunities, b) immunization at an age when maternal antibody interfered with vaccine virus replication, and c) the 2-10 percent primary vaccine failure rate.[22]

Vaccine efficacy was estimated for children less than 15 years of age using vaccine coverage figures for children aged from 12-23 months. To determine if this bias affected the VE estimate further calculation of VE were conducted using only cases who fell between the 12-23 month age limit. Although the number was small, the estimate of VE was approximately the same (90%). The case definition used was applied blindly without knowledge of the immunization status and would not have introduced bias into the VE calculation. Biases would not have been introduced from immunization status ascertainment, since this information was collected from the child health card (children who were inappropriately immunized were classified as unimmunized) or by incomparability of exposure since

both immunized and unimmunized children were assumed to have been equally likely to be exposed. Children with a history of measles were as likely to receive measles vaccine as other children. Vaccine was withheld only from children who had appropriately completed child health cards.

Since we had no access to records of about 24% of cases, the estimated case fatality ratio was underestimated. However, it does not seem these missed cases affect other findings.

Mass immunization of children in the beginning of an outbreak has been demonstrated to result in shortening of the epidemic and prevention of a high proportion of cases.[28] To control the outbreak, the Local Office of Ministry of Health and Medical Education have administered an additional dose of measles vaccine to all primary school children independently of previous immunization which probably kept down the rate of occurrence in this age group. By June 1990, the measles immunization coverage had been increased to more than about 80% (unpublished personal communication). Since then, no new measles outbreaks have been reported. However, revaccination without evaluation of vaccine efficacy risks the loss of confidence of the public and health workers in the immunization programme as well as wasting the vaccine in children with documented immunization and seropositive results.

Finally mathematical models predict that immunity levels of 93.5-96 percent would be necessary to eliminate measles transmission.[29,30] The upper estimate implies that nearly 100% of the population would need to be immunized. Assuming that the lower estimate is correct, 98.5% of the population would have to be immunized with a vaccine of 95% efficacy to answer elimination. If efficacy is 98%, at least 95.5% of the population would have to be immunized.[31] Despite the fact that immunization of Iranian children has been improved since the beginning of EPI in early 1983, it is far behind the original goal of 90% coverage of complete immunization by 1990.[32] Although the goal of complete immunization coverage of 90% by 1990 was not achieved, and there is evidence of known or suspected risk factors for vaccine failure, the Islamic Republic of Iran has made great strides to maintain this immunization coverage. However, the goal of eliminating measles is premature in this country where control of measles has not yet been fully achieved. There seems to be two implications if elimination is to succeed and be maintained. First, the target for immunization coverage should be 100% of children by the time they reach their second birthday. Second, probably revaccination at school age will need to be considered. Also surveillance to identify new foci of transmission and prompt containment will be necessary.

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