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In 1984, the authors first conducted a nationwide survey of deaf children with a history of maternal rubella (HMR) in special schools for the deaf in Japan. The survey showed that the incidence of congenital rubella syndrome in the Japanese mainlands was similar to those in the United States and Europe. In 1993, a second nationwide survey by the authors evaluated the efficacy of the vaccination program for schoolgirls begun in 1977. This second survey yielded 272 deaf children with HMR born between 1981 and 1989. Per 100,000 annual livebirths, the incidence rates were 1.56–9.95 in the epidemic years 1981–1982 and 1987–1988 and 0.20–0.72 in the interepidemic years. During the 1987–1988 epidemic, the incidence rates per 100,000 livebirths were 1.52 among mothers eligible for the vaccination program and 5.52–7.44 among mothers not eligible, and the difference was significant. However, only 21.7% of the women who delivered children during the 1987–1988 rubella epidemic were eligible for the vaccination program, and because the majority of deaf children with HMR were born to mothers not eligible, a decrease in the birth rate of deaf children with HMR was not observed. These data suggested the need to introduce a new vaccine program to suppress rubella epidemics.

The epidemiology of congenital rubella syndrome in Japan has been unique. A hypothesis that the American rubella virus was more virulent than the Japanese virus has been proposed (1, 2). On the basis of our seroepidemiologic study in Okinawa (3) and our 1984 nationwide survey of special schools for the deaf (4), we have proven that the rubella virus in Okinawa was not virulent and that the incidence of congenital rubella syndrome in the Japanese mainlands was not lower, i.e., the rate in Japan was similar to those in the United States and Europe (4). In 1977, a rubella vaccination program for schoolgirls similar to the one in the United Kingdom was started in Japan, with the goal of preventing congenital rubella syndrome (5). In addition, immunization of children of both sexes by using the measles-mumps-rubella vaccine was started in 1989 (6–8). To investigate the change in the epidemiology of the Japanese congenital rubella syndrome under these circumstances, we conducted a second nationwide survey on congenital rubella syndrome in Japan among schoolchildren attending special schools for the deaf. This paper documents the continuing birth of many children with congenital rubella syndrome in Japan and also the negligible influence of rubella immunization on the prevention of congenital rubella syndrome.

Before the 1975–1977 nationwide rubella epidemic in Japan, rubella epidemics had occurred there in 10-year cycles. That is, an epidemic developed and continued for 4–5 years, followed by an interval of 4–5 years with no reported rubella cases. However, this pattern changed to one that is similar to those in the United States and Europe, i.e., rubella occurred endemically, with periodic epidemics (9, 10). Rubella epidemics in Japan were observed in 1965–1969, 1975–1977, 1981–1982, 1987–1988, and 1992–1993 (2–6, 9, 10). In addition, 351 children with congenital rubella syndrome were born between 1963 and 1980 (4).

In 1977, Japan instituted rubella immunization of junior high school girls (aged 12–14 years) who did not have a history of clinical rubella (5). Females less than age 30 years on April 1, 1993, i.e., those born in 1962 or later, should have been eligible for this program. The annual rubella immunization rates in 1977 and in 1978–1989 among schoolgirls were 27.3 and 63.7–74.0 percent, respectively (11). The mean age of
women giving birth in Japan between 1981 and 1989 was 28.2–28.9 years, and the mean ages of those giving birth to the first, second, and third children were 26.5–27.0, 28.9–29.4, and 30.8–31.7 years, respectively (12).

Immunization of children of both sexes using the measles-mumps-rubella vaccine was begun in 1989. The main reasons for starting this program were that 1) it has been confirmed that human rubella antibodies persist for at least 10 years after vaccination (6); 2) an epidemic of rubella could not be prevented by vaccinating female junior high school students only, and babies with congenital rubella syndrome continue to be born; 3) the number of rubella epidemics and cases of congenital rubella syndrome decreased rapidly in the United States when measles-mumps-rubella vaccination was promoted earlier than in other countries; and 4) the patent on the measles-mumps-rubella vaccine had expired (8). However, use of the Japanese measles-mumps-rubella vaccine was stopped because of occurrences of aseptic meningitis caused by the mumps vaccine, and use of the monovalent live rubella vaccine began in 1995 (6).

MATERIALS AND METHODS

During the school year from April 1993 to March 1994, 7,842 deaf kindergarten and older schoolchildren attended the 107 public or private schools for the deaf in the 47 prefectures in Japan. A total of 4,065 were kindergarten and primary schoolchildren, and the remaining 3,777 were junior and senior high school students (13). In our 1984 survey, the investigation of kindergarten and older schoolchildren born in or before 1980, i.e., junior and senior high school students in the 1993 survey, had been completed. The study population enrolled in the 1993 survey were those born in or after 1981, i.e., those aged 11 years or younger who were kindergarten and primary schoolchildren on April 1, 1993. In June 1993, questionnaires were sent to all 107 schools for the deaf; 92 schools (86.0 percent) replied. The total number of deaf kindergarten and primary schoolchildren born in or after 1981, i.e., those aged 11 years or younger who were kindergarten and primary schoolchildren bom in or before 1980, i.e., junior and senior high school students in the 1993 survey, had been completed. The study population enrolled in the 1993 survey were those born in or after 1981, i.e., those aged 11 years or younger who were kindergarten and primary schoolchildren on April 1, 1993. In June 1993, questionnaires were sent to all 107 schools for the deaf; 92 schools (86.0 percent) replied. The total number of deaf kindergarten and primary schoolchildren bom in or after 1981, i.e., those aged 11 years or younger who were kindergarten and primary schoolchildren.

Table 1 shows the regional distribution of these 272 deaf children. The overall prevalence was 0.22 cases per 100,000 population. Although differences were observed between districts during the previous survey (a higher prevalence in southwestern Japan and a lower prevalence in northeastern Japan) (4), no difference was observed in the 1993 survey. Only one case was noted in Okinawa, where a severe congenital rubella syndrome epidemic was observed in 1965 (3).

Table 2 shows the clinical manifestations other than deafness in these 272 children with HMR. Twenty-four children (8.8 percent) were found to have cataract with and without congenital heart disease, and 31 children (11.4 percent) had congenital heart disease without cataract. The remaining 217 children (79.8 percent) had deafness alone.

Table 3 shows the distribution of these 272 deaf children with HMR on the basis of their year of birth, along with the annual incidence rates per 100,000 population.

RESULTS

Among the 3,465 kindergarten and primary schoolchildren attending the 92 special schools for the deaf that replied to the questionnaire, 272 children (7.8 percent; 145 males, 127 females) were deaf children with HMR. These children were studied.

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TABLE 2. Clinical manifestations in 272 deaf children with a history of maternal rubella attending special kindergartens and primary schools for the deaf in Japan, June 1993

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>No. of children</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Cataract</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Cataract + congenital</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>heart disease</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>122</td>
<td>95</td>
</tr>
<tr>
<td>Deafness alone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>127</td>
</tr>
</tbody>
</table>

TABLE 3. Annual incidence rate by year of birth of 272 deaf children with a history of maternal rubella attending special kindergartens and primary schools for the deaf in Japan, 1981-1989

<table>
<thead>
<tr>
<th>Year of birth</th>
<th>No. of cases</th>
<th>Incidence rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981</td>
<td>24</td>
<td>1.56</td>
</tr>
<tr>
<td>1982</td>
<td>45</td>
<td>2.97</td>
</tr>
<tr>
<td>1983</td>
<td>8</td>
<td>0.53</td>
</tr>
<tr>
<td>1984</td>
<td>3</td>
<td>0.20</td>
</tr>
<tr>
<td>1985</td>
<td>8</td>
<td>0.56</td>
</tr>
<tr>
<td>1986</td>
<td>8</td>
<td>0.58</td>
</tr>
<tr>
<td>1987</td>
<td>134</td>
<td>0.95</td>
</tr>
<tr>
<td>1988</td>
<td>33</td>
<td>2.51</td>
</tr>
<tr>
<td>1989</td>
<td>9</td>
<td>0.72</td>
</tr>
</tbody>
</table>

* Cases/100,000 livebirths.

livebirths. The numbers of deaf children with HMR born in 1981 and 1982, or the prekindergarten children in our previous survey, were eight and six, respectively (4). However, the numbers of deaf schoolchildren with HMR in the 1993 survey were 24 and 45, respectively. In Japan, special schools for the deaf educate preschool children who are age 3 years or older at the beginning of the school year in kindergartens. Those prekindergarten children younger than age 3 years would also be admitted to special schools if their parents preferred. Therefore, our previous survey might have identified fewer deaf children with HMR born in 1981 and 1982 than were identified in our 1993 survey. So, the latter data on the numbers of deaf children born with HMR were used in the 1993 survey. The incidence rate was 1.56-9.95 per 100,000 annual livebirths in the epidemic years 1981-1982 and 1987-1988, presumably during the rubella epidemics (4-6).

To evaluate the efficacy of the rubella vaccination program for schoolgirls in preventing congenital rubella syndrome among the 236 deaf children with HMR born during the 1981-1982 and 1987-1988 rubella epidemics, we studied 199 children whose mothers’ ages were listed on the questionnaire. The mothers eligible for the vaccination program for schoolgirls begun in 1977 were aged 18-19 years or younger and were aged 24-25 years or younger during the 1981-1982 and 1987-1988 rubella epidemics, respectively. Their proportions among the total number of mothers were 0.8 and 21.7 percent, respectively. Thus, this vaccination program had almost no influence on the earlier epidemic but a partial influence on the later epidemic. Table 4 shows the number and incidence rate of deaf children with HMR born during the 1981-1982 and 1987-1988 rubella epidemics by the different age groups of their mothers.

Per 100,000 livebirths, the rates of deaf children with HMR born to mothers aged 20-24, 25-29, and 30-44 years during the 1981-1982 epidemic were 3.41, 1.74, and 1.33, respectively. On the other hand, the rates for the same age groups during the 1987-1988 epidemic were 1.52, 5.52, and 7.44, respectively, showing a significantly lower rate for the group aged 20-24 years (p < 0.01) and a higher rate for the group aged 30-44 years, although the difference was not significant.

DISCUSSION

Our 1984 survey confirmed that 351 deaf children with HMR were born between 1963 and 1980 on the Japanese mainlands (4). Nine years later, our 1993
TABLE 4. Incidence rate of deaf kindergarten and primary school children with a history of maternal rubella by the age of the mother in the 1981-1982 and 1987-1988 rubella epidemics, Japan

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of births</td>
<td></td>
<td></td>
<td>No. of births</td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>48,858</td>
<td>0</td>
<td>51,948</td>
<td>0</td>
</tr>
<tr>
<td>20-24</td>
<td>674,620</td>
<td>23</td>
<td>525,002</td>
<td>8</td>
</tr>
<tr>
<td>25-29</td>
<td>1,496,186</td>
<td>26</td>
<td>1,250,113</td>
<td>69</td>
</tr>
<tr>
<td>30-44</td>
<td>824,746</td>
<td>11</td>
<td>833,073</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
<td>3,044,410</td>
<td>60</td>
<td>2,660,136</td>
<td>139</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01.
† Data show summation of the 2 years at the same age cohort.
‡ Cases/100,000 livebirths.
§ The age of the mother was unknown in 9 cases.
¶ The age of the mother was unknown in 28 cases.

The 1993 survey and our previous nationwide surveys (4) showed that births of deaf children with HMR occurred annually, coinciding with a peak number of such births during the rubella epidemics. Information gathered on clinical manifestations other than deafness showed cataract and/or congenital heart disease in 21 percent of these children in Okinawa (1965) (3), 19 percent in the 1984 survey (4), and 20 percent in the 1993 survey. From our clinical information, deaf children with HMR in the 1993 survey were congenital rubella syndrome compatible or possible cases according to Centers for Disease Control criteria (16). All of our surveys could therefore be considered to share similar epidemiologic and clinical backgrounds.

The rubella vaccination program for schoolgirls was adopted in the United Kingdom, Australia, and Japan. In addition, a program to vaccinate nonpregnant rubella-seronegative adult women was implemented in the former two countries (17, 18) but not in Japan (19, 20). The number of rubella-seropositive women in these countries has been confirmed to be rising, and the rubella vaccination program has been reported to be effective in reducing the number of children with congenital rubella syndrome born in the United Kingdom (15, 17, 21, 22) and Australia (18, 23-26).

The Japanese rubella vaccination program for junior high school girls who do not have a history of clinical rubella was started in 1977 (5). Our 1993 survey found that during the 1987-1988 rubella epidemic, the birth rate of deaf children with HMR to vaccine-eligible mothers was significantly lower than that to ineligible mothers.

Table 5 gives the prevalence of rubella hemagglutination inhibition antibodies among Japanese women in different age groups, as released in the 1981 and 1987 reports of National Epidemiological Surveillance
of Infectious Diseases (19, 20). This table also shows data from our 1993 survey on the birth rate of deaf children with HMR during the 1981–1982 and 1987–1988 rubella epidemics. The high birth rate of deaf children with HMR to mothers aged 20–24 years during the 1981–1982 rubella epidemic suggests a low rubella seropositivity rate in this age group, a gap in immunity that we had already pointed out (9). Furthermore, the low birth rate of deaf children with HMR to mothers aged 20–24 years during the 1987–1988 rubella epidemic was considered attributable to the high seropositivity rate that resulted from the rubella vaccination program for mothers in this age group.

However, this difference in birth rates during the two epidemics suggests two possible biases. The first is the age effect: It has been shown that the risk of exposure to rubella in pregnancy is several times higher in parous than in nulliparous women, because the former contract rubella from their own children. Since parity increases with age, women with rubella in pregnancy were shown to be older than the general population of pregnant women in the United Kingdom (15, 27). A similar age effect has been reported for women who have parvovirus B19 infection in pregnancy, among whom those aged 30 years or older are overrepresented (28). The birth rate of deaf children with HMR among the oldest age group (30–44 years) was higher, although not significantly so, than that among the group aged 25–29 years during the 1987–1988 rubella epidemic (table 4), and this significantly low birth rate of deaf children with HMR among mothers aged 20–24 years could not be explained by age alone.

The second possible bias is that vaccine-eligible mothers were far more concerned about rubella than were those mothers who were not eligible, and a higher rate of therapeutic abortion after rubella infection might have occurred in the vaccine-eligible group. Therapeutic abortion after rubella infections is illegal in Japan, and official statistical data on this problem are therefore unavailable. In cooperation with a group of obstetricians in the city of Fukuoka (number of births in 1987: 15,017), we conducted a survey on the number of abortions attributable to rubella infection in the first trimester of pregnancy in the 1987 epidemic and found 63 cases. The ages and number of cases were as follows: 10 cases at age 20–24 years, 26 cases at age 25–29 years, and 27 cases at age 30–44 years, with abortion rates of 4.6, 3.7, and 4.6 per 1,000 livebirths in each age group, respectively. Therefore, the higher rate of therapeutic abortions among the group of vaccine-eligible pregnant women might also be considered a result of the vaccine program. From these data, it is evident that during the 1987–1988 rubella epidemic, the birth rate of deaf children with HMR to vaccine-eligible mothers aged 20–24 years was lower than that to ineligible pregnant women.

Although the efficacy of the vaccination program has already been discussed in this paper, the total number of births of deaf children with HMR did not decrease. The reason was that the proportion of vaccine-eligible mothers was small (21.7 percent of the total number of pregnant women during the 1987–1988 epidemic). Therefore, although the number of births of deaf children with HMR to vaccine-eligible mothers was decreasing, a much larger number of deaf children with HMR were born to ineligible mothers during the 1987–1988 rubella epidemic. Thus, a decrease in the total number of such births could not be observed.

In the United Kingdom, the number of abortions that resulted from rubella infection during the epidemics has been reported to be 10 times the number of children born with congenital rubella syndrome (16, 27). If the same rate of therapeutic abortions as that observed in Fukuoka had occurred throughout Japan in the 1987 rubella epidemic, the estimated number of abortions in the entire country (number of births in 1987: 1,346,658) would have been about 5,650, regardless of the vaccine program. Therefore, to eliminate rubella epidemics, children of both sexes must be immunized.

The policy of controlling rubella epidemics by routinely administering a measles-mumps-rubella vaccine to all children began in the United Kingdom in 1988.
(15) and in Australia in 1990 (26). In Japan, measles-mumps-rubella vaccination began in 1989. However, because of the adverse effects of the mumps vaccine, monovalent rubella live vaccine will be administered to all children, per the amended vaccination law effective April 1995 (6).

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REFERENCES