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The epidemiology of measles in Poland: prevalence of measles virus antibodies in the population

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SUMMARY

WHO has adopted a goal of eliminating indigenous measles from the European Region by the year 2007. The strategy focuses on reducing the proportion of susceptible individuals in the population to low levels and maintaining these low levels of susceptibility. Routine vaccination against measles for children aged 13–15 months was introduced in Poland in 1975, and a second dose added in 1991. High coverage (> 95%) is achieved with both doses. In order to assess progress towards measles elimination in Poland, a serological survey was performed to evaluate the impact of vaccination on the susceptibility profile of population. Three thousand residual serum samples from individuals aged 1–30 years were collected from hospitals in six selected voivodeships (administration units) in Poland. These were tested for measles-specific IgG using a commercial ELISA. Overall 4% (120/3000) were negative for measles virus antibody. The highest proportion of negatives (8·2%) occurred among cohorts born 1977–81 – the only cohorts in which susceptibility exceeded the WHO targets. 'Catch-up' vaccination strategies should target these cohorts.

INTRODUCTION

Measles is one of the most infectious human diseases, causing many complications and deaths [1–4]. Effective vaccines provide the means to prevent this morbidity [2, 5, 6]. WHO has adopted a goal of eliminating indigenous measles from the European Region by the year 2007 [7]. The strategy focuses on reducing the proportion of susceptible individuals in the population to low levels and maintaining these low levels of susceptibility [7]. WHO age-specific susceptibility targets for developed countries were established by mathematical modelling based on vaccination coverage data and age-specific disease incidence. These proportions differ according to specific age groups. The proportion of susceptible individuals must not exceed 15% in children aged 1–4 years, 10% in 5–9-year-olds, 5% in 10–14-year-olds and 5% in each cohort of adults above this age. The concept of an epidemic threshold is crucial for elimination programmes. Elimination of measles will depend on all countries in the Region reaching and maintaining these targets.

Routine vaccination against measles for children aged 13–15 months was introduced in Poland in 1975. A second dose of measles vaccine was added to the vaccination schedule of 9-year-old children in 1991, and was brought forward to 7-year-olds in 1994. High vaccination coverage has led to changes in measles epidemiology, and a high level of control has been achieved.

In order to assess progress towards measles elimination in Poland, a serological survey was performed to evaluate the impact of vaccination on the susceptibility profile of the population. This survey is

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reported and the results are interpreted with reference to measles surveillance data.

METHODS

Measles surveillance

Data collected routinely for measles surveillance in Poland included statutory case notifications, death certifications and vaccine coverage. Clinically diagnosed measles cases were reported to field sanitary epidemiological stations. These are centres of Public Health Service concerned with problems of infection diseases control. Sanitary epidemiological stations are organized in each voivodeship and county. In 1997 Poland was divided into 49 voivodeships. Each voivodeship comprised some counties. The data for each voivodeship were collated by the voivodeship sanitary epidemiological stations, which reported, twice monthly, the number of cases according to age, sex, region and vaccination status to the Epidemiology Department in the National Institute of Hygiene. These data are elaborated in the 'Annual Bulletin of Communicable Diseases in Poland'. Clinical diagnosis of measles cases has been based on the case definition proposed by WHO [7]. There has been no change in the case definition over the period of surveillance shown in this paper.

Each child had an immunization card for recording vaccinations. Cards for pre-school children were held at paediatric clinics in urban areas, and at health centres in rural areas. Cards for school children were held by the school health service. At the end of each year, the measles vaccination status of all children aged 1–14 years (1–4 years until 1990) was reviewed. The 'Annual Bulletin of Vaccinations in Poland' reported the vaccination status of all children by birth cohort and voivodeship.

The vaccination status on 31 December 1997 of children born in 1984–96 was determined on the basis of annual reports sent from all voivodeships. The vaccination status of older children and adults was obtained from similar reports from the most recent year. This provided the proportion of individuals in cohorts born in 1966–96 who have received 0, 1 and 2 doses of measles vaccine.

Vaccine efficacy

Measles attack rates in vaccinated (ARV) and attack rates in unvaccinated (ARU) children aged 1–4 years were calculated by year of age for each year 1985–97. The vaccine efficacy (of a single dose) was estimated as 1-ARV/ARU.

Serum samples

The study group comprised the population in six voivodeships of Poland (Warsaw, Lublin, Wroclaw, Poznan, Tarnobrzeg, Zielona Góra). The total population in the selected voivodeships was 7212838 in 1996, which represented about 18·6% of the Polish population.

Anonymized residual serum samples were collected from individuals born in 1966–95 attending selected hospitals and Public Laboratories between March and October 1997. One hundred samples were collected from each year birth cohort, giving a total of 3000 samples. Leftover serum samples collected at obstetric, surgery and traumatology wards at Regional General Hospitals and from casualty, surgery and ophthalmology wards at the Regional Paediatric Hospitals were included in the study. Each sample was accompanied by a form containing information about year of birth, sex, place of residence (urban or rural), and the date and hospital ward of collection.

Measles antibody assays

Serum samples were assayed for measles-specific IgG using a commercially available enzyme-linked immunosorbent assay kit (ELISA-Behringwerke™). Assays were standardized to the 2nd International Standard for human anti-measles serum. Inclusion of the International Reference for anti-measles serum in assay reduced the variation between assays and between studies.

On each assay plate, 48 samples were tested; this included 40 test samples and 2 replicates of 4 standard sera (each calibrated against the 2nd International Standard for human anti-measles sera). A standard curve was obtained for each plate through a regression of optical density against log antibody concentration; for all plates the coefficient of correlation (r) was $\geqslant$ 0·97.

Antibody concentrations were expressed in International Units per millilitre (IU/ml). Samples with titres below 0·5 IU/ml were regarded as negative (non-protected). From our experience measles virus antibody titres below 0·5 IU/ml may be not enough sometimes for measles protection. All negative samples were retested to confirm the result. The retested samples have been confirmed in 80%. Results for

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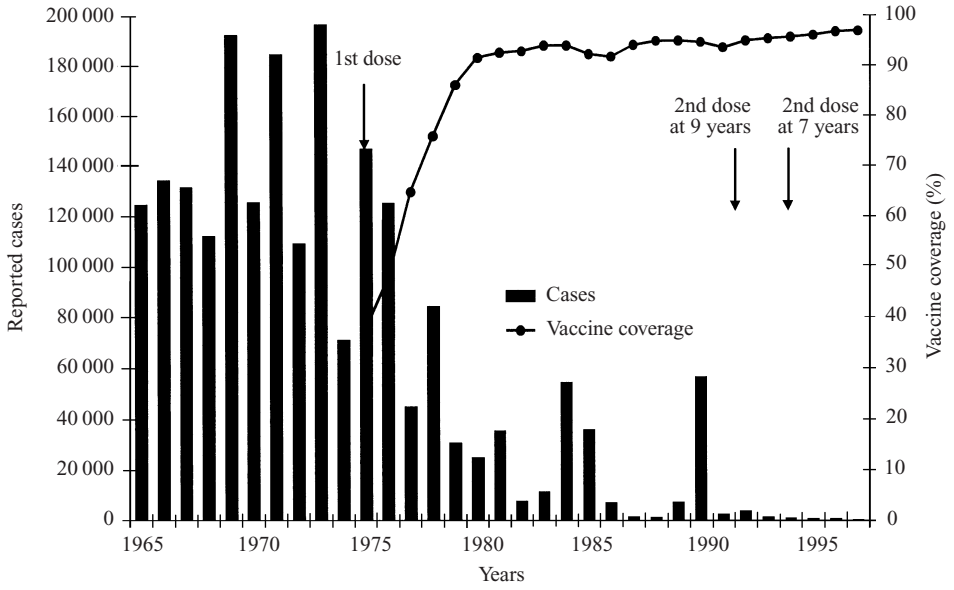

Fig. 1. Reported measles cases and vaccine coverage in Poland, 1965–97.

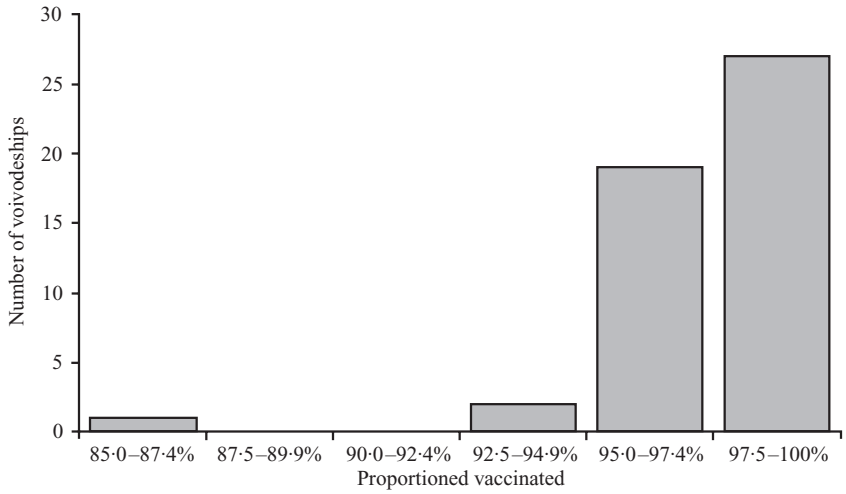

Fig. 2. Frequency distribution of measles vaccination coverage by voivodeship: proportion of children born in 1995 who were vaccinated before the end of 1997.

each cohort were summarized by the geometric mean titre. For mean antibody titres comparison between age groups the *t*- test for unpaired samples was used.

RESULTS

Routine vaccination against measles for children aged 13–15 months was introduced in Poland in 1975, at which time some vaccine was also given to some older children (aged 1–4 years). Until 1990 a monovalent measles vaccine prepared from the Leningrad 16 (L-16) strain was used. Since then a monovalent vaccine prepared from Schwarz strain (Rouvax, Pasteur Merieux) has been used. National coverage for the first dose of measles vaccine in 2-year-old children increased during the 1970s and has exceeded 90% since 1980. Data from annual reports show that most vaccinations were given in the second year of life. For example, at the end of 1997, 77·0% of children born in 1996 (then aged 12–23 months) had been vaccinated. Since some of this cohort had not yet reached the scheduled age of vaccination, this suggests that most vaccinations were given on schedule. Coverage evaluated at age 24–35 months reached 96·9% by 1997 (Fig. 1). In almost all (46/49) voivodeships vaccination coverage exceeded 95% by the third year of life (Fig. 2). Coverage in Krakow was less good, 86·5% of children born in 1995 had been vaccinated

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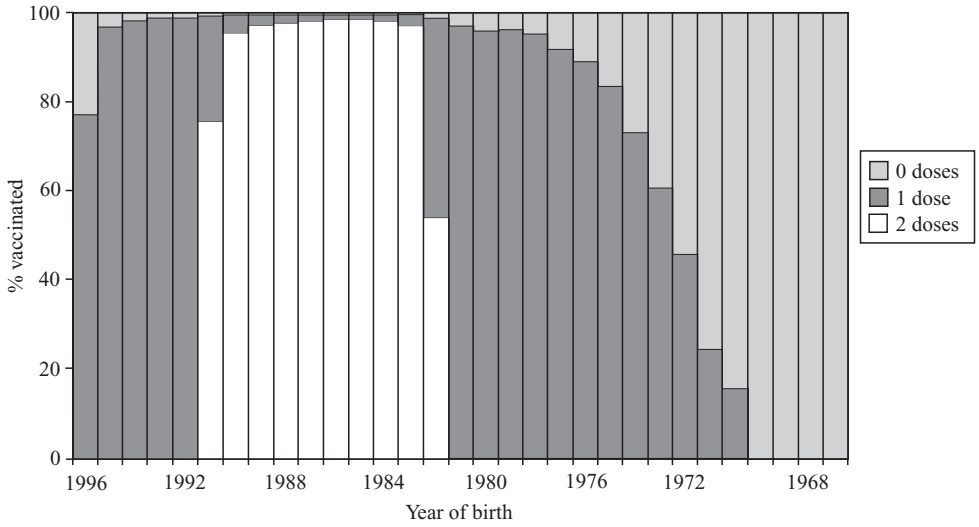

Fig. 3. Vaccination status of the population of Poland (excluding Krakow) on 31 December 1997.

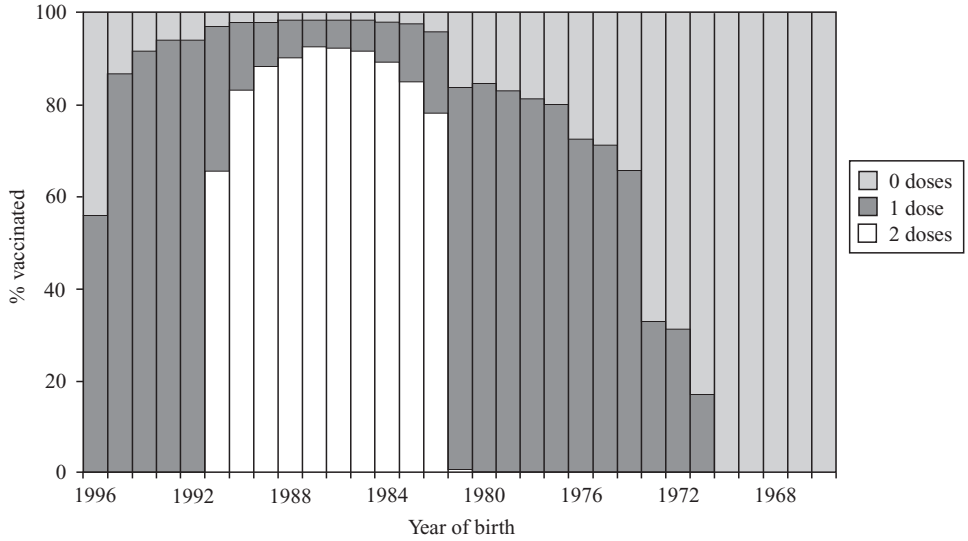

Fig. 4. Vaccination status of the population of Krakow on 31 December 1997.

by the end of 1997. Nevertheless, this represented an improvement from levels of 70–80% in Krakow during 1980–95.

A second dose of measles vaccine was introduced for children aged 9 years in 1991, and brought forward to 7 years in 1994. The 1982 cohort was the first in which 53·6% of children received two doses of measles vaccine. In subsequent cohorts (born in 1983–90) 97·6% of children in Poland had received two doses of vaccine. The vaccination status for Poland (excluding Krakow voivodeship) is shown in Figure 3. Coverage in Krakow was significantly lower (Fig. 4).

Before the introduction of measles vaccination, epidemics occurred every 2–3 years (Fig. 1). The number of reported cases during the pre-vaccinated era was 140–200 thousands in epidemic years and 70–120 thousands in inter-epidemic years. Since acquisition of infection was almost universal, it is estimated that approximately 25–30% of infections were reported. Since 1975, the number of reported cases has shown a sharp downward trend, from 70857 cases in 1974 to 338 cases in 1997. The size of epidemics decreased and the inter-epidemic period lengthened to 5 years in the 1980s and 8 years in the 1990s. The reporting of measles cases in Poland is based on a clinical diagnosis; the predictive value of clinical diagnosis is expected to be highest in epidemic years.

Before the introduction of vaccination about 50% of reported cases occurred in children aged less than 5 years of age and approximately 90% were in children

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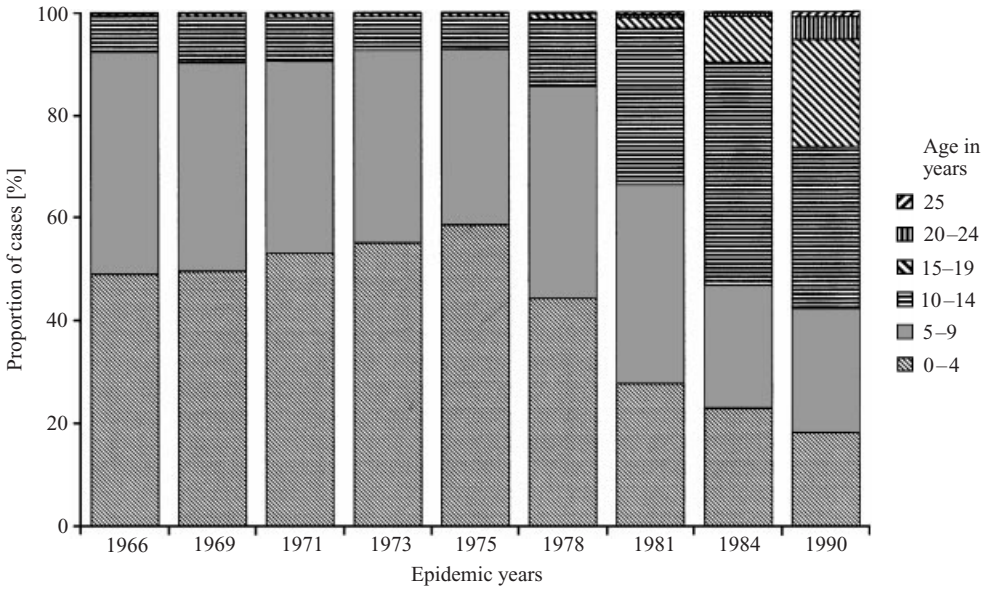

Fig. 5. Age distribution of measles cases in epidemic years.

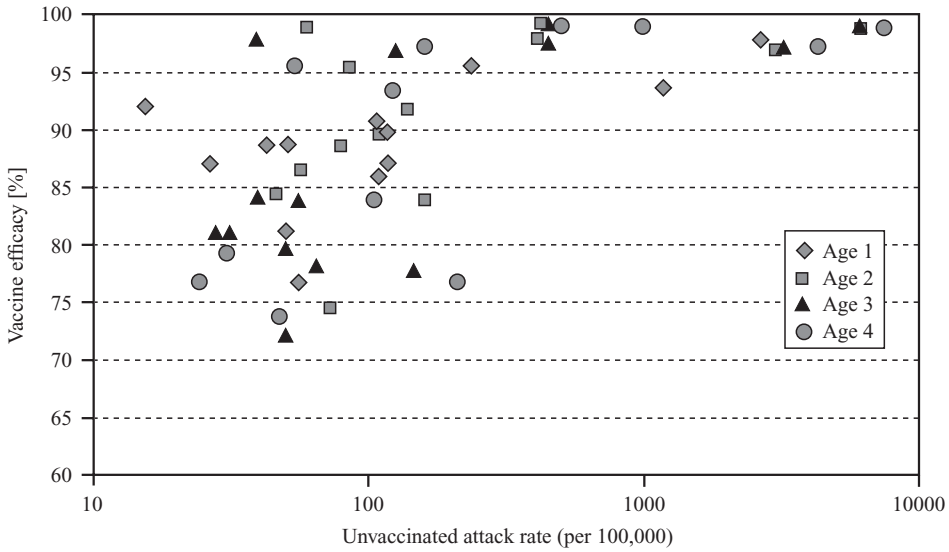

Fig. 6. Annually calculated vaccine efficacy in each cohort aged 1–4 by incidence of measles.

less than 10 years of age (Fig. 5). Following the introduction of routine vaccination an increasing proportion of cases among older children and young adults was observed. In the 1990 epidemic 57·8% of cases occurred in persons aged 10 years or more (Fig. 5). The number of measles deaths declined before vaccination was introduced, from 800 in 1965–9 to 461 in 1970–4, due to a reduction in the case fatality ratio. Following the introduction of measles vaccination, the decrease in the measles mortality was accelerated. The case fatality ratio decreased further to 20 per 100000 cases in 1990–4. The last death caused by measles was reported in 1991.

The estimates of vaccine efficacy are uniformly high (> 95%) in epidemic years (when the attack rate in the unvaccinated population exceeds 300/100000), but lower in non-epidemic years (Fig. 6). The lower efficacy in non-epidemic years is probably due to a higher proportion of misdiagnosed non-measles infections amongst the reported measles cases. Vaccine efficacy in excess of 95% is higher than that observed in many other countries. Such high efficacy may be due in part to the age at vaccination (13–15 months or more). However, it is possible that the estimates are biased upwards by differing exposure of vaccinated and unvaccinated children, resulting from some

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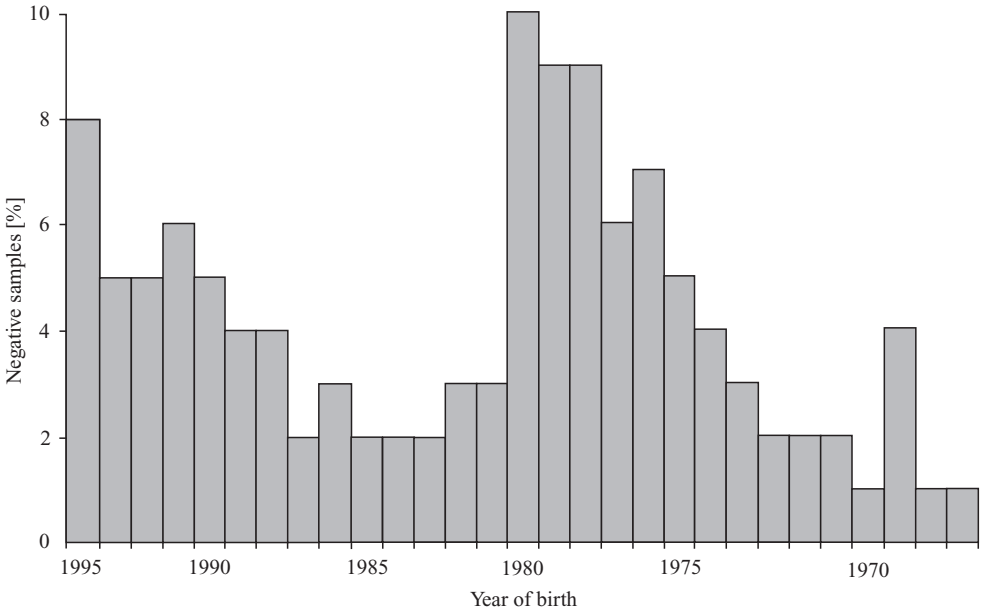

Fig. 7. Proportion of serum samples negative for measles virus antibody by year of birth.

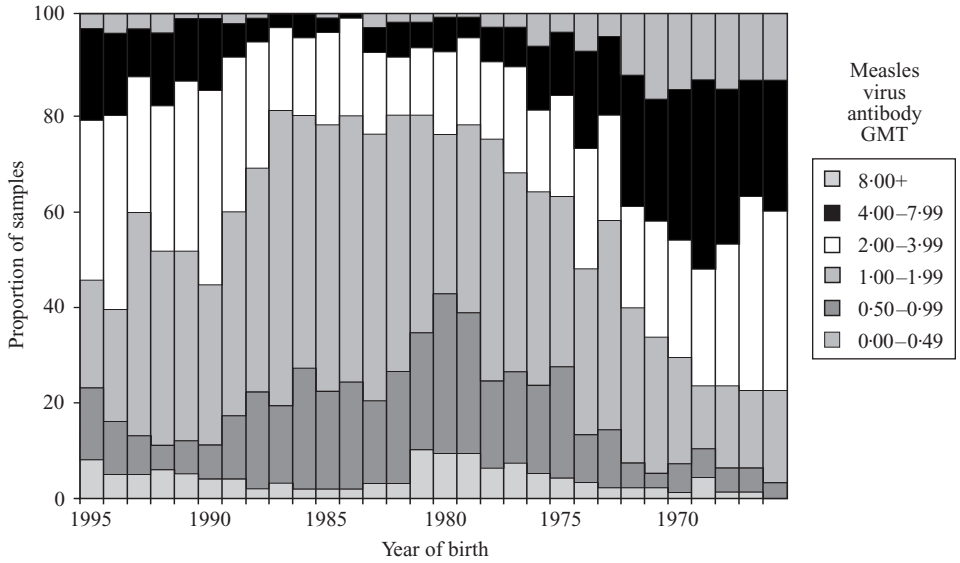

Fig. 8. Distribution of measles virus antibody titres by year of birth.

heterogeneity in coverage (particularly the low coverage in Krakow).

In all, 4% (120/3000) of serum samples were negative for measles antibody; the proportion negative varied with age (Fig. 7). The level of measles antibodies also showed considerable age-dependence (Fig. 8, Table 1). There was no significant difference between prevalence in males and females, or between voivodeships.

In 1997, when serum samples were collected, the children who were born in the period 1992–5 had received one dose of measles vaccine. All these children were at least 14 months of age. The

Table 1. *Proportion antibody negative and geometric mean measles virus antibody titre of positive serum samples according to age group and vaccination schedule*

Year of birth	Vaccination schedule (doses)	% negative ($< 0{\cdot}5$ IU/ml)	GMT of positives ($\geqslant 0{\cdot}5$ IU/ml)
1992–5	1	6·0	2·30
1982–91	2	3·0	1·65
1975–81	1	7·1	1·65
1966–74	0	1·8	3·18

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proportion negative was 6·0% and the geometric mean titre (GMT) of measles antibody in positives was 2·30 IU/ml. Almost all children born in 1982–91 have received two doses of measles vaccine. In this group 3·0% were antibody negative and the GMT of positives was 1·65 IU/ml. It seems that the second dose mainly provided protection to children not previously immunized (unvaccinated or vaccine failures). No booster effect was apparent. Probably the observed waning level of vaccine-induced measles virus antibody titres between these two groups is connected with time since the first vaccination. The cohorts born in 1975–81 had been vaccinated only once and had little exposure to natural measles infection. They had the highest proportion negative (7·1%); the GMT of positives was 1·65 IU/ml. The proportion negative was highest (9·3%) in the cohorts born in 1979–81 who were just too old to have received a second dose. Persons who were born in 1974 or before were generally unvaccinated and have acquired immunity by natural measles infection. The proportion negative in this group was the lowest (1·8%) and the GMT in positives was the highest (3·18 IU/ml). The mean measles antibody titre in this group was significant higher than in all other groups ($P < 0{\cdot}0001$).

DISCUSSION

Over 20 years of measles vaccination in Poland has had a substantial impact on disease morbidity and mortality. The changes in measles epidemiology are typical of countries that have achieved high vaccination coverage [6, 8–10]. The number of reported cases has shown a sharp downward trend (99·5% reduction between 1974 and 1997). A changing age distribution of cases was observed, with an increasing proportion of cases occurring among older children and adults. No measles deaths have been reported since 1991.

Achieving high coverage with a single dose of vaccine can produce prolonged periods of freedom from measles. However, it is inevitable that cohorts of susceptible persons will accumulate during these periods and epidemics of measles will occur, predominantly among older children [6]. In some countries, such epidemics may be associated with a higher case-fatality amongst adolescents and the costs of outbreak control and investigation may be large. Some countries have managed to interrupt measles transmission by achieving high vaccination coverage using a two-dose schedule [8, 11]. In Poland, a second dose was introduced in 1991. The lower susceptibility in cohorts who have received two doses is evidence of the benefit of the second dose.

The elimination strategy for the European Region focuses on the estimation and reduction of susceptible individuals in the population [7]. Data from the measles serological survey in Poland suggest that a high proportion of the tested population (96%) was protected against measles infection. The only cohorts in which the proportion susceptible exceeded the WHO targets were those born in 1977–81. Lower coverage with a single dose of vaccine and little exposure to natural measles infection combine to give a higher proportion of susceptible persons in this group.

In 1998, there was a resurgence of measles in Poland, although the number of cases was smaller than in previous epidemics (2255 cases in 1998 compared with 56471 in 1990). In this epidemic the highest incidence was in young adults, the cohorts with the highest susceptibility in the serosurvey; 70% of cases occurred in persons aged 10 years or more, 36% of cases were aged 15–19 years.

The high vaccine coverage achieved in most voivodeships with the current two-dose schedule is successful in achieving high levels of immunity in each new cohort and maintaining susceptibility below the WHO target levels. The current programme with the first dose at age 13–15 months and second dose at age 7 years should be maintained. Considerable progress has been made recently in improving coverage in the voivodeships with the lowest coverage. Further efforts should be made to achieve coverage of at least 95% for two doses in every voivodeship. The higher level of susceptibility in persons born in 1977–81 provides the potential for further limited outbreaks. These cohorts should, where possible, be targeted to receive a second dose of measles vaccine. Establishments in which many persons of this age live (such as universities, colleges and military camps) are the most likely settings for outbreaks, but also provide the greatest opportunity for vaccination to be delivered at low cost.

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