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A LABORATORY STUDY OF AGE-RELATED VARICELLA INCIDENCE AND PREVALENCE IN THE CZECH SOCIALIST REPUBLIC

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Summary. — During 1972—1981, ten representative population samples totalling 2 916 individuals were tested for antibodies to varicella-zoster virus (VZV) by an indirect-haemagglutination assay (IHA). Statistical analysis of the results provided estimates of age-related varicella prevalence and incidence rates. It transpired that 45 % of the child population had encountered varicella at preschool age and another 45 % during the attendance of school. Adult seropositivity rates amounted to 97.5—100 %. The highest varicella incidence was observed in the 4-year age interval of 2—6 years. For control, additional 324 and 297 individuals were tested by RIA and ELISA IgG, respectively; there was good correlation of results. For the period 1970—1985 varicella morbidity was also studied from notification data. As far as the authors are aware, the present investigation performed on a total of 3537 subjects furnishes the most comprehensive information on nation-wide varicella incidence and prevalence obtained by laboratory methods.

Key words: *indirect haemagglutination*; *radioimmunoassay*; *enzyme-linked immunosorbent assay*; *varicella prevalence*; *varicella incidenc*

Introduction

Varicella incidence and prevalence among the population of the Czech Socialist Republic (western greater half of the Czechoslovak Socialist Republic) were studied on a long-term basis by serological testing representative population samples. The investigations were carried out within a programme of immunological surveys of infections that is being conducted by the Institute of Hygiene and Epidemiology (IHE), Prague. This brief report sums up the results obtained.

Materials and Methods

Sets of sera. A total of 3537 individuals constituting 12 representative population samples were tested serologically. The sera were obtained from the WHO Serum Bank at Prague. Ten of the sets, jointly totalling 2916 serum specimens and collected in different parts of the country, were tested by an indirect haemagglutination (IHA) assay. In this subtotal, age categories were represented as follows: 1 year, 169 sera; 2 years, 216; 3 years, 246; 4 years, 256; 5 years, 252;

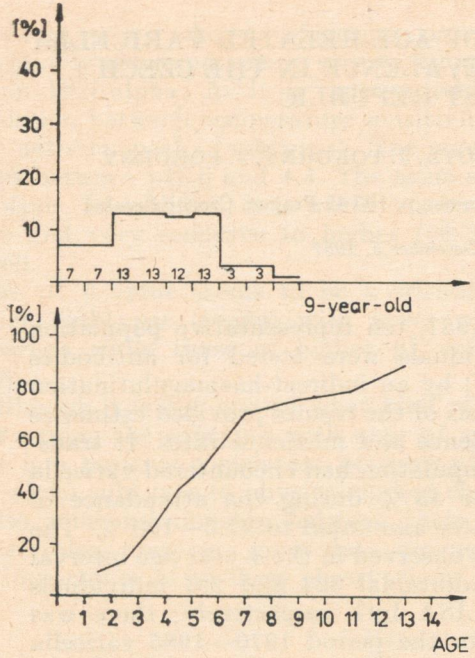

Fig. 1.
Varicella prevalence and incidence according to age groups
Indirect haemagglutination. Total of subjects tested: 2916. Incidence was estimated in terms of the difference between the percentages of seropositive children in every two consecutive years of age.

6—9 years, 499; 10—14 years, 237; 15—19, 224; in the adult age groups (5-year span each) the numbers of tested individuals varied between 107 and 62; the eldest age group, above 60, was represented by 104 sera. Radioimmunoassay (RIA) was used for testing 324 sera, a representative sample collected in the district of Beroun in 1977, and an enzyme-linked immunosorbent assay (ELISA IgG) was used to test 297 sera, a representative sample assembled at the district of Frýdek-Místek in 1985.

Serological tests. The IHA assay was described previously (Trlifajová *et al.*, 1973, 1974). Evidence for seropositivity was a positive reaction in serum diluted at least 1 : 8. The mean positive titre was 1 : 134.5. Sera were diluted 1 : 8—1 : 4096. The RIA used was also described previously (Trlifajová et al., 1979). Sera were diluted 1 : 10—1 : 10 240; the mean positive titre was 1 : 229.8. ELISA IgG was performed as it is used at the Parasitology Laboratory, IHE. Briefly, Kohinoor plates were coated with varicella-zoster virus (VZV) antigen or LEP-cell antigen (control), either diluted 1 : 400; if required, they were stored for up to several weeks in a humid chamber at 4 °C. The serum dilution range was 1 : 40—1 : 5 120. Incubation of antigen and serum at 37 °C in humid chamber lasted for 1 hr, that of the conjugate (SwAHu IgG-Px, Institute of Sera and Vaccines, Prague; dilution 1 : 8000) for 30 min. O-Phenylendiamine, 0.1 mol/l citrate buffer pH 4.0, and H_2O_2 as substrate, were added to detect peroxidase activity (15 min, 37 °C, in the dark). The reaction was stopped by adding 4 N H_2SO_4. OD was measured at 492 nm on a Dynatech photometer. Positivity: difference between reaction of VZV antigen and control antigen (used in first four serumdilntions) and in higher serum dilutions, reaction of the virus antigen only, equal to 0.200 of the absorption value. Seropositivity: a positive result in serum dilutions from 1 : 640; the mean positive titre was 1 : 2 384.

Results

In 1972—1981 ten serum sets collected from a total of 2 916 individuals of different age groups were tested by the IHA assay. Statistical analysis of the results provided a curve for age-related prevalence of varicella (Figs. 1 and 2).

According to the data obtained, the age-related seropositivity rates as an indication of past varicella infection were, during preschool and school ages (Fig. 1), as follows: 4 years, 33 %; 5 years, 45 %; 6 years, 56 %; 14 years, 90 %. Thus, varicella had been encountered by 45 % of the tested children at preschool age and another 45 % of children during school age. In the age group of 15—19-year-olds, seropositivity had reached 93.8 %, to rise to 97.5—100 % during adulthood (Fig. 2). No decrease in seropositivity rate or mean antibody titre was observed in the older age categories.

The age-related varicella incidence was estimated in terms of the difference in the percentage of seropositive children between each two consecutive years of age in the 10 population samples tested (Fig. 1). As Fig. 1 shows, the highest age-related incidence was found for the four-year interval from 2 to 6 years of age. Previous serological tests of one group only (Trlifajová *et al.*, 1980) had shown the highest number of new varicella cases in 2-year-old children. In individual epidemics, highest varicella incidence may apparently occur in a 1-year age interval of the 4-year age span indicated above.

In addition, two representative population samples were tested for control: 4 individuals from the district of Beroun by RIA in 1977 and 297 individuals from the district of Frýdek-Místek by ELISA IgG in 1985 (Fig. 2).

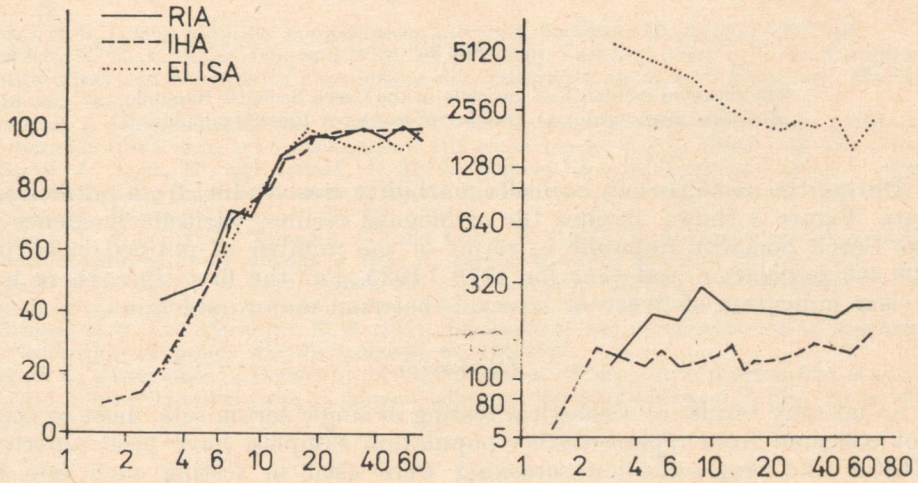

Fig. 2.

Varicella prevalence estimated by testing 3537 subjects by an indirect haemagglutination assay

Ten representative population samples, ELISA (one sample), and RIA (one sample); see Materials and Methods. The curve representing ELISA geometric mean titres reflects the marked difference between VZV antibody titres during convalescence after varicella and anamnestic titres and is conditioned by the maximal incidence of varicella in the low-age groups.

In the left: abscissa: age groups; ordinate: per cent positives.

In the right: abscissa: age groups; ordinate: geometric mean titre.

Although it was impossible, because of shortage of sera, to test the sera of any population sample by all the methods in paralell, the data obtained were, nevertheless, indicative of a high level of agreement. Good agreement was also obtained in an experimental simultaneous testing of 104 blood donors by ELISA and IHA (results not shown).

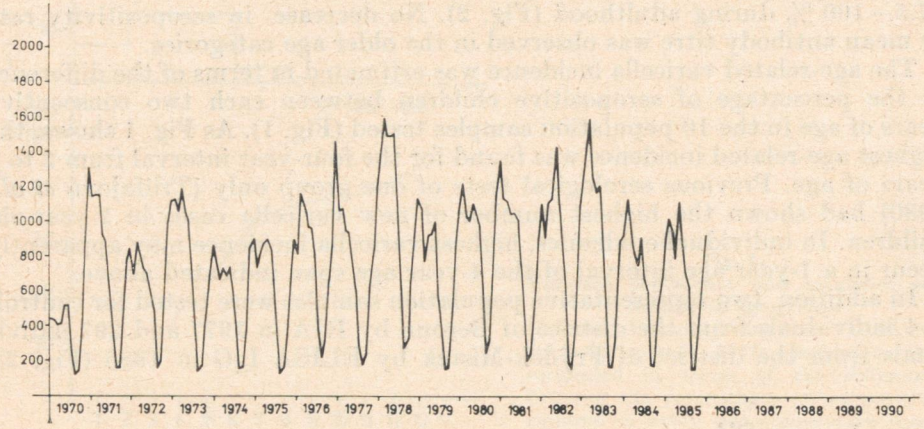

Fig. 3.

The reported incidence of varicella in the Czech Socialist Republic
Abscissa: years; ordinate: number of cases per 100 000 population

During the same period, varicella morbidity was studied from notification data. Figure 3 shows, besides the serological results, varicella incidence in the Czech Socialist Republic in terms of the number of notified cases per 100 000 population and year for 1970—1985. For the first time, there was a clear indication of five-year intervals between major epidemics.

Discussion

So far only results of serological testing of single serum sets, most of them not collected from representative population samples, have been reported. ELISA and single-dilution screening were used in testing such sets by Schneweis *et al.* (1985) and Muench *et al.* (1986). Other serological methods have been used by Tomlinson and Mac Callum (1970), Wentworth and Alexander (1971), Leventon-Kriss *et al.* (1978), Wong *et al.* (1978), Ozaki *et al.* (1980), and Gershon and Steinberg (1981). Testing a single set is liable to greater bias by the local epidemiological situation at the time and, of course, the smaller the set the greater the 95 % reliability interval. All considered, therefore, most of these studies do not show gross discrepancy with our results. However, our results do not confirm a decrease in VZV antibodies in the older age categories, which has sometimes been claimed, especially

in studies using the less sensitive method of complement fixation. In recent years, several detailed epidemiological studies on varicella incidence/prevalence have been published in association with the use of the live OKA varicella vaccine (Preblud, 1984, 1985, 1986). The present intention has been to provide a more accurate picture of varicella incidence and prevalence using laboratory methods.

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