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## Seroepidemiology of varicella-zoster virus antibodies among health-care workers and day-care-centre workers

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### SUMMARY

Inclusion of live varicella vaccine in the routine occupational health vaccination schedule requires knowledge of the natural immunity to varicella zoster virus (VZV) among high-risk occupations. This study aims were to evaluate VZV antibody positivity among health-care workers (HCWs) and day-care-centre workers (DCWs) and to assess its association with potential risk factors. Three groups of workers were tested for VZV antibody positivity: hospitals and community clinic HCWs ( $n=335$ ), DCWs ( $n=117$ ) and blue-collar workers as controls ( $n=121$ ). The total VZV antibody positivity was 94·4%. There was no significant difference in VZV antibody positivity among study groups. DCWs had the lowest VZV seroprevalence (90·9%, 95% CI 85·7–96·1) and controls the highest (96·6%, 95% CI 93·2–99·9). This high VZV antibody positivity suggests that no special occupational measures are indicated in health-care or day-care occupational settings in Israel. On-going monitoring of the natural immunity to VZV is necessary to detect trends over time.

### INTRODUCTION

Although adults account for only 5% of all cases, they make up more than half of the deaths due to varicella (chicken pox) each year in the United States. As with children, the majority have no identifiable risk factor for severe disease [1]. Varicella in adults is often associated with a higher frequency of pneumonia, encephalitis and death. Although infection with VZV generally results in lifetime immunity, the virus persists latently in the sensory nerve ganglia and may reactivate, causing zoster in approximately 15% of adults [2].

Before the varicella vaccination programme was introduced in the United States, varicella was responsible for more than 100 deaths and more than 10 000 hospitalizations annually. According to the American Academy of Pediatrics (AAP) guidelines, published in January 2000, health- and child-care workers who do not have a history of varicella, should be tested for VZV antibody, and those who are VZV antibody negative should be immunized unless they have contraindications [3]. Health- and child-care workers should be considered immune from varicella infection after receiving their second dose of varicella vaccine and need not be excluded from work if subsequently exposed to VZV infection. Although morbidity has substantially declined due to this policy, there has been a recent report of an outbreak of varicella in a day-care centre despite vaccination [4]. The outbreak included 25 cases and 17 cases (68%)

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occurred in vaccinated children. In this outbreak, the effectiveness of the varicella vaccine was only 44%. This finding raises concerns that the current vaccination policy may not protect all children and staff. In deciding whether or not to include a vaccine in the routine vaccination schedule, knowledge of the natural immunity to the disease is fundamental. To date, no seroprevalence study has been carried out in Israeli health- and child-care workers to enable an evidence-based decision on the need for VZV vaccination primary prevention of varicella infections.

Since the epidemiology of varicella varies worldwide, adopting foreign prevention policies may not always be applicable. In addition, reliable data on the local epidemiology of varicella in Israel are limited. Data from countries in Europe with statutory reporting of chickenpox (e.g. Northern Ireland, Spain, Italy and Greece) are restricted in terms of compliance or population size. Neither Canada nor the United States collect notification data on a national scale with reliable completeness [5]. In countries without varicella notification process, some cases may not be seen by family doctors and many cases go unreported. Thus, local data on the epidemiology of VZV is essential for the establishment of local evidence-based decision making regarding vaccination against the disease.

A study of 900 samples which were taken from young adult Israeli army recruits showed that 98% tested positive for VZV antibodies [6]. These high natural immunity rates raise questions about the applicability of the AAP recommendation to Israel. The purpose of the current study was to better evaluate the proportion of health- and child-care workers who are susceptible to VZV and to assess possible occupational risk or other factors associated with susceptibility to the virus. The study results will permit evidence-based decision making on the proper prevention policy for VZV in Israel.

## METHODS

### Study population

Serum samples were obtained from three groups: health-care workers (HCWs) in a tertiary medical centre and in community clinics, day-care-centre workers (DCWs), and blue-collar workers (non-HCW and non-DCW).

We randomly obtained serum samples from 335 health workers. Of these, 179 were employed in the

largest children's hospital in Israel and one of the largest medical centres in Israel and 156 were HCW employed in 42 different community clinics belonging to the largest HMO-like organization in Israel [7].

We tested 121 serum samples which were previously obtained from a random sampling of staff in 37 day-care centres [8]. Serum samples which had previously been collected from a group of blue-collar workers that consisted of 118 factory workers, blood donors and women in maternity were used as control specimens [8].

The local and national Ministry of Health ethics committees approved the study. Written informed consent was obtained before completing the questionnaire and obtaining venous blood samples.

### Questionnaire

A questionnaire was completed by all workers. It contained data on sociodemographic and occupational variables potentially associated with exposure to infections, including demographic and socioeconomic characteristics: age, gender, nationality (Jewish or Arab), birthplace, year of immigration to Israel, current residence (rural or urban), number of children, number of siblings, current persons per room and during childhood. Other data collected related to occupational characteristics (for DCWs and HCWs only): type of occupation, age of children under workers' responsibility and duration of professional experience.

### VZV antibody assays

Serum samples were blindly analysed for VZV IgG with a commercial ELISA kit (Panbio, Columbia, MD, USA) according to the manufacturer's instructions. The test had a sensitivity of 99.76% and a specificity of 98.75% [9].

### Statistical analysis

The  $\chi^2$  test was used to analyse differences between proportions when categorical variables were applied. Confidence intervals (CIs) were calculated according to formula presented by Newcombe et al. [10]. The Mantel-Haenszel test for trends was used to evaluate statistical significance in univariate analyses. Odds ratios (ORs) and 95% CIs of immunity to varicella were derived from logistic regression models. The analysis was conducted by means of SPSS 10.0 for Windows (SPSS Inc., Chicago, IL, USA).

Table. VZV antibody positivity among hospital and community-clinic health-care workers and day-care-centre workers, according to age and gender

Age group (years)	Females		Males	
	<i>n</i>	Seroprevalence (%)	<i>n</i>	Seroprevalence (%)
<26	44	90.91	7	100.00
26–35	104	95.19	31	100.00
36–45	122	95.90	37	100.00
46–55	108	88.89	38	100.00
>55	66	90.91	11	100.00
Total ( <i>n</i> =444)	444	92.79	124	100.00

## RESULTS

The total study sample size was 573 persons, comprised of 335 HCWs (physicians and nurses), 121 DCWs and 117 controls. A total of 541 participants (94.4%) were VZV antibody positive. There was no observed association between age and VZV antibody positivity. A significant difference ( $P < 0.01$ ) was, however, noted between genders as all of the VZV antibody negative participants ( $n = 32$ ) were female (Table).

There was no significant ( $P = 0.146$ ) difference in the observed seroprevalence among study groups, as the lowest rate was recorded among the DCWs (90.91%, 95% CI 85.71–96.11) and the highest among the control group (96.58%, 95% CI 93.24–99.92) (Fig. 1).

Of all variables examined, only years of education showed a significant ( $P = 0.03$ ) association with VZV immunity as every year of study increased the probability of positive results by an OR of 1.22 (95% CI 1.02–1.47) (Fig. 2). Assuming one VZV antibody-negative male case for statistical analysis, gender was associated with immunity to VZV as females present higher susceptibility (OR 0.11, 95% CI 0.01–0.95). No significant differences in immunity rates were found among HCWs, DCWs and controls. Other sociodemographic variables, nationality, number of siblings or number of children showed non-significant association with VZV immunity.

## DISCUSSION

The high (94.4%) natural immunity to VZV found in the current study is similar to that in a recently published seroepidemiological study of 333 employees at

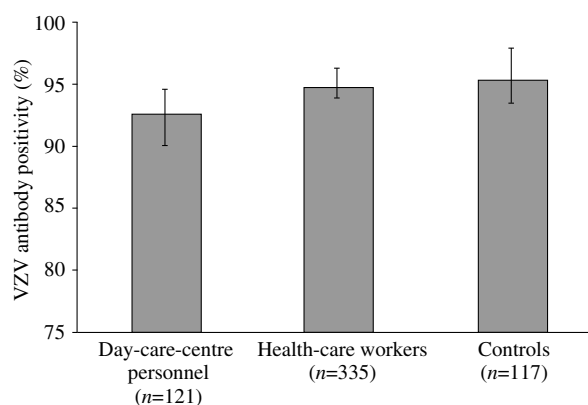


Fig. 1. Age- and gender-adjusted VZV IgG seroprevalence (and 95% CI) among different occupations in Israel.

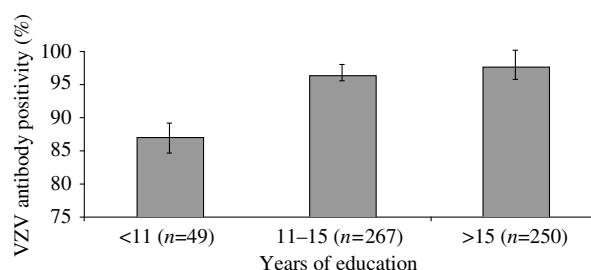


Fig. 2. Age- and gender-adjusted VZV IgG seroprevalence (and 95% CI) among health-care workers according to years of education.

Padova University Hospital (Italy) which found that 97.9% of the workers were positive for VZV antibody [11]. Similar VZV antibody positivity (96%) was reported amongst 365 applicants for nursing training enrolled at an occupational health department in the NHS in Scotland [12]. The authors stated that screening for susceptible workers using past clinical history compatible with VZV infection would have missed 40% of those possibly susceptible to VZV on the basis of the ELISA IgG test. Thus, although screening those with a negative history seems more cost-effective, it is still problematical.

The current ACIP (Advisory Committee on Immunization Practices) recommendations regarding VZV vaccination recommend VZV vaccination for personnel known, or likely to be, susceptible to varicella and who have close and prolonged exposure to infectious HCWs or patients, particularly those at high risk for complications, such as pregnant or immunocompromised persons [1]. Although the outbreak described by Galil et al. [13] raises concerns regarding the possibility of a varicella outbreak among vaccinated persons, because of the high prevalence of naturally immune

workers, we do not recommend an active varicella vaccination campaign of all HCWs and DCWs.

The high VZV antibody positivity found amongst all occupational groups did not allow the detection of any increased occupational exposure to the virus and suggests that no special occupational measures should be taken in paediatric or child-care settings in Israel.

The single factor directly associated with VZV immunity was years of education. One of the speculations to explain this is the effect of socioeconomic status. For example, persons of high socioeconomic class that were previously reported to have a significantly lower VZV antibody prevalence at a young age, were exposed later in life and, therefore, present higher rates at adulthood [14], while persons of lower social class have lower serum antibody levels. We could not support this speculation by other socioeconomic variables associated with socioeconomic status, such as number of siblings.

Studies in the United States have suggested the yearly cost for infection control varies from US\$41500 to US\$55934 and that the costs to control individual outbreaks vary from US\$9100 to US\$19000 [15]. Similarly, a 5-year prospective study from the United Kingdom estimated the annual hospital expense on VZV control to be £13204. The largest components of this total cost were the exclusion of staff from work (46%), prophylactic varicella-zoster immune globulin treatment (30%) and patient isolation (15%) [16]. More data are needed regarding the total impact of such events in Israel at paediatric and adult hospitals in primary-care as well as tertiary-care settings. Similar to other infectious diseases, the epidemiology of VZV infection is open to changes with time. In addition there is no currently available evidence of an increase over time in the rate of breakthrough disease that would suggest waning immunity after vaccination. We, therefore, recommended that seroprevalence surveys among potentially exposed populations should be repeated to monitor VZV immunity trends in the future.

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