

## SHORT REPORT

# Changes in age related seroprevalence of antibody to varicella zoster virus: impact on vaccine strategy

G Kudesia, S Partridge, C P Farrington, N Soltanpoor

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**Aim:** To study changes in the seroprevalence of varicella zoster virus (VZV) antibody over the past 25 years with a view to determining the target age group for any future vaccination strategy.

**Methods:** Stored sera collected from different age groups over a period of 25 years were tested by a commercial VZV IgG enzyme immunoassay at a four year time interval. Data were analysed by logistic regression to investigate the evidence for changes in incidence and hence seroprevalence over that period.

**Results:** There was a significant rise in VZV antibody prevalence in the 1–4 year age group during the study period.

**Conclusions:** A universal childhood VZV vaccination strategy will need to take account of the increase in incidence of VZV infection in children under the age of 4 years; hence, the suggested target age would be between 12 and 18 months—soon after the disappearance of maternal antibody.

It has been suggested that the pattern of primary infections with varicella zoster virus (VZV) has changed in recent years, with an upward shift in age distribution. Monitoring of cases reported by “spotter” general practices has shown a significant increase in both the absolute number and the proportion of cases in those over 14 years over the past 20 years.<sup>1</sup> A review of notifications in a Scottish health region for 1988–92 showed that 24% of cases were in patients aged 15 or over.<sup>2</sup>

The epidemiology of VZV has important implications for future vaccine strategies. This study of age related VZV seroprevalence over the past 25 years was undertaken to ascertain whether the increase in reported cases of chicken-pox in adults results from the decrease in numbers of immune adults as reflected by a change in seroprevalence.

“The epidemiology of VZV has important implications for future vaccine strategies”

## SUBJECTS AND METHODS

The sera for our study were drawn from a series of independent cross sections of anonymised patients divided into the following age groups: 1–4, 5–9, 10–19, 20–29, and 30–39 years, from whom blood samples were submitted for routine tests during the months of June and July each year over the past 25 years and an aliquot stored at –20°C. An upper age limit for testing of 39 years was chosen because > 95% seroprevalence rates in over 40 year olds<sup>3</sup> would not have allowed us to detect changes in seroprevalence with the small numbers of samples available for testing. The children under 10 years old were subdivided to distinguish between preschool and school age children. Samples from infants aged less than 1 year were excluded because it would not be possible to distinguish passively acquired maternal antibody from that resulting from infection. As far as possible within the limitations of available sera, specimens were tested from each age group at four yearly intervals with substitutions from preceding or following years if necessary.

A total of 1530 sera were tested by a commercially available VZV IgG assay (Bio-Stat Diagnostic). Samples giving an equivocal result by the manufacturer's criteria were repeated. Those giving a repeat equivocal result were excluded from the analysis.

## RESULTS

Four samples giving a repeated equivocal result by the manufacturer's criteria were excluded from the analysis. Table 1 shows the seroprevalence of VZV, stratified by age cohort, for each of the sampling years. For all years the seropositive rate in subjects older than 20 years exceeded 90%.

We analysed the data in table 1 by logistic regression, with the aim of investigating the evidence for changes in incidence over the period. If there were no changes in incidence, one would expect the prevalence to remain the same within age groups. Therefore, we estimated the trends in prevalence over time within each age group. Our model confirms the fact that

**Abbreviations:** CI, confidence interval; OR, odds ratio; VZV, varicella zoster virus

**Table 1** Age related varicella zoster virus antibody prevalence

Age of cohort (years)	Year of survey						
	1966	1970	1974	1978	1984	1988	1992
1–4	1/14 (7)	2/46 (4)	11/54 (20)	3/12 (25)	5/21 (24)	8/34 (24)	37/73 (51)
5–9	18/32 (56)	24/37 (65)	23/43 (53)	9/30 (30)	24/43 (56)	9/26 (35)	23/36 (64)
10–19	4/6 (67)	40/40 (100)	23/28 (83)	37/47 (79)	31/39 (79)	51/58 (88)	44/46 (96)
20–29		48/49 (98)	66/67 (99)	45/48 (94)	43/48 (90)	50/55 (91)	49/53 (92)
30–39		31/31 (100)	41/45 (91)	46/47 (98)	22/30 (73)	49/52 (94)	52/54 (96)

Figures in parenthesis are percentages.

prevalence increases significantly with age, at least to age 19, representing the acquisition of infection ( $p < 0.0001$ ). We found significant differences in prevalence trends over time between age groups ( $p < 0.0001$ ). These differences are primarily attributable to a sharp increase in prevalence in the 1–4 year age group (odds ratio (OR), 1.09; 95% confidence interval (CI), 1.05 to 1.13). Other changes are less clear. Prevalence in the 20–29 year age group declined marginally (OR, 0.93; 95% CI, 0.88 to 1.00) with no significant changes in other age groups.

## DISCUSSION

A previous study by Joseph and Noah<sup>4</sup> had reported an increase in the incidence of chickenpox in the 0–4 year age group. They reported that although before 1982 the highest incidence of clinical chickenpox was in 5–14 year olds, subsequently the highest incidence of clinical chickenpox shifted to the 0–4 year age group. Our study is consistent with their findings and shows a pattern of increasing prevalence of chickenpox in the 1–4 year age group, which was noticeable during the latter half of the 1980s. This implies that the incidence has increased in children under the age of 4 years. A recent study from the USA<sup>5</sup> also reports varicella incidence rates in preschool children that were two to 2.5 times higher than those reported previously. This is probably because of exposure at preschool age in crèches and nurseries. It has been reported that 14% and 16% of children attending day care centres in the USA and France develop chickenpox, respectively.<sup>6,7</sup>

“Approximately 6% of women of childbearing age are probably not immune to varicella zoster virus”

The evidence for changes in incidence in older individuals is less clear cut: a decline in prevalence in the 20–29 year age group, combined with constant prevalence in the 30–39 year age group, suggests an increase in incidence in persons over 30. However, this needs to be confirmed by further serial seroprevalence studies, with larger sample sizes. The VZV seroprevalence of 94% in over 20 year olds is consistent with other work,<sup>3</sup> and indicates that approximately 6% of women of childbearing age are probably not immune. The risk of infection may be greater for susceptible parous women, in view of the increased incidence in under 4 year olds, which would in turn lead to an increased risk of exposure to infected children in the home.

At present, 50% of all varicella zoster immunoglobulin issued for passive prophylaxis is for pregnant contacts and neonates.<sup>8</sup> A live, attenuated safe and effective VZV vaccine is available.<sup>6</sup> Targeting women of reproductive age group, especially in a post partum programme, may be an effective

## Take home messages

- There has been a sharp increase in the prevalence of chickenpox in the 1–4 year age group over the past 25 years
- A universal childhood VZV vaccination strategy will need to take these changes into account; hence, vaccine should be targeted at an age group of between 12 and 18 months, soon after the disappearance of maternal antibody

vaccination strategy.<sup>9</sup> If VZV vaccine were to be introduced as a universal childhood vaccine in the UK, then the increase in prevalence in the 1–4 year age group seen in our study would suggest that, as in the USA, for the vaccination programme to be effective,<sup>6</sup> vaccine should be targeted at an age group of between 12 and 18 months; that is soon after the disappearance of maternal antibody.

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## Authors' affiliations

**G Kudesia**, Public Health Laboratory, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK

**S Partridge, P Farrington, N Soltanpoor**, Public Health Laboratory Service Statistics Unit, 61 Colindale Avenue, London NW9 5EQ, UK

Correspondence to: Dr G Kudesia, Public Health Laboratory, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK

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