

## Varicella prevention – a lifelong and challenging affair

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Varicella, or chickenpox, is a common infectious disease that is caused by varicella zoster virus (VZV), a double-stranded DNA alpha-herpesvirus. VZV is transmitted from humans to humans by droplets [1, 2]. It is a widely held belief that varicella is a harmless childhood disease. While this is true for the majority of cases, there are noteworthy and serious exceptions. First, varicella does cause serious complications in approximately 1 of 1000 affected children [3] and up to 10-fold more in adults [2]. Second, in the western world, about 5% of children escape VZV infection (especially those who grow up without siblings) and, in the absence of immunisation, therefore remain susceptible [4]. They will more likely acquire varicella on the first occasion of VZV exposure, which is frequently in adulthood when they have become parents and their own child comes down with varicella. This should be avoided, as the risk for complications, primarily secondary bacterial infections and pneumonia, increases with age at acquisition of varicella [2].

Effective live-attenuated vaccines against varicella are available, but only a few countries have established general varicella childhood immunisation programmes [5]. In contrast, many countries, including Switzerland, recommend varicella catch-up immunisation for adolescents and adults with a negative or uncertain disease history for varicella or without proof of immunity by means of VZV-IgG serum antibody analysis. Of note, a positive varicella disease history is highly reliable [6].

With this background, Freuler and colleagues set out to study VZV-IgG seroprevalence in adults seeking travel advice at the travel clinic of the University of Zürich, Switzerland [7]. Importantly, they selected their study cohort based on lack of a reliable varicella disease history and they identified 1757 such individuals by taking their history during an almost 7-year study period. Incidentally, we unfortunately do not learn how many of their clients during the same study period did have a reliable history – in other words, what proportion of such clients fall into the risk category for varicella. Of these 1757 individuals, 91% were VZV-IgG positive and can therefore be considered immune. This results in a negative predictive value of only 9% and translates to a number needed to immunise of 11. This number is substantially lower than those which we and others obtained in adolescents [6, 8]. For understandable reasons, Freuler et al conclude that adults without a reliable

varicella disease history should all be tested for VZV-IgG to identify those few seronegative individuals who qualify for the two-dose vaccination schedule. However, as a note of caution, this two-step strategy requires compliance of the patients as they will need to return to the clinic for immunisation if seronegative, whereas immediate initiation of the immunisation series based solely on history would get rid of the compliance issue, at least for the first of the two doses. The disadvantage of missing the opportunity to immunise immediately needs to be weighed against the advantage of avoiding superfluous immunisation in seropositives, and although this does not confer an increased risk of side effects (live-attenuated viruses will rapidly be neutralised in the presence of pre-existing specific IgG antibodies), costs are considerable. A further argument brought forward by the investigators supporting their two-step approach regardless of age is the observation of VZV susceptibility in individuals older than 40 years. This is the age threshold for the immunisation strategy in Switzerland as it is assumed that hardly any adult beyond that age would still be susceptible to varicella. In accordance with this assumption, the great majority of clients with Swiss nationality among this study population, selected on the basis of varicella disease history, were VZV-IgG seropositive, whereas amongst those of South Central, South Eastern or Eastern Asian origin approximately 35% were seronegative. Several of those individuals were older than 40 years.

A major limitation of this study, which is acknowledged by the authors, is the lack of follow-up so that we remain unclear about the success of the intervention in terms of following the advice for varicella immunisation in those travellers who were VZV-IgG negative.

Where shall we go from here and which conclusions can be drawn? Although risk-based varicella immunisation recommendations are laudable, they are prone to fail, by and large due to mal-compliance, ignorance and complexity. It is my strong belief, supported by scientific evidence [9–11], that general varicella childhood immunisation programmes are by far the most, if not the only, successful strategy to better control varicella in general and to protect those who cannot be immunised themselves (such as immunocompromised patients and seronegative pregnant women). It is time for saving money spent for VZV-IgG serology testing and rather to invest it in vaccinating our children against varicella.

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