VOLUME 59 • JANUARY 1977 • NUMBER 1

Pediatrics

COMMENTARY

Protection against varicella

Asano and his colleagues have reported rather remarkable preliminary observations of experiments in which children were immunized against varicella with a live virus vaccine.[1] Before efforts are made to confirm and expand these observations, however, we must consider the potential advantages and disadvantages of such a vaccine.

It is well to remember that immunization with live virus vaccines involves infection of individuals with live viruses which are intended to produce less morbidity than the natural illness while inducing immunity similar to that following natural infection. In this instance the infection is produced with varicella-zoster (V-Z) virus.

Of the numerous experiments using vesicular fluid virus to immunize against varicella which have been reported during the past 150 years, one of the more notable was that reported by Bruusgaard.[2] He observed that when susceptible children were inoculated with zoster vesicle fluid many developed varicella. This confirmed the epidemiologic observations, reported by Bokay at the turn of the century, that zoster and varicella are caused by the same virus.[3] It is now generally accepted that initial exposure to V-Z virus causes varicella. Following clinical recovery, virus infection is believed to persist in a latent form, *i.e.*, in the absence of clinical manifestations. Decades following varicella, for yet unexplained reasons, the latent virus may be activated to produce the clinical illness we recognize as zoster. Our knowledge of why latent virus becomes activated or what controls virus latency is rather rudimentary at the present time.

In assessing a V-Z virus vaccine, data are required to evaluate its effects on zoster as well as on varicella. One must be able to predict or provide evidence that infection with the vaccine virus will result in less frequent and less severe zoster than natural infection. As the time period between onset of varicella and zoster may be several decades, the results of the experiments evaluating the effect of a V-Z vaccine on zoster may not be available until most of us have passed on. "Markers," or characteristics, have been distinguished for some other viruses that identify them as being suitable candidates for vaccines. Unfortunately, markers have not been recognized which can be used to predict how a given strain of V-Z virus will behave with respect to causing zoster.

In contrast to zoster which produces considerable morbidity, chicken pox in normal children is usually a mild disease. During the past decade there have been only approximately 130 deaths per annum reported due to varicella. Although the exact causes of these deaths cannot be determined, it is likely that the vast majority occurred in certain high-risk groups. In contrast to the

findings in normal children, varicella can be quite severe in adults and children with malignant diseases or those who are immunocompromised. Morbidity in these high-risk groups could probably be diminished by a well-organized program of passive immunization.[4] The mortality and morbidity produced by varicella in normal children could hardly justify a major effort to eradicate varicella.

One of the possible results of the routine use of a V-Z vaccine in infants and children might be to postpone infection from childhood when it is a mild illness to adulthood when it may be quite severe. This would occur if immunity produced by immunization of infants and children were to wane during adult life or if the epidemiology of the disease were to be changed by routine immunization. It would be most unfortunate if vaccine-induced immunity were to diminish during the third and fourth decades when adults might then be exposed to their children with varicella. Efforts to "eradicate" varicella might decrease the chances of contracting varicella during childhood. Those who were not immunized or infected as children would then become susceptible high-risk adults. At the present time it is estimated that only about 4% of our urban adult population is probably susceptible to varicella.[5]

Could one use this vaccine for protection of immunocompromised patients at high risk? Who would be willing to find out? The Japanese group has immunized some children, who might be considered at high risk, without untoward effects.[6] It is clear, however, that "immunocompromised" describes a spectrum of disability. Most children who are receiving steroids[7] or patients with leukemia,[8] although "immunocompromised," recover uneventfully from varicella. Although most high-risk children who have received zoster immune globulin have been protected against varicella, at least two have succumbed to varicella. It may be inferred that response of "immunocompromised" children to infection with live V-Z virus vaccine would vary. Unfortunately, the determinants of host response to V-Z infection are poorly understood at this time. There are no tests which one could use to predict which "immunocompromised" children could safely be immunized. One might assume, moreover, that even some so-called "normal" children might react adversely to immunization with a live V-Z vaccine. In the case of polio vaccine, unfortunately, some children were revealed to be "immunocompromised" only after they were paralyzed by infection with live attenuated poliovirus vaccine.

A judgment must now be made as to whether we should embark on an effort to further evaluate this live V-Z vaccine. Should we support with our tax monies and could we sanction morally a trial involving thousands of children? In weighing the benefits of a V-Z vaccine against the possible hazards, I would judge that even additional clinical trials at this time would be ill-advised.

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