

“Let’s Talk” Teleconference
November 19, 2002

Varicella – Barbara Watson MD (Assoc. Professor of Pediatrics –
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(Note: The conference notes were abstracted by J. Aronson MD and reviewed by Dr. Watson prior to posting on website.)

Varicella disease and vaccine efficacy statements derive from:

- CDC statements;
- 7 year surveillance data from two Varicella Active Surveillance Programs: Philadelphia and Los Angeles (Antelope Valley);
- On-going research.

Surveillance data shows that varicella vaccine use i) decreases varicella disease by 85% in 1-4 year old children and ii) provides herd immunity throughout the community.

Questions of clinical concern from surveillance programs:

1. Is a clinical history of varicella at any age a reason to NOT vaccinate with varicella vaccine? In particular, are mild disease and disease before age 1 year reasons to not immunize with VARIVAX?
2. Are there special circumstances even with confirmed disease that one might choose to vaccinate with varicella vaccine?

Comments:

- CDC recommends immunization of all susceptible individuals defined as a positive history of exposure without evidence of prior disease and/or immunization.
- Validation of prior clinical varicella disease is difficult. 20% of physicians were not certain that the observed clinical rash was varicella. Let alone the number of phone diagnosis – LaRussa study in NEJM (August 9, 2001) demonstrated ~30% wrong diagnosis over the phone
- Measles (rubeola) may be a good analogy to the challenge of varicella validation. The current clinical recommendation is to obtain IgM rather than depend upon rash to confirm diagnosis. This technique is not currently recommended for varicella. But the changes in epidemiology will eventually make it so
- Note - Other rash producing illnesses include: Coxsackie, scabies, adenovirus, etc.
- Individuals residing in the following locations should be immunized during outbreak situations unless prior severe disease is documented:
 - Homeless Shelter
 - Prison

- Household contacts (note – a recent death of a 4 month old child in Lancaster Co. was due to exposure to 6 y/o. sibling with disease who was allegedly not immunized because of prior clinical disease.)
- Schools

Miscellaneous Issues:

Children <1 year of age have:

- Increased likelihood of getting clinical zoster <10years of age.
- A varicella re-infection rate (mild disease <50 lesions) of approximately 10%
- The reasons for the above observations require further study – if interested in participating in this type of surveillance study, contact B. Watson.

Varicella vaccine immunity:

- Requires serum antibody + cell mediated immunity.
- Immunized individuals with varicella ELISA levels of 5 or > have less breakthrough disease
- Immunity duration – Japanese clinical trial data: > 25 years
- US data: 10-15 yrs with high antibody titers persisting. Cell mediated immunity is not measured re: difficult technique.
- Varicella anamnestic memory exists.
- Natural disease incubation period is 21 days; vaccine anamnestic memory responds 3-4 days.

Subgroups of individuals with poorer response to varicella vaccine:

- Adults: therefore 2 dose at older than age 13 yrs. is necessary to get sero-conversion.
- Asthmatics – have an increase in breakthrough Varicella disease based upon surveillance data from parents. However, the asthma patient's current medication status is unclear from the studies. A parent may answer, "Yes" to disease; however, the child may not be on asthma medication currently. Therefore, prior steroid use is not measured. (Note – all poor response varicella vaccine studies related are related to parenteral, not inhaled or topical steroids). A two-dose varicella vaccine schedule is NOT routinely recommended for children with asthma. 10% of the birth cohort will develop asthma at some time.
- Nephrotic syndrome = 2 dose routine recommended if the patient is not currently immunosuppressed.
- HIV = 2 dose routine recommended if the patient is not currently immunosuppressed.

Varicella immunization, varicella disease breakthrough and rash post vaccine administration:

- Breakthrough varicella disease is more common if immunized at 12-15 months of age compared with >15 months of age. However, children immunized at 12 months of age have a good antibody response. Therefore:
 - 2 dose varicella vaccine routine – NOT NOW!!

- Clinicians should NOT change the timing of initial vaccination (currently at 12 months of age) since vaccine coverage rates drop significantly as the child gets older (per CASA studies re: DTaP#4).
- Breakthrough varicella disease is mild.
- Optimum community protection against varicella disease requires high herd immunity
- Varicella vaccine virus is attenuated. The attenuated varicella virus does not grow well in humans. Reference – Paul Offit tape on “How vaccines are made”. For information about the tape, contact P. Offit MD at CHOP.
- Post vaccine administration rash occurs rarely:
 - 1-4% injection site (day 5-7)
 - 1-2% generalized rash (Note – there is no documented outbreak in a child care or school setting from a vaccine-associated rash, hence child can attend school.)
- And in contrast, Only 3 cases of varicella vaccine transmission have been documented from a household setting.
- Health care workers receiving varicella vaccine should be allowed to return to work. However, if rash appears, the workers should either be furloughed or re-located. The transmission of attenuated virus is rare.
- Note: Wild varicella virus attack rate is 87%; compare with 1-4% for vaccine virus rash.
- All childcare workers should be vaccinated with varicella vaccine; the literature documents childcare outbreaks due to an infected worker.
- Break-through rash
 - Occurs >42 days after immunization
 - Median interval breakthrough = children age 2-3 years
 - No increase in % breakthrough as children get older
 - Incidence = 2%;
 - 2 dose varicella vaccine studies yielded higher titers and decrease clinical disease breakthrough
 - Physician should see child in office to confirm that it is varicella breakthrough
 - Contact B. Watson for information on varicella confirmation techniques.
 - Surveillance project is working with 25 Philadelphia offices to get lesion scraping + acute IgG and IgM and convalescent IgG's
- Varicella vaccine should not be given to children less than 1 year of age:
 - The vaccine is licensed for children > 1 year of age.
 - Clinical trials data re: maternal antibody compromise the vaccine take, and showed that 85% of mothers of children < 1 year of age have titres that would not block vaccine.
 - Protect a child <1 year of age exposed to clinical disease with Acyclovir rather than off-label use of vaccine.

MMR-V: Efficacy? When?

- Probably less breakthrough disease because it will be given on a 2 dose schedule
- Current MMR-V product in US testing is frozen.

- Release date: ???? FDA has data. Issues remain: Clinicians do not want frozen product re: risk of measles vaccine failure with frozen vaccine.
- Dose timing – Finland has eradicated measles with 2 dose routine given 1 month apart!! This is not a current US recommendation.
- A refrigerator stable vaccine exists – data with FDA; Italy/France using refrigerator stable vaccine
- Note: Simultaneous vaccine can be given e.g. Comvax, Tetramune, MMR2 at the same time as varicella vaccine, per package insert. The pharmacokinetic studies confuse individuals since they show a decrease in VZV titers. However, the VZV titers remain within the protective bell-shaped curve of when VZV was given on its own.

Varicella vaccine and shingles:

- Varicella vaccine (live, attenuated) administration cannot treat shingles.
- Killed varicella vaccine trial – 60,000 individuals > age 50 years in VA study, placebo controlled and still blinded. End point is to show no shingles after varicella vaccine. Pilot studies suggest that killed varicella vaccine may be used to prevent shingles. There is no US recommendation for this at present.
- Varicella vaccine will prevent shingles long term. The challenge is obtaining sufficient community coverage. Note: Varicella vaccine coverage in North and South Dakota is only 40%.
- Varicella vaccine does not cause shingles. In cases where varicella virus was recovered, 80% of individuals had a history of natural disease < age 1 or early in life and wild virus was recovered; in 20% individuals with zoster only– wild virus recovery only
- Treat shingles like varicella.
- Shingles can start varicella outbreak. Not in textbooks. However, household setting, homeless shelter, schools, jails have documented outbreaks

Pregnancy and varicella disease and vaccine:

- ACOG and Varicella Active Surveillance Projects are currently reviewing NHANES serology; Nationally, 95% of Caucasian women are immune by history;
- Clinical study is underway with varicella serology
- Adult/teen Health – varicella vaccine should not be administered in pregnant women;
 - Immunize post-partum, no pregnancy for 1 month (CDC says 3 mo.)
- Varicella Registry – no teratogenicity in pregnant women exposed to child immunized with Varicella vaccine.