

Today, I will be discussing the varicella vaccination program, highlighting the many success and outlining some of the challenges.

As you can see in this slide, the varicella vaccination coverage for children 19-35 months of age has increased progressively over time from 26% in 1997 when the National Immunization started asking about varicella vaccination, to 81% in 2002. The vaccination coverage, however, varies by state with coverage ranging from 59 to 91%. Our goal is to reach > 90% coverage for this age group by 2010.

Many states have implemented requirements for varicella vaccination for child care or school entry as recommended by the advisory committee on immunization practices (ACIP).

By September 2003, 39 states implemented childcare or school entry requirements for varicella vaccination. 11 states have childcare, elementary, and middle or high school entry requirements, 20 states have childcare and elementary school requirements, 5 states have requirements for childcare only, and 3 states have only elementary school requirements.

This slide shows monthly varicella cases (white bars) from 1995 to July of 2003 in Antelope Valley, CA. one of the varicella active surveillance sites. As you can see, the number of cases declined dramatically over time. The decline started in 1999 and has continued since. By mid 2003, there was about a 90% decline in varicella disease, compared to 1995. The decline is associated with an increase in varicella vaccination (shown in red) that ranged from about 40% in 1997 to about 87% in 2002 for children 19-35 months of age.

This slide shows varicella disease reduction by age groups in the two varicella active surveillance sites (Antelope Valley, Ca and West Philadelphia, Pennsylvania). Over all, there was about 85% disease reduction in both sites comparing cases in 2002 to 1995. The highest decline at about 90% in both sites occurred among children 1-4 and 5-9 who are receiving most of the vaccine. Infants less than one year of age who are not eligible for vaccination, and adults over 20 years of age, who are not receiving a lot of the vaccine also experienced declines in varicella disease, indicating herd immunity.

The pattern of disease reduction was also seen in passive surveillance. Here we show data from 4 states that report to the National Notifiable Disease Surveillance System. The 4 states experienced reduction in varicella cases in 2002 compared to average cases in 1993-1995 ranging from 65% in Illinois to 85% in Texas. These declines corresponded to vaccination coverage among children 19-35 months of age, ranging from 70% in Illinois to 83% in Texas.

In addition to declines in varicella incidence, varicella hospitalizations also declined. Data from the varicella active surveillance project showed that the annual varicella hospitalizations rates declined from about 2.5 per 100,000 population in 1995 to less than 1.00 per 100,000 population in 2002. (60%)

This graph shows the number of varicella deaths in the US from 1990-2001. Before vaccine licensure, there was an average of 107 death each year. Starting in 1999, we saw a dramatic drop in number of varicella deaths, consistent with incidence data. In 2001, there was only 26 varicella deaths, one fourth of the average annual number of deaths before vaccine licensure.

This table summarizes the reduction in varicella age-specific mortality rates in 2001 compared with the average rates for 1990-1995. Overall, for all ages there was a 78% reduction in mortality rates in 2001 compared with the average rates in 1990-1995. Children aged 1-4 years and 5-9 who receive most of the vaccine had a 100% reduction and 94% reduction respectively. Infants <1 year, who are not eligible for vaccination, and persons 20-49 years, not receiving a lot of the vaccine experienced over 80% mortality reduction. Finally, persons aged 50 years and older had a 28% reduction, however, some of these may be zoster deaths. If we excluded adults aged 50 years and older, the overall reduction in mortality in 2001 compared with 1990-1995 increases to 92%.

In summary, with about 80% vaccination coverage nationally among children 19-35 months of age in 2002, varicella cases have declined by over 80% in both active and passive surveillance. This was also associated with declines in varicella hospitalizations and deaths.

Now, I will discuss varicella vaccine effectiveness

In clinical trials the Varicella vaccine was 70-90% effective in preventing any disease and over 95% effective in preventing severe disease (defined as > 300 lesions).

Since vaccine licensure and use, many studies and outbreaks have examined vaccine effectiveness after using the vaccine in real life conditions where storage and handling issues are not controlled as in clinical trials.

In the first few years after routine vaccination, 1996-2002, most outbreaks were occurring in day care centers. VE results from these outbreaks were reassuring with VE ranging from 71% in CA to 86% in GA against any disease and 93 to 100% against moderate to severe disease. (more than 50 lesions)

Starting in 2001, we started to hear of outbreaks occurring in schools. Most cases were occurring in K to first grade. Again VE results were also reassuring and within the expected range reported in clinical trials before vaccine licensure. VE ranged from 72% in OR to 90% in ME against any disease and over 95% against moderate to severe disease.

Between 2002 and 2003, most outbreaks were reported in schools with cases occurring mostly in children in first to third grade. Here again the VE results were within the expected range with VE against any disease ranging from 83% in Arkansas to 89% in Maine, and over 95% against moderate to severe disease.

Post licensure vaccine effectiveness in the majority of day care and school outbreaks have been reassuring in that they replicated the findings of clinical trials results. VE in 17 outbreak investigations that we assisted with or knew about range from 71-100% against any disease and 93-100% against moderate to severe disease. Two outbreak investigations, however, resulted in lower than expected VE. One of these was in a day care center where the index case was a vaccinated healthy child with over 300 lesions. In this outbreak in NH, VE was the lowest observed to date at 44% against any disease. VE against moderate to severe disease was 86%. The other outbreak occurred in a school on MD, with VE against any disease at 59% and the lowest observed against moderate to severe disease at 75%. We know that outbreaks tend to under-estimate true VE because we only investigate outbreaks where we suspect the vaccine not to perform well, that is outbreaks with high vaccination coverage and a large number of vaccinated cases. Outbreaks with few cases where the vaccine is performing well are not likely to be considered high priority for investigation.

Finally studies that are designed to examine varicella vaccine effectiveness are less likely to have biases than outbreak investigations for the reasons mentioned earlier. 4 studies examined vaccine effectiveness as seen on this slide. One was a cohort in NC, two case control studies in Connecticut and one utilizing secondary attack rates in House holds in CA have resulted in reassuring VE estimates ranging from 79% to 87% against any disease and over 92% against moderate to severe disease.

A few factors have been identified in published studies and in outbreak investigations that are associated with vaccination failure and a higher risk of breakthrough, varicella disease in a vaccinee. The results of the studies have not been consistent with some factors being important in some studies, and not in others. Some of these factors are:

Age of child, which is highly correlated with the likelihood of exposure. Earlier outbreak occurred mostly in day cares, and more recent ones in schools.

Asthma/reactive airway disease and or steroids. Most outbreak investigation don't allow the simultaneous examination of these factors. In one cohort study in which the effect of asthma and steroids were examined, only prescription of oral steroids 3 months before disease was associated with a higher risk of BT.

In some outbreaks and one case control study, vaccination at 12-14 months of age was associated with a higher risk of BT compared to vaccination at 15 months or older.

Longer time since vaccination. Some outbreaks have identified time since vaccination as a risk factor for BT, ranging from 3 to 5 years since vaccination depending on the age of the cases. Time since vaccination is highly correlated with age at exposure and disease. Earlier when outbreaks were occurring in day cares, 3 or more years was identified as a risk factor. In school based outbreak, 4-5 years since vaccination is identified.

Receipt of the varicella vaccine within less than 28 days of receiving MMR vaccine

Other including eczema with children who have eczema having a higher risk of BT compared to those without eczema.

In summary, most outbreak investigations and all designed study that examined VE have confirmed pre licensure estimates of VE ranging from 70-90 against any disease and over 93% against moderate to severe disease. Therefore, we know that the vaccine is performing as well as in clinical trials before licensure. We also identified potential risk factors for vaccination failure as mentioned earlier.