Varicella

http://www.cdc.gov/mmwr/preview/mmwrhtml/00056339.htm

Evaluation of Varicella Reporting to the National Notifiable Disease Surveillance System -- United States, 1972-1997

MMWR Weekly January 29, 1999/ 48(03);55-58

Before 1995, an estimated 4 million cases of varicella occurred each year in the United States, approximately 100 patients died (1), and approximately 10,000 persons were hospitalized because of varicella and related complications. Approximately 95% of cases (2), 66% of hospitalizations, and 45% of the varicella-related deaths occurred among persons aged less than 20 years (CDC, unpublished data, 1998). In 1972, varicella became nationally notifiable in the United States; subsequently, 46 states * and the District of Columbia (DC) provided weekly reports to CDC's National Notifiable Disease Surveillance System (NNDSS). In 1981, varicella was deleted from the weekly morbidity report, and in 1982, states were encouraged to report varicella to NNDSS annually.

In 1995, a live, attenuated varicella vaccine was licensed in the United States for routine use in children. This report describes changes in the annual reported incidence of varicella from 1972 to 1997 and discusses the need for increased surveillance with the availability of a vaccine.

Varicella cases reported to NNDSS during 1972-1997 were reviewed. The annual population estimates for the states, DC, and the nation from the Bureau of the Census were used to calculate annual incidence. Because, without a vaccination program, the average annual number of cases of varicella is approximately equal to the size of the birth cohort each year (2), the annual birth cohort was used to estimate the completeness of reporting.

In 1972, the reported national incidence of varicella was 78.4 cases per 100,000 population. During 1972-1987, the reported incidence of varicella ranged from 66.3 in 1974 to 94.1 in 1984, peaking every 3-5 years. From 1987 to 1997, the reported national incidence decreased 58%, from 88.0 to 36.9 (Figure 1).

[78 *2500=195000 = 4.875% of 4 million, or less than 1 in 20.]

The decrease from 1987 to 1997 corresponded with decreases in the number of states reporting to NNDSS and the completeness of reporting. The number of areas reporting varicella weekly to NNDSS declined from 46 states and DC in 1972 to 20 states ** and DC in 1997. In 1972, cases constituting greater than or equal to 3% of the birth cohort were reported in 27 states and DC (range: 0.1%-34.3%); the number of states reporting cases constituting greater than or equal to 3% declined to 21 in 1982 and 17 in 1994. By 1997, of 20 states and DC reporting varicella, 10 states reported cases constituting greater than or equal to 3% of their birth cohorts; three reported greater than or equal to 10% (range: less than 0.1%-20.4%)

During 1972-1997, 14 states maintained continuous reporting to CDC of varicella. In these states, the incidence of reported varicella increased from 107.0 in 1972 to 212.1 in 1987, then decreased to 95.9 in 1996 and 107.1 in 1997. These rates corresponded with levels of reporting, which were 6.2%-9.7% of the birth cohort in the 1970s, 9.1%-14.4% in the 1980s, and 6.6%-11.8% in the 1990s.

Editorial Note The data presented in this report suggest that the decline in the reported national incidence of varicella since 1987 resulted from the changes in state reporting requirements and practices. The low number of reporting states in 1997 and the incomplete reporting from participating states limits the use of NNDSS data to monitor the impact of vaccination against varicella at the national level. Three states have stopped reporting varicella since vaccine licensure. Among the 14 states that have reported continuously, the decline in incidence is due to a decrease in their level of reporting, which will make it difficult to interpret the expected decline in those states resulting from the varicella vaccination program. In these states, annual decreases in incidence that are higher than decreases for previous years might reflect the impact of the vaccination program. Improvements in the quality of varicella reporting are needed to properly monitor vaccine use and its impact on disease trends.
Age <1yr
60 * 2490 = 149400 = 3.7%
immunity = 96.3% for 1 year.

Age 1-4
100 * 2490 = 249000 = 6.225%
immunity = 93.8% /year.

Reference the graph at the above right:
The population of the USA in 1990 was 249 million. Taking the numbers for each age group above and adding:
60+100+85+20+5+1 = 271*2490=674790 /4,000,000 = .1686975 about 17% of birth cohort.

Death at 1 per 60,000 cases, and 103 deaths * 60,000 = 6,180,000 cases = 155 percent of birth cohort.(Only 45% of deaths occur in age 20. 45 * 60,000 = 2.7 million or 67.5 % of birth cohort.)
Prevacine Hospitalization at 11,000 per year associated with varicella and
2-3 hospitalizations per 1000 cases = 4400 * 1000 or 4,400,000 or 110 percent of birth cohort.
Varicella vaccine coverage increased progressively in all age groups over time. Coverage was highest among children 2 years old, ranging from <1% in 1995 to 65% in 2002, followed by coverage among children 6 years old, ranging from <0.1% to 45%. Coverage among older children (12 and 15 years old), increased modestly, to 9% and 5%, respectively, in 2002.

Figure 2. Age-specific incidence rates of varicella, 1992–2002

[Note: the relative incidence of varicella changed in the under 1 year old group from less than 10 per 1000 person years in 1992 to about 4 per 1000/person years in 2002. This drop is in a totally unvaccinated population (<1 yr olds) and reflects the downward trend that was established pre-vaccine use. The above graph reflects the trend based on annual incidence rates divided by person-years for the age group registered with the HMO (Seattle). Roughly one child in a hundred under one year old and one in 62 in the one to four years old range had registered cases of varicella. The vaccinated and unvaccinated alike registered similar downward trends.]

Source: lifeissues.net
During March 1995 to July 1998, a total of 9.7 million doses of varicella vaccine were distributed in the United States. During this time, the CDC’s Vaccine Adverse Event Reporting System (VAERS) received 6,580 reports of adverse reactions to the vaccine, which included 14 deaths. Routine underreporting of adverse vaccine reactions suggests mortality and morbidity rates were far higher. The GAO estimates as few as 1 percent of all serious adverse reactions are actually reported to VAERS: "Studies show that adverse events are often substantially underreported in a passive surveillance system ... only about 1 percent of serious events attributable to drug reactions are reported to FDA."
Varicella-Related Hospitalization and Emergency Department Visit Rates, Before and After Introduction of Varicella Vaccine, Among White and Black Children in Hamilton County, Ohio

TABLE 1 Demographic Characteristics for Incident Cases
Five years before Licensure <1yr 39 hospitalized versus 21 after Licensure
Five years before Licensure <1yr 243 Emergency Department versus 112 after.

Results
From the prevaccination period to 2002, hospitalizations due to varicella declined by 88% (from 2.3 to 0.3 per 100,000 population) and ambulatory visits declined by 59% (from 215 to 89 per 100,000 population). Hospitalizations and ambulatory visits declined in all age groups, with the greatest declines among infants younger than 1 year. Total estimated direct medical expenditures for varicella hospitalizations and ambulatory visits declined by 74%, from an average of $84.9 million in 1994 and 1995 to $22.1 million in 2002.

Varicella vaccine coverage has increased steadily, reaching 81% in 2002 among children aged 19 to 35 months nationally, while varicella disease incidence has declined in all age groups.10-12

Centers for Disease Control and Prevention (CDC).
Varicella (chickenpox) is a common, highly infectious, and vaccine-preventable disease. Before the introduction of the live attenuated varicella vaccine in 1995, approximately 4 million cases of varicella occurred annually in the United States, resulting in approximately 11,000 hospitalizations and 100 deaths. In 1996, the Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination of all children at age 12–18 months, catch-up vaccination of all susceptible children before age 13 years, and vaccination of susceptible persons with close contact to persons at high risk for serious complications. In 1999, ACIP updated these recommendations to include vaccination requirements for child care and school entry and for postexposure; ACIP also strengthened recommendations for vaccination of susceptible adults and indicated that varicella vaccine should be considered for outbreak control. Changes in the national annual reported incidence of varicella disease during 1972-1997 have been reported previously. This report summarizes trends in the annual reported incidence of varicella disease in selected states during 1990-2001. The findings underscore the continued need to improve varicella surveillance to monitor the impact of the varicella vaccination program and assess any changes in varicella transmission and disease.   PMID: 13679791 [PubMed - indexed for MEDLINE]
Complications of varicella infection in children in southern Taiwan

![Graph showing varicella-related complications, annual rates of hospitalizations due to varicella per 1000 admissions, and vaccination doses used, 1998-2004.]

**Fig. 1.** Varicella-related complications, annual rates of hospitalizations due to varicella per 1000 admissions, and vaccination doses used, 1998-2004


**Varicella Epidemiology: Postvaccine Era**

Varicella epidemiology data in the postvaccine era are limited. In a study of 11 daycare centers in North Carolina, the rate of vaccine coverage increased from 4% in 1995 to 63% in December 1999.\(^{[97]}\) During that same period, the incidence of disease decreased from 17 cases/1000 person-months to 2 cases/1000 person-months.
FIG. 1. Rates (per 100 000 person-years) of varicella-related hospital discharge by age group, 1988 to 1999. Bars, standard errors of estimates. Statistical analysis by one way ANOVA showed no difference in any of the displayed age groups. The final point (1998 to 1999) in both the 5- to 14- and 15- to 44-year age groups is based on fewer than 60 actual discharges in the NHDS data set and must be considered a potentially unreliable estimate. , (diamond), 0 to 4 years; , (square), 5 to 14 years; , x, 15 to 44 years.

DISCUSSION

Analysis of hospital discharges is an inexpensive, relatively simple alternative to active surveillance for monitoring disease trends. Active surveillance allows direct measurement of disease rates but is both time-and resource-intensive. Hospital discharge data has been used to measure patterns of respiratory illnesses,15 rotavirus disease16 and pediatric hospitalizations.17 We investigated changes in VRHD during 12 years using a nationally representative database. This methodology has several limitations, including the assumption that hospital coding for varicella did not change during this period. Varicella is a common, recognizable entity, presumably less subject to miscoding than other diagnoses. Omission of federal and long term facilities certainly resulted in missing cases, more likely in adults than in children. However, we calculated prevaccine rates of VRHD similar to those found in a recent study utilizing active surveillance.4 Others have reported lower rates of hospitalization,18, 19 but these generally used a stricter case definition (a first or second coded diagnosis) than ours. Despite increasing use of VV since its licensure,6 we observed neither a significant decrease in the incidence of VRHD nor a shift toward an older, unvaccinated cohort. This
finding was concordant with data reported by Seward et al.,10 which demonstrated a similar, nonsignificant trend in three counties with above average vaccination rates. Although data from the National Immunization Survey indicate that the national rate of VV coverage was 43.2% for children 19 to 35 months old in 1998, there was significant regional variation. South Dakota reported a 12.9% rate of coverage, whereas the District of Columbia had nearly 60%, both below levels used in prelicensure models.1 State hospital discharge data might allow comparison of VRHD among regions with disparate vaccination rates.
3.2 Safety of the varicella vaccine

3.2.1 Adverse events in healthy individuals

VZV vaccine has been well tolerated in children. The most commonly observed adverse events in the 4-8 weeks post vaccination are mild tenderness (19.3%), redness at the injection site (3.8%) and low grade fever (14.7%). In one double blind, placebo-controlled trial, the only complaint that occurred more often in vaccinated children, than in those who received placebo, was pain and redness at the injection site (26).

Four to 10 percent of VZV vaccine recipients may develop a generalized maculo-papular rash within 7-21 days post vaccination, consisting of usually less than 50 lesions. Reactivation of the VZV virus, resulting in herpes zoster, has been reported in eight children (27). From this study the incidence of herpes zoster was estimated to be 1.8 /10,000 person-years after VZV vaccination. This is clearly lower than the incidence of 7.7/10,000 person-years following natural infection, found in an earlier study (28).

3.2.2 Adverse events in children with immunosuppression

A rash occurs in up to 40% of children with acute lymphoblastic leukemia who have been vaccinated with VZV vaccine. This is more frequent in children on steroid therapy and ongoing chemotherapy. Reactivation of VZV vaccine virus, resulting in herpes zoster may be less frequent than after natural infection (29). No severe illness or dissemination in children with vaccine-caused herpes zoster has been reported.

3.2.3 Transmission of VZV vaccine strain

Transmission of VZV vaccine strain to susceptible persons, diagnosed by seroconversion has been reported from normal recent vaccine recipients and from children with ALL, who developed a rash. In a double-blind, placebo controlled trial there were 1% asymptomatic seroconversions in susceptible household contacts in the eight weeks following vaccination. (26).

3.3 Efficacy of the varicella vaccine

3.3.1 Efficacy in healthy children

Normal children show a seroconversion rate of 94%-100% after one dose of the vaccine. The efficacy in normal children, who were exposed to wild-type varicella virus in the first year after vaccination, has been estimated in two randomized placebo-controlled trials to be 100% and 88% respectively (26,31). Several other studies have reported that each year post vaccination 1% to 3% of vaccinated children develop a mild varicella disease (mild varicella like syndrome, or MVLS) after exposure to wild-type varicella (31-33). These breakthrough infections are generally mild, with few skin lesions and do not result in dissemination or serious illness.
Since introduction of varicella vaccine in 1995, incidence of varicella has decreased as vaccination coverage has increased. Nevertheless, varicella outbreaks continue to occur, even among populations with high vaccination coverage. Although varicella typically is mild, the outbreaks can last for several months and be challenging and costly for health departments to control. In 2005, CDC conducted a national survey to determine the distribution and extent of reported varicella outbreaks during 2003-2004 and the public health response. This report summarizes the results of that survey, which indicated that varicella outbreaks are still common and that health jurisdictions are responding to these outbreaks, although they have varying definitions and guidelines for varicella-outbreak management.

PMID: 16971888 [PubMed - indexed for MEDLINE]
was significantly higher than for 1 dose of varicella vaccine. This higher efficacy translated into a 3.3-fold lower risk of developing varicella >42 days after vaccination in 2- vs 1-dose recipients. Of the children receiving 2 doses, 99% achieved a glycoprotein-based enzyme-linked immunosorbent assay level of > or =5 units (considered a correlate of protection) 6 weeks after vaccination compared with 86% of children who received 1 dose. The 6-week glycoprotein-based enzyme-linked immunosorbent assay level of > or =5 units has been shown to be a good surrogate for protection from natural disease. Ten years after the implementation of the varicella vaccination program, disease incidence has declined dramatically, and vaccination coverage has increased greatly. However, varicella outbreaks continue to occur among vaccinated persons. Although varicella disease among vaccinated persons is mild, they are contagious and able to sustain transmission. As a step toward better control of varicella outbreaks and to reduce the impact on schools and public health officials, in June 2005, the Advisory Committee on Immunization Practices recommended the use of a second dose of varicella vaccine in outbreak settings. Early recognition of outbreaks is important to effectively implement a 2-dose vaccination response and to prevent more cases. Although the current recommendation of providing a second dose of varicella vaccine during an outbreak offers a tool for controlling outbreaks, a routine 2-dose recommendation would be more effective at preventing cases. Based on published data on immunogenicity and efficacy of 2 doses of varicella vaccine, routine 2-dose vaccination will provide improved protection against disease and further reduce morbidity and mortality from varicella.

PMID: 16740809 [PubMed - indexed for MEDLINE]

Vaccine effectiveness and severity of varicella among previously vaccinated children during outbreaks in day-care centers with low vaccination coverage.

- Miron D, Lavi I, Kitov R, Hendler A.
Pediatric Department A, Infectious Disease Consultation Service, HaEmek Medical Center, Afula, Israel.

BACKGROUND: Varicella vaccine effectiveness (VE) during outbreaks has been reported to be 71-100% against any disease and >90% against moderate/severe disease even in day-care centers (DCCs) and schools with low vaccination rates. A recent report suggested an effectiveness rate of 44% during a DCC outbreak despite a high vaccination rate. AIMS: To reassess vaccination coverage, VE and severity of disease among previously vaccinated children after exposure during DCC outbreaks in northern Israel, where vaccination rates are low. METHODS: During January to June 2003, active surveillance for varicella among children in northern Israel revealed outbreaks in 8 DCCs with children 3-6 years of age. Data concerning symptoms of the disease and the age at vaccination (for previously vaccinated children) were obtained from parents and health care providers for children who contracted the disease. Analysis of VE was limited to children who were continuously enrolled in DCCs during the outbreaks. RESULTS: The overall vaccination rate was 37%. The incidences of natural varicella and breakthrough varicella (BV) were 79 of 153 [52%; 95% confidence interval (CI) 44-60%] and 37 of 89 (41.5%; 95% CI 31-52%), respectively. VE was 20% (95% CI 0-40%) against disease of any severity and 93.4% (95% CI 75-98%) against moderate/severe disease. Ninety-four percent and 14% of children with BV and natural varicella, respectively, had mild disease (P < 0.001). The odds ratio for BV was 17 (95% CI 2.18-118) for children vaccinated >2 years before the outbreak. CONCLUSIONS: During varicella outbreaks in DCCs with low vaccine coverage, previous vaccination provided poor protection against chickenpox, mostly among children who had been vaccinated >2 years earlier, but the disease appeared to be much milder among children with BV than among nonvaccinated children.

PMID: 15750459 [PubMed - indexed for MEDLINE]

http://www.immunizationinfo.org/vaccineInfo/vaccine_detail.cfv?id=11
(National Network for Immunization Information)

Varicella is generally a mild disease, but it is highly contagious and can be severe and even fatal in otherwise healthy children (less than 1 out of every 10,000 cases).

Prior to the introduction of the varicella vaccine, there were 3 to 4 million cases of varicella in the United States each year. About 10,000 people were hospitalized with complications, and approximately 100 patients died. While only 5% of reported cases of varicella are in adults, adults account for 35% of the deaths from the disease.
Varicella vaccination in England and Wales: cost-utility analysis

The predicted 651,000 cases of varicella per year in England and Wales result in an estimated 384,000 physician visits, 2,200 hospitalisations, and 20 deaths. [1/32550]

Estimating case fatality
We used general practitioners' consultation rates to estimate the number of cases of clinical chickenpox in the population. The case fatality was 9.22/100,000 for 1985-97. In each year, the number of deaths certified generally closely paralleled the consultation rate for chickenpox.

In 1995-7, 81% of consultations for clinical chickenpox were for children aged 0-14 years (table 2). Of the certified confirmed deaths due to chickenpox, 61 (81%) were in adults, 58 of whom were aged over 25 years. The case fatality, based on age specific consultation rates, showed considerable variation (table 2). Mortality from chickenpox was most likely in those aged 65 years or older and least likely in those aged 5-14 years (table 3). The sex ratio of two male deaths to one female death was especially apparent in those aged 15-44 years, although the consultation rates for chickenpox in both sexes were similar.

During 1995-7, 81 deaths were recorded by the Office for National Statistics. However, we received 119 certificates that mentioned chickenpox or varicella. After detailed inquiries, we estimated that at least 75 were genuine cases of chickenpox. This suggests at least 25 deaths from chickenpox annually.

[Another study suggests this figure of 25 may be high, closer to 20 average.]

[From Table 2: 456,444 cases in 0-4, 2.63 deaths/100,000 cases .94 deaths per 100,000 cases 211,930 cases in 5-14 years.]

This was pre-vaccine era

Deaths from chickenpox in adults are decreasing
Editor—On the basis of death certificates from the Office for National Statistics from 1995 to 1997, Rawson et al conclude that deaths as a result of chickenpox are increasing in adults in England and Wales. More up to date figures from the Office for National Statistics, however, show that chickenpox mortality is decreasing in adults (from 32 deaths in 1996 to 18 in 2000—see figure (a)). Furthermore, the number of deaths from chickenpox and case fatality rates were significantly higher in 1995-7 (period of the analysis) than at any other period. The claim by Rawson et al that deaths in adults are rising is therefore misleading.

The change in age related varicella mortality is the result of a shift in the age distribution of infection. Over the past two decades there has been an increase in cases in the youngest age group (possibly due to greater attendance of day-care). Over the same time period there has been a gradual increase in reported incidence in adults, which peaked in the late 1980s and has been falling since (figure (b)). This is broadly reflected in the gradual decrease in deaths in adults during the past decade. The exception to this trend are 1996 and 1997—exactly the time period when Rawson et al performed their study. What has caused these large shifts in the incidence of varicella in adults is still largely unexplained.
Chicken Pox is another common disease and is mild with low mortality if occurs in childhood. Primary Varicella has a mortality rate of 2-3 per 1,00,000 cases with lowest case fatality rates among children 1-4 years and 5-9 years(approximately 1 death per 1,00,000 cases). The mortality rate of untreated primary infection in immuno compromised children is 7-14% and may approach 50% in adults. Most of the children are infected by the age of 15 years with fewer than 5% adults remaining susceptible. Disease is often severe if it occurs after adolescence or in adults. Natural infection provides life long immunity.

In the meantime, 6,580 adverse events--including 14 deaths--were reported to the Vaccine Adverse Events Reporting System in association with varicella vaccination between March 17, 1995 and July 25, 1998. (23) The actual number could be at least 10 times higher, if we take into consideration the proven fact that only 10% of adverse events are commonly reported.

59% Varicella 1 or more doses in Montana in 2002.

ACIP req proof of immunity to varicella includes Born in the US prior to 1966. Found in Montana's Immune Response.

VAERS 66 Found 66 records with Vaccine contains 'VARCEL' and Patient Died and Vaccination Date after '1995-01-01' and Vaccination Date before '2006-07-01'
20 records contained only Varcel, plus ⅘ of the 46 remaining = 11 +20 = 31 /11 =3 meaning that Varicella vaccine kills 30 (minimum) to a maximum of 300 per year. The likely figure would be 90-150.
Objective: To examine the epidemiology of chickenpox in Wales from 1986 to 2001.

Design: Descriptive analysis of chickenpox consultations reported by the Welsh general practice sentinel surveillance scheme for infectious diseases, compared with annual shingles consultation rates from the same scheme to exclude reporting fatigue and data from a general practice morbidity database to validate results.

Setting: A total of 226,884 patients registered with one of 30 volunteer general practices participating in the sentinel surveillance scheme.

Main outcome measures: Age standardised and age specific incidence of chickenpox.

Results: Crude and age standardised consultation rates for chickenpox declined from 1986 to 2001, with loss of epidemic cycling. Rates remained stable in 0–4 year olds but declined in all older age groups, particularly those aged 5–14 years. Shingles consultation rates remained constant over the same period. Data from the morbidity database displayed similar trends.

Conclusion: General practitioner consultation rates for chickenpox are declining in Wales except in pre-school children. These findings are unlikely to be a reporting artefact but may be explained either by an overall decline in transmission or increased social mixing in those under 5 years old, through formal child care and earlier school entry, and associated increasing rates of mild or subclinical infection in this age group. Further investigation, particularly by serological surveillance, is necessary before universal varicella immunisation can be considered in the UK.

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