

OREGON PUBLIC HEALTH DIVISION • DEPARTMENT OF HUMAN SERVICES

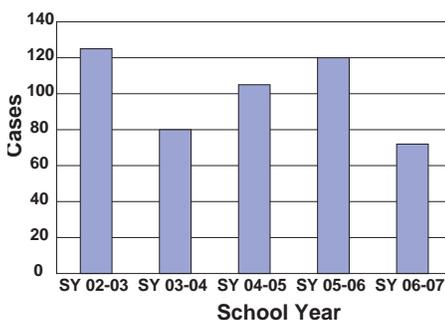
CHICKENPOX: EPIDEMIOLOGY AND PREVENTION UPDATE

This issue of the *CD Summary* presents the latest in vaccine-era chickenpox epidemiology in Oregon, stuff about the new 2-dose varicella vaccination recommendation for children, and how to find the new varicella zoster immune globulin (VariZIG™).

CHICKENPOX IN OREGON

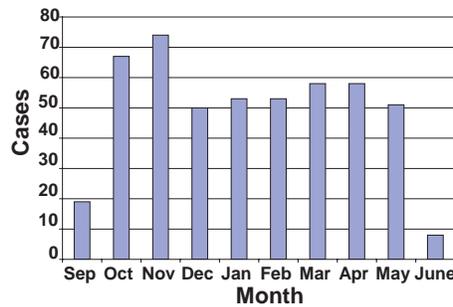
Chickenpox isn't reportable in Oregon, so to get some information on its incidence, we asked school nurses in Multnomah County to collect data on absenteeism due to chickenpox among elementary school students in school years 2002–2007.^{1,2} Cases were defined clinically.* An average of 100 chickenpox cases per year (range, 72–125) occurred within the population of approximately 50,000 students 5–9 years of age (Fig. 1). These numbers translate to annualized incidence rates of 0.2%–0.3% — much lower than the 9% average annual incidence reported among 5–9-year-olds during the pre-vaccine-era.³

Fig. 1 Chickenpox by school year



Among other interesting epidemiologic details we found that: (a) chickenpox cases peaked early in October and November (Fig. 2); (b) 60% of cases occurred in grades K-2 (Fig. 3); (c) 5% of cases had allegedly had chickenpox once before; (d) just two cases had complications (a bacterial skin infection and conjunctivitis); (e) only 54% of cases were provider-diagnosed; and

Fig. 2. Chickenpox by month



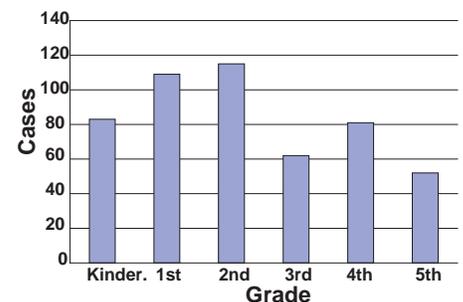
(f) none of these diagnoses were based on the “gold standard” of varicella zoster virus (VZV) culture.

Varicella vaccination coverage of our vaccine-eligible (i.e. without prior varicella) school students was 92%. In children exposed to varicella in a classroom, vaccine effectiveness against any chickenpox was 81%, and, in contrast to what we found in a 2001 outbreak in an Oregon elementary school, time since vaccination of ≥5 years was not significantly associated with breakthrough varicella.⁴ As would be expected with a 92% vaccination rate, most cases (62%–75% per year) occurred among the vaccinated. This is good news. Cases who were unvaccinated were sicker longer (and thus out of school longer) than vaccinated cases (median seven vs. five days absent), and had more severe illness with rashes of ≥50 lesions (74% vs. 19%), fevers (86% vs. 62%), and headaches, sore throats, malaise, and anorexia (60% vs. 28% taken together). To their parents, 65% of susceptible cases, but only 13% of vaccinated cases, appeared “moderately” or “severely” ill.

The majority (53%) of cases occurred in 27 outbreaks. During 2001–2005, the national Centers for Disease Control and Prevention (CDC) reports, frequent outbreaks of breakthrough chickenpox with high vaccine effectiveness (72%–85%) indicated that even in well vaccinated populations, the 1-dose varicella vaccination program has not

eliminated varicella outbreaks — a key part of the rationale for the 2-dose recommendation made this year by CDC's Advisory Committee on Immunization Practices (ACIP).⁵

Fig. 3 Chickenpox by grade



ACIP RECOMMENDATIONS

The FDA licensed the single-antigen varicella vaccine in 1995 and the combination measles-mumps-rubella-varicella vaccine in 2005. The ACIP released varicella vaccination recommendations in 1996, 1999, and 2007.

The 1996 recommendations called for routine 1-dose varicella vaccination of susceptible children aged 12–18 months, catch-up vaccination of susceptible children aged 19 months–12 years, targeted two-dose vaccination (4–8 weeks apart) of susceptible persons ≥13 years old (4–8 weeks apart) who have close contact with persons vulnerable to serious complications, and a “should be considered” suggestion for vaccinating persons likely to be exposed to varicella.⁶

The 1999 edition upgraded the vaccination of persons likely to be exposed to varicella from a suggestion to a recommendation.^{6,7} Persons likely to be exposed to chickenpox include: (a) persons who live or work in environments in which transmission of VZV can occur; (b) nonpregnant women of child-bearing age; (c) international travelers; and (d) adolescents and adults living in households with children. Also called for was making varicella vaccination a child care and elementary school entry

* acute illness with maculo-papulo-vesicular rash without other apparent cause persisting longer than 24 hours, regardless of previous episodes of the same or similar illness



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requirement (a policy adopted in Oregon at the start of the 2000–01 school year), giving vaccine 3–5 days after exposure, and vaccinating asymptomatic or mildly symptomatic children infected with HIV (in CDC immunologic and clinical categories N1 or A1 with age-specific CD4+ T-lymphocyte percentages $\geq 25\%$).⁷

The 2007 recommendations now call for routine 2-dose varicella vaccination, the first dose to be given at 12–18 months and the second at 4–6 years of age (harmonized with recommendations for MMR use); and catch-up vaccination for everyone who has received but one dose. Prenatal assessment and post-partum vaccination is newly recommended, as is a 2-dose vaccination policy for outbreak control.⁵

The second dose of vaccine is expected to provide protection to the 15%–20% of children who do not respond adequately to the first dose. Data from a randomized clinical post-licensure trial indicated that vaccine efficacy in children after two doses was 98.3% (95% confidence interval [CI] 97.3%–99.0%) — significantly higher than that after a single dose (94.4%; 95% CI, 92.9%–95.7%). Put another way, the risk for breakthrough disease was 3.3-fold lower among children who received two doses.⁵

VZIG

Varicella-zoster immune globulin (VZIG) is indicated for persons who have no evidence of immunity to chickenpox, have an exposure likely to result in infection, and are at greater risk for complications than the general population. This sounds straightforward enough, but the devil's in the details.

Evidence of immunity to chickenpox consists of (a) age-appropriate varicella vaccination; (b) laboratory evidence of immunity or infection; (c) birth in the U.S. before 1980 except for pregnant women and health care workers (who had best have lab evidence of immunity); or (d) diagnosis of chickenpox or shingles by a health care provider.

Exposures “likely to result in infection” include continuous household contact; playmate contact of more than an hour; hospital contact in the same 2- to 4-bed room; or prolonged direct contact.⁸ VZIG must be given within 96 hours of such exposure to prevent varicella.

Individuals “at greater risk for complications” are (a) children and adults immunocompromised by immune deficiencies, neoplastic disease, or current immunosuppressive therapy; (b) neonates of mothers with chickenpox onset 5 days before to 48 hours after delivery; (c) premature infants (including extreme premies born after ≤ 28 weeks' gestation or who weigh $\leq 1,000$ grams at birth); and (d) pregnant women.⁸

Chickenpox in the first 20 weeks of gestation is associated with congenital varicella syndrome about 2% of the time. There's no evidence that VZIG will prevent congenital varicella syndrome if given as post-exposure prophylaxis to a pregnant woman.⁸

After all the right boxes are checked, however, it is tricky to get VZIG into a patient within the 96-hour window required for it to be effective. The only manufacturer of U.S.-licensed VZIG, Massachusetts Public Health Biologic Laboratories, discontinued production in 2006 at the same time that a new,

unlicensed VZIG product (manufactured by Cangen Corporation, Winnipeg, Canada) became available under an investigational new drug (IND) application protocol. Clinicians can request the product, called VariZIG™, from FFF Enterprises (Temecula, California) by calling 1-800-843-7477, submitting a request form, and, because it's an IND, completing a plethora of paperwork after giving VariZIG™.

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