

Status of varicella surveillance and challenges in the 2-dose varicella vaccination era

Adriana Lopez, MHS

Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Outline

- ❑ Varicella and varicella vaccine background
- ❑ Varicella surveillance
- ❑ Implementation and impact of the varicella vaccination program
- ❑ Varicella surveillance in Arizona
- ❑ Challenges with varicella surveillance
- ❑ Summary

Varicella: Transmission, Incubation Period, Contagiousness

- Humans only reservoir of infection
 - Primary infection → varicella (chickenpox)
 - Reactivation → herpes zoster (shingles)
- Person-to-person transmission through
 - Direct contact
 - Inhalation of aerosols from vesicular fluid of skin lesions, or infected respiratory tract secretions
- Average incubation period
 - 14-16 days after exposure to rash (range: 10-21 days)
- Contagiousness
 - 1-2 days before rash onset until all lesions crusted or disappear if maculopapular rash (typically 4-7 days)
- Varicella in unvaccinated persons is highly contagious
 - 61-100% secondary household attack rate



Varicella: Clinical Features in Unvaccinated Persons

- ❑ Can start with prodrome of fever, malaise, headache, abdominal pain 1-2 days before rash
- ❑ Vesicular rash, occurring in crops, lesions in different stages of development, centralized distribution
- ❑ Rash usually starts on face and trunk, then spreads to extremities
- ❑ Rash involves 250-500 lesions that are pruritic
- ❑ Lesions typically crusted 4-7 days after rash onset



Varicella Complications

Virally mediated

- Neurological
- Pulmonary
- Hemorrhagic, other

Bacterially mediated

- Skin and soft tissue
- Sepsis
- Pneumonia, other

□ Certain groups at increased risk of complications

- Adults
- Immunocompromised persons
- Pregnant women
- Newborns

□ However, most severe complications and deaths occur in healthy persons

Varicella Disease Burden in the U.S. Before Varicella Vaccine Introduction

- Annually, before 1996, varicella caused:
 - Cases ~ 4 million
 - 15.0 – 16.0/1,000 population per year
 - Highest incidence children < 10 years
 - Hospitalizations ~ 11,000 to 13,500
 - ~ 4.0-6.0/100,000 population per year
 - Deaths ~ 100 – 150
 - ~ 0.4-0.6 /million population per year
 - Congenital varicella syndrome ~ 44
 - Risk = 1-2% for pregnancies affected 0-20 weeks

- Greatest disease burden in children
 - >90% cases, 70% hospitalizations, 50% deaths

US Varicella Vaccination Program

- ❑ 1996 - Universal one-dose varicella vaccination program recommended by Advisory Committee on Immunization Practices (ACIP)
- ❑ 2007 - ACIP changed from a routine 1-dose to a 2-dose varicella vaccination program for children
 - First dose: 12-15 months
 - Second dose: 4-6 years
- ❑ Rationale for routine 2 dose program
 - Outbreaks in highly vaccinated school populations placed resource burden on state health departments
 - Incomplete protection after 1 dose
 - Improved disease control anticipated with 2 dose program
 - 2nd dose expected to provide protection to the 15-20% of children who do not respond to the 1st dose
 - Risk of varicella 3-fold lower in 2-dose vaccinees compared to 1-dose vaccinees



Varicella: Clinical Features in Vaccinated Persons ("Breakthrough Varicella")

- ❑ ~15-20% of 1-dose vaccinated persons develop breakthrough varicella if exposed to VZV
- ❑ Varicella in vaccinated persons usually milder than varicella in unvaccinated persons
- ❑ 25-30% breakthrough cases not mild and have clinical features more similar to unvaccinated cases
- ❑ 1-dose vaccinees with <50 lesions 1/3 as contagious as unvaccinated persons
- ❑ Vaccinees with ≥ 50 lesions as contagious as unvaccinated persons



Varicella Surveillance

History of varicella surveillance

- ❑ 1999 – Varicella deaths become reportable
- ❑ 2002 – Council of State and Territorial Epidemiologists (CSTE) recommended states move to case-based reporting by 2005
- ❑ 2003 – Varicella added back to national notifiable diseases list for case reporting
- ❑ 2007 – 2nd dose varicella vaccination program implemented
- ❑ 2010 – Varicella reportable in 39 states and 38 states conducting case-based surveillance

Case-Based Surveillance

- ❑ Needed to monitor impact of the varicella vaccination program
- ❑ Critical variables:
 - Standard case-based surveillance data:
 - Demographics
 - Clinical information (e.g., rash description, fever, medications)
 - Epidemiologic (e.g., transmission setting, outbreak-related)
 - Outcomes of case (e.g., hospitalized, died)
 - Varicella-specific variables needed to monitor varicella surveillance program:
 - Age
 - Vaccination status and number of doses
 - Disease severity (i.e., number of lesions)

Sources of Varicella Surveillance Data

- ❑ Varicella Active Surveillance Project (VASP)
 - Established in 1995 in 3 sites (Antelope Valley, CA, West Philadelphia, PA, and Travis County, TX) to monitor impact of varicella vaccination program
 - Not nationally representative – only 2 sites participated from 2000-2012
 - Expensive to maintain
 - Project ended June 2012

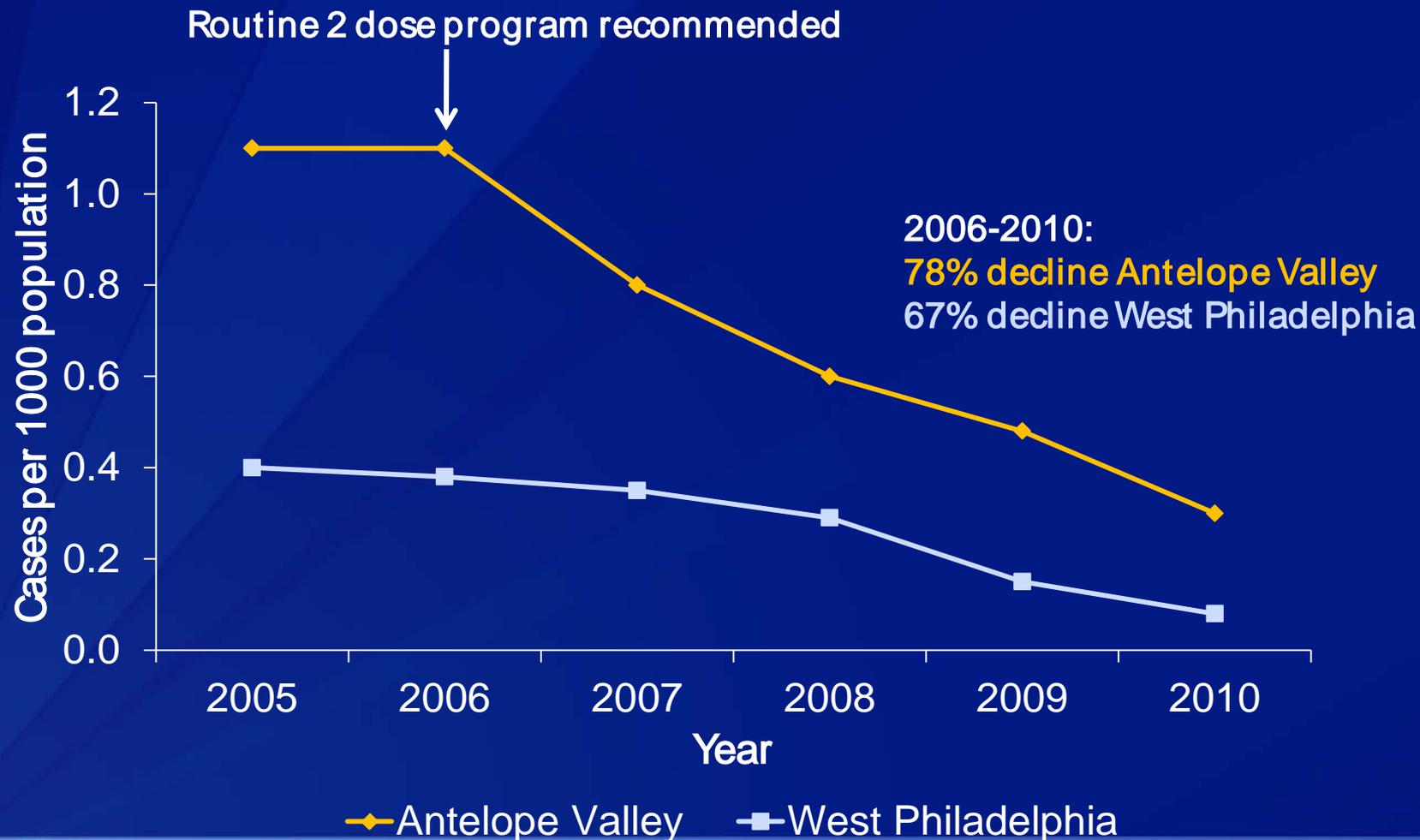
- ❑ National Notifiable Diseases Surveillance System (NNDSS)
 - Relies on passive reporting from sites to state
 - Limited to states where varicella reportable

Implementation and Impact of the Varicella Vaccination Program

One-dose Varicella Vaccination Program (1996-2005)

- ❑ One-dose vaccine effectiveness 80-85% against all varicella; >95% against severe varicella
- ❑ National one-dose varicella vaccination coverage reached 90% in 2010
- ❑ One-dose varicella vaccination coverage in Arizona reached 88.2% in 2010
- ❑ Varicella active surveillance sites reported 90% decline in varicella incidence

Varicella Active Surveillance Project sites experience further declines in varicella incidence during two-dose vaccination era, 2006-2010

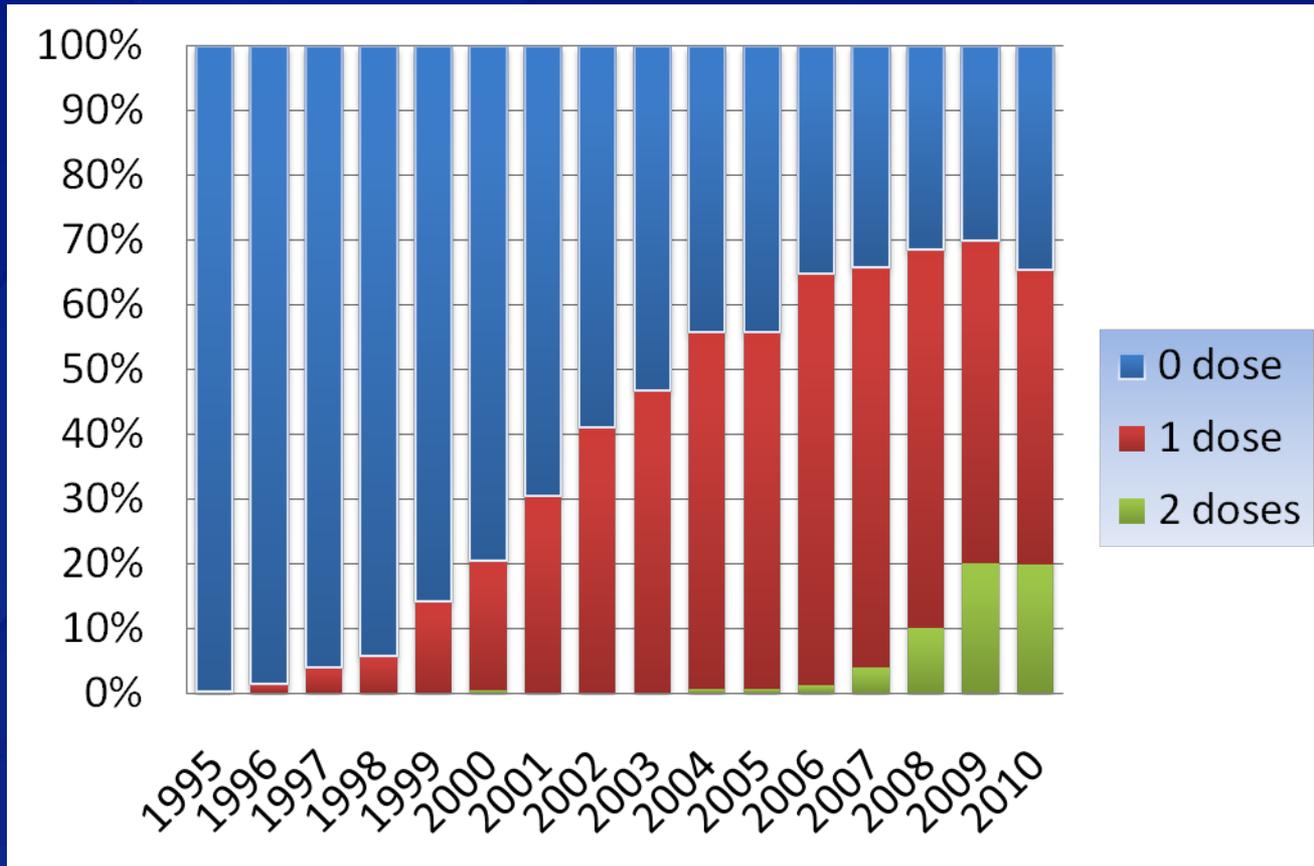


Reductions in age-specific incidence greatest in age groups targeted for 2nd dose – Varicella Active Surveillance Project sites, 2006-2010

Age (years)	Antelope Valley, CA (%)	West Philadelphia, PA (%)
<1	-81.3	40.8
1-4	-54.0	-72.7
5-9	-88.3	-78.7
10-14	-75.3	-91.4
15-19	-29.3	-25.1
20+	-50.0	-17.3
Total	-76.3	-67.1

Proportion of Case-patients with Breakthrough Varicella

Varicella Active Surveillance Project, 1995-2010



National varicella incidence rates from states meeting inclusion criteria* (n=12-31 states) that reported to NNDSS, 2000-2010



* Inclusion criteria includes: reporting a minimum incidence of 1/100,000 for at least 3 consecutive years between 2000-2010.

Characteristics of varicella cases reported to NNDSS, 2009-2010

Varicella-specific variable (N states reporting data)	Total number of cases reported	Number of cases with characteristic, n (%)
Vaccinated with varicella-containing vaccine (N=15)	12,313	7906 (64.2)
Number of lesions <50 (N=12)	3942	2062 (52.3)
Fever present (N=12)	5934	1406 (23.7)
Itchy rash (N=11)	3193	1801 (56.4)
Hospitalized (N=14)	8884	132 (1.5)
Vaccinated (N=14)	5448	17 (0.3)
Laboratory testing for varicella performed (N=13)	8035	964 (12)
Outbreak-related (N=33)	31,793	4309 (13.6)
Case status (N=34)	35,676	
Probable		14,896 (41.8)
Confirmed		20,596 (57.7)

Impact on Varicella Outbreaks

- ❑ Connecticut (Kattan JID 2011)
 - 42 outbreaks 2005-2006, median size 14 cases
 - 2 outbreaks 2008-2009, median size 5 cases
- ❑ 6 state and local health departments funded to conduct varicella outbreak surveillance in schools
 - New York City: 120-330 schools (93,000-224,000 students)
 - reported 1 outbreak (n=7 cases) in a non-participating school during 2009-10 school year
 - Minnesota: 80 schools statewide (41,000 students)
 - reported 15 outbreaks from non-participating schools
 - Average outbreak size=9 cases
 - West Virginia: ~700 schools (281,000 students)
 - Reported 19 outbreaks (n=167 cases)
 - Case-control study being conducted to assess 2-dose VE
- ❑ VASP – Antelope Valley, CA
 - 46 outbreaks 2002-2005, median size 9 cases (range 5-45)
 - 21 outbreaks 2006-2009, median size 9 cases (range 5-17)

Varicella surveillance in Arizona

Varicella Reporting Form

Outbreak

- Indicate on School-based Case Form
- Also fill out the Outbreak Reporting Form

Received Varicella Vaccine?

- 1 dose
- 2 doses
- No
- Unknown

* *Outbreak*: 5+ cases (if ≤ 13 years old) or 3+ cases (if > 13 years old) within 21 days

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Varicella (Chickenpox) Reporting Form

School-based Varicella Sentinel Surveillance System

For schools and child care facilities for reporting of ***chickenpox ONLY***

School or Child Care reporting _____

Person reporting _____ Phone _____

Date of report _____ Outbreak*: **Y N**

Name of Child or Staff With Lesions	Date of Birth	Date of Onset	Received Varicella Vaccine?		Date(s) Vaccinated	Grade of Lesions**		
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III
			1-dose No	2-doses Unknown		I	II	III

* *Outbreak*: 5+ cases (if ≤ 13 years old) or 3+ cases (if > 13 years old) within 21 days

** *Grade of lesions*: Estimated number of chickenpox lesions/spots easily counted by parent or nurse.

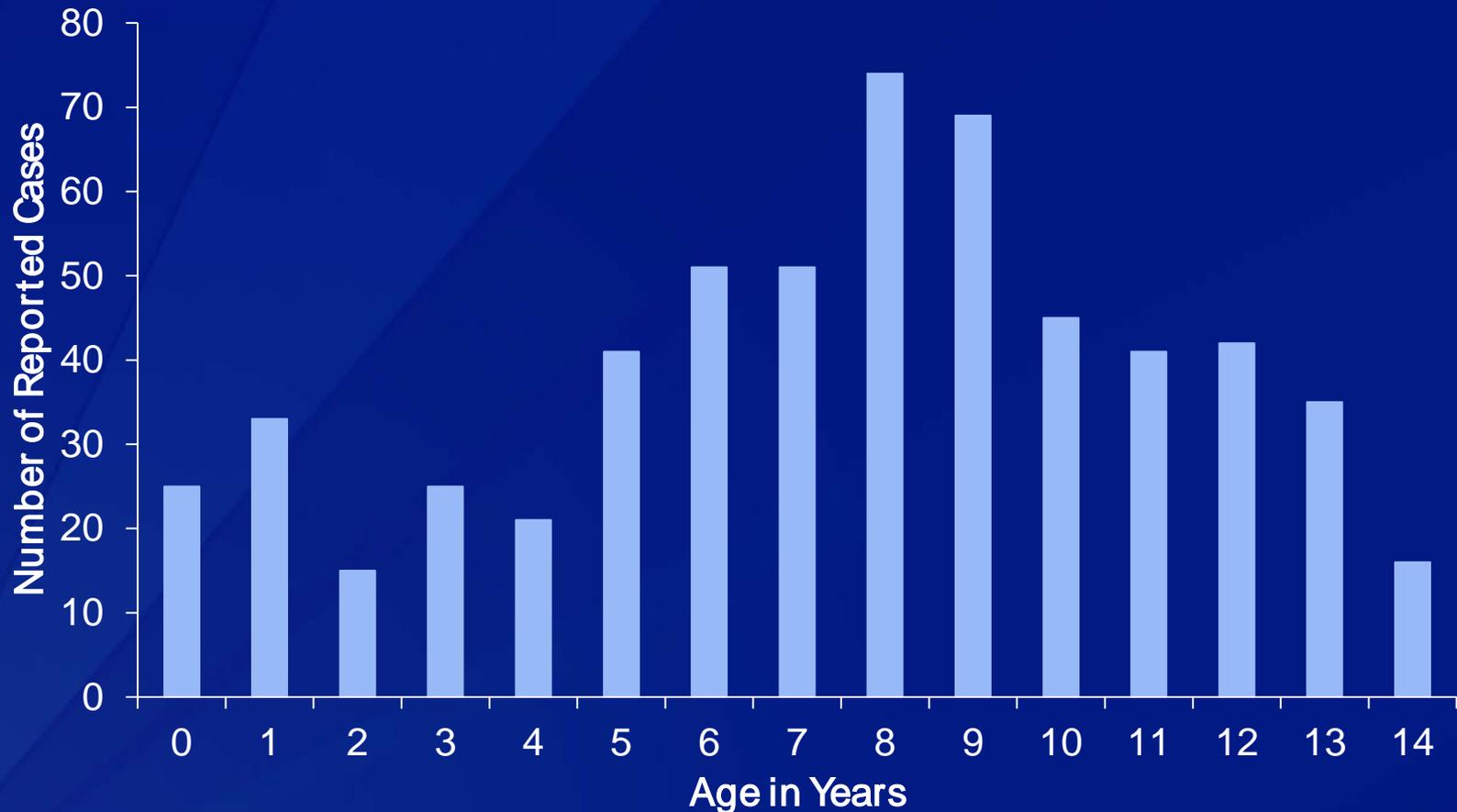
Grade I: 50 spots or less easily counted within 30 seconds

Grade II: 50-500 spots (between Grades I and III)

Grade III: 500 or more spots, or spots clumped so close together that little normal skin is visible

Please submit this form to your county health department.

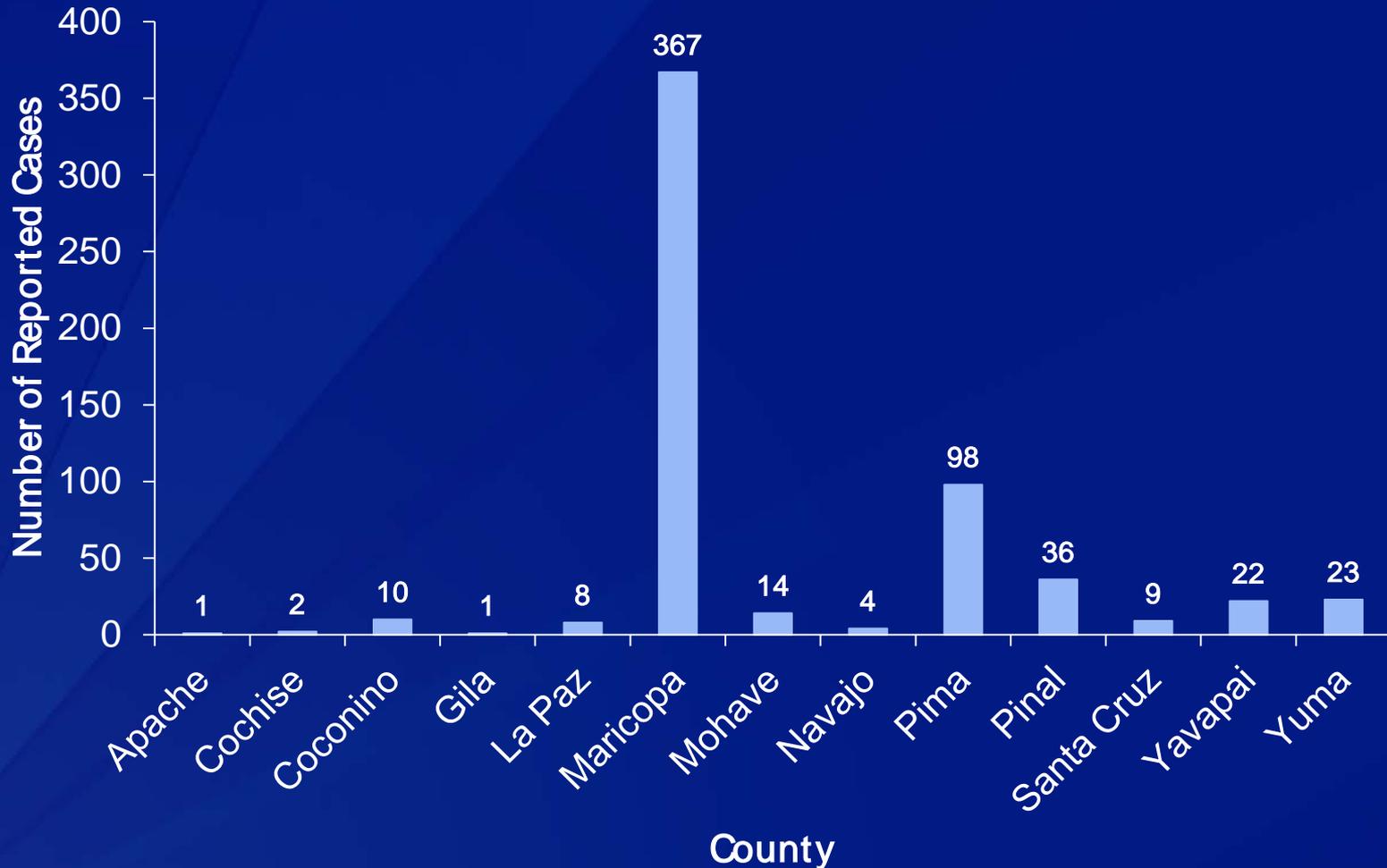
Reported Varicella Cases by Age (≤ 14 years), Arizona, 2010



Reported Varicella Cases by Month (≤14 years), Arizona, 2010



Reported Varicella Cases by County (≤14 years), Arizona, 2010

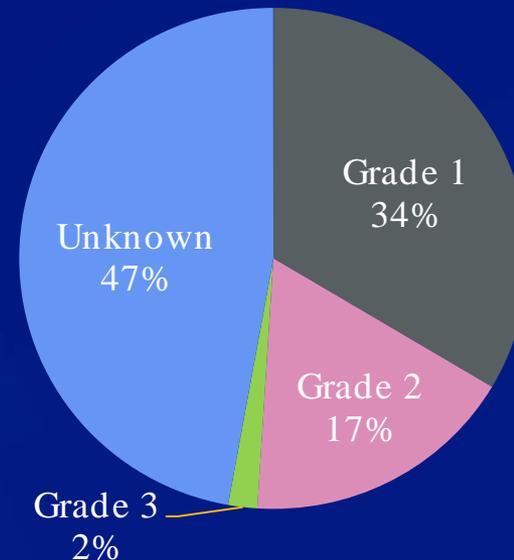


Vaccination Status and Grade of Lesions for Reported Varicella Cases, Arizona, 2010

□ 593 varicella cases in 2010

- 340 (57%) were vaccinated
 - 232 (68%) received one dose
 - 108 (32%) received two doses

Grade of lesions for reported varicella cases, 2010



Grade I: 50 spots or less easily counted within 30 seconds
Grade II: 50-500 spots (between Grades I and III)
Grade III: 500 or more spots or spots clumped so close together that little normal skin is visible

Challenges with varicella surveillance

Defining and identifying varicella cases in the 2-dose vaccination era

- Varicella case definition not sensitive or specific
 - Probable case: acute illness with generalized maculopapulovesicular rash
 - Confirmed case: acute illness with generalized maculopapulovesicular rash epi-linked to another probable or confirmed case or has lab confirmation
 - Two probable cases that are epi-linked considered confirmed even in absence of lab confirmation
- Rash presentation modified by vaccination
 - Increasingly challenging in 2 dose vaccine era to diagnose cases in vaccinated persons because often lack “classical” vesicles
 - Can be confused with other rashes or bug bites

Importance of laboratory testing for confirmation of varicella cases

- ❑ Laboratory testing not routinely done
 - Providers don't rely on it for patient management and don't recognize it is important for control to properly advise regarding exclusion from school, etc
 - If providers test, often not aware of best specimen to collect or test to order
 - Lesions/scabs better than serologic testing
 - IgM testing using commercial assays not sensitive
 - PCR of lesions most sensitive/specific for diagnosis
- ❑ Timing of specimen collection affects results and limits ability to confirm cases/outbreaks

Summary

□ Impact

- Varicella incidence has declined in all age groups coincident with implementation of routine 2-dose varicella vaccination program for children
 - Greatest declines among children aged 5-14 years
- Outbreaks have become less common

□ National varicella surveillance improving with more states reporting cases and varicella-specific variables to CDC

- Data are now robust enough for monitoring impact of the varicella vaccination program

Varicella Surveillance Needs You...

- ❑ To identify cases
 - Identification and exclusion of mild cases can help prevent transmission
- ❑ To collect specimens for laboratory testing
 - Useful for diagnosis of mild cases that may be confused with other rash illnesses
 - Important for confirmation and implementation of appropriate control measures during outbreak investigations
- ❑ To report cases to your local/state health department
 - Data from Arizona will be used in analysis of national data for monitoring impact of the 2-dose varicella vaccination program

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Varicella outbreak surveillance in schools project

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Resources

- ❑ Manual for the Surveillance of Vaccine Preventable Diseases – Varicella chapter:
<http://www.cdc.gov/vaccines/pubs/surv-manual/chpt17-varicella.html>
- ❑ Strategies for the Control and Investigation of Varicella Outbreaks, 2008: <http://www.cdc.gov/vaccines/vpd-vac/varicella/outbreaks/manual.htm>
- ❑ How to collect specimens for VZV testing:
<http://www.cdc.gov/shingles/lab-testing/collecting-specimens.html>
- ❑ Instructions for sending specimens for VZV testing at CDC
<http://www.cdc.gov/shingles/lab-testing/collecting-specimens.html>

Contact Information

- For questions regarding varicella reporting, outbreak investigations, and laboratory testing in Arizona, please contact:
 - Office of Infectious Disease Services
 - Clarisse Tsang: **602-364-3817 (phone)**
602-509-7970 (cell)
tsangc@azdhs.gov (email)

For questions about national varicella surveillance and testing at the CDC National VZV Laboratory, please contact:

CDC, Division of Viral Diseases, Herpes Virus Team

Adriana Lopez: alopez@cdc.gov (email) or 404-639-8369 (phone)

Thank you!

Severe Varicella Complications

Group A Strep



Severe disseminated varicella
in child with ALL



Staph aureus

Varicella Vaccines

□ Monovalent vaccine (VARIVAX)

- Licensed 1995
- Live, attenuated vaccine with VZV strain (Oka)
- Vaccine-strain virus has potential to cause symptoms similar to those seen with wild-type infection (e.g., reactivation to cause herpes zoster, meningitis)

□ Quadrivalent vaccine (MMRV; PROQUAD)

- Licensed 2005 for children 1-12 years of age
- Includes Measles, Mumps, Rubella, Varicella

Published Estimates of 2-Dose Varicella Vaccine Effectiveness

Study	1-dose VE	2-dose VE	
Vaccine Efficacy			
Kuter PIDJ 2004	94%	98%	
Vaccine Effectiveness			
Gould PIDJ 2009	84%	88%	Incremental vaccine effectiveness of 2 nd dose =28%
Nguyen PIDJ 2010	79%	95%	Incremental vaccine effectiveness of 2 nd dose =76%
Shapiro JID 2011	86%	98%	