Etiologic Investigation of Sporadic Cases of Parotitis

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Disclaimer: The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention

Overview

- Background and epidemiology of mumps
- Challenges with sporadic cases of parotitis
- Project objectives
- Methods
- Findings
- Assessing a mumps diagnosis
- Summary and conclusions

Mumps

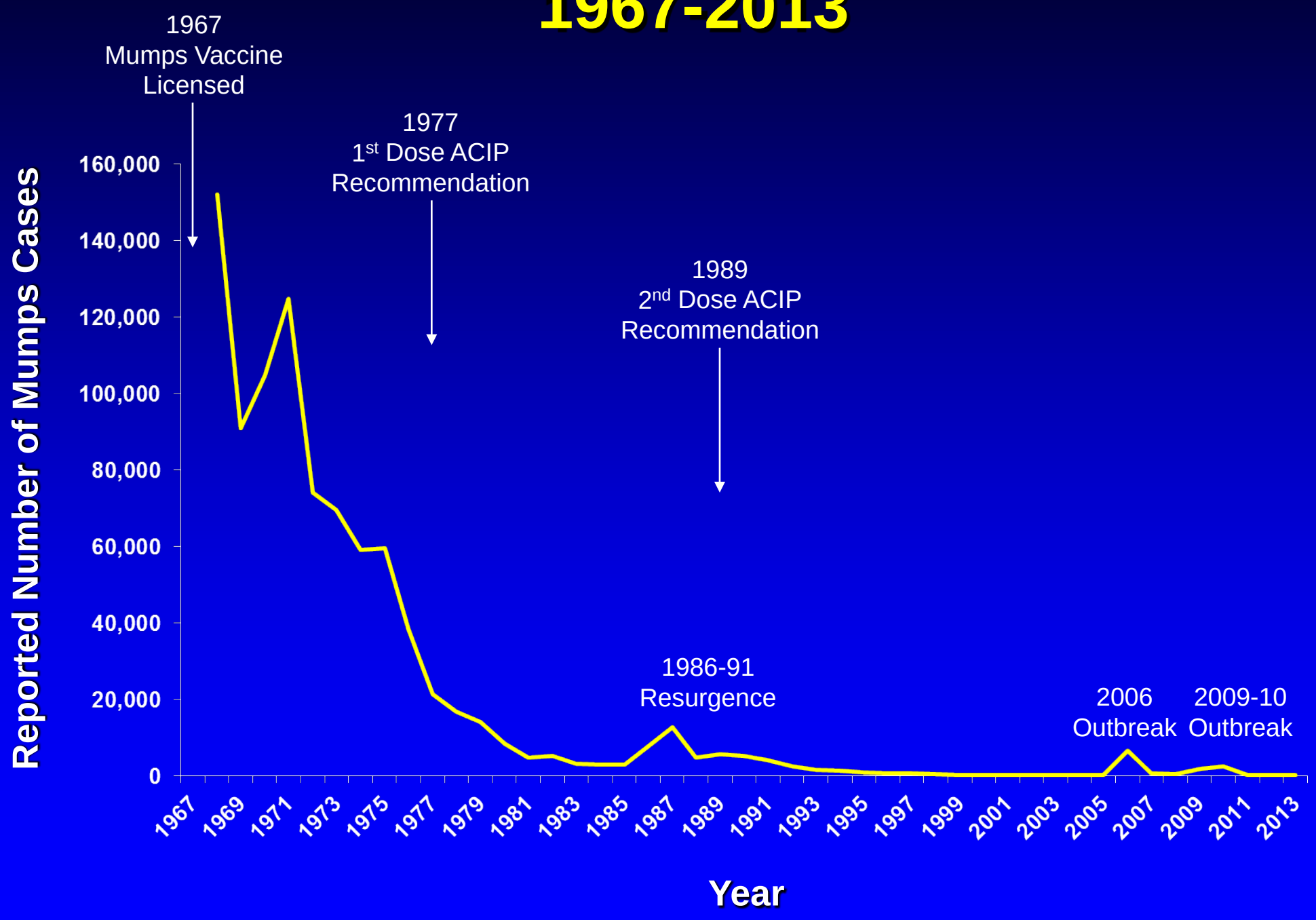
- Acute, viral illness that can present with
  - **Parotitis** (60-70%)
  - Other salivary gland swelling
  - Orchitis (in post-pubertal males)
  - Aseptic meningitis
  - Non-specific respiratory symptoms
  - Asymptomatic (~30%)
- Transmission
  - Respiratory droplet
  - Direct contact (saliva)
- Only known cause of epidemic parotitis

Mumps Vaccine

- The United States uses the Jeryl Lynn mumps vaccine strain
- Effectiveness[1]
  - 1 dose ~78% (49-92%)
  - 2 doses ~88% (66-95%)
- Coverage during 2011 in the U.S.
  - 1 dose, 19-35 month-olds: ~92%[2]
  - 2 doses, 13-17 year-olds: ~91%[3]

1 MMWR 2013; 62(RR4):1-34
2 MMWR 2012; 61:689-96
3 MMWR 2012; 61:671-7

Mumps in the United States, 1967-2013



Laboratory Criteria for Mumps Diagnosis*

- Detection of mumps IgM antibody, or
- Demonstration of specific mumps antibody response in the absence of recent vaccination: either a 4-fold increase in mumps IgG titer as measured by a quantitative assay or a seroconversion from negative to positive using a serologic assay of paired acute and convalescent serum specimens, or
- Detection of mumps RNA (using RT-PCR), or
- Isolation of mumps virus in culture

*CSTE Position Statement 09-ID-50

Recent Laboratory Positivity Rates

- 2006 Midwest U.S. outbreak – low proportion of cases were able to be laboratory-confirmed using IgM, RT-PCR, and viral isolation[1]
- Fall 2006 UVA outbreak[2]
  - IgM: 6/47 (13%)
  - RT-PCR and/or viral isolation: 12/39 (31%)
- 2009-10 Northeast U.S. outbreak[3]
  - IgM: 550/1563 (35%)
  - RT-PCR: 373/530 (68%)
  - Viral isolation: 283/443 (64%)
- 2009-10 Guam outbreak[4]
  - IgM: 60/309 (19%)
  - RT-PCR: 28/34 (82%)
  - Viral isolation: 14/34 (41%)

1 Dayan et al. *N Engl J Med* 2008;358:1580-9
2 Rota et al. *J Med Virol* 2009;81:1819-25
3 Barskey et al. *N Engl J Med* 2012;367:1704-13
4 Nelson et al. *Pediatr Infect Dis J* 2013;32374-80

Previously Infected or Vaccinated Individuals

- May not mount an IgM response
- May not have a 4-fold rise in IgG titer
- May already be IgG-positive on initial blood draw
- May have a viral load below the assay detection level
  - Cannot rule-out a suspected mumps case based only on a negative lab test result

“Outbreaks” of Mumps-like Illness

- Maine (throughout the state)
  - September 2007 – February 2008
  - 102 cases, 97 had parotitis
  - Very few were epi-linked
  - 29/83 (35%) were IgM+
  - 1*/61 (2%) was RT-PCR+
- Nevada (throughout greater Las Vegas)
  - December 2007 – May 2008
  - 35 cases, all had parotitis or jaw swelling
  - 2 were epi-linked
  - 1/22 (5%) was IgM+
  - 0/7 were RT-PCR+

*Confirmed exposure to mumps in Africa

Challenges with Sporadic Cases of Parotitis

- Are sporadic cases of parotitis really mumps?
- Cannot rule-out a suspected mumps case based solely on a negative lab result, especially in a previously vaccinated individual
- Non-mumps causes of parotitis exist on a non-epidemic scale
- Mumps cases require a large amount of resources to investigate and respond to

Objectives

- Assist state health departments in determining the etiology of sporadic cases of parotitis (suspected mumps)
- End fewer investigations of sporadic cases of parotitis with ambiguous findings
- Characterize the profile of viruses and epidemiologic features associated with sporadic cases of parotitis

Surveillance Population

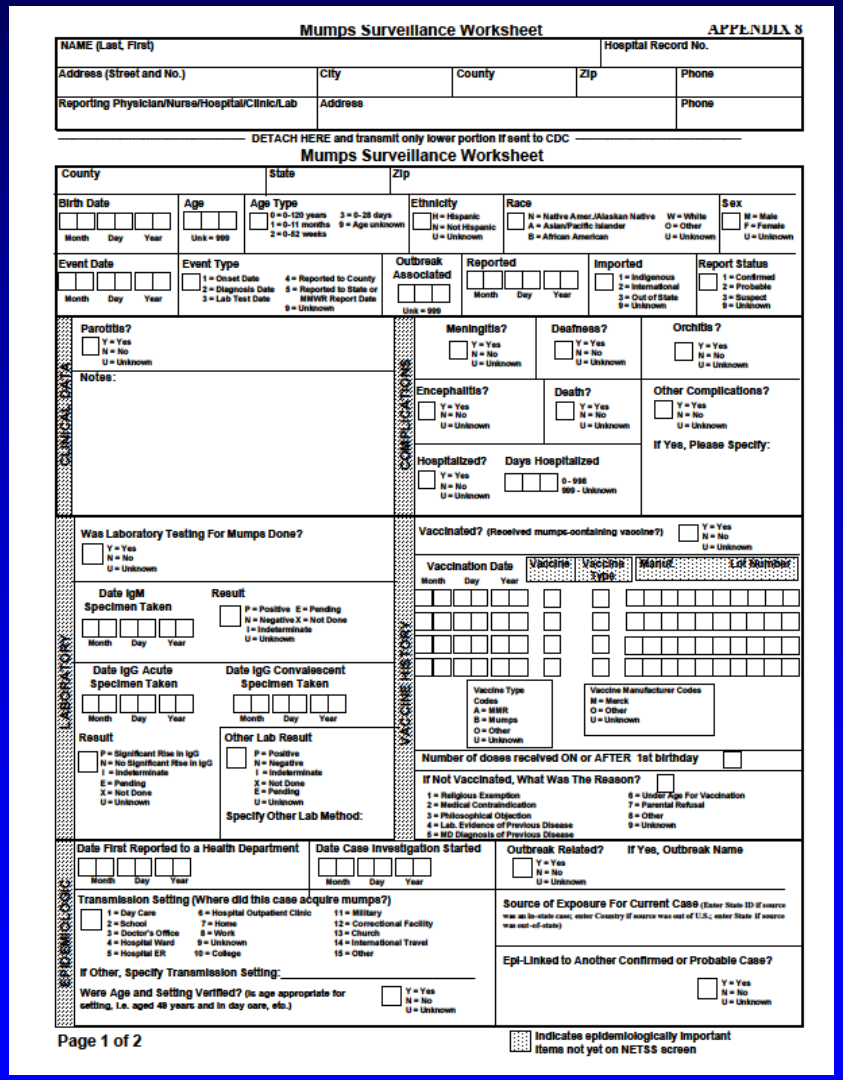
- Sites
  - Arizona, California, Kansas, Michigan, North Carolina, Philadelphia, Tennessee, and Washington State
- Duration
  - 2009-2011

Case-patient Inclusion Criteria

- Must have parotitis
- Must be sporadic
  - Not epi-linked to 2 or more other cases of parotitis
  - Not epi-linked to a laboratory-confirmed mumps case
  - No recent travel to an area known to be experiencing high mumps activity

Procedures – State/Local

- Standard mumps case investigation performed
  - Relevant information collected
    - Demographic
    - Clinical
    - Epidemiologic
    - Vaccination
  - Specimens collected
    - Serum
    - Buccal swab
    - Oropharyngeal swab



Mumps Surveillance Worksheet

APPENDIX 8

NAME (Last, First) | Hospital Record No.

Address (Street and No.) | City | County | Zip | Phone

Reporting Physician/Nurse/Hospital/Clinic/Lab | Address | Phone

DETACH HERE and transmit only lower portion if sent to CDC

Mumps Surveillance Worksheet

County | State | Zip

Birth Date (Month Day Year) | Age (Unk = 999) | Age Type (0 = 0-120 years; 1 = 0-11 months; 2 = 0-52 weeks; 3 = 0-28 days; 9 = Age unknown) | Ethnicity (H = Hispanic; N = Not Hispanic; U = Unknown) | Race (N = Native Amer./Alaskan Native; A = Asian/Pacific Islander; B = African American; W = White; O = Other; U = Unknown) | Sex (M = Male; F = Female; U = Unknown)

Event Date (Month Day Year) | Event Type (1 = Onset Date; 2 = Diagnosis Date; 3 = Lab Test Date; 4 = Reported to County; 5 = Reported to State or MMWR Report Date; 9 = Unknown) | Outbreak Associated (Unk = 999) | Reported (Month Day Year) | Imported (1 = Indigenous; 2 = International; 3 = Out of State; 9 = Unknown) | Report Status (1 = Confirmed; 2 = Probable; 3 = Suspect; 9 = Unknown)

COMPLICATIONS

Parotitis? (Y = Yes; N = No; U = Unknown)

Notes:

Meningitis? (Y = Yes; N = No; U = Unknown) | Deafness? (Y = Yes; N = No; U = Unknown) | Orchitis? (Y = Yes; N = No; U = Unknown)

Encephalitis? (Y = Yes; N = No; U = Unknown) | Death? (Y = Yes; N = No; U = Unknown) | Other Complications? (Y = Yes; N = No; U = Unknown)

If Yes, Please Specify:

Hospitalized? (Y = Yes; N = No; U = Unknown) | Days Hospitalized (0 - 998; 999 - Unknown)

LABORATORY

Was Laboratory Testing For Mumps Done? (Y = Yes; N = No; U = Unknown)

Date IgM Specimen Taken (Month Day Year) | Result (P = Positive; E = Pending; N = Negative; X = Not Done; I = Indeterminate; U = Unknown)

Date IgG Acute Specimen Taken (Month Day Year) | Date IgG Convalescent Specimen Taken (Month Day Year)

Result (P = Significant Rise in IgG; N = No Significant Rise in IgG; I = Indeterminate; E = Pending; X = Not Done; U = Unknown)

Other Lab Result (P = Positive; N = Negative; I = Indeterminate; X = Not Done; E = Pending; U = Unknown)

Specify Other Lab Method:

VACCINE HISTORY

Vaccinated? (Received mumps-containing vaccine?) (Y = Yes; N = No; U = Unknown)

Vaccination Date (Month Day Year) | Vaccine | Vaccine Type | Manuf. | Lot Number

Vaccine Type Codes: A = MMR; B = Mumps; O = Other; U = Unknown

Vaccine Manufacturer Codes: M = Merck; O = Other; U = Unknown

Number of doses received ON or AFTER 1st birthday

If Not Vaccinated, What Was The Reason?

1 = Religious Exemption; 2 = Medical Contraindication; 3 = Philosophical Objection; 4 = Lab. Evidence of Previous Disease; 5 = MD Diagnosis of Previous Disease; 6 = Under Age For Vaccination; 7 = Parental Refusal; 8 = Other; 9 = Unknown

EPIDEMIOLOGY

Date First Reported to a Health Department (Month Day Year) | Date Case Investigation Started (Month Day Year)

Outbreak Related? (Y = Yes; N = No; U = Unknown) | If Yes, Outbreak Name

Transmission Setting (Where did this case acquire mumps?)

1 = Day Care; 2 = School; 3 = Doctor's Office; 4 = Hospital Ward; 5 = Hospital ER; 6 = Hospital Outpatient Clinic; 7 = Home; 8 = Work; 9 = Unknown; 10 = College; 11 = Military; 12 = Correctional Facility; 13 = Church; 14 = International Travel; 15 = Other

If Other, Specify Transmission Setting:

Were Age and Setting Verified? (Is age appropriate for setting, i.e. aged 48 years and in day care, etc.) (Y = Yes; N = No; U = Unknown)

Source of Exposure For Current Case (Enter State ID if source was an in-state case; enter Country if source was out of U.S.; enter State if source was out-of-state)

Epi-Linked to Another Confirmed or Probable Case? (Y = Yes; N = No; U = Unknown)

Page 1 of 2

Indicates epidemiologically important items not yet on NETSS screen

Procedures – CDC

- Nucleic acids extracted from swab specimens
- Presence of viral nucleic acids was tested for using PCR methods
  - Mumps virus (MuV)
  - Enteroviruses (EV), including human parechovirus (HPeV)
  - Human herpesvirus 6A & 6B (HHV-6A & HHV-6B)
  - Epstein-Barr virus (EBV)
  - Human parainfluenza virus 1-3 (HPIV 1-3)
  - Adenoviruses (AdV)
  - Human bocavirus (HBoV)

Findings*

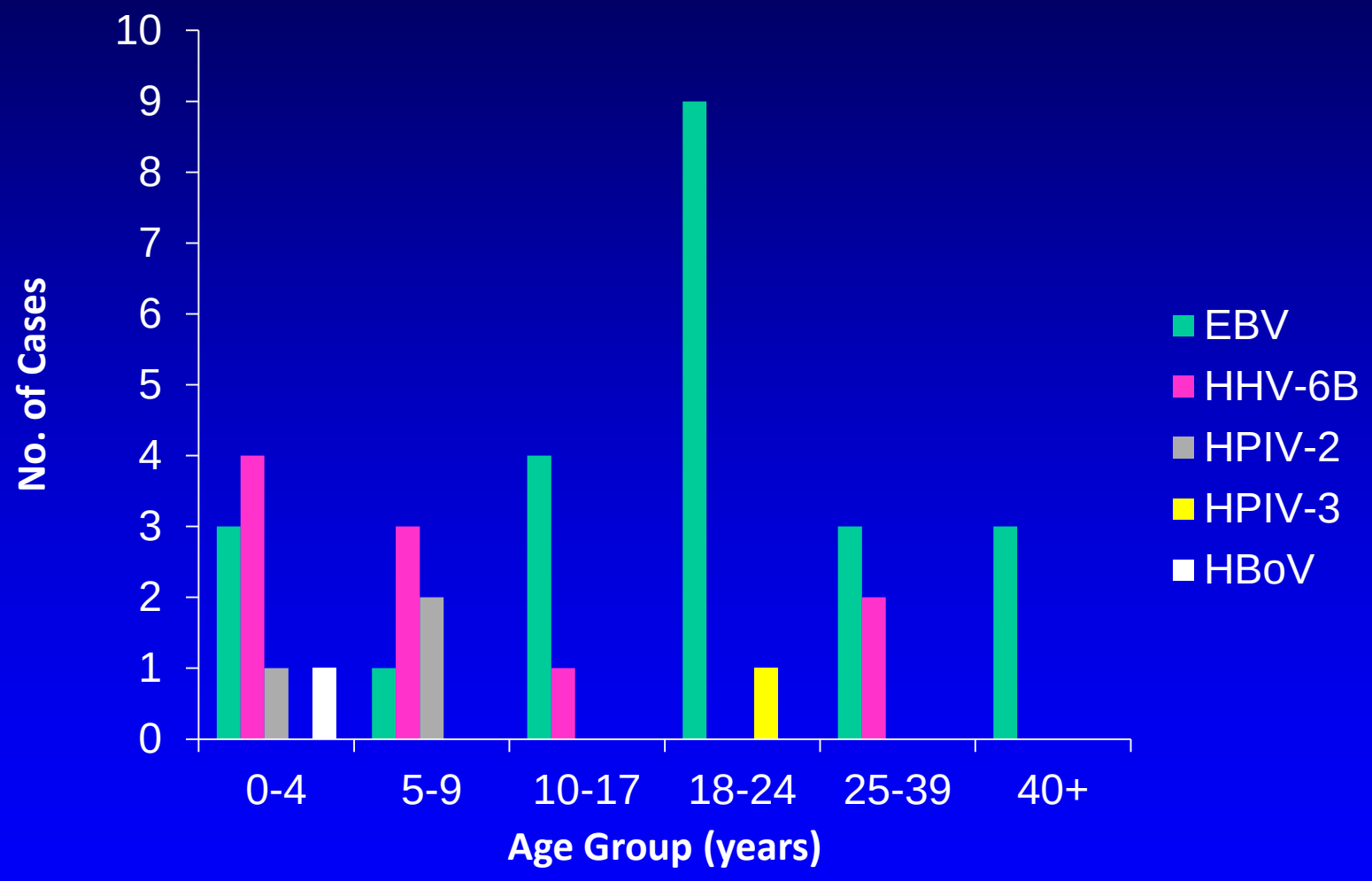
- 101 patients
- Median patient age: 19 years (range: 0.3 – 76 years)
- Sex: 46% female
- Vaccination documented for 65/101 patients
  - 0 Doses: 18%
  - 1 Dose: 20%
  - 2 Doses: 62%
- Number of patients from each jurisdiction
  - AZ (6), CA (4), KS (13), MI (33), NC (15), PHL (10), TN (1), WA (19)

*Barskey et al. *J Infect Dis* in press.

Viruses Detected

Virus	Number positive (n)	Percent positive (n/101)
Epstein-Barr virus (EBV)	23	23%
Human herpesvirus 6B (HHV-6B)	10	10%
Human parainfluenza virus 2 (HPIV-2)	3	3%
Human parainfluenza virus 3 (HPIV-3)	1	1%
Human bocavirus (HBoV)	1	1%
Mumps (MuV)	0	0%
Enteroviruses (EV)	0	0%
Human parechovirus (HPeV)	0	0%
Human herpesvirus 6A (HHV-6A)	0	0%
Human parainfluenza virus 1 (HPIV-1)	0	0%
Adenoviruses (AdV)	0	0%
Total	**38**	**38%**

Viral Detection by Age Group



Viral Detection by Onset Month

Figure 2

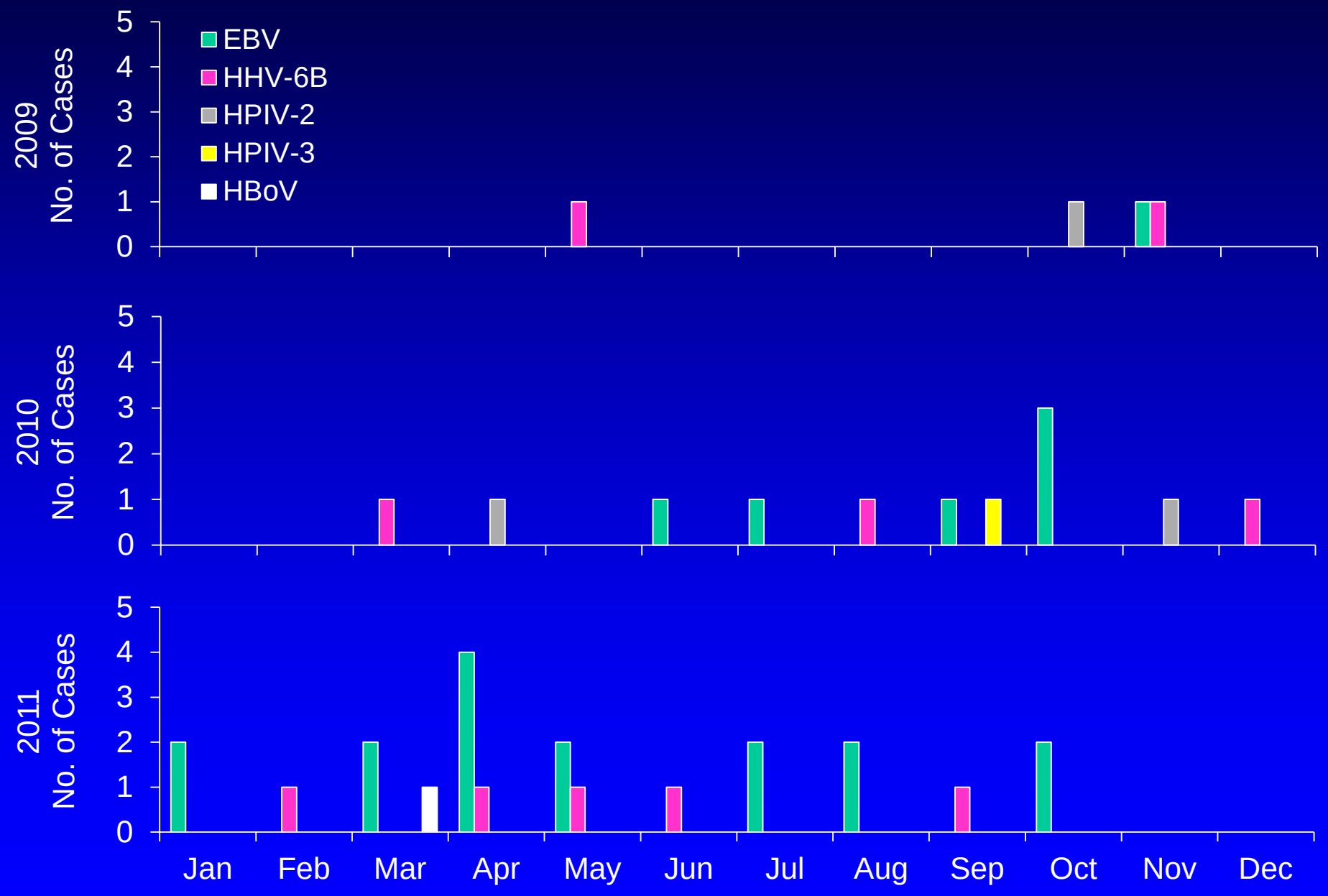
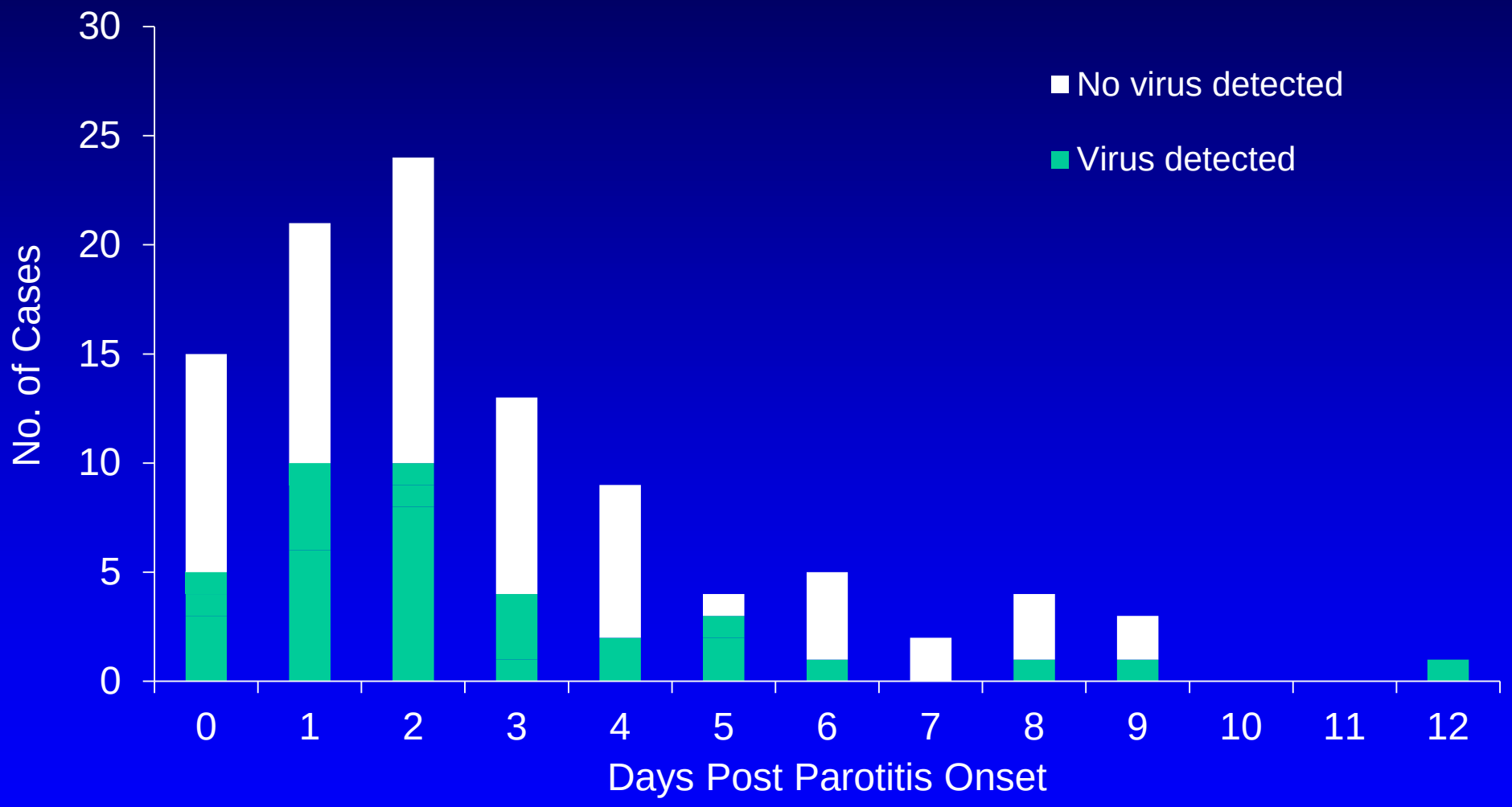


Figure 1

Timing of Swab Collection



Mumps IgM Results

Assay	No Virus Detected Number Mumps IgM Positive (%)	Virus Detected Number Mumps IgM Positive (%)	Total Number Mumps IgM Positive (%)
EIA	3/27 (11%)	3/17 (18%)	6/44 (14%)
IFA	1/2 (50%)	2/3 (67%)	3/5 (60%)
Unknown	2/15 (13%)	1/6 (17%)	3/21 (14%)
Total	6/44 (14%)	6/26 (23%)	12/70 (17%)

Mumps Vaccination History of Patients*

Doses	No Virus Detected n = 35 n (%)	Virus Detected n = 30 n (%)	Total n = 65 n (%)
0	6 (17%)	6 (20%)	12 (18%)
1	9 (26%)	4 (13%)	13 (20%)
2	20 (57%)	20 (67%)	40 (62%)

*Where vaccination history was documented

Considerations When Assessing a Mumps Diagnosis in a Sporadic Case of Parotitis

- Mumps RT-PCR and culture results
- Laboratory results for other agents
- Mumps IgM test results
- Patient vaccination history
- Timing of specimen collection
- Time of year

Summary and Conclusions

- Mumps virus was not detected among any sporadic cases of parotitis
- A non-mumps virus was detected in 38% of sporadic cases of parotitis
  - Most were EBV
- Mumps vaccine effectiveness and coverage estimates within the U.S. are high
- Sporadic cases of parotitis within the U.S. may have a lower likelihood of being mumps
- Until more reliable methods for ruling-out a mumps etiology are developed, sporadic cases of parotitis should be treated as if they were mumps

Limitations

- Passive surveillance system
- Small numbers and convenience sample, so results might not be generalizable
- Obtaining specimens within 2 days of parotitis onset not always possible
- No control group, so causation should not be assumed
- Other infectious etiologies for parotitis exist, but were not tested for (e.g., HIV, cat scratch disease, and influenza)

Acknowledgments

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Thank you