2015 Science Writers Symposium

Mumps Resurgence and Our Work to Prevent New Epidemics

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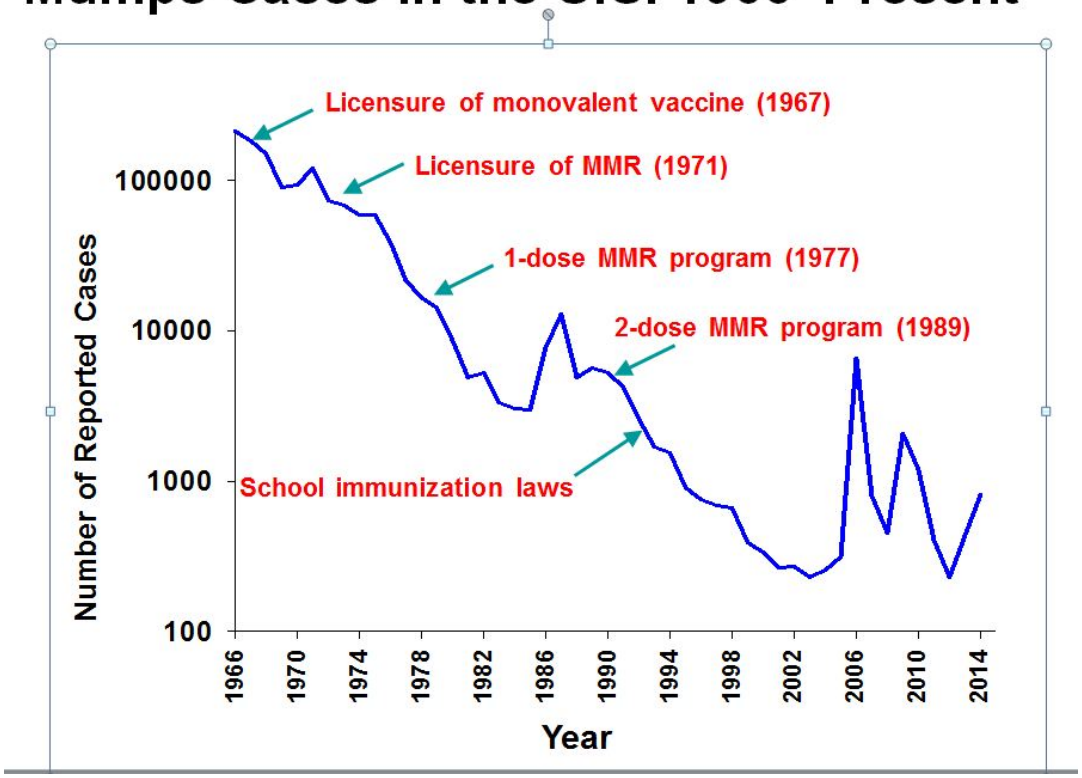
September 18, 2015

Mumps: Brief History and Intro

- First described by Hippocrates in the 5th century BC
- Viral etiology demonstrated in 1935
- Acute infection transmitted by respiratory droplets
- Parotitis (salivary glands), orchitis (testes), meningitis
- Prevaccine era
  - Disease of childhood
  - Leading cause of viral aseptic meningitis and encephalitis
  - Most common cause of unilateral acquired deafness in children

Graph shows rapid decline in the number of mumps cases, from the prevaccine era (prior to 1967) when well over 100,000 cases were reported annually, to about 10,000 cases per year following the 1977 recommendation from the Advisory Committee of Immunization Practices (ACIP) that all children receive one dose of MMR vaccine, to less than 5,000 cases per year following the 1989 ACIP recommendation that all children receive two doses of MMR vaccine (at 12–15 month of age and at 4–6 years of age). The number of reported mumps cases precipitously declined even further following the 1991 institution of immunization laws for school attendance, so that by the early 2000s only a few hundred cases were being reported annually. However, a massive resurgence occurred in 2006 and has continued since.



Vaccine Failure or Failure to Vaccinate?

- **U. Iowa**: 97% of cases vaccinated
- **U. Kansas**: 99% of cases vaccinated
- **U. Virginia**: 100% of cases vaccinated
- **Ohio St. Univ.**: "Nearly all persons vaccinated"
- **U. Idaho**: "Most persons vaccinated"
- **U. Illinois:** "Most up to date on their MMR vaccine"

Vaccine Failure? NO

- Review of 54 mumps vaccine immunogenicity studies
- Mean rate of primary vaccine failure: 5%
- Nearly all individuals failing to respond to the first dose of vaccine will develop antibodies following a second dose

Dayan G and Rubin S. Clin Infect Dis. 2008; v47(11):p1458-67

Longitudinal Study: 87 subjects, each tested at two time points

Mumps virus neutralizing antibody titers in sera of MMR vaccinees

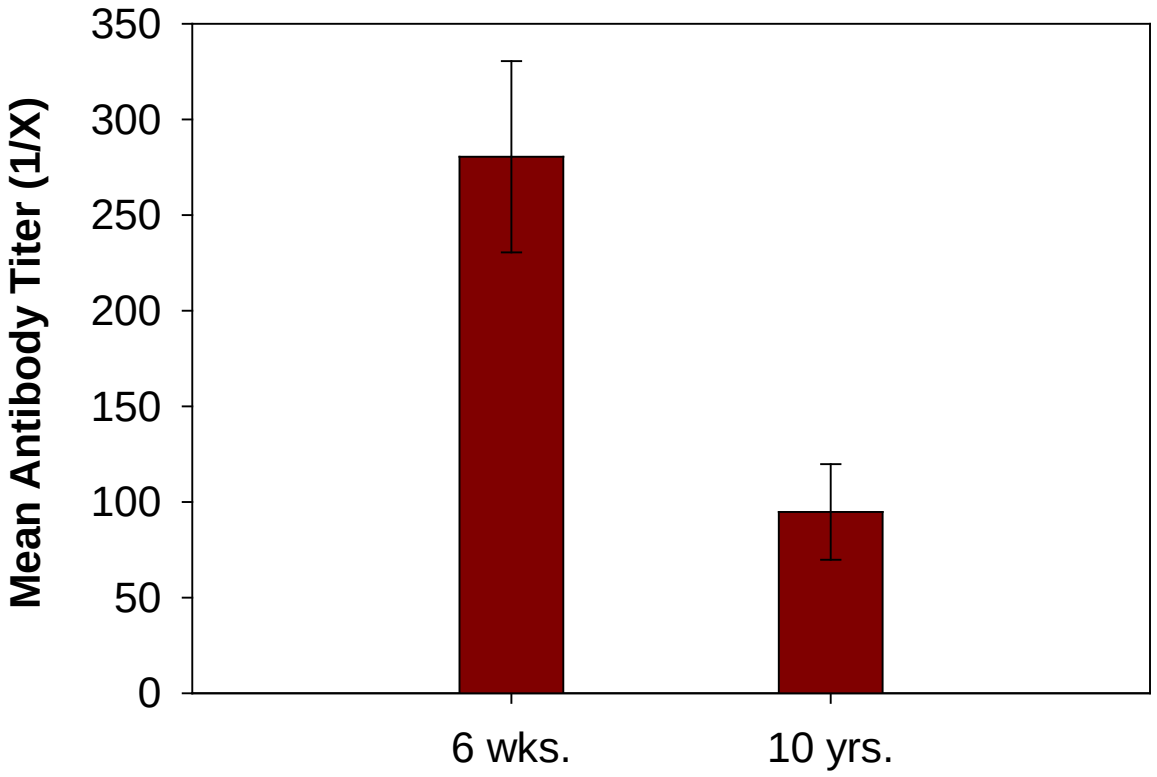


Figure shows declining levels of anti-mumps virus antibodies over a 10-year period after vaccination. The geometric mean titer of mumps virus neutralizing antibody declined from 280 to 95 over this time frame.

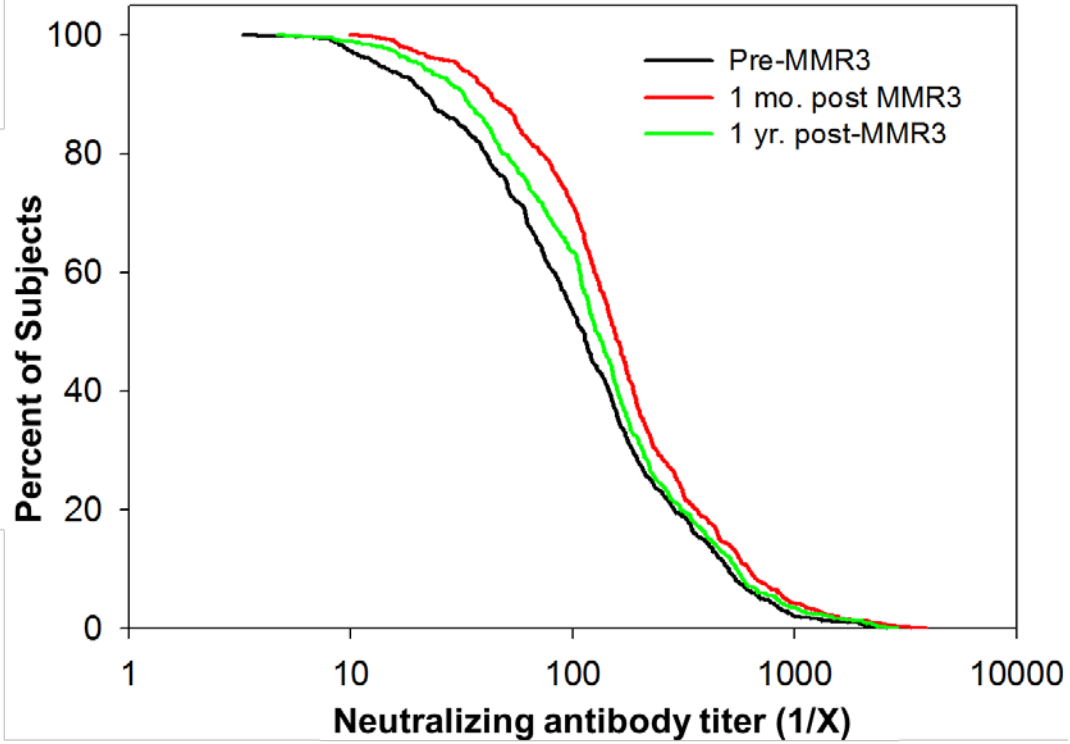
Rubin et al. J Infect Dis. 2008; v198(4):p508-15

What To Do About Declining Immunity With Time Post Vaccination?

- Current vaccine schedule
  - First dose as 12–15 months of age
  - Second dose at 4–6 years of age
  - Perhaps add a third dose, to be administered during adolescence?
  - Collaboration with the CDC to assess the magnitude and duration of virus neutralizing antibody responses after a third dose of MMR in 685 young adults

Fiebelkorn et al. Open Forum Infect Dis. 2014; v1(2)

Figure shows the reverse cumulative distribution curves of antibody titers among 685 young adults sampled at three time points: prior to receipt of a third dose of MMR, 1 month after the third dose, and 1 year later. The figure shows a significant shift of the curve to the right 1 month after the third dose of MMR, indicating a boost in antibody titers. However, 1 year later, the curve returned close to baseline, indicating that the boost was only transient. These data argue against consideration for a three-dose MMR program.



What's Next?

- **Consideration for development of better mumps vaccines**
  - Compared to measles and rubella responses to MMR vaccine:
    - There are fewer mumps virus antibody secreting cells (CDC)
    - Avidity (strength) of mumps antibodies is lower (NIH Helsinki)
  - Suggests deficiencies in memory B-cell development
    - Calls for optimization of the amino acid sequence of vaccine virus antigens
    - Not possible when vaccines were developed in the 1960s, but now can easily be done with reverse genetics

Rubin et al. J Virol. 2012; v86(1):p615-20

Current Mumps Vaccine Is Efficacious

- The occurrence of mumps in vaccinated persons does not mean that the vaccine is not efficacious, it means that the vaccine is not 100% effective.
  - Field studies show that two doses of vaccine is 88% effective (very good)

Scenario: Student with mumps attends college campus of 10,000

Assume 20% exposed, 50% of infections are asymptomatic

If no one is vaccinated: 1,000 cases

If everyone is vaccinated: 120 cases

Disease is mild in vaccinees.