

Mumps resurgence in the United States

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The recent mumps epidemic in the central United States has generated a large amount of public concern. A total of 2597 mumps cases have been reported in the United States in 11 states since January 1, 2006, representing a marked resurgence of mumps in a single year. The majority of these recent cases have occurred in college students age 18 to 25 years. Most were vaccinated with 2 doses of measles, mumps, and rubella-containing vaccines. Such outbreaks provide an opportunity for clinicians to review the clinical presentation, diagnosis, and morbidity of vaccine-preventable infections and also to review immunologic mechanisms and practice guidelines that might contribute to poor vaccine responses. A review of mumps is provided with discussion of potential mechanisms for vaccine failure. (*J Allergy Clin Immunol* 2006;118:938-41.)

Key words: Mumps, outbreak, mumps complications, parotitis, orchitis, incomplete immunization

The US Centers for Disease Control and Prevention has received reports on more than 515 possible mumps cases from the Iowa Department of Public Health through April 2006.¹ Since January 2006, the total number of reported mumps cases in the United States is 2597, and this represents a marked increase in reported cases in a single year. By comparison, only 231 cases were reported nationally in 2003.²

The majority of recent cases have occurred in patients age 18 to 25 years, but infection has been identified in all age groups. Most infected patients were vaccinated in childhood with 2 doses of mumps-containing vaccine. In the Iowa college-age cohort, approximately 6% were unvaccinated, and 12% had received a single mumps-containing vaccine. The strain of mumps under investigation has been described as that present in the current mumps vaccine licensed for use in the United States; therefore, full vaccination should be protective. The same strain has been identified in more than 70,000 cases in the United Kingdom within the past 2 years.³ In contrast with

Abbreviations used

HAI: Hemagglutination inhibition assay

MMR: Measles, mumps, rubella

the reported US cases, the majority of the United Kingdom cases occurred in unvaccinated young adults.

Such outbreaks provide an opportunity for physicians with limited experience evaluating mumps disease to revisit the clinical presentation, diagnosis, and morbidity of vaccine-preventable infections. A review is provided of the immune mechanisms and practice guidelines that might contribute to poor vaccine response.

MUMPS VIRUS

Mumps is an acute, self-limited viral infection occurring most often in school-age children and adolescents. The classic feature of mumps is nonsuppurative swelling and tenderness of the salivary glands. The infection is usually benign, and many cases are subclinical. Complications of infection include meningitis and epididymo-orchitis. In the recent US outbreak, reported clinical symptoms included parotitis in 66% of cases. Other serious complications (orchitis, sialadenitis, deafness) occur in lesser numbers of affected individuals and may manifest without evidence of parotitis. Unapparent infection may be more common (15% to 20% asymptomatic) among adult-age than pediatric-age patients.⁴

Mumps is a member of the Paramyxovirus genus. The virus genome is composed of single-stranded RNA. The 2 major surface glycoproteins are hemagglutinin-neuraminidase and fusion protein. The virus is transmitted by fomites, respiratory droplets, or direct contact. Mumps is most contagious right before or at the onset of parotitis. Humans are the only natural host for the mumps virus.

The incubation period of the virus is 16 to 18 days. Prodromal symptoms include low-grade fever, anorexia, headache, and malaise. Within 24 hours of the prodrome, patients may complain of earache and tenderness of the ipsilateral parotid gland. Once parotid swelling reaches its peak, the tenderness and fever resolve rapidly, with the gland usually returning to its normal size in 7 to 10 days.

The diagnosis of mumps is based on history of exposure, and parotid swelling with tenderness. Laboratory

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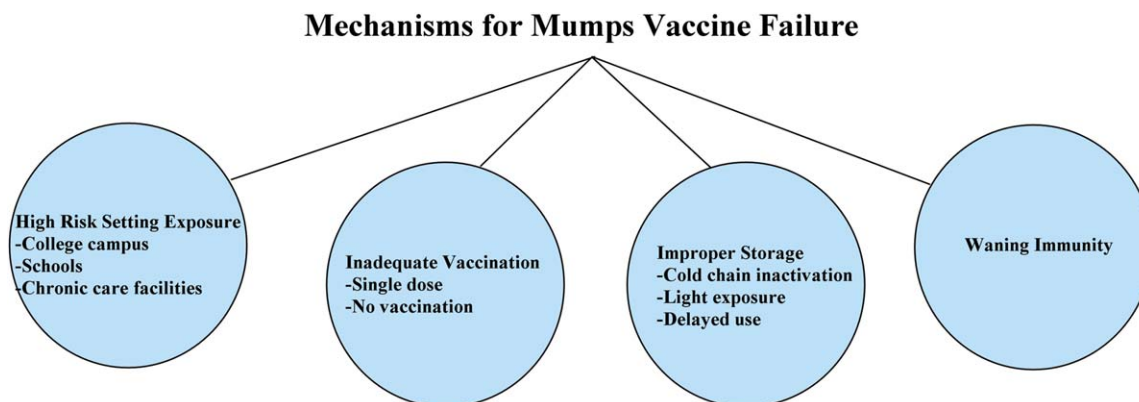


FIG 1. Mechanisms for mumps vaccine failure in the current US outbreak may include the following: high viral burden in close settings like college campuses that overcomes herd immunity; suboptimal vaccination in high-risk populations; poor storage and handling practices that lead to virus inactivation, ie, cold chain interruption; and possible waning immunity in previously vaccinated individuals.

confirmation of typical mumps becomes important in outbreaks and in cases with subclinical symptoms. Specific assays include viral isolation from the throat or nasal washings, IgG titers (hemagglutination inhibition assay [HAI], complement fixation assay, enzyme immunoassay), IgM assays, and RT-PCR testing.⁴

Infection is confirmed by viral isolation or nucleic acid from a clinical specimen. Serology should reveal a significant rise in IgG titers between acute and convalescent specimens or a positive IgM mumps antibody.

Parainfluenza 3 virus can also cause parotitis and can produce a heterologous antibody response affecting the mumps HAI test. It is important to rule out this infection when using the HAI test for diagnosing mumps.

Management of mumps infection includes isolation until the parotid swelling resolves. However, this may not be an effective measure because the virus is shed from saliva days before the development of parotitis. Therefore, patients without clinical symptoms can effectively transmit mumps virus, especially in crowded settings. Delayed diagnosis may lead to enhanced transmission.

MUMPS VACCINE

The measles, mumps, rubella (MMR) vaccine most commonly used in the United States is a sterile lyophilized preparation of (1) Attenuvax (Measles Virus Vaccine Live; Merck, Whitehouse Station, NJ); (2) Mumpsavax (Mumps Virus Vaccine Live; Merck), the Jeryl Lynn (B level) strain of mumps virus grown in cell cultures of chick embryo; and (3) Meruvax II (Rubella Virus Vaccine Live; Merck). The 3 viruses are mixed before lyophilization.

The vaccine should be stored at 2°C to 8°C, and light exposure should be avoided to minimize inactivation before reconstitution. The reconstituted vaccine is delivered by subcutaneous administration at a dose of 0.5 mL. Each dose contains approximately 25 µg neomycin. The product contains no preservative. Sorbitol and hydrolyzed gelatin are added stabilizers.

INDICATIONS FOR MUMPS VACCINE DELIVERY

Presumptive evidence of mumps protection is (1) birth before 1957, (2) physician-diagnosed mumps, (3) laboratory evidence of immunity, or (4) documentation of delivery of 2 mumps-containing vaccines. The Advisory Committee for Immunization Practices, selected experts who provide advice to the Centers for Disease Control and Prevention, in collaboration with the American Academy of Family Physicians and the American Academy of Pediatrics recommends that all US children older than 12 months receive a measles-containing vaccine, and the MMR is most often delivered.⁵ A second dose delivered at 4 to 6 years of age was added to MMR dosing in the United States in 1998.⁶ Most states now require evidence of immunity to mumps (ie, documented 2 doses of vaccine, physician-diagnosed disease, or positive antibody studies) for school entry and attendance. Updated recommendations for mumps vaccination of healthcare workers include receipt of 2 doses of MMR vaccine (28 days apart) for those without a history of mumps vaccination or any evidence of immunity. Healthcare workers with only single dosing documentation should receive a second dose. Birth before 1957 has been associated with presumptive evidence of immunity. In the context of the current outbreak, a single dose is recommended in healthcare workers in this age group who have no history of physician-diagnosed mumps or evidence of immunity (see laboratory tests outlined).⁷

VACCINE EFFICACY

Immunologic responses to viral vaccines typically elicit both humoral and cellular responses. More than 97% of persons who are susceptible to mumps develop measurable antibody after vaccination. In controlled clinical trials in the United States, 1 dose of vaccine was

approximately 95% efficacious in preventing mumps disease.⁸⁻¹⁰ However, field studies have documented lower estimates of vaccine efficacy, ranging from 75% to 95%.¹¹ Antibody levels induced by the vaccine are lower than antibody levels resulting from natural infection.^{8,12,13} The duration of vaccine-induced immunity is unknown, but serologic and epidemiologic data collected during 30 years of live vaccine use indicate both the persistence of antibody and continuing protection against infection.¹³ Cellular responses (lymphoproliferation and cytokine production) to MMR vaccination are described in correlation with measles antibody production. After measles vaccination, HLA class 1 genes have been associated with a differential measles antibody response that correlates with T_H1 (IFN- γ) measles-specific stimulation but not T_H2 (IL-4).¹⁴

MECHANISMS FOR VACCINE FAILURE

Immunologic mechanisms and clinical practices that might contribute to poor vaccine responses are outlined in Fig 1.

School settings (preschool through 12th grade and university settings), camps, and chronic care facilities are often the setting for transmission of droplet-spread vaccine-preventable diseases, such as mumps and influenza.⁸ Mumps transmission is facilitated by both subclinical cases and undiagnosed cases that may shed infectious particles in populations at risk. In reported outbreaks in camp/school settings, adherence to school entry regulations for 2 doses of MMR have been excellent (90% to 96%), but outbreaks of mumps have still occurred in the setting of close contact and shared secretions (normal youth behavior). Therefore, mumps exposure in high-risk settings may overcome established immunity in individuals with optimal vaccination delivery.

Updated recommendations (2006) stress the importance for university students to receive 2 doses of MMR vaccines.⁸ Although these and earlier guidelines (1998) have been adopted by many universities, adherence is not complete. Mumps exposure can result in infection in a high-risk setting like university campuses when only single dosing of MMR is prevalent.

The MMR vaccine is a live attenuated vaccine and, as previously outlined, requires fastidious storage and handling for best potency and resultant efficacy at delivery.¹⁵ Interruption of the cold chain can lead to significant changes in potency and resultant decrease in immune response. Delay in use after reconstitution (>30 minutes) and exposure to light can inactivate the virus. Practices that violate the vaccine cold chain (inappropriate storage or handling) are important potential sources of vaccine failure. In outbreak settings, affected individuals with documented vaccine delivery and IgM serologic responses to mumps could represent such failure.

Concerns about waning immunity to mumps or MMR vaccine have been raised but not documented in outbreak or at-risk populations to date.¹⁶ This important issue must

be considered in outbreaks such as the current US mumps outbreak, in which affected individuals may have been appropriately vaccinated.

SUMMARY

Practicing physicians in the United States have limited experience with vaccine-preventable disease recognition. Delayed diagnosis may be associated with more widespread transmission because prevention practices may not be implemented early in high-risk environments like schools/colleges, camps, and healthcare settings. Poor adherence to recommended dosing guidelines may provide suboptimal herd immunity and permit breakthrough in vulnerable populations and is the likely cause of the recent outbreak in the Midwest. Inappropriate storage and handling affects potency, which may in turn reduce efficacy. Waning vaccine immunity has not been proven with live viral vaccines but should be evaluated in outbreak settings. Clinical immunologists/allergists are well versed in the immune mechanisms necessary for efficacious vaccine delivery because they deliver allergy injections. Vaccine-preventable outbreaks allow an opportunity to consider storage/handling practices related to both childhood/adult vaccine delivery and other allergy vaccines/biologicals that we deliver daily in our practices. In outbreak settings, recommendations for control and elimination of mumps should be considered in geographically affected allergy/immunology practices in the United States.

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