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LEARNING OBJECTIVES After studying the literature presented in this issue, participants will be able to:

- Describe the relationship of the 2006 outbreak of mumps to the effectiveness of the 2-dose mumps vaccine
- List the most common viral causes of acute laryngeal croup in young children

TARGET AUDIENCE This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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Resurgence of Mumps in the United States in 2006

Mumps is an acute viral infection that causes fever and inflammation of the salivary glands. In the prevaccine era, children in primary grades had the highest attack rate. The extensive use of a second dose of the measles-mumps-rubella (MMR) vaccine among US school-aged children beginning in 1990 yielded historically low counts of mumps cases. Although a 2010 elimination goal was set, the largest mumps outbreak in 2 decades occurred in 2006. In this study, Dayan and colleagues reviewed mumps cases that were reported during the 2006 outbreak through the National Notifiable Diseases Surveillance System from state health departments to the Centers for Disease Control and Prevention.

In January 2006, mumps cases were initially reported on college campuses in Iowa; in February, mumps cases were reported on other college campuses; and by April, the outbreak had peaked. This unexpected and abrupt outbreak involved 6,584 cases, with 76% occurring between March and May. There were no large outbreaks at primary or secondary schools. Additionally, 198 persons had complications, 85 hospitalizations, and no deaths were reported. Complications were due mostly to orchitis. Male gender and increasing age up to 50 years were significantly associated with an increased complication rate.

The reported national incidence of mumps during the preresurgence period (2000-2005) was less than 1 case per million persons. In contrast,

the reported national incidence during the 2006 resurgence was 2.2 cases per 100,000 persons, with the highest incidence among persons aged 18 to 24 years (31.1 per 100,000; 3.7-fold higher than all other age groups combined). A subgroup analysis revealed that 83% of these patients were currently attending college. Although mumps was reported in 45 states, 8 contiguous midwestern states (Illinois, Iowa, Kansas, Minnesota, Missouri, Nebraska, South Dakota, and Wisconsin) had the most cases (85%).

Among those in the 8 highly affected states with known vaccination status, 63% overall and 84% of those aged between 18 and 24 years had received 2 doses of mumps vaccine. During the 12 years preceding the outbreak, national coverage of 1-dose mumps vaccination among preschoolers was 89% or more nationwide and 86% or more in highly affected states. In 2006, the national 2-dose coverage among adolescents was 87%, the highest in US history.

Given the low case counts of mumps throughout the early 2000s, the outbreak in 2006 was indeed unexpected. Regardless of a high coverage rate with 2 doses of mumps vaccine, a large mumps outbreak occurred that preferentially involved midwestern college-aged adults who probably received the second dose as school-aged children. This outbreak suggested failure of the 2-dose vaccine. However, case counts of mumps during the 2006 outbreak were still far below those observed during the prevaccine era.

Continued

Disclosures:

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Resurgence of Mumps in the United States in 2006 *(Continued)*

The authors speculated that this outbreak might be attributed to loss of efficacy of mumps vaccine-induced immunity (derived from genotype A virus) against heterologous strains (eg, G genotype). The authors proposed that a more effective mumps vaccine or changes in vaccine policy (eg, administration of a second dose of MMR vaccine

at a later age or administration of a third dose) may be required to circumvent future outbreaks and eliminate mumps.

Dayan GH, Quinlisk MP, Parker AA, et al. Recent resurgence of mumps in the United States. *N Engl J Med*. 2008;358(15):1580-1589.

COMMENTARY

The 2006 Mumps Epidemic: A Perfect Storm or a Shot Across the Bow?

JOHN P. DEVINCENZO III, MD, Associate Professor of Pediatrics and Molecular Sciences, University of Tennessee School of Medicine, Memphis, Tennessee.

The *Perfect Storm* was a recent popular novel and film illustrating the devastating effects on a fishing boat crew of the statistically improbable confluence of 3 major storms, including a Nor'easter and a hurricane. The paper reviewed here describes the 2006 mumps outbreak occurring primarily in a highly vaccinated population of college attendees in the upper Midwest in much the same terms. This epidemic may have been the result of a "perfect storm." The factors coming together to produce this epidemic were crowded living conditions of college campuses; likely waning immunity from a single strain mumps vaccine; vaccination rates that, although high, were around the threshold but certainly not higher than that predicted to provide herd immunity; and importantly, the presumed importation of mumps from an ongoing much more serious epidemic occurring in Great Britain. Although not mentioned in the paper, the "storm" continued in large part because of the relatively large percentage of mumps infections that do not manifest pathognomonic signs of parotid swelling and the transmissibility of the infection prior to the development of this sign.

Rather than being regarded as a "perfect storm" that is unlikely to happen again, this epidemic should instead be considered a warning "shot across the bow." We need to take notice. This epidemic was not even the first such shot. Several smaller epidemics of mumps occurring in highly vaccinated populations have been previously described. The maintenance of vaccination-induced immunity will be an ongoing challenge, especially when the diseases (eg, pertussis, mumps, measles, varicella) themselves are pushed to such infrequent occurrences that they fail to provide ongoing booster immunity. Global mumps eradication will likely not be soon achieved (>40 countries do not routinely vaccinate against this virus). Therefore immigration policy needs to address more seriously the importance of diseases of epidemic potential.

The good news from this epidemic was twofold. First, the US epidemic was orders of magnitude less severe than that occurring in the United Kingdom, likely because of high US vaccination rates. Second, breakthrough disease is likely to have been less severe in those who were previously vaccinated. As clinicians, we cannot become complacent in vaccinating nor in considering vaccine-preventable diseases occurring in our vaccinated patients because these and other vaccine-preventable epidemics are likely to continue to occur.

Respiratory Viruses in Acute Laryngeal Croup in Childhood

Respiratory viruses have been implicated in laryngeal croup in young children. Virus isolation and antigen detection have shown that parainfluenza viruses (PIVs) are the most important single agents causing croup. However, polymerase chain reaction (PCR) assays for respiratory viruses are more sensitive methods of detection than virus culture and immunologic techniques. Rihkanen and associates performed PCR assays for rhinovirus, enterovirus, coronavirus, PIV 1 through 3, respiratory syncytial

virus (RSV), influenza A and B viruses, human metapneumovirus, adenovirus, human bocavirus (HBoV), and *Mycoplasma pneumoniae* using nasopharyngeal swabs from children with acute laryngeal croup and age- and season-matched children with acute wheezing illnesses.

This prospective study was carried out from October 2003 through September 2004 at the 2 pediatric emergency departments of Helsinki University Central Hospital (Hospital for Children and Adolescents and Jorvi Hospital) in Finland.

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Respiratory Viruses in Acute Laryngeal Croup in Childhood (Continued)

A total of 144 children (median age, 1.9 years) with inspiratory stridor and barking cough or hoarse voice were in the study group of croup children; 76 control subjects (median age, 1.5 years) had expiratory dyspnea caused by wheezing (median age was significantly different between croup and wheezing groups; $P<0.01$).

Virus infection was detected in 79.9% of patients with croup and 71.1% of control subjects. There was a seasonal difference for most of the tested viruses. Cases of croup appeared in 2 peaks, one from October through January and the other from March through April. Among patients with croup, rhinovirus and enterovirus infections predominated during October and November. However, rhinovirus and enterovirus genome was detected as frequently in children with croup as in those with wheezing, including during the late fall, with rhinovirus and enterovirus being detected in 39% of children with croup and 40% of children with wheezing.

During the study year, PIV types 1 to 3 genomes were detected in 41.8% of the children with croup and 5.2% of the children with wheezing. Compared with children with wheezing, children with croup had significantly more infections with PIV 1 (30.6% vs 3.9%; $P<0.001$) and PIV 2 (4.9% vs 0%; $P<0.05$). Further, there were significantly fewer RSV infections among children with croup than among those with wheezing (14.6% vs 27.6%, respectively; $P<0.01$). Children with croup and those with wheezing had the same frequencies

of rhinovirus (11.8% vs 11.8%) and enterovirus (9.0% vs 13.2%, respectively). There were no significant differences between children with croup and those with wheezing in the frequencies of influenza A virus (9.0% vs 13.2%) and HBoV (12.5% vs 10.5%). Few patients with croup or wheezing had adenovirus infections (1.4% and 0%, respectively) or *M. pneumoniae* infections (0.7% and 1.3%, respectively). Overall, 22% of children with croup and 16% of those with wheezing exhibited coinfections with 2 or more pathogens.

This study revealed viral causes of laryngeal croup by using highly sensitive PCR methods and included recently recognized viruses in the analysis. As shown here, 8 out of 10 children with croup had common respiratory virus genome detected in their nasopharynx. Acute laryngeal croup in childhood was associated with several different virus types, most commonly PIV, RSV, rhinovirus, and enterovirus. PIV 1 and 2 predominated in children with croup compared with children with wheezing; whereas RSV was less commonly detected among children with croup compared with children with wheezing. The remaining viral genome detections were similar in both groups. Additionally, there was a clear seasonal predilection for most of the tested virus genomes.

Rihkanen H, Rönkkö E, Nieminen T, et al. Respiratory viruses in laryngeal croup of young children. *J Pediatr*. 2008;152(5):661-665.

Clinical Insights® in Pediatric Respiratory Care Post-Test

- During the 2006 outbreak, cases of mumps were most prevalent in which group?
 - School-aged children in northeastern states
 - School-aged children in midwestern states
 - College-aged adults in northeastern states
 - College-aged adults in midwestern states
- In the PCR analysis conducted by Rihkanen et al, which of the following viruses predominated among children with acute laryngeal croup compared with children with acute wheezing?
 - Enterovirus
 - PIV 1 and PIV 2
 - Rhinovirus
 - RSV

ANSWERS

Question 1 answer: d. In 2006, a large mumps outbreak occurred that preferentially involved midwestern college-aged adults.
Question 2 answer: b. Compared with children with wheezing, children with croup had significantly more infections with PIV 1 (30.6% vs 3.9%; $P<0.001$) and PIV 2 (4.9% vs 0%; $P<0.05$). There were significantly fewer RSV infections among children with croup than among those with wheezing (14.6% vs 27.6%; $P<0.01$). Children with croup and those with wheezing had the same frequencies of rhinovirus (11.8% vs 11.8%) and enterovirus (9.0% vs 13.2%).

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