Is mumps making a comeback?

JM Conly MD[1], BL Johnston MD[2]

Mumps is a viral disease caused by a paramyxovirus that exhibits glandular and nervous system tropism. It is a disease that has affected humankind for centuries. The classical clinical form of mumps was first described by Hippocrates in the fifth century BC as a disease associated with unilateral or bilateral swelling of the parotid glands and, in certain cases, unilateral or bilateral swelling of the testicles (1). Before the introduction of mumps vaccination, it was mainly a disease affecting children and young adults (2). Although mumps is a relatively benign disease in childhood, meningitis and orchitis are not uncommon complications in adults (1,2).

Effective vaccines have been available for many years, and in settings where high coverage has been achieved and maintained, the incidence of mumps has declined markedly (1,2).

Mumps, a member of the *Paramyxoviridae* family, is in the same group as parainfluenza and Newcastle disease viruses (2). Mumps virus has a single-stranded RNA genome and can be isolated and propagated in cultures of various human and monkey cell lines and in embryonated eggs. It has been recovered from multiple body fluids, including saliva, cerebrospinal fluid, urine, blood and milk, as well as from the infected tissues of patients with mumps.

Humans are the only known natural host for mumps virus. The virus is spread by direct contact or through droplets from the upper respiratory tract of infected individuals. It then replicates in the nasopharynx and regional lymph nodes. After replication in the host tissues, viremia occurs, lasting from three to five days. During the viremia, the virus spreads to multiple body sites, including the meninges, salivary glands, pancreas, testes and ovaries. It is the spread and subsequent inflammatory response in infected tissues that leads to the characteristic symptoms of parotitis and aseptic meningitis seen with mumps. A natural infection from the wild type virus typically confers lifelong protection against the virus, but cases of relapse have been reported (1).

Mumps has a usual incubation period of 16 to 18 days but can range from 14 to 25 days. Persons with mumps are contagious for the two days preceding swelling of the salivary glands and for up to nine days after the onset of swelling (2). A typical illness in persons with 'classical' mumps begins with nonspecific symptoms such as myalgia, headache, anorexia, malaise and high fever, followed 24 h later by characteristic swelling, either unilateral or bilateral, of the parotid glands. One to three days later, other salivary glands are visibly affected in almost 10% of cases. However, only 30% to 40% of mumps infections produce typical acute parotitis; 15% to 20% of infections are asymptomatic and up to 50% of infections are associated with nonspecific or primarily respiratory symptoms (3,4). Asymptomatic or inapparent infection may be more common among adults than children; parotitis occurs more commonly among children aged two to nine years (4,5). Serious complications of mumps infection can occur without evidence of parotitis (3,6,7). After approximately one week, the fever and swelling subside, and if there are no complications, recovery is complete (1,2).

Although mumps may produce many complications, the most serious ones are more common in adults than in children (3,8). The neurological complications are dominated by aseptic meningitis, which is asymptomatic in 50% to 60% of subjects and symptomatic in only 4% to 6% of clinical mumps cases (2,9). Aseptic meningitis is usually mild; the outcome is generally favourable, and complete resolution usually occurs within three to 10 days. The more serious neurological complication is meningoencephalitis, which can cause permanent sequelae, including paralysis, seizures, cranial nerve palsies, aqueductal stenosis and hydrocephalus (10,11). Mumps was a major cause of sensorineural deafness among children in the prevaccine era; this deafness may be sudden in onset, bilateral, and permanent (12,13).

Orchitis, most often unilateral, appears in 20% to 50% of boys contracting mumps before puberty. Both testicles may be affected in up to 30% of cases, but mumps-related orchitis is rarely associated with irreversible sterility (2). Pancreatitis is uncommon and reported in 2% to 5% of cases. The mortality associated with mumps is estimated at one to three cases per 10,000 subjects (2). Mumps infection during pregnancy is not associated with congenital malformations (14).

The first attenuated live virus mumps vaccines were developed during the 1960s, and most industrialized countries have introduced vaccination against mumps into their national vaccination programs. Vaccines for measles, mumps and rubella (MMR) are combined into a single MMR vaccine. The current vaccine strain used in Canada is prepared from the Jeryl Lynn attenuated virus and was licensed for use in 1969 (15). The MMR vaccine was introduced as a single dose to children aged 12 to 15 months. In Canada, a recommendation for providing a booster dose to children was made in the mid-1990s. The National Advisory Committee on Immunization currently recommends vaccination of all children at 12 months of age with the MMR vaccine, followed by a booster dose at either 18 months of age or at four to six years of age (15).

In both Canada and the United States (US), the reported incidence of mumps decreased steadily after the introduction of live mumps vaccine in the late 1960s and the subsequent recommendation for its routine use. In Canada, 87 to 205 cases

[1]*Departments of Medicine, Pathology and Laboratory Medicine, and Microbiology and Infectious Diseases, University of Calgary, Calgary, Alberta;* [2]*Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, Nova Scotia*

Correspondence: Dr JM Conly, Foothills Medical Centre, 1403–29 Street South, Calgary, Alberta T2N 2T9. Telephone 403-944-8222, fax 403-944-1095, e-mail jconly@ucalgary.ca

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have been reported annually over the past several years, without sustained transmission or frequent complications (16). In the US, by the mid-1990s, just over 900 cases were reported annually, representing a 99% decrease from the 185,691 cases reported in 1968 (17). Despite the substantial reduction in mumps incidence over the past few decades in both Canada and the US, recent multiple outbreaks of mumps have suggested a resurgence of the disease and serve to underscore the need to maintain high immunization levels.

Since August 2005, two outbreaks of mumps in Nova Scotia have been reported (18). The first outbreak involved 13 high school students, nine of whom had previously received two doses of MMR and four who received a single dose. The second outbreak involved 19 cases among students and staff at a local university, of whom 18 had received only one dose of MMR (the other individual received a second dose). The viruses identified in the outbreaks were phylogenetically similar and belonged to a genotype commonly reported in the United Kingdom (UK). The virus from the second outbreak was identical to the strain currently circulating in the UK and US, which has been responsible for widespread outbreaks (18).

In the US, between January 1 and October 7, 2006, a total of 5783 confirmed or probable mumps cases were reported to the US Centers for Disease Control and Prevention from 45 states and the District of Columbia (19). The majority of cases occurred within the US Midwest. Six states reported 84% of the cases, including Iowa (n=1968), Kansas (n=904), Wisconsin (n=750), Illinois (n=591), Nebraska (n=357) and South Dakota (n=288). The median age was 22 years, and 63% were female. The highest incidence was recorded in persons aged 18 to 24 years, many of whom were college students. In Iowa (which had the most complete data), among 1798 patients, 123 (7%) were unvaccinated, 245 (14%) had received one dose of MMR vaccine, and 884 (49%) had received two or more doses of MMR vaccine. The vaccination status of 546 (30%) patients, the majority of whom were adults, was unknown (20).

In addition to cases of mumps occurring in North America, during the 2005/2006 season, the UK experienced a nationwide epidemic of mumps, which peaked during 2005, when 56,390 cases were reported in England and Wales (21). The majority of confirmed cases were in the 15- to 24-year-old age group, most of whom had not been eligible for routine mumps vaccination.

Multiple factors may have contributed to the spread of these mumps outbreaks. The outbreaks in Halifax, Nova Scotia, occurred in both a singly vaccinated cohort of young adults and a doubly vaccinated cohort of adolescents (18). These outbreaks raise questions as to the efficacy of the MMR vaccine in each of these cohorts. Although the Jeryl Lynn mumps vaccine strain is thought to induce antibodies in 95% of people after a single dose, recent studies have estimated the efficacy of a single dose to be less than 70% (22). Thus, a naturally occurring primary vaccine failure may offer an explanation for these cases. In light of the Halifax outbreaks, the National Advisory Committee on Immunization reviewed its mumps vaccine recommendations and decided to 'stay the course', recommending no changes to the current program, which presently recommends a two-dose schedule for mumps (16).

Although primary vaccine failure has been suggested as a potential cause of the outbreaks occurring in the US Midwest, field studies suggest that reductions in vaccine efficacy likely reflect a combination of both primary and secondary failure of the mumps component of the MMR vaccine (22). Improper handling or administration of the vaccines by providers may have been a contributing factor in leading to some degree of 'failure' in these cases. Another factor that may have contributed to the US outbreak is the college campus environment, with its frequent and extended close contact among students living in dormitories, which facilitates transmission of mumps. In addition, only 25 states require two doses of MMR vaccine, and two-dose coverage with mumps-containing vaccine among college students is likely lower than coverage for measles-containing vaccine (almost exclusively administered as MMR vaccine) for students entering elementary school. Delayed recognition and diagnosis of mumps may have also contributed to spread in this outbreak; younger physicians may not have seen mumps, and thus may not consider the diagnosis in vaccinated persons. The potential for waning immunity has been postulated as another contributing factor because young adults in the 18- to 24-year-old age group would most commonly have received their most recent dose of mumps-containing vaccine six to 17 years ago. In the UK, the contributing factors were different, and the large number of cases may have been primarily related to a lost unvaccinated cohort. During November 1994, approximately eight million school children aged five to 16 years (ie, born between 1978 and 1989) were offered combined measles-rubella vaccine to prevent a predicted epidemic of measles. At that time, a global shortage prevented offering MMR to this group, leaving a proportion of the eight million children susceptible to mumps (21).

The recent resurgence of mumps in North America and the UK underscores the need for health care providers to remain alert for suspected mumps cases and the need to readdress current and past approaches to mumps management. Mumps transmission has occurred in past outbreaks involving hospitals and long-term care facilities housing adolescents and adults, thus reinforcing the need for vigilance in these settings as well. The US Centers for Disease Control and Prevention has recently updated its guidelines for preventing mumps transmission in health care settings (23). The predominance among university-aged students in these outbreaks not only highlights an environment conducive for increased transmission, but also raises questions about the efficacy of the MMR vaccine itself. Clinicians should remain vigilant for symptoms of mumps, conduct appropriate diagnostic testing, and report these cases to regional or provincial public health authorities. Appropriate specimens for laboratory testing include serum to test for mumps immunoglobulin M antibodies and a swab from the parotid duct or other affected salivary gland ducts for viral isolation, reverse transcriptase polymerase chain reaction testing, or both. Negative laboratory tests, especially in vaccinated persons, should not be used to rule out a mumps diagnosis, because these tests may not be sensitive enough to detect infection in all persons with clinical illness.

Related to vaccine use, it is becoming clear that two-dose schedules of mumps-containing vaccine preparations, used in Canada since 1996, have a greater chance of eliminating mumps, most likely by reducing the rate of primary vaccine failure (16,18). From a Canadian perspective, ensuring full compliance with current recommendations and continuous vigilance by clinicians for clinical cases of mumps must be maintained.

REFERENCES

1. Plotkin SA. Mumps Vaccine. In: Offit PA, Orenstein WA, eds. Vaccines, 4th edn. Philadelphia: WB Saunders Co, 2003:441-70.
2. Centers for Disease Control and Prevention. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. Epidemiology and Prevention of Vaccine-Preventable Diseases, 9th edn. Washington DC: Public Health Foundation, 2006.
3. Falk WA, Buchan K, Dow M, et al. The epidemiology of mumps in Southern Alberta, 1980-1982. Am J Epidemiol 1989;130:736-49.
4. Cooney MK, Fox JP, Hall CE. The Seattle Virus Watch. VI. Observations of infections with and illness due to parainfluenza, mumps and respiratory syncytial viruses and *Mycoplasma pneumoniae*. Am J Epidemiol 1975;101:532-51.
5. Philip RN, Reinhard KR, Lackman DB. Observations on a mumps epidemic in a virgin population. 1958. Am J Hyg 1959;69:91-111.
6. Centers for Disease Control and Prevention. Mumps outbreaks on university campuses – Illinois, Wisconsin, South Dakota. MMWR Morb Mortal Wkly Rep 1987;36:496-8, 503-5.
7. Hersh BS, Fine PE, Kent WK, et al. Mumps outbreak in a highly vaccinated population. J Pediatr 1991;119:187-93.
8. Centers for Disease Control and Prevention. Mumps surveillance, January 1977-December 1982. Atlanta: US Department of Health and Human Services, US Public Health Service, 1984.
9. Reed D, Brown G, Merrick R, Sever J, Feltz E. A mumps epidemic on St. George Island, Alaska. JAMA 1967;199:113-7.
10. Bray PF. Mumps – a cause of hydrocephalus? Pediatrics 1972;49:446-9.
11. Azimi PH, Cramblett HG, Haynes RE. Mumps meningoencephalitis in children. JAMA 1969:207:509-12.
12. Hall R, Richards H. Hearing loss due to mumps. Arch Dis Child 1987;62:189-91.
13. Westmore GA, Pickard BH, Stern H. Isolation of mumps virus from the inner ear after sudden deafness. Br Med J 1979;1:14-5.
14. Siegel M. Congenital malformations following chickenpox, measles, mumps, and hepatitis. Results of a cohort study. JAMA 1973;226:1521-4.
15. National Advisory Committee on Immunization (NACI), Health Canada. Canadian immunization guide, 6th edn. Ottawa: Canadian Medical Association, 2002. Also available at <www.phac-aspc.gc.ca/publicat/cig-gci/pdf/cdn_immuniz_guide-2002-6.pdf> (Version current at January 24, 2007).
16. Gemmill IM. Mumps vaccine: Is it time to re-evaluate our approach? CMAJ 2006;175:491-2.
17. Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L. Measles, mumps, and rubella – vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1998;47:1-57.
18. Watson-Creed G, Saunders A, Scott J, Lowe L, Pettipas J, Hatchette TF. Two successive outbreaks of mumps in Nova Scotia among vaccinated adolescents and young adults. CMAJ 2006;175:483-8.
19. Centers for Disease Control and Prevention (CDC). Brief report. Update: Mumps activity – United States, January 1-October 7, 2006. MMWR Morb Mortal Wkly Rep 2006;55:1152-3.
20. Centers for Disease Control and Prevention (CDC). Update: Multistate outbreak of mumps – United States, January 1-May 2, 2006. MMWR Morb Mortal Wkly Rep 2006;55:559-63.
21. Centers for Disease Control and Prevention (CDC). Mumps epidemic – United kingdom, 2004-2005. MMWR Morb Mortal Wkly Rep 2006;55:173-5.
22. Harling R, White JM, Ramsay ME, Macsween KF, van den Bosch C. The effectiveness of the mumps component of the MMR vaccine: A case control study. Vaccine 2005;23:4070-4.
23. Centers for Disease Control and Prevention. Prevention and Control of Mumps in Healthcare Settings. <www.cdc.gov/nip/diseases/mumps/control-hcw.htm> (Version current at January 24, 2007).