ORIGINAL ARTICLE

Recent Resurgence of Mumps in the United States

Gustavo H. Dayan, M.D., M. Patricia Quinlisk, M.D., M.P.H., Amy A. Parker, M.S.N., M.P.H., Albert E. Barskey, M.P.H., Meghan L. Harris, M.P.H., Jennifer M. Hill Schwartz, M.P.H., Kae Hunt, B.A., Carol G. Finley, B.S., Dennis P. Leschinsky, B.S., Anne L. O'Keefe, M.D., M.P.H., Joshua Clayton, B.S., Lon K. Kightlinger, Ph.D., M.S.P.H., Eden G. Dietle, B.S., Jeffrey Berg, Cynthia L. Kenyon, M.P.H., Susan T. Goldstein, M.D., Shannon K. Stokley, M.P.H., Susan B. Redd, Paul A. Rota, Ph.D., Jennifer Rota, M.P.H., Daoling Bi, M.S., Sandra W. Roush, M.T., M.P.H., Carolyn B. Bridges, M.D., Tammy A. Santibanez, Ph.D., Umesh Parashar, M.B., B.S., M.P.H., William J. Bellini, Ph.D., and Jane F. Seward, M.B., B.S., M.P.H.

ABSTRACT

BACKGROUND

The widespread use of a second dose of mumps vaccine among U.S. schoolchildren beginning in 1990 was followed by historically low reports of mumps cases. A 2010 elimination goal was established, but in 2006 the largest mumps outbreak in two decades occurred in the United States.

METHODS

We examined national data on mumps cases reported during 2006, detailed case data from the most highly affected states, and vaccination-coverage data from three nationwide surveys.

RESULTS

A total of 6584 cases of mumps were reported in 2006, with 76% occurring between March and May. There were 85 hospitalizations, but no deaths were reported; 85% of patients lived in eight contiguous midwestern states. The national incidence of mumps was 2.2 per 100,000, with the highest incidence among persons 18 to 24 years of age (an incidence 3.7 times that of all other age groups combined). In a subgroup analysis, 83% of these patients reported current college attendance. Among patients in eight highly affected states with known vaccination status, 63% overall and 84% between the ages of 18 and 24 years had received two doses of mumps vaccine. For the 12 years preceding the outbreak, national coverage of one-dose mumps vaccination among preschoolers was 89% or more nationwide and 86% or more in highly affected states. In 2006, the national two-dose coverage among adolescents was 87%, the highest in U.S. history.

CONCLUSIONS

Despite a high coverage rate with two doses of mumps-containing vaccine, a large mumps outbreak occurred, characterized by two-dose vaccine failure, particularly among midwestern college-age adults who probably received the second dose as schoolchildren. A more effective mumps vaccine or changes in vaccine policy may be needed to avert future outbreaks and achieve the elimination of mumps.

From the Division of Viral Diseases (G.H.D., A.A.P., A.E.B., S.T.G., S.B.R., P.A.R., J.R., D.B., U.P., W.J.B., J.F.S.), the Immunization Services Division (S.K.S., T.A.S.), the Bacterial Diseases Division (S.W.R.), and the Influenza Division (C.B.B.), National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta; the Iowa Department of Public Health, Des Moines (M.P.Q., M.L.H.); the Kansas Department of Health and Environment, Topeka (J.M.H.S.); the Illinois Department of Public Health, Springfield (K.H., C.G.F.); the Nebraska Department of Health and Human Services, Lincoln (D.P.L., A.L.O.); the South Dakota Department of Health, Pierre (J.C., L.K.K.); the Missouri Department of Health and Senior Services, Jefferson City (E.G.D.); the Wisconsin Department of Health and Family Services, Madison (J.B.); and the Minnesota Department of Health, St. Paul (C.L.K.). Address reprint requests to Amy Parker at MS A-47, the Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Atlanta, GA 30333.

N Engl J Med 2008;358:1580-9.

Mumps is an acute viral infection characterized by fever and inflammation of the salivary glands.[1] The spectrum of illness ranges from subclinical infection to meningoencephalitis, deafness, and orchitis, and severity increases with age.[2] In the prevaccine era, the highest attack rate was among children in primary school, and most adolescents showed evidence of previous infection.[2]

After the implementation of a policy for the administration of a one-dose mumps vaccine (Jeryl Lynn strain) for children in 1977,[3] reports of mumps cases fell dramatically. However, in the late 1980s, outbreaks occurred in both unvaccinated and vaccinated adolescents and young adults.[4] Widespread use of the recommended second dose of measles–mumps–rubella (MMR) vaccine for measles control among schoolchildren[5] was followed by historically low rates of mumps,[4] and an elimination goal for mumps was set for 2010.[6]

In 2006, the United States had the largest mumps epidemic in two decades. We examined the epidemiology of that outbreak to assess whether mumps elimination can be achieved through the current two-dose childhood-vaccination strategy.

Methods

Mumps Case Reports

We reviewed and classified mumps cases that were reported through the National Notifiable Diseases Surveillance System from state health departments to the Centers for Disease Control and Prevention (CDC), according to the standard clinical case definition and case classifications of the Council of State and Territorial Epidemiologists. A case that met the clinical case definition (i.e., an illness with an acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary gland that lasted at least 2 days, without other apparent cause[7]) and that was not laboratory-confirmed was classified as a probable case. A patient with a confirmed case had a positive laboratory test or met the clinical case definition and was epidemiologically linked to a confirmed or probable case.

We defined three time periods: preresurgence (from 2000 to 2005), resurgence (2006), and postresurgence (from January 1 to June 30, 2007). Case data from the eight most severely affected states (Illinois, Iowa, Kansas, Minnesota, Missouri, Nebraska, South Dakota, and Wisconsin) included vaccination status from written records and self-reported race or ethnic group; for four of the states, data were also included about patients' college attendance. Inclusion criteria for the detailed analysis were the presence of parotitis, other salivary gland inflammation, or one of seven common mumps complications (orchitis, oophoritis, mastitis, meningitis, encephalitis, deafness, and pancreatitis). Routine procedures for reporting adverse events to the Vaccine Adverse Events Reporting System after immunization were followed.

Mumps Vaccination Coverage

Due to a lack of standard methods for the national assessment of vaccine coverage from 1980 to 2006, we reviewed data regarding mumps vaccination coverage from four surveys: the U.S. Immunization Survey (USIS),[8] the National Immunization Survey (NIS),[9] the National Health Interview Survey (NHIS),[9] and school vaccination surveys.[9] Population data were derived from Census data for 2006.[10]

Statistical Analysis

In bivariate comparisons, we used the chi-square test and Fisher's exact test for the analysis of categorical variables and the Wilcoxon rank-sum test and analysis of Pearson's correlation for continuous variables. To evaluate the complications of mumps, we examined age, sex, race or ethnic group, and vaccination status as risk factors and included in multivariate analyses those factors with a bivariate P value of less than 0.05.

Results

Temporal Patterns

After the introduction of the mumps vaccine in 1967, reported cases dropped by 98%, from 152,209 cases in 1968 to 2982 cases in 1985 (Fig. 1). Increased numbers of cases and outbreaks in the late 1980s were followed by low case counts during the period from 2000 to 2005 (the preresurgence period) when fewer than 350 cases (<30 per month) were reported annually. In contrast to recurrent spring peaks in previous years, no seasonal variation was apparent, and transmission was sporadic: only 60 of 1677 cases (4%) during the period from 2000 to 2005 were related to an outbreak.

In January 2006, mumps cases were noted on college campuses in Iowa[12]; in February, mumps

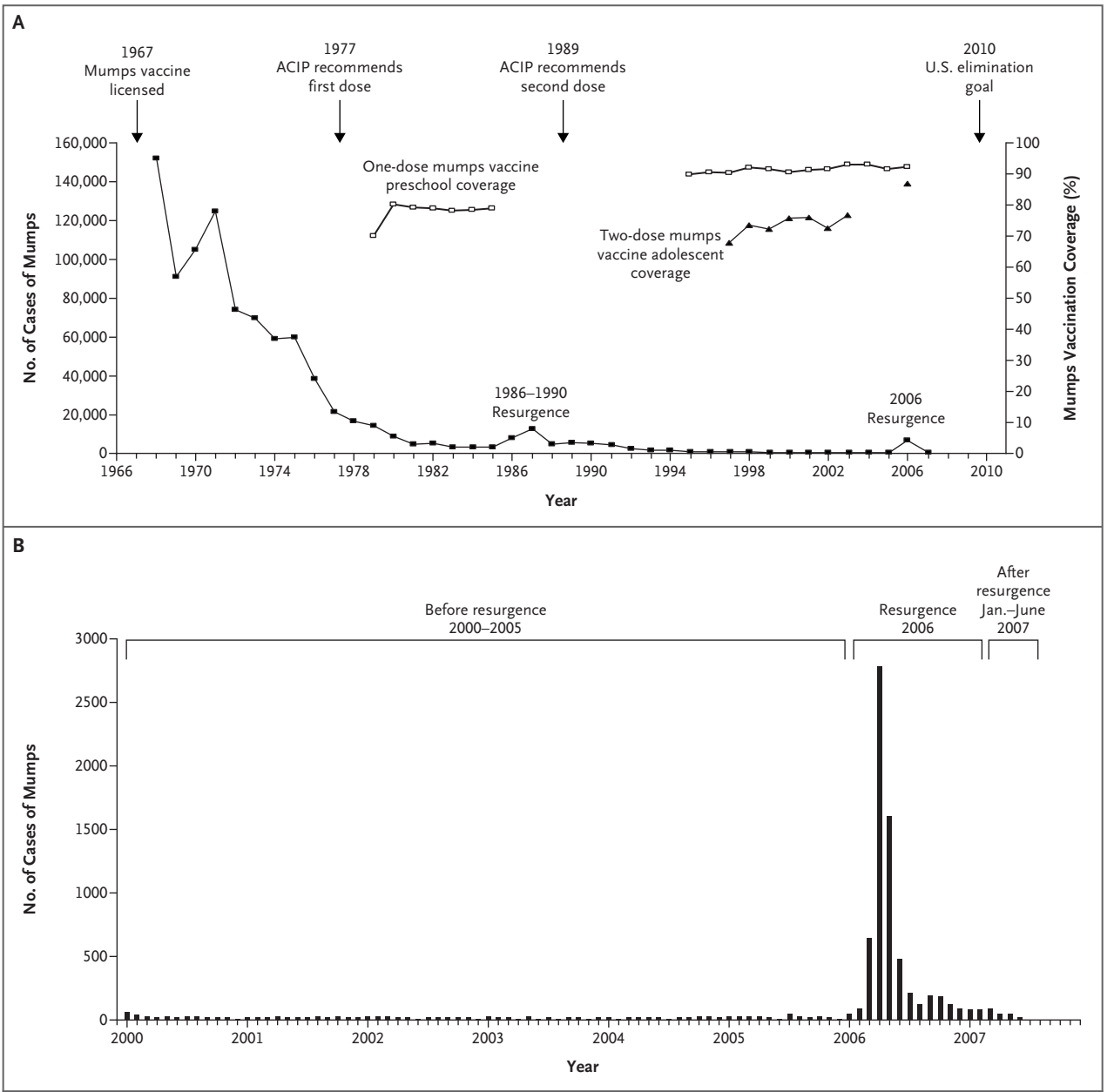

Figure 1. Association between Mumps Cases and Vaccination Coverage (1968–2007) and Monthly Reports of Mumps Cases (2000–2007).

Panel A shows the annual number of reported mumps cases from January 1968 to June 2007, as reported by the National Notifiable Diseases Surveillance System (solid rectangles). In 1977, the Advisory Committee on Immunization Practices (ACIP) recommended universal childhood vaccination with one-dose mumps-containing vaccine[3] (open rectangles). Data from 1979 to 1985 are from the U.S. Immunization Survey (USIS)[8] and were verified by vaccination cards for 24-month-olds; data from 1995 to 2006 are from the National Immunization Survey (NIS)[9] and were verified by providers for children between the ages of 19 and 35 months. In 1989, the ACIP recommended that children entering kindergarten or first grade receive a second dose of measles-containing vaccine, preferably administered as combined measles–mumps–rubella (MMR) vaccine,[3] which had been available since 1971 (solid triangles). Coverage data were verified for 1997 to 2003 by vaccination cards for adolescents between the ages of 13 and 15 years, according to the National Health Interview Survey (NHIS),[9,11] and for 2006 by providers, according to the NIS.[9] Panel B shows monthly case reports of mumps from 2000 to 2007. Data are from the National Notifiable Diseases Surveillance System for January 2000 through June 2007. Data for the post-resurgence period represent provisional counts of cases received by June 30, 2007.

was reported on other college campuses, and by April, the outbreak had peaked, with 40 states reporting 2786 cases.[13] Thereafter, reported cases steadily declined. From August to November, three outbreaks consisting of 22 to 93 cases each were reported at colleges in Illinois, Kansas, and Virginia. By December 31, a total of 6584 cases and 85 hospitalizations had been reported; no deaths occurred. No large outbreaks were reported at primary or secondary schools. During the postresurgence period (from January 1 to June 30, 2007), 359 cases (60 per month) and no outbreaks were reported.

GEOGRAPHIC PATTERNS

During the preresurgence period, the reported national incidence of mumps was less than 1 case per million persons, and cases were reported in proportion to the population of the state (r^2=0.73, P<0.001) (Fig. 2). During the 2006 resurgence, the reported national incidence was 2.2 cases per 100,000 persons. Although mumps was reported in 45 states, the above-mentioned 8 states had the highest case counts (range, 170 to 1964) and incidence rates (2.9 to 65.9 per 100,000 persons). These states accounted for 5586 of 6584 cases (85%), although they comprised only 37.7 million of 299.4 million (13%) of the U.S. population and in the preresurgence period reported only 193 of 1677 cases (12%). Contiguously located in the Midwest, these 8 states tended to have a lower population density than did the 37 less-affected states (56.2 persons vs. 96.9 persons per square mile, P=0.08).

Of 3141 U.S. counties, 879 (28%) reported mumps cases in 2006, and 47 (1%) reported having at least 25 cases, which accounted for 3548 of 6584 cases (54%). Of the 47 counties, 44 (94%) were within a 400-mile radius in the Midwest, and most of the counties were rural; the remaining 3 were in Arizona, Washington, and Virginia. The 47 counties were home to 20.9 million of the total U.S. population of 299.4 million (7%) and in the preresurgence period reported having 104 of 1677 cases (6%). Of the 47 counties, 22 (47%) had colleges that reported clusters of mumps activity. During the 2007 postresurgence period, the eight states with the highest case counts accounted for 182 of 359 cases (51%), and 47 counties accounted for 134 of 359 reports of mumps (37%). No clusters of serious adverse events after immunization campaigns were reported during the outbreak.

LABORATORY AND GENOTYPING

Mumps was confirmed by polymerase-chain-reaction (PCR) assay or viral isolation in all highly affected states. During the main outbreak period, specimens from 25 patients were genotyped at the CDC. Genotype G virus was identified in samples from 24 patients from 12 states, and genotype H virus was identified in a sample from a case imported from Bulgaria. Only a small proportion of cases could be confirmed with the use of viral isolation, PCR analysis, and classic serologic methods at the CDC.

VACCINATION COVERAGE

One Dose among Preschoolers

During the first half of the 1980s, according to the USIS, rates of one-dose coverage for mumps-containing vaccine among 24-month-old children (as verified by vaccination cards) ranged from 78 to 80% (Fig. 1). From 1995 to 2006, according to the NIS, provider-verified one-dose coverage for mumps-containing vaccine among children between the ages of 19 and 35 months was 90 to 93% nationwide and 86 to 96% in the eight highly affected states.

Two Doses among Schoolchildren

From 1997 to 2003, according to the NHIS, vaccination-card–verified two-dose coverage for mumps-containing vaccine among adolescents between the ages of 13 and 15 years rose from 68 to 77%. In 2006, according to the NIS, provider-verified two-dose coverage for mumps-containing vaccine among adolescents between the ages of 13 and 17 years was 87%. By 1992, the eight highly affected states had enacted requirements for a second dose of measles vaccine (commonly administered as MMR vaccine) for at least one cohort of schoolchildren. From the beginning of each state's requirement through the 2006–2007 school year, annual, state-specific second-dose coverage for measles-containing vaccine for kindergartners and first-graders ranged from 81 to 100% (mean, 97).

CHARACTERISTICS OF PATIENTS IN EIGHT HIGHLY AFFECTED STATES

Of the 5127 cases reported from the eight states between January 1 and July 31, 2006, 4039 (79%) met the inclusion criteria. Of these patients, age was known for 4017 (99%) (Fig. 3). Of the 4017 patients, 1184 (29%) were between the ages of 18 and 24 years; in this age group, the incidence of

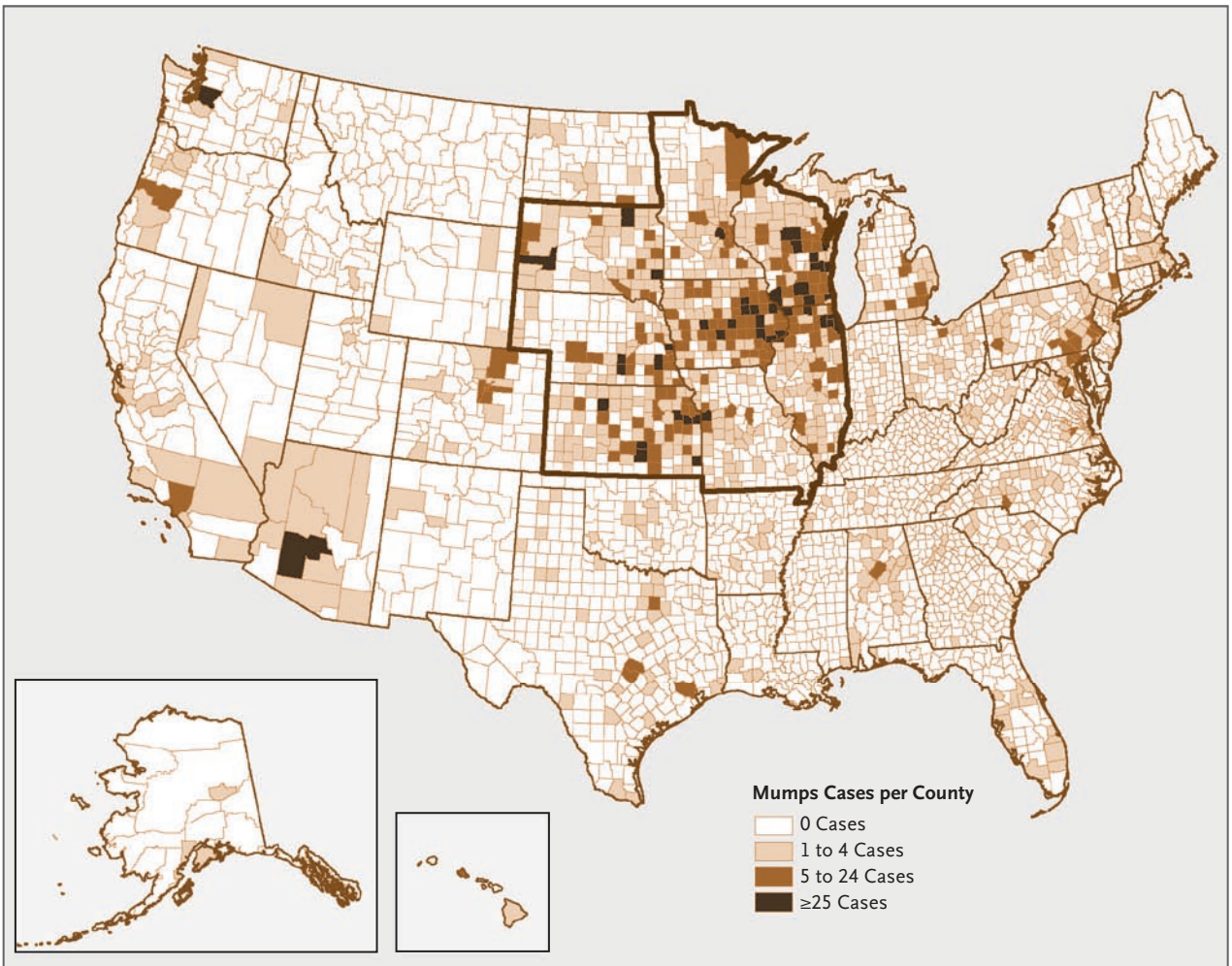

Figure 2. Mumps Cases, According to County, for 2006.

Enclosed by a dark line are the eight states that had both the highest case counts and the highest incidence rates. Of the nation's 3141 counties reporting 6584 cases of mumps, 2262 counties (72%) reported no cases (white); 653 (21%) reported 1 to 4 cases each (shaded tan), providing an aggregate of 1132 cases (17% of total); 179 (6%) reported 5 to 24 cases each (shaded light brown), providing an aggregate of 1886 cases (29% of total); and 47 (1%) reported 25 or more cases each (shaded dark brown), providing an aggregate of 3548 cases (54% of total). For 18 cases (<1%), the county of residence was unknown.

mumps was higher than in all the other age groups combined by a factor of 3.7 (31.1 vs. 8.4 per 100,000, P<0.001). Data on college attendance were collected from Iowa, Kansas, Nebraska, and South Dakota. Of 768 patients between the ages of 18 and 24 years, 486 of 589 with available data (83%) reported current college attendance.

The number of doses of mumps vaccine was known for 3115 of 4039 patients (77%); of the 3115 patients, 396 (13%) had received no vaccine, 772 (25%) had received one dose, and 1947 (63%) had received two or more doses. Of the patients with known vaccination status, less than 4% of those under the age of 30 years were unvaccinated; 858 of 1020 patients (84%) between the ages of 18 and 24 years had received two doses of mumps vaccine. For patients who were 30 years of age or older, the proportion who were unvaccinated rose progressively to 73%; 38% had unknown vaccination status.

The sex was known for 4012 of 4039 patients (99%), of whom 2578 (64%) were female (Fig. 4A). The incidence among female patients was higher than that among male patients by a factor of 1.8 (13.5 vs. 7.7 per 100,000, P<0.001), a finding that was not explained by differences in either vacci-

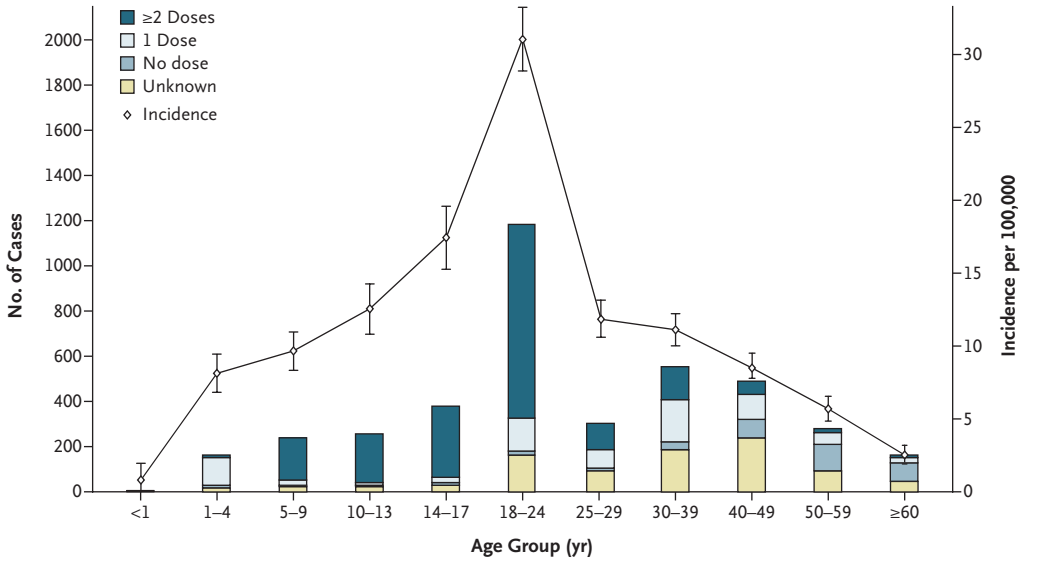

Figure 3. Mumps Cases and Incidence, According to Age Group and Vaccination Status.

Data are from the eight most highly affected states (Illinois, Iowa, Kansas, Minnesota, Missouri, Nebraska, South Dakota, and Wisconsin) for the period from January 1 to July 31, 2006. Age was reported for 4017 patients. The national age-specific incidence rates per 100,000 population were 6.2 for persons between the ages of 18 and 24 years, 3.3 for those between the ages of 14 and 17 years, and 2.8 for those between the ages of 10 and 13 years. The I bars represent 95% confidence intervals.

nation status or age (proportions differed by <3% for both comparisons).

Race or ethnic group was known for 3337 of 4039 patients (83%), of whom 88% were non-Hispanic white (Fig. 4B). The incidence among whites was twice as high as the aggregate for all other racial or ethnic groups (9.95 vs. 4.88 per 100,000, P<0.001), a finding that was not explained by differences in either vaccination status or age (proportions differed by <4% for both comparisons).

COMPLICATIONS

Complications were reported for 5% of patients, and 2% of patients were hospitalized (Table 1 and Fig. 5). Due primarily to orchitis, the proportion of male patients with complications was higher than that of female patients by a factor of 3.4 (P<0.001). With the exclusion of sex-specific complications, the relative proportion of complications was higher in male patients by a factor of 1.5 (P=0.16). The complication rate increased with age up to 50 years (P<0.001). Both age and sex remained significant predictors of complications when paired in a multivariate model. Neither vaccination status nor race or ethnic group was significantly associated with complications.

OUTBREAK RESPONSE

States, in collaboration with the American College Health Association and the CDC, recommended that colleges implement a requirement that students receive two doses of MMR vaccine. The CDC and states recommended that patients with mumps be isolated for 5 to 9 days. Iowa conducted a statewide vaccination campaign for adults between the ages of 18 and 46 years, and Kansas, South Dakota, and Wisconsin conducted targeted campaigns. In June 2006, the Advisory Committee on Immunization Practices recommended the administration of two routine doses of mumps vaccine for children and health care workers and a second dose for one-dose vaccine recipients during outbreaks.[14] Third doses of vaccine were not recommended.

DISCUSSION

The largest U.S. mumps epidemic in approximately 20 years occurred in 2006, involving 6584 patients. After historically low case counts throughout the country in the early 2000s, the outbreak was unexpected, abrupt,[12,13,15] and focal, primarily affecting midwestern states and colleges. However, even at the peak of the epidemic, case counts

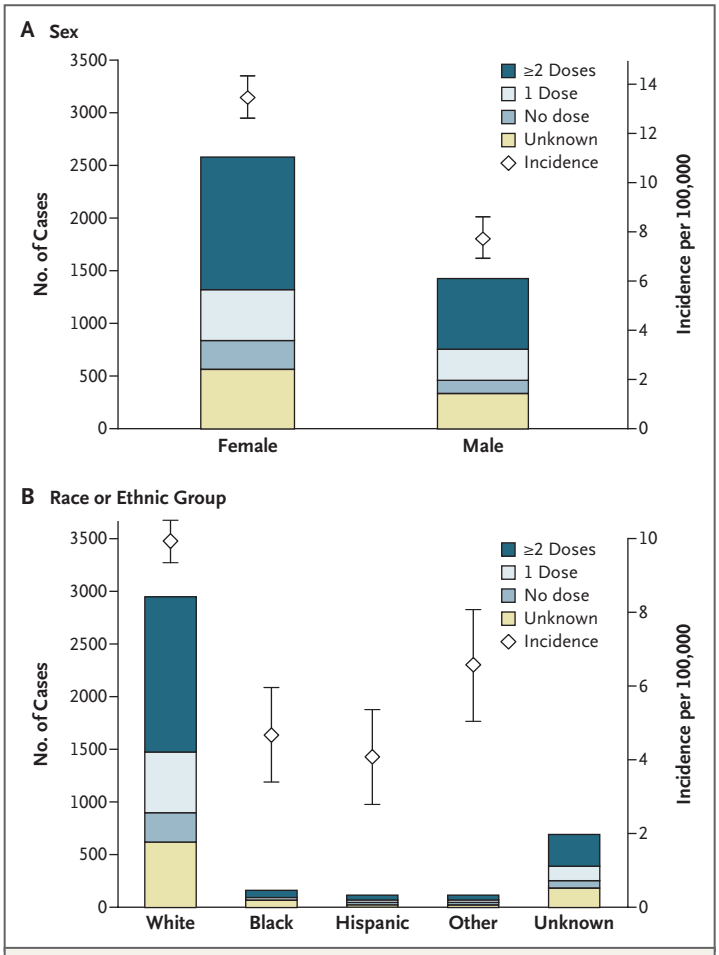

Figure 4. Mumps Cases and Incidence, According to Sex, Race or Ethnic Group, and Vaccination Status.

Data are from the eight most highly affected states (Illinois, Iowa, Kansas, Minnesota, Missouri, Nebraska, South Dakota, and Wisconsin) for the period from January 1 to July 31, 2006. Data were available regarding sex for 4012 patients (Panel A) and regarding race or ethnic group for 3337 patients (Panel B). The I bars represent 95% confidence intervals.

were far below those of the prevaccine era, during which tens of thousands of cases were reported monthly. The incidence was highest among college-age youths between the ages of 18 and 24 years and recipients of two doses of mumps vaccine.

Although similarities with the ongoing mumps outbreak in Canada are striking,[16] the 2006 outbreak was the first account of a large-scale mumps epidemic characterized by two-dose–vaccine failure. The outbreak occurred in the context of sustained, high one-dose preschool vaccine coverage, high adolescent two-dose coverage, and implementation of a requirement for two-dose coverage for all schoolchildren in almost every state by 2007.[17] Although there was no single explanation for the outbreak, multiple factors may have contributed, including waning immunity, high population density and contact rates in colleges, and incomplete vaccine-induced immunity to wild virus. Transmission from patients with subclinical and mild vaccine-modified disease may have also contributed to sustaining transmission.[18]

The estimated herd-immunity threshold for mumps ranges from 88 to 92%.[19] Numerous outbreaks have occurred in populations with high one-dose coverage,[20-22] and the effectiveness of one dose of mumps vaccine of approximately 80%[1,2,20,21,23] is considered inadequate to provide population protection.[24] The effectiveness of two doses of vaccine has been less extensively studied, but estimates range from 88 to 95%.[23,25,26] Nevertheless, even 95% coverage with 95% vaccine effectiveness brings population immunity (90%) near the putative herd-immunity threshold. Situations of high population density and contact rates that facilitate transmission (e.g., college dormitories) may require an increased level of group-specific immunity.[21,27]

The 2006 outbreaks on college campuses resemble those among schoolchildren who received one dose of vaccine during the 1980s,[4,20-22] which raised the issue of waning immunity after one dose of mumps vaccine. Some studies have suggested that antibody levels[28,29] and vaccine effectiveness[25] can wane after a second dose of mumps vaccine. Findings regarding the age group that was most affected in the 2006 outbreak (persons between the ages of 18 and 24 years) and results from two studies that were conducted on college campuses support the hypothesis of waning immunity after the second dose. One study showed that students who contracted mumps had higher odds of having received a second dose of MMR vaccine 10 or more years previously than did their roommates without mumps.[18] The other study showed lower levels of mumps-neutralizing antibodies among students who had been vaccinated with a second MMR dose 15 or more years previously than among those who had been vaccinated 1 to 5 years previously.[30] If population immunity is already near the herd threshold, even negligible waning immunity, particularly when combined with increased exposure, could potentiate an outbreak.

Waning immunity may be secondary to a lack of natural exposure. Persons between the ages of

18 and 24 years were born during the 1980s, when mumps activity was sufficiently low that many of them were never exposed to the disease. They probably received a second dose in the early 1990s, when opportunities for boosting from exposure to wild virus became increasingly rare. These young midwesterners entered college at a time of increased risk of the importation of mumps virus from abroad (e.g., when the 2004–2006 mumps epidemic in the United Kingdom with >70,000 patients was peaking).[25,31]

Besides waning immunity, other explanations are possible. The mumps virus in the U.S. outbreak was the same genotype G virus circulating during the 2004–2006 outbreak in the United Kingdom.[31] Some observers have speculated that mumps vaccine–induced immunity (derived from genotype A virus) may be less effective against heterologous strains (e.g., G genotype).[29,32,33] Although it is possible that antigenic differences may lead to some decrease in effectiveness, mumps vaccine was highly effective during the U.K. outbreak,[25] during a small New York outbreak in 2005 that was probably caused by genotype G virus,[23] and against the circulating strain in the 2006 U.S. outbreak. The U.S. outbreak was an order of magnitude lower in incidence than the U.K. outbreak, which primarily affected unvaccinated persons.[31] Attack rates in the most highly affected colleges in the 2006 outbreak were less than 6%,[12] considerably lower than attack rates in both the prevaccine and one-dose–vaccine eras.[1] Thus, mumps vaccine probably prevented U.S. patients from numbering in the tens or hundreds of thousands.

We explored the possibility of errors in vaccine records (in which MMR vaccine was mistakenly recorded when measles vaccine was administered) as an explanation for the outbreak. However, from 1984 to 2006, 244.2 million doses of MMR vaccine were delivered, as compared with only 13.1 million doses of measles vaccine — more than enough mumps-containing vaccine to provide two doses to every cohort annually. Thus, on the basis of these data, it would be difficult to attribute the epidemic to "pseudo-vaccination."

Male patients had a higher rate of complications than did female patients, primarily because of their risk of orchitis. As in some previous mumps outbreaks,[21,34] female patients were disproportionately affected, accounting for 64% of cases. Disparities between the sexes probably reflected the sex distribution in postsecondary institutions, in which 57% of students in the eight highly affected states were women.[35] Differences in behavior patterns or differential reporting patterns may also have contributed.

Mumps subsided in the summer of 2006, and sustained epidemic patterns did not return at the start of college in the fall or during the first half of 2007. Since two-dose coverage was already high and third doses were not offered, major changes in vaccine-derived immunity may not have been instrumental in stopping the outbreak or preventing its return. The resurgence may have arisen from circumstances that are unlikely to be repeated: students in rural areas with little boosting from disease entered crowded dormitories when importations were maximal. However, in the prevaccine era, mumps activity followed 3-year cycles,[1]

Table 1. Clinical Manifestations and Complications.*

Variable	Patients with Mumps (N=4039)
	no. (%)
Clinical manifestation	
Any	4031 (>99)
Parotitis†	3724 (92)
Other salivary-gland inflammation	294 (7)
Constitutional symptom (headache, myalgia, or fatigue)	2293 (57)
Fever	1178 (29)
Complication	
Any	198 (5)
Orchitis	112 (10)
Oophoritis	25 (1)
Mastitis	22 (1)
Meningitis	22 (<1)
Encephalitis‡	13 (<1)
Deafness§	11 (<1)
Pancreatitis	2 (<1)

* Patients could have more than one clinical manifestation or complication. The percentage of patients with orchitis was calculated on the basis of 1168 male patients who were 12 years of age or older. The percentages of patients with oophoritis or mastitis were calculated on the basis of 2307 female patients who were 12 years of age or older.
† The median duration of parotitis was 5 days (range, 1 to 30).
‡ Of the 13 patients with encephalitis, only 1 was known to have long-term unresolved sequelae; follow-up information was unavailable for 2 patients.
§ Of the 11 patients with deafness, the condition was unilateral and transient in 5 patients, bilateral and transient in 3 patients, and transient with no information regarding the extent of involvement in 2 patients; data were missing for 1 patient.

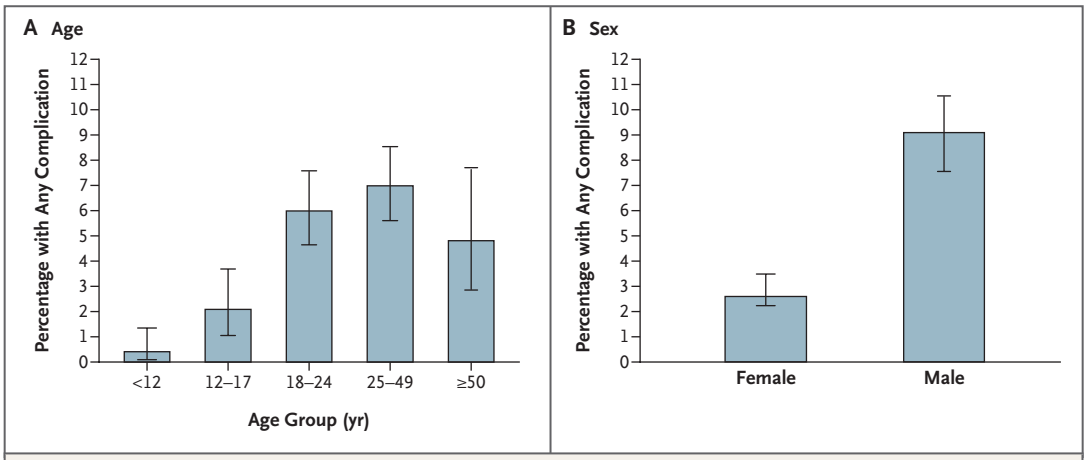

Figure 5. Proportion of Patients with Complications, According to Age Group and Sex.

Data are from the eight most highly affected states (Illinois, Iowa, Kansas, Minnesota, Missouri, Nebraska, South Dakota, and Wisconsin) for the period from January 1 to July 31, 2006. Graphs represent data for risk factors that were significant on multivariate analysis. Data were available for the proportion of mumps cases with any complication for 4017 patients according to age (Panel A) and for 4012 patients according to sex (Panel B). The I bars represent 95% confidence intervals.

so the current low activity rate may be transient while another critical mass of susceptible persons accrues. Since 43% of the world's nations do not vaccinate against mumps,[36] importations are likely to continue.

Our study had some limitations. Cases of mumps were reported through a passive surveillance system with unknown sensitivity. We consider it unlikely that differential reporting was responsible for variations in reported cases among states owing to the reporting in the national media and enhancement of surveillance nationwide. Because of low numbers of unvaccinated children and young adults, our findings that show no difference in complications according to vaccination status were driven largely by data in adults who were at least 30 years old, among whom approximately 40% had unknown vaccination status and no available written records. The resulting misclassification of vaccination status may have biased findings toward the null hypothesis. The decrease in reported rates of mumps complications, as compared with the prevaccine era,[1,37] suggests that disease was modified by vaccination, although incomplete reporting of complications is an alternative explanation. We could not assess vaccine effectiveness with the use of outbreak surveillance data because of high vaccine coverage among patients with mumps.

Conventional virologic and serologic diagnostic methods (with analysis of IgM and both acute and convalescent IgG), which have been of value in confirming mumps in unvaccinated persons,[23] had limited use in the highly vaccinated population in this outbreak. IgM may be transient or absent in a secondary immune response in vaccinated persons. Our experience in detecting IgM antibodies with the use of a capture assay developed by the CDC was at the lower end of the range of 15 to 50% reported in various studies in vaccinated or previously infected persons with the use of IgM antibody-capture enzyme immunoassays.[38-40] The unavailability of appropriately timed specimens and the presence of low virus titers in vaccinated persons often made IgG, PCR, and isolation methods unhelpful in diagnosis. Consequently, laboratory testing was able to confirm but not rule out mumps. Future studies will help to evaluate national vaccine policy, including whether the administration of a second dose of MMR vaccine at a later age or the administration of a third dose would provide higher or more durable immunity.

Dr. Dayan, who was employed at the CDC during the preparation of this article, reports being employed at Sanofi Pasteur; Dr. O'Keefe, having an equity interest in Abbott Laboratories; and Ms. Kenyon, receiving a federal Emerging Infections and Protection grant. No other potential conflict of interest relevant to this article was reported.

The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the CDC, U.S. Department of Health and Human Services.

We thank Gregory Wallace, M.D., M.P.H., and Lisa Galloway for providing data from the National Biologics Surveillance System; Diane Simpson, M.D., Ph.D., for her kind permission to adapt USIS data regarding mumps coverage from her study of various immunization surveys; Shannon Graham, M.A., for her tireless work in producing maps of mumps activity; Larry Anderson, M.D., for his scientific leadership and guidance; and all the state, local, and CDC public health officials and the university staff members who were involved in the response to the 2006 mumps outbreak.

REFERENCES

1. Plotkin SA. Mumps vaccine. In: Plotkin SA, Orenstein WA, eds. Vaccines. 4th ed. Philadelphia: Elsevier, 2004:441-69.
2. Galazka AM, Robertson SE, Kraigher A. Mumps and mumps vaccine: a global review. Bull World Health Organ 1999; 77:3-14.
3. Mumps vaccine. MMWR Morb Mortal Wkly Rep 1977;26:393-4.
4. van Loon FPL, Holmes SJ, Sirotkin BI, et al. Mumps surveillance — United States, 1988–1993. MMWR CDC Surveill Summ 1995;44:1-14.
5. Measles prevention: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Morb Mortal Wkly Rep 1989;38:Suppl 9:1-18.
6. Department of Health and Human Services. Healthy People 2010: understanding and improving health. 2nd ed. Washington, DC: Government Printing Office, November 2000. (Accessed March 17, 2008, at www.healthypeople.gov/document/html/objectives/14-01.htm.)
7. Council of State and Territorial Epidemiologists. CSTE position statement 1999-ID 9. (Accessed March 17, 2008, at http://www.cste.org/ps/1999/1999-id-09.htm.)
8. Simpson DM, Ezzati-Rice TM, Zell ER. Forty years and four surveys: how does our measuring measure up? Am J Prev Med 2001;20:Suppl:6-14.
9. Centers for Disease Control and Prevention. Statistics and surveillance: immunization coverage in the U.S. (Accessed March 17, 2008, at http://www.cdc.gov/vaccines/stats-surv/imz-coverage.htm#nis.)
10. Census Bureau. Population estimates. (Accessed March 17, 2008, at http://www.census.gov/popest/datasets.html.)
11. Stokley S, McCauley M, Fishbein D, Stevenson J. Adolescent vaccination coverage levels: results from the 1997-2003 National Health Interview Survey. Presented at the 40th National Immunization Conference, Atlanta, March 6–9, 2006. (Accessed March 17, 2008, at http://cdc.confex.com/cdc/nic2006/techprogram/P10373.HTM.)
12. Mumps epidemic — Iowa, 2006. MMWR Morb Mortal Wkly Rep 2006;55: 366-8.
13. Update: multistate outbreak of mumps — United States, January 1–May 2, 2006. MMWR Morb Mortal Wkly Rep 2006;55: 559-63.
14. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP) for the control and elimination of mumps. MMWR Morb Mortal Wkly Rep 2006;55:629-30.
15. Exposure to mumps during air travel — United States, April 2006. MMWR Morb Mortal Wkly Rep 2006;55:401-2. [Erratum, MMWR Morb Mortal Wkly Rep 2006;55:434.]
16. Public Health Agency of Canada (PHAC) home page. (Accessed March 17, 2008, at http://www.phac-aspc.gc.ca/index-eng.php.)
17. Kolasa MS, Klemperer-Johnson S, Papania MJ. Progress toward implementation of a second-dose measles immunization requirement for all schoolchildren in the United States. J Infect Dis 2004;189: Suppl 1:S98-S103.
18. Cortese MM, Jordan HT, Curns AT, et al. Mumps vaccine performance among university students during a mumps outbreak. Clin Infect Dis (in press).
19. Anderson RM, May RM. Vaccination and herd immunity to infectious diseases. Nature 1985;318:323-9.
20. Hersh BS, Fine PEM, Kent WK, et al. Mumps outbreak in a highly vaccinated population. J Pediatr 1991;119:187-93.
21. Cheek JE, Baron R, Atlas H, Wilson DL, Crider RD Jr. Mumps outbreak in a highly vaccinated school population: evidence for large-scale vaccination failure. Arch Pediatr Adolesc Med 1995;149:774-8.
22. Briss PA, Fehrs LJ, Parker RA, et al. Sustained transmission of mumps in a highly vaccinated population: assessment of primary vaccine failure and waning vaccine-induced immunity. J Infect Dis 1994;169:77-82.
23. Schaffzin JK, Pollock L, Schulte C, et al. Effectiveness of mumps vaccine in a summer camp outbreak. Pediatrics 2007; 120(4):e862-e868.
24. Mumps virus vaccines. Wkly Epidemiol Rec 2007;82:51-60.
25. Cohen C, White JM, Savage EJ, et al. Vaccine effectiveness estimates, 2004-2005 mumps outbreak, England. Emerg Infect Dis 2007;13:12-7.
26. 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.
27. Anderson RM, May RM. Infectious disease of humans: dynamics and control. New York: Oxford University Press, 1991:89-90.
28. Davidkin I, Valle M, Julkunen I. Persistence of anti-mumps virus antibodies after a two-dose MMR vaccination: a nine-year follow-up. Vaccine 1995;13:1617-22.
29. Rubin SA, Qi L, Audet SA, et al. Antibody induced by immunization with the Jeryl Lynn mumps vaccine strain effectively neutralizes a heterologous wild-type mumps virus associated with a large outbreak. J Infect Dis (in press).
30. Date A, Kyaw M, Rue A, et al. Long-term persistence of mumps antibody after receipt of two MMR vaccinations and antibody response after a third MMR vaccination among a university population — Nebraska 2006. J Infect Dis (in press).
31. Mumps epidemic — United Kingdom, 2004–2005. MMWR Morb Mortal Wkly Rep 2006;55:173-7.
32. Jin L, Brown DWG, Litton PA, White JM. Genetic diversity of mumps virus in oral fluid specimens: application to mumps epidemiological study. J Infect Dis 2004; 189:1001-8.
33. Nöjd J, Tecle T, Samuelsson A, Örvell C. Mumps virus neutralizing antibodies do not protect against reinfection with a heterologous mumps virus genotype. Vaccine 2001;19:1727-31.
34. Wharton M, Cochi SL, Hutcheson RH, Bistowish JM, Schaffner W. A large outbreak of mumps in the postvaccine era. J Infect Dis 1988;158:1253-60.
35. Department of Education, National Center for Education Statistics. 2004 and 2005 Integrated Postsecondary Education Data System (IPEDS), Spring 2005 and Spring 2006. (Accessed March 17, 2008, at http://nces.ed.gov/programs/digest/d06/tables/dt06_196.asp.)
36. Global status of mumps immunization and surveillance. Wkly Epidemiol Rec 2005;80:418-24.
37. Werner CA. Mumps orchitis and testicular atrophy: occurrence. Ann Intern Med 1950;32:1066-74.
38. Gut J-P, Spiess C, Schmitt S, Kirn A. Rapid diagnosis of acute mumps infection by a direct immunoglobulin M antibody capture enzyme immunoassay with labeled antigen. J Clin Microbiol 1985;21: 346-52.
39. Krause CH, Eastick K, Ogilvie MM. Real-time PCR for mumps diagnosis on clinical specimens — comparison with results of conventional methods of virus detection and nested PCR. J Clin Virol 2006;37:184-9.
40. Sanz JC, Mosquera Mdel M, Echevarría JE, et al. Sensitivity and specificity of immunoglobulin G titer for the diagnosis of mumps virus in infected patients depending on vaccination status. APMIS 2006;114:788-94.