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Mumps resurgences in the United States: A historical perspective on unexpected elements☆

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ABSTRACT

In 2006 the United States experienced the largest nationwide mumps epidemic in 20 years, primarily affecting college dormitory residents. Unexpected elements of the outbreak included very abrupt time course (75% of cases occurred within 90 days), geographic focality (85% of cases occurred in eight rural Midwestern states), rapid upward and downward shift in peak age-specific attack rate (5–9-year olds to 18–24-year olds, then back), and two-dose vaccine failure (63% of case-patients had received two doses).

To construct a historical context in which to understand the recent outbreak, we reviewed US mumps surveillance data, vaccination coverage estimates, and relevant peer-reviewed literature for the period 1917–2008.

Many of the unexpected features of the 2006 mumps outbreak had been reported several times previously in the US, e.g., the 1986–1987 mumps resurgence had extremely abrupt onset, rural geographic focality, and an upward-then-downward age shift. Evidence suggested recurrent mumps outbreak patterns were attributable to accumulation of susceptibles in dispersed situations where the risk of endemic disease exposure was low and were triggered when this susceptible population was brought together in crowded living conditions. The 2006 epidemic followed this pattern, with two unique variations: it was preceded by a period of very high vaccination rates and very low disease incidence and was characterized by two-dose failure rates among adults vaccinated in childhood.

Data from the past 80 years suggest that preventing future mumps epidemics will depend on innovative measures to detect and eliminate build-up of susceptibles among highly vaccinated populations.

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1. Introduction

Mumps is an infectious viral disease, classically manifested by inflammation of salivary glands and fever [1]. Mortality is rare, but aseptic meningitis can affect 10% of case-patients [2]. Mumps is an important cause of pediatric deafness, and up to 37% of post-pubertal males develop orchitis, 13% of whom have impaired fertility [1]. In the absence of vaccination, most persons have been infected by young adulthood [2]. In 1967 a live, attenuated mumps virus vaccine was licensed in the United States, and by 2005 high two-dose childhood vaccination coverage reduced disease rates by >99% [3,4].

In 2006 the US experienced a multi-state outbreak involving 6584 reported cases, with the highest attack rate among persons 18–24 years of age, many of whom were college students [4]. In affected colleges, most case-patients had received a second dose of the measles–mumps–rubella vaccine (MMR) ≥10 years previously [5,6]. This was the first large-scale US mumps outbreak among two-dose vaccinees.

Waning immunity appeared to play a role in facilitating this outbreak, consistent with effectiveness data from the United Kingdom [7] and serological data from Finland [8]. However, certain epidemiologic features were unexpected. The onset was sudden – a >50-fold rise in case counts within a 30-day period, followed by a sudden decrease, so that three-quarters of the epidemic's total cases occurred within 3 months [4]. After a decade in which the geographical distribution of mumps cases had been proportional to population, 85% of case-patients during the 2006 epidemic came from eight rural states located in the central US, followed by a return to an unremarkable geographic pattern [4]. In parallel, the peak age-specific attack rate shifted suddenly from primary school children to the college age group, then began moving back toward primary school children [4,9].

Previous resurgences of vaccine-preventable diseases in the United States had not shown these characteristics. The 1989–1991

☆ The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, US Department of Health and Human Services.

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measles resurgence had been preceded in the mid-1980s by a rising tide of incidence and increasing mean age of disease acquisition [10]. Lasting for 3 years, the measles resurgence saw outbreaks distributed widely across the US, but incidence was most intense in urban, rather than rural, areas [10]. The pertussis resurgence of the 1990s differed markedly from measles in many respects, but it too was widely distributed across the US, without any clear rural focality, and showed a slowly progressive pattern, both in terms of incidence and changing age-distribution [11].

We reviewed the history of mumps disease reports in the US to assess whether the 2006 resurgence patterns should have been unexpected – or whether they reflected recurrent phenomena that might shed light on the behavior of the mumps virus in the population, thereby helping us to anticipate and prevent future epidemics.

2. Methods

2.1. Surveillance data

2.1.1. Data sources

National notification of mumps cases was begun in 1922, discontinued in 1950 (though some states continued to report voluntarily), then restored in 1968 [12]. Where incidence was unavailable (1922–1967), we used the method of Sistrom and Mergo to scan graphic data four times, recorded the average value, and then used a cubic spline to interpolate missing values [12,13]. In 1968, printed monthly case counts by state were available. Beginning in 1977, case-patients' age group was increasingly included. In 1990 computerized case reporting was initiated, and more variables were progressively included, though completeness ranged 22–99%.

2.1.2. Inclusion criteria

Reporting criteria (including clinical case definition and case status classification) evolved over time. Because sufficient data were not available to allow application of the current definitions (Council of State and Territorial Epidemiologists, Position Statement 07-ID-02, accessed 12/1/08, http://www.cste.org/PS/2007ps/2007psfinal/ID/07-ID-02.pdf) to the whole period under examination (1917–2008), we included all reports of confirmed and probable mumps cases according to the case definition in use at the time.

2.1.3. Peak/trough analysis

We measured incidence amplitude by calculating a peak/trough ratio, obtained by dividing a peak incidence by the previous nadir incidence.

2.2. Population data

We calculated mumps incidence (overall, state-specific, and age group-specific), using annual US population estimates (Census Bureau, Population Estimates, accessed 12/1/08, http://www.census.gov/popest/datasets.html).

2.3. Vaccination coverage

One- and two-dose mumps-containing vaccine coverage was assessed from three national surveys whose methods have been described in detail elsewhere:

(1) US Immunization Survey (USIS): vaccination-card-verified, one-dose coverage of 24-month-old children, 1979–1985 [14].
(2) National Health Interview Survey (NHIS): vaccination-card-verified, two-dose coverage for 13–15-year-old adolescents, 1997–2003 [15].
(3) National Immunization Survey (NIS): (Centers for Disease Control and Prevention, Immunization Coverage in the US, accessed 12/1/08, http://www.cdc.gov/vaccines/stats-surv/imz-coverage.htm#nis).
    (a) Provider-verified, one-dose coverage for 19–35-month-old children, 1995–2008.
    (b) Provider-verified, two-dose coverage for 13–17-year-old adolescents, 2006–2008.

2.4. Mumps in the military

We obtained mumps case counts and population denominators for 1998–2007 (Armed Forces Health Surveillance Center, Defense Medical Epidemiology Database, accessed 12/1/08, http://www.afhsc.mil/dmed_overview.asp). Policy memoranda supplied by the Military Vaccine Agency provided a history of military vaccination practices.

2.5. Literature review

We reviewed available peer-reviewed literature concerning mumps outbreaks and epidemic patterns, particularly for the years where original reporting data were not available.

2.6. Analytic periods

We defined four time periods:

(1) Pre-vaccine 1917–1967.
(2) Vaccination Program Implementation 1968–1982.
(3) First Resurgence 1983–1992.
(4) Second Resurgence 1993–2008.

We chose to end the Period of Vaccination Implementation when a steady baseline incidence appeared to have been reached. We ended the Period of the First Resurgence when the annual incidence had returned to the level observed at the beginning of this period.

2.7. Modeling

To evaluate the multi-annual periodicity of mumps in the pre-vaccine era, we performed Fourier decomposition, identifying a single cycle with a 3-year period. As the annual rates also increased from early to mid-century and decreased thereafter, our harmonic regression model also includes terms for non-cyclic secular variation. We estimated its coefficients via least squares.

3. Results

3.1. Pre-vaccine Period: 1917–1967

Irregular epidemic cycles of relatively moderate amplitude (mean peak/trough 1.6, range 1.1–2.5) had a periodicity of approximately 3 years, and a superimposed secular trend peaked during World War II (Fig. 1A). By age 14 years, approximately 90% of urban children had been infected, with peak incidence at age 5–9 years [12,16], suggesting that millions of cases occurred each year, but reported incidence was much lower (50–251/100,000). Cases were reported throughout the year, with highest incidence during winter and spring [12,17]. No geographic patterns were reported, but in the early years of this period, disease acquisition may have been delayed among rural children, as explosive outbreaks occurred when young military recruits, particularly those from rural areas, were crowded into barracks [18,19]. A report from World War

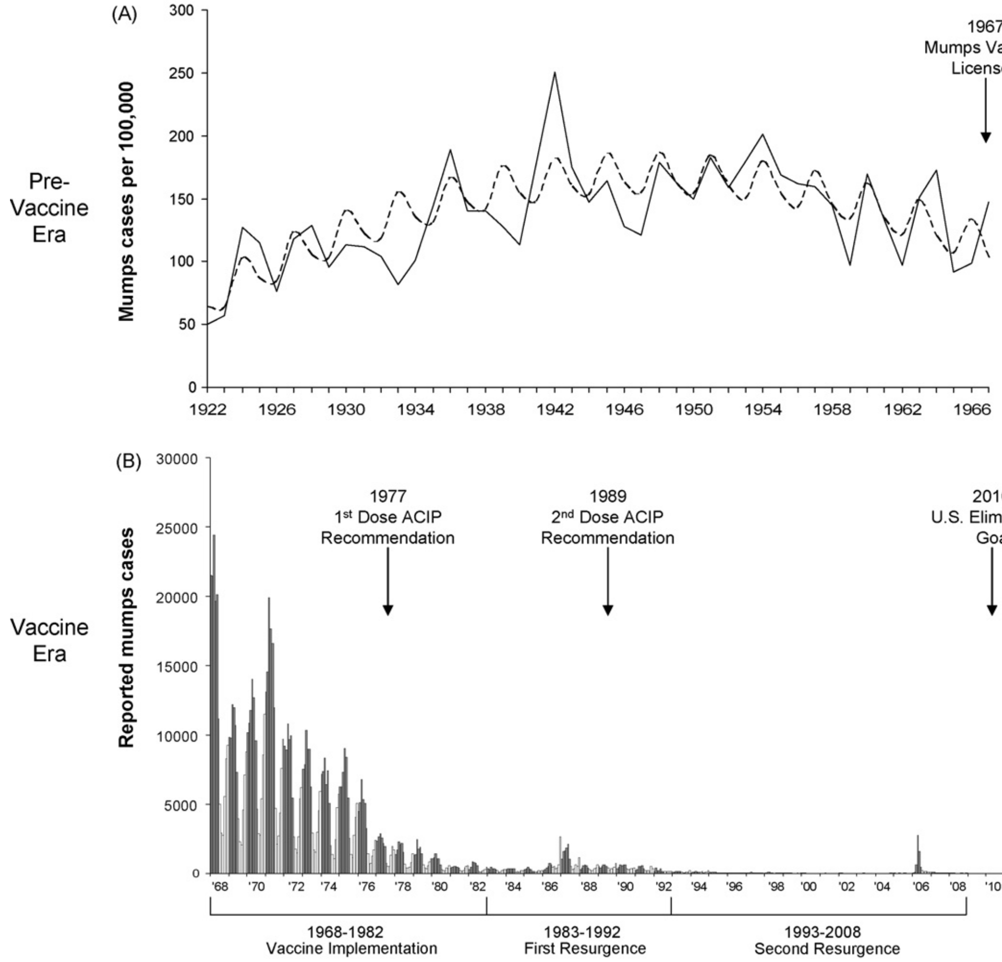

Fig. 1. Mumps Activity in the US, 1922–2008. (A) Pre-vaccine era mumps incidence, 1922–1967. Reported incidence (solid line); 3-year epidemic cycle with secular trend (broken line). (B) Vaccine era monthly mumps cases, 1968–2008. Cases of mumps reported to the Centers for Disease Control and Prevention (CDC) by month of onset date are shown in bars: cases that occurred January to June (dark bars) and cases that occurred July to December (white bars).

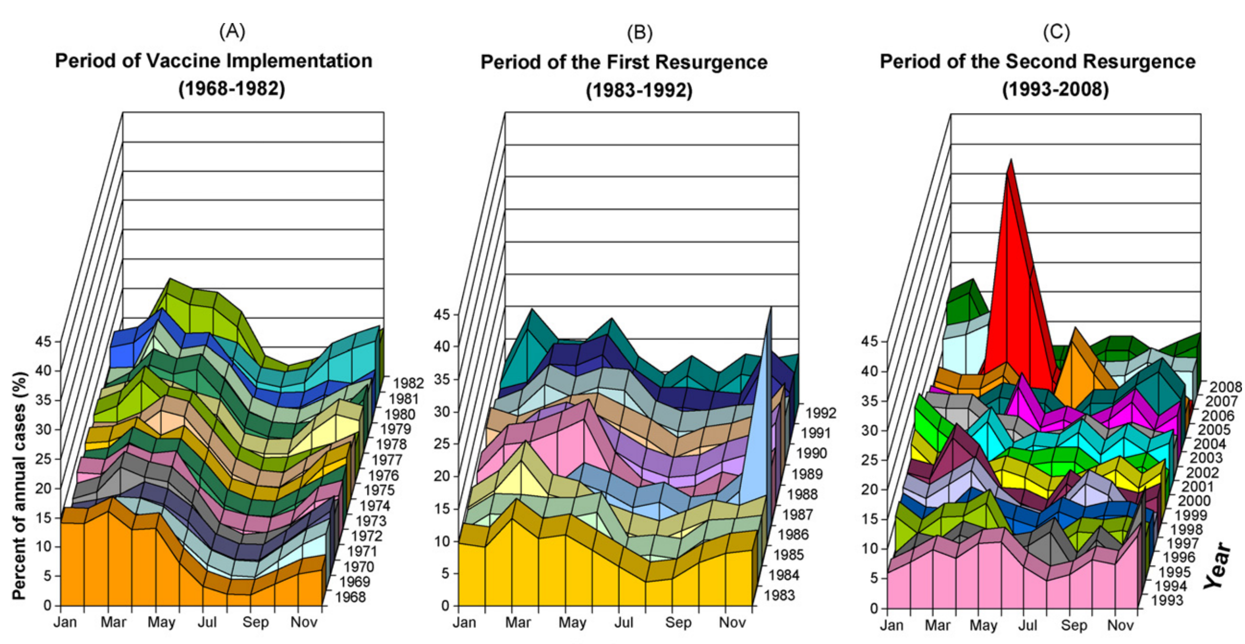

Fig. 2. Mumps Seasonality, 1968–2008. For each graph, percent of annual cases is plotted on the *z*-axis, with months on the *x*-axis and years on the *y*-axis.

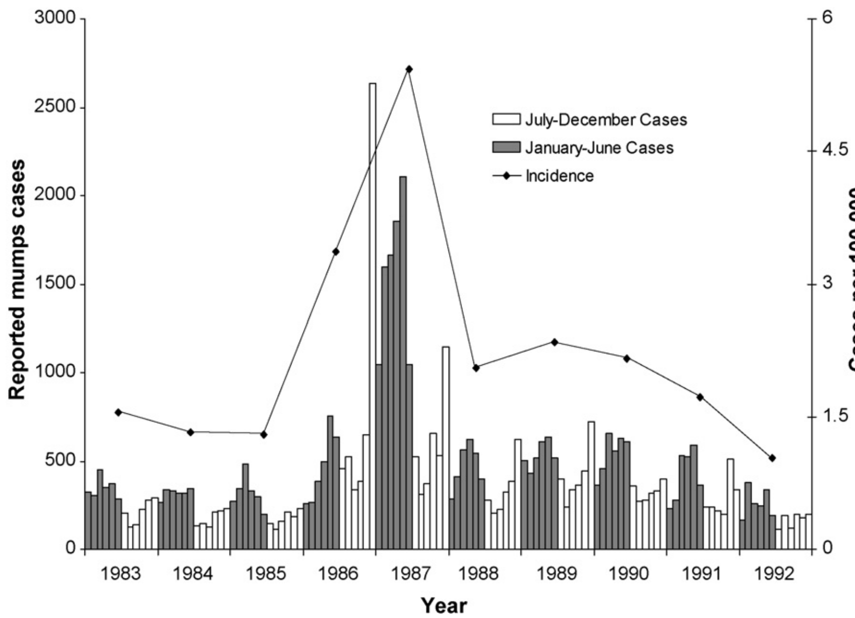

Fig. 3. Period of the First Resurgence, 1983–1992. Monthly mumps cases (bars): cases of mumps reported to CDC by month of onset date are shown in bars: cases that occurred January to June (dark bars) and cases that occurred July to December (white bars). Annual mumps incidence (solid line): number of annual cases reported to CDC per 100,000 US population.

I stated: "…mumps has appeared most frequently among rural rather than urban troops. Our percentage has been 85 per cent rural and 15 per cent urban." [18] Another World War I report attributed this rural preponderance to lack of prior exposure: "They had not been accustomed, like their urban cousins, to epidemics of any sort and therefore, from their lack of immunity, geographically furnished good soil for the virus" [20].

3.2. Period of Vaccination Implementation: 1968–1982

Progress toward universal childhood vaccination was gradual. In 1967, after mumps vaccine licensure, the Advisory Committee on Immunization Practices (ACIP) stated the "vaccine may be considered for use in children approaching puberty, in adolescents, and in adults, especially males," but "the vaccine is not recommended for routine use" [3]. In 1968, this was modified to indicate "that consideration be given to immunizing all susceptible children over 1 year of age" [21]. Finally, in 1977, ACIP recommended mumps vaccination "for all children at any age after 12 months" [22]. Annual mumps coverage rates for 24-month olds ranged 70–80% according to a national survey conducted 1979–1985 [14]. Enactment of school mumps vaccination requirements was gradual: by 1982 twenty states still lacked such laws [23]. However, because combined MMR was used in school-based measles elimination efforts, 95% of school enterers had been vaccinated for mumps according to a 1982 survey, though state-specific rates were as low as 69% [23]. The number of reported mumps cases decreased by 97% compared to the Pre-Vaccine Era: 152,209 (incidence 88/100,000) in 1968 to 5270 (incidence 2.5/100,000) in 1982. Winter-spring seasonality persisted (Fig. 2A), but the 3-year cycles were gradually eliminated (Fig. 1B). Although incidence declined across all age groups, reduction was greatest in the primary school ages targeted for immunization, producing a relative up-shift in the age of case-patients [23]. However, the peak attack rate remained age 5–14 years [23].

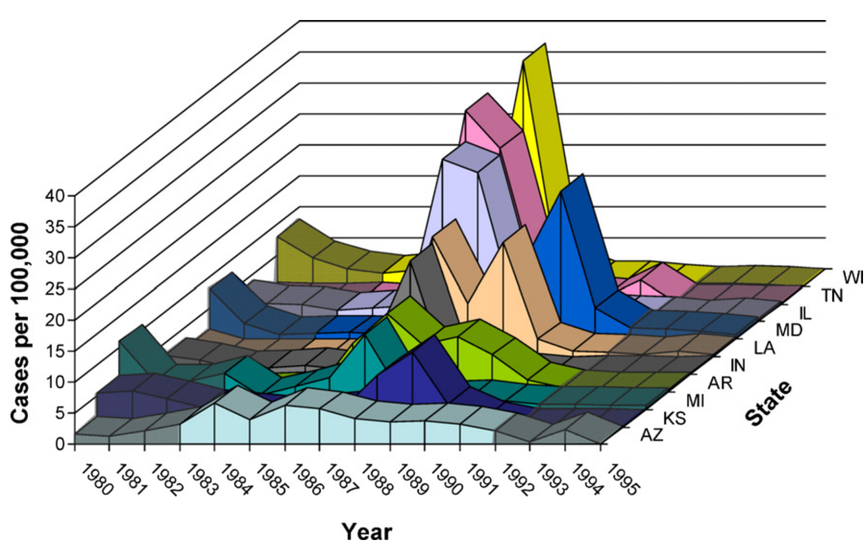

Fig. 4. Highest incidence states in the Period of the First Resurgence, 1983–1992. The ten states shown along the y-axis had the highest aggregate incidence reported to CDC during 1983–1992. Annual incidence for each state is shown on the z-axis. Bracketing years 1980–1982 and 1993–1995 are shown in shaded colors.

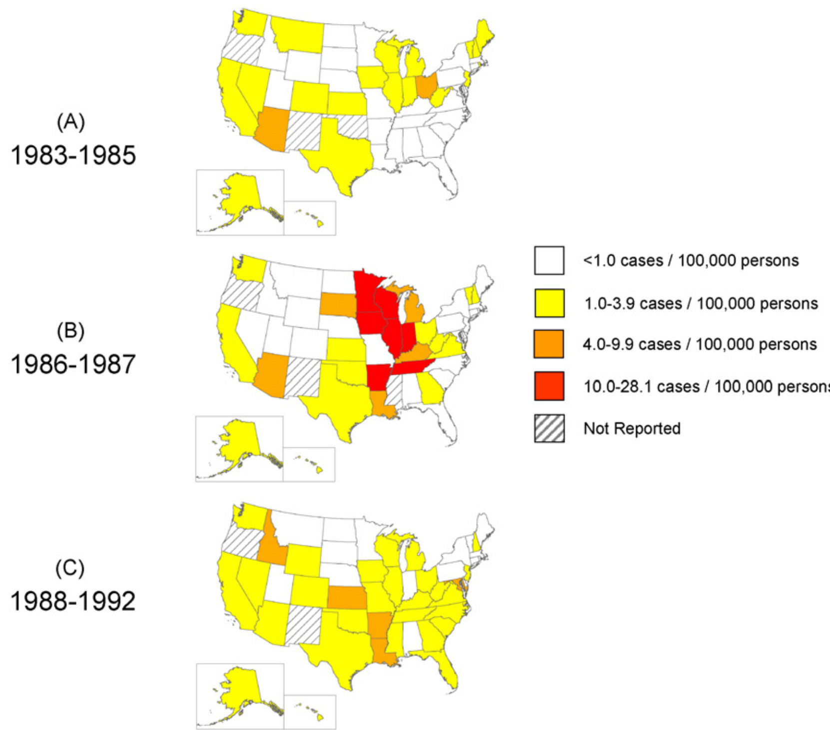

Fig. 5. Geography of the Period of the First Resurgence, 1983–1992. For each map, the state's aggregate incidence reported to CDC over the given time period is shown.

3.3. *Period of First Resurgence: 1983–1992 (Fig. 3)*

After 17 years of marked decline in mumps incidence, a historical nadir of 2982 cases (incidence 1.3/100,000) was reached in 1985. Abruptly in December 1986 a resurgence began, with the single-month case count (2633) nearly equaling the previous year's total. The outbreak peaked in 1987 with 12,848 annual cases (incidence 5.4/100,000). Of the 10 states with the highest incidence for 1983–1992 (Fig. 4), 9 showed an explosive pattern (mean peak/trough 64, range 2–419). Compared to a diffuse geographic incidence before and after, the 1986–1987 resurgence was highly focal: the eight states with highest incidence were contigu-

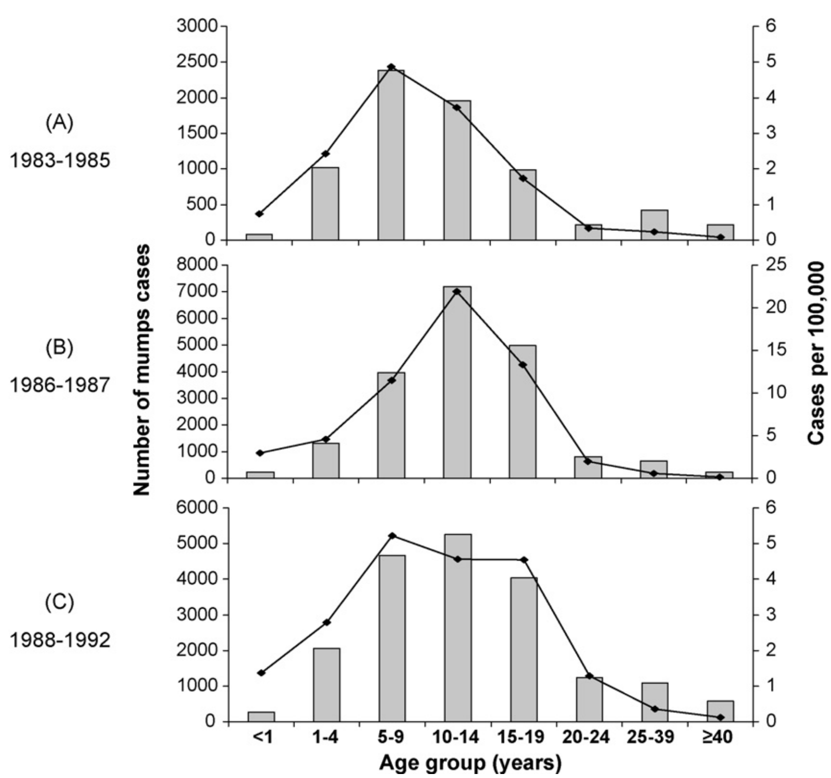

Fig. 6. Age-specific incidence and case numbers, Period of the First Resurgence, 1983–1992. For each graph, bars represent total cases of mumps reported to CDC, and the solid line represents aggregate incidence. Note that *y*-axes are on a different scale for each graph.

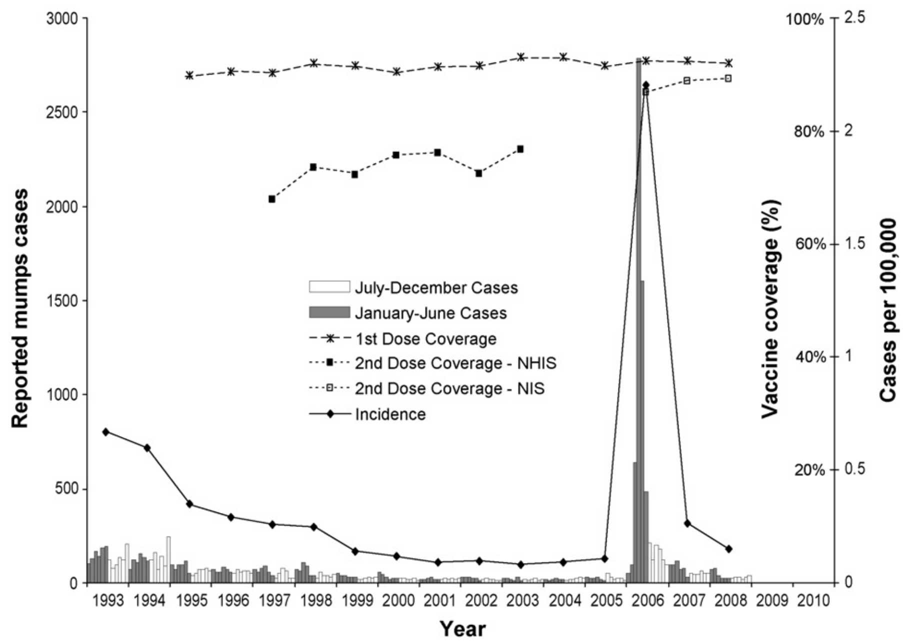

Fig. 7. Period of the Second Resurgence, 1993–2008. Monthly mumps cases (bars): cases of mumps reported to CDC by month of onset date are shown in bars: cases that occurred January to June (dark bars) and cases that occurred July to December (white bars). Annual mumps incidence (solid line): number of annual cases reported to NNDSS per 100,000 US population. First dose coverage (broken line): Single dose coverage with the measles–mumps–rubella vaccine (MMR) among 19–35-month olds measured by the National Immunization Survey and verified by provider records. Second dose coverage – NHIS (dotted line with solid square markers): second dose coverage with MMR among 13–15-year olds measured by the National Health Interview Survey and verified by vaccination cards [15]. Second dose coverage – NIS (dotted line with hollow square markers): Second dose coverage with MMR among 13–17-year olds measured by the National Immunization Survey and verified by provider records.

ously located in the central, rural US, and two states accounted for 57% of the nation's cases in 1986 (Fig. 5). Outbreaks were often reported from high schools and colleges serving rural populations [24,25]. During 1986–1987, incidence increased for all age groups, but the peak shifted from the 5–9-year age group into 10–19-year olds where 63% of cases occurred (Fig. 6). Vaccination status of case-patients was not quantified nationally, but the resurgence was attributed to an increase in susceptibility among older cohorts of children who had not been vaccinated but who had been spared previous disease exposure by declining mumps incidence [26]. During the post-resurgence years (1988–1992), outbreaks associated with one-dose vaccine failure were first reported [27–29]. In December 1989, ACIP, for improved measles control, recommended a second dose of measles vaccine, but suggested it be administered

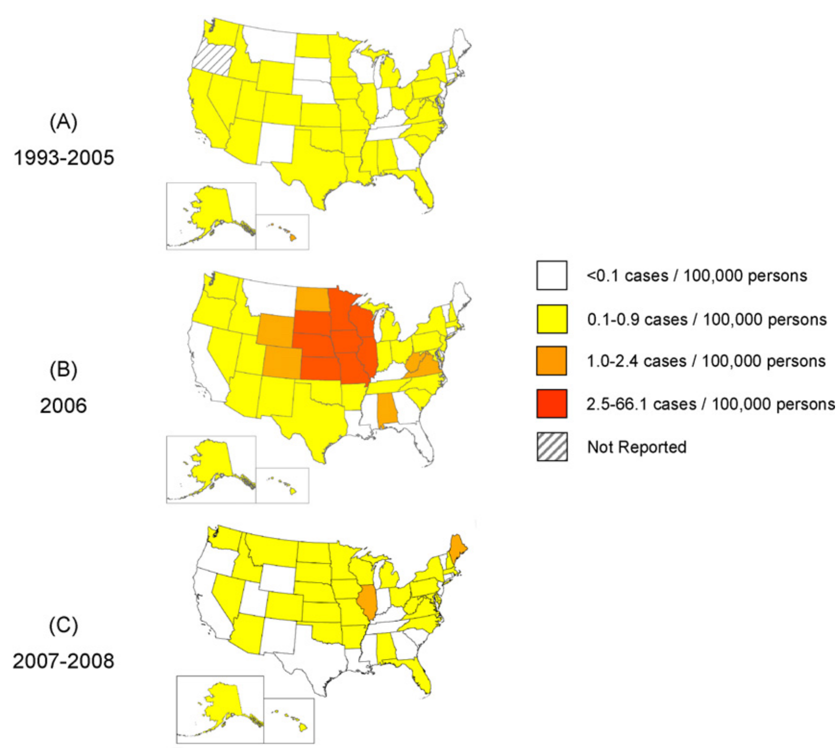

Fig. 8. Geography of the Period of the Second Resurgence, 1993–2008. For each map, the state's aggregate incidence reported to CDC over the given time period is shown.

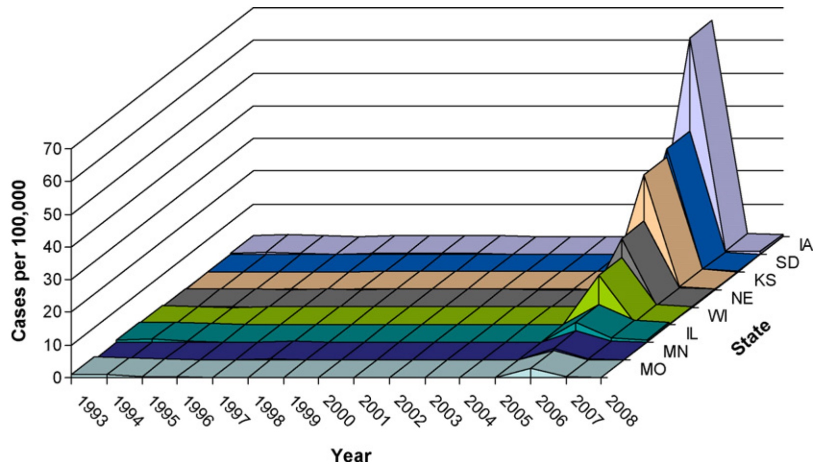

Fig. 9. Highest Incidence States in the Period of the Second Resurgence, 1993–2008. The eight states shown along the *y*-axis had the highest aggregate incidence reported to CDC during 1993–2008. Annual incidence for each state is shown on the *z*-axis.

as MMR, stating "Mumps revaccination is particularly important" [30]. By 1992, mumps incidence finally returned to pre-resurgence levels at 1.0/100,000.

3.4. Period of Second Resurgence: 1993–2008 (Fig. 7)

3.4.1. Coverage

Annual national immunization coverage surveys resumed in 1995 with NIS: for every year through 2008, first dose preschool mumps vaccination coverage was ≥90%, with a slow upward trend. Second dose coverage among adolescents was measured by two different surveys. The first showed coverage rose from 68% in 1997 to 77% in 2003 [15], and the second (NIS) showed a rise from 87% in 2006 to 89% in 2008.

3.4.2. Pre-resurgence (1993–2005)

Reported annual mumps cases continuously declined from 1989 through 2001, then plateaued through 2005, averaging 268 (average incidence 0.1/100,000) with a historical nadir of 231 in 2003. Of case-patients, 72% were vaccinated, 37% with two doses. Peak incidence remained primarily in the 5–9-year age range. Seasonal patterns were no longer recognizable (Fig. 2C). The eight Midwestern states most affected in the subsequent resurgence (representing 13% of the US population) accounted for 10% of total cases (Fig. 8A). Compared to these eight states, cumulative mumps incidence in the rest of the country was 41% higher (0.24 vs. 0.17/100,000).

3.4.3. Resurgence (2006)

Abruptly the number of cases rose from 13 in December 2005 (the third lowest month in US history) to 2786 in April 2006 (the highest month in 29 years) with an annual total of 6584 (incidence 2.2/100,000). Eight states contiguously located in the central US (13% of US population) accounted for 85% of 2006 cases (Fig. 8B). These states tended to have a lower population density than the rest of the country (56.2 persons vs. 96.9 persons per square mile,

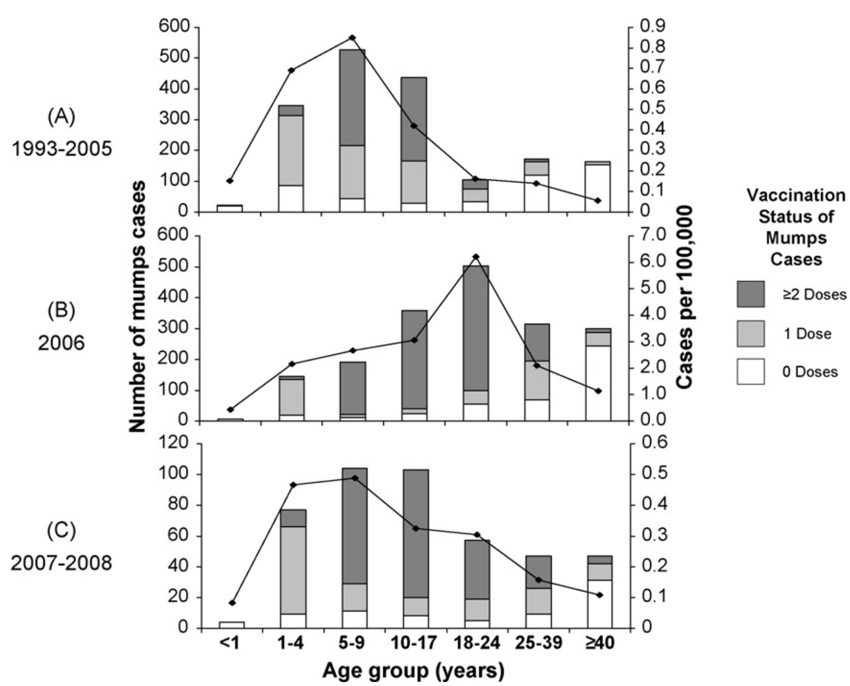

Fig. 10. Age-specific incidence and case numbers by vaccination status, Period of the Second Resurgence, 1993–2008. For each graph, bars represent total cases of mumps reported to CDC by vaccination status, and the solid line represents aggregate incidence. Note that *y*-axes are on a different scale for each graph.

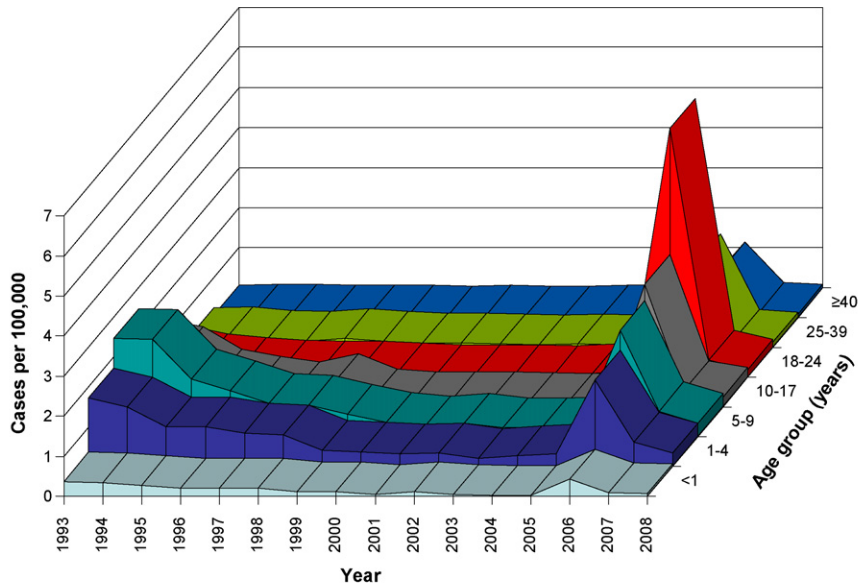

Fig. 11. Annual incidence by age group, 1993–2008. Year is plotted along the *x*-axis, and age group in years is plotted along the *y*-axis. Mumps incidence for each year and age group, as reported to CDC, is plotted along the *z*-axis.

$P = 0.08$). For each of the preceding 11 years, each of these states had $\geq$86% first dose mumps vaccination coverage according to NIS and near-zero mumps incidence. Each experienced explosive epidemic onsets (mean peak/trough 165, range 13–350, excluding one infinite value) and almost equally abrupt decreases (Fig. 9). Peak incidence shifted abruptly to 18–24-year olds (Figs. 10 and 11). Of case-patients, 76% were vaccinated, 57% with two doses. However, for the most highly affected 18–24-year age group, 80% had received two doses (Fig. 10B). Studies suggested 83% of case-patients in this age group were college students, mainly in rural states, 89–99% of whom had received two doses of vaccine, most $\geq$10 years before [4–6].

3.4.4. Post-resurgence (2007–2008)

Case counts declined rapidly toward pre-resurgence levels. Of case-patients, 82% were vaccinated, 53% with two doses. Peak incidence progressively shifted back toward the 5–9-year age group, and the geographic pattern was unremarkable.

3.4.5. Military

Military recruits were apparently spared involvement in the resurgence, despite belonging to the same age group and residing in barracks across the US. During the years for which data are available (1998–2007), the number of first-occurrence mumps cases in an ambulatory setting averaged 30 annually (range 16–53) in a total military population that averaged 1.38 million (range 1.36–1.41 million) for an aggregate incidence of 2.2/100,000. During the 2006 nationwide resurgence, 53 cases but no outbreaks were reported. In 1991, the military had begun routine administration of MMR to recruits without regard to prior vaccination status. In 1995 this was changed to provide measles and rubella vaccination regardless of prior history and mumps vaccination (either as MMR or as single antigen) to those without written proof of prior vaccination or mumps disease. In 2006 this policy was updated again to provide MMR to those without documentation of vaccination or serologic evidence of immunity against measles and rubella. Under these policies, an unknown proportion of recruits may have received a third dose of a mumps-containing vaccine [31,32].

4. Discussion

Many of the unexpected features of the 2006 mumps resurgence had occurred before in the history of mumps activity in the United States. Both the 1986–1987 and 2006 resurgences were immediately preceded by historic low points in disease activity. Both resurgences had extremely abrupt onsets, with incidence rising 10- to >100-fold over baseline within a month. In both resurgences, a few states contiguously located in the central US contributed most cases. In both the 1986–1987 and 2006 resurgences, there was a sudden upward shift in peak attack rate from children 5–9 years old to teenagers/young adults, followed by a return to the 5–9-year age group after the resurgence had subsided.

However, in two important respects, the 2006 resurgence appears to have been unique. First was the apparent near-elimination of viral transmission in the preceding decade: vaccination levels higher than the estimated herd immunity threshold (88–92%) [33], disease incidence rate <1 case per million, loss of seasonality, and absence of any foci of ongoing transmission.

Second was the preponderance of cases among two-dose vaccinees. Though outbreaks attributable to one-dose vaccine failure were first reported in the late 1980s, and sporadic cases of two-dose failure were common after the early 1990s, large-scale outbreaks attributable to two-dose failure had not been reported in the US or elsewhere, to our knowledge, prior to 2006. After the US reported the 2006 resurgence, however, other nations have begun reporting mumps outbreaks attributed to two-dose failure. The Czech Republic, which had implemented a routine two-dose mumps vaccination policy just 2 years prior to the US, experienced a large outbreak in 2006 with characteristics similar to that of the US: 70% of cases had received two doses, and among these, the median age was 15 years [34]. In 2008–2009, North Wales experienced an outbreak in which 87% of case-patients had received two doses of MMR, and the median age was also 15–16 years [35].

These apparently novel outbreak characteristics may have historical precedents, however. The 1986–1987 resurgence has been explained as resulting from the growth of a population who had missed vaccination as children but who had been spared previous disease exposure, so that when they entered into high school and college environments where transmission was facilitated, a resurgence resulted [26]. Though the 2006 resurgence involved a highly vaccinated, rather than an unvaccinated population, one can speculate that the conditions which gave rise to it may not have been so different from the 1986–1987 resurgence. In rural sections of Midwestern states, where population density was very low and vaccination coverage high, natural boosting attributable to importations or endemic disease may have been rare, allowing vaccine-induced immunity to wane. Although susceptibles accumulated, mumps is much less infectious than measles [36], and the force of infection in sparsely populated areas was insufficient to cause outbreaks until young adults entered concentrated living conditions in colleges [5,6]. Such an outbreak pattern has been reported as far back as World War I, in which outbreaks occurred among rural populations placed in barracks conditions [17–20].

In support of this hypothesis is the fact that these eight Midwestern states had an aggregate population density almost half of the rest of the United States and a much lower cumulative mumps incidence in the period preceding the resurgence. Compared to other rural areas in the country (e.g., the Southeast or Mountain West), they also had higher rates of college attendance (National Center for Education Statistics, Total fall enrollment in degree-granting institutions, by state or jurisdiction: Selected years, 1970 through 2005, accessed 6/25/09, http://nces.ed.gov/programs/digest/d06/tables/dt06_193.asp). Studies in the eight Midwestern states during the resurgence suggested that among 18–24-year olds (the most affected group) 83% of cases were college-associated, with the highest attack rate among first-year students living in dormitories [4–6]. Thus it is possible that these Midwestern states may have been at increased risk because of the relatively larger numbers of well-vaccinated young adults leaving home in rural areas to live together in dormitory conditions. While lower preceding disease incidence, lower population density, and greater rates of college attendance may have contributed to higher attack rates in the Midwest, the extreme focality of the 2006 mumps resurgence – which contrasts dramatically with the geographic patterns of the measles and pertussis resurgences of the 1990s – suggests that other factors, not accounted for in this analysis, may also have played a role.

Regardless of hypothetical mechanisms, the patterns of mumps outbreaks, both in 2006 and in the past, have implications for mumps surveillance and vaccination programs. First, given the explosive characteristics of mumps outbreaks in the past, historically low disease rates may not be proof that the risk of epidemic disease is remote. Thus, the usual indicators of an impending epidemic (e.g., gradually rising numbers or increasing spread rates) may not occur. Similarly, if epidemics arise specifically from lack of wild disease boosting, the search for foci of ongoing transmission may not be helpful in identifying locations at risk. Coverage surveys to identify pockets of under-vaccination will not be fruitful when outbreaks occur among highly vaccinated populations. And when mumps does occur among highly vaccinated populations, data suggest clinical manifestations may be atypical, the proportion of asymptomatic case-patients may be greater than the previous estimate of 30%, and the usual laboratory tests (e.g., IgM) may have lowered yield [6]. Thus silent or unrecognized transmission can contribute to difficulties in identifying and containing disease introductions, problems in recognizing outbreaks, and diminished effectiveness of isolation/quarantine measures.

This may be particularly important since mumps disease patterns in 2007 and 2008 appeared to be returning to those existing in the period leading up to the 2006 resurgence. Provisional data from the first 6 months of 2009 seem to confirm this trend (CDC, unpublished data).

Novel strategies are needed for identifying disease and detecting and eliminating build-up of susceptible individuals. Neutralizing antibodies may be protective against mumps disease [37], and their titers have been shown to decline over time [38]. If the 2006 resurgence occurred because the protective value of a second dose waned in a proportion of vaccinated cohorts, particularly in rural populations who had been spared disease exposure, then serologic monitoring of antibody levels may be needed in addition to monitoring vaccination and disease rates. Studies to better characterize the protective level of mumps antibody would be particularly useful in interpreting such surveys. Improved laboratory methods for diagnosing mumps in vaccinated populations would also be valuable. Evidence suggests the 2006 US resurgence was preceded and possibly seeded by mumps epidemics in nations such as the United Kingdom and Canada with which the US has substantial contact [7,39]. Expanding and improving global surveillance for mumps, particularly in developed countries with vaccination programs, will assist in evaluating the potential risk of mumps activity in the US. The relative absence of mumps activity in the military during the 2006 resurgence raises the possibility that a third dose could be effective in preventing or controlling future epidemics. The immunogenicity, long-term efficacy, and adverse events associated with a third dose of mumps vaccine in young adults need to be studied so that data will be available to guide vaccination response in future resurgences.

There are several limitations to this study. The data analyzed were obtained from a passive surveillance system, with much missing data. For the pre-vaccine era, we relied on data summaries, sometimes drawing on a limited number of individual studies to make inferences about population-based conditions. Viral strain differences may affect the level of antibodies needed to neutralize mumps virus [40,41], but too few viral specimens were available to examine the potential role of virus strains in mumps epidemiology (1917–2008).

Nonetheless, we believe our findings demonstrate many aspects of the 2006 resurgence were consistent with patterns of mumps epidemiology for the preceding 80 years. Following periods of low disease, explosive outbreaks occurred when young adults from rural areas were brought into close contact. These recurrent patterns help provide insight into how to anticipate and prevent future mumps epidemics. As in the past, this will depend on detecting and eliminating build-up of susceptible individuals – now among highly vaccinated populations.

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