

# Upward Trends of Parotitis and Mumps in Atlanta over a Decade

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## Abstract

Rising rates of mumps in Georgia have been reported. We hypothesize that the incidence of parotitis and mumps presenting to Children's Healthcare of Atlanta (CHOA) has increased over the past decade among immunized children. Retrospective chart reviews were conducted using ICD9/10-codes for parotitis and mumps from January 2007 to December 2017. Data on demographics, vaccination status, labs, management and disposition were collected. 1017 parotitis cases were diagnosed; an upward trend in incidence occurred over time. Mumps testing was done in 47 (4.6%) parotitis cases; 9 mumps cases were identified, with 6 diagnosed in 2017. Seven patients (78%) were fully vaccinated. Median age for mumps was 13 years. Few symptoms differentiate mumps from non-mumps-parotitis. The incidence of parotitis and mumps in children has increased since 2007 in the Atlanta area, reflecting a nationwide trend. Mumps is likely underreported as rates of testing are low, and should be considered in children with parotitis regardless of vaccination history.

## Keywords

parotitis, mumps, MMR-vaccine, immunized, pediatric emergency departments

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## Highlights

### What do we already know about this topic?

- The incidence of parotitis and mumps in children is increasing nationwide

### How does your research contribute to the field?

- This research demonstrates that the majority of new mumps cases occurred in younger children than expected who were fully vaccinated, and evaluation of parotitis in the pediatric emergency department commonly involved bloodwork, imaging and antibiotics that may not have been necessary.

### What are your research implications towards theory, practice or policy?

- This research suggests that mumps should be considered in the differential diagnosis for

children with parotitis regardless of vaccination history; masking, droplet-precautions, isolation for 5 days from the development of symptoms, and supportive care is recommended for all parotitis cases.

## Introduction

Mumps is a viral infection caused by a paramyxovirus transmitted through contact with respiratory secretions. Risk increases with duration and close proximity to a

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positive contact and infection ranges from a mild sub-clinical course to significant parotitis, orchitis, oophoritis, pancreatitis, and especially in the pre-vaccine era, meningoencephalitis and deafness. By far the most common clinically significant manifestation of mumps is parotitis (75%-95%).<sup>1,2</sup> In the past, the Measles-Mumps-Rubella (MMR) vaccine has a reported median effectiveness of 78% in preventing mumps for 1 dose (range, 49%-91%) and 88% for 2 doses (range 66%-95%).<sup>3-8</sup> Despite greater than 90% uptake of the vaccine in the US over the last decade, the incidence of mumps has increased. Between the years of 2007 to 2015, there were consistently less than 3000 cases of mumps reported per year, whereas in 2016, there were 6369 cases reported.<sup>9</sup> The most recent mumps outbreaks have occurred in multiple states, with New York, Pennsylvania and Alaska reporting the highest number of cases.<sup>9</sup> Cases were common among college campuses and most notably, amongst vaccinated individuals.<sup>10</sup> A total of 2954 mumps cases in 2016 were identified in Arkansas; the majority of those cases (57%) were in school-aged children (5-17 years), and 92% of those children had completed the mumps vaccination schedule.<sup>11</sup> At the University of Washington, Seattle campus, 100% of individuals diagnosed with mumps (N=42) received 2 doses of the MMR vaccine and the overall rate of MMR uptake in the University was >99%.<sup>12</sup> Data suggests that contraction of mumps may be associated with close living situations.<sup>13,14</sup> The most likely explanation for mumps cases in previously immunized persons may be secondary vaccine failure, or waning immunity. Data from a recent study suggest that specific immune outcomes may wane at different rates and highlight our currently incomplete understanding of protective immune responses to mumps and measles.<sup>15</sup>

A confirmed case of mumps is defined by positive reverse transcription polymerase chain reaction (RT-PCR) or viral culture for mumps along with symptoms of mumps including parotitis, orchitis, aseptic meningitis, meningoencephalitis, oophoritis, mastitis, pancreatitis, and/or hearing loss. Probable mumps requires presence of mumps symptoms in addition to IgM-positivity or close contact with an epidemiological link to a probable or confirmed mumps case or in times of outbreak. Suspected mumps is defined as any subject with unexplained parotitis, orchitis or oophoritis; or mumps IgM positivity without clinical symptoms.<sup>1</sup> In Georgia, there have been 110 cases of mumps (52 suspected, 29 probable, and 29 confirmed) from January 2017 to December 2017, a significant increase from prior years (2016 had 16 cases of suspected, probable, and confirmed mumps combined). Of the 110 Georgia

mumps cases, 82 have available vaccination history, of which 61 (74.4%) have documentation of receiving 2 doses of MMR vaccine.<sup>16</sup>

Children's Healthcare of Atlanta (CHOA) has recently seen an increase in parotitis cases, with several anecdotally noted to be younger than the college-aged cases of mumps described in the literature. We hypothesize that the incidence of parotitis and mumps has increased over the past decade including among those who are fully immunized. This study examines the trends in parotitis and mumps evaluated in the emergency departments (ED) of CHOA over the past decade as well as presenting symptoms, clinical characteristics, vaccination status, and management of this condition.

## Material and Methods

### Study Design

An institutional review board (IRB) approved retrospective chart review of patients presenting to 3 CHOA pediatric EDs with the diagnosis of mumps, sialoadenitis or parotitis using ICD-9 codes (527.2 for parotitis and 072 for mumps) and ICD-10 codes (K11.2 for parotitis and B26 for mumps) from January 1, 2007 to December 31, 2017 was performed. ED encounters were charted through Epic electronic medical records (EMR) and scanned handwritten paper charts. Immunization information was obtained through the Georgia Registry of Immunization and Transaction Services. The Georgia Department of Public Health (DPH) was consulted for up-to-date numbers on suspected and confirmed mumps cases statewide, and specifically those reported from CHOA.

Charts that did not show evidence of parotitis through documentation in medical records were excluded. Patients with recurrent parotitis or multiple ED visits for parotitis/mumps were counted as 1 subject. Patients were considered to have been tested for mumps if blood test for mumps IgM and/or buccal swab for mumps RT-PCR or viral culture were sent. Subjects meeting inclusion criteria were reviewed for immunization status, presentation, management and disposition. Patients were considered to have fever if reported by family and documented in physician chart or according to ED recorded temperature >38°C. Patients were considered to have blood tests done if any non-microbiological blood test was performed such as complete blood count (CBC), C-reactive protein (CRP), or amylase. Patients who had blood cultures obtained as part of their workup were noted. Patients were considered to have had imaging studies if they had an ultrasound, CAT scan (CT) or magnetic resonance imaging (MRI) as part of their

evaluation. Administration of antibiotics, disposition status, and number of visits for parotitis were noted.

### Statistical Analysis

Descriptive statistics were calculated for variables of interest, including medians and interquartile ranges (25th-75th percentiles) for continuous variables, and counts and percentages for categorical variables. Distributions of continuous variables were assessed using Anderson-Darling normality tests. Patients with parotitis not inclusive of mumps were compared to mumps positive patients using Fisher's exact tests for categorical variables (gender, vaccine-status, unilateral versus bilateral nature of parotitis, presence of fever, rate of imaging, whether or not antibiotics were administered and admission rate) or Wilcoxon rank-sum tests for continuous variables due to non-normality. A linear trend of parotitis cases during the 2007 to 2017 study period was assessed using Pearson's correlation coefficient and Fisher's  $z$  transformation to compute 95% confidence intervals for the correlation coefficient. All statistical analyses were performed using SAS 9.4 (Carey, North Carolina). A  $P$ -value of  $<.05$  assumed statistical significance.

### Ethical Approval and Informed Consent

This retrospective chart review was approved by the Children's Healthcare of Atlanta IRB (study ID #17-174). A waiver of informed consent was approved by the IRB, as the research involved no more than minimal risk to the subjects included in the electronic chart review.

## Results

### Patient Characteristics of Parotitis and Mumps at Children's Healthcare of Atlanta

A total of 1052 ED charts were reviewed based on ICD codes; 35 were excluded due to lack of parotitis diagnosis confirmation. Of the 1017 children (ages birth to 20 years) with parotitis evaluated over the decade in the CHOA EDs, 47 (4.6%) were tested for mumps and 9 (19%) of those tested were positive for mumps either by serology and/or PCR. Five of those cases were considered probable mumps and 4 were confirmed mumps.

Demographics, clinical characteristics, vaccination status and ED disposition of patients are summarized in Table 1. Mumps-positive cases were more commonly associated with bilateral parotitis than presumed non-mumps parotitis (56% vs. 9%,  $P < .001$ ). No other statistically significant differences in mumps cases were observed, although there was a trend towards higher frequency of fever, male gender and older age.

### Serious Complications

Of the 1008 patients with non-mumps parotitis, 22% (N=219) required hospitalization to the general pediatrics ward and 0.4% (N=4) required pediatric intensive care unit (PICU) admission. Of the 9 mumps cases, 2 required admission to the ward and 1 required PICU admission. There were no reports of orchitis or meningoencephalitis in any children with parotitis or mumps. Two children developed airway involvement and retropharyngeal spread related to parotitis, one of whom was confirmed-positive for mumps while the other was not tested for mumps and did not have any viral testing or cultures performed. Neither of them required an advanced airway. One additional child had a ring-enhancing brain lesion found on MRI after the patient was admitted to the hospital for parotitis, however no mumps testing was performed.

### Incidence and Trends in Mumps Testing over a Decade

The number of cases of parotitis have increased in the Atlanta area over the last decade (Figure 1,  $r = +0.75$ , 95% CI 0.25-0.93,  $P = .0074$ ). There was a significant spike of cases during December 2014 (64 cases), while the median (25th-75th) case per month was approximately 6 (4-10) throughout the 2007 to 2017 study period. Nine children (0.9%) with parotitis were ultimately diagnosed with mumps.

Testing for mumps is infrequently performed in the CHOA EDs (Table 2). In total, 47 children with parotitis (4.6%) were screened for mumps, although testing increased in 2017 (Figure 1B). All 4 cases of confirmed mumps occurred in 2017. Of these 47 patients tested for mumps, 19% were positive; 9 children had positive serology, RT-PCR and/or viral culture. Of note, 35% of subjects tested from 2014 to 2017 were positive while no cases of mumps were identified in years 2007 to 2013. No tests for mumps were sent in 2016.

In 2017, 2 patients were RT-PCR positive for mumps but with a negative mumps IgM titer while 2 patients had positive mumps IgM titer but negative RT-PCR and/or viral culture (Table 3). Prior to 2017, there were no RT-PCR tests sent for mumps and there was only 1 case which had a viral culture performed.

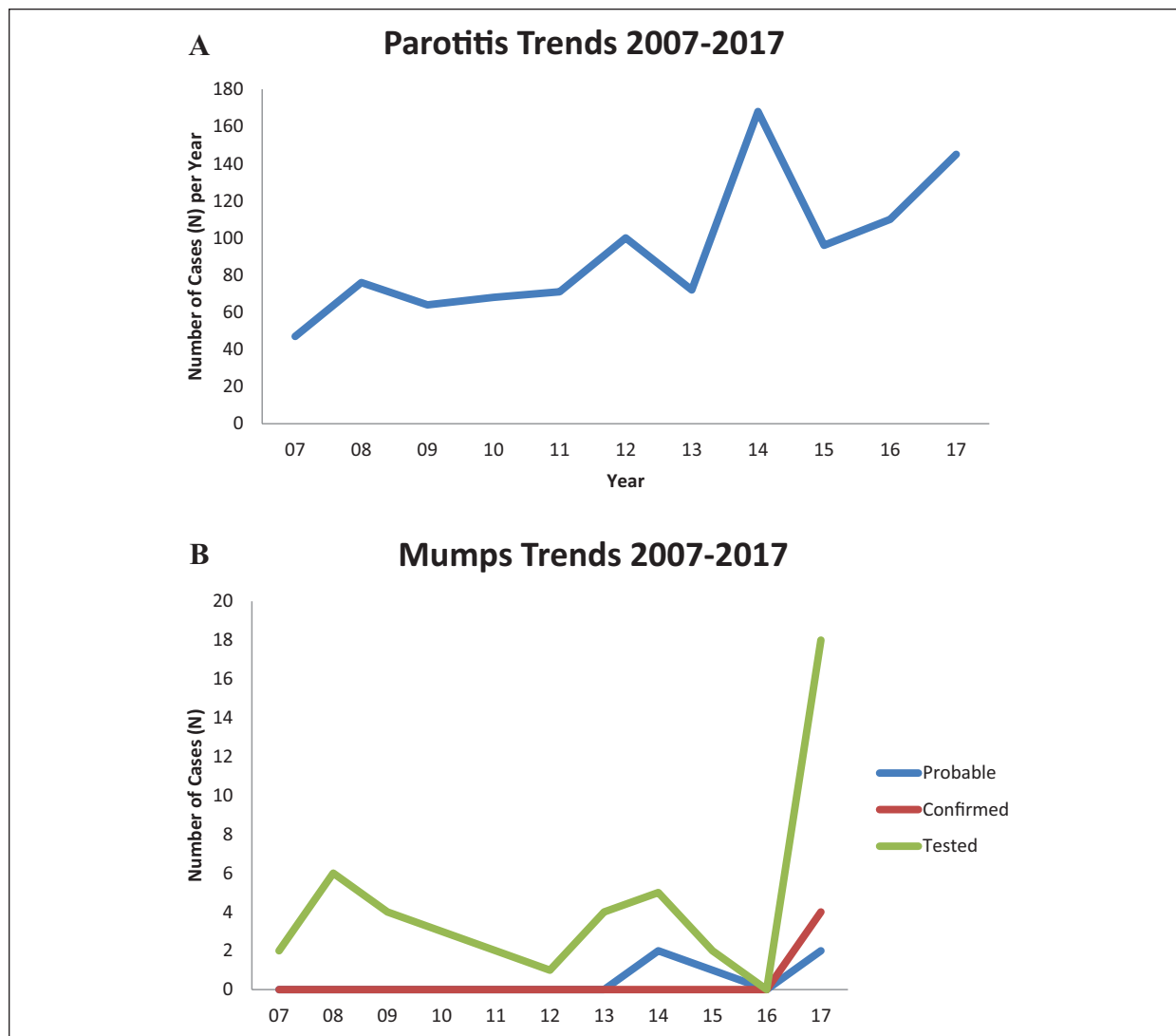
There were no statistically significant differences in clinical characteristics between patients tested for mumps who were found to be mumps-positive vs. mumps-negative.

Although parotitis is seen in the ED throughout the year, an increase in cases commonly occurred during winter months (Figure 2). However, of the 9 mumps-positive cases, 78% were seen between May and August,

**Table 1.** Demographics, Clinical Characteristics, Vaccination Status and Management of Parotitis and Mumps.

Year	Cases (N)	Gender (male %)	Median age in years (Q range 25%, 75%)	Vaccine+ status (%)	Fever (%)	Bilateral (%)	Bloodwork (%)	Blood culture (%)	Imaging (%)	Antibiotic given (%)	Admit (%)
<b>Parotitis<sup>a</sup></b>											
All	1008	56	6 (4, 10)	92	34	9	53	26	50	62	22
2017	139	58	8 (5, 12)	91	36	12	50	27	66	62	25
2016	110	57	6 (3, 9)	89	26	5	35	14	63	59	18
2015	95	49	7 (4, 10)	84	31	11	43	14	45	48	16
2014	166	60	7 (4, 10)	96	32	11	52	23	52	55	19
2013	72	64	6 (3, 10)	89	42	8	67	29	48	75	33
2012	100	54	6 (4, 10.5)	97	35	10	58	28	48	60	21
2011	71	49	7 (5, 10.5)	99	46	11	65	31	31	69	27
2010	68	63	5 (3, 8)	85	37	12	50	24	28	71	16
2009	64	55	6 (4, 9)	98	30	9	66	34	47	69	25
2008	76	59	4.5 (3, 8)	93	34	4	55	36	50	66	32
2007	47	53	5 (3, 8)	89	40	2	64	40	40	59	15
<b>Mumps positive<sup>b</sup></b>											
All	9	78	13 (7, 15.5)	78	67	56	67	67	33	56	33
2017	6	67	14 (5.5, 16.2)	83	67	67	83	67	33	67	33
2007-2016	3	100	7	67	67	33	33	67	33	33	33
P-value <sup>c</sup>		.314	.0257	.154	.29	.0007	.514	.0551	.506	.739	.425

<sup>a</sup>Parotitis group includes undifferentiated (untested?) cases.<sup>b</sup>These are cases that tested positive (probable/confirmed) for mumps (see Table 3).<sup>c</sup>P-value: comparison between All Parotitis and All Mumps Positive cases using Wilcoxon-rank sum tests and Fisher's exact tests.



**Figure 1.** (A) Number of parotitis and (B) mumps cases from 2007 to 2017. The number of parotitis and mumps cases as well as mumps testing has increased at Children’s Healthcare of Atlanta over the last decade.

**Table 2.** Mumps Testing per Year among Parotitis Cases.

Year	Mumps tested (N)	Mumps tested <sup>a</sup> (%)	% of tested with probable or confirmed mumps
2017	18	12%	33%
2016	0	0	0
2015	2	2%	50%
2014	5	4%	40%
2013	4	6%	0
2012	1	1%	0
2011	2	3%	0
2010	3	4%	0
2009	4	6%	0
2008	6	8%	0
2007	2	4%	0

<sup>a</sup>Percent of all parotitis cases (n = 1017) tested for mumps.

**Table 3.** Characteristics of Probable and Confirmed Mumps Cases.

Year	Gender	Age (years)	MMR doses	Laterality	Fever	Mumps labs tested	Positive	Dispo	Dx
2017	F	17	2	Bilateral	No	1; 2, 3 (buccal)	1, 2, 3	PICU	Confirmed mumps parotitis and retro-pharyngeal collection
2017	M	7	2	Left	Yes	1, 2 (buccal and urine)	1, 2 (buccal)	Admit	Confirmed mumps parotitis
2017	M	1.5	1	Left	Yes	1; 2, 3 (buccal)	1	Home	Probable mumps parotitis
2017	M	13	2	Bilateral	Yes	1, 2 (buccal)	1	Home	Probable mumps parotitis
2017	M	15	0	Bilateral	Yes	1, 2 (buccal)	2	Home	Confirmed mumps parotitis
2017	F	16	2	Bilateral	No	2 (buccal)	2	Home	Confirmed mumps parotitis
2015	M	7	1	Left	Yes	1	1	Home	Probable mumps parotitis
2014	M	7	2	Right	No	1	1	Home	Probable mumps parotitis
2014	M	15	2	Bilateral	No	1	1	Admit	Probable mumps parotitis

Mumps testing: (1) mumps IgM; (2) RT-PCR; (3) viral culture.

while one presented in October and the other in January. A seasonal trend is noted for parotitis, however there does not seem to be a seasonal trend for mumps; given limited testing for mumps, a conclusion about mumps seasonality cannot be assumed.

### Immunization Status

Ninety-two percent of children presenting with parotitis were fully vaccinated with 2 doses of MMR and of the 47 patients tested for mumps, 84% were fully immunized. Of the 9 patients identified with probable or confirmed mumps, 78% (N=7) were fully immunized, 1 was incompletely immunized (1 MMR dose) and 1 child was unvaccinated.

### Clinical Management of Parotitis

Bloodwork was commonly obtained in children with parotitis (53%). Blood cultures were obtained in 26% of children with parotitis of which 1 (0.4%) was noted to be positive (methicillin-resistant *Staphylococcus aureus*). Imaging was a commonly used diagnostic tool (50% of parotitis cases); CT use decreased over the past decade while ultrasound use increased. Antibiotics were commonly prescribed (Table 1); 1 child with mumps and 1 child with parotitis not tested for mumps required pediatric intensive care due to concern for airway involvement, although no advanced airway was necessary.

### Discussion

Over the past decade, national trends indicate an increase in both parotitis and mumps in a largely fully-immunized population,<sup>17</sup> which is consistent with our data. Less than 1% of subjects in our study presenting to the

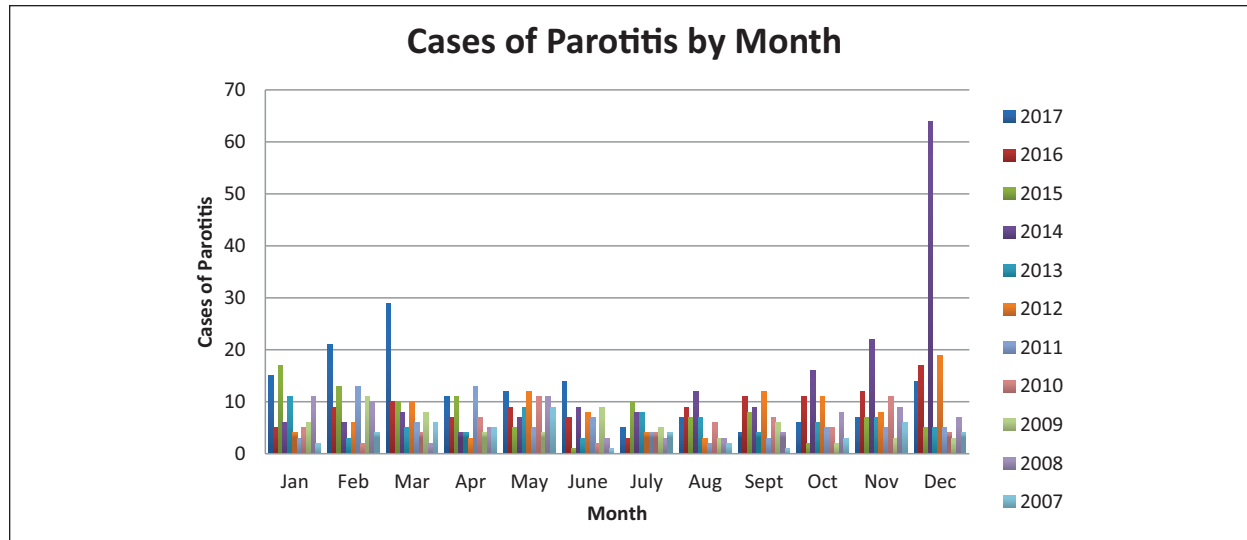
ED with parotitis were diagnosed with probable or confirmed mumps. However, since only 4% of all children with parotitis were tested for mumps, this is likely an underestimation of the true incidence, particularly given mumps outbreaks reported around the country. Of children with parotitis tested for mumps, 19% had positive mumps IgM and/or PCR while more than a third tested from 2014 to 2017 were positive. This suggests that there is a resurgence of mumps in the Atlanta area. Of note, there were no patients tested for mumps in 2016.

In previously reported studies, mumps has been seen mostly in college-aged populations and those living in close quarters. Our data, however, identifies a younger group of children contracting mumps, with a median age of 13 years. Data on living situations of the patients were not noted in the charts.

In the pre-vaccine era, complications of mumps were more significant with orchitis (11-66%), pancreatitis (3.5%), encephalitis (0.02%-0.3%) associated with mumps cases and very rare cases of death (2/10 000; 1966-1971).<sup>1,18,19</sup> In the post-vaccine era, rates of orchitis ranged from 3.3% to 10% and pancreatitis and encephalitis rates are less than 1%.<sup>1,14,20</sup> None of these complications were observed in our cohort over a decade. One patient with mumps and 1 patient with parotitis (not tested for mumps) had serious complications of airway impingement requiring a PICU admission, which serves as a reminder that parotitis can have serious consequences in rare instances. However, the majority of mumps-positive subjects and children with parotitis in general were discharged home from the ED.

The ED evaluation of parotitis in our cohort commonly involved bloodwork, imaging and antibiotics. Since parotitis is a self-limited condition typically caused by viral etiologies, the utility of blood tests, particularly blood cultures, and antibiotic usage is questionable.





**Figure 2.** Parotitis cases per month from 2007 to 2017. Although there is a seasonal trend for parotitis, there does not seem to be a seasonal trend for mumps.

Parotitis is a clinical diagnosis easily made with a good history and physical exam, however the use of imaging, particularly low-risk ultrasound may be justified when the diagnosis is unclear or to evaluate for a potential abscess. A complete blood count (CBC) with a differential may help differentiate between a viral vs. bacterial illness to help guide treatment, however antibiotics are not indicated when viral etiology is suspected.

Screening for mumps with RT-PCR or viral culture is more sensitive than serology and serologic testing can have false positives and cross-reaction with several other viruses.<sup>21,22</sup> Thus, if testing for mumps is indicated, RT-PCR or viral culture are better options.

The concern of waning efficacy of the MMR vaccine series has led to approaches to boost immunity. A third booster dose of MMR has been trialed with mixed results.<sup>23</sup> A third dose vaccination campaign was performed on the University of Iowa campus, and found that there were fewer cases of mumps post-campaign. The attack rate of mumps in students who received 3 doses versus 2 doses of the MMR vaccine was lower (6.7 vs. 14.5 cases per 1000  $P < .001$ ).<sup>24</sup> However, another study notes that the impact of an additional immunization had a negligible long-term effect on antibody titers.<sup>25</sup> The possible utility of a polyvalent mumps vaccine has also been suggested.<sup>26</sup> Ultimately, increased antibody levels induced by a third dose of MMR vaccine may protect against mumps virus infection for longer than previously assumed and is expected to be a good and safe intervention for controlling a mumps outbreak.<sup>27</sup>

Although few differences in clinical characteristics of mumps-positive children would help identify them from the parotitis group, significant differences may

have been missed due to a small sample size in the mumps group. Bilateral parotitis was 1 significant observation that should raise clinical suspicion for mumps, however 44% of children with mumps presented with unilateral parotid swelling. Testing for mumps in the larger parotitis cohort was done in <5% of all cases. Since nearly 20% of all children tested throughout the decade, and over a third of parotitis cases tested for mumps since 2014 were mumps-positive, it is likely that mumps cases were missed and inadvertently included among the parotitis group, which is another limitation of this study. In addition, cases of parotitis could have been overlooked, a limitation of the retrospective study design. This study reports from 3 urban pediatrics EDs which may not be reflective of other hospital experiences in other locations.

Mumps is likely underreported as rates of testing are low and cases of parotitis have clearly increased over the past decade. These data from Atlanta add to reports from other states of a resurgence of mumps despite appropriate vaccination<sup>28,29</sup>; mumps should be considered in the differential diagnosis of all children with parotitis regardless of immunization history.<sup>28,30</sup> Masking, droplet precautions and supportive care is recommended for all parotitis cases. The clinical management of uncomplicated, undifferentiated parotitis and mumps-positive parotitis are similar, and the rate of complications appears to have decreased over the last decade compared to older reports.

The differential diagnosis of parotitis is broad and includes infectious and non-infectious etiologies. While the viral differential includes mumps, it also includes influenza, parainfluenza, Epstein-Barr virus,

cytomegalovirus and human immunodeficiency virus. In 2014 to 2015, there were 257 cases of influenza-associated parotitis reported to the CDC.<sup>31,32</sup> Clinicians should have a high level of suspicion for mumps in a child who is fully vaccinated even during a non-outbreak period.

During a period of known mumps outbreaks or for a patient for whom other sources of parotitis have been ruled out, it is reasonable to test for mumps for hospital and outpatient isolation, hospital infection control cohorting purposes, and epidemiologic surveillance and contact tracing for outbreak investigation. However, routine testing in an ED can be problematic as it may expose potentially high-risk patients (non- or incompletely vaccinated young children or immunocompromised patients) to disease in waiting rooms before droplet isolation has been implemented. The high-volume and quick pace of the ED also may not be the most appropriate place to work up parotitis for patients without respiratory compromise and otherwise mild symptoms. Patients seen by primary care providers for whom the provider suspects mumps should therefore not be referred to the ED merely for testing. The health department should be notified about any patient in whom mumps is suspected, both to facilitate testing if preferred, and to conduct appropriate follow up and prevent transmission in the community, particularly among school- and college-aged students. Testing can also be arranged outside of the ED through predetermined DPH locations, although this would require an additional visit to a healthcare provider, an increased likelihood of transmission, and a decreased possibility of a positive RT-PCR test result, if delayed. The management of patients with both undifferentiated and uncomplicated parotitis and mumps is conservative and focuses on rest and isolation.

## Conclusion

The incidence of parotitis and confirmed mumps cases has increased over the last decade across the United States. This trend is confirmed in the Atlanta area and includes immunized subjects and children younger than college-age. Few clinical symptoms differentiate mumps from non-mumps parotitis. Mumps should be considered when evaluating a child with parotitis; all patients with parotitis should be masked and isolated for 5 days from the development of symptoms.

## Author Contributions

LMR: contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be

accountable for all aspects of work ensuring integrity and accuracy.

DB: contributed to conception and design; contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

AM: contributed to analysis; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

PK: contributed to analysis and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

JF: contributed to design; contributed to analysis and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

LK: contributed to design; contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

AC: contributed to design; contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

JT: contributed to design; contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

ET: contributed to design; contributed to interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

CRM: contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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