# Mumps Virus Detection During an Outbreak in a Highly Unvaccinated Population in British Columbia

Kennard E. Tan, MD,[1] Maureen Anderson, MSc,[2] Mel Krajden, MD,[3] Martin Petric, PhD,[3] Annie Mak, BSc,[3] Monika Naus, MD[2]

## ABSTRACT

**Objectives:** Control measures of mumps involve isolation of those symptomatic or potentially exposed. Recent guidelines have recommended shortening the isolation period from 9 days to 5 days after the onset of parotitis, despite using mainly historical evidence. In British Columbia, mumps circulated in a predominantly unvaccinated population in 2008. We compared laboratory findings between the different vaccination groups and assessed the period of mumps viral detection after onset of parotitis.

**Methods:** Demographic and clinical data were collected according to guidelines during the course of the outbreak. Clinical specimens, including buccal swabs, urine, CSF and sera, were collected on a single visit upon presentation for diagnosis. Laboratory diagnosis of mumps was confirmed by either virus detection by PCR and/or isolation in cell culture from clinical specimens, or by serology.

**Results:** Laboratory testing confirmed mumps on 85 (74%) of 115 cases by virus detection and/or serology. Thirty-nine (78%) of 50 cases had virus detected within the first 5 days after onset of parotitis, with the rate highest in specimens collected early. However, virus could be detected in 5 (56%) of 9 cases after day 5 and up to day 9.

**Conclusion:** Our study questions whether a 5-day isolation period is sufficient to prevent mumps transmission in a susceptible population. Our observations are based on single specimen submission, whereas an optimal study design would entail serial collection after presentation of parotitis, as this reflects true viral shedding. Further investigations are warranted to validate patient isolation guidelines.

**Key words:** Mumps; polymerase chain reaction; virus shedding; patient isolation

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Mumps is an acute viral illness characterized by fever and parotitis that typically affects young children.[1] Clinical manifestations start with a non-specific prodrome, which can include malaise and headache, and are followed by painful swelling of the parotid glands. Less common presentations include epididymo-orchitis, oophoritis, pancreatitis and meningo-encephalitis. Approximately half of those infected develop classical disease, the remainder having non-specific or respiratory symptoms and 15-20% being asymptomatic.[2,3] Most of those who are symptomatic recover fully. There is currently no specific antiviral treatment available, but mumps vaccine has been available since the 1960s.[4]

The introduction of the scheduled mumps-measles-rubella (MMR) childhood vaccination in 1967 has resulted in a dramatic decrease of disease incidence in North America.[5] However, mumps has reemerged since 2004, with outbreaks reported in Europe,[6] US[7] and Canada.[8] These outbreaks have been documented in vaccinated populations, frequently affecting older children and young adults, suggesting that current vaccines are not adequately protective over the long term.[9]

Control measures for mumps consist of immunization of susceptible populations and isolation of those symptomatic or potentially exposed. Post-exposure prophylaxis with vaccine or immunoglobulin is not known to prevent infection.[10] Recently, the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics have recommended shortening the isolation period from 9 days to 5 days after the onset of parotitis.[11] This was based on limited historical studies performed prior to the availability of mumps vaccination, and one small 2008 study in a highly vaccinated population[12] in which virus detection, hence the potential for transmission, was observed to be highest prior to the onset of parotitis and within the subsequent 5 days. This recommendation was also based in part on improved compliance among university students isolated for shorter periods (4 days) compared to those isolated for up to 9 days.[13] The Canadian guidelines for the prevention and control of mumps have similarly adopted a 5-day case isolation period.[14]

A mumps outbreak occurred in a highly unvaccinated population in British Columbia (BC), Canada, from February to October 2008. Most of the affected unimmunized population belonged to a small faith-based community who opted out of scheduled vaccination. The outbreak was managed by using provincial mumps control guidelines, including programs for enhanced surveillance and public awareness, in the specific geographic region of the epidemic. After the outbreak resolved, we retrospectively utilized clin-

**Author Affiliations**

1. Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC
2. Epidemiology Services, British Columbia Centre for Disease Control, Vancouver, BC
3. Laboratory Services, British Columbia Centre for Disease Control, Vancouver, BC

**Correspondence:** Dr. K.E. Tan, Department of Pathology and Laboratory Medicine, UBC, Rm 1501, Vancouver General Hospital, 899 12th Ave W, Vancouver, BC V5Z 1M9, Tel: 604-875-4892, Fax: 604-875-4988, E-mail: kennard@interchange.ubc.ca

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ical and laboratory data to investigate the period of mumps virus detection following the onset of parotitis and to compare laboratory findings with mumps vaccination status.

## METHODS

Mumps is a reportable disease in British Columbia. Upon recognition of the outbreak, a series of advisories were issued to health care providers and the public. People presenting with mumps-like illness were seen and assessed by their family physicians or community health nurses. Those who met the case definition were reported to the local medical health officer and thereby to the British Columbia Centre for Disease Control (BCCDC). Public health staff collected clinical, demographic and epidemiologic data during the course of the outbreak, including contact tracing and follow-up. This information was obtained either through discussions with the patients' health care providers or directly by telephone interviews with the patients or their parents.

Types and timing of diagnostic laboratory tests for mumps were determined by the health care provider and patient preferences, and specimens were submitted from a single visit. For laboratory diagnosis, public health guidelines recommend specimen collection for mumps virus detection and/or both acute and convalescent serology. Mumps virus was detected from buccal swab, urine and CSF specimens using reverse-transcriptase PCR (RT-PCR) and isolation in cell culture. RT-PCR performed was a semi-quantitative assay with primers targeting the F and SH genes.[15,16] This assay was performed in parallel with the National Microbiology Laboratory (NML) in Winnipeg, Manitoba during the initial course of the outbreak for validation of the RT-PCR. CT-values of the assay <35 were considered positive for the presence of mumps virus RNA. Sequencing of the SH gene identified outbreak strain as genotype G, which was consistent with other outbreaks in Canada.[8] Serology for IgG and IgM were also performed semi-quantitatively with the VIDAS (bioMérieux, Marcy l'Etoile, France) automated immunoassays. A positive laboratory result is defined as either: virus detection by RT-PCR or isolation in cell culture; significant increase of convalescent IgG; or having detectable IgM in either acute and/or convalescent serology.

Data captured in a database throughout the course of the outbreak were analyzed. Cases with both the date of parotitis reported and a buccal swab collected were evaluated as a subset to assess the viral shedding period. Because these activities were performed as part of the outbreak investigation, under public health legislative authority, ethics board approval was not required. Statistical analysis was performed with SPSS software[17] with chi-square testing to assess statistical significance.

## RESULTS

### Demographics

In this outbreak, 180 cases of mumps were reported. Of these, 115 (64%) cases had at least one laboratory test performed, 38 (33%) reported no history of prior mumps vaccination and 37 (32%) had unknown vaccination status.

### Laboratory testing

Of the 115 cases tested, results confirming mumps virus infection were available on 85 (74%). Laboratory testing is categorized as either virus detection by RT-PCR or isolation in cell culture, or serology (Table 1). In 59 cases, both virus detection and serology were performed. While serology was the more common test performed, most laboratory-confirmed cases were identified by virus detection. An increase in convalescent IgG did not identify any cases that were not diagnosed by virus detection or by the presence of mumps specific IgM antibody.

**Table 1.** Diagnostic Testing Results

| | Test | Performed | Positive/ Reactive* (%) |
|---|---|---|---|
| Virus Detection | Buccal swabs | 75 | 55 (73) |
| | Urine | 26 | 8 (31) |
| | CSF | 2 | 1 (50) |
| Serology* | Acute IgM serology | 86 | 35 (41) |
| | Convalescent IgM† | 11 | 6 (55) |
| | Acute IgG serology | 96 | 79 (82) |
| | Rise in convalescent IgG signal | 16 | 4 (25) |

* Equivocal serology results excluded.
† Where IgM was not detected in acute serum.

**Table 2.** Virus Detection in Buccal Specimens (n=61), by Days After Parotitis

| | RT-PCR | | Isolation in cell culture | | RT-PCR or isolation |
|---|---|---|---|---|---|
| # Days Post-parotitis | Performed n | Positive n (%) | Performed n | Positive n (%) | % Positive |
| 0-1 | 24 | 21 (88) | 23 | 16 (70) | 88 |
| 2-3 | 15 | 11 (73) | 16 | 6 (38) | 69 |
| 4-5* | 10 | 7 (70) | 10 | 2 (20) | 70 |
| 7-9 | 9 | 5 (56) | 9 | 3 (33) | 56 |
| >9† | 2 | 0 | 2 | 0 | 0 |

* No specimens collected on day 6.
† Specimens collected on day 13 and 20.

Most specimens for virus detection were assessed by both RT-PCR and isolation in cell culture, with RT-PCR assay being more sensitive. Mumps was detected by RT-PCR in 94% of all specimens, and in only 57% of the specimens by isolation on cell culture. Of the 18 urine specimens tested, the virus was detected in 5 by RT-PCR and in 2 by isolation in cell culture. The specimens were collected up to 16 days after onset of parotitis, and virus was detected up to day 5. None of the cases with virus detected in urine reported having orchitis or oophoritis. CSF specimens were collected for two cases one day after onset of symptoms of meningitis, with the virus detected in one by both isolation and RT-PCR.

### Assessment of shedding duration

Viral shedding is believed to occur from nasal and oral secretions, with buccal swab specimens offering the highest yield for virus detection.[18] The date of parotitis onset was used as the starting point of shedding duration because this is the most specific symptom of mumps. This approach is consistent with prior studies,[11] although it should be acknowledged that shedding can precede onset of parotitis. Detailed clinical history with dates of parotitis onset and detection of virus from buccal swabs were available for 61 cases. Specimens from these cases had been collected over a number of days after the onset of parotitis, but mostly within the first three days. As shown in Table 2, virus was detected by RT-PCR in 5 specimens (56%) collected at day 7-9 and in 3 (33%) by isolation in cell culture. Moreover the virus was detected by both RT-PCR and isolation in cell culture in 2 specimens that were collected day 9 post onset of parotitis.

**Table 3.** Lab Results in Comparison With Vaccination Status

| Comparison | Cases With History of Vaccination (%) | Cases With No History of Vaccination (%) | p-value* |
|---|---|---|---|
| Laboratory test performed | 40 / 49 (82) | 37 / 84 (44) | <0.01 |
| Virus detected in buccal swabs | 20 / 28 (71) | 15 / 19 (79) | 0.56 |
| Mumps IgG† detected in acute serum | 32 / 33 (97) | 20 / 30 (67) | <0.01 |
| Mumps IgM‡ detected in serum | 13 / 31 (42) | 17 / 24 (70) | 0.03 |

* Chi squared.
† Equivocal findings excluded.
‡ Reactive in either initial or convalescent, and equivocal findings excluded.

The above findings cannot be directly used to correlate the length of viral shedding with factors such as vaccination status and age as specimens were not collected every day to test for presence of virus. However, of 3 patients with known vaccination status and detectable virus in buccal swabs at days 7 to 9 post-parotitis, 2 reported and 1 denied prior vaccination. In patients with detectable virus by RT-PCR, no correlation could be found between CT-values of the RT-PCR assay and the timing of specimen collection after onset of symptoms.

### Laboratory findings in vaccinated and non-vaccinated patients

As shown in Table 3, laboratory testing was more often performed in cases with a history of vaccination. A history of vaccination did not significantly affect the detection of mumps in buccal swab specimens. As expected, mumps IgG antibody was detected in nearly all vaccinated cases and was detected in only 67% of unvaccinated cases in acute serum specimens. On the other hand, mumps IgM antibody was detected in 70% of the non-vaccinated cases and in only 42% of the vaccinated cases.

## DISCUSSION

Isolation of cases while they are shedding an infectious agent is an important control measure for many communicable diseases. For mumps, this isolation period was determined by studies that assess viral detection in patient specimens in relation with clinical symptoms[18] and/or epidemiologic data.[2] Up until recently, investigations into mumps transmission have been largely ignored as effective vaccination had greatly reduced the incidence of the illness in our population.

The BC mumps outbreak was similar to many other recent outbreaks, although it included a substantial number of cases who were unvaccinated and in the pediatric age group. As with recent studies, the rate of viral detection was highest in specimens collected immediately after the onset of parotitis (88%) and decreases up to day 9 (56%). However, in contrast with previous studies,[12] virus could be detected in a subset up to day 9 by both RT-PCR and isolation in cell culture.

Our findings are consistent with the mathematical model from Polgreen et al.,[19] which estimates that 8-15% of patients would still be shedding virus five days after the onset of symptoms. Their model was based on data from the 2006 Iowa outbreak, in which virus was isolated in cell culture from 10 of 71 specimens collected during days 6 to 9. In neither their study nor ours could the virus be detected after day 9. However, our detection rates between days 6 to 9 were higher, and we hypothesize this to be due to the use of more sensitive RT-PCR technology and to selection bias; those still unwell several days after onset of parotitis may have been more likely to have sought medical attention and diagnostic testing.

We are unable to show a difference of viral shedding between populations of different vaccination status. However, in both groups, rates of viral detection were similar with virus detected after day 5. We also found that virus was more readily detected in buccal specimens (73%) than in urine (31%), in agreement with other studies.[20]

Due to the observational nature of our study, our results are limited by single specimen submissions and by retrospective clinical data. Ideally, specimens should have been collected serially after initial presentation of parotitis, as this reflects true viral shedding. Furthermore, detection of virus shedding, especially by RT-PCR, may not be the only factor in determining infectivity,[19] and further work is required for accurate modeling of virus transmission in a susceptible population.

Despite these limitations, our study indicates that mumps viral shedding continues for up to 9 days after onset of parotitis. While a 5-day isolation period may be pragmatic in the context of low compliance with self-isolation, patients with mumps should be informed that while viral shedding may be maximal in the patients up to 5 days, it continues up to 9 days and they should be asked to limit activities associated with direct respiratory contact for the full 9-day period. Our study also brings into question whether a 5-day isolation period is sufficient to prevent transmission of mumps in a susceptible population. Further investigations to prospectively assess viral shedding and epidemiological studies to correlate this to transmission are warranted to validate patient isolation guidelines.

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## RÉSUMÉ

**Objectifs :** La lutte contre les oreillons consiste à isoler les personnes symptomatiques ou potentiellement exposées. Des lignes directrices récentes recommandent de réduire la période d'isolement de 9 à 5 jours après l'apparition d'une parotidite, mais les preuves à l'appui sont principalement de nature historique. En Colombie-Britannique, les oreillons ont circulé en 2008 dans une population majoritairement non vaccinée. Nous avons comparé les résultats de laboratoire des deux groupes (vaccinés et non vaccinés) et déterminé le délai de détection virale des oreillons après l'apparition de la parotidite.

**Méthode :** Nos données démographiques et cliniques ont été recueillies selon les lignes directrices, durant l'éclosion. Des prélèvements cliniques (buccaux, urinaires, de liquide céphalorachidien et de sérum) ont été obtenus au cours d'une même visite de diagnostic. Le diagnostic d'oreillons obtenu en laboratoire a été confirmé soit au moyen d'une détection virale par RPC et/ou par isolement en culture cellulaire à partir des prélèvements cliniques, soit par sérologie.

**Résultats :** Les épreuves de laboratoire ont confirmé les oreillons dans 85 des 115 cas (74 %), par détection virale et/ou par sérologie. Dans 39 cas sur 50 (78 %) le virus a été détecté dans un délai de 5 jours après l'apparition de la parotidite, le taux le plus élevé ayant été observé dans les échantillons prélevés tôt. Cependant, on pouvait encore détecter le virus dans 5 cas sur 9 (56 %) après le jour 5 et jusqu'au jour 9.

**Conclusion :** On peut se demander si une période d'isolement de 5 jours est suffisante pour prévenir la transmission des oreillons dans une population réceptive. Nos observations reposent sur une seule séance de prélèvement, tandis qu'un protocole d'étude optimal impliquerait une série de prélèvements après l'apparition de la parotidite, pour tenir compte de l'excrétion réelle du virus. Il faudrait pousser la recherche pour valider les lignes directrices sur l'isolement des patients.

**Mots clés :** oreillons; réaction de polymérisation en chaîne; excrétion virale; isolement du patient