Alberta Health Services
Public Health
Central Zone

Nuclear Acid Testing (NAT) for Measles, Mumps, and Rubella

Date: **Friday, January 17, 2020**

To: **Family Physicians; University of Alberta Residency Program; Nurse Practitioners; Emergency Department Physicians and Staff**

Cc: **Infection Prevention Control (IPC); Workplace Health & Safety (WHS); Communicable Disease Control (CDC)**

From: **Dr. Digby Horne, on behalf of Medical Officers of Health, Central Zone**

NAT (reverse-transcription polymerase chain reaction (RT-PCR)) is an important lab diagnostic tool which should be done at initial presentation of suspect cases of measles, mumps, and rubella. It offers several potential advantages over serologic testing for IgM and IgG antibodies:

- *NAT is positive earlier in illness than IgM antibodies and can thus expedite diagnosis.*
- *A positive NAT on a single occasion is diagnostic whereas sometimes more than one serology specimen is required.*
- *NAT does not require blood collection at an outpatient laboratory, which carries with it a potential transmission risk to other patients and laboratory staff.*
- *NAT false-positive results are very infrequent compared with serologic testing, particularly for patients without typical signs and symptoms and/or no history of exposure to a suspect case or travel to an area with an outbreak.*
- *Positive NAT results permit differentiation between wild type virus and vaccine virus in persons recently immunized.*

Since viral shedding decreases over time and infected, previously immunized persons may shed for a shorter time than unimmunized persons, NAT must be done early in the course of illness. Another important consideration is that NAT requires swab submission in universal transport media (UTM).

Three recent Central Zone cases help illustrate the importance of early NAT and use of the appropriate transport media:

1. **Suspect measles:** A sixteen-month-old child developed a cough and runny nose on December 7 and a rash on December 10. He was immunized with measles, mumps, rubella, and varicella vaccine (MMR-V) at twelve months of age and had not been exposed to anyone ill. On December 13, measles serologic testing was done; measles IgG and IgM were both reported positive on December 14. Measles NAT (RT-PCR) was done on December 14 on nasopharyngeal (NP) swabs and urine; results were reported negative on December 15 and used to rule out measles.

2. **Suspect mumps:** A five-year-old developed headache, fatigue, and fever on December 11, and presented December 13 with right-sided facial swelling, sore throat, and neck pain. On December 14, he tested positive for mumps IgM and IgG antibodies. He had been immunized with two doses of MMR-V and had not travelled or had contact with anyone with mumps. On December 16, a buccal swab saliva specimen for mumps NAT (RT-PCR) was submitted to Provincial Lab in the incorrect transport medium and therefore not tested. Further NAT was not recommended due to the length of time since illness onset; additional IgM antibody testing for December 23 was recommended but declined. On December 27, since mumps could not be ruled out, follow-up of community and health care worker contacts (for possible work exclusion in the absence of immunity) was undertaken.

3. **Suspect rubella:** A thirty-nine-year-old male presented December 12 with a three-day history of cough, productive sputum, chest pain, malaise, fever, and a widespread papular rash. He was admitted to ICU for respiratory distress; blood cultures grew Staphylococcal aureus, and rubella IgM and IgG antibodies were positive. There was no history of rubella immunization in Netcare. A throat swab and urine for rubella NAT were collected on December 14. However, the throat swab was tested for Group A Strep DNA and a nasopharyngeal swab collected on December 17 was cancelled due to submission in Routine rather than Universal Transport media. On the basis of the relatively low IgM rubella positive result and no history of exposure to a suspect case or travel, the IgM was considered a false positive, and community and health care worker contact follow-up did not take place. On December 24 the urine specimen was reported as rubella NAT negative.

For reference, information on the use of NAT and serologic testing in the lab diagnosis of measles, mumps, and rubella is provided below.

Measles Laboratory Testing (adapted from *Public Health Disease Management Guidelines – Measles*): https://open.alberta.ca/dataset/cddcf8b0-9193-4fd7-aa49-def3fded69cf/resource/a4b8b797-ab30-4154-bdcd-6296b91a3c1c/download/guideline-measles-2019-06.pdf.

Test	**Sample**	**Recommended Timing for Collection (Days Since Rash Onset)**		
NAT	**Nasopharyngeal (NP) Swab**	OPTIMAL (0-4 Days)	Viral Load Declines (5-7 Days)	
	Urine	OPTIMAL (0-7 Days)		
IgM	**Serology**	False Negatives Likely[A] (0-3 Days)	OPTIMAL (4-28 Days)[B]	False Negatives Likely (29-42 Days)
IgG[C]	**Serology**	ACUTE[D] (0-7 Days)	CONVALESCENT[E] (10-27 Days)	

(A) If a person meets the clinical illness definition for measles and the IgM serologic results from an early acute phase are inconclusive or negative for measles, and if no other pathogen is identified, a second blood sample is indicated.
(B) Testing for IgM antibody also has the potential for false positive findings. If the clinical presentation is inconsistent with measles or in the absence of recent travel/exposure history, positive IgM antibody results must be confirmed by NAT or paired IgG serology.
(C) IgG antibody serology using paired acute and convalescent specimens is a reliable test for measles, provided that specimens are collected at the appropriate times and tested simultaneously.
(D) Acute samples should be obtained as soon as possible after the onset of the rash, and no later than seven days afterwards.
(E) Convalescent samples, if necessary, should be collected 10-20 days after the acute sample.

Information relating to requisition requirements, and specimen collection and transportation is available at Alberta Precision Laboratories Test Directory – *Measles – Public Health*: https://www.ahs.ca/webapps/labservices/indexAPL.asp?id=5516&tests=&zoneid=1&details=true

Mumps Laboratory Testing (adapted from *Alberta Health Public Health Disease Management Guideline – Mumps*): https://open.alberta.ca/dataset/776b7b8e-ad3c-48f4-b2a5-4a2a048fb9c8/resource/a89cc8c3-5f67-4ba8-b860-bbd5bb7495c0/download/guidelines-mumps-2018-06.pdf

Interval in days from onset of parotitis to testing	Immunization status	Test request and sample
0, 1, 2, or 3	Not applicable	Order mumps NAT on buccal swab
4 or 5	Not immunized or unknown status	Order mumps NAT on buccal swab Order mumps IgM & IgG serology
	Immunized (1 or 2 doses)	Order mumps IgM & IgG serology **after day 5**
6 to 10	Not applicable	Order mumps IgM & IgG serology
When orchitis/oophoritis and/or meningitis are present	Not applicable	Order mumps NAT on buccal swab AND urine (prior to 8 days following onset) Order mumps IgM & IgG serology (3-10 days following onset)

- A positive mumps NAT result is definitive of recent infection.
- In vaccinated individuals, the length of viral shedding, (and therefore the number of days NAT testing will be positive), is decreased compared to unvaccinated individuals. Also, the IgM response can be delayed or absent; collecting blood 6-10 days from onset of parotitis has been shown to increase the IgM positive rate to 70%.
- In unvaccinated individuals the IgM response is nearly always detected at 3 to 5 days after the onset of parotitis, reaching a maximum level at 7 days.
- A urine sample should also be collected in individuals with orchitis, oophoritis, and meningitis to maximize virus detection. Urine samples may test positive for up to 7 days post symptom onset.

Information relating to requisition requirements, specimen collection and transportation, and ordering in Meditech is available at Alberta Precision Laboratories Test Directory – *Mumps*: https://www.ahs.ca/webapps/labservices/indexAPL.asp?zoneid=1&SearchText=mumps&submit=Submit+Query&upperTest=-1&lowerTest=-1 (click on *Mumps-Public Health, Mumps NAT Central Zone,* and *Mumps Serology Central Zone* tabs).

Rubella Laboratory Testing (adapted from *Public Health Disease Management Guidelines - Rubella***:** https://open.alberta.ca/dataset/f13a2867-26e0-4012-919e-3bfaa4754ce8/resource/715d1f70-1bc6-41df-bace-c042c2b30ea0/download/guidelines-rubella-2018-12.pdf.

Test	Sample	Recommended Timing for Collection (Days Since Rash Onset)	
NAT	**Nasopharyngeal (NP) or Throat Swab**	OPTIMAL: 0-5 days	
	Urine	OPTIMAL: 0-7 days	
IgM	**Serology**	OPTIMAL: 5 days	
IgG	**Serology**	ACUTE – OPTIMAL: 5 days	CONVALESCENT: 10-27 Days

- Since NAT is done at the National Microbiology Lab in Winnipeg and result turnaround time can be 10-14 days, specimens are only submitted following IgM positive results.
- If IgM testing is done earlier than 5 days following rash onset and is negative, it should be repeated 5 to 7 days after the initial blood to rule out a seroconversion (negative result changing to a positive result).
- Convalescent IgG testing would only be required if NAT had not been done or was done late, posing a risk of a false negative result.

Information relating to requisition requirements, and specimen collection and transportation is available at Alberta Precision Laboratories Test Directory – *Rubella – Public Health*: https://www.ahs.ca/webapps/labservices/indexAPL.asp?id=5312&tests=&zoneid=1&details=true

For assistance in selecting appropriate test specimens or to report suspect cases of measles, mumps, and rubella, please contact CDC: ph.: 403-356-6420 (8:30am – 4:30pm Monday – Friday) or 403-391-8027 (all other times). Reporting of suspect cases may expedite testing, patient isolation, and contact follow-up.

Thank you for your attention and assistance.

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