
Date: December 8, 2010

To: Alberta Health and Wellness, Alberta Micronet, CDC Nurses, Infection Prevention and Control, Laboratory Directors and Managers, Medical Officers of Health, Transplant Services and All Physicians

From: ProvLab

Re: Laboratory Testing for Measles

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Background:

Measles is a highly infectious disease, transmitted person to person by the airborne route, direct contact with nasal or throat secretions from an infected person, and less commonly, indirectly by articles freshly soiled by these secretions. Despite high levels of vaccination, sporadic cases and outbreaks have been recently documented in Alberta. Measles is a notifiable disease and all suspected cases **must be reported immediately** to the zone Medical Officer of Health, **who will arrange for STAT testing** if required. The Provincial Laboratory (ProvLab) provides serological and molecular testing to assist with the diagnosis of measles.

Diagnosis:

Measles clinical illness¹ is characterized by ALL of the following features:

- Fever 38.3° C or higher
- Cough, coryza OR conjunctivitis
- Generalized maculopapular rash for at least 3 days (red blotchy rash appears 3-7 days after symptom onset, beginning behind the ears and on the face and spreading down to the trunk - then to the extremities).

Note: Do not wait for a 3 day rash history to report suspected cases of measles to the zone Medical Officer of Health

¹Alberta Health and Wellness Public Health Notifiable Disease Management Guidelines *Measles* July 2008

Viral shedding occurs in the prodrome phase and for at least four days after the appearance of the rash. Measles specific IgM antibody may be detectable in some patients three days after the rash onset, although at five days most patients will be positive. Individuals who received a single dose of a measles-containing vaccine or have waning immunity can demonstrate a variable serological response. In vaccinated persons or those with prior exposure, the presentation of measles may be atypical.

Laboratory confirmation of measles is based on the serological detection of IgM antibody in the acute serum sample or seroconversion of measles IgG antibody between acute and convalescent samples. Patients recently vaccinated with a measles-containing vaccine, e.g. MMR vaccine, will also produce a similar serological picture; hence providing the dates of vaccination as well as the clinical presentation is necessary for the accurate interpretation of serology results. The molecular detection of measles virus can precede a serological response thereby presenting a significant advantage in the early and definitive detection of this virus which is important in initiating public health management of contacts.

The Provincial Laboratory now has a validated measles PCR assay for the detection of the virus in nasopharyngeal swab and urine samples. Positive samples will be referred to the National Microbiology Laboratory for genotyping and surveillance.

The development of immunity is attributed to the production of neutralizing antibody to the virus. Following vaccination, neutralizing antibody is usually detectable after twelve days. In a natural measles infection, neutralizing antibody is usually detectable after sixteen days after exposure, which generally corresponds to the onset of the rash. Peak antibody titres occur about one month after natural infection or vaccination. The detection of measles IgG antibody by enzyme immunoassays is used as a surrogate for the presence of neutralizing antibody.

Infection Control Measures:

As measles virus is highly infectious, appropriate infection prevention measures MUST be made prior to collecting samples. Follow the guidelines provided by your zone Medical Officer of Health when collecting the nasopharyngeal swab (and urine) at the physician’s office. Notify the Collection Site prior to sending the patient to have blood taken for serology, so that the appropriate measures can be taken to prevent other patients from being exposed.

Laboratory Testing (see Table 1):

Laboratory confirmation by molecular testing and serology in all suspected cases of measles is recommended due to the highly infectious nature of this virus. Therefore collection of **all** of the following samples, nasopharyngeal swab, urine and serum, in the acute phase of illness (at rash onset to 4 days later) is **strongly recommended**. Determination of the viral genotype is important for public health surveillance in discriminating vaccine strains from wild type and in determining the probable origin of wild-type strains. As required, additional testing may be performed on the nasopharyngeal swab to rule out other viral agents, such as enterovirus, that are also associated with a rash-like presentation.

Table 1: Laboratory Testing and Sample Type

Phase	Samples to be Collected (in order of priority)	Test Request	Samples/Transport/Other
Acute illness (From rash onset to 4 days later)	1. Nasopharyngeal swab in Universal Transport Medium AND 2. Urine [10 to 20 mL in sterile container] AND 3. Serum [collect 3-5 mL blood in Serum Separator tube (SST)]	Request measles PCR on nasopharyngeal swab and urine Request measles IgM antibody on acute blood (see serology note adjacent*)	Nasopharyngeal (NP) swab – follow collection instructions given in the collection insert or on the ProvLab website Urine samples - should preferably be the first void of the day (morning sample) Note: Store the NP swab and urine in a cool place or in the fridge prior to transport *Send a convalescent serum 7 to 10 days after the acute blood if the measles IgM antibody is negative and measles is still strongly suspected
Immunity determination/ previous exposure	Serum [collect 3-5 mL blood in Serum Separator tube (SST)]	Request measles IgG antibody	Routine testing for immunity is performed three times weekly

Requisition information:

- **Complete the appropriate ProvLab requisition** (*one per patient for all samples is acceptable, providing that ALL samples collected at that time are sent with this requisition*).
- Include **all** of the following information: ordering physician, patient’s name, date of birth, gender, PHN, home address and phone number, specimen type and source, date and time of sample collection, lab tests required and clinical history*
***Clinical history:** Provide date of onset of illness, symptoms, measles vaccine history and travel history within the past 3 weeks.
- The ordering physician and office address must be clearly provided. If copies to another physician are required, provide the physician name and complete address where copies should be sent to comply with current privacy legislation.

Note: As measles is a highly infectious virus and this disease is notifiable by fastest means possible, it is imperative that all of the patient demographics and physician contact information, specified above, is given on the requisition. This will allow laboratory staff to contact the ordering physician, and when necessary, provide the appropriate information to public health for follow-up of the patient and contacts.

Transport:

- Each sample should be submitted together with absorbent material in the re-sealable pouch of the biosafety specimen bag. Ensure the seal is zip-locked and place the requisition in the adjoining pouch.
- When sending blood, nasopharyngeal swab and urine together with **ONE requisition**, ensure that **EACH** of these samples are placed in **SEPARATE** baggies with absorbent material, which can then be put into one biosafety bag with a zip-lock seal. If one sample leaks, then the other samples will not become contaminated and have to be discarded.
- Samples can be sent at ambient temperature if within 8 hours of collection. If more than 8 hours – use a Cold-Pak or ice-pack to maintain the integrity of the virus in the sample.

Note: If the MOH has approved STAT testing the samples should be sent to the ProvLab as soon as possible, and the requisition clearly labeled STAT.

Interpretation of Laboratory Tests:

In Table 2 below are some of the most likely combinations of test results and their probable interpretations. The patient clinical presentation, including vaccination history, must always be considered in the context of the interpretation.

Table 2: PCR and Serology Results and Interpretation

Assay/Test	Result	Interpretation	Comments
Measles PCR	Positive	Measles virus present	Patient should be considered infectious Note: Patients receiving measles containing vaccine in the past 14 days could test positive
	Indeterminate	Low titre of virus present	Patient may still be infectious due to low viral load (Also see note above) Samples with indeterminate PCR results are sent to NML for verification, which can take up to one week
	Negative	Measles virus absent	Patient not infectious
Measles Serology	IgM - Positive & IgG - Negative	Suggestive of acute infection	IgM antibody may be detectable 3 days after rash onset and can persist for 4 to 6 weeks Infrequently, a positive IgM result alone may be a false positive
	IgM - Positive & IgG - Positive	As above	Measles IgG antibody is detectable shortly after the IgM antibody becomes positive Note: Individuals receiving measles containing vaccine can give a similar serology result
	IgM - Indeterminate & IgG - Positive	Indicates convalescence	In some vaccinated patients or those with prior natural exposure, the IgM response can be short lived or indeterminate in the acute phase of a re-infection. (Also see note above)
	IgM - Negative & IgG - Positive	Patient likely immune due to vaccination or natural infection	Patients with a single dose of the vaccine can produce a detectable IgG response but may be susceptible to infection

Positive measles PCR and IgM antibody results are automatically notified to the zone Medical Officer of Health and Communicable Diseases, Alberta Health Services

Supplies:

If nasopharyngeal swabs and Universal Transport medium are not available from your local laboratory or collection site, contact the respective ProvLab site as indicated below:

Laboratory Information	Calgary Site	Edmonton Site
General Inquiries	Phone: 403-944-1200	Phone: 780-407-7121
Supplies	Phone: 403-944-2583 FAX: 403-944-2317	Phone: 780-407-8971 FAX: 780-407-8984
Address	3030 Hospital Drive NW Calgary, AB T2N 4W4	Walter Mackenzie Health Sciences Centre University Hospital Room 2B4.04 8440-112 Street Edmonton, AB T6G 2J2

Inquiries and feedback regarding the content of this bulletin may be directed to:

Dr. Kevin Fonseca, Clinical Virologist, ProvLab

Phone number: (403) 944-1263

E-mail: kevin.fonseca@albertahealthservices.ca

This bulletin has been reviewed and approved by Dr. Marie Louie, Acting Medical Director of ProvLab