MEASLES

Disease Overview

Measles is a highly contagious disease caused by a virus. Measles is a vaccine preventable disease.

While Canada has been free of endemic measles since 1998; the risk of importing measles remains a reality due to travel to and from countries with disease activity and the existence of susceptible individuals and communities who are either unimmunized or under-immunized.

Maintaining elimination of this disease requires enhanced surveillance activities, widespread immunization coverage, and ongoing public and professional education about the importance of immunization. For more information see *Public Health Agency of Canada, Guidelines for the Prevention and Control of Measles Outbreaks in Canada*, October 2013.

Symptoms

Measles has non-distinct early symptoms (prodrome) that begin with fever and malaise. The more distinct syndrome can include conjunctivitis, coryza (sneezing, nasal congestion, and nasal discharge), cough, photophobia, and Koplik's spots. These spots are seen as bluish-white specks on a rose-red background appearing on the buccal mucosa (on the inside of the cheek) usually opposite the molars. These symptoms generally appear 2–4 days before the rash.

Body temperature may exceed 40°C (104°F), and usually falls 2–3 days after rash onset. High fever persisting beyond the third day of the rash suggests that a complication (e.g., otitis media) may have occurred.

The rash is maculopapular (flat, red area on the skin that is covered with small confluent bumps) and begins on the head often along the hairline and spreads downward reaching the hands and feet. In severe cases, the lesions usually become confluent, especially on the face and upper body. The rash usually lasts 4-7 days.

Typically, the disease is more severe in infants, adults, and individuals with compromised immune systems. Diarrhea occurs in some cases. Complications of measles include otitis media, pneumonia, and encephalitis.

Individuals who have 1 or 2 doses of Measles vaccine may not present with typical symptoms.

Reservoir

Humans.

Mode of Transmission

Measles virus is spread from person to person by inhalation of suspended droplet nuclei (airborne) or when infectious nasopharyngeal secretions come into contact with the mucous membranes of a susceptible person (direct). Measles virus is sensitive to strong light and drying but remains infectious in aerosol form in air for approximately 2 hours. Measles is one of the most **highly communicable** diseases with attack rates of >90% among susceptible close contacts.

Incubation Period

Incubation period for measles is defined as **the time from exposure to the onset of fever,** ranging usually from 7–18 days (average 10 days). The rash onset usually occurs within 2–4 days

after the first symptoms appear and up to 21 days after the initial exposure (average of **14 days from exposure to onset of rash).**

Note: The incubation period may be extended in an exposed individual who has received Immune globulin (IG) for passive protection early in the incubation period.

Period of Communicability

Measles is most communicable from **one day before onset of prodromal symptoms (usually 4 days before rash onset) to 4 days after rash onset.** However, given the incubation period of this disease, the risk of the appearance of secondary cases is possible up to 21 days.

Risk Factors

Increased risk of acquiring and/or severe illness:

- Persons who have not had the disease, are unimmunized against the disease, or immunocompromised (regardless of immunization status) are at risk of developing measles when exposed to a measles case for as little as 15 minutes.
- Most individuals born before 1970 likely had measles as a child and are considered to be protected. Anyone born after 1970 who has not had two doses of measles vaccine and has never had measles is at risk.
- Recent travel or exposure history to an endemic or known outbreak area.

Surveillance Case Definition

Confirmed case

Laboratory confirmation of infection in the absence of recent immunization [1]with measles-containing vaccine:

- isolation of measles virus from an appropriate clinical specimen.

OR

- detection of measles virus RNA.

OR

- seroconversion or a significant (e.g., fourfold or greater) rise in measles IgG titre by any standard serologic assay between acute and convalescent sera.

OR

- positive serologic test for measles IgM antibody using a recommended assay in a person who is either epidemiologically linked to a laboratory-confirmed case or has recently travelled to an area of known measles activity.

OR

- Clinical illness[2] in a person with an epidemiologic link to a laboratory-confirmed case.

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[1] The most frequent reaction to measles-mumps-rubella (MMR) immunization is malaise and fever (with or without rash) occurring 7-12 days after immunization. However, this should be determined for each case, as these reactions and the time frame can vary (*Canadian Immunization Guide,* Evergreen Edition, 2023).

[2] Clinical illness is characterized by all of the following features: fever of 38.3° C or greater; cough, coryza or conjunctivitis; generalized maculopapular rash for at least 3 days.

Probable case

Clinical illness

- in the absence of appropriate laboratory tests.

OR

- in the absence of an epidemiologic link to a laboratory-confirmed case.

OR

- in a person who has recently travelled to an area of known measles activity.

Diagnosis and Laboratory Guidelines

Measles virus infection can be diagnosed by a positive serologic test result for measles immunoglobulin (Ig) M antibody, a significant increase in measles IgG antibody concentration in paired acute and convalescent serum specimens by any standard serologic assay, or isolation of measles virus or identification of measles RNA (by RT-PCR) from clinical specimens, such as urine, blood, throat or nasopharyngeal secretions.

The laboratory diagnosis of measles is most often made by detection of measles IgM antibody in a single serum specimen. Approximately 80% of measles cases have detectable IgM antibody by IgM capture EIA within 72 hours of rash onset. Nearly 100% of measles cases demonstrate IgM antibody 72 hours after rash onset. Cases suspected to have measles in which serum is collected ≤ 3 days after rash onset, and initially tests IgM negative, should have a second serum specimen collected > 3 days after rash onset for retesting for IgM.

In general, a positive IgM result obtained at any time during the illness is diagnostic for measles. However, false positive IgM results can occur, particularly when testing is being performed in a low prevalence population (i.e., people who do not meet the clinical case definition, people with no recent travel/exposure history to endemic or known outbreak area, or people with no obvious risk factors for measles). In such instances, when a positive IgM result is obtained, the result should be interpreted with caution. Further testing is recommended as follows:

- The diagnosis can be confirmed by demonstrating a significant rise in measles IgG antibody level in acute and convalescent sera. A fourfold or greater increase in IgG is enough to confirm a case. Demonstrating a rise in measles IgG or seroconversion is not necessary when measles has been confirmed by another method.
- The diagnosis can also be made by detection of measles virus from a clinical specimen using RT-PCR. Urine specimen, nasopharyngeal (NP) swab and throat swab are good clinical specimens for viral detection. **A negative result for measles detection does not rule out the diagnosis.**

Further strain characterization may be performed by NML on request for epidemiologic, public health and control purposes.

Contact your laboratory for more information on testing and required type of sample.

Summary of laboratory diagnostics for measles[3]

Laboratory Diagnostic Element	Description
Specimen collection	Upon suspicion of measles, clinicians should immediately collect specimens for serology and virus detection for the purpose of laboratory confirmation. For viral detection, nasopharyngeal (preferably) or throat swabs (or washes) should be collected as soon as possible and no later than 4 days from the onset of rash. Measles virus may be still detected after 7 days from the onset of rash, but with rapidly decreasing sensitivity. Specimens should be collected using a swab approved for virus isolation and placed in virus transport media. Although nasopharyngeal specimens are preferred, the measles virus can also be detected in urine, which should be collected within 7 days from the rash onset, for maximum sensitivity. For serological testing, a serum specimen should be collected as soon as possible, when the patient is first seen. For IgM serology, a sample collected before 3 days and after 28 days from rash onset may yield a false negative result. For IgG serology, the first (acute) sample should be collected no later than 7 days from rash onset and a second (convalescent) sample 10 to 30 days after the first.
Serology	Presence of measles-specific IgM-class antibody is indicative of acute measles infection when rash was present and there is a history of exposure to measles through travel to an endemic area or an epidemiological link to a confirmed case. Positive IgM results not associated with acute measles infection may be due to the following reasons: • A positive measles IgM result in a sporadic case of rash without a history of exposure is possibly a false positive and it should be carefully investigated. Anti-measles IgM are frequently elevated in patients who received the MMR vaccine within 6 weeks prior to rash onset. Negative IgM results in a true measles case may also occur: • if the specimen is taken from the patient earlier than 3 days or later than 28 days after rash onset. The immune response to measles infection in previously immunized individuals or those with pre-existing immunity may not be typical of the response in a measles naive individual, and such cases may not have an IgM response. Virological confirmation and/ or acute and convalescent IgG testing should be conducted to confirm the infection in such cases. Seroconversion (i.e., negative to positive result) or a four-fold or greater rise in IgG titre between the acute and convalescent sera is indicative of an acute measles infection. Previously vaccinated individuals (secondary vaccine failure) may represent an exception in that rapid elevation of anti-measles IgG titre would be expected causing strong positive anti-measles IgG results in acute sera and the likely absence

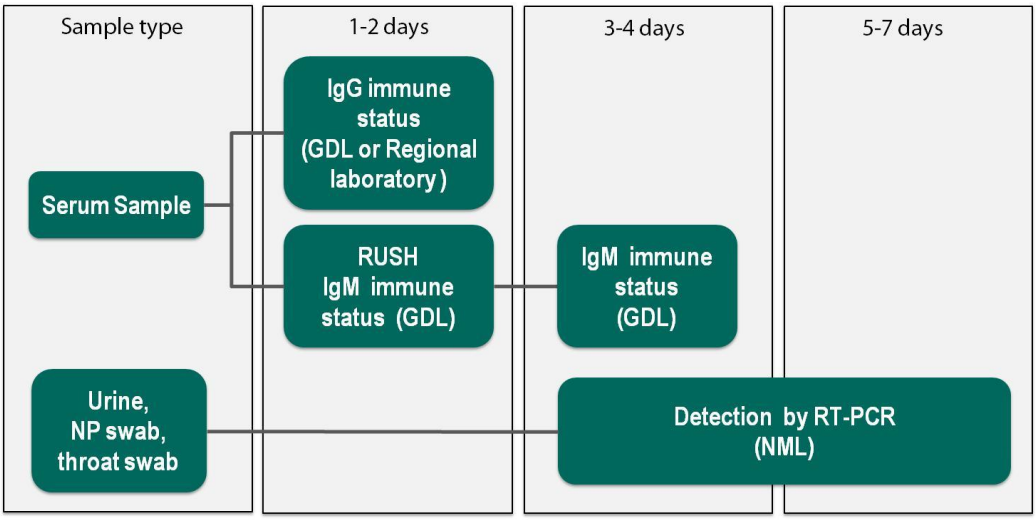
[3] PHAC, Guidelines for the Prevention and Control of Outbreaks of Measles in Canada, October 2013.

Laboratory Diagnostic Element	Description
	of a four-fold rise in IgG titre in the convalescent sera (36,37). The presence of measles-specific IgG antibodies, as determined using an enzyme immunoassay (EIA) predicts protective immunization, but it does not necessarily correlate with protective neutralizing antibodies measured by the gold standard, the plaque reduction neutralization test – PRNT (38). The absence of detectable measles IgG using EIA may reflect the lower sensitivity of the EIA in comparison to a more sensitive assay, especially in young infants. The protective level of measles IgG has been estimated between 120 (39) and 200 mIU (40), but it is not precisely known.
SSPE diagnosis	Sub-acute sclerosing panencephalitis (SSPE) is a rare complication caused by persistent measles virus infection in the central nervous system. In the presence of the characteristic clinical, neurological and pathology signs, the diagnosis can be confirmed by detecting an increase of measles IgG titre in the cerebrospinal fluid (CSF) relative to the titre in serum.
Measles virus detection	The RT-PCR assay is the most reliable test for the definitive diagnosis of measles infection, but its sensitivity can be influenced by the following: • timing of the specimen collection • specimen integrity (rapid specimen processing) • prior vaccination history Measles virus isolation in culture is also a very specific test (when confirmed by immunofluorescence or RT-PCR), but it is less sensitive than RT-PCR and is heavily dependent on timely collection and specimen integrity.
Genotyping	Measles virus genotyping is needed to distinguish post-vaccine rash from wild type measles infection. Virus genotyping is useful for linking cases, linking outbreaks and tracking importations. PAHO requires genotype information for monitoring the efforts of elimination. It is advisable to genotype as many cases as possible of measles, ideally all the sporadic cases and representative cases of all the outbreaks. The National Microbiology Laboratory (NML) performs measles genotyping in Canada and will accept all suitable specimens. The genotyping test requires the same type of specimens as RT-PCR.
Interpretation of laboratory results	In order to properly interpret laboratory results and to assess the performance of measles diagnostic assays, both clinical and epidemiologic information need to be considered along with the laboratory information (e.g., prior vaccination history, travel history, timing of sample collection relative to onset of symptoms). Therefore, communication and information sharing between public health and the laboratory are essential. A positive RT-PCR result or positive IgM result in a patient with rash and with history of travel in a measles endemic area or with an epidemiological link to a confirmed case, are diagnostic for measles infection.

Laboratory Diagnostic Element	Description
	Seroconversion or a fourfold increase of measles IgG in a patient with rash and no history of recent MMR vaccination is also diagnostic for measles. Negative results by RT-PCR and negative IgM-class antibody detection may not be sufficient to rule out measles infection in some cases, particularly if the specimen for PCR was collected later than 7 days after symptom onset. Serological results for previously vaccinated individuals (secondary vaccine failure) will likely not follow the paradigm associated with acute primary measles in unvaccinated individuals. Anti-measles IgM antibody response may be weak or not detectable, and a rapid elevation of anti-measles IgG titre would be expected causing strong positive anti-measles IgG results in acute sera and the likely absence of a four-fold rise in IgG titre in the convalescent sera (36,37). In these individuals, the timely collection of specimens for measles virus detection (RT-PCR) is recommended.

Laboratory Testing

An overview of testing timelines for samples after the sample has been received by the laboratory. Turnaround times are averages and may change depending on the urgency of the situation.



Notification and Reporting

Per Policy 2.2 Disease and Event Notification to OCMOH and Disease and Event Reporting section.

- CD Urgent Notification for all confirmed and probable cases of measles
- Enhanced Surveillance. For all confirmed and probable cases an enhanced surveillance form should be completed, and information sent to OCMOH within 24 hours of completing interview.
- Routine surveillance (RDSS) for all confirmed cases.

Case Management

Education

The case or relevant caregiver should be informed about:

- Nature of the infection, length of the communicable period, and mode of transmission.
- Hand washing.
- Respiratory disease precautions.
- Cough/sneeze etiquette.

Investigation

Upon receipt of information from a clinician or laboratory of a person suspected to have measles, immediately begin investigation, and treat a patient as a "case under investigation" for public health management purposes. Initiation of control measures must not wait laboratory confirmation of the case.

For investigation purposes: the first day of exposure can range from 7 to 18 days prior to prodrome onset. The last day of exposure is 7 days prior to the first onset of prodrome.

Exclusion/Social Distancing

Index case(s) is infectious from 4 days before the onset of rash (1 day before the onset of prodrome symptoms) until 4 days after the onset of rash. **Therefore, all case(s) under-investigation should be isolated i.e., not allowed to attend day care, school, workplace, or other social settings, and stay home for 4 days after onset of rash (with the day of the rash onset being day 0) or until measles is ruled out**.

Regardless of the case's vaccination history, exclusion applies to all childcare settings, schools, post-secondary educational institutions, workplaces, health care and other group settings. Cases should also self-isolate away from non-household contacts until the end of the 4th day after the rash onset.

Treatment

Immunoglobulin (IM or IV) is not used to treat cases of measles. No specific antiviral therapy is available and treatment is mostly supportive.

Immunization

Measles disease typically provides life-long immunity; therefore, there is no need to vaccinate individuals who had diagnosed disease. In the absence of documented laboratory confirmation of measles, a history of suspect or probable illness does not preclude further vaccination.

Contact Management

Education

Advise susceptible contacts (or parents/guardians) of the risk of infection and counsel them to watch for signs or symptoms beginning 7 to 18 days after the first contact with an infectious case.

Contacts should avoid contact with other susceptible people and immunocompromised people during this period.

If symptoms develop, they should also be advised to call ahead before visiting doctors' rooms, hospital ERs or pathology services so as to avoid mixing with other people, and to telephone the local PH if measles is suspected.

Investigation

Measles is one of the most contagious diseases known. **As little as 15 minutes of exposure to a case may lead to disease in a susceptible (non-immune) person**.

Different thresholds for exposure time should be used for assessing the significance of exposure in contacts. Consideration should be given to the distance between the index case and potential contacts, as well as ventilation systems, size of room, crowding, and the wearing and type of protective equipment such as masks.

Immunocompetent persons (this category also includes healthy pregnant women and infants):

- Face-to-face contact of any length or exposure for 15 minutes or longer in the same room; level of risk remains after case has left the room/space i.e., shared airspace during the case's presence in that setting.
- Spent time in a room previously occupied by a measles case, during that case's infectious period, within 2 hours after that individual left the room/space, may constitute a significant exposure. Advice from the Medical Officer of Health should be sought to assess such situations.

Immunocompromised persons (e.g. persons with primary or acquired immunodeficiency, those on high dose steroid treatment or other immunosuppressive agents, patients with hematologic malignancies, patients post Haemopoetic Stem Cell Transplant (HSCT):

- If immunocompromised individuals are identified as contacts, advice from the Medical Officer of Health and/or attending physician should be sought on the nature of immunocompromising condition.
- Measles infection in these populations carries a much higher risk of severe outcomes and complications, and such immunocompromised cases may themselves remain infectious for a longer period of time. As such, prompt identification and comprehensive follow up of these contacts is important.
- Spent time in a room previously occupied by a measles case, during that case's infectious period, within 2 hours after that individual left the room/space is likely to be a significant exposure.

Assess Susceptibility of Contacts

Immune	Susceptible
Individuals born before 1970 are generally presumed to have acquired natural immunity to measles; however, exceptions occur.	Individuals born in 1970 or later with unknown immunization history; or evidence of receiving only 1 dose of measles - containing vaccine or not receiving any doses.
Individuals born in 1970 or later with documented evidence of receiving 2 valid doses of live measles - containing vaccine after their first birthday and given at least 1 month apart.	Infants younger than 12 months; including those born to vaccinated mothers or if maternal immunity is lacking or uncertain. This group also includes infants born before 32 weeks gestation even if their mothers are naturally immune to measles.
Individuals with laboratory evidence of immunity or a history of laboratory confirmed measles infection (regardless of birth date).	
Infants born to mothers with natural immunity to measles are likely to have protective antibodies until 6 months of age.	

Assess Immunocompromised Contacts

If any immunocompromised individuals are identified as contacts, advice from the Medical Officer of Health and/or attending physician should be sought on the nature of immunocompromising condition. Serological testing for measles IgG antibody is generally recommended. Some immunocompromising conditions may render individuals with previously acquired immunity (through natural disease or adequate immunization) non-immune. As a guide these conditions include severe primary immunodeficiencies, AIDS (not just HIV), receiving HSCT until 12 months after stopping all immunosuppressive treatment and ALL until after 6 months after finishing immunosuppressive therapy.

Exclusion/ Social Distancing

Susceptible contacts who are not immunized within 72 hours of exposure should be excluded (e.g., from work, school, daycare) for 2 weeks after the onset of rash in the case(s) to which the contacts were exposed.

HCWs should also be excluded from direct patient contact from the 5th day after exposure until 21st day after exposure.

Prophylaxis

Post-exposure prophylaxis involves either administration of MMR vaccine as soon as possible and within 3 days after exposure or immunoglobulin within 6 days after exposure, mostly in situations where MMR vaccine is contraindicated. Post-exposure prophylaxis should be offered to those contacts meeting *all* of the following criteria:

- Contact was exposed to a sporadic case within infectiousness period.
- The nature of exposure is considered significant.
- Contact is assessed to be susceptible (non-immune).

For an on-going exposure, MMR is the preferred method of PEP.

Infants under 6 months of age:

- Infants under 6 months of age may receive immunoglobulin unless considered immune and advice from the Medical Officer of Health should be sought.

Infants between 6 months of age and 12 months of age:

- Infants between 6 months of age and 12 months of age can receive either MMR vaccine or immunoglobulin; as determined by the time since exposure.
- In the outbreak settings, MMR can be administered as early as 6 months of age, however the efficacy of MMR given at this age is likely to be lower compared when given at 12 months of age or older (2 scheduled doses of measles-containing vaccine should be administered in addition to the dose given before 12 months of age).

Pregnant women and immunocompromised individuals:

- Immunoglobulin should be given to pregnant women or to individuals with immunocompromising conditions within 6 days after exposure.
- In some circumstances, MMR vaccine can be given to individuals with HIV without significant immunosuppression.
- For individuals on regular intravenous immunoglobulin (IVIg) therapy who received the last dose within 3 weeks, intramuscular immunoglobulin (IMIg) is not required.

Immunoglobulin and MMR vaccine:

- For those susceptible individuals who are not infants, not pregnant, or not immunocompromised, Ig following measles exposure is no longer recommended.
- Immunoglobulin should not be given to persons with isolated IgA immunodeficiency and to those with severe thrombocytopenia or coagulation disorder. Some hospitals may maintain a supply of immunoglobulin from other sources for other indications.
- For an optimum immune response to a measles vaccine, the vaccine should be administered at least 14 days before administering an Ig preparation or blood product.
- Those who received an Ig preparation or blood product should delay administering a measles vaccine until the antibodies in the IG preparation or blood product have degraded. Refer to Table 1: *Guidelines for the interval between administration of immunoglobulin (Ig) preparations or blood products and measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV) or monovalent varicella vaccine to maximize immunization effectiveness*, Canada Immunization Guide, 2023 for timeline according to product and dose.
    - Note: there are no additional safety concerns if Ig is inadvertently administered with, or shortly before or after the vaccine. If unable to delay administration of measles vaccine, repeat the vaccine dose after the recommended interval.
- Although IV immunoglobulin products are not indicated for use as measles PEP in Canada, NACI now recommends them as an alternative to IMIg because there are no comparable appropriate prophylaxis strategies in some situations.
- The Regional Medical Officer of Health is able to provide the designated specialist/clinical expert consultation as required by Health System Bulletin PS2030, for this unlabeled use and therefore must be consulted before IVIG is released from the Blood Bank.

- For susceptible contacts who are pregnant or immunocompromised, if injection volume is not a concern, IMIg can be provided at a concentration of 0.5 mL/kg, understanding that recipients weighing 30 kg or more will not receive the measles antibody concentrations that are considered to be fully protective. In cases where injection volume is a major concern or for recipients weighing 30 kg or more, IVIg can be provided alternatively at a dose of 400 mg/kg.
- Measles vaccine can be provided in MMR combination vaccines and is available from the Central Serum Depot and local sub-depots.

Overview prophylaxis See NACI Recommendations for PEP, September 2018

Age/ immune status	Time since exposure to Measles		Considerations
	Within 6 days		
Less than 6 months	Immunoglobulin IMIg (0.5 mL/kg)		If injection volume is a major concern, IVIg can be provided at a concentration of 400 mg/kg
Pregnant women	Immunoglobulin IVIg (400 mg/kg) or IMIg (0.5 mL/kg), limited protection		For individuals weighing 30 kg or more, IMIg will not provide complete protection but may provide partial protection
Immunocompromised persons 6 months of age or older	Immunoglobulin IVIg (400 mg/kg) or IMIg (0.5 mL/kg), limited protection		For individuals weighing 30 kg or more, IMIg will not provide complete protection but may provide partial protection.
	Within 72 hours/ 3 days after exposure	**Between 3 days and 6 days after exposure**	
Immunocompetent persons 12 months and older	MMR	MMR	Even though MMR vaccine will not provide PEP protection after 72 hours of exposure, the 2-dose series should not be delayed since it provides long term protection.
6-12 months	MMR*	Immunoglobulin** IMIg (0.5 mL/kg)	*2 scheduled doses of measles –containing vaccine should be administered in addition to the dose given before 12 months

			of age. **If injection volume is a major concern, IVIg can be provided at a concentration of 400 mg/kg.

Management of Special Situations

Considerations for Health care workers (HCW)

- HCWs should have their immune status recorded, ideally before exposure occurs.
- If HCWs have had two documented doses of measles-containing vaccine or documentation of antibodies to measles, they can be considered immune and can continue work.
- HCWs who had significant exposure to a case of measles within the infectious period and who cannot provide documentation that they have received 2 doses of measles vaccine on or after their first birthday or other evidence of immunity to measles, should receive 1 or 2 doses of MMR (based on prior vaccine history and if not contraindicated).
- HCWs should also be excluded from direct patient contact from the 5th day after exposure until 21st day after exposure with a measles case.
- Personnel from healthcare institutions that become ill should be relieved of patient contact for 4 days after rash develops.

Considerations for pregnant women

- Pregnant women should receive MMR after delivery if not considered immune.

Considerations for schools and child day care centers

- Immunization is the intervention of choice for control of measles outbreaks in schools and child care centers. Immunize or encourage immunization for those not up to date according to the New Brunswick Routine Immunization Schedule.

Considerations for travel to areas with high measles activity

- Advise to contact local travel clinic. During outbreaks or for travel to regions where measles is a concern, the vaccine may be given as early as six months of age. Under these circumstances, the routine two dose series must be then restarted on or after the first birthday, for a total of three doses.
- For travel purposes adults should review their vaccination records to ensure they are up-to-date.

Outbreak Management

Activate the local outbreak plan when an outbreak is declared.