



Measles

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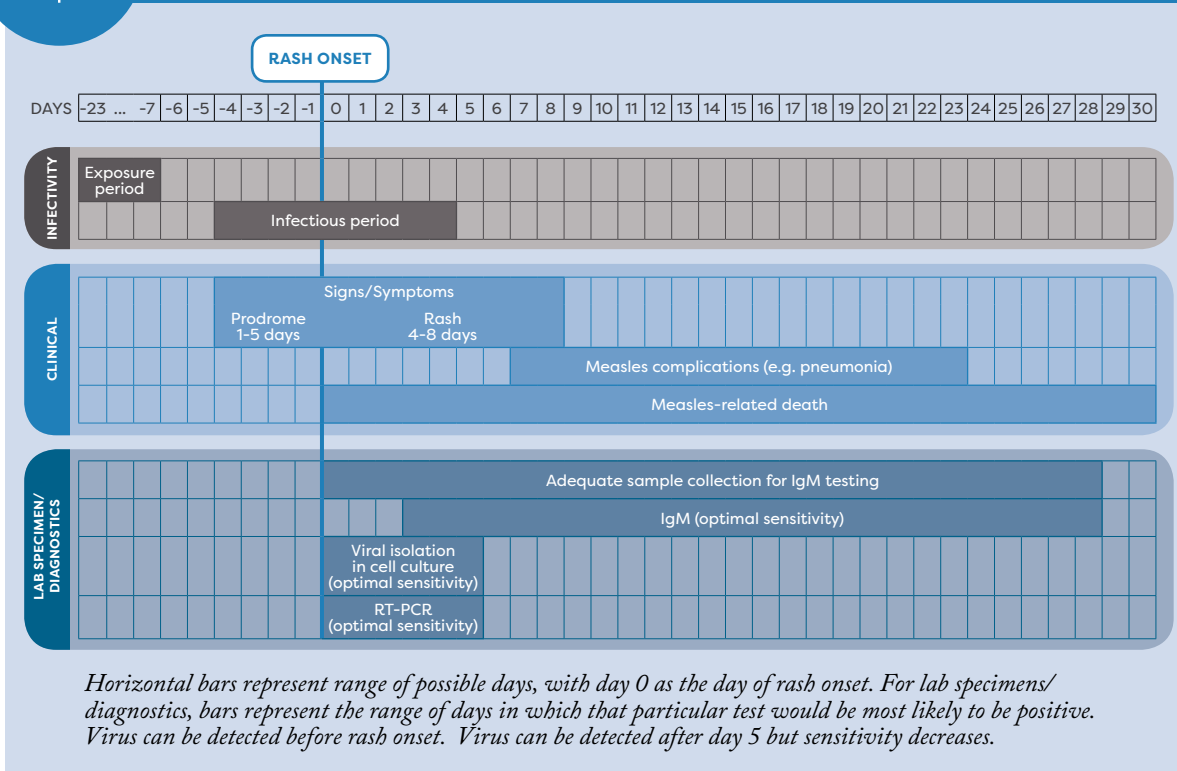
DISEASE AND VACCINE CHARACTERISTICS

Measles is one of the most contagious diseases for humans. It is caused by a paramyxovirus virus, manifesting as a febrile rash illness. The incubation period for measles usually is 10–14 days (range 7–23 days) from exposure to symptom onset (1). Initial symptoms (prodrome) generally consist of fever, malaise, cough, conjunctivitis, and coryza. The characteristic maculopapular rash appears two to four days after onset of the prodrome. Patients are usually contagious from about four days before rash onset until four days after its appearance. The exact source of transmission is frequently unknown because the patient is often infected by someone in the pre-rash prodrome stage. Measles complications such as

pneumonia, diarrhea and encephalitis can occur in up to 30% of persons depending on age and predisposing conditions, such as young age, malnutrition and immunocompromising conditions. These complications usually occur two to three weeks after rash onset. Measles can infect anyone of any age, but most of the burden of disease globally is still among children < 5 years of age.

The measles vaccine is a live attenuated virus vaccine; two doses are recommended by WHO to provide protection from disease. Currently, all six WHO regions have measles elimination goals by or before 2020, and surveillance is a key element to achieving elimination (2).

FIGURE 1
Timeline of infectivity, clinical disease and laboratory findings for measles virus infection





RATIONALE AND OBJECTIVES OF SURVEILLANCE

GLOBAL OR REGIONAL LEVEL

The key objective of measles surveillance is to identify areas of measles virus transmission and immunity gaps. This will guide effective public health responses to achieve elimination of endemic measles and sustain elimination in post-elimination settings.

NATIONAL OR LOCAL LEVEL

The objectives of measles surveillance at these levels are to:

- detect and confirm cases to ensure proper case management and implement appropriate public health strategies to control further transmission
- investigate cases to determine the source of infection, including who infected the individual and whether the infection was imported, importation-related or endemic
- identify populations and areas with low coverage and at higher risk of outbreaks that require enhanced vaccination efforts, and determine the reason for each measles case:
 - » vaccine was recommended but person did not get it (programmatic failure)
 - » person was vaccinated according to the recommended schedule (vaccine failure)
 - » vaccine was not received because it is not normally recommended for this person (for example, younger than the routine age for a second dose of vaccine).
- verify the absence of endemic measles cases to document elimination of endemic virus.

The rationale for surveillance in the 2003 VPD surveillance standards described different surveillance standards for countries with different goals or at different points along the measles prevention continuum: control, accelerated control/mortality reduction, and elimination. However, now that all regions have measles elimination goals, all countries should strive to achieve elimination-standard surveillance. This document provides the standards for surveillance in countries moving towards or maintaining elimination. Guidance on how to transition from surveillance in mortality-reduction settings to elimination settings is published elsewhere (2).

BOX 1

Integration with rubella surveillance

Integrate measles surveillance with rubella surveillance, whenever possible. Both diseases present as clinically similar with a rash illness, and both have regional targets of elimination. As such, both should have similar approaches to surveillance. Test for suspected cases of both measles and rubella either in parallel or in series, depending on local epidemiology and public health priorities. This chapter specifically addresses measles surveillance, although many details would also pertain to rubella surveillance. See the Rubella chapter for additional information about rubella.



TYPES OF SURVEILLANCE RECOMMENDED

MINIMAL SURVEILLANCE

In elimination mode, measles surveillance must be case-based. The surveillance system should be able to do the following in a timely manner: detect, notify and investigate suspected measles cases and outbreaks; correctly classify cases as confirmed or discarded; determine if they were due to failure of programme implementation (for example, should have been vaccinated but were not), due to vaccine failure, or occur in someone for whom vaccination is not recommended; and inform actions that reduce morbidity and mortality and prevent further virus transmission (2).

Active surveillance in health facilities, such as regular review of clinic logbooks for missed cases, is essential so no cases are missed. Surveillance should be nationwide with inclusion of all health facilities (both private and

public), with a system for zero reporting (reporting that there were no cases). If desired and resources exist, consider implementing community-based surveillance (such as notification of cases by community health workers or teachers) in areas that are at risk for measles, during outbreaks, and in populations where not all measles cases seek care in health facilities.

LINKAGES TO OTHER SURVEILLANCE

Surveillance for measles should be done together with rubella (see Box 1). Also consider integrating other rash-causing diseases such as dengue into this surveillance system, given the broad case detection definition for measles.



CASE DEFINITIONS AND FINAL CLASSIFICATION

SUSPECTED CASE DEFINITION FOR CASE FINDING

A suspected case is one in which a patient with fever and maculopapular (non-vesicular) rash, or in whom a health-care worker suspects measles.

FINAL CASE CLASSIFICATION

➤ **Laboratory-confirmed measles:** A suspected case of measles that has been confirmed positive by testing in a proficient laboratory, and vaccine-associated illness has been ruled out (see the section below, **Other definitions for measles cases**). A proficient laboratory is one that is WHO-accredited or has established a recognized quality assurance programme, such as International Organization for Standards (ISO) or Clinical Laboratory Improvement Amendments (CLIA) certification (3).

- **Epidemiologically linked measles:** A suspected case of measles that has not been confirmed by a laboratory, but was geographically and temporally related with dates of rash onset occurring 7–23 days apart from a laboratory-confirmed case or another epidemiologically linked measles case.
- **Clinically compatible measles:** A suspected case with fever and maculopapular (non-vesicular) rash and at least one of cough, coryza or conjunctivitis, but no adequate clinical specimen was taken and the case has not been linked epidemiologically to a laboratory-confirmed case of measles or other communicable disease. **As countries get closer to elimination, the vast majority of measles cases should be confirmed by laboratory or epidemiological linkage.** Clinically compatible cases are highly unlikely to be measles when the country is at or near elimination.

► **Non-measles discarded case:** A suspected case that has been investigated and discarded as a non-measles (and non-rubella) when any of the following are true:

- » negative laboratory testing in a proficient laboratory on an adequate specimen collected during the proper time period after rash onset (see Figure 1)
- » epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is not measles

- » confirmation of another etiology
- » failure to meet the clinically compatible measles case definition.

If the case is also negative for rubella, this is a non-measles non-rubella discarded case.

See Figure 2 for a summary of the classification process for measles and rubella.

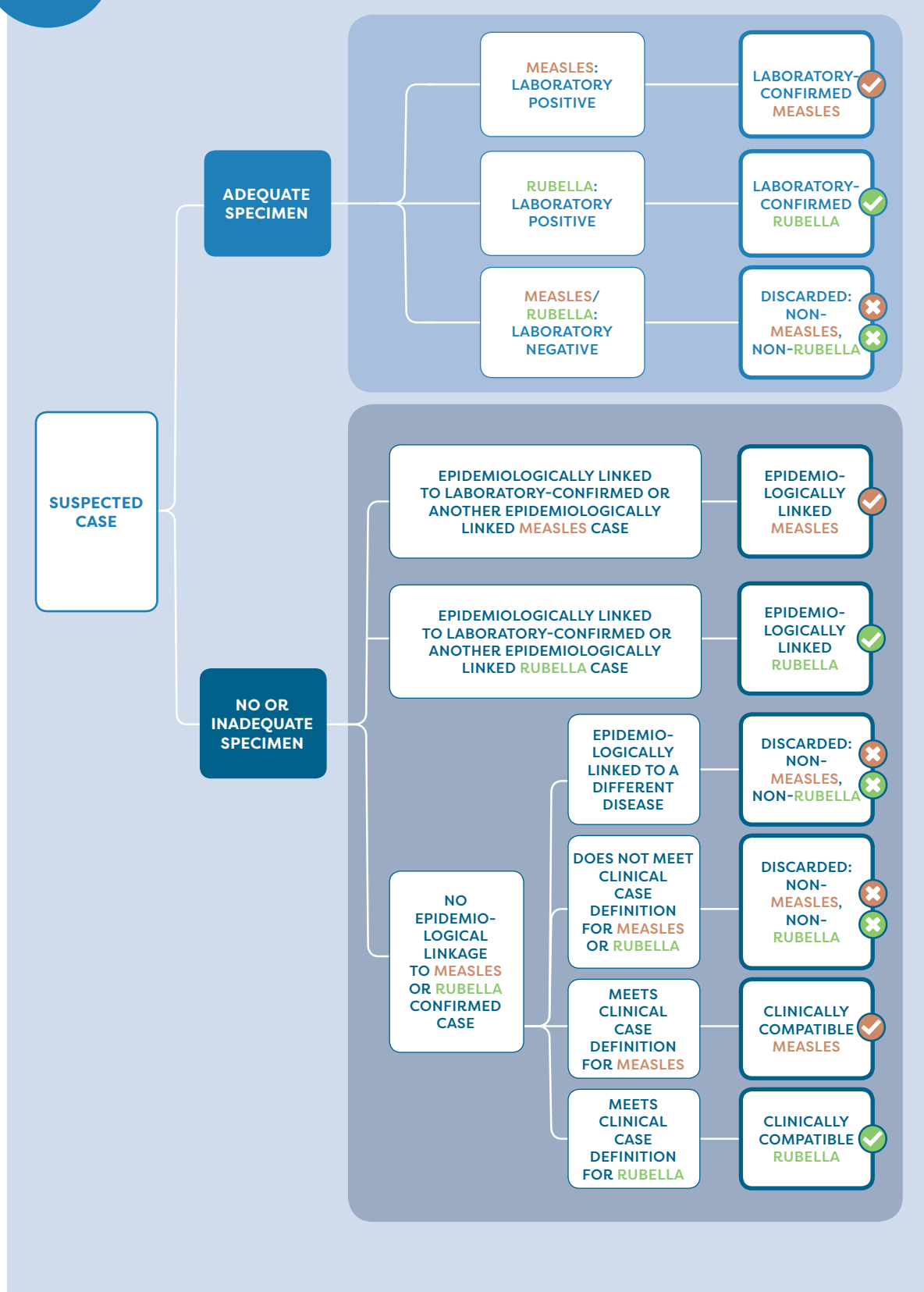
BOX
2

Measles case classification in countries post-elimination or close to elimination

In countries that have eliminated measles or are close to elimination, review both positive and negative IgM results for each measles case closely before assigning a final classification. As measles prevalence decreases, the positive predictive value of IgM testing becomes low, which means that false positive IgM results are to be expected. Additional sources of data such as the clinical presentation, epidemiological context (including travel and case contact history) and the timing and quality of specimen collection and testing are required to confirm a case. IgM may also be negative in a true measles case if the specimen is collected early or too late in the course of illness (< 4 days and > 28 days). This is especially important in outbreak settings where it is necessary to determine if there is sustained transmission. In outbreak settings, review discarded cases within 46 days (i.e. 2 incubation periods) from the last confirmed measles case to ensure that they are truly negative and transmission has ended.

FIGURE
2

Classification of suspected measles and rubella cases



OTHER DEFINITIONS

- **Endemic measles case:** Confirmed case of measles resulting from endemic transmission of measles. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥ 12 months within a country. To the greatest extent possible, this chain of transmission should be defined based on genotyping evidence along with epidemiological investigation. It is often the case that chains of transmission are unclear for measles, given the infectivity and mass movements of people.
- **Imported measles case:** A returning traveler or visitor exposed to measles outside the country during the 7–23 days prior to rash onset and supported by epidemiological or virological evidence. For cases that were outside the country for only a part of the 7–23 day period prior to rash onset, investigate whether the exposure to another measles case likely occurred outside or within the country to determine the source of infection and whether the case can be considered imported. Imported cases are defined by the place where the case was infected, not the country of residence or origin of the case.
- **Importation-related measles case:** A locally acquired infection that occurs as part of a chain of transmission originating from an imported case as supported by epidemiological or virological evidence. In countries with strong genotyping data, it is possible that a case with no identified epidemiological link to an imported case has viral genetic evidence linking the case to a chain of transmission from an imported measles case. If transmission of measles from cases related to importation persists for ≥ 12 months within a country, cases are no longer considered import-related but endemic.
- **Unknown source measles case:** A confirmed case for which no epidemiological or virological link to importation or endemic transmission can be established after a thorough investigation.
- **Measles vaccine-associated reaction:** A suspected case that meets **all five** of the following criteria:
 1. The patient had a rash illness, but did not have cough or other respiratory symptoms related to the rash
 2. The rash began 7–14 days after vaccination with a measles-containing vaccine
 3. The blood specimen, which was positive for measles IgM, was collected 8–56 days after vaccination
 4. A thorough field investigation did not identify any secondary cases
 5. Field and laboratory investigations failed to identify other causes, or genotype A was isolated from the suspected case (genotype A is only vaccine-related and does not occur as wild-type infection).
- **Acute measles-related death:** Any death occurring within 30 days of rash onset of a measles case (laboratory-confirmed, epidemiologically linked, clinically compatible) that is related to a complication of measles (such as pneumonia). Rare deaths from post-infectious encephalitis and subacute sclerosing panencephalitis (SSPE) occur months to years after measles infection and would not be detected by surveillance for acute measles illness.



CASE INVESTIGATION

Countries nearing elimination of measles should investigate all suspected cases and obtain clinical specimens for laboratory testing. Notify the public health authorities of all suspected measles cases within 24 hours of identification and investigate within 48 hours of notification. Collect the minimum data elements on the case investigation form. Additionally, collect data on potential risks of exposure and spread among contacts to identify transmission patterns and ways to interrupt chains of transmission. The source of infection is likely a person who interacted with the case during the source patient's infectious period and 7–23 days before the case's rash onset. Sometimes, however, the source patient cannot be identified, such as when the infection is travel related.

Once the case investigation form has been completed and laboratory test results are available, suspected cases should be classified both by confirmation status (laboratory-confirmed, epidemiologically linked,

clinically compatible, discarded) and by source of infection (imported, importation-related, endemic, unknown). Whenever possible, classify as few cases as possible as clinically compatible or unknown source, as these indicate that either a substandard investigation was conducted or that surveillance is substandard because a source case was unreported. In some cases, interpretation of the laboratory results is challenging (for example, in persons with a recent history of vaccination, cross reactivity with other infections or non-specific stimulation of the immune system due to other pathogens, indeterminate test results, or positive test results for both measles and rubella). False positive serologic results become relatively more frequent in elimination settings where the positive predictive value decreases as the measles incidence approaches zero. These situations are elaborated in more detail in the WHO manual for the laboratory diagnosis of measles and rubella virus infection (3).



SPECIMEN COLLECTION

Several different types of specimens can be collected from suspected measles cases based on the timing of investigation (3). Collect specimens on first contact with the case; do not wait for the ideal window or the case might be lost to follow up. An adequate specimen for antibody detection is defined as a sample collected within 28 days after rash onset that consists of ≥ 0.5 mL of sera. The volume of whole blood to be collected is defined in Table 1 based on age. In some regions where suitable testing is available, you may also use a sample of oral fluid or dried blood on a filter paper (≥ 3 fully filled circles).

At a minimum, all cases should have a specimen collected for antibody detection (unless they can be epidemiologically linked to a laboratory-confirmed or another epidemiologically linked case). Additionally, if the case is not part of a known chain of transmission,

collect a viral detection (genotyping) sample at first contact from 5–10 cases early in the chain of transmission, and every two months thereafter if transmission continues. Use laboratory testing and epidemiologic linkage for case confirmation together in a sustainable way that allows maximization of laboratory resources. Particularly in endemic settings, epidemiologic linkage should be prioritized during case investigations for routine case confirmation, during confirmed outbreaks and in times and places where sample collection or transportation is extremely difficult, such as during disasters and remote locations.

In countries that are close to elimination or have been verified, make an attempt to collect for each case a serum specimen and a specimen for viral detection (throat, nasal, or nasopharyngeal [NP] swab; oral fluid, urine or nasopharyngeal aspirates) at the correct time.

TABLE

1

Specimen types for diagnosis of measles (and rubella)

TYPE OF SPECIMEN	TYPE OF TEST	VOLUME TO BE COLLECTED	TIMING OF COLLECTION
WHOLE BLOOD/ SERUM (BY VENIPUNCTURE)	Antibody detection* (measles specific IgM, paired sera to document IgG seroconversion or significant rise in IgG between acute and convalescent phase sera)	Volume of 4–7 mL of blood for older children and adults; 1 mL for younger children; 0.5 mL from infants	≤ 28 days after rash onset. Paired sera are normally collected 10–20 days apart. The interval between the two serum samples can be shorter if virus-specific IgG was not detected in the first serum sample.
ALTERNATIVE SPECIMEN: DRIED BLOOD SPOTS (DBS) (WHOLE BLOOD)	Antibody detection* (measles specific IgM, paired sera to document IgG seroconversion or significant rise in IgG) Detection of viral RNA by RT-PCR	At least 3 fully filled circles on a filter-paper collection device	≤ 28 days after rash onset
THROAT (RECOMMENDED), NASAL, OR NASOPHARYNGEAL (NP) SWABS OR NASOPHARYNGEAL ASPIRATES**	Viral isolation by cell culture Detection of viral RNA by RT-PCR***	Swab or NP aspirate	Ideally, the sample should be collected within 5 days, but can collected up until 14 days after onset of rash for virus detection.
ORAL FLUID (OF)	Antibody detection* (measles specific IgM) Detection of viral RNA by RT-PCR	Using a sponge collection device that is rubbed along the gums for > 1 minute to ensure the device is thoroughly wet (~0.5 mL crevicular fluid).	Ideally, the sample should be collected within 5 days, but can collected up until 14 days after onset of rash for virus detection. Up to 28 days if antibody testing.
URINE	Viral isolation by cell culture Detection of viral RNA by RT-PCR	Minimum 10 mL (preference first morning void). Larger volumes have a higher chance of detection.	Ideally, the sample should be collected within 5 days, but can collected up until 14 days after onset of rash for virus detection.

* Antibody detection. Adequate samples are those collected within 28 days after onset of rash. However, IgM detection by ELA for measles is more sensitive when collected 4–28 days after the onset of rash. In the first 72 hours after rash onset, a negative result for measles IgM may be obtained from up to 30% of measles cases. A second serum sample may be required for additional testing under the following circumstances:

- Detection of virus-specific RNA by RT-PCR is either unavailable or the results were inconclusive
- The first serum specimen was collected ≤ 3 days after rash onset and is negative for measles IgM, or is negative in serum collected ≤ 5 days for rubella IgM by ELA
- Repeat testing of the initial serum specimen fails to resolve an equivocal result for IgM.

TABLE 1 CONTINUATION: SPECIMEN TYPES FOR DIAGNOSIS OF MEASLES (AND RUBELLA)

STORAGE CONDITIONS	ADVANTAGES	DISADVANTAGES	COMMENTS
Whole blood: 4–8°C (never freeze whole blood) for up to 24 hours or for 6 hours at 20–25°C before the serum is separated from clotted blood through centrifugation. Serum should be stored 4–8°C until shipment to laboratory, ideally no longer than 7 days.	<ul style="list-style-type: none"> » Most widely collected and tested, technically simple and standardized » WHO correlate of protection exists 	<ul style="list-style-type: none"> » Sensitivity of the test is lower ≤ 3 days after rash onset* » Positive predictive value of IgM in elimination settings is low 	Laboratories should report results for IgM within 4 days of receipt of the specimens.
Does not require cold chain. Should be dried before storage at low humidity.	<ul style="list-style-type: none"> » Does not require cold chain » Potentially lower transportation cost » Can collect from finger or heel prick » Potential for viral RNA isolation and antibody detection from same sample 	<ul style="list-style-type: none"> » Sensitivity reduced if not dried/stored properly » Increased workload in laboratory » No quality control on extraction process » Insufficient blood collected in field » Lower sensitivity for RT-PCR 	Preference is for serum to be collected, with DBS reserved for situations where it's hard to collect venous blood (e.g. infants), reverse cold chain cannot be maintained, or where expedited shipping is not possible.
4–8°C	<ul style="list-style-type: none"> » Superior to oral fluid for virus isolation » Can be more sensitive for confirmation than serum within first 3 days 	<ul style="list-style-type: none"> » Requires cold chain » Should get to lab within 48 hours ideally 	Both NP and OF samples can be stabilized on FTA® cards for transport at ambient temperature. In this case, detection of antibodies is not possible, but viral RNA can be detected by RT-PCR.
Does not require cold chain if < 22°C ambient temperature and shipped to the laboratory within 24 hours. At higher temperatures, the OF samples should be kept at 4–8°C until the samples can be shipped on cold packs.	<ul style="list-style-type: none"> » Less invasive than blood collection » Does not require cold chain » Potentially lower transportation cost » Viral detection and antibody detection from same sample 	<ul style="list-style-type: none"> » Somewhat less sensitive for antibody detection than serum when collected early » Not suitable for virus isolation (cell culture) » External quality control programmes have not been established » Limited number of EIA test kits validated for OF » If stored at room temperature, need to ship samples to lab within 24 hours of collection 	Both NP and OF samples can be stabilized on FTA® cards for transport at ambient temperature. In this case, detection of antibodies is not possible, but viral RNA can be detected by RT-PCR
Stored at 4–8°C until the urine can be centrifuged. Original urine sample should not be frozen prior to centrifugation.		<ul style="list-style-type: none"> » Often difficult to collect, transport and process » Less sensitive than throat swabs » May contain substances that are inhibitory for RT-PCR 	

*** Properly collected serum tested for IgM is still considered by some labs as the only adequate specimen to rule out measles. A negative RT-PCR from the upper respiratory tract is not considered to rule out measles because specimen timing and quality are critical. However, some countries are collecting only upper respiratory tract specimens from infants because of the difficulty of drawing blood. In some countries with very low measles prevalence, these samples can be a significant fraction of the total.*

****Virus detection (by cell culture or RT-PCR). Because virus is more likely to be isolated (and RNA detection rate is higher) when specimens are collected early, the collection of specimens for virus detection should not be delayed until laboratory confirmation by antibody detection of a suspected case is obtained. Samples for antibody and viral detection should be collected at first contact with a suspected case.*

STORAGE AND TRANSPORT

- **Whole blood/serum.** Collection of whole blood is done by venipuncture using a sterile, plain collection tube or gel separator tube without additives. Whole blood can be stored at 4–8°C (never freeze whole blood) for up to 24 hours or for 6 hours at 20–25°C before the serum is separated from the clotted blood through centrifugation. After this time, whole blood must be transported to a facility equipped to separate the serum in order to avoid haemolysis.

Serum should be stored at 4–8°C until shipment, but ideally should not be held at 4–8°C for longer than seven days. For longer periods, such as when a delay is anticipated in shipping or testing, serum samples must be frozen at –20°C or below and transported to the testing laboratory on frozen ice packs in a sufficiently insulated container. Avoid cycles of repeated freezing and thawing, as this can have detrimental effects on the integrity of IgM antibodies. Aliquots of important serum specimens should be prepared prior to freezing. As a general rule, serum specimens should be shipped to the laboratory as soon as possible, and shipment should not be delayed for the collection of additional specimens.

Blood can be dried onto filter paper (dried blood spots, or DBS) if venipuncture is not possible, or if a cold chain or economical method to ship serum samples are not available. While venous blood can be collected for DBS, normally DBS are prepared using capillary blood. Collect blood by finger- or heel-prick using a sterile lancet, preferably a single-use disposable lancet. Allow blood specimens that have been spotted on filter paper to air dry completely. Wrap individual cards in wax paper and place them in a sealable plastic bag with a desiccant pack. DBS should be stored at 4°C until they can be shipped to the laboratory. It is acceptable to transport DBS at ambient temperatures up to 42°C if the sample is delivered to the laboratory within three days.

- **Oral fluid (OF).** An adequate OF sample is one that is collected by gently rubbing along the base of the teeth and gums for at least one minute, which should allow the sponge to absorb about 0.5 mL of crevicular fluid. If the daily ambient temperature is below 22°C, OF samples should be shipped to the laboratory within 24 hours. At higher temperatures, the OF samples should be kept at 4–8°C until the samples can be shipped to the laboratory on cold packs. The OF samples are not considered a biohazard and can be shipped without special documentation from the site of collection to the laboratory.

- **Nasopharyngeal (NP), nasal or throat swabs.** An oropharyngeal (throat swab) is the recommended sample for both viral detection and virus isolation for suspected cases. NP swabs will serve as good samples for both virus isolation and detection but are more difficult to collect. NP aspirates and nasal swabs are variations that have been used successfully to detect measles virus. Swabs should be collected using only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts as they may contain substances that inactivate viruses and/or inhibit PCR testing.

The throat swab is collected by swabbing the posterior pharynx, avoiding the tongue. The NP swab has a flexible shaft. Tilt the patient's head back and insert the swab into the nostril parallel to the palate. The swab should contact the mucosal surface. Place the sample in sterile tubes containing 2–3 mL of viral transport media (VTM) or phosphate-buffered saline (PBS). It is important to prevent the swabs from drying out. The throat and NP swabs may be refrigerated at 2–8°C for up to 48 hours and shipped on ice/frozen ice packs. If arrangements cannot be made for shipment within this timeframe, it is best to preserve the sample at –70°C. After freezing at –70°C, the samples are shipped on dry ice. Avoid freeze/thaw cycles. If storage at –70°C is not available, store samples at –20°C; viral viability will be lost, but the integrity of the viral RNA may be maintained and detected by RT-PCR.

- **Urine.** Urine is collected in a suitable sterile, leak-proof container. The urine sample should be stored at 4–8°C until the urine can be centrifuged. Do not freeze the original urine sample prior to centrifugation. Whole urine samples may be shipped in sealed containers at 4°C, but centrifugation within 24 hours of collection is recommended. The urine is centrifuged at 500 × g (approximately 1500 rpm) for 5–10 minutes, preferably at 4°C and with the supernatant removed. Add sterile VTM, tissue culture medium or PBS to the sediment to bring the final volume to 2 mL. If a pellet is not visible, remove all but 1 mL at the bottom of the centrifuge

tube and mix with equal volume of VTM. Store the processed urine sample at 4°C and ship within 48 hours. Alternatively, the urine sample may be frozen at -70°C in viral transport medium and shipped on dry ice. If storage at -70°C is not available, samples can be stored at -20°C; viral viability will be lost, but the integrity of the viral RNA may be maintained and detected by RT-PCR.

Regardless of specimen type collected, all specimens should arrive to the lab within five days of collection, except in the case of oral fluids as noted above.



LABORATORY TESTING

CONFIRMATION METHODS

Laboratory case confirmation for measles can yield the following testing results:

- detection of anti-measles IgM antibody by enzyme immunoassay (EIA). This is the gold-standard. Results of IgM should be reported within four days of the specimen's arrival to the laboratory (Figures 3b/3c).
- diagnostically significant titer change in IgG antibody level in acute or convalescent sera, or documented seroconversion (IgG negative to IgG positive) (Figures 3b/3c).
- positive reverse transcription-polymerase chain reaction (RT-PCR) or viral isolation in cell culture (Figure 3a).

See Figures 3a, b and c for more information.

GENOTYPE TESTING

Measles genotype testing and the use of named strains can help to identify the chain of transmission to which the case belongs. It is recommended that ≥ 80% of laboratory-confirmed outbreaks have their genotype determined. In some situations, extended window or whole genome sequencing may be considered to assess whether an outbreak is ongoing or the result of a new importation. Results from genotyping samples should be reported within two months of the specimen's arrival to the laboratory.

SPECIAL LABORATORY CONSIDERATIONS

- **Laboratory testing for rubella.** Laboratories can perform testing on specimens from suspected measles/rubella cases using different testing algorithms, depending on the local epidemiology and available resources. When possible, it is best to integrate the testing of measles and rubella. If resources are sufficient or both diseases occur at similar prevalence, do measles and rubella testing in parallel, with all samples tested simultaneously for both diseases. If resources are limited or measles burden is high, do serial testing in which measles testing is done first, followed by rubella testing on samples that are negative for measles. If rubella burden is higher than measles, do the rubella testing first followed by measles testing on samples that test negative for rubella.
- **Laboratory testing for other febrile rash illnesses.** In countries that use the fever-rash case definition and have a high burden of other fever-rash diseases (such as dengue, Zika and Chikungunya), additional testing can be integrated into the measles/rubella testing algorithm. Weigh the burden of disease and the risk of delayed diagnosis when determining the proper algorithm.

➤ **Laboratory testing in an elimination setting.** In an elimination setting, critically evaluate both positive and negative IgM testing results. False positives become more likely as the positive predictive value of IgM testing decreases as measles prevalence decreases. Epidemiological data can strengthen the argument for or against an IgM-positive result representing a true case. A second sample may need to be collected if the original sample that tested negative for measles was collected less than four days after rash onset, to ensure the case is truly negative. Figures 3a, 3b and 3c demonstrate the process for laboratory testing for suspected measles and rubella cases when a country is near or at elimination. Suspected cases in low incidence settings should be evaluated and classified after taking into consideration all laboratory and epidemiological data.

LABORATORY NETWORKS

WHO coordinates the Global Measles and Rubella Laboratory Network (GMRLN), a network of over 700 labs at national and subnational laboratories that meet rigorous standards to provide accurate results (4). Regional and global reference laboratories can provide specialized testing (such as avidity testing) and virus isolation with molecular techniques to those countries that are unable to do this in their own laboratories. Ensure that samples are tested in a WHO accredited or proficient laboratory, or in laboratories with quality assurance support from national laboratories in GMRLN. If this is not possible, then use a laboratory that has an established recognized quality assurance programme such as ISO 15189 or ISO 17025 accreditation, or CLIA certification.

FIGURE
3a

Laboratory testing for suspected measles or rubella cases in countries at or near elimination, part I

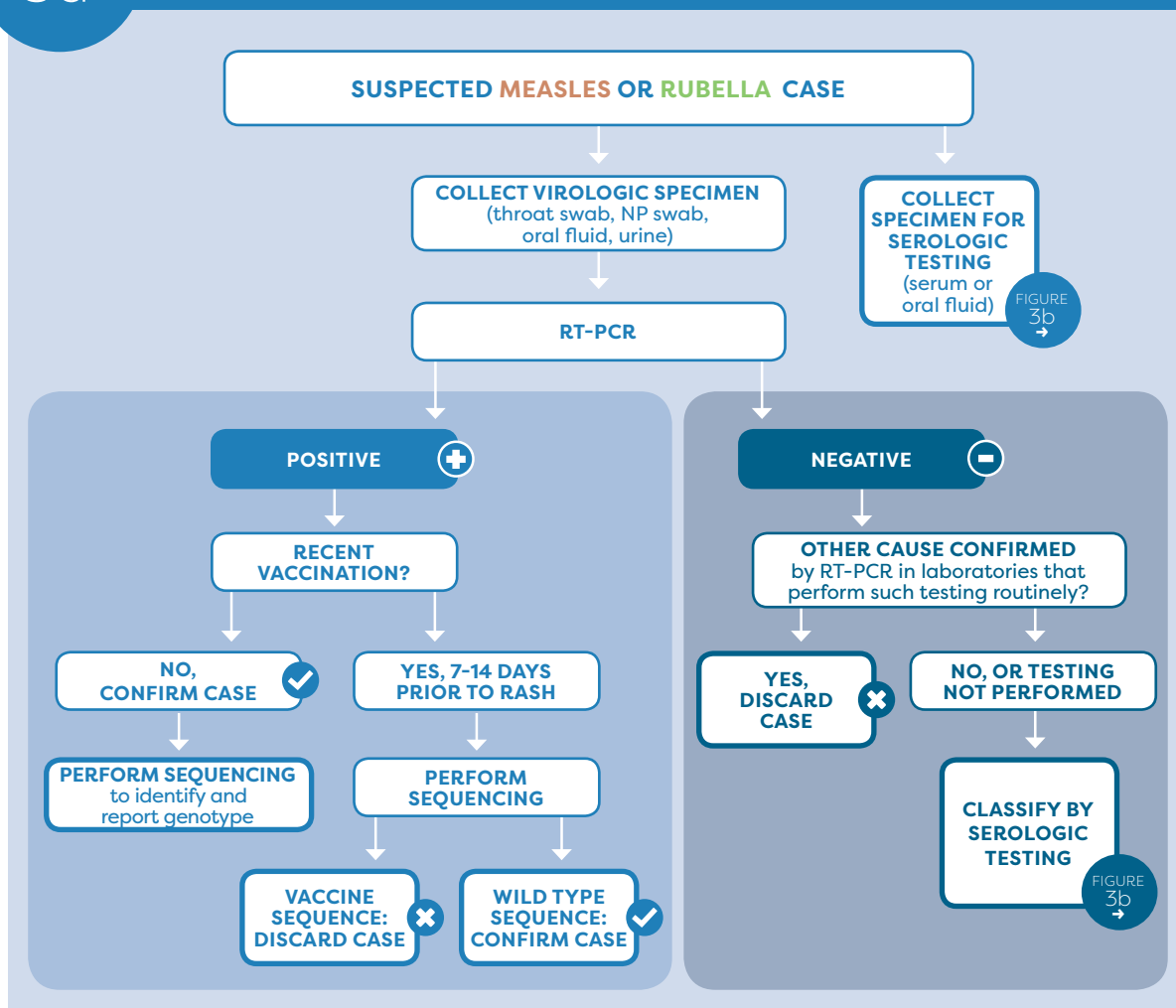
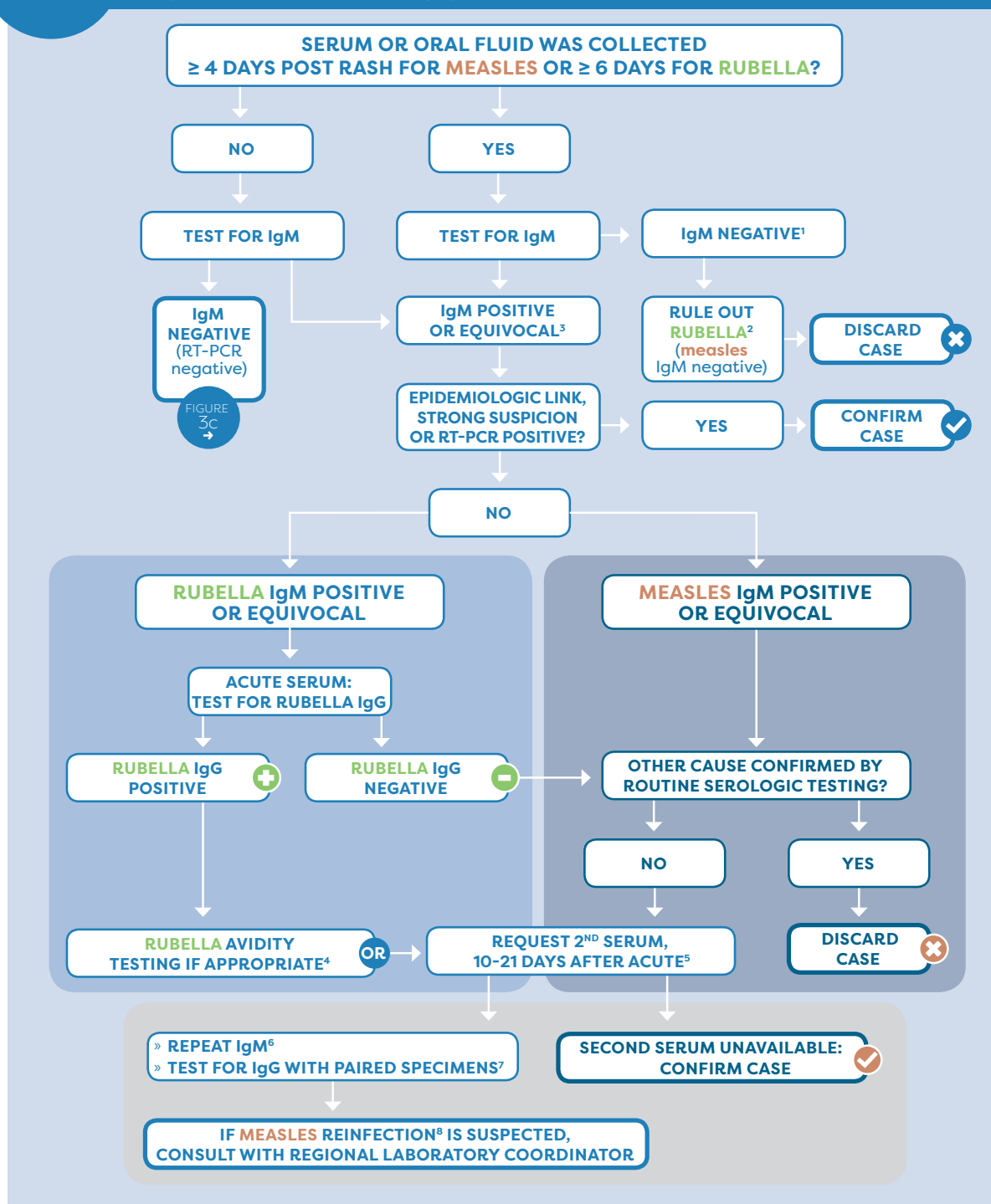


FIGURE
3b

Laboratory testing for suspected measles or rubella case in countries at or near elimination (sample collected in the optimal time window), part II



Notes for Figure 3b:

- 1 A measles reinfection case can have a negative IgM result. If measles reinfection is suspected, consult with the regional laboratory coordinator. Reinfection cases can be confirmed by RT-PCR, a rise in IgG titer or by measuring high levels of measles neutralizing antibody levels ($\geq 40,000$ mIU/mL) by plaque reduction neutralization testing.
- 2 Parallel, or reflex, testing should be performed according to the resources available and regional surveillance recommendations.
- 3 An equivocal IgM result is obtained after repeat of test. The equivocal or positive IgM result was obtained using a validated assay in accredited laboratory.

4 A positive IgG result and an equivocal IgM for rubella are inconsistent with primary rubella. If acute serum was IgM positive, rubella avidity testing or evaluation of IgG titers with paired specimens may be necessary to resolve the case. Low avidity is associated with recent primary rubella infection; high avidity is associated with past infection, vaccination, or reinfection.

5 If the acute serum was IgG negative, the absence of seroconversion can be demonstrated with a second serum collected ≥ 10 days post rash.

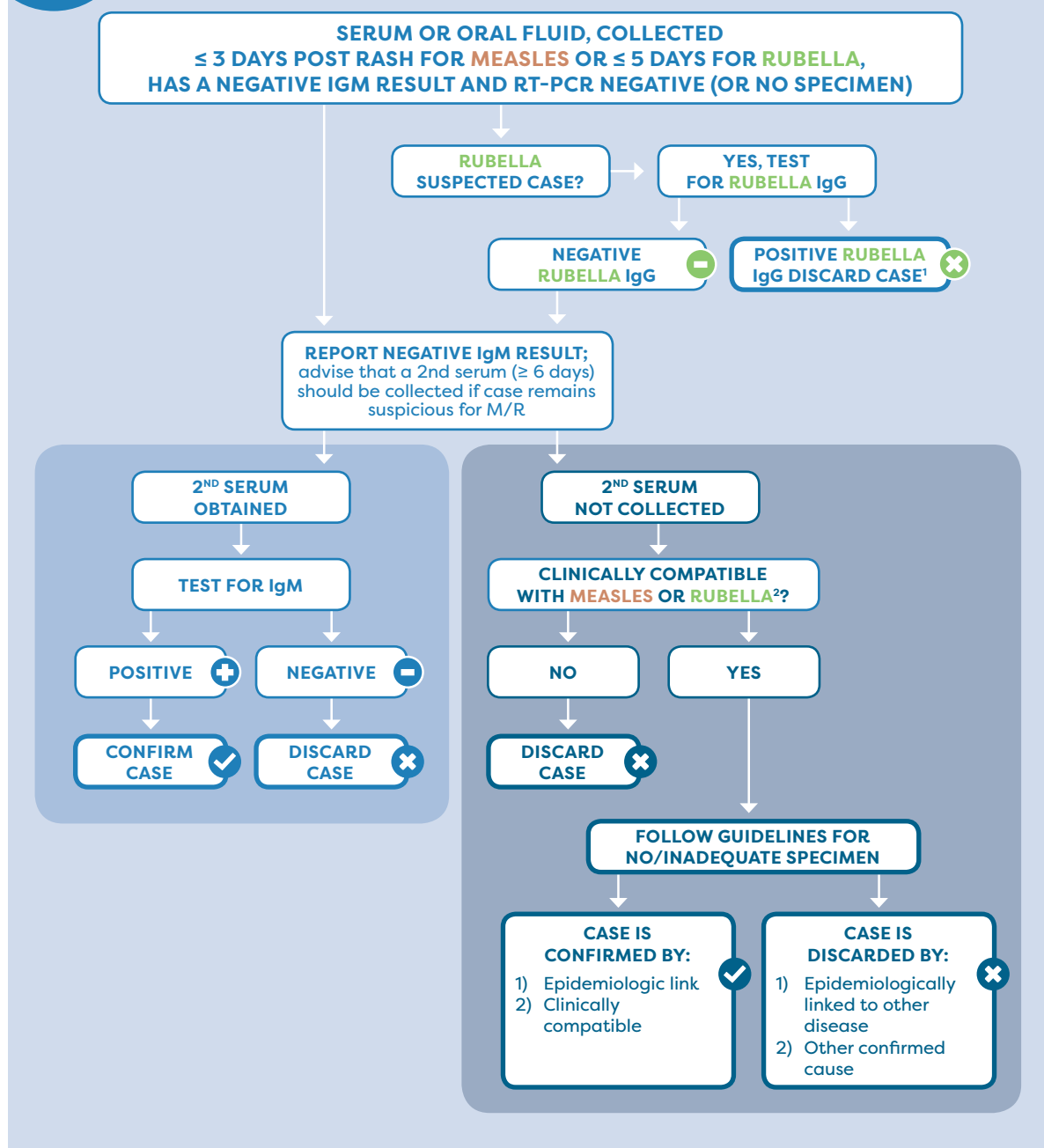
6 In most instances, a suspected case with an equivocal IgM result obtained from acute serum and a positive IgM from the second serum confirms the case. However, an evaluation of IgG titers may be deemed necessary to support the IgM result.

7 Test for IgG if test is available (by semi-quantitative ELA) using appropriately timed paired specimens, tested together. Seroconversion or demonstration of a diagnostically significant rise confirms the case. Absence of seroconversion (both IgG negative) rules out the case. Note: failure to measure a diagnostically significant rise in titer must be interpreted with caution since the ideal timing for demonstration of a rise in titer can vary among individuals.

8 The rise in IgG titer from a measles reinfection case is rapid and remarkably high titers in acute serum are typical. Consultation with the regional laboratory coordinator is recommended to determine if additional testing is warranted and feasible.

FIGURE
3c

Laboratory testing for suspected measles or rubella case in countries at or near elimination, part III



Notes for Figure 3c:

- 1 Cases who are rubella IgM negative and rubella IgG positive are inconsistent with acute infection.
- 2 Expert review as appropriate



DATA COLLECTION, REPORTING AND USE

Because it is recommended that measles and rubella surveillance be integrated, the case investigation forms, databases and data reporting are usually done together for both diseases. Below is a list of general data elements for both diseases, with rubella-specific data points indicated by *.

RECOMMENDED DATA ELEMENTS

► Demographic information

- » Name (if confidentiality is a concern the name can be omitted so long as a unique identifier exists)
- » Unique identifier
- » Place of residence (city, district, and province)
- » Place of infection (at least to third administrative level, if known)
- » Date of birth (or age if date of birth not available)
- » Sex
- » Race and/or ethnicity, if appropriate in country setting
- » Country of birth

► Reporting source

- » Place of reporting (for example, county or district)
- » Date of notification
- » Date of investigation
- » Name of clinician who suspects measles (or rubella)

► Clinical

- » Date of rash onset
- » Symptoms
 - Fever
 - Maculopapular rash
 - Cough
 - Conjunctivitis
 - Coryza
 - Lymphadenopathy*
 - Arthralgia or arthritis*

- » Severe complications
 - Pneumonia
 - Persistent diarrhea
 - Encephalitis
 - Thrombocytopenia*
 - Other
- » Hospitalizations
 - History of hospitalization in 23 days prior to rash onset?
 - Dates of hospitalization
 - Hospitalized because of this current fever-rash diagnosis?
- » Outcome (patient survived or died)
 - Date of death
- » For women of childbearing age
 - Number of previous pregnancies*
 - Pregnancy status*
 - Number of weeks gestation at onset of illness*
 - Prior evidence or date of rubella serologic immunity, or both*
 - Number and dates of previous pregnancies and location (second administrative level or country) of these pregnancies*
 - Pregnancy outcome, when available (normal infant, termination, infant with congenital rubella syndrome, etc.)*

► Laboratory methods and results

- » Type(s) of specimen(s) collected
- » Date of specimen(s) collection
- » Date specimen(s) sent to laboratory
- » Date specimen(s) received in laboratory
- » Date of results from laboratory
- » Laboratory results (serology, viral detection, genotype)

► Vaccination status

- » Number of doses of measles-containing vaccine
 - Dates of all doses of vaccine given (if card available)

- » Number of doses of rubella-containing vaccine*
 - Dates of all doses of vaccine given (if card available)

► Contact tracing

- » Persons who came in contact with the case 7–23 days before symptom onset (source of case's infection). Determine if any of them had rash illness with fever.
- » Persons who came in contact with the case in the four days prior to and four days after rash onset (potential persons exposed by the case)

► Epidemiological data

- » Transmission setting (infection acquired at home, health care setting, daycare, school, workplace, etc.)
- » Enrolled in a school?
 - If enrolled, name of the school
- » Visited a health facility in the 7–23 days before symptom onset?
 - If yes, name of the facility
- » Travel history in the past 7–23 days?
- » Relationship to outbreak (Is the case part of an outbreak or is it sporadic?)

► Classification

- » Final case classification (laboratory-confirmed, epidemiologically-linked, clinically compatible, discarded)
- » Source (import, importation-related, unknown, endemic)

Note: The time period of 7–23 days is used to cover both measles and rubella exposure periods.

REPORTING REQUIREMENTS AND RECOMMENDATIONS

Report and analyse case-based data on all suspected cases, regardless of final classification, from local to national level, to allow for adequate epidemiological analysis. Report measles cases regularly to the next level within the Ministry of Health (at least monthly, preferably weekly), including zero reporting (reporting even when no suspected cases have been detected during the designated reporting time period).

Every WHO Member State uses the Joint Reporting Form (JRF) to report confirmed cases of measles annually. Additionally, WHO recommends that all

countries submit monthly case-based data to WHO. Measles is not currently a notifiable disease under the International Health Regulations (IHR); however, measles outbreaks may be considered as events involving epidemic-prone diseases of special national or regional concern that “have demonstrated the ability to cause serious public health impact and to spread rapidly internationally”. As such, they may be reported through IHR mechanisms.

RECOMMENDED DATA ANALYSES

- Number of suspected and confirmed cases by age, date of onset (month and year at a minimum, by week in outbreak setting) and geographic area
- Incidence per million population by 12-month period and geographic area (because of seasonality, it is not appropriate to calculate incidence for shorter periods of time)
- Age-specific, sex-specific and district-specific incidence rates
- Proportion of confirmed cases by age group and immunization status. Suggested age groups are < 6 months, 6–8 months, 9–11 months, 1–4 years, 5–9 years, 10–14 years, 15–19 years, 20–24 years, 25–29 years, 30–44 years, ≥ 45 years, but base the age groups on the epidemiology of the disease, vaccination schedule and history of the vaccine programme.
- Measles vaccine status among confirmed and discarded cases by year and geographic area
- Epidemic curve showing cases over time by genotype/named strain (see Figure 4a, b and c)
- Proportion of cases by final classification and source
- Maps of cases
- Proportion of complications and death, stratified by age
- Proportion of cases that are preventable (for example, age ≥ age of first recommended dose), separated into vaccine failures and programmatic failures; proportion of cases not preventable by vaccination (age below that of first recommended dose).
- Data summaries for endemic and imported virus genotype and lineage characterization

Figures 4a, b and c are examples of how to present genotyping data alongside epidemiologic data.

FIGURE
4a

Example of an epidemic curve of measles outbreak by source, week of onset, and genotype

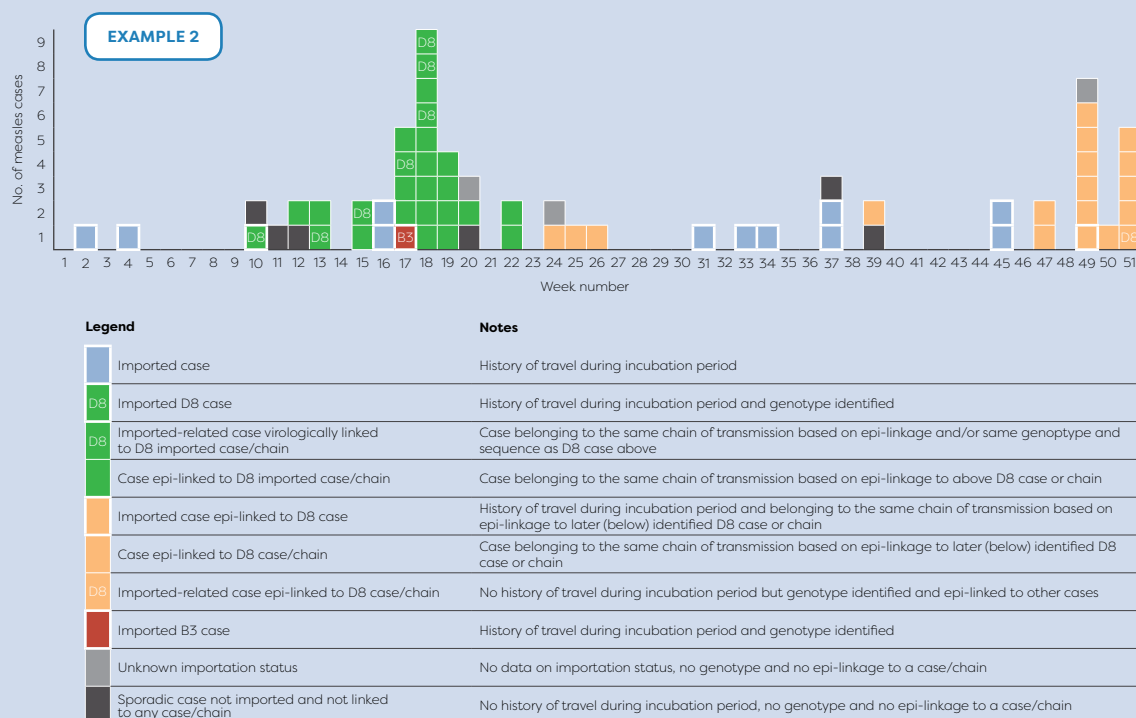
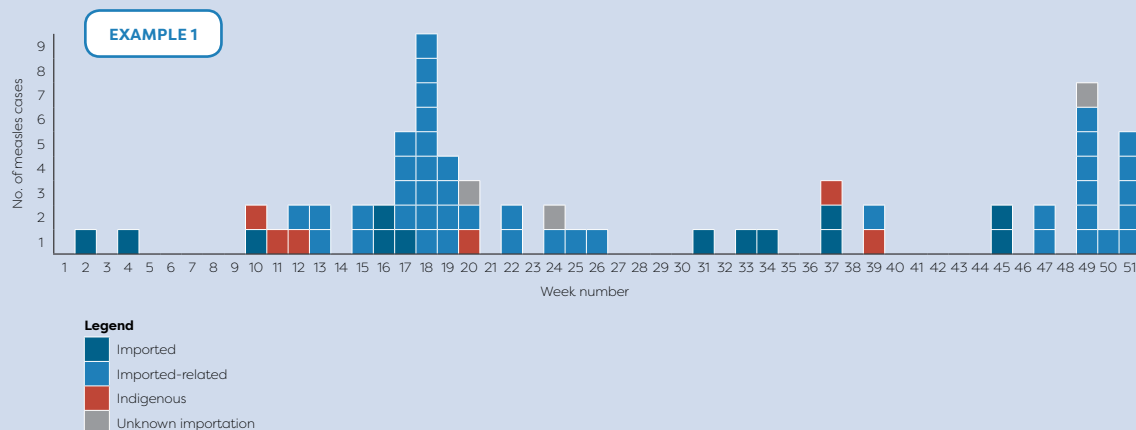


FIGURE
4b

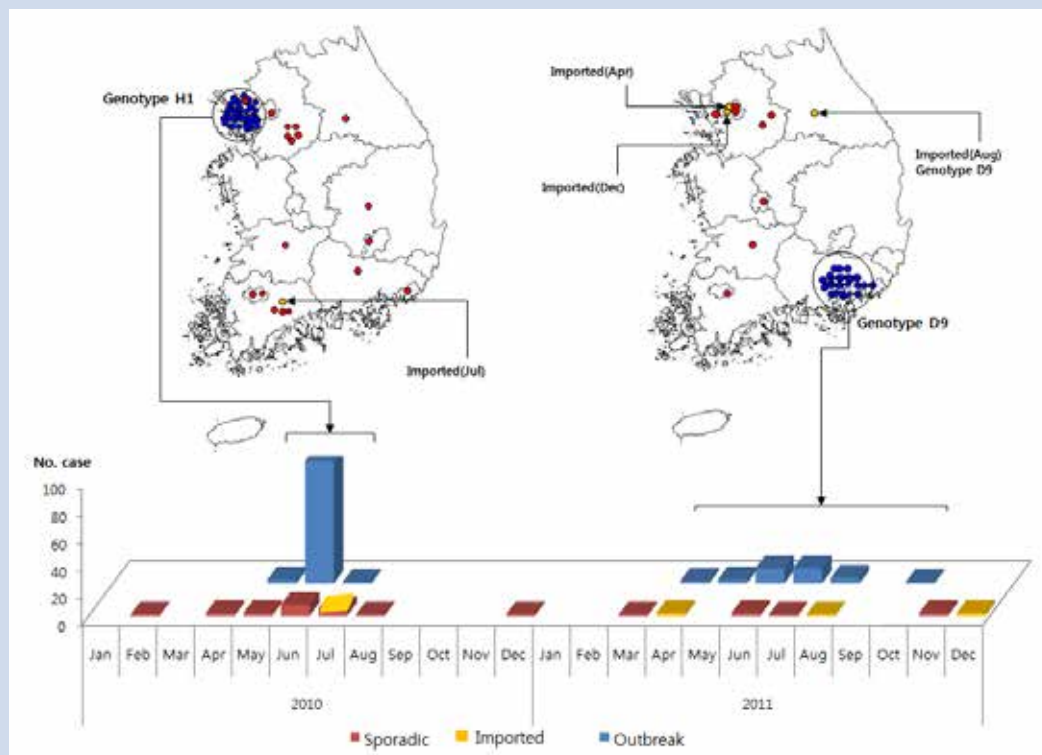
Predominant measles virus sequence variants in Germany, by federal state and week of onset

	2016				2017												Federal State
	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	
B3-4686			1														Sachsen-Anhalt
		1	14	2	1												Thüringen
				2	2												Rheinland-Pfalz
						1											Hamburg
B3-4686					8	5	1										Sachsen
					2	1											Baden-Württemberg
							1										Sachsen-Anhalt
B3-4299, MVs/ DUBLIN.IRL/ 08.16					2	1	8		1		1						Baden-Württemberg
						1	1										Saarland
						5	7	16	27	9	5	4					Nordrhein-Westfalen
						1			2								Sachsen
						1				5	2	2					Berlin
							1										Hamburg
			1				1		6				1			6	Bayern
											1	1	1				Brandenburg
												3					Sachsen-Anhalt
												1					Mecklenburg-Vorpommern
										2	7					1	Niedersachsen
													1				Hessen
D8-4221, MVs/ OSAKA.JPN/ 29.15					2	4											Hessen
					1												Baden-Württemberg
	1						1	1									Bayern
		1								1			1				Nordrhein-Westfalen
	3										1	1	1				Berlin
D8-2283, MVI/ HULU LANGAT.MYS/ 26.11			2														Saarland
				1													Brandenburg
					6	6	1										Berlin
						3											Baden-Württemberg
D8-4807						9	12	1									Hessen
						2	1		1								Rheinland-Pfalz
						1	1	1									Nordrhein-Westfalen
								1									Baden-Württemberg
	2016				2017												Federal State
	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	

The number of detected cases is given in each field.
Sample collection date as of 31.12.2017.

FIGURE
4c

Epidemiologic curve of measles cases by source with supplemental mapping to highlight geographic distribution of cases



Note about counting measles cases: total measles cases are usually the sum of laboratory-confirmed cases, epidemiologically linked cases and clinically compatible cases. However, when disease incidence is very low or a country has achieved or nears measles elimination, the positive predictive value of the clinically compatible case definition is low and most are likely not measles. Therefore, in eliminated and near-eliminated settings, total cases are usually the sum of laboratory-confirmed and epidemiologically linked cases. Imported cases should be included in a country's total case count unless the source country accepts the cases as part of their case count. Imported cases should be included in analysis but can be analysed separately.

All confirmed cases should be further classified to determine the proportion of cases attributable to programme failure – that is, cases in persons who should have been vaccinated according to the national schedule, but were not. Strive for this even in outbreaks, though it might be not feasible due to the large number of cases. A programmatically preventable measles case is a confirmed measles case for whom the vaccine was indicated based on the national immunization schedule, but who did not receive the recommended doses. A programmatically non-preventable measles case is a confirmed measles case who had been appropriately vaccinated as per the national schedule, or for whom vaccine is not routinely recommended. This distinction can help immunization programmes determine the need to improve delivery of recommended measles vaccines or change the national policy, such as changing the timing of vaccination doses.

USING DATA FOR DECISION-MAKING

Conduct regular epidemiological analysis and synthesis of data informed by local knowledge of the context in order to capture patterns of disease and any immunity gaps. Such analysis will provide insight into likely future issues requiring action, and indicate whether or not control and elimination status will be sustained. The synthesis and interpretation should include an epidemiological description of who is infecting whom, particularly with respect to the source of infection for infants and where immunity gaps seem to be most evident amongst birth cohorts or underserved populations. Such a synthesis should be derived from and informed by the analysis of surveillance data. The most important uses of data are the following:

- identify proportion of disease due to endemic circulation versus importation
- characterize transmission patterns including which age groups are the main transmitters of infection to infants, and effectiveness of methods to interrupt transmission
- determine risk factors for infection, complications and death
- determine major reasons that cases are non-immune and act to fill gaps or modify vaccination programme
- verify elimination and sustainability of elimination
- identify birth cohorts with immunity gaps; assess risk for outbreak spread and protect neighboring areas
- confirm cases and outbreaks to take appropriate action to prevent further transmission.



SURVEILLANCE PERFORMANCE INDICATORS

Measles surveillance should be evaluated routinely at national and subnational/local levels, and are frequently important in decision-making by national and regional verification commissions. It is recommended that countries review their national measles surveillance system annually as the country approaches, achieves and sustains elimination. Additionally, measles surveillance

should be reviewed within the context of comprehensive VPD surveillance reviews which should be conducted at least every five years.

Table 2 lists indicators established by WHO, against which the measles surveillance system can be evaluated in order to help pinpoint problems and make improvements.

TABLE
2

Indicators of the quality of surveillance for measles (and rubella)

SURVEILLANCE ATTRIBUTE	INDICATOR	TARGET	HOW TO CALCULATE (NUMERATOR / DENOMINATOR)	COMMENTS
TIMELINESS OF REPORTING	Percentage of surveillance units reporting to the national level on time, even in the absence of cases	≥ 80%	# of surveillance units in the country reporting by the deadline / # of surveillance units in the country x 100	At each level, reports should be received on or before the requested date.
TIMELINESS OF REPORTING (WHO REGION)	Percentage of countries reporting to their WHO Regional Office on time, even in the absence of cases	100%	# of countries in the region reporting to WHO by the deadline / # of countries in the region x 100	At each level, reports should be received on or before the requested date.
TIMELINESS AND COMPLETENESS OF INVESTIGATION	Percentage of all suspected measles and rubella cases that have had an adequate investigation initiated within 48 hours of notification	≥ 80%	# of suspected cases of measles or rubella for which an adequate investigation was initiated within 48 hours of notification / # of suspected measles and rubella cases x 100	<p><i>Note 1:</i> An adequate investigation includes collection of all the following data elements from each suspected measles or rubella case: name or identifiers, place of residence, place of infection (at least to district level), age (or date of birth), sex, date of rash onset, date of specimen collection, measles-rubella vaccination status, date of all measles-rubella or measles-mumps-rubella vaccination, date of notification, date of investigation and travel history.</p> <p><i>Note 2:</i> Some variables may not be required for cases that are confirmed by epidemiological linkage (for example, date of specimen collection).</p>
SENSITIVITY	Reporting rate of discarded non-measles non-rubella cases at the national level	≥ 2/100,000 population per 12 months	# suspected cases that have been investigated and discarded as a non-measles and non-rubella case using (a) laboratory testing in a proficient laboratory or (b) epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is neither measles nor rubella in a 12 month period / national population x 100,000	

SURVEILLANCE ATTRIBUTE	INDICATOR	TARGET	HOW TO CALCULATE (NUMERATOR / DENOMINATOR)	COMMENTS
SOURCE CLASSIFICATION	Percentage of confirmed cases for which source of transmission is classified as endemic, imported or importation-related.	≥ 80%	# confirmed cases in which the source can be classified as endemic, imported, or importation-related / total number of confirmed cases x 100	Unknown source should be kept to a minimum but will continue to occur even with thorough field investigations. This target might not be achievable in large outbreaks
REPRESENTATIVENESS	Percentage of subnational administrative units (at the province level or its administrative equivalent) reporting at least 2 discarded non-measles non-rubella cases per 100,000 population per year	≥ 80%	# of subnational units achieving ≥ 2 per 100,000 population discard rate / # of subnational units x 100	<p><i>Note 1:</i> If the administrative unit has a population <100 000, the rate should be calculated by combining data over more than 1 year for a given administrative unit to achieve ≥100,000 person-years of observation, or neighboring administrative units can be combined for the purpose of this calculation.</p> <p><i>Note 2:</i> Administrative units should include all cases reported from their catchment area, including import and importation-related cases, and cases residing in neighboring administrative units but reported in this one.</p>
SPECIMEN COLLECTION AND TESTING ADEQUACY	Percentage of suspected cases with adequate specimens for detecting acute measles or rubella infection collected and tested in a proficient laboratory	≥ 80%	# of suspected cases with an adequate specimen tested in a proficient lab / # of suspected cases - # of suspected cases of measles or rubella that are not tested by a laboratory and are (a) confirmed as measles or rubella by epidemiological linkage or (b) discarded as non-measles and non-rubella by epidemiological linkage to another laboratory-confirmed communicable disease case x 100	<p><i>Note 1:</i> Adequate specimens are: a blood sample by venipuncture in a sterile tube with a volume of at least 1 mL for older children and adults and 0.5 mL for infants and younger children; a dried blood sample, at least 3 fully filled circles on a filter-paper collection device; an oral fluid sample using a sponge collection device that is rubbed along the gums for > 1 minute to ensure the device is thoroughly wet; a properly collected upper respiratory tract specimen for RT-PCR. Adequate samples for antibody detection are those collected within 28 days after onset of rash, and for RT-PCR within 5 days of rash onset.</p> <p><i>Note 2:</i> A proficient laboratory is one that is WHO accredited or has established a recognized quality assurance programme (such as the International Organization for Standards (ISO) or Clinical Laboratory Improvement Amendments (CLIA) certified).</p>

SURVEILLANCE ATTRIBUTE	INDICATOR	TARGET	HOW TO CALCULATE (NUMERATOR / DENOMINATOR)	COMMENTS
VIRAL DETECTION	Percentage of laboratory-confirmed outbreaks with samples adequate for detecting measles virus collected and tested in an accredited laboratory	≥ 80%	# of outbreaks for which adequate samples have been submitted for viral detection / # of outbreaks identified x 100	Where possible, samples should be collected from at least 5–10 cases early in a chain of transmission and every 2–3 months thereafter if transmission continues. For virus detection, adequate samples are those collected within 14 days of rash onset.
TIMELINESS OF SPECIMEN TRANSPORT	Percentage of specimens received at the laboratory within 5 days of collection	≥ 80%	# of specimens received within 5 days of collection by laboratory / # of specimens x 100	Indicator only applies to public laboratories.
TIMELINESS OF REPORTING LABORATORY RESULTS	Percentage of IgM results reported to national public health authorities by the laboratory within 4 days of specimen receipt	≥ 80%	# of IgM test results reported within 4 days of specimen receipt / # of specimens received by lab x 100	Indicator only applies to public laboratories.



CLINICAL CASE MANAGEMENT

There is no specific treatment for measles virus apart from supportive care along with vitamin A. Vitamin A should be administered to all acute cases irrespective of the timing of previous doses of vitamin A. Vitamin A oral dosage should be given immediately on diagnosis and repeated the next day; give 50,000 IU to infants < 6 months, 100,000 IU to infants aged 6–11 months, and 200,000 IU to children ≥ 12 months. If the child has clinical ophthalmic signs of vitamin A deficiency such as Bitot's spots, give a third dose four to six weeks later (5).

Case management for complications of measles such as otitis media, pneumonia and diarrhoea should be managed using the Integrated Management of

Childhood Illness (IMCI) case management algorithm or based on recommendations in country (6). Severe measles cases, such as those with severe pneumonia, dehydration or seizures, require specific treatment (antibiotics, rehydration, anticonvulsants) and should be treated as inpatients due to the increased risk of mortality. IMCI specifically recommends assessment and treatment of measles cases with eye and mouth complications among children (6). Measles cases should be isolated from non-measles cases in health facilities; non-hospitalized measles cases should be isolated in the home until four days after rash onset.



CONTACT TRACING AND MANAGEMENT

Because of its infectious nature, contact tracing is essential to determine both the source of infection for the measles case (endemic versus imported/importation-related), as well as identify those whom the case may have subsequently infected. Any person who had contact with the case in the four days before and after rash onset may have been infected and should be monitored by public health authorities for 23 days from last contact with the confirmed case. Contact refers to sharing the same air space, usually an enclosed area (example living in the same household or being in the same room, school, health facility waiting room, office or transport) for any length of time with a case during the case's infectious period. Additionally, the virus remains contagious in the air or on infected surfaces for up to two hours; this should be considered when conducting contact tracing as transmission can occur even if the contact was not in the same room at the exact same time as the case. In some investigations, contacts are considered those sharing an enclosed airspace with a case within two hours of when the case was there. Contact tracing is particularly important in schools due

to the intensity of exposure and the presence of non-immune children. In health care settings measles can also be amplified, with an elevated risk due the presence of vulnerable, susceptible populations such as the very young, the immunocompromised and patients with underlying immunocompromising illnesses.

Unvaccinated contacts ≥ 6 months of age who are eligible for vaccination should be vaccinated for prophylaxis, if possible within 72 hours of exposure. This can prevent or ameliorate clinical presentation of measles infection. Any doses given younger than the age of routine first measles dose (MCV1) at 9–12 months of age, are referred to as MCV0 and do not count. For contacts that have contraindications to measles vaccine, human immune globulin may be administered intramuscularly within six days of exposure. This includes pregnant women, infants < 6 months of age and individuals with impaired immune systems. If administered within six days of exposure, this method of passive immunization can prevent illness or reduce its severity.



SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

DEFINITION OF AN OUTBREAK

A single laboratory-confirmed measles case should trigger an aggressive public health investigation and response in an elimination setting. An outbreak is defined as two or more laboratory-confirmed cases that are temporally related (with dates of rash onset occurring 7–23 days apart) and epidemiologically or virologically linked, or both.

An outbreak is considered over after there have been no further epidemiologically or virologically linked cases for two incubation periods (46 days) from the date of onset of the last case.

CHANGES TO SURVEILLANCE DURING AN OUTBREAK

Countries should develop a detailed outbreak response plan before an outbreak occurs. This plan should include how surge capacity will be managed to provide staff for epidemiological investigations and response, as well as supplies and staffing for an increased volume of laboratory testing. Consider the following changes to surveillance during outbreaks:

- Routine passive surveillance should be enhanced during an outbreak (for example, increasing awareness and messaging to clinicians and laboratories). Active surveillance should be established, with laboratory confirmation of cases that are identified by regular visits and record review at health facilities (both public and private, and other settings). The investigation should also include efforts to retrospectively find any cases that preceded the first reported case to help determine the time and circumstances of the beginning of the outbreak and better assess its full extent. Establish intensified surveillance in neighbouring villages, districts and possibly provinces in response to laboratory-confirmed cases or outbreaks to detect and minimize the spread of the outbreak.
- When outbreaks become too large to maintain normal case investigation protocols, deprioritize contact tracing and prioritize a large public health response.
- Public health can move to line listing cases and decrease the number of elements required to be collected for each individual case. However, continue to collect at a minimum the unique identifier, name, age, clinical symptoms, date of rash onset, date of specimen collection, vaccination status, travel history and residence. When possible, also assign an outbreak identifier to all cases associated with an outbreak. More detailed information such as potential sources of infection (medical settings, school settings, etc.) should be collected on a sample of cases to help determine major transmitters and transmission settings.
- Laboratory specimens should be collected from approximately the first 5–10 suspected cases in an outbreak; at least 80% (4 of 5 or 8 of 10) of these suspected cases in the same village or neighbourhood should be laboratory-confirmed before moving to epidemiologically linking cases. If less than 80% of the suspected cases are laboratory-confirmed as measles, continue with sample collection. Specimens are not needed from suspected cases that satisfy the clinical case definition and that can be epidemiologically linked to a laboratory-confirmed or other epidemiologically linked case. Epidemiological linkage should be the primary way that new cases are classified during a confirmed outbreak. However, criteria for epidemiological linkage must be sufficiently strict to provide confidence of a high positive predictive value that the epidemiologically linked case is a true measles case. Criteria for epidemiological linkage include being a known contact, being in the same physical setting as the case during their infectious period (shared enclosed airspace such as at home, school or workplace). In elimination settings, as well as where possible in endemic settings, it is no longer recommended that all cases in a given district in a month all be categorized as epidemiologically linked. It is preferable to do better investigations to understand potential relationships between cases. If epidemiological linkage is not established, laboratory testing of the suspected case should be done. After initial confirmation of the outbreak, laboratory testing should be done for suspected cases that arise in new locations or in previously unaffected groups. It is important that the field teams and the laboratory coordinate their work to make sure laboratory results can be interpreted in the context of the field investigation.
- If an outbreak continues over a protracted period, another 5–10 samples should be collected every two months to ensure that the outbreak is still due to measles. Genotyping becomes particularly important when the duration of an outbreak is approaching 12 months in a country in which measles was previously eliminated, in order to determine whether cases are part of the same outbreak or due to new importations of a different measles virus strain.
- Establish intensified passive reporting and active surveillance in neighbouring villages, districts and possibly provinces in response to laboratory-confirmed cases or outbreaks to characterize the extent of the outbreak.
- Analyse epidemiological data rapidly to identify vulnerable groups with low immunity and targeting responsive immunization activities appropriately.

OUTBREAK INVESTIGATION

Conduct local risk assessments such as rapid community surveys and health facility vaccination record review in outbreak areas, neighboring villages, health center catchment areas, districts, and possibly provinces, depending on the extent of the outbreak. This includes ensuring that 1st and 2nd dose measles vaccination coverage in the area is sufficiently high ($\geq 95\%$) to prevent measles transmission. Children who are unvaccinated or under-vaccinated should receive vaccine through routine services.

In some settings, it may be important to do epidemiological studies, such as case-control/cohort studies to determine vaccine effectiveness or risk factors and transmission patterns, to investigate the outbreak, complete the epidemiological synthesis and decide what action is required. At a minimum, all outbreak investigations should include an evaluation of which age/birth cohorts are most affected and why the affected individuals and communities are unvaccinated, in order to guide the programme in the future. This can be done after the outbreak is over rather than during the outbreak, when many resources are already taxed.

In outbreak settings, it is especially important to determine potential sources of infection. Surveillance is often focused on reports from health care facilities. However, not all measles cases will seek health care. For example, an older person with measles may have been exposed to school-aged children, who may be missed if investigation is focused solely on persons who visit health care facilities. Such persons may be playing a major role in transmission. Going into communities and asking families of persons with measles whom they

might have been exposed to during the relevant time period can help identify persons with measles who are the major transmitters. In family investigations, it is also important to determine whether there are additional cases as well as the characteristics of the index (initial) case in the family.

PUBLIC HEALTH RESPONSE

Outbreak response immunization is usually indicated. The extent of the vaccination response will depend on the epidemiological picture. For sporadic cases and small outbreaks of fewer than 10 cases in geographically limited (same village) or low-risk areas, it may be sufficient to do selective immunization of contacts and children 6–59 months of age in the immediate area of the outbreak (involved and surrounding villages). Older children may need to be immunized as well, depending on the local disease epidemiology. In outbreak settings, the lower age of vaccination should be reduced to six months of age. Susceptible health staff should also be vaccinated to prevent possible transmission in health care settings to high-risk individuals. Routine immunization services should be reinforced. For larger outbreaks, or when the risk assessment indicates there are large areas at risk, consider doing an immunization campaign that non-selectively targets larger areas. The target age group should be determined by disease epidemiology and population immunity profiles.

As part of post-outbreak recovery, conduct an assessment of the immunity profile and gaps and develop a strategy to ensure measles control will be sustained.



SPECIAL CONSIDERATIONS FOR MEASLES SURVEILLANCE

SEROSURVEYS

High-quality representative serosurveys can provide ancillary evidence that a country has achieved high population immunity in line with achieving and sustaining measles elimination. The main purpose of conducting serosurveys in the context of measles and rubella elimination is to identify areas and age cohorts with potential immunity gaps. Serologic testing cannot distinguish between immunity from natural measles infection and vaccine-derived immunity. Serosurveys should not be used as a substitute for surveillance, and can be quite costly and time consuming to undertake.

RISK ASSESSMENTS

A multitude of factors must be evaluated when assessing the risk of an area for a measles outbreak. The WHO *Measles Programmatic Risk Assessment Tool* was developed to help national programmes to identify areas not meeting measles programmatic targets, and use the findings to guide and strengthen measles elimination programme activities and reduce the risk of outbreaks. This tool triangulates data from surveillance and the

immunization programme to give a more complete map of subnational risk of measles outbreaks. One limitation of the tool is that it focuses primarily on early childhood risk. Further information on this tool is available here: http://www.who.int/immunization/monitoring_surveillance/routine/measles_assessment/en/ (7).

HUMANITARIAN EMERGENCIES

Measles is a highly infectious disease with grave consequences during humanitarian emergencies, especially those emergencies with displaced populations and among the malnourished. In these setting, surveillance must be able to identify suspected measles cases and may need to be modified to include, for example, daily reporting and community-based surveillance. Further information is available in Vaccination in Acute Humanitarian Emergencies: A Framework for Decision Making, available here: <http://apps.who.int/iris/bitstream/10665/255575/1/WHO-IVB-17.03-eng.pdf> (8).



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