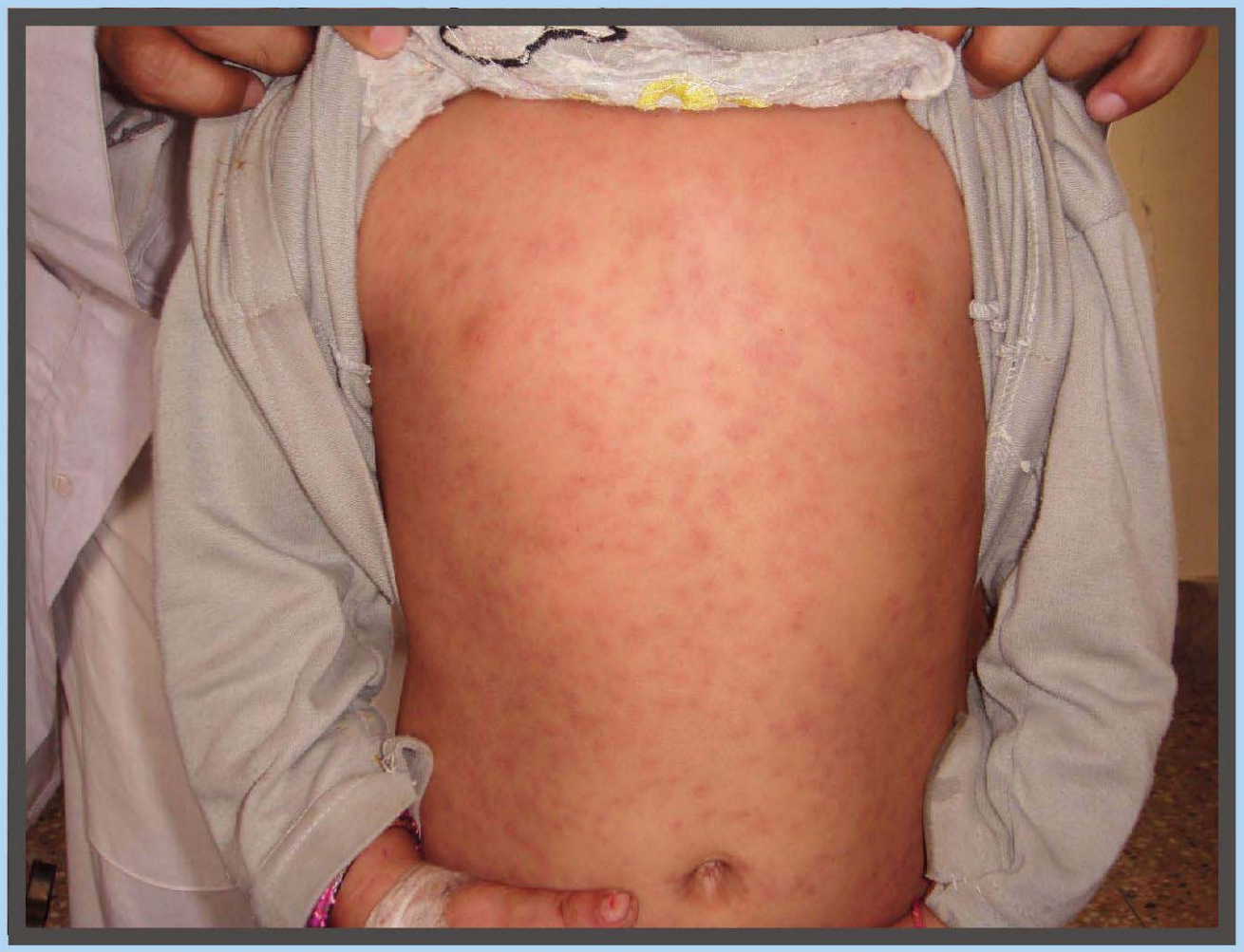
EMRO Technical Publications Series 36

Field guidelines for surveillance of measles, rubella and congenital rubella syndrome



World Health Organization
Regional Office for the Eastern Mediterranean

EMRO Technical Publications Series 36

Field guidelines for surveillance of measles, rubella and congenital rubella syndrome

World Health Organization
Regional Office for the Eastern Mediterranean

WHO Library Cataloguing in Publication Data

World Health Organization. Regional Office for the Eastern Mediterranean
Field guidelines for surveillance of measles, rubella and congenital rubella syndrome / World Health Organization. Regional Office for the Eastern Mediterranean
p. .- (EMRO Technical Publications Series ; 36)
ISBN: 978-92-9021-742-8
ISBN: 978-92-9021-743-5 (online)
ISSN: 1020-0428
1. Measles - epidemiology 2. Rubella - epidemiology 3. Rubella Syndrome, Congenital - epidemiology 4. Epidemiologic Methods 5. Guideline I. Title II. Regional Office for the Eastern Mediterranean III. Series
(NLM Classification: WC 590)

Design, layout and printing by WHO Regional Office for the Eastern Mediterranean, Cairo, Egypt

Contents

In the name of God, the Compassionate, the Merciful

Foreword

Great progress has been made toward measles elimination in the Eastern Mediterranean Region since 1997 when the WHO Regional Committee for the Eastern Mediterranean passed a resolution (EM/RC44/R.6) to eliminate measles by 2010. This progress has been achieved thanks to the successful implementation of measles elimination strategies in the Region, particularly the high attainment of measles vaccine coverage and the implementation of a laboratory-supported measles case-based surveillance system in most countries.

Countries within the Region are at different stages of elimination. Some countries are still experiencing a high burden of disease and measles surveillance remains suboptimal. Other countries appear close to elimination, however surveillance systems are not up to the standards of elimination. Therefore, as most performance indicator targets are still not being met, measles elimination cannot be validated. There is an urgent need for a well-performing measles surveillance system to assess the burden of the disease and to measure the progress towards measles elimination in the Region.

The WHO Regional Office for the Eastern Mediterranean, in collaboration with other partners, particularly the US Centers for Disease Control and Prevention (CDC), Atlanta, has developed these guidelines to help establish high-quality measles, rubella and congenital rubella syndrome (CRS) surveillance systems. These guidelines provide practitioners in the field with the tools to identify, report and investigate cases of measles, rubella and congenital rubella syndrome. They also provide information on laboratory testing, identifying measles and rubella suspected cases, analysing data and monitoring the performance of the surveillance system.

It is hoped that, through the use of these guidelines, better information on measles and rubella can be obtained, which, in turn, will improve the performance of prevention programmes and reduce the incidence of morbidity and mortality due to measles and rubella.

Hussein A. Gezairy MD FRCS

WHO Regional Director for the Eastern Mediterranean

Preface

One of the strategies to reduce measles mortality is to enhance the surveillance of measles and rubella and integrate epidemiological and laboratory information. Since 2006, 19 countries of the Eastern Mediterranean Region have conducted case-based surveillance and a regional laboratory network has been established in all 22 countries, including two regional reference laboratories– one in Oman and the other in Tunisia. However, in most countries, the surveillance system for measles, rubella and congenital rubella syndrome (CRS) is not up to the same standard as the surveillance system for measles.

In 2006, the regional measles technical advisory group recommended that the Regional Office develop guidelines for the surveillance of measles, rubella and CRS. An extensive review of the literature was conducted to ensure that the guidelines were supported by all available evidence on the methods used to design and implement these surveillance systems. The review included measles surveillance guidelines already developed by the World Health Organization and the Pan American Health Organization (PAHO), WHO position papers on measles and rubella and guidelines and articles on the progress towards measles elimination produced by Centres for Disease Control and Prevention, Atlanta, USA. The first draft of these guidelines was reviewed by staff of the vaccine preventable diseases and immunization programme of the Regional Office and then by staff of the Global Immunization Division, Centres for Disease Control and Prevention. The document was also shared with country managers of the Expanded Programme on Immunization and surveillance and laboratory staff of all countries in the Region. In 2008, the guidelines were further reviewed during an intercountry meeting on measles held in the United Arab Emirates and by members of the regional measles/rubella technical advisory group. Finally, the document was reviewed by the surveillance officer focal point for measles at WHO headquarters. All steps have been taken to identify and manage any circumstances that could give rise to a conflict of interest. The development process was reviewed and approved by the WHO Guidelines Review Committee.

These field guidelines for the surveillance of measles, rubella and CRS are to be used as technical resource material in developing comprehensive standard operating procedures for measles, rubella and CRS surveillance. The largest part of these guidelines is devoted to developing a surveillance system for cases of measles, rubella and CRS, including case investigation, outbreak response, laboratory procedures for measles and rubella testing and surveillance monitoring and feedback.

This publication is primarily intended for use by surveillance and national immunization managers and their staff, but many other health professionals and technical staff working in surveillance, immunization and laboratories at the country level will find it useful in improving measles, rubella and CRS surveillance. It can be used at various levels of the health care system and by all countries. Countries may need to adapt these guidelines to their local situations. It will provide information to relevant staff on how to comply with the requirements needed in order to ensure a well performing measles/surveillance system that is able to validate measles and rubella elimination.

This is the first edition of the *Field guidelines for the surveillance of measles, rubella and congenital rubella syndrome* developed by the Regional Office for the Eastern Mediterranean. Comments, suggestions and recommendations from users of these guidelines are welcome. The elimination of measles in general, and surveillance in particular, are part of an evolving and dynamic process, and hence, it is expected that the guidelines will be updated as needed.

Acknowledgements

This publication is the product of contributions by several individuals. The publication was written by Boubker Naouri, WHO Regional Office for the Eastern Mediterranean, Egypt. The development process was reviewed and approved by the WHO Guidelines Review Committee. The draft was reviewed by Susan Reef, Amra Uzicanan and James Alexander (Centres for Disease Control and Prevention, Global Immunization Division, United States of America), Alya Dabbagh and David Featherstone (Immunization, Vaccines and Biologicals, WHO headquarters, Switzerland), Hinda Ahmed and Raef Bekhit (Vaccine Preventable Diseases, WHO Regional Office for the Eastern Mediterranean, Egypt). Reviewers also included all EPI managers, surveillance officers and laboratory staff in the WHO Eastern Mediterranean Region.

1. Introduction

Measles, rubella and congenital rubella syndrome (CRS) remain important preventable causes of infectious disease morbidity and mortality. Measles remains a leading cause of death among young children, despite the availability of a safe and effective vaccine since the early 1960s. In 2007, the latest year for which figures are available (*1*), globally, an estimated 197 000 people died from measles, most of whom were children. In the WHO Eastern Mediterranean Region, 15 670 cases of measles were reported in 2007 compared to 38 592 in 2000 (*2*). An estimated 10 000 measles deaths[1] occurred in 2007, compared with 106 000 in 2000, representing a 95% decrease (*3*). Thus, the goal of the Global Immunization and Vaccination Strategy (GIVS) of reducing measles mortality by 95% by 2010 was reached three years earlier in the Region. However, the number of measles cases reported to the WHO Regional Office for the Eastern Mediterranean does not represent the true number of cases as some countries (Morocco, Pakistan and Somalia) have not yet developed a nationwide case-based measles surveillance system.

In 2006, globally, 251 311 cases of rubella and 191 cases of CRS were reported (2007 data not available). During the same year, 3685 rubella cases were reported to the Regional Office. However, only 10 countries[2] in the Region have developed surveillance systems to monitor CRS cases. In 2007, these 10 countries reported 23 cases of CRS to the Regional Office.

In 1997, the Member States of the Region resolved to eliminate measles by 2010 (*4*). Since then, many countries have implemented measles elimination strategies, have been working towards the elimination of the measles virus and have elected to accelerate rubella control/elimination.

One of the strategies for eliminating measles is to enhance measles and rubella surveillance through integration of epidemiological and laboratory information. As the number of cases of measles declines, the importance of surveillance will become even greater, to identify and aggressively respond to cases and outbreaks. It will become increasingly crucial that all suspected cases of measles are reported, using surveillance for febrile rash illnesses, and that samples from sporadic cases are submitted for full laboratory investigation. Specific performance indicators have been developed to regularly monitor the measles/rubella surveillance system.

2. The diseases

2.1 Measles

2.1.1 The organism

Measles is an acute illness caused by a virus of the genus *Morbillivirus* (a member of the *Paramyxovirus* family); humans are the only reservoir.

2.1.2 Transmission

Transmission is primarily person-to-person via aerosolized respiratory droplets or by direct contact (*5*). Measles is highly infectious and the disease spreads easily in areas where infants and children gather, for example, in health care centres and schools. Individuals with measles are infectious from 2–4 days before until 4 days after rash onset. Conditions such as high birth rates, overcrowding and the influx of large numbers of susceptible children from rural areas can facilitate measles transmission. A small percentage of susceptible individuals

[1] The number of deaths is estimated by a model, and the reported number of cases likely reflects gross under-reporting of measles, which explains the apparent discrepancy between the reported number of cases and estimated number of deaths.

[2] Bahrain, Egypt, Jordan, Lebanon, Morocco, Oman, occupied Palestinian territory, Qatar, Saudi Arabia, Syrian Arab Republic.

are sufficient to maintain virus circulation in populations of a few hundred thousand. In areas with tropical climates, most cases of measles occur during the dry season, whereas in areas with temperate climates, the incidence peaks during late winter and early spring (5).

2.1.3 Clinical features

After an incubation period of approximately 10–14 days (range 8–15 days), from exposure to onset of rash, prodromal symptoms of fever, malaise, cough, coryza (runny nose) and conjunctivitis appear in non-immune persons exposed to the virus.

The rash appears behind the ears and on the face, accompanied by a high fever. Fever can be as high as 40.6°C (105°F). The rash is maculo-papular, made up of large, blotchy red spots (macules are circumscribed areas of change in normal skin colour, with no skin elevation or depression; they may be of any size). The rash typically spreads from the head to the trunk and then extremities, lasts 3–7 days, and may be followed by a fine desquamation. Koplik spots may occur on the buccal mucosa shortly after the onset of rash and for about 1–2 days afterwards.

A modified form of measles, with generally mild symptoms, may occur in infants who still have partial protection from maternal antibodies and occasionally in persons who received only partial protection from the vaccine.

2.1.4 Differential diagnosis

Infections with a number of other viruses can present with a rash resembling that of measles, including rubella virus, *parvovirus, enterovirus*, *adenovirus* and human *herpesvirus 6*.

2.1.5 Complications

Complications of measles include otitis media, pneumonia, diarrhoea, febrile seizure, blindness and encephalitis. Less common complications include protein energy malnutrition, convulsions and brain damage. Unless managed early and aggressively, these complications may lead to death within the first month after rash onset. The case-fatality rate from measles is estimated to be 3%–5% in developing countries but may reach more than 10% during epidemics in certain settings. Malnutrition and infection with human immunodeficiency virus (HIV) are risk factors for complications and mortality.

2.1.6 Immunity

Measles-specific immunoglobulin M (IgM) antibodies are detectable within 4 days after onset of the rash and can persist for up to 4–12 weeks. Natural infection produces lifelong immunity. Infants born to mothers who have either had measles or been vaccinated are protected by trans-placental acquired maternal antibodies. The protection from this passive immunity lasts 6 to 9 months on average (5).

2.1.7 Measles vaccines

Measles vaccines contain live, attenuated virus. Following vaccination, the long-term persistence of neutralizing measles antibodies (26–33 years) and long-lasting protection against measles have been demonstrated by several investigators. However, it is not definitively known whether a single dose of measles vaccine, without natural boosting by recurrent measles exposure, will result in lifelong protection. Studies using IgG avidity measurements to separate primary vaccination failures from secondary vaccination failures suggest that secondary failures may occur at least occasionally (5,6,7).

Measles-containing vaccine can be safely and effectively administered to children with mild acute illnesses, such as low-grade fever, diarrhoea and upper respiratory tract infections. However, severely-ill children with high fever should not be vaccinated until they have recovered. People who

have experienced an anaphylactic or severe hypersensitivity reaction to a previous dose of measles/mumps/rubella (MMR) vaccine or its component vaccines or who have experienced an anaphylactic reaction to neomycin, gelatine or another component of the vaccine should not be vaccinated (*5*). In countries where HIV infection is prevalent, infants and children should be immunized with the EPI antigens according to standard schedules. However, measles vaccine is contraindicated in people who are severely immunocompromised due to congenital disease; severe HIV infection; advanced leukaemia or lymphoma; serious malignant disease; treatment with high-dose steroids, alkylating agents or antimetabolites; or who receive immunosuppressive therapeutic radiation (*5*). As vaccinated persons do not transmit vaccine virus, the risk to these patients of being exposed to measles may be reduced by vaccinating their direct susceptible contacts. Rubella-containing vaccine should not be administered to pregnant women (*5*). This contraindication is based on theoretical reasons, as there is currently no evidence to suggest that children born to pregnant women who received measles or MMR vaccines during pregnancy are adversely affected (*5*).

2.1.8 Treatment

There is currently no specific treatment for measles infection. Administration of vitamin A to children with measles has been shown to decrease both the severity of disease and the case-fatality rate, and WHO recommends that vitamin A be administered to all children with acute measles (*8*). Case management of measles cases is discussed in detail in Section 6.2.

2.2 Rubella

2.2.1 The organism

Rubella is an acute illness caused by a virus of the family *Togaviridae*.

2.2.2 Transmission

The rubella virus, while less contagious than that of measles, is also transmitted by respiratory droplets and by direct contact with the nasal and throat secretions of infected persons. While individuals with rubella may shed virus from 7 days before to 14 days after the onset of rash, 25% to 50% of infections are asymptomatic.

2.2.3 Clinical features

Rubella is a common cause of maculopapular rash illness with low-grade fever. Symptoms in children and adults are often mild, and children often do not have fever. In addition to fever and rash, individuals with rubella frequently have lymphadenopathy, and up to 60% of adult women with rubella have joint symptoms. Up to 50% of rubella infections are subclinical or asymptomatic.

2.2.4 Differential diagnosis

Other causes of rash illness with fever include measles, dengue, *parvovirus* B19, human *herpesvirus* 6, Ross River virus, Chikungunya virus, *enteroviruses*, *adenoviruses* and *Streptococcus* group A (beta hemolytic).

2.2.5 Complications

Rubella has few complications unless the virus is contracted by a susceptible pregnant woman. A primary rubella infection (i.e. infection of a susceptible woman) during pregnancy may result in spontaneous abortion, stillbirth or fetal death; an infant born with CRS; an infant born with congenital rubella infection (CRI) without congenital defects; or birth of a normal infant.

2.2.6 Immunity

Rubella-specific IgM antibody usually appears within 4 days after onset of the rash and can persist for up to 4–12 weeks. Rubella-specific IgG antibody begins to rise after the onset of the rash, peaks about 4 weeks later, and

generally lasts for life; it is a long-term marker of previous rubella infection. Natural infection produces lifelong immunity.

2.2.7 Rubella vaccine

The rubella vaccine widely used around the world is based on the live attenuated RA27/3 strain of rubella virus. Protective antibodies against rubella develop in >95% of vaccinees 21–28 days after vaccination. One dose of rubella vaccine probably confers lifelong immunity in more than 95% of people immunized.

The primary purpose of rubella vaccination is to prevent the occurrence of CRS. Two approaches are recommended for CRS prevention (*9*), which are:

- prevention of CRS only through immunization of adolescent girls and/or women of childbearing age.
- elimination of rubella, as well as CRS, through universal routine vaccination of infants with/without mass campaigns, surveillance and ensuring immunity in women of childbearing age.

Rubella vaccine is very safe. Most adverse reactions reported following MMR vaccination (such as fever and rash) are attributable to the measles component. The most common complaints following vaccination are fever, lymphadenopathy and arthralgia. Rubella vaccination should be avoided in pregnancy because of the theoretical, but never demonstrated, teratogenic risk (*9*).

2.2.8 Treatment

There is no specific treatment for rubella or for CRS. Patients with rubella should drink plenty of fluids and may take medication to reduce mild fever. Infants with CRS should be treated for their specific problems.

2.3 Congenital rubella syndrome

A rubella-infected fetus carried to term may be born with CRS. Some defects associated with CRS may be recognizable at birth, while others are detected months or even years later. CRS manifestations may be transient (e.g. purpura), permanent structural manifestations (e.g. deafness, central nervous system defects, congenital heart disease, cataract), or late-emerging conditions (e.g. diabetes mellitus).

At birth, the sera of infants with CRS contain maternally derived rubella-specific IgG antibodies, as well as IgG and IgM antibodies synthesized by the fetus. In contrast, only maternal rubella-specific IgG is found in the sera of normal infants born to women who are immune to rubella. Infants with CRS may shed rubella virus from body secretions for up to 27 months, although most infants stop shedding by one year of age. Infants who shed rubella virus are infectious, and rubella outbreaks have occurred among health care workers caring for infants with CRS.

3. Measles, rubella and CRS surveillance objectives

Surveillance is the ongoing systematic collection, analysis and interpretation of outcome-specific data for use in planning, implementing and evaluating public health practice. The primary surveillance goal is to detect and investigate all suspected measles cases, including imported ones, and to implement activities which prevent or limit secondary transmission (*10*). Besides the rapid detection of cases, a surveillance system that maintains a satisfactory record over several years will be crucial to the eventual validation of measles elimination.

3.1 Measles surveillance objectives

Every measles case could potentially spark an outbreak, especially if under-vaccinated groups are exposed. Surveillance and prompt investigation of cases and contacts contribute to halting the spread of disease. Information obtained through surveillance is also used to assess progress towards disease elimination goals. Surveillance data are used to characterize persons, groups or areas in which additional efforts are required to reduce disease incidence. Surveillance data are essential for:

- documenting disease burden and describing the characteristics of measles cases;
- identifying high-risk populations;
- understanding the reasons for the occurrence of the disease and developing appropriate control measures;
- predicting, detecting and investigating outbreaks to ensure proper case management and to determine why outbreaks have occurred (e.g. failure to vaccinate, vaccine failure, or an accumulation of susceptible persons). Measles surveillance also helps to determine when the next outbreak might occur due to the build-up of susceptible persons and accelerates prevention activities beforehand;
- providing evidence that, in countries with low measles incidence, the absence of reported cases is attributable to the absence of disease rather than to inadequate detection and reporting;
- detecting any importation of virus into a community and determining whether transmission is sustained, following an importation, from the size, nature and duration of clusters and the genotypic diversity of circulating viral strains;
- monitoring progress towards achieving disease control and elimination goals.

3.2 Rubella/CRS surveillance objectives

Case-based surveillance of rubella is essentially conducted in exactly the same way as measles. The objectives of rubella/CRS surveillance are:

- identifying populations at risk and guiding vaccination strategies;
- determining where the virus is circulating;
- detecting cases in a timely manner in order to carry-out outbreak control and CRS prevention measures;
- providing evidence of the impact of interventions.

4. Establishing and strengthening an integrated measles/ rubella/CRS surveillance system

In order to achieve regional measles elimination goals, one of the important strategies is establishing effective surveillance for measles, including laboratory confirmation of cases and outbreaks and an opportunity to assess the population immunity profile through the vaccination status of cases.

4.1 General principles

The three main components of a measles/ rubella and CRS surveillance system are:

- detection and notification of suspected cases;
- investigation, including active case searches, timely collection of blood samples and laboratory workup and final classification;
- using surveillance data for action.

Effective surveillance systems are necessary at the district, provincial and national levels. Such systems need to be country-wide, sensitive and case-based. Legislative changes may be required in countries where mandatory reporting does not exist for measles, rubella and CRS, to facilitate the operation of the surveillance system. Countries are encouraged to use the infrastructure and operating procedures (zero reporting, active surveillance, etc.) of the existing acute flaccid paralysis (AFP) surveillance system to develop measles, rubella and CRS surveillance systems.

Measles, rubella and CRS surveillance should be case-based. A case-based surveillance system collects a core data set at national level on each case, including but not limited to, information on age, gender, vaccination status, date of last vaccination received, place of residence, travel history, date of rash onset, disease outcome, etc. Case-based surveillance allows for analysis of measles epidemiology to guide control efforts.

4.1.1 Integrated disease surveillance

Many countries have multiple reporting systems for measles, such as programmes managed by the communicable disease programme, EPI programme and school health programme. Ideally, countries should integrate these efforts in a unified system. This might be done within the frame of integrated disease surveillance that should carry out many functions using similar structures, processes and personnel. The surveillance activities that are well developed in one area may act as driving forces for strengthening other surveillance activities, offering possible synergies and common resources. The integrated disease surveillance strategy aims to improve the availability and use of surveillance and laboratory data for control of priority infectious diseases that are the leading cause of death, disability and illness in a country.

Given the similarities in clinical presentation, epidemiologic investigation and laboratory workup, surveillance for measles/rubella should be fully integrated (*11*). Reporting and investigation of suspected cases of measles or rubella should thus follow the same channels and procedures. Except for outbreaks, all serum specimens of suspected cases should be tested for both measles- and rubella-specific IgM.

4.1.2 Core surveillance functions

Core surveillance functions are case detection, reporting, investigation (including confirmation of diagnosis), data analysis, interpretation and control activities. The national level should establish the following standards for surveillance to achieve maximum efficiency and ensure that data are comparable throughout the country.

- Case definitions and guidance on final classification of cases
- Identification and reporting of measles/rubella and CRS cases
- Type of surveillance to be conducted (zero reporting, active surveillance)
- Data to be collected and forms/data collection tools to be used
- Laboratory diagnosis methods
- Minimum data analysis by level (district, provincial, national)
- Procedures and indicators for monitoring surveillance quality
- Routine reports to be produced
- Surveillance data dissemination and the use of data in decision-making.

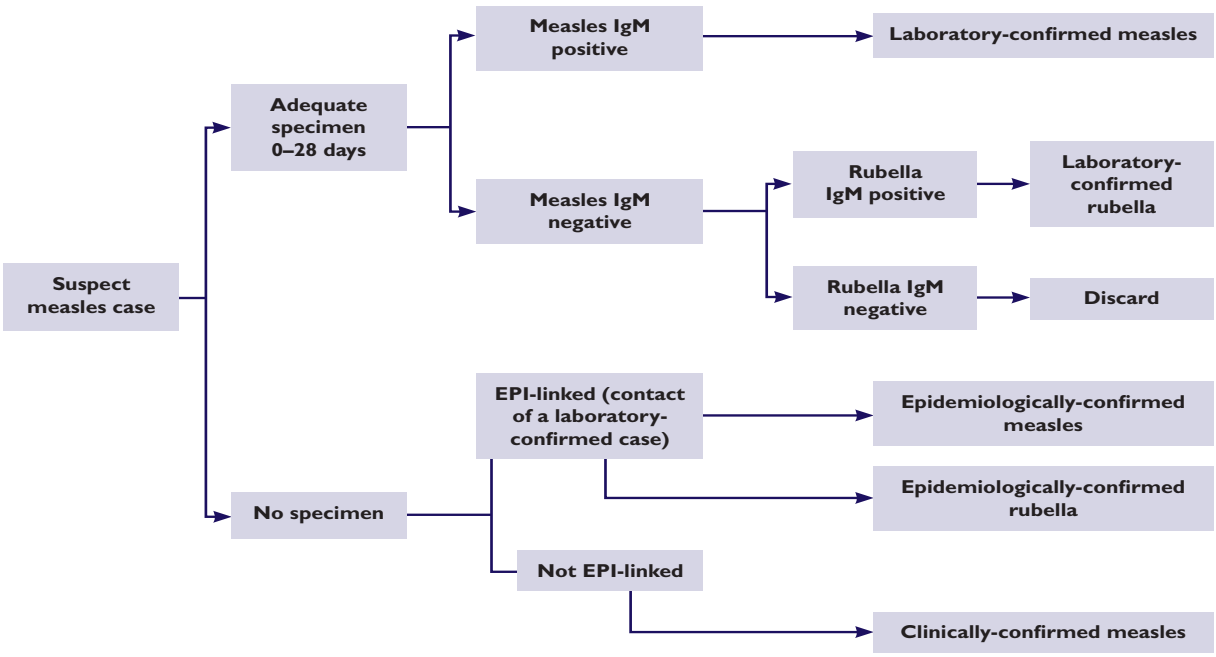
4.2 Case definitions

4.2.1 Measles case definition

Case definitions according to which a measles case can be classified are presented below. There should be widespread dissemination of the national case definition to all health

workers, together with encouragement to report cases, as needed. WHO recommends the following clinical and laboratory case definitions of measles (*10*).

- The clinical case definition of measles is:
  - any person in whom a health care worker suspects measles infection, *or*
  - any person with fever and maculo-papular rash (i.e. non-vesicular), and one or more of the following: cough or coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes).
- Measles laboratory criteria for diagnosis: presence of measles-specific IgM antibodies.
  - All suspected cases should be classified into one of the four following mutually exclusive categories, i.e. laboratory-confirmed cases, clinically-confirmed cases, EPI-linked cases or discarded cases, by using the laboratory classification of measles/rubella (Figure 1).
  - Clinically confirmed: a case that meets the clinical case definition and for which no adequate blood specimen was taken.
  - Laboratory confirmed: a case that meets the clinical case definition and is laboratory confirmed by detection of IgM antibody in serum.
  - Epidemiologically confirmed: a case that meets the clinical case definition and that is linked epidemiologically to a laboratory-confirmed case. Epidemiological linkage is defined as direct contact with another laboratory-confirmed measles case or another epidemiologically-linked case within the last 7 to 21 days before onset of illness.



Source: Pan American Health Organization, Pan American Sanitary Bureau, Regional Office of the World Health Organization. Measles and rubella surveillance integration in the Americas. *EPI Newsletter*, 2000, 22:4–5.

Figure 1. Laboratory classification of measles/rubella scheme

– Discarded: A suspected case that has had an adequate investigation, including collection of a blood specimen during the appropriate time frame, but lacks serologic evidence of a measles virus infection.

Suspected cases that have no specimen or equivocal laboratory results but are also confirmed as another disease may be discarded. Also, cases that are EPI-linked to confirmed cases of other communicable diseases should also be discarded as non-measles (e.g. a suspected case that is EPI-linked to a laboratory-confirmed rubella case during a rubella outbreak). Suspected measles cases should be classified by qualified health workers (doctors, epidemiologists, laboratory personnel, etc.) at the district or provincial level.

The case definition given above has a high sensitivity for measles. However, countries may elect to choose to use the case definition "rash and fever" to make the surveillance sensitive enough to detect all measles cases and meet the criteria for measles elimination. However, suspected cases may not be "true measles cases", particularly in areas of low measles prevalence. As the incidence of measles decreases, individuals meeting the clinical case definition will increasingly have rash illnesses other than measles, such as rubella, roseola infantum, scarlet fever, etc. For these reasons, WHO recommends enhanced measles surveillance based on the serological confirmation of all suspected cases of measles, once the case load has been brought down through the implementation of effective measles control interventions (*10*).

4.2.2 Vaccine-related cases

Two situations exist in which an IgM-positive result is not associated with a case having a wild-type measles virus. First, patients (up to 5% of those vaccinated) who were recently vaccinated with measles- or rubella-containing vaccines and who subsequently develop a rash, would ideally be reported as a suspected case and usually have an IgM-positive result (11). Second, the specificity of the kits for the detection of measles- or rubella-specific IgM (i.e. the ability to rule out a measles or rubella virus infection) is not 100%. Some patients with eruptive (rash) illness, such as dengue or erythema infectiosum, may test positive for measles- or rubella-specific IgM. The Pan American Health Organization (PAHO) uses the following five clinical and epidemiological criteria for the classification of measles case as vaccine-related (*11*).

- The patient had a rash illness, with or without fever, but did not have cough or other respiratory symptoms related to the rash.
- The rash began 7–14 days after vaccination with a measles-containing vaccine.
- The blood specimen which was IgM-positive was collected 8–56 days after vaccination.
- A thorough field investigation did not identify an index case or any secondary cases; and
- Field and laboratory investigation failed to identify other causes (including the inability to identify wild-type measles virus in culture).

Based on the infection source, confirmed cases should further be classified into one of three mutually exclusive categories.

- An imported measles case is a confirmed case which, as supported by epidemiological and/or virologic evidence, was exposed outside of the country during the 7–21 days prior to rash onset. For rubella, the time frame is 12–23 days.
- An import-related case is a confirmed case which, as supported by epidemiological and/or virologic evidence, was exposed

locally as part of a transmission chain initiated with an imported case.
- A case with unknown source of infection is a confirmed case for which the source of infection was not identified.

Classification of confirmed cases by infection source is critical to evaluate whether endemic circulation of measles virus has been interrupted or, if interrupted, re-established in a country. In particular, re-establishment of endemic transmission is defined as a situation in which a chain of transmission continues uninterrupted for a period of more than 12 months. Classification of measles cases should be done through regular and frequent meetings of surveillance, laboratory and EPI staff.

For surveillance purposes, a measles death is defined as any death from an illness that occurs in a confirmed case of measles within one month of the onset of rash.[3] The immediate and delayed complications of measles, such as pneumonia or persistent diarrhoea, which are the complications most responsible for measles deaths, may manifest and result in death much later than the disappearance of the rash.

4.2.3 Rubella case definition

The following case definitions are recommended for the surveillance of rubella (*12*).

- Suspected rubella case: a patient of any age in whom a health worker suspects rubella. A health worker should suspect rubella when a patient presents with fever, maculopapular rash and cervical, sub-occipital or post-auricular adenopathy or arthralgia/arthritis.
- Clinical confirmation: rubella cannot be confirmed clinically; laboratory confirmation is required.
- Laboratory-confirmed rubella case: a laboratory-confirmed case is a suspected case with a positive blood test for rubella-specific IgM. The blood specimen should be obtained within 28 days of rash onset.
- Epidemiologically-confirmed rubella case: a patient with a rash illness that is linked epidemiologically to a laboratory-confirmed rubella case.

4.2.4 CRS case definition

The following case definitions are recommended for the surveillance of CRS (*12*).

- Suspected CRS case: an infant less than one year of age in whom a health worker suspects CRS. A health worker should suspect CRS when an infant (0–11 months of age) presents with heart disease or suspicion of deafness or one or more of the following eye signs: cataract, diminished vision, nystagmus, squint, microphthalmos or congenital glaucoma. A health worker should also suspect CRS when an infant's mother has a history of suspected or confirmed rubella during pregnancy, even when the infant shows no signs of CRS.
- Clinically-confirmed CRS case: An infant in whom a qualified physician detects two of the complications listed in a) below or one in a) and one in b).
  a) cataract, congenital glaucoma, congenital heart disease, loss of hearing, pigmentary retinopathy.
  b) purpura, splenomegaly, microcephaly, mental retardation, meningocephalitis, radiolucent bone disease, jaundice that begins within 24 hours after birth.
- Laboratory-confirmed CRS case: An infant with clinically-confirmed CRS who has a positive blood test for rubella-specific IgM (100% of such infants will be positive at age 0–5 months and 60% at age 6–11 months). Where special laboratory resources are available, detection of rubella virus in specimens from the pharynx or urine of an infant

[3] This definition should exclude deaths due to obvious non-measles causes (e.g. accidents, etc.).

with suspected CRS provides laboratory confirmation of CRS (60% of such infants shed rubella virus at age 1–4 months, 30% at 5–8 months, and 10% at 9–11 months).

- Congenital rubella infection (CRI): When a woman is diagnosed with suspected or confirmed rubella during pregnancy, her infant should have a rubella-specific IgM blood test. An infant who does not have clinical signs of CRS but has a positive rubella-specific IgM test is classified as having CRI.

4.3 Reporting sites

Each country may decide about the reporting sites to include in the surveillance system for measles, rubella, CRS or for vaccine-preventable diseases in integrated disease surveillance. However, this decision needs to be made without compromising representativeness, accuracy and quality of information and resources. The following are suggested sites.

- Primary health care facilities: health centres, health units and inpatient and outpatient clinics;
- Hospitals, both inpatient and outpatient units;
- Private medical practitioners and private hospitals;
- Private and public laboratories: it is important to establish routine communication with all local laboratories that may receive serum specimens for diagnosis of suspected measles/rubella cases;
- Community sources: pharmacists, village leaders, school personnel and anyone else likely to learn about or have contact with sick children.

For CRS surveillance, reporting sites may include the following.

- Antenatal clinics visited by women during the first 16 weeks of pregnancy (the risk of CRS is low in women infected after the first trimester);
- Maternity hospitals, paediatric hospitals and neonatal intensive care units;
- Reference facilities treating children with cataract, deafness or congenital heart disease.

5. Surveillance activities and procedures for measles, rubella and CRS

In establishing and conducting measles, rubella and CRS surveillance activities, the roles and responsibilities of health workers and authorities at different levels of the health care system need to be defined and reporting procedures developed.

5.1 Health facilities

5.1.1 Reporting and investigating measles and rubella cases

- Identify suspected measles/rubella cases. Health care workers should use the case definitions described above to identify suspected measles/rubella cases. The definition of suspected cases is meant to be broad and sensitive.
- Notify all suspected measles/rubella cases. Designate one individual and one or two alternates to be responsible for keeping track of suspected measles cases and to report immediately all new suspected measles cases. Health care workers should immediately notify all suspected cases to district surveillance authorities. The channel of notification should be simple and efficient, with a designated reporting form used for notification. A sample form that may be considered for notification

and investigation of suspected cases of measles and rubella is given in Annex 1.

Regional measles elimination goal: measles suspected cases reported within 7 days of rash onset ≥80%

- Immediately collect specimens for laboratory testing. Blood and clinical specimens for virus isolation should be collected in designated health facilities from all suspected cases. A copy of the notification and investigation form should be sent with the specimen. Preparation of the specimen for shipment is discussed in detail in Section 8.
- Investigate all suspected measles cases. See Sections 6 and 7 for details.
- Conduct case-based measles/rubella surveillance by collecting a minimum data set on each case. A standard reporting form should be completed for each case of suspected measles/rubella. The following items of information are of major importance.[4]
  - date of birth or age
  - date of rash onset
  - date of blood specimen collection
  - district of residence at time of rash onset
  - history of immunization against measles and rubella and date of last vaccination
  - manage measles cases appropriately (see Sections 7 and 8 for details).
- Identify clusters or outbreaks and immediately notify them to the district.
- Conduct an intense search for pregnant women exposed and potentially infected with rubella. Any pregnant women who have been infected need to be followed-up to document their outcome. All suspected CRS cases in infants under one year of age should be investigated and both clinical and analytical findings should be included.
- Send the weekly surveillance report summarizing the number of suspected cases seen in the previous week to the district surveillance unit. This is usually done on a specific day each week. Maintain weekly reporting even if there are zero cases (often referred to as "zero reporting"). The health facility should use a standard form to report suspect measles/rubella cases, acute flaccid paralysis and other vaccine-preventable diseases (for an example of a form see Annex 2).

5.1.2 Information system and data analysis

- Record all suspected measles cases in a registry with the age and vaccination status for each case.
- If possible, data should be entered into a database at health facility level. Initial data can be analysed at the health facility level and further case-based data can be forwarded to the district.
- Data from notifications, investigation forms and line-listings should be analysed to monitor reported suspected and confirmed cases by age, sex, location and vaccination status, and to determine whether standards for case reporting and investigation are being met.
- Health facilities should promptly detect all suspected outbreaks during analysis of the data, through an investigation of the distribution of cases by area and reporting unit.
- Case-based information collected through case investigation forms and line-listings (Annex 3) should be sent (on a specific day of the week) from the reporting site to the district surveillance unit, as a file

[4] Recommendations of the regional measles technical advisory group. *Report on the Intercountry meeting on measles and rubella control and elimination and laboratory network*, 27–30 November, Amman, Jordan. Cairo, WHO Regional Office for the Eastern Mediterranean 2006 (WHO-EM/EPI/259/E).

containing all individual case forms and a line list. If a reporting site has the capacity for data entry, then the case investigation forms can be entered into a database or spreadsheet, and soft versions can be sent on a memory device or through e-mail.

5.2 Districts

5.2.1 Supporting health facilities

- Respond to the needs of the reporting units (health facilities), assist and supervise their work, and resolve any technical problem as soon as possible. Surveillance staff should monitor surveillance quality indicators through field visits, surveillance review meetings, and regularly-organized training workshops.
- Conduct periodic active case searches to ensure that all suspected cases are identified and notified. Active case-finding is particularly important in areas that do not notify cases, such as "silent" and high-risk areas. Case-finding is primarily conducted in health facilities (clinics and hospitals) but can also be performed in institutions, schools and in the community. In health facilities, registration records, discharge diagnoses and hospital charts are reviewed to identify patients with fever and rash illnesses, such as dengue and scarlet fever. In local laboratories, the logbook should also be checked to ensure that all suspected cases are being reported promptly. If potential cases are spotted, medical records should be reviewed carefully and the physician or nurse who provided care to the individual should be interviewed to determine whether the patient met the criteria of a suspected measles/rubella case. If so, it must then be determined if the case was reported and adequately investigated.
- Investigate and document outbreaks of measles (see Section 7 for details).
- Investigate all CRS cases and monitor CRS rates (an example of a CRS case investigation form is given in Annex 4). The annual number of CRS cases should be reported to the national level. To calculate the rates, it will be necessary to define the catchment area for cases and the annual number of live births in that catchment area. CRS surveillance should be enhanced in the context of a rubella outbreak, particularly during 6–12 months post-outbreak to identify births to women who may have been infected during the outbreak. Up to 50% of rubella infections may be asymptomatic, which means that pregnant women may not have been ill and may not have known that they had rubella infection.

5.2.2 Information system and data analysis

- Generate a measles/rubella database. Data on all reported cases from all reporting sites should be entered into database within 3 days. A weekly report should be sent to the provincial level.
- Analyse measles/rubella/CRS data. The district officials should analyse weekly and should send a monthly report (in the first week of every month) to the provincial surveillance unit. The data entered should be transferred immediately from the district database to the PSU data provincial surveillance unit by uploading through the Internet or through a computer storage device.
- Interpret surveillance data in conjunction with routine immunization coverage data. Analyses should be aimed at understanding the reasons for the occurrence of measles, obtaining guidance for control strategies, predicting potential outbreaks in order to implement vaccination strategies for

the prevention of outbreaks and planning measles elimination strategies (*13*). A few simple graphs can provide the essential data (i.e. time, place and person).
  - Number of cases by month of report compared over several years.
  - Number of cases reported by health facility (spot map). Cases should be plotted on a map according to their place of residence and the map compared with vaccination coverage data and sites reporting in the surveillance system. These maps can be useful for coordinating activities, such as setting up vaccination sites.
  - Number of cases by age group and vaccination status (cumulative for the year). Tabulating the age distribution of cases permits health authorities to detect any changes in the epidemiology of the disease and to establish which age groups to target for vaccination. Determining the vaccination status of confirmed cases is essential for evaluating vaccine effectiveness and detecting potential problems with the cold chain.
- Whenever information on vital status/deaths is available, analyse the number of measles-related deaths by age group and vaccination status (cumulative for the year). Such data are essential for measuring progress towards measles mortality reduction and for targeting appropriate control measures.
- Review any areas that do not report cases for extended periods. If such areas exist, it is important to identify at least one reporting site, e.g. a hospital or large clinic and include it in training programmes and prompt reporting procedures.

5.3 Provinces

- Ensure adequate and proper supervision and provide technical support to the districts.
- Review and clean up data received from the district before merging and transferring it to the national level. In case of delays in data transfer, provincial staff should contact district staff by phone to urge them to send the data. Transfer of data to the national level could be done through uploading or by sending a storage device.
- Transmit reports received from the districts to the national level on a weekly basis.
- Analyse disease patterns and trends, interpret surveillance data in conjunction with routine immunization coverage data, produce routine and activity reports and share results with district, provincial and national staff. The calculation of incidence rates, e.g. the number of measles cases divided by the population at risk, is especially useful at the provincial level for comparing the occurrence of disease at different places and times. In order to calculate rates accurately, it is important to obtain accurate population figures. Population data can be obtained from the census bureau or can be assessed by special surveys performed by various institutions or by health facilities.
- Monitor the surveillance performance using standard indicators and assess the programme as a whole by implementing an evaluation plan every six months (see Section 9 for details).

5.4 National level

- Supervise and provide technical support, as well as training, guidelines and logistic support to all levels of the surveillance programme, including assistance with

budgeting and finance and managerial support. The national level should produce and distribute surveillance guidelines, including case definitions, reporting forms and case investigation guidelines.

- Develop and support data management software to be used at the provincial and district level, including data entry screens, report generators and electronic reporting procedures from provincial to national level.
- Receive and merge data transferred from all provinces on a weekly basis and ensure consistency and validity of national data.
- Monitor the surveillance performance using standard indicators (Section 9). In case of delays in data transfer from any site, the coordinator should contact the province by phone and urge officials to send data and solve any technical problems causing delay.
- Confirm cases and outbreaks using IgM serologic testing in a WHO proficient national measles/rubella laboratory, and organize a possible shipment of specimens for viral isolation and genotyping. The national level needs to coordinate epidemic preparedness at all levels and to function as the central point for response for reported or identified outbreaks or rumoured outbreaks.
- Use measles surveillance data to evaluate national objectives and to direct the control programme. National officials should analyse disease patterns and trends, interpret surveillance data in conjunction with the routine immunization coverage data and produce routine reports. They should conduct in-depth epidemiological analysis (disease trends, high-risk groups, high-risk areas and progress towards elimination) from national surveillance data.
- Coordinate and integrate national surveillance activities and provide reliable surveillance data and reports to responsible public health officials.
- Generate a monthly (or more frequently) report about the current situation of vaccine-preventable diseases under surveillance. Surveillance staff at national level should conduct monthly surveillance meetings, data analysis, the epidemiologic situation and progress in all provinces and districts (such a meeting can be conducted quarterly or twice a year with staff at each province and district).
- Provide surveillance data and summaries to relevant ministry of health disease control programmes and officials and other stakeholders, i.e. EPI diseases, other communicable diseases, public health laboratories, WHO Regional Office, national immunization technical advisory group (NITAG), and other relevant departments. Timely data should be provided to the Regional Office and other related programmes in the country. Reporting to the Regional Office involves monthly reporting of case counts according to an agreed-upon standardized format (Annex 5).

6. Investigating and managing measles, rubella and CRS cases

Prompt recognition, reporting and investigation of measles/rubella cases are important because the spread of the disease can be limited with early case identification and vaccination of susceptible contacts. Once endemic transmission has become rare or has been interrupted, the surveillance goal is to detect and investigate all suspected measles cases and outbreaks, including those imported,

and to implement activities that prevent or limit secondary transmission.

6.1 Measles case investigation

Investigation of measles/rubella suspected cases should be conducted within 48 hours of notification. If the patient meets the case definition for measles, use the case investigation forms (Annex 1), submit them to district and/or provincial surveillance coordinators, and update the line list of suspected measles/rubella cases (Annex 3). Health care workers should ask parents if they know anyone else in their household or village/town that has a fever and rash. It is important to ensure completeness of all data collected, such as date of notification and date of investigation.

Regional measles elimination goal: percentage of suspected measles cases investigated within 48 hours of notification ≥80%

Suspected measles cases should receive a case identification number (case ID number) to aid in case tracking. This case number should begin with one or more three-letter combinations to designate the geographic location, followed by the year and the case number. All communications and forms related to the case should cite the identification number. For example, a unique EPID number in the case investigation form to each suspected case with the following format.

Country code/Province code/District ID/Year/MSC/Case serial # # # #. Some countries add MSC: measles suspected case. The four digit serial case # will be an incremental number per year.

A suspected case of measles needs to be investigated thoroughly. Clinicians, epidemiologists and/or other specially trained staff should be in charge of the investigation.

During the elimination phase, plans should be made to visit the home of the patient within 48 hours of notification. An investigation includes, at a minimum, a home visit with clinical and epidemiologic investigation of the suspected case and contacts of the suspected case and completion of relevant data (district, age, gender, date of onset, known vaccination status, date of last measles/rubella vaccinations, date when specimen was collected, travel history). The health facility then needs to complete an individual case investigation form for each patient (Annex 1).

Correct timing of specimen collection with respect to onset of clinical signs is important for the interpretation of results and reaching an accurate conclusion. A serologic specimen needs to be collected within the 28 days of the onset of rash. Investigators should collect a specimen and arrange for its transportation to the national measles laboratory. The blood sample should be taken during the first contact with the suspected patient as soon as possible following rash onset, unless it can be arranged for the patient to provide a sample on day 3 or 4 of the rash. The sample could be collected either at the health facility or during a home visit, using a specimen collection kit and ensuring a well-executed reverse cold chain when transporting the specimen to the health facility. Blood specimens must arrive at the laboratory within 7 days of collection. Laboratory request information should be included in the case investigation form. For countries using a separate form for measles/rubella laboratory testing, a template is provided in Annex 6.

Regional measles elimination goal: percentage of cases with blood specimen collected (exclude epidemiologically-linked cases from denominator) ≥80%

Active case-finding should be conducted even if there are more than 10 suspected cases and should be combined with AFP active surveillance. However, this would depend on time and resources. Contact tracing may identify the source of infection and determine whether other areas have been exposed.[5] Surrounding areas should be visited to find additional cases. Inquiries should be made to determine whether cases are occurring in places visited by the 'case under investigation' between 7 and 21 days prior to the onset of the rash, such as a preschool centre, school or another town or village. Surveillance sites and surveillance coordinators in nearby areas should be informed that a suspected case has been identified and the public should be kept well informed. Community leaders should also be asked to assist in case-finding. Investigators should call local private medical doctors and inform them about the suspected measles/rubella outbreak, as well as the mandatory notification of any suspected patient, and ask if they have seen any cases of fever and rash illness.

Evaluation of vaccination coverage levels is important to provide measles vaccination to unvaccinated persons.

Regional measles elimination goal: percentage of identification of source of infection ≥80%

6.2 Measles case management

Measles case management should be conducted through the IMCI approach, with the supplementation of vitamin A.

[5] In elimination settings, contact tracing and, if necessary, active case search should be a routine practice. However, this would not be feasible in countries where measles remains highly endemic

6.2.1 Case management of uncomplicated measles (14)

Many children will experience uncomplicated measles and will require only supportive measures.

- Give vitamin A if the child lives in an area of known deficiency or high measles case-fatality rates.
- Advise mothers to treat the child at home as long as no complications develop.
- Provide nutritional support: continue breastfeeding or give weaning foods and fluids at frequent intervals and treat mouth ulcers.
- Control fever by keeping the child cool.
- Instruct the caregiver to return for further treatment if the child's general condition worsens or if any of the danger signs develop.
- Explain to mothers that there is an increased risk in the weeks following a measles infection of diarrhoea, acute respiratory infections and other infections, and encourage them to seek medical advice promptly if these complications develop.
- Immunize direct contacts if they are identified within 72 hours of exposure. Prophylactic use of antibiotics is not recommended for uncomplicated cases. However, a Cochrane Review suggested a beneficial effect of antibiotics in preventing complications such as pneumonia, purulent otitis media and tonsillitis in children with measles (*15*).

6.2.2 Case management of complicated measles

Even in industrialized countries, about 10% of cases can be expected to develop complications of measles. In severe outbreaks in developed countries, this proportion will be higher and some children may have several complications. In developing countries, at least three-quarters

of all cases can be expected to have at least one complication and some may have multiple systems involvement. The following actions should be taken when complications occur.

- Refer to health facility for further management.
- Follow the above recommendations for case management of uncomplicated measles.
  and
- Ensure that two age-appropriate doses of vitamin A are given.
- Clean eye lesions and treat with 1% tetracycline eye ointment three times a day for 7 days (for corneal lesions, cover the eye with a patch). Vitamin A administration is particularly important to minimize the risk of potentially blinding eye lesions. In this situation, use a third dose of vitamin A four weeks later using the same dosage and age as in Table 1 (*16*).
- Clean ear discharge and treat with antibiotics. Antibiotics should be used for cases complicated by otitis media.
- Refer suspected cases of encephalitis to a hospital.
- Treat malnutrition and diarrhoea with sufficient fluids and a high-quality diet.
- Treat pneumonia with antibiotics.

Table 1. Recommended vitamin A schedule for measles treatment

Age group	Immediately on diagnosis	Next day
Infants <6 months	50 000 IU	50 000 IU
Infants 6–11 months	100 000 IU	100 000 IU
Children 12 months and above	200 000 IU	200 000 IU

7. Outbreak investigations and control for measles and rubella

7.1 Measles outbreak investigation

Health facilities and district staff will be responsible for investigating clusters of measles cases and conducting good quality outbreak investigations, including active case-finding in the community, maintaining a line-list of cases and implementing public health measures.

7.1.1 Definition of a measles outbreak

All countries in the Region have conducted a one-time measles catch-up campaign. Hence, using the WHO guidelines, a suspected outbreak of measles is defined as the occurrence of five or more reported suspected cases of measles in one month per 100 000 population living in a geographical area (e.g. district/health facility). (*14*) A confirmed measles outbreak is defined as the occurrence of three or more confirmed measles cases (at least two of which should be laboratory confirmed; IgM positive) in a district/health facility (approximate catchment population of 100 000) in a month.

7.1.2 Reporting measles outbreaks

The health facility surveillance focal person should notify the district team about the occurrence of clusters of cases using the quickest available means of communication (phone, fax, e-mail, etc).

All outbreaks should be reported to WHO Regional Office using a specific form (Annex 7) and thoroughly investigated using WHO guidelines for outbreak investigations (*14*).

Regional measles elimination goal: percentage of suspected measles outbreaks investigated ≥80%

7.1.3 Measles outbreak investigation

The district team should conduct the outbreak investigation. All cases need to be investigated to confirm that they meet the clinical case definition, to assess the extent of the suspected outbreak and to determine the population at risk. The investigation is best performed by health workers trained to identify clinical measles cases, using a standard form to obtain details on cases and contacts (Annex 1). If there are >10 suspected cases in each single area, the household visits may be reduced or eliminated, depending upon the availability of investigators. However, the suspected case line-listings should be filled out for each suspected case and particular attention should be given to obtaining basic demographic data, including the age and vaccine history of the patient.

All suspected measles outbreaks should be confirmed as having resulted from measles virus infection. Blood samples, as well as other clinical specimens for viral isolation and genotyping, should be taken from the first 5–10 suspected cases within an affected geographical area for laboratory confirmation (the presence of measles-specific IgM antibodies) of the outbreak in that area. If there is any suspicion that the outbreak has spread to an adjacent area, 5–10 blood specimens should also be collected from suspected cases in that area, unless there is clear epidemiologic linkage between the two areas/districts. Once a measles outbreak is laboratory confirmed, it is unnecessary to collect specimens from every suspected case. Additional cases can be confirmed if they meet the clinical case definition and are epidemiologically linked to a laboratory-confirmed case or to another EPI-linked case.

Laboratories are recommended to report laboratory results within 7 days of receipt; however, during outbreaks, laboratories should provide the IgM results within 24 hours after the receipt of specimen. If laboratory confirmation is not possible, an outbreak may be documented through a sustained and progressive rise in clinically-confirmed cases over a 3-week period (*14*).

The district team needs to create a line-listing of all subsequent cases to include the age, vaccination status, address, date of rash onset, outcome and case ID number (Annex 2) Provincial staff should inform national authorities and the community through the effective use of public health messages regarding appropriate treatment of cases, immunizations to be given, and other control measures. Figure 2 illustrates the importance of conducting an active search of cases during a measles outbreak.

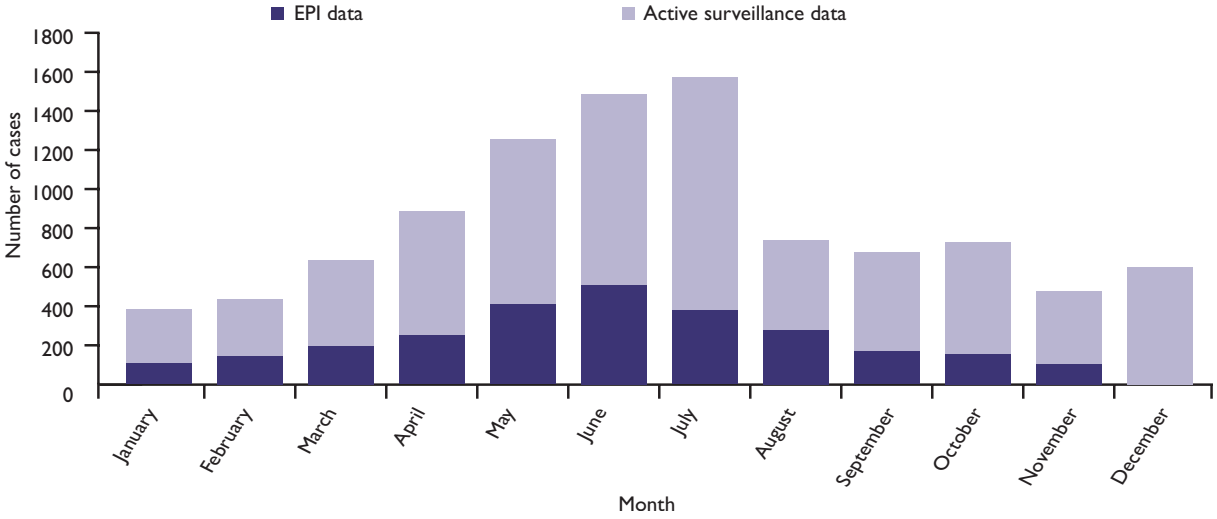
The data collected should be analysed rapidly at the local level to determine the extent of the outbreak and the population at risk. This can be done by analysing a line-listing of cases with key variables (Annex 3) or, more efficiently, by entering the data into a computer program such as Epi-InfoTM, Access or SPSS. Figure 3 shows the distribution of suspected measles cases by age group reported in a province in Iraq in 2008. It shows that 58% of total cases were under-5 years of age and 17% of cases were above 15 years of age, which reflects weaning of immunity at the older age group.

7.1.4 Measles outbreak response

Types of outbreak response

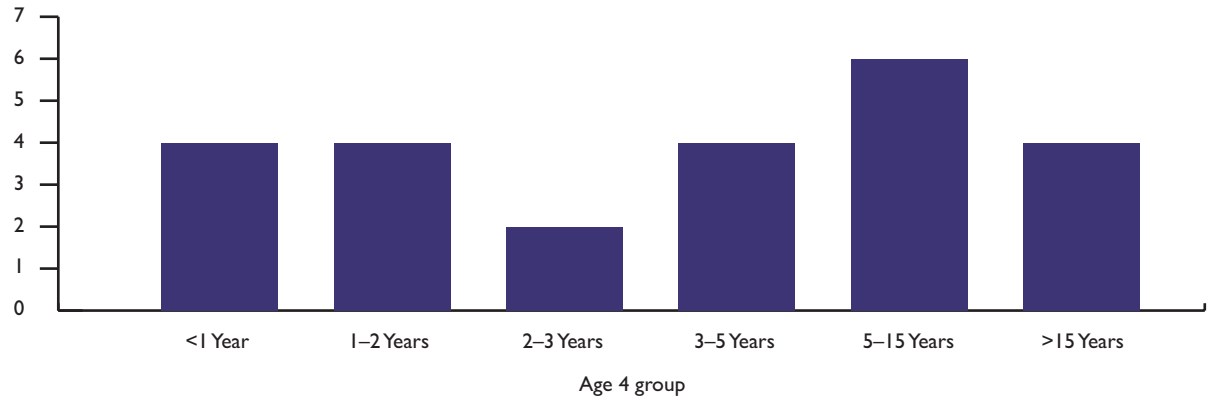
The response to the outbreak needs to be developed fast and aggressively (*14*). The type of outbreak response varies, depending on a number of factors, including the level of susceptibility in the population, risk for spread and complication and the existing health service infrastructure.

In order to enhance the capacity to respond to measles outbreaks, a district level outbreak coordination committee or any equivalent subnational level multidisciplinary group



Source: Technical report from the Expanded Programme on Immunization, Ministry of Health, Pakistan, 2005 (unpublished data).

Figure 2. Comparison of measles cases by EPI data and active search data, Pakistan 2005



Source: Technical report from the Expanded Programme on Immunization, Ministry of Health, Iraq, 2008 (unpublished data).

Figure 3. Suspected cases of measles by age group, Ninawa, Iraq, 2008

should be created prior to the occurrence of outbreaks. The outbreak coordinating committee should ensure that the following actions are carried out.

- laboratory confirmation of the outbreak
- ensuring adequate clinical management of cases
- administration of vitamin A
- supportive treatment should be provided for all cases, including additional fluids (such as oral rehydration solution) and antipyretics.
- antibiotics should be used for cases complicated by otitis media or pneumonia, and nutritional therapy is indicated for children with malnutrition.
- Intensifying surveillance and notification of suspected cases.

Once an outbreak is confirmed (or before, if circumstances indicate), surveillance

staff should immediately notify other health facilities, clinicians, and surveillance coordinators in surrounding areas and the appropriate surveillance staff at the district and provincial levels. Active surveillance and case-finding need to be intensified in the outbreak area and surrounding areas.

Health staff at the health facility or district level should be vigilant and investigate any reports or rumours of measles cases occurring in the community, or when there is an epidemic occurring in a neighbouring area. Such investigations should either confirm (or reject) the existence of measles virus circulation.

Assessing the risk of a large outbreak with high morbidity and mortality

As soon as the outbreak is suspected the risk of a large outbreak with high morbidity and mortality must be assessed. This assessment is needed to determine what type of vaccination response is most appropriate to control the outbreak. For this, the following evaluations should be carried out.

- Evaluate the susceptibility of the population and potential for spread both in the affected and neighbouring areas.
- Evaluate the risk of further transmission, morbidity and mortality. For this, the following factors should be taken into account.
  - population characteristics, such as size, density, movement and setting (e.g. community spread throughout a district, or limited spread within a subpopulation; resource-poor settings).
  - under-5 mortality rates
  - nutritional, including vitamin A, status
  - HIV prevalence in the population
  - period of the year (considering potential for seasonal outbreak) and plans for any festivals or other social events that will result in increased opportunities for spread
  - number of cases reported and comparison with data from previous years
  - access to health services.

Implementing control and preventive measures (including vaccination activities)

- Managing cases and contacts to limit spread. It is important to ensure adequate clinical management of measles cases in order to reduce measles mortality. In addition, if time and resources permit, the following measures should be implemented, as follow-up of all cases and contacts may not be possible if the epidemic is large and if resources are limited.

As soon as the outbreak is confirmed, the district outbreak coordination committee should review risk-assessment results and decide accordingly whether to continue with the selective vaccination activities or to carry out a nonselective vaccination campaign.

Selective vaccination activities

The following selective vaccination activities should be undertaken.

- Enhance social mobilization activities to inform affected communities about the suspected outbreak, which specific age groups of previously unvaccinated children is targeted for measles vaccination, and where parents should bring their at-risk children for vaccination.
- Vaccinate all children (6 to 59 months of age or determine the target age group according to the local disease epidemiology) presenting to a health facility or an outreach vaccination site without a history of measles vaccination (either written or verbal).

- Vaccinate hospital staff at risk of exposure, and who have not been vaccinated.
- Reinforce routine vaccination.

Non-selective vaccination activity

As soon as the outbreak is confirmed, and if the risk-assessment results indicate that there is a high risk of a large measles outbreak, then the capacity to carry out a high-quality large-scale immunization campaign should be rapidly evaluated. Once the decision to intervene has been made, it is critical to act as quickly as possible to minimize the number of severe measles cases and deaths.

- Target population: choosing the target population depends upon the susceptibility profile of the population. Key elements to consider are: 1) routine vaccination coverage and coverage during supplementary immunization activities (SIAs) in each birth cohort; 2) age-specific attack rates; 3) absolute number of cases.
- Ensuring effective community involvement and public awareness: when an outbreak is confirmed, there is likely to be widespread public concern and media attention. It is important to keep the public informed, to calm fear and encourage cooperation. Messages to the community should be clear and concise, using local terminology, and should convey the following.
  - existence of an outbreak and the benefits of measles vaccination;
  - signs and symptoms of the disease;
  - encouragement to parents whose children have had a recent rash and fever illness;
  - the need to consult a health care facility early after symptom onset;
  - instruction to parents to bring their children to a health facility/vaccine post for vaccination;
  - information on locations and opening hours of health facility/vaccine posts.

The district team should also complete and send the analysis of the outbreak by person (age distribution, vaccination status, etc. of cases), place (spot map), and time ("epidemic curve") to the provincial level within 2 weeks. More comprehensive documentation needs to be performed at the close of the outbreak.

An outbreak of measles in a district is said to have ended when no new suspected case of measles is identified for more than 3 weeks, and when all neighbouring districts have also not reported any cases for a similar period of time. Step-by-step guidelines for measles outbreak investigations are presented below. It should be noted that the placement of these actions is not intended to indicate a chronological order for implementation. Many of these actions should be taken simultaneously whenever the outbreak is suspected or confirmed.

7.1.5 Step-by-step guidelines for measles outbreak investigation

It should be noted that the order of these actions is not intended to indicate a chronological order for their implementation. Many of these actions should be undertaken concurrently as soon as the outbreak is suspected or confirmed.

Confirm the diagnosis

- Serological testing for suspected measles cases
  - Collect one blood specimen at first contact from 5–10 suspected measles cases.
  - Take the opportunity simultaneously to collect appropriate throat swab/ nasopharyngeal swab or urine for viral isolation from cases presented within 5 days of rash of onset.
  - Establish virological link to a laboratory-confirmed case.

  - Virus identification of the strain genotype.

Identify and investigate suspected measles cases

- Basic surveillance variables
  - age, sex, residence
  - date of rash of onset
  - date of last measles vaccination and number of doses received
  - date of collection of blood specimen
  - possible source of exposure 7–21 days prior to rash of onset
  - exposure to another laboratory-confirmed measles case
  - travel to foreign country with known measles virus circulation
  - possible transmission to others 3 days prior to onset of rash to 4 days after rash of onset.
- Questions to be asked
  - Where was the patient born?
  - When did patient move to current residence?
  - Have there been other cases within the household?
  - Where does the patient work/study?
  - How does the patient travel to work/school?
  - Are there other cases in the workplace/school?
  - Where does the patient socialize (e.g. market, club, school)?
  - Are there other cases in these social groups, mosques, places of worship?

Describe the outbreak

- What was the total number of confirmed cases?
- What were the age distribution and vaccination status of confirmed measles cases?
- Which municipalities have measles circulation occurring? (map)
- In each affected household, what was the age and vaccination status of the first case?
- How long did the epidemic last? (EPI-curve)

Determine the source of outbreak

- Classical epidemiology (Who acquired the infection from whom?).
- Molecular epidemiology via genotyping analysis of measles virus isolates.

Determine risk factors for measles infection (analytical epidemiology)

- Age and vaccination status of cases
- Place of exposure (school, office, etc.)
- Attack rates
- Possible risk factors:
  - age group and vaccination status
  - travel to areas where measles is endemic
  - occupation (e.g. health care, tourism industry)
  - school/day care attendance
  - visit to health facility

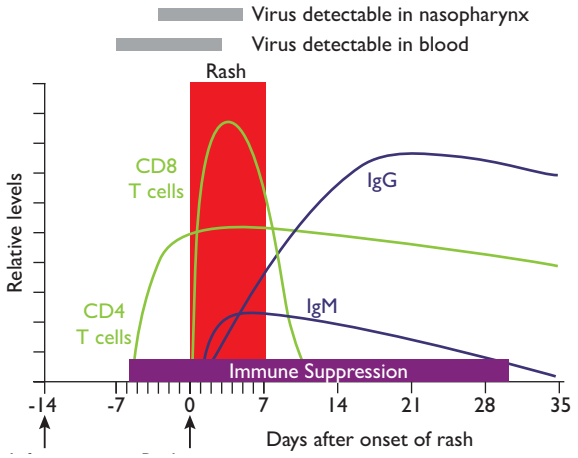
The national level, in collaboration with the provincial and district levels, should document the outbreak. Careful investigation of measles outbreaks can provide useful information regarding factors that may have facilitated measles virus circulation. The investigation may help to identify risk factors for measles infection and provide information that can be used to refine and improve the measles elimination. To benefit from the investigation and outbreak control activities, data and conclusions from the outbreak need to be published. The report should include the following sections: introduction; surveillance methods; description of the outbreak; analysis of the outbreak; control measures; problems; conclusions and recommendations.

7.2 Rubella/CRS outbreak investigation

There should be a special emphasis placed on the investigation of rubella outbreaks as such outbreaks may provide an opportunity to obtain information on the CRS disease burden. CRS cases are likely to be under-reported in areas and among populations where a high proportion of births occur at home and where neonatal and childhood deaths are often unreported. In such settings, outbreak investigations can help to identify CRS cases. Because rubella outbreaks tend to persist for several months or more and because CRS is a late outcome of these outbreaks, there is time to conduct active surveillance for CRS.

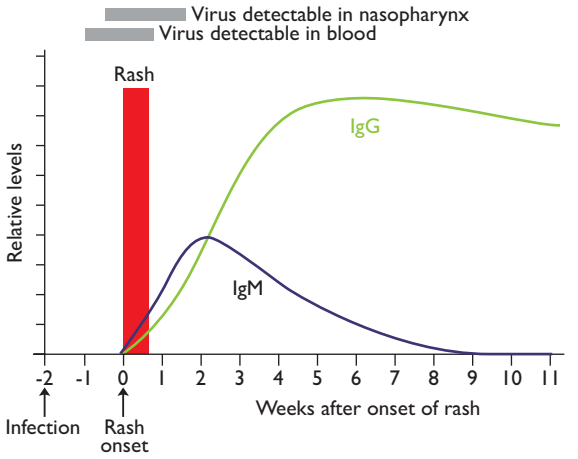
When a rubella outbreak is detected, investigations need to be conducted, including laboratory tests of a small number of suspected rubella cases per month (5 to 10 investigations per month, except in the accelerated or elimination control phase when all cases need to be investigated). All febrile rash illnesses during pregnancy should be identified, investigated and followed. If rubella cases are reported in individuals >15 years of age, active surveillance should be conducted until 9 months after the end of the outbreak, to identify suspected CRS cases in infants 0–11 months of age.

All pregnant women infected with rubella should have their pregnancy monitored to document the outcome. Follow-up of pregnant women should be an integral part of CRS surveillance. A pregnancy registry should be created to assist districts in the follow-up of these women. CRS surveillance should be established in hospitals where these women will be delivering and at specialty hospitals and clinics or specialists where these infants will be diagnosed or treated. All CRS cases should be investigated using the form in Annex 4. There should be a protocol in place for the clinical evaluation, laboratory testing and infection control guidelines for these infants.



Source: *(17)*

Figure 4. Immunity responses of an acute measles infection



Source: *(17)*

Figure 5. Immunity response in typical rubella infection (*15*)

8. Laboratory support in measles and rubella surveillance

Laboratory testing to confirm a clinical diagnosis of measles/rubella is an essential part of the surveillance system. Each country needs to establish a system and procedures for collecting and testing blood samples from cases of suspected measles and rubella following the Regional Office guidelines. Laboratory testing should be done in a WHO proficient national measles/rubella laboratory. To be discarded, a suspected measles case must undergo an adequate epidemiological investigation and have a negative laboratory result for measles-specific IgM in a blood sample collected within an appropriate time period (28 days from rash onset).

8.1 Measles/rubella serology

Any suspected measles case should have a laboratory test undertaken. Accurate laboratory confirmation depends on the proper and timely collection, processing, shipment and storage of specimens, as well as accurate testing by a proficient laboratory.

Regional measles elimination goal: percentage of cases with blood specimen collected (exclude epidemiologically-linked cases from denominator) ≥80%

For measles surveillance, a single blood specimen obtained shortly after rash onset may be sufficient to confirm or discard suspected measles cases. Specimens taken on day of rash may be IgM negative and a repeat serum may be needed.

Once specimens are collected, they must be shipped to an official laboratory as soon as possible. Blood specimens must arrive at the laboratory within 3 (maximum 7) days of collection. If specimens for viral isolation are collected but not shipped along with the blood specimen, they should be kept in an adequate storage. Procedures for the collection, handling and shipment of specimens for measles/rubella testing are presented in Annex 8.

It is critical for the laboratory to receive case information with specimens. Blood specimens must be sent with a completed copy of the case investigation form, including the following information: case identification number, patient's name, age, county/municipality, travel history, number of vaccine doses received, date of last measles/rubella vaccination, date of rash onset, date of notification, date of investigation, date of blood specimen collection, date specimen was sent to the laboratory and case classification.

Laboratories should conduct ELISA testing to detect specific IgM class antibodies to measles. WHO recommends using commercially available ELISA assays that are independently validated, have high sensitivity and specificity, and are unaffected by haemolytic, lipaemic and icteric sera (*17*).

Measles-specific IgM antibodies appear first and can be detected shortly after rash onset. They attain peak levels approximately one week later, then gradually decline and are rarely detectable at 6 weeks after rash onset (Figure 4) (*17*). Ig G antibodies peak about 2 weeks following rash onset and are detectable for years after infection.

Regional measles elimination goal: percentage of laboratory results available within 7 days ≥80%

Serum samples that are negative for measles IgM should be tested for rubella IgM. Rubella can be confirmed only by laboratory testing. Laboratory confirmation of rubella is made by detection of rubella-specific IgM in a blood

specimen, which should be obtained within 28 days of rash onset (Figure 5).

If measles or rubella is suspected and a serum sample obtained within the first 2 to 3 days after rash onset is negative for measles and rubella IgM, it is recommended to obtain a second serum specimen within 10 to 20 days of onset (*13*). This is especially true for rubella-infected pregnant women. When serum samples are taken within 2 to 3 days after the rash onset, up to 30% of ELISA tests for measles-specific IgM may give false negative results and up to 50% of rubella-specific IgM tests may give false negative results.

False-positive results of IgM tests can also occur; for example, exanthemata (rash illnesses) caused by *Parvovirus* B19, rubella and *Human herpesvirus* 6, among others, can be misdiagnosed as suspected measles cases. Each IgM positive test that is thought to be false–positive needs to be considered on a case-by-case basis, taking into account clinical presentation, vaccination history, epidemiological data and laboratory results.

If IgM results are thought to be false-positive, the IgM test should be repeated with the same enzyme immunoassay (EIA) to measure IgG titer levels in paired sera (first sample collected within 7 days of rash onset, second sample 2 to 3 weeks thereafter). When possible, viral detection/isolation and avidity assays (rubella only) should be done.

To discard a suspected case with an IgM-positive result that is not related to a recent vaccination, laboratory results must confirm a diagnosis other than measles/rubella that is compatible with the clinical presentation of the suspected patient. In addition, a thorough field investigation must have been conducted and failed to identify any measles/rubella cases (whether an index or secondary case). A suspected case should never be discarded merely on the basis of a clinical presentation that is not viewed as typical for measles/rubella (*9*).

Serology cannot be used to rule out measles. A diagnosis should be considered confirmed in the presence of good clinical and/or epidemiologic evidence, even in the absence of confirmatory serology. However, all suspected cases with an IgM-positive result should be considered laboratory-confirmed and control measures need to be initiated immediately.

8.2 Viral detection/isolation/genotyping

Efforts should be made to collect specimens for virus isolation simultaneously with the blood samples for serological confirmation of measles and rubella as the cause of the outbreak. Collection of specimens for virus isolation should not be delayed until laboratory confirmation of a suspected case of measles is obtained. Throat swabs, nasopharyngeal specimens, or 10–50 ml of urine for virus isolation must be collected within 3–5 days of rash onset when the virus is present in high concentration.

Viruses are sensitive to heat and their infectivity decreases when samples are not kept cooled. It is important to transport samples to the laboratory under cold chain conditions within 48 hours of specimen collection.

Genomic sequencing of wild-type measles virus isolates from laboratory-confirmed cases will distinguish the origin of measles viruses as indigenous or imported, and thus will corroborate whether the transmission of indigenous measles strains has been fully eliminated. Genotyping can also identify vaccine-related suspected cases. If the person has been vaccinated within 6 weeks prior to serum collection, refer to *Manual for the laboratory diagnosis of measles and rubella infection*. Geneva, (*17*).

8.3 Measles/rubella laboratory network

The WHO Regional Office for the Eastern Mediterranean has organized a network of national measles laboratories in all countries of the Region. The network's structure and functions at each level are described below.

8.3.1 Regional reference laboratories

There are two regional reference laboratories, one in Oman and one in Tunisia, which serve as centres of excellence for the Region. The functions of the regional reference laboratories include:

- collaboration and evaluation of new diagnostic assays
- diagnosis of clinically-suspected measles and rubella cases by serologic testing, virus isolation, and characterization of viruses, from samples collected by national and subnational laboratories
- training and advising national laboratory staff
- quality control (validation of their own and national laboratory results using a gold standard)
- internal quality assurance through assessing the sensitivity and specificity of their work through proficiency testing.

The Oman and Tunisia regional reference laboratories have been identified as the measles sequencing reference laboratories for the Region, though several national laboratories within the Region also have the capacity to sequence viruses.

8.3.2 National laboratories

All countries should have an accredited national laboratory for measles and rubella testing. National laboratories should have strong links to the immunization and surveillance units at the ministry of health. National laboratories should be closely linked with the national programme managers to ensure that patients with suspected measles have access to laboratory testing with full integration of laboratory and surveillance data. Every effort must be made to ensure that laboratory, epidemiologic and operational personnel work closely together and possess: accredited capability to perform testing, in addition to the need for well-trained scientists and technicians, adequate laboratory facilities and resources to cover operating costs.

The duties of the national laboratory include:

- confirmation of the diagnosis of clinically-suspected measles using validated commercial IgM ELISA kits;
- collection and dispatch of samples for virus isolation to the regional reference laboratory in Oman or Tunisia. For viral isolation and genotyping, shipment to a regional reference laboratory can be delayed until serological results are known;
- quality assurance which includes performing annual proficiency testing, referral of selected specimens to a reference laboratory for validation, and performance of epidemiologically essential serological surveys;
- training activities.

Some countries experiencing logistical difficulties in shipping samples to the central laboratory are encouraged to maintain subnational laboratories to facilitate the shipment of samples for retesting and strengthening virus detection capabilities and genotyping in the Region. Before establishing subnational laboratory networks, however, use of alternative sampling techniques should be considered as a means of overcoming logistical and economic challenges.

8.4 Alternative sampling techniques

The collection of blood specimens from infants and young children is always a challenge, and

maintaining the cold chain during transportation of specimens to the laboratory is not always possible. Recently, two approaches have been validated for use in the WHO measles and rubella laboratory network which have the potential to be useful tools for measles/rubella surveillance, namely, the use of dried blood spots and oral fluid samples (*17,18*). Therefore, countries are encouraged to utilize alternative sampling and transportation techniques, where appropriate, for their measles and rubella control programmes. Dried blood filter paper and oral fluid can be used for case confirmation in areas where a reverse cold-chain is not feasible logistically. Antibody and viral RNA (ribonucleic acid) are sufficiently stable at up to 37 °C for a week when such collection methods are used. The standard protocols recommended by the measles and rubella LabNet are outlined in *Manual for the laboratory diagnosis of measles and rubella infection (17).*

8.4.1 Dried blood samples

Dried blood spots have been used for a number of epidemiological studies as an alternative specimen to serum for the detection of virus-specific immunoglobulin G (IgG) and IgM. Studies have shown that antibodies present in dried blood spots collected on filter papers are stable for at least a month in the absence of a cold chain, and can be detected for both measles and rubella viruses (*19,20,21*). See Annex 8 for specimen collection and transportation.

8.4.2 Oral fluid sampling

Since the early 1990s, the United Kingdom has successfully used oral fluid sampling for almost all measles, rubella and mumps laboratory-based surveillance. Use of oral fluid samples enables field workers to obtain a more complete sampling of suspected cases (*21,22*). Oral fluid samples are easy to collect and, because the procedure is less invasive than drawing blood, they are more accepted by the population. Beside the detection of IgM specific to measles and rubella viruses, oral fluid can also be used for viral genome detection using reverse transcriptase-polymerase chain reaction (RT-PCR). Oral fluid testing provides almost equivalent sensitivity and specificity for measles-specific IgM detection, though it shows moderately lower sensitivity for rubella IgM (*22*). In addition, oral fluid samples have a higher sensitivity for nucleic acid detection than dried blood samples. Use of oral fluid samples creates an additional opportunity to test for both antibody response (IgM) and the presence of virus in the same sample.

9. Surveillance monitoring and feedback

A high-quality surveillance system is essential to monitor progress toward and success in sustaining measles elimination and rubella/CRS control. A quality surveillance system must be maintained even after endemic measles virus transmission has been interrupted. All Member States should regularly and systematically assess the capacity of their surveillance systems to ensure sufficient quality to monitor, measure and report on measles, rubella and CRS, according to their elimination, control and prevention goals. A set of standard indicators should be used to monitor the quality of a measles/rubella surveillance system, and feedback should be provided to other levels and local staff.

9.1 Surveillance performance indicators for countries with elimination goal

9.1.1 Reporting rate

At national level, a rate of two non-measles suspected measles cases per 100 000 population should be considered a minimum. These cases must have been investigated and discarded as non-measles cases using laboratory testing in a

proficient laboratory[6] and/or epidemiological linkage to another confirmed disease and /or epidemiological linkage to an IgM negative case.

In addition, at least one non-measles suspected measles case should be reported annually per 100 000 population in at least 80% of the administrative units at the provincial level or its administrative equivalent or at an administrative level that has a population of at least 100 000.

9.1.2 Laboratory confirmation

Specimens adequate[7] for detecting measles IgM should be collected from at least 80% of suspected measles cases and tested in a proficient laboratory. Any cases that are epidemiologically linked to a laboratory-confirmed case of measles or other communicable disease should be excluded from the denominator.

9.1.3 Viral detection

Samples[8] should be collected for virus detection from at least 80% of identified outbreaks and tested in an accredited laboratory. The numerator is the number of outbreaks with sufficient samples for viral detection and the denominator is the number of outbreaks identified.

9.1.4 Adequacy of investigation

At least 80% of all reported suspected measles cases should have had an adequate investigation initiated within ≤48 hours of notification. The numerator is the number of suspected measles cases for which an adequate[9] investigation was initiated within 48 hours of notification and the denominator is the total number of suspected measles cases.

9.2 Measures of progress towards measles elimination

To monitor progress towards elimination, there is a need to monitor population immunity and measles incidence. One suggested indirect measure of population immunity is vaccination coverage. The incidence of measles cases per million population should be monitored to assess progress towards reaching elimination, and is another indirect measure of population immunity. Incidence monitoring is reliable only when surveillance is of high quality (as indicated by meeting the surveillance performance indicators above) and when thorough outbreak investigation is carried out.

Countries should conduct thorough outbreak investigations of all outbreaks that include contact tracing and active case-finding, and should determine the size, duration and origin of all outbreaks. As countries approach elimination, the size and duration of the outbreaks will diminish and the majority of outbreaks should be import-related in origin. These measures are useful for providing general guidance and may not apply to small populations (particularly isolated small populations, e.g. small islands).

[6] A proficient laboratory is a WHO network laboratory that uses a validated assay and has passed the annual WHO proficiency test.

[7] Adequate specimens are: serum; minimum of 0.5 ml, dried blood sample; at least three fully filled circles on filter paper collection device, oral fluid; sponge collection device should be rubbed along the gum until the device is thoroughly wet. This usually takes one minute. Samples should be collected within 0–28 days post onset.

[8] Where possible, samples should be collected from 5–10 cases early in the outbreak and every 2–3 months thereafter if transmission continues. For virus isolation, throat or urine samples should be collected within 5 days after rash onset. For virus detection using molecular techniques, throat samples can be collected up to 14 days and for oral fluid samples up to 21 days after rash onset.

[9] An adequate investigation includes at a minimum collection of all of the following data elements from each suspected measles case: name or identifiers, age (or date of birth), sex, date of rash onset, date of specimen collection, vaccination status, date of last vaccination, date of notification and date of investigation, travel history, and district. In addition, the investigation should include contact tracing and additional case-finding. Cases that do not require specimen collection (e.g. have been epidemiologically linked to a laboratory-confirmed case) are considered as adequately investigated if they have all the above information except the date of specimen collection.

The two measures below will be monitored at the global level and are accompanied by markers that suggest elimination has been achieved. Regions and countries may add additional measures and markers as is appropriate for the Region. Certification of elimination will entail further analysis of the measures below (for example, an assessment of the reliability of coverage data in each country) and the use of additional data elements such as an analysis of the sources and genotypes of all confirmed cases in the country in question.

9.2.1 Vaccination coverage

Vaccination coverage should be continuously monitored by countries to enable the assessment of population immunity.

- Vaccination coverage: vaccination coverage of both first routine measles dose (MCV1) and second dose (MCV2, either through routine or SIA coverage)
- Vaccination coverage marker: achieving and maintaining at least 95% coverage with both MCV1 and MCV2 in all districts or their equivalent, and nationally.

9.2.2 Incidence

- Incidence: measles incidence per million population per year should be used to monitor progress towards elimination. The numerator should exclude measles cases confirmed as imported;[10]
- Incidence marker;
- Achieving a measles incidence of zero confirmed measles cases per million population per year, excluding cases confirmed as imported.

Other indicators are used for monitoring measles/rubella surveillance performance.

- Percentage of suspected cases notified ≤7 days of rash onset: ≥80%
- Proportion of reporting sites that report weekly: ≥80%
- Percentage of suspected cases with a blood specimen received at the laboratory within 3 (maximum 7) days of being taken: >80%
- Percentage of suspected cases with blood specimen processed within 7 days of laboratory receipt: ≥80%
- Percentage of suspected cases that were laboratory discarded: ≥90%
- Percentage of confirmed cases with infection source identified: ≥80%.

These indicators should be monitored at all levels: district, provincial and national. While all are important, three indicators are critical: 1) the proportion of suspected cases with adequate investigation; 2) the proportion of suspected cases with a blood specimen collected within 28 days of rash onset or an epidemiologic link to a laboratory-confirmed case; and 3) the proportion of transmission chains with representative samples for viral isolation.

9.3 Feedback

Regular feedback to everyone involved in the surveillance system is important to ensure that sustainability and refinements to the system are implemented as necessary. Feedback may be given in writing or verbally during on-site supervisory visits and during the periodic surveillance review meetings. Feedback includes providing surveillance participants with the following.

- The number and location of reported cases
- An assessment of the level of promptness and accuracy of their surveillance reports
- Information on the effectiveness of vaccination and control activities
- Specific recommendations on how to solve common problems

[10] All import-related cases and sporadic or endemic measles cases that are not imported should be included.

- Commendations for personnel doing excellent work.

Feedback can be provided effectively in writing by sending weekly or monthly measles surveillance bulletins to the reporting sites, to interested parties and to all partners. To encourage reporting, it is important to respond to all reports with at least an acknowledgement of the report.

References

1. Measles fact sheet number 286. Geneva, World Health Organization, revised December 2009 (http://www.who.int/mediacentre/factsheets/fs286/en/print.html, accessed 24 May, 2010).
2. *Immunization, vaccines and biologicals, WHO vaccine-preventable diseases: monitoring system - 2007 global summary*. Geneva, World Health Organization, 2007.
3. Centers for Disease Control and Prevention. *Progress in global measles control and mortality reduction, 2000–2007*. Morbidity and Mortality Weekly Report, 2008, 57:1303–1306.
4. Forty-fourth Session of the Regional Committee for the Eastern Mediterranean, Teheran, Islamic Republic of Iran, 4 to 7 October 1997 (Resolutions available at http://www.emro.who.int/governance/PDF/RC44_Resolutions.pdf, accessed 24 May 2010).
5. WHO position paper. Measles vaccine. *Weekly Epidemiological Record*, 2009, 84(35):349–360 (htt://www.who.int/wer, accessed 24 May, 2010).
6. Anonymous. Vaccination against measles: clinical trial of live measles vaccine given alone and live vaccine proceeded by killed vaccine. Second report to the medical research council by the measles vaccines committee. *British Medical Journal* 1968, 2:449–452.
7. Paunio M et al. IgG avidity to distinguish secondary from primary measles vaccination failures: prospects for a more effective global measles elimination strategy. *Expert Opinion on Pharmacotherapy*, 2003, 4:1215–1225.
8. WHO/UNICEF/IVACG Task Force. *Vitamin A supplements: A guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia*. Second edition. Geneva, World Health Organization, 1997.
9. WHO position paper. Rubella vaccines. *Weekly Epidemiological Record*. 2000, 75:161–172. http://www.who.int/wer, accessed 24 May 2010.
10. WHO-recommended surveillance standard of measles (http://www.who.int/immunization_monitoring/diseases/measles_surveillance, accessed 24 May 2010).
11. *Measles elimination: field guide*. Washington, D.C. Pan American Health Organization, 2005, Scientific and Technical Publication, Number 605.
12. WHO-recommended surveillance standard of rubella and congenital rubella syndrome (http://www.who.int/immunization_monitoring/diseases/rubella_surveillance, accessed 24 May 2010).
13. 13. Guris D. *Module on best practices for measles surveillance* (WHO/V and B/01.43). Geneva: World Health Organization, 2001.
14. *Response to measles outbreaks in measles mortality reduction settings*. Geneva, World Health Organization, 2009 (http://www.who.int/immunization/documents/WHO_IVB_09.03/en/print.html, accessed 24 May 2010).
15. Kabra SK, Lodha R, Hilton DJ. Antibiotics for preventing complications in children with measles. *Cochrane Database of Systematic Reviews* 2008, Issue 3. Article Number: CD001477. DOI: 10.1002/14651858.CD001477.pub3.

16. WHO/UNICEF/IVACG Task Force. *Vitamin A supplements: A guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia*. Second edition. Geneva, Wolrd Health Organization, 1997.

17. *Manual for the laboratory diagnosis of measles and rubella infection*. Second edition. Geneva, World Health Organization, 2007 (WHO/IVB/07.01).

18. Mosquera Model, M et al. Use of whole blood dried on filter paper for detection and genotyping of measles virus. *Journal of Virological Methods*, 2004, 117:97–9.

19. Helfand, R.F et al. Comparative detection of measles and rubella IgM and IgG derived from filter paper blood and serum samples. *Journal of Virological Methods*. 2001, 65:751–757.

20. Vyse AJ et al. Evolution of surveillance of measles, mumps, and rubella in England, and Wales: providing the platform for evidence-based vaccination policy. *Epidemiologic Reviews*, 2002, 24:125–136.

21. Jin L et al. The role of RT-PCR assay of oral fluid for diagnosis and surveillance of measles, mumps and rubella. *Bulletin of the World Health Organization*, 2002, 80:76–7.

22. Van Binnendijk RS et al. Evaluation of serological and virological tests in the diagnosis of clinical and sub clinical measles virus infections during an outbreak of measles in The Netherlands. *Journal of Infectious Diseases*, 2003, 188:898–903.

Annex 1

Notification and case investigation form for measles/rubella

Date of notification: _____ Province/territory _____ Reporting district _____ Reporting health facility _____	Case ID /_____ /_____ /_____ / Date of case investigation: _____ /_____ /_____ Initial diagnosis (measles/rubella/other specify)
Name/Patient's father's name ----------/---------- Date of Birth: _____ /_____ /_____OR Age: Years _____ Months _____ Days _____ Sex: _____ M=Male F=Female Address: House _____ Village/Neighbourhood/Housing Scheme _____ _____ Street no/name _____ Town/City _____ District _____	Is case linked to another case or index case? Yes ☐ No ☐ Unk ☐ if yes, write the ID of that case /_____ /_____ /_____ Is case outbreak associated? _____ (Y, N, Unk). If Yes, give the outbreak ID _____ Date seen at health facility _____ /_____ /_____ Date of onset of rash: _____ /_____ /_____ No. of measles/rubella vaccine doses received _____ (9=Unk) Vaccination information obtained by: Vaccination card ☐ Health services ☐ Parents ☐ Self (adult) ☐ Date of last dose of measles vaccine: _____ /_____ /_____ Date of last dose of rubella vaccine: _____ /_____ /_____ Pregnancy status of women: _____

Outcome:

Recovered ☐ Complicated Unknown Died ☐Date death: _____ /_____ /_____

Hospitalized: Yes ☐ No ☐

Complications: _____

Date notified to District: _____ /_____ /_____

Possible Source of infection

Did the person have contact with anyone suspected of having measles 7–21 days before onset of rash? Yes ☐ No ☐ Unk ☐

If yes, who? _____ where? _____

Where there any suspected cases of measles/rubella in the area before this case? Yes ☐ No ☐ Unk ☐

Did the person travel 7–21 days before onset of rash? Yes ☐ No ☐ Unk ☐.If yes, where? _____

Source of infection identified: Yes ☐ No ☐ Unk ☐. (Other epidemiological, import status, travel history) :_____

_____

Final classification: measles rubella

Clinically confirmed ☐ Epidemiologically linked to importation ☐

Laboratory confirmed ☐ Virology evidence of importation ☐

Epidemiologically confirmed ☐ Unknown source ☐

Discarded other classifications:

International importation ☐

Indigenous ☐

Date of final classification: _____ /_____ /_____

Laboratory

Date blood specimen collected: ___ /___ /___ Date blood specimen sent to laboratory: ___ /___ /___ Date blood specimen received by laboratory: ___ /___ /___ Condition of blood specimen: Adequate ☐ Inadequate ☐ Unk. ☐

Date measles serology results reported ___ /___ /___ Results of measles serology: positive ☐ Negative ☐ not tested ☐ indeterminate ☐ Unknown ☐. Results of differential serology (make separate variable for each disease): Positive ☐ Negative ☐ Not tested ☐ Indeterminate ☐ Unknown ☐. Rubella confirmed: Yes ☐ No ☐ Not tested ☐

Collection of specimen for viral culture/identification: Yes ☐ No ☐ Unk ☐

Specimen type: _____ 1 = Urine; 2 = Throat swab; 3 = Oral fluid. Date specimen (culture)/PCR received: ___ /___ /___

Results of measles viral culture/identification: Positive ☐ Negative ☐ Not tested ☐ Unk ☐

Investigator: _____ **Position:** _____

Signature: _____ **Date:** _____ /_____ /_____

Annex 2

Weekly surveillance report

Reporting unit: _____

Dates: from _____ to _____

1. Number of suspected measles cases: _____

(Attach forms on any case; if no cases to report, indicate 0.)

2. Number of acute flaccid paralysis cases: _____

(Attach forms on any case; if no cases to report, indicate 0.)

3. Other: _____; _____

(other designated disease or condition.)

Person filling out report: _____

Date : _____

Annex 3

Line-listing elements of data for measles reporting after investigation

Measles surveillance data elements	
Element of data	**Options**
Country	Standard Name
Province	Standard Name
District	Standard Name
Health formation	Urban HU; Rural HU; Urban HC; Rural HC; Hospital; Health insurance
Date of notification	DD/MM/YYYY
Date of onset of rash	DD/MM/YYYY
EPI.ID	EPID agreed by the country "Same as polio case coding"
Name	
Age in years	Number of years; zero for cases less than one year
Age in months	Number of months
Gender	Male; Female; Unknown
Nationality	
Address	
Date of investigation	DD/MM/YYYY
Vaccination with MCV	0; 1; 2; Blank for unknown
Date last vaccination	DD/MM/YYYY
Link with another measles case	Yes; No
Link with another rubella case	Yes; No
For travellers number of days of arrival	Number of days after your arrival
Destination of travel	
Date specimen collected	DD/MM/YYYY
Date specimen received at the laboratory	DD/MM/YYYY
Type of specimen	Serum; Dry blood; Oral fluid; Urine; Throat swab; Serum and urine; Serum and throat swab; Oral fluid and urine; Oral fluid and throat swab
Condition of specimen and reason of inadequacy for serology	Adequate; Poor due to delay of specimen receiving; Poor due to quantity; Poor due to cold chain; Poor due to delay in specimen collection; Poor due to other reasons

Measles surveillance data elements	
Kit type for measles serology	Brand of assay
Measles serology result	IgM+ve; IgM-ve; Equivocal; not tested
Kit type for rubella serology	Brand of assay
Rubella serology result	IgM+ve; IgM-ve; Equivocal; not tested
Date result shared with EPI	DD/MM/YYYY
Case classification	Measles laboratory confirmed; Measles EPI-linked; Measles clinically diagnosed; Rubella laboratory confirmed; Rubella EPI-linked; Discarded case;Vaccine-related case; Double infection; Imported case
Epidemiologic situation	Sporadic case; chain of transmission, epidemic; imported case
If epidemic index case	EPI.ID Code of index case "should be the same index case for the whole chain of transmission"
Outcome of the case	Recovered; died; complication
Type of complication	Type the complication diagnosed

Annex 4

Congenital rubella syndrome case investigation form

Infant's identification

Name of child: _____

Date of birth: _____ / _____ / _____

Sex: M ☐ F ☐Place infant delivered: _____

Hospital/clinic record number: _____

Name of mother: _____

Address: _____

_____

Notification

Source: _____

Date of notification: _____ / _____ / _____

Name of referring health worker: _____

Address of referring health worker: _____

_____

Telephone number: _____

Clinical signs and symptoms

Group (a)

Congenital heart disease: Yes ☐ No ☐

If yes, describe: _____

_____

Cataract(s): Yes ☐ No ☐

Glaucoma: Yes ☐ No ☐

Pigmentary retinopathy: Yes ☐ No ☐

Hearing impairment: Yes ☐ No ☐

Group (b)

Purpura: Yes ☐ No ☐

Splenomegaly: Yes ☐ No

Annex 5

Case-based measles reporting elements to the Regional Office

1.	Use country standard name
2.	Use location standard name province, district, locality, village, etc.
3.	Unique identifier in surveillance database same as polio
4.	Age in years (less than one year counts" 0 "in the column of years and number of months registered in age-month)
5.	Gender (Male, female, unknown)
6.	Date of onset of rash (dd/mm/yyyy)
7.	Number of measles vaccination doses, leave blank for unknown zero for unvaccinated
8.	Date of last measles vaccination (dd/mm/yyyy)
9.	EPI-linked to a confirmed measles case (Yes/No)
10.	Date specimen collected (dd/mm/yyyy)
11.	Measles IgM (+, -, equivocal, not tested, unknown)
12.	Rubella IgM (+, - , equivocal, not tested, unknown)
13.	Date specimen received in the laboratory (dd/mm/yyyy)
14.	Date laboratory reported back to EPI (dd/mm/yyyy)
15.	Condition of specimen: adequate, poor
16.	Type of specimen collected (Serum, whole blood, Dried blood, Blood and urine, Blood and throat swab, Blood and nasopharyngeal swab)
17. 18.	Final diagnosis (measles laboratory confirmed, measles EPI linked, measles clinically diagnosed, rubella laboratory confirmed, rubella EPI linked, discarded case, vaccine-related, imported)
19.	Lab-ID number
20.	Measles virus isolate (Yes, No)
21.	Measles genotype done (Yes, No)
22.	Measles genotype (A, B1, B2, B3, C1, C2, D1, D2, D3, D4, D5, D6, D7, D8, D9, D10, E, F, G1, G2, G3, H1, H2)
23.	Rubella virus asólate (Yes, No)
24.	Rubella genotype done (Yes, No)
25.	Rubella genotype (1a, 1B, 1C, 1D, 1E, 1F, 1g, 2A, 2B, 2c)

Annex 6

Laboratory request form for measles

Country code _____ Province/territory _____ Reporting District _____

Reporting health facility _____ Date sent: _____ /_____ /_____

Case ID: _____ /_____ /_____ /_____ /_____

Patient's name: _____ Father's name _____ Sex: _____ M=male F=female Uk=unknown

Age: Years _____ Months _____

Address Complete: _____

Date of birth: _____ /_____ /_____ Date of onset of rash: _____ /_____ /_____

S.no Specimen Type Date of collection Date of shipment Date received at laboratory Condition Date of result Result

1. Blood _____ /_____ /_____ _____ /_____ /_____ _____ /_____ /_____ _____ _____ /_____ /_____ _____

2. Throat ___ /_____ /_____ ___ /_____ /_____ _____ /_____ /_____ _____ ___ /_____ /___ _____

3. Oral fluid _____ /_____ /

4. Urine ___ /_____ /_____ ___ /_____ /_____ _____ /_____ /_____ _____ ___ /_____ /___ _____

Suggestions from laboratory, for future sampling, if any_____

Results to be sent to: surveillance focal point at reporting site and country measles surveillance cell

Complete address: _____

Telephone no: _____

Fax number: _____

Name of laboratory: _____

Person received sample: _____

Annex 7

Final report of measles outbreak and control measures

Country:				**Province/State:**				
District/locality				**Town/City:**				
Indicate surrounding areas where there are measles outbreaks if any?								
Date of rash onset of first confirmed case:	DD	MM	YYYY	**Date of rash onset of last confirmed case:**	DD	MM	YYYY	

Number of cases by age in years									
Age	<1	1–4	5–9	10–14	15–19	20–24	25–29	>29	Total
Suspected									
Confirmed									
Deaths									

Documented vaccination history of the confirmed cases							**District/Locality coverage**		
Age in Years	Non-vaccinated	1 dose	2 doses	3 doses	Unknown	Total	Age in Years	MCV1	MCV2
<1									
1–4									
5–9									
10–14									
15–19									
20–24									
25–29									
>29									
Total									

Immunization response to the outbreak						
District/ City name	Date immunization started			Target age group	Target population	Vaccination coverage
	DD	MM	YYYY			

Laboratory investigation									
District/ City name	Date serum sp. collected	No. serum specimens	No. Lab confirmed measles	No. Lab confirmed rubella	Date Oral fluid or throat S. collected	No. Oral fluid sp.	No. throat swabs	Genotype of the virus	Date reported back

Discriptive analysis of outbreak origin	
Discriptive control activities	
Discriptive follow-up activities	

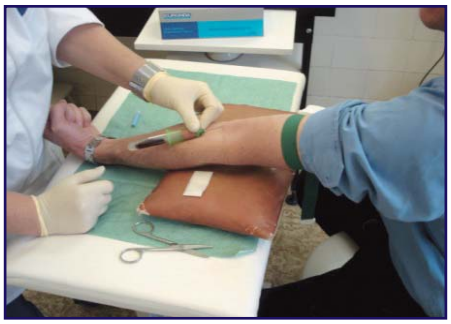
Investigator's name		Date of report	DD	MM	YYYY

Annex 8

Laboratory procedures for measles/rubella

1. *Collecting and handling of blood specimen for serologic confirmation*

- Collect 5 ml blood for adults and older children and 1ml for infants and young children by venipuncture into a sterile tube labelled with patient identification and collection date (Figure 1).
- Fill in case investigation forms completely. Three dates are very important:
  - Date of rash onset
  - Date of collection of sample
  - Date of last measles vaccination.
- To separate the serum from red cells, one of the following three methods described below can be employed. To prevent bacterial over-growth, ensure that the serum is aseptically transferred to a sterile test tube.
- Let the blood sit at an angle for at least 60 minutes (without shaking or being driven in a vehicle), then pour off carefully or remove the serum by using Pasteur pipette to pour into a sterile test tube and label with patient ID.
- If a refrigerator is available, put the sample in a refrigerator for 4–6 hours until the clot retracts, then pour off the serum the next morning. Do not freeze whole blood.
- If a centrifuge is available, let the blood sit for 30–60 minutes, then centrifuge the specimen at 2000 RPM for 10–20 minutes and pour off the serum into sterile tube.



Courtesy of David Featherstone, World Health Organization.

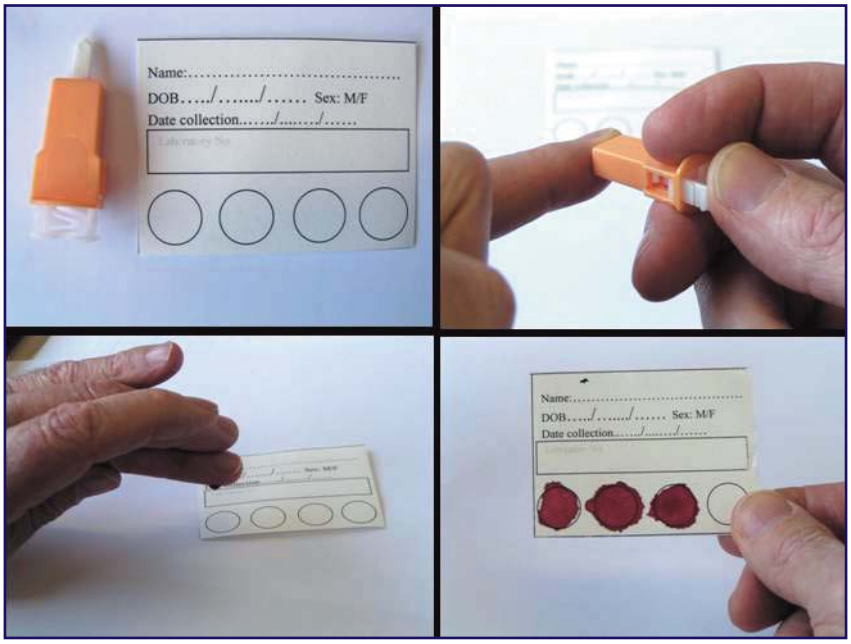
Figure 1. Serum collection by venipuncture

2. *Storage and shipment of serum specimens*

- Store serum at 4 °C–8 °C until it is ready for shipment. The serum can be stored in the refrigerator for a maximum of 7 days. Serum must be frozen at -20 °C if it is going to be stored for longer periods.
- Place specimens in plastic bags. Specimens from different patients should never be sealed in the same bag. Place specimen form and investigation form in another plastic bag and tape to inner top of the specimen transport box.
- If using ice packs (these should be frozen), place ice packs at the bottom of the box and along the sides, place samples in the centre, then place more ice packs on top. When shipping arrangements are finalized, inform receiver of time and manner of transport.

3. *Handling and transport of dried blood specimen using the filter paper method*

- For the collection of a blood sample using the filter paper (e.g. Whatman S&S No. 903), method, a skin puncture may be performed on the finger or heel (in infants and children). For the finger, the area with optimal vasculation and lowest sensitivity is the side of the finger tip about 3 mm from the nail bed. The middle and ring finger are best. The pulp on the tip of the finger should be avoided as it is very sensitive. For the heel the puncture should be performed on the lateral or medial edges of the heel rather than the centre of the heel.
- Label the filter paper with necessary information for identification. The filter paper should be in a standard format 14–15 mm circle to place the blood drops (Figure 2).
- Make sure the patient sits comfortably. A baby should be held gently but firmly by the parent. For Finger prick, the hand should be warm and relaxed. The patient's fingers should be straight but not tense. Clean the puncture site with an alcohol wipe and allow drying.
- Use thumb to lightly press the finger from the top of the knuckle to the tip. With the thumb's gentle pressure at the tip of the finger, place the lancet at the side of the fingertip. Press the lancet firmly against the finger or heel and allow the tip to penetrate the skin by 2 mm. Dispose the used lancet into a sharps container.
- Wipe away the first drop of blood with a clean piece of dry gauze. Allow one drop to fall onto each circle of the filter paper. Fill at least three circles and four if possible. Ensure that the blood soaks completely through the paper over the complete area of the circle. Do not hold the filter paper against the puncture site (Figure 2).
- Allow the filter paper to air dry thoroughly (at least 60 minutes) before enclosing in a bag or storing. Drying stabilizes the IgM and reduces the chance of microbiological contamination.



Courtesy of David Featherstone, World Health Organization.

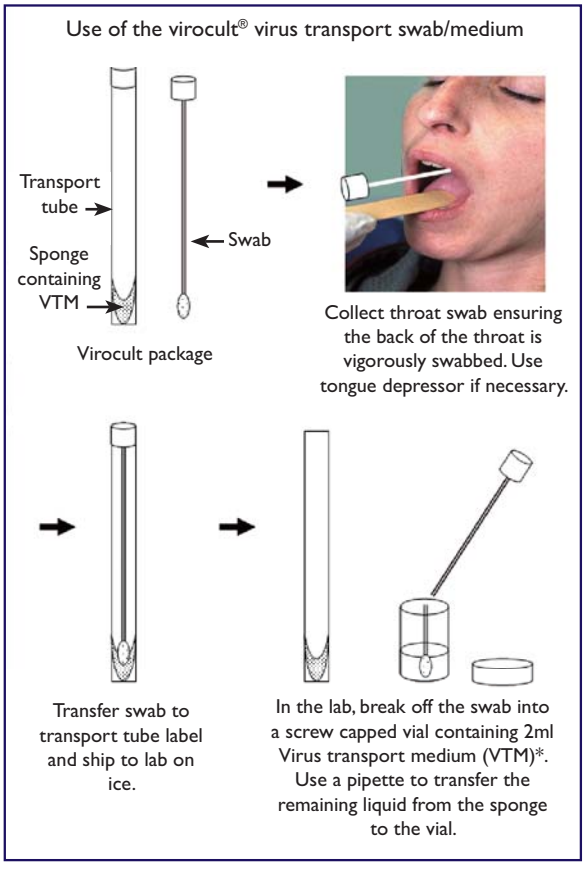
Figure 2. Dried blood sampling technique

- Wrap each dried blotting paper in paper/foil/plastic or an envelope to prevent possible cross contamination. Store each filter paper out of sunlight preferably inside a plastic zip bag to protect it from dust and moisture. Store if possible in a cool place and transport to the laboratory as quickly as possible under reverse cold chain. The dried serum is stable at room temperature and can be shipped in an envelope by mail within a week. For a longer period the dried serum should be kept at +4 °C until shipment.

4. *Handling and transporting naso-pharyngeal swabs for viral isolation*

- Nasopharyngeal specimens for virus isolation must be collected as soon as possible after onset and not longer than 5 days after the appearance of the rash, when the virus is present in high concentration.
- The patient is asked to open the mouth wide and say "ah". The tongue should be depressed with a spatula, and a nasopharyngeal swab is obtained by firmly rubbing the nasopharyngeal passage and throat with sterile cotton swabs to dislodge epithelial cells. The swab is then placed in a labelled viral transport tube ensuring that the swab is immersed in the sponge containing the viral transport medium (Figure 3).
- The tube is transported to the laboratory at 4 °C–8 °C, using frozen ice packs and appropriate insulated shipping container within 48 hours.

A number of swab collection devices (such as the Orocol™ and OraSure™) have been developed specifically to collect these fluids from the mouth. The swabs are designed to be used like a toothbrush (Figure 3). Oral fluid samples are collected by gently rubbing a small sponge on a stick along the gum and dentine interface for about 1 minute. The sponge absorbs approximately 0.5 ml of crevicular fluid during this period. It is sealed in a tube and transported to the laboratory at ambient temperature. The laboratory adds buffer to the sponge, extracts the crevicular fluid by centrifugation and tests the supernatant for specific IgM or viral RNA, or both.



Courtesy of David Featherstone, World Health Organization.

Figure 3. Technique of naso-pharyngeal specimen collection

Courtesy of Ruth Parry, World Health Organization.

Figure 4. Technique of oral fluid sampling

Field guidelines for surveillance of measles, rubella and congenital rubella syndrome *provides countries with a technical resource to use in developing comprehensive standard operating procedures for measles, rubella and congenital rubella syndrome surveillance. The largest part of these guidelines is devoted to developing a surveillance system for cases of measles, rubella and congenital rubella syndrome, including case investigation, outbreak response, laboratory procedures for measles and rubella testing and surveillance monitoring and feedback. This publication is primarily intended for use by surveillance and national immunization managers and their staff, but many other health professionals and technical staff working in surveillance, immunization and laboratories at the country level will find it useful in improving measles, rubella and congenital rubella syndrome surveillance. It can be used at various levels of the health care system and countries can adapt the guidelines according to their local situations.*

9 789290 217909