Integrated Surveillance Guideline for selected Vaccine Preventable Diseases

Measles, Rubella, Congenital Rubella Syndrome, AFP, Diphtheria, Pertussis, Neonatal Tetanus and Japanese Encephalitis

1st Edition, 2018

VACCINE PREVENTABLE DISEASE PROGRAMME

Department of Public Health

Ministry of Health

BHUTAN

Forward

Expanded Programme for Immunization (EPI) which is now known as Vaccine Preventable Disease Programme (VPDP) is oldest public health program launched on 15th November 1979 with an objective of reducing the incidence of six vaccine preventable diseases namely tuberculosis, diphtheria, whooping cough, tetanus, polio and measles. As of now, country has introduced 12 antigens in the routine immunization services.

An immunization service has been one of the successful public health programme and archived many milestone. Bhutan has achieved Universal Childhood Immunization in 1991 and since then Bhutan has sustained high immunization coverage above 95%. Bhutan remained polio free since 1986 and received polio-free certification in 2014. Subsequently, Bhutan eliminated neonatal tetanus in 2014 and Measles in 2017. Bhutan has also rubella and congenital rubella syndrome (CRS) control targets and awarded certificate for control of rubella CRS in 2018.

In the past, Vaccine Preventable Disease (VPD) surveillance has been conducted in isolation with each VPD having separate surveillance guideline. This has caused inconvenience for health care workers in field for implementation. As a result, integrated surveillance guideline was for VPD by SEARO, WHO in 2018. In line with the SERO guideline, VPDP has also developed the VPD integrated surveillance guideline for the country. This is the first integrated surveillance guideline developed for selected Vaccine Preventable Disease.

We hope that this VPD integrated surveillance guideline will be more users friendly and practical for implementation in the field to further strengthen the Vaccine Preventable Disease Surveillance.

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DIRECTOR

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Chapter 1: Introduction

1.1. Surveillance definition

An ongoing, systematic collection, analysis, and interpretation of health-related data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those responsible for prevention and control.

1.2. Surveillance goals

1. Early detection and notification of suspected cases
2. Monitoring trends of VPD's over the period of time
3. Ensuring adequate and timely response to cases/outbreak notified
4. Identifying risk population for institution of appropriate prevention measures
5. Monitoring and evaluation of vaccine preventable Disease programme performance
6. Resource prioritization and mobilization for implementing preventive and control measures based on the information obtained through the surveillance
7. To determine the effectiveness and impact of vaccination programme

1.3 Existing VPD Surveillance systems

Existing VPD surveillance is disease specific surveillance system and all health centers are reporting centers. AFP, measles and rubella are case based surveillance while diphtheria, pertussis, tetanus are reported as aggregate on monthly basis including zero-reporting by health centers to district health office and to VPDP. CRS and AES/JE are sentinel based surveillance. However, after introduction of National Early Warning Alert and Response Surveillance, VPD reporting has been integrated in NEWARS.

1.4 National Early warning Alert and Response Surveillance (NEWARS)

The National Early Warning Alert and Response Surveillance (NEWARS) was introduced in 2014 as the national surveillance and response system for various priority diseases or syndromes of public health concern including vaccine preventable

diseases for early detection and efficiently response . The NEWARS was developed to replace previous National Notifiable Diseases Surveillance introduced in 2010 which was indicator based surveillance. The NEWARS guideline revised to update and incorporate electronic web-based and mobile SMS reporting system introduced for NEWARS in 2015.

The NEWARS information system has three platforms for reporting:

1. Weekly Reporting: There are 11 diseases and syndromes to be reported including zero reporting every week (Monday and Tuesday).
2. Immediately Reporting: There are 15 diseases and syndromes to be reported as and when detected including weekly zero reporting (Monday and Tuesday). All vaccine preventable diseases are immediately notifiable by healthcare professionals. Immediately reported diseases or syndromes are verified and responded.
3. Event Reporting. Any outbreak of can be reported as and when detected not limited to diseases by healthcare professionals. Events are verified and responded.

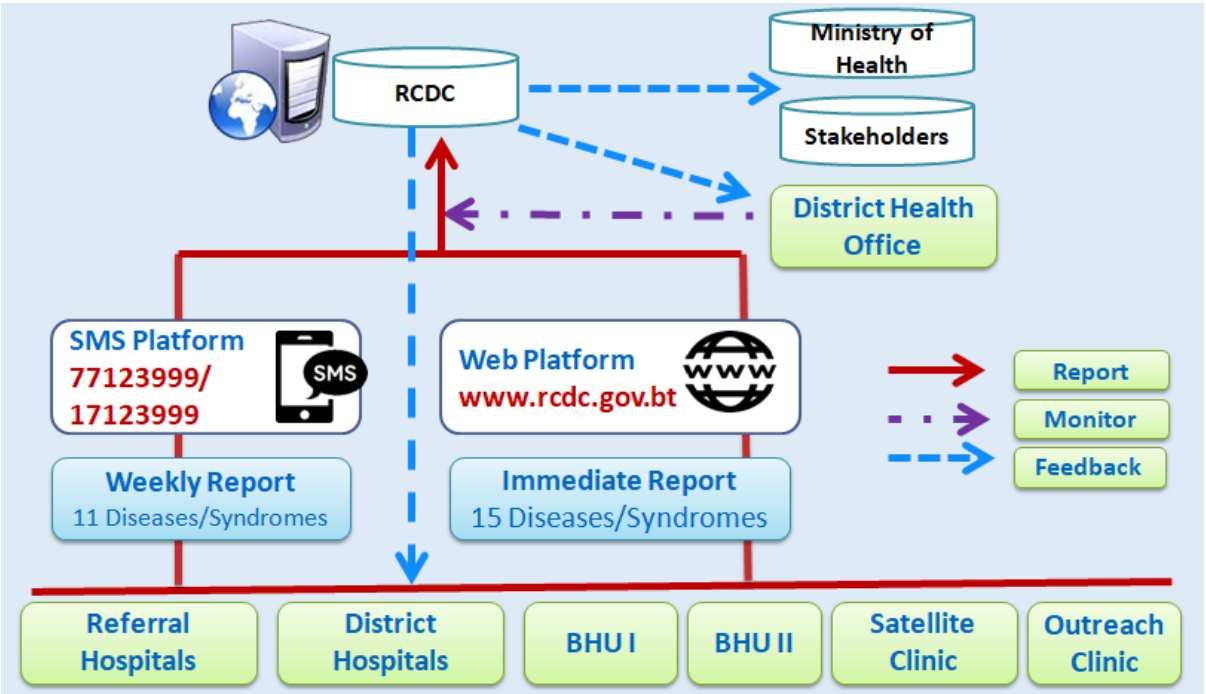


Figure 1: Flowchart of notifiable disease surveillance

1.5. Overview of operational aspect of VPD's integrated surveillance system

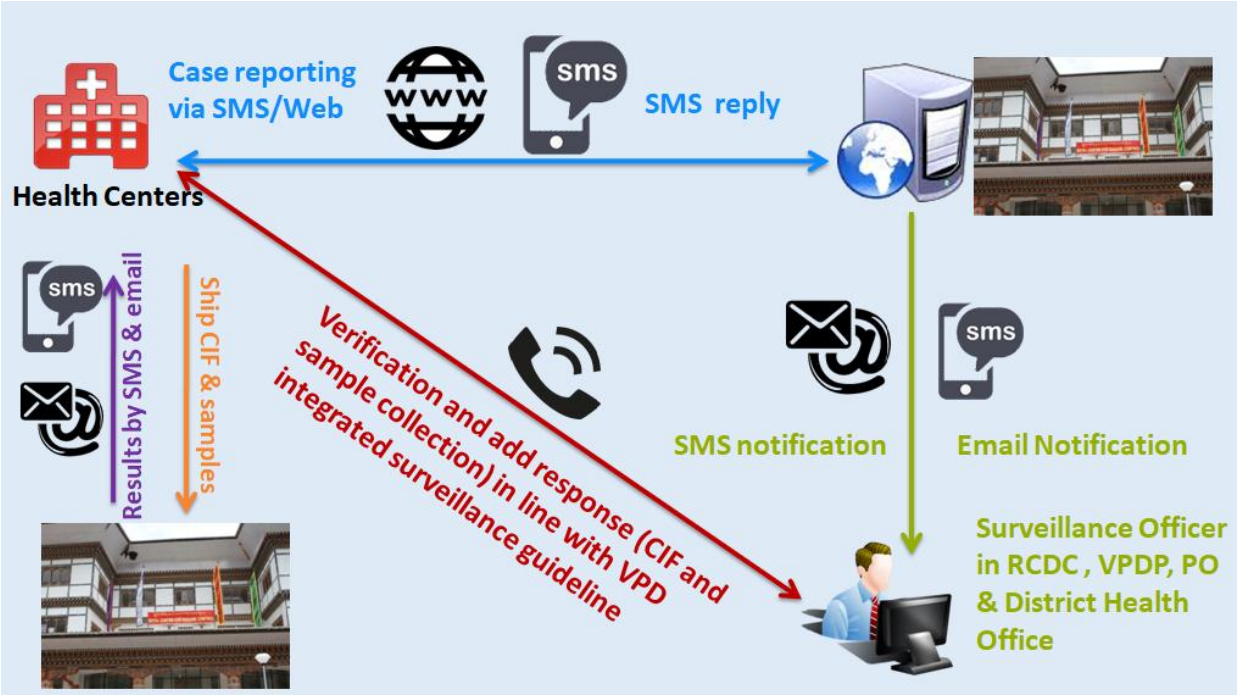


Figure 2: Flowchart of VPD surveillance

1.5.1 All clinicians including specialists, nurses and health workers should:

- Identify VPDs as per the case definition
- Report suspected case immediately through web based or mobile SMS if any and zero reporting weekly in the National Early Warning Alert and Response Surveillance (NEWARS) Information System.
- Collect information as require by standard case investigation form
- Refer patient to laboratory with case-based reporting form duly filled for sample collection.
- Refer suspected case to hospitals (from BHU) if require.
- Contact tracing in household or village or community with similar illness.
- Organize a network of community reporters who will report cases to the health center through support of local government and community leaders.
- Ensure samples referral to RCDC as early as possible.

- Share lab results to hospitals and BHU for referral samples.

1.5.2 Laboratory personnel should:

- Collect suitable sample as per the SOP's
- Aliquot and store in proper refrigerator or freezer if available
- Ship samples to RCDC in proper cold chain

1.5.3 District Health Office should:

- Conduct surveillance monitoring and supervision in respective health centers
- Follow up and monitor the reports including zero reporting in NEWARS system
- Monitor case based information reported by health centers and sample referral to RCDC
- Support case investigation and active case searches.
- Activate District Rapid Response Team, if needed, to investigate any VPD's outbreaks

1.5.4 Surveillance officers at RCDC should:

- Verify VPD's events reported and provide appropriate recommendation for response
- Routinely validate data reported by health centers
- Coordinate outbreak investigation
- Provide feedback through monthly report and quarterly disease surveillance
- Conduct training for health professionals on VPD's surveillance

1.5.5 National Reference Laboratory at RCDC should:

- Providing confirmatory diagnosis for vaccine preventable diseases promptly for samples referred by health centres
- Referring samples to supranational reference laboratories if required

1.5.6 Vaccine Preventable Disease Programme should:

- Regularly review surveillance data along with the surveillance and data team and provide timely feedback as and when required
- Ensure corrective actions are initiated as per the findings of the data review.

Chapter 2: Measles and Rubella Surveillance

2.1. Introduction

Bhutan has eliminated measles in 2017 and goal of measles and rubella surveillance is to sustain measles elimination status and monitor progress towards rubella elimination. To sustain measles elimination and monitor progress towards rubella elimination, a sensitive quality case-based surveillance system should be maintained. The goal of case-based surveillance is to detect, investigate and classify all suspected cases; and response to confirmed outbreaks. For case confirmation, case-based surveillance includes laboratory testing at an accredited laboratory within the Global Measles and Rubella Laboratory Network.

The measles and rubella surveillance is a nation-wide surveillance **case-based surveillance** whereby every health center should actively look for suspected cases during OPD and IP service. The single suspected case of fever with rashes (maculopapular) is an immediately notifiable syndrome in the country.

2.2. Case/Outbreak detection and Reporting

2.2.1 Case definition

Suspected case of measles and rubella – A patient with acute fever and maculopapular (nonvesicular) rash, or a patient whom a health-care worker suspects has measles or rubella irrespective of the age.

Measles or rubella outbreak in an elimination setting is defined as laboratory confirmation of any single case and evokes a public health response.

2.2.2 Case Reporting

All health-care workers – physicians/clinicians, nurses, health workers– should immediately report every suspected case of fever with rashes (maculopapular) to the Royal Centre for Disease Control web-based National Early Warning Alert and Response surveillance information system under immediately reporting platform using either through mobile SMS or web-based system (refer NEWARS guideline). If no suspected case is detected, Zero reporting should be made weekly through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform.

All health-care workers should know how to identify and report suspected cases. District health authority /designated surveillance officers are responsible for ensuring that health-care workers know how to identify and report cases, and maintain surveillance of adequate quality.

District health authority/ designated surveillance officers should also regularly conduct active surveillance visits to health facilities to check hospital records, outpatient and inpatient registers and interview health staff to find any missed case of suspected measles or rubella. Such visits also provide an opportunity to sensitize health staff on case reporting and resolve any issues that they may have.

2.3. Case investigation

Case investigation is important to identify the magnitude of public health response required. Trained health staff should be responsible for case investigation within 48 hours of case reporting and lab confirmation. Every single measles or rubella laboratory confirmed should be considered as an outbreak and case should be investigated using standard Measles Rubella Case Investigation Form (**Annexure 2.1**) in a community/locality with serology and virology sample collection from suspected cases. In case of rubella, sera should be obtained from all pregnant women with suspected rubella.

2.4. Unique cases identification number

It is critical to assign a unique case identification number to each suspected case and outbreak. The case identification number begins with one or more three-letter combinations to designate the geographic location, followed by the year and the case number. Forms, specimen labels and all communications related to the case should cite the unique case identification number. Since MR case-based surveillance is the web-based surveillance, unique case identification number to each suspected case and outbreak is generated automatically by the system. E.g: BHU-MR/MRR/2018/001 if MR suspected case is the first case Mongar Regional Referral hospital in 2018.

2.5. Specimen collection and transport

Country has been verified as measles eliminated, and rubella control/near elimination. Therefore every suspected case should have a serum sample for serology and a throat swab for virology.

If there is a suspected large outbreak, laboratory specimens should be collected from at least the first five suspected cases. If an outbreak continues over a protracted period, another 5-10 samples for virology and serology should be collected every two months to ensure that the outbreak is still due to measles or rubella or chains of transmission are part of the same outbreak or due to new importations of a different measles virus strain.

2.5.1. Serology

Whenever measles/rubella is suspected, designated personnel should secure specimens for laboratory confirmation. Adequate blood sample should be collected on first contact with the patient during the case investigation. A throat swab should be obtained for virology along with the serology specimen. **The likelihood of detecting IgM antibodies is high if the blood specimen is collected between 3 and 28 days after onset of rash**. Shipment of the sample to a recognized laboratory should take place as soon as possible, maintaining appropriate cold chain (4–8 ºC).

Venous blood collection

- Venipuncture in sterile labelled tube (3-5 ml for older children and adults and 1mL for infants and younger children).
- Whole blood can be stored at 4–8 ºC for up to 24 hours before the serum is separated.
- Whole blood should be allowed to clot and then centrifuged at 1000 × g for 10 minutes to separate the serum.
- The serum should be carefully removed with a fine-bore pipette to avoid extracting red cells and transferred aseptically to a sterile labelled vial.
- Serum should be stored at 4–8 ºC until shipment takes place, but not more than a maximum of 5 days. When kept for longer periods, serum samples must be frozen at a temperature of –20 ºC.

Dried blood spot collection (alternate specimen collection for serology when venipuncture is not feasible)

- Skin puncture the finger or heel (for young children before they start to walk) using sterile lancet.
- Up to four full-circles of whole blood are collected on standardized filter paper.
- For an adequate specimen, ensure that each entire circle is completely filled.
- One to two drops are collected to completely fill each circle of a filter paper (*whatman protein saver)* properly labelled for each case. (1st circle for Measles IgM, 2nd circle for Rubella IgM, 3rd circle for repeat test if required, 4th circle for quality assurance processes in the lab).
- Allow the filter paper to dry thoroughly before enclosing in a plastic bag or envelope, and store with a desiccant to keep dry.
- Samples do not need to be kept refrigerated or frozen during transport; it is advisable to store in a cool, dry place and transport to the laboratory as soon as possible, preferably within 5 days.
- Thoroughly dried blood spot samples are no longer subject to IATA (International Air Transport Association) dangerous goods regulations.

2.5.2. Virology

Throat swabs should be collected within 5 days of onset of rash for viral detection/isolation for both measles and rubella viruses. In our setting, blood and throat swabs are collected together during first visit to health center service contact.

Throat swab collection

- Firmly rub the back of the throat with sterile cotton swabs to dislodge epithelial cells.
- The swabs are placed in a sterile viral transport medium in labelled screw capped tubes.
- The swab should be refrigerated and shipped to the laboratory with ice packs (4 to 8 ºC) to arrive at the testing laboratory within 48 hours.
- If arrangements cannot be made for rapid shipment, swabs should be shaken in the medium to elute the cells and then removed.

2.6. Case classification

Laboratory-confirmed case A suspected case of measles or rubella that has been confirmed by a proficient laboratory through detection of IgM in sera (or oral fluid) for measles or rubella in the laboratory by ELISA

Epidemiologically linked case: A suspected case of measles, or rubella, that has not been confirmed by a laboratory but was geographically and temporally related, with dates of rash onset occurring 7–21 days apart for measles (or 12–23 days for rubella) to a laboratory-confirmed case or, in the event of a chain of transmission, to another epidemiologically-confirmed measles or rubella case.

Discarded: A suspected case which was investigated and discarded, either through negative results of adequate laboratory testing for measles or by an epidemiologic linked to a laboratory-confirmed case of another disease that is neither measles nor rubella

Clinically compatible measles case: A suspect case with fever and maculopapular (non-vesicular) rash and one of cough, coryza or conjunctivitis, for which no adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory-confirmed case of measles, rubella, or another laboratory-confirmed communicable disease.

Clinically compatible rubella case: A case with maculopapular (non-vesicular) rash and fever (if measured) and one of arthritis/arthralgia or lymphadenopathy, for which no adequate clinical specimen was taken and which has not been linked epidemiologically to a laboratory-confirmed case of rubella, measles or another laboratory-confirmed communicable disease.

Non-measles non-rubella case: A suspected case that has been investigated and discarded as non-measles and non-rubella using

(a) laboratory testing in a proficient laboratory or

(b) epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is neither measles nor rubella

Measles vaccine-associated illness: A suspected case that meets **all** five of the following criteria:

i. the patient had a rash illness, with or without fever, but did not have cough or other respiratory symptoms related to the rash;
ii. the rash began 7–14 days after vaccination with a measles-containing vaccine;

iii. the blood specimen, which was positive for measles IgM, was collected 8–56 days after vaccination;

iv. thorough field investigation did not identify any secondary cases; and

v. Field and laboratory investigations failed to identify other causes.

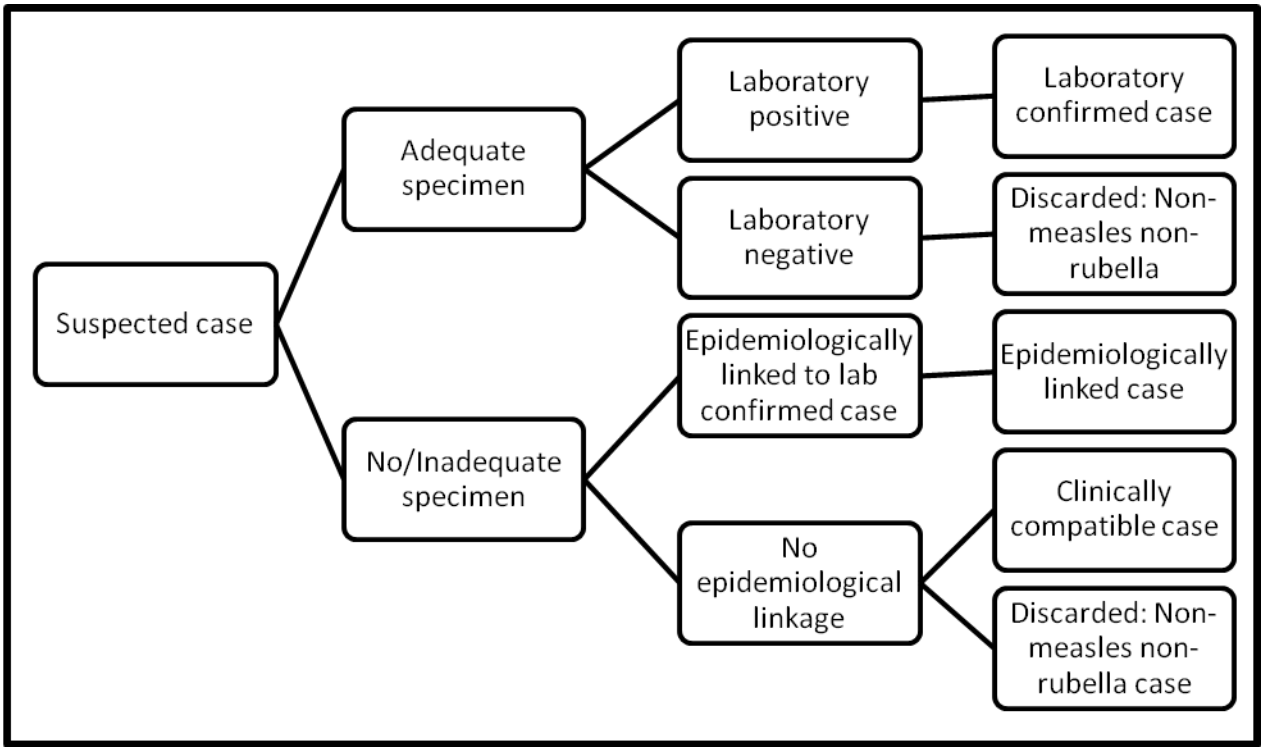


Figure 2.1: Flowchart for classification of suspected cases

Endemic cases

Endemic measles transmission is the existence of any continuous indigenous chain or re-established chain of transmission of measles/rubella virus persisting for >1 year in any defined geographic area. An endemic measles case is a laboratory or epidemiologically confirmed measles case resulting from endemic transmission of the measles virus. For rubella, any case that cannot be proved imported is considered endemic.

Imported cases:

An imported measles case is a confirmed case which, as supported by epidemiologic and/or virologic evidence, was exposed outside the country or region during the 7–21 days prior to rash onset. For rubella, the time frame is 12–23 days. A travel history to an area where measles/rubella occurs and during a plausible time frame must be demonstrated; results of molecular sequencing of the virus isolated from the cases

should be compatible with the areas/countries visited. The possibility of local exposure to measles/rubella must be excluded after a careful community investigation.

Import-related cases: An import-related case is a confirmed case, which, as supported by epidemiologic and/or virologic evidence, has locally acquired infection as part of a transmission chain related to an imported case. A chain of transmission is two or more confirmed cases that are epidemiologically linked. The investigation should thus demonstrate that the import-related case had direct contact 7–21 days with an imported case or another import-related case (12–23 days before rash onset for rubella). Molecular sequencing data of the isolated virus, if available, could support the link.

Cases with unknown source of infection: A confirmed case for which the source of infection was not identified. It is possible that an epidemiological link to an imported case or an import-related case cannot be found even after a thorough investigation, and sporadic cases with unknown source of infection are not necessarily indicative of endemic transmission. However, the identification of sporadic cases might indicate gaps in surveillance. The pattern of occurrence of these cases (e.g. number of transmission chains and number of cases involved, geographical and temporal distribution) is as important as their number.

2.7. Case Management

There is currently no specific antiviral treatment for measles or rubella. Administration of vitamin A to children with measles has been shown to reduce both the severity of disease and the case-fatality rate, and WHO recommends that vitamin A be administered to all children with measles: **50 000 I.U. for infants aged less than 6 months, 100,000 I.U. for infants aged 6–11 months and 200,000 I.U. for children aged 12 months of age and older**. Administration of vitamin A should be provided at the first health service contact and one dose should be administered the following day. If the child has clinical signs of vitamin A deficiency (such as Bitot's spots), a third dose should be given 4–6 weeks later. For children who are being cared at home, health workers should ensure that they receive vitamin A doses. Treatment should be provided for a measles complication. All cases of measles do not require hospitalization and many can be managed at home. For uncomplicated cases, fluids (such as oral rehydration solution), antipyretics and nutritional therapy are commonly

indicated. Many children require 4 to 8 weeks to fully recover their pre-measles nutritional status.

All hospitalized cases of measles should be isolated to prevent further transmission inside the hospital. Suspected measles patients should be isolated until 4 days after appearance of rash. Care should be taken in hospital settings to use proper infection control practices (e.g. isolation, negative pressure) as measles is extremely contagious. There is high risk of nosocomial transmission among non-immune health-care workers and other patients, including unimmunized infants. Unless measles patients have complications requiring hospitalization or follow-up, it is recommended for them to be cared for at home. Other measles complications, such as diarrhoea, pneumonia and otitis media, should be treated following the WHO protocol for Integrated Management of Childhood Illness.

For rubella, care is supportive for non-pregnant persons. For pregnant women with suspected rubella, blood sample should be collected and a comprehensive investigation including laboratory testing should be conducted. Pregnant women with confirmed rubella should be followed till the completion of her pregnancy to document the outcome (i.e., normal, CRS, miscarriage, stillbirth, etc). For those pregnancies that go to delivery, the newborn should be placed in contact isolation and evaluated for suspected CRS.

2.8. Public Health Intervention

The key components of public health response are:

a. **Contact tracing:** contact tracing should be conducted for every single laboratory confirmed measles or rubella case to identify the source of infection and determine whether other areas have been exposed or are also experiencing outbreaks (**Annexure 2.2**). Identify all people that the case had contact with the cases during the time he/she was contagious (**4 days before and until 4 days after the onset of rash for measles and for rubella, 7 days before until 7 days after the onset of rash**) and determine whether they are or were ill. If rubella is suspected, pregnancy status for all women of childbearing age should be obtained.

In large outbreaks, it may not be feasible to identify all contacts due to time, resources, and logistical constraints. In this situation, contact tracing should be deprioritized, and a large public health immunization response should be triggered along with a risk

communication and awareness campaign. However, the following groups and individuals should be considered priority contacts during outbreaks: household contacts, schools/institutes contacts, including all school employees and students, Child care/day care contacts, workplace contacts health care facility (individuals who shared the same room, including waiting room without appropriate protection).

The following actions should be taken to minimize spread.

- Contacts without documented evidence of measles and/or rubella vaccination should be vaccinated and the symptoms of measles and rubella should be explained to them. During the second week after exposure, and at the first sign of possible fever and maculopapular rashes the contact should be instructed to stay at home.
- Follow-up should be done to till 21 days to determine if a contact subsequently became ill, laboratory specimens should be collected.
- Pregnant women with suspected rubella should be followed until the completion of her pregnancy to document the outcome especially if the outbreak is rubella. (i.e., normal, CRS, miscarriage, stillbirth, etc).

b. Enhanced case-based surveillance and active case searches: Country has been verified as measles eliminated, and rubella control/near elimination. Therefore, every single laboratory confirmed case of measles or rubella should response as outbreak and active case searches should be conducted to detect unreported cases to ensure that all cases are identified and reported.

In the community and in schools, active case searches should be conducted by asking key people if they know of anyone with fever and rash. This activity should be aided by using pictures of measles/rubella patients with maculopapular rash. Such searches should be conducted in a perimeter of an entire village, cluster of villages, ward of town or entire town, etc. depending upon a local epidemiological assessment mostly within the radius of 100–1000 metres from the confirmed case (may not applicable in the community and small urban towns). In addition, health facilities should also be included for active case searches. In health facilities, health staff interviews and review of registration records, discharge diagnoses, hospital charts, etc. should be performed to identify patients with fever and rash illnesses and their final diagnosis. During rubella outbreaks, active CRS surveillance should be implemented with special attention to

investigation and active follow-up of pregnant women with suspected rash illness in the affected area. Additional measures could include investigation and vaccination of susceptible contacts to reduce the risk of exposure to pregnant women.

c. Survey of population immunity/gaps: should be conducted to review coverage trend for MRCV1 and MRCV2, review coverage of MCV SIA or other Periodic Intensification of Routine Immunization (PIRI) if any in the area to identify any immunity gaps especially on any hard-to-reach populations. Such survey will be conducted by national programme if required.

d. **Enhancing population immunity against measles and rubella:** ORI or SIA should be conducted based on epidemiological data (**Annexure 2.3**). Since country has already achieved elimination and MR vaccination should be provided among close contact of every lab confirmed cases if they are unimmunized and those including children who cannot produce immunization cards or records during the investigation.

Isolation of suspected cases: Children with mild illness may preferably be managed at home without compromising on access to health care and avoiding contact with other vulnerable children. Seriously ill children should preferably be hospitalized for proper management. Since the measles virus is highly infectious, all hospitalized children with suspected measles should be cared for in an isolation facility. School-aged children and working adults should avoid public places and remain confined at home for at least 5 days after the onset of the rashes.

For confirmed rubella infection, persons with rubella should be isolated up to 5 days after rash onset. Emphasis should be placed on preventing exposure of susceptible pregnant women to prevent CRS.

2.9. Dealing with larger outbreaks (>two suspected cluster cases)

In such situation, laboratory specimens should be collected from all suspected cases.

- If two or more specimen are positive for either measles/rubella IgM, the outbreak should be classified either as **Measles/Rubella outbreak**
- If less than two samples are positive for measles or rubella IgM, the outbreak should be **discarded** and the cases are treated as sporadic cases and public health response initiated accordingly.

During large outbreaks, the principles of public health response remain the same with case based measles /rubella case:

1. Contact tracing should be conducted and a large public health immunization response along with risk communication and awareness campaign should be prioritized.
2. Outbreak ID should be assigned to all cases associated with an outbreak.
3. Epidemiological linkage should be the primary way classifying new cases during confirmed outbreak. However, it is not recommended that all cases in a given area during the particular period be all categorized as epidemiologically linked; all IgM negative cases should be discarded and do better investigations to establish potential relationships between cases to have epidemiological linkage.
4. If epidemiologic linkage is not established, laboratory testing of the suspect case should be done. After initial confirmation of the outbreak, laboratory testing should be conducted among suspected cases that may arise in new locations or in previously unaffected groups.
5. If the outbreak continues over a protracted period, another 5-10 samples should be collected every 2-3 months to ensure that the outbreak is still due to measles. Genotyping becomes particularly important to determine whether chains of transmission are part of the same outbreak or due to new importations of a different measles virus strain.

2.10. Data Management

For successful measles and rubella elimination, a well-developed information system is needed that provides programme managers and health workers with the information they need for taking appropriate actions. Information from the surveillance system should be used to produce regular summary reports, and distribute to the personnel responsible for taking actions on identified problems. All surveillance information should be standardized.

Data Collection: For optimal monitoring and meaningful analysis of surveillance data, systematic and standard collection of critical parameters is essential. These limited numbers of variables called ‘core variables’ are required to properly manage such information which include: unique case identification number; basic demographic data

on each case; basic clinical data on each case; data on vaccination status; recording and monitoring of laboratory specimens from collection to final laboratory results; case classification and outcomes. These core variables are incorporated into a standardized case investigation form which is designed in the NEWARS MR web-based surveillance. All suspected cases should be notified immediately and all information required by the standard cases investigation form should be collected by all health centers. If no suspected cases are identified, all health centers should do weekly "zero-reporting" in the NEWARS. The national programme should then forward the collated report to the WHO regional office every week. The timeliness of those reports (on time or late) should be regularly recorded for each health centers.

Data analysis: Data from the investigation form and line-listings should be analysed to monitor reported suspected, clinically compatible, epidemiologically linked and laboratory confirmed cases by age, sex, location and vaccination status as well as to determine whether standards for case reporting and investigation are being met.

Age distribution: 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.

Geographic location: 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.

Source of infection: Surveillance and investigation information will help to identify areas where the measles/rubella virus is still actively circulating or imported.

Source of reporting: This information will help to determine whether improvements are needed regarding personnel reporting suspected cases.

Vaccination history of cases: Accurate information on the vaccination history of confirmed cases is essential for evaluating vaccine coverage, vaccine effectiveness and detecting potential problems with the cold chain.

Surveillance Performance Indicators

- Timeliness of reporting
  - Proportion of surveillance units sending measles and rubella reports, including 'zero-reporting' to the national level on time (target: ≥80%).

$$\frac{\text{Surveillance units reporting measles and rubella data to the national level on time}}{\text{Total number of surveillance units}} \times 100$$

- Reporting rates of cases discarded as non-measles and non-rubella as a proxy to sensitivity of surveillance
  - Reporting rate of discarded non-measles non-rubella cases at national level (target: ≥2 per 100 000 total population).

$$\frac{\text{Total number of discarded non-measles non-rubella cases}}{\text{Total population}} \times 100\,000$$

- Representativeness of reporting
  - Proportion of second administrative level units reporting at least two non-measles non-rubella cases per 100 000 population (target: ≥80% of second-level administrative units).

$$\frac{\text{Total number of second administrative level units reporting at least two non-measles non-rubella cases per 100 000 population}}{\text{Total number of second administrative level units}} \times 100$$

- Adequacy of investigation
  - Proportion of suspected cases with adequate investigation initiated within 48 hours of notification (target: ≥80% of suspected cases).

$$\frac{\text{Total number of cases with adequate investigation within 48 hours of notification}}{\text{Total number of suspected cases}} \times 100$$

  - Adequate investigation includes collection of all the following data elements from each suspected case of measles or rubella: Name or identifier; place of residence; place of infection; age or date of birth; sex; date of onset of rash; date of specimen collection; measles-rubella vaccination status; date of last measles-rubella containing vaccination; date of notification; date of investigation and travel history.

- Laboratory confirmation
  - Proportion of suspected cases with adequate specimen collection[3] for detecting acute measles and rubella infection collected and tested in a proficient laboratory (target: ≥80% of suspected cases, excluding epidemiologically linked cases).

$$\frac{\text{Total number of cases in which adequate serum sample is collected and tested in a proficient laboratory}}{\text{Total number of suspected cases}} \times 100$$

- Timeliness of specimen transport
  - Proportion of serology and virology specimens received at the laboratory within 5 days of collection (target: ≥80%).

$$\frac{\text{Total number of specimens received at laboratory within 5 days of collection}}{\text{Total number of specimens collected}} \times 100$$

- Viral detection
  - Proportion of laboratory-confirmed chains of transmission (defined as one or more confirmed measles cases) with specimens adequate for detecting measles virus collected and tested in an accredited laboratory (target: ≥80%).

$$\frac{\text{Total number of laboratory-confirmed cases with specimens adequate for detecting measles virus collected and tested in an accredited laboratory}}{\text{Total number of laboratory-confirmed cases}} \times 100$$

- Timeliness of laboratory reporting
  - Proportion of serology results reported by the laboratory within 4 days of specimen receipt (target: ≥80%).

$$\frac{\text{Total number of results reported by laboratory within 4 days of specimen receipt}}{\text{Total number of serology specimens received}} \times 100$$

  - Proportion of virology results reported by the laboratory within 2 months of specimen receipt (target: ≥80%).

$$\frac{\text{Total number of results reported by laboratory within 2 months of specimen receipt}}{\text{Total number of virology specimens received}} \times 100$$

2.11. Review and Feedback

Periodic review of surveillance performance should be conducted through various mechanisms:

- Annual review meeting with District Health Authority
- Annual desk review using the WHO Measles Programmatic Risk Assessment Tool
- Periodic (every 2-3 years) Joint national and international VPD surveillance e review activity

At the national level, preferably updated weekly/monthly bulletin should be issued with results on suspected and confirmed cases. In addition, this bulletin should indicate the number of units reporting each week (including zero-case reporting). Information about the current epidemiology of acute flaccid paralysis, neonatal tetanus and other EPI target diseases could also be included, and bulletins should be distributed to all health-care providers and other interested health-care personnel regularly.

Annexure 2.1 MR Case investigation form

1. Patient Information **Case Identification Number:**

Name of Health Facility:-
Patient Name:
Age in Year: _____ Month: _____
Gender: ☐ Male ☐ Female
Occupation:_____
Resident address:
Dzongkhag (District):
Duration of stay:_____
Contact Number of Patient/Parents Mobile No:

(dd/mm/yyyy)
Date of Birth: (_____/_____/_____)
Date of visit: (_____/_____/_____)
Date of Onset fever: (_____/_____/_____)
Date of onset of rash: (_____/_____/_____)
Date of notification: (_____/_____/_____)
Date of Investigation: (_____/_____/_____)

2. Vaccination Status (by card / history): ☐**Yes** ☐**No** ☐**Don't know**

	No. of Doses	Date 1st dose	Date 2nd dose
Measles containing vaccine:	_____	(_____/_____/_____)	(_____/_____/_____)
Rubella containing vaccine:	_____	(_____/_____/_____)	(_____/_____/_____)

Date of last Measles/Rubella containing vaccine: (_____/_____/_____)

3. Clinical Information

Fever: ☐Yes ☐No ☐Unknown
Maculopapular Rash: ☐Yes ☐No ☐Unknown
Cough: ☐Yes ☐No ☐Unknown
Coryza: ☐Yes ☐No ☐Unknown
Conjunctivitis: ☐Yes ☐No ☐Unknown

Adenopathy: ☐Yes ☐No ☐Unknown
If yes, place……..
Arthralgia: ☐Yes ☐No ☐Unknown
If yes, joint……..
Pregnant: ☐Yes ☐No ☐Unknown
If yes, week of gestation:…….
Others:

4. Patient Status

Hospitalization? ☐Yes ☐No if yes, Name of Hospital:
Date of admission: (_____/_____/_____) Date of discharge: (_____/_____/_____)
Final status: ☐ Recovered ☐ Referred ☐ Died ☐Unknown

5. Epidemiological Information

Any similar illness in family/community: ☐Yes ☐No If yes, number……..
Travel History (7-21 days before the onset of rash): ☐Yes ☐No If yes, place/country visited:
Travel dates: From (_____/_____/_____) To (_____/_____/_____)
Attended social gathering/events: ☐Yes ☐No If yes, specify:_____

Name of the Investigator with Designation:

6. **Laboratory Information**

To be filled at specimen collection point	**To be filled by Royal Centre for Disease Control**
A. Serology Samples and Test Results	
Specimen Collected? ☐ Yes ☐ No If yes, types of Specimen: ☐ Serum ☐ DBS ☐ Both serum & DBS Others, specify:_____	Date of sample received: (_____/_____/_____) Sample received by: Sample status: ☐ Satisfactory ☐ Unsatisfactory If unsatisfactory, give details:

Date of Collection: (_____/_____/_____) Specimen Collected By: Sample Shipment date: (_____/_____/_____) Sample sent by:	**Serology Result:** Specimen ID:_____ Test Done by: Date of Test: (_____/_____/_____) Date of Report to VPDP: (_____/_____/_____) Measles: ☐ Positive ☐ Negative ☐ Equivocal ☐ Test Not done Rubella: ☐ Positive ☐ Negative ☐ Equivocal ☐ Test Not done
B. Virology samples and Test Results	
Specimen Collected? ☐ Yes ☐ No If yes, types of Specimen: ☐ Throat swab ☐ Others, specify:_____ Date of Collection: (_____/_____/_____) Specimen Collected By: Sample Shipment date: (_____/_____/_____) Sample sent by:	Date of sample received: (_____/_____/_____) Sample received by: Sample status: ☐ Satisfactory ☐ Unsatisfactory If unsatisfactory, give details: **Virology Result:** Specimen ID:_____ Test Done by: Date of Test: (_____/_____/_____) Date of Report to VPDP: (_____/_____/_____) ☐ Measles Positive ☐ Rubella Positive ☐ Negative ☐ Test Not done
C. Genotyping	
Specimen submitted for genotype? ☐ Yes ☐ No If yes, Date specimen sent: (____/_____/_____)	Genotype results: Measles: ____ Rubella:_____ Date results received by RCDC: (____/____/_____) Date results received by VPDP: (____/____/_____)
7. Classification (to be filled by the VPDP)	
Final Classification: ☐ Confirmed Measles ☐ Confirmed Rubella ☐ Discarded Basis for classification: ☐ Laboratory ☐ Epidemiological Linked ☐ Clinical Source of infection: ☐ Endemic ☐ Imported ☐ Import-related ☐ Unknown Reason for discard…….	
8. Follow-up	
Active case search done? ☐ Yes ☐ No If yes, number of additional suspected cases detected: _____ Outcome at 30 days follow-up: : ☐ Alive ☐ Died ☐ Lost to follow-up ☐Complications, specify:___ Follow-up date: (____/_____/_____) Investigator Name: Institution: Telephone: Date:	

Annexure 2.2 Measles Outbreak Investigation: Contact Tracing Forms

MR OB FORM-2

Measles outbreak investigation : CONTACT TRACKING FORMS

District:_____ Gewog (Block):_____

Supervisor name:_____ Investigator name:_____

Outbreak ID:MR/BTN/_____ Survey Dates: _____

CONTACTS four days before to four days after the rash onset						ONLY SUSPECTED CASES (Onset between _____ & ____				
(1)	(2)	(3)	(4)		(5)	(6)	(7)	(8)	(9)	(10)
Name	Age	Sex (M/F)	Total number of measles vaccine doses	Date of last dose	Suspected measles case (fever , rash, 3 C's) (Yes/No)	Date of rash onset	Samples taken: (serum, throat swab,)	Places visited four days before to four days after rash onset	Date(s) of investigation of places described in column 10	Geo - cordinates , if available

MR OB FORM-2

Exposure to suspected cases 7-21 days before the onset of rash (dated between _____ & _____)										
(1)	(2)	(3)	(4)		(5)	(6)	(7)	(8)	(9)	(10)
Name and address	Birth date/Age in years	Sex (M/F)	Total number of measles vaccine doses	Date of last dose	Suspected measles case (fever, rash, 3 C's) (Yes/No)	Date of rash onset	Samples taken: (serum, throat swab,)	Places visited 7-21 days before rash onset (possible exposure sites)	Date(s) of investigation of places described in column 8	Geo - cordinates of the contact, if available

Remarks

Annexure 2.3 Community Census Form

Village/locality name---------- Date ----------Team No-------

Dzongkhag---------- Surveyors name ----------

Note: During community survey please ask for any cases of fever with rashes and include them in contact tracing form

Age-group	MR Vaccination status by Card or History	House Number									
		1	2	3	4	5	6	7	8	9	10
0-9 months	Zero dose										
	1 dose										
	2 or more dose										
	unknown										
1-4 years	Zero dose										
	1 dose										
	2 or more dose										
	unknown										
5-9 years	Zero dose										
	1 dose										

	2 or more dose										
	unknown										
10-14 yrs	Zero dose										
	1 dose										
	2 or more dose										
	unknown										
15-19 yrs	Zero dose										
	1 dose										
	2 or more dose										
	unknown										
20-29 yrs	Zero dose										
	1 dose										
	2 or more dose										
	unknown										
30-39 yrs	Zero dose										
	1 dose										
	2 or more dose										
	unknown										
40 + yrs	Zero dose										
	1 dose										
	2 or more dose										
	unknown										

Chapter 3: Congenital Rubella Syndrome (CRS) surveillance

3.1. Introduction

CRS surveillance allows for detection of infants with clinically apparent manifestations. Early identification of infants with CRS is necessary to ensure appropriate testing conducted and the infant is entered into the CRS surveillance system. Detection of infants with CRS is necessary to ensure infection control and prevent further spread of rubella, as infants with CRS may shed the virus for a prolonged period – up to 1 year of age or longer. Immediate diagnosis of CRS also facilitates early intervention for specific defects.

Bhutan has been declared as one of the SEARO member states that has controlled rubella successfully by Regional Verification Commission in July 2018. The country now plans to embark for rubella elimination for which quality CRS surveillance is critical to monitor the progress towards elimination.

The CRS surveillance is **case-based surveillance** and single suspected case of CRS is an immediately notifiable syndrome in the country and all health centers should notify if suspected case is detected during OPD and IP service and refer to the referral hospitals for case investigation. In addition **sentine**l **surveillance** are conducted in three referral hospitals to complement the case based surveillance.

3.2. Sentinel sites

CRS sentinel surveillance is carried out in the two regional referral hospitals (Mongar Eastern Regional Referral Hospital and Gelephu Central Regional Referral Hospital) and the national referral hospital (Jigme Dorji Wangchuk National Referral Hospital) (Figure 3.1).

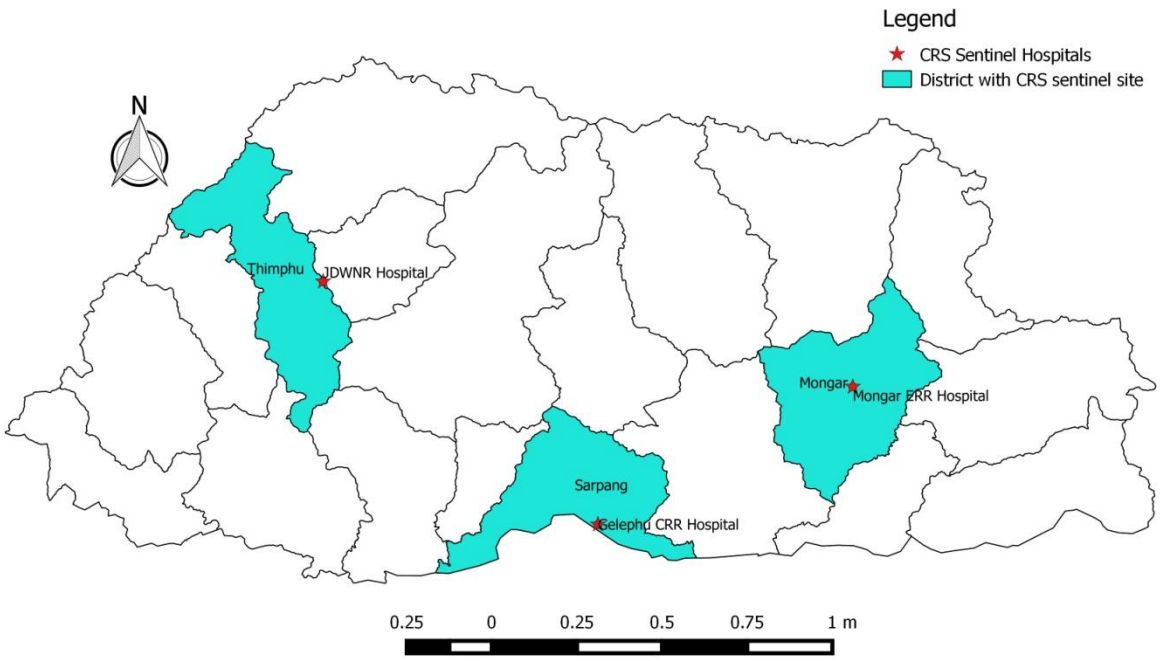


Figure 3.1: CRS Surveillance Sentinel Sites

3.3. Case Detection and Reporting

Suspected CRS case

Any infant, less than one year of age that a health worker suspects of having CRS.

- A health worker should suspect CRS when an infant aged 0–11 months presents with heart disease and/or suspicion of hearing impairment and/or one or more of the following eye signs: white pupil (cataract), larger eye ball (congenital glaucoma) or pigmentary retinopathy.
- an infant's mother has a history of suspected or confirmed rubella during pregnancy, even when the infant shows no signs of CRS.

Case reporting

Suspected CRS should be reported in NEWARS information system under immediately reporting platform using either through mobile SMS or web-based system (refer NEWARS guideline). If no suspected case is detected, Zero reporting should be made

weekly through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform.

The infants with most common defects associated with CRS – cataracts, heart defects or hearing impairment are likely to be referred to referral hospitals. Therefore, these defects are most likely to be evaluated and treated in referrals hospitals and therefore three referrals hospitals are identified as sentinel sites for CRS surveillance.

In referral hospitals, multiple specialties (departments), such as paediatrics, obstetrics, otorhinolaryngology, cardiologists and ophthalmology should be involved in diagnosing defects associated with CRS, a mechanism of coordination between these departments should be developed at all three referral hospitals and one nodal person should be identified by the management of the hospitals. The nodal person should ensure collection of clinical and epidemiologic data, completion case investigation forms and appropriate collection and transportation of specimens, ensuring that laboratory data can be linked to clinical and epidemiologic information. A line list of suspected CRS cases should be maintained in respective referral hospitals. There should be regular communication with the programme regarding identification and follow-up of suspected cases of CRS identified in the respective referral hospitals.
If neonatal-perinatal database and birth defect surveillance are in place, suspected cases of CRS should be reported through this network to the vaccine preventable Disease Programme and vice-versa.

3.4. Case Investigation

When a suspected CRS case is reported, a case investigation (**Annexure 3.1**) should be filled in after clinical evaluation by specialists of different departments as per symptoms/signs suspected and sent to the nodal person of the same reporting site for further action. It is critical to note receipt of MR doses through routine service or campaigns (i.e. in children 6 to <12 months) so that laboratory results can be correctly interpreted when classifying cases.

3.5. Unique identification number

Each suspected CRS case will be assigned a unique identification number. This unique identification will be assigned by three sentinel sites as follow: Country CRS surveillance code + referral hospital code + year + sequential number by order of reporting. Example:

JDWNRH: BHU-CRS/JDNR/2018/001 unique identification number assigned for 1st CRS case from JDWNRH detected in 2018,

MRRH: BHU-CRS/MRR/2018/001 unique identification number assigned for 1st CRS case from MRRH detected in 2018,

GRRH: BHU-CRS/GRR/2018/001 unique identification number assigned for 1st CRS case from GRRH detected in 2018,

3.6. Specimen collection and transportation

Efforts should be made to obtain clinical specimens for antibody levels and for viral detection/isolation from infants at the time of the initial investigation. For serological diagnostics, 1 mL sample of blood should be taken and then centrifuged to separate out the serum, which should then be kept under refrigeration at temperatures from 2–8 °C. The serum should then be transported in cold chain to the laboratory. Throat swabs should also be collected for isolation of the virus or virus detection.

Laboratory criteria for confirmation of suspected CRS cases include any one of the following:

- rubella IgM antibody over cut-off-point detected; or
- sustained rubella IgG antibody level as determined on at least two occasions (at least 1 month apart) between 6 and 12 months of age in the absence of receipt of rubella vaccine; or
- rubella virus detection (e.g. nucleic acid detection by reverse transcription polymerase chain reaction (RT-PCR) or rubella virus isolation) in an appropriate clinical sample (throat swab).

Depending on the age of the suspected CRS case at initial testing, the following considerations should be made when interpreting laboratory results and determining final classification of suspected CRS cases.

- Children >9 months may have received rubella-containing vaccine through routine service or campaigns. Serology results cannot be used to confirm CRS after a child with suspected CRS has received rubella-containing vaccine.

- Infants with congenital rubella will usually be positive for rubella-specific IgM at or shortly after birth. Although IgM antibodies may persist for up to 1 year, they normally peak within the first 6 months of life. Because IgM may not be detectable in some infants tested shortly after birth, IgM negative cases with suspected CRS should be retested at 1 month of age or shortly thereafter.

- Laboratory confirmation of CRS in an infant aged over 6 months should not rely on the IgM test alone if the result is negative. In such cases, serial IgG testing should also be included to check for a sustained level of antibody on two occasions separated by >1-month interval. After confirming IgG+ in the first serum sample collected, this sample should be saved and retested again with the second serum sample to compare antibody levels. If IgM and IgG testing are performed concurrently in ages 6–11 months, any infant testing IgG- should be discarded (all infants with CRS are IgG+).
- Infants with congenital rubella should also be tested for shedding rubella virus through virus isolation techniques. Congenitally infected infants may shed and transmit rubella virus for up to 1 year of age and be the source of rubella outbreaks. Therefore, it is important to continue testing the infant for virus throughout the first year of life so that infection control measures can continue until virus shedding stops. This has to be confirmed by two negative results of viral testing of specimens obtained 1 month apart from infants at least 3 months of age.

3.7. Case classification

Case classification will follow an algorithm based on the age of the child, the algorithm is described in Figure below:

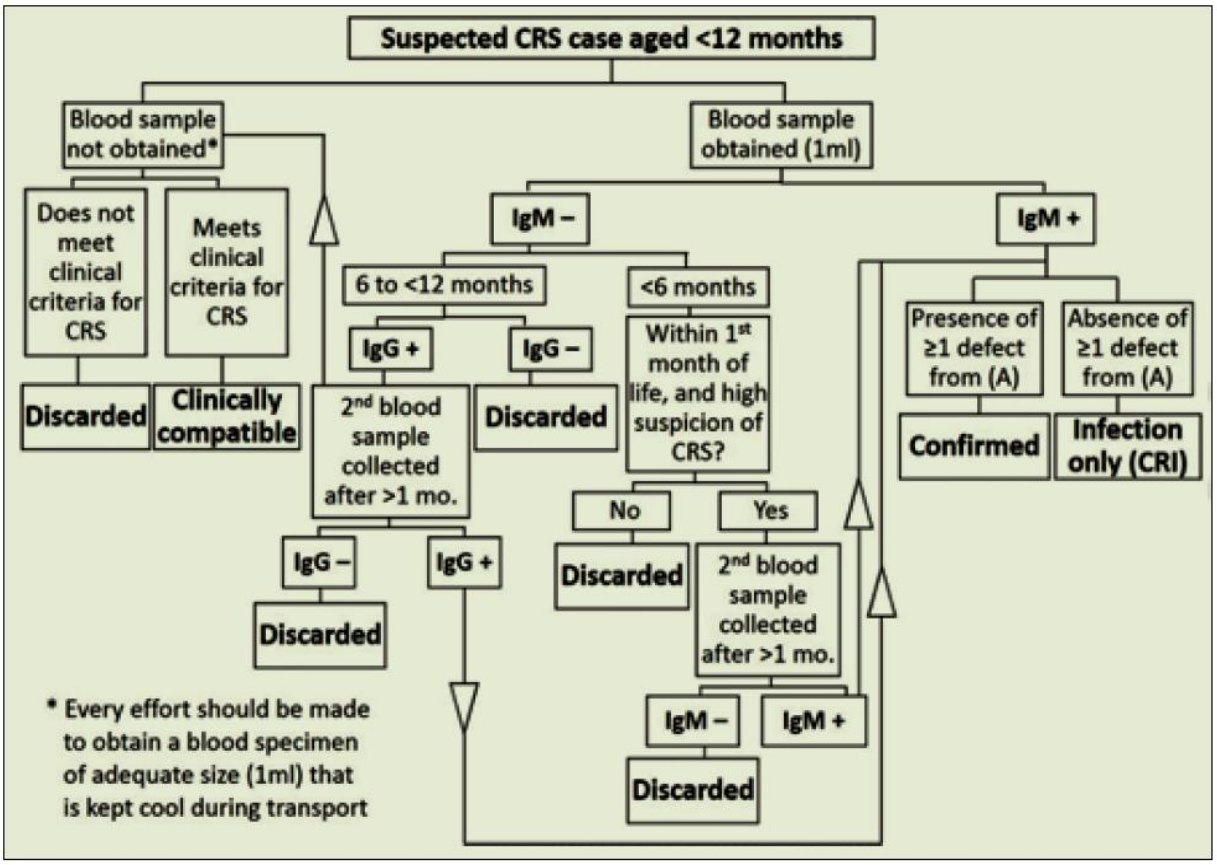


Figure 3.2: Flow chart describing the CRS diagnosis

Clinically confirmed CRS case: An infant in whom a qualified physician detects at least two of the findings listed in (a) or one in (a) and one in (b) and without any other obvious clinical cause that has not been adequately tested by a laboratory:

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 who is a suspected case (who has one condition from group (a) who meets the laboratory criteria for CRS case confirmation.

Congenital rubella infection (CRI): An infant who does not have group (a) clinical signs of CRS but who meets the laboratory criteria for CRS is classified as having CRI.

Discarded: A suspected case that does not meet the definition of clinically compatible case and has negative laboratory results after adequate testing.

3.8. Case Management

Case should be cared for and follow-up done by experienced personnel according to national treatment guidelines. Ensure infection control measure for CRS cases. Virus excretion should be monitored until at least two tests for virus detection/isolation (with 1 month gap) are negative after 3 months of age. Until this time, infection control procedures should be followed, as infants with CRS can be highly infectious.

3.9. Public Health Intervention

Infants with CRS may shed rubella virus for up to 1 year and may cause rubella outbreaks. Only person immune to rubella should have contact with these infants. In hospitals, infants should remain in isolation. Persons caring for the infant should follow universal precautions and should be immunized against rubella. Family members and friends involved in the care or handling of the infant should be immune or given immunization against rubella following the national policy. An active search should be conducted in the community for more CRS cases as well as to review the vaccination status of children in the locality. All children in the same locality who are found to be unimmunized and those who cannot produce immunization cards or records during the community survey should be vaccinated with MMR vaccine.

3.10. Data Management

Data Anlysis

CRS surveillance data should be analyzed on a monthly basis, or more frequently if necessary.

Epidemiologic variables that should be assessed include the following:

- number of cases reported throughout time frame assessed (e.g. year);
- case classification status;
- geographic location of CRS cases within the country;
- whether or not cases were clustered and/or associated with rubella outbreaks;
- maternal characteristics (age, race/ethnicity, country of birth and immunization

status);

- location of maternal exposure to rubella.

Monitoring indicators

Surveillance quality assessments need to be conducted at the sentinel sites at least every 6 months to assess completeness of CRS surveillance at the site.

- This should be done by reviewing hospital records by the surveillance officer of the hospital or designated from other referral hospital officer to identify any missed cases.
- Missed cases can be identified by comparing the list of reported CRS cases with the list of all cases that meet the entry criteria for CRS surveillance (i.e. criteria for suspected CRS cases). The proportion of missed cases at a sentinel site can be assessed as the percent of missed cases identified by the surveillance officer among all cases that meet the CRS surveillance entry criteria (total of both reported and unreported cases).
- Similarly, the proportion of suspected CRS cases that have been reported but have not been tested by the laboratory can be assessed as the percentage of reported cases without laboratory testing among all reported suspected CRS cases (both tested and untested).

Monitoring surveillance data quality:

CRS surveillance case reports should be assessed for any missing variables. If records are incomplete, the findings should be discussed with information providers at the site and the need for completeness of data and case reporting should be emphasize.

Criteria	Indicator	Target
Reporting rate	National annual rate of suspected CRS cases $\frac{\text{number of suspected CRS cases for the year}}{\text{live birth cohort of the population in which the cases occurred}} \times 10{,}000$	≥1 per 10 000 live births
Adequate investigation	Percentage of suspected CRS cases with the following data points completed: name and/or identifier, place of residence, sex, date of birth, date of reporting, date of investigation, date of specimen collection, history of rash illness of mother, travel history of mother, vaccination history of mother, age of mother, clinical examinations for hearing impairment, cataract, and congenital cardiac/heart defects and clinical outcome of the CRS case (alive or dead) $\frac{\text{number of suspected CRS cases for which an adequate investigation *was initiated after three 3 months of age of the child}}{\text{total number of suspected CRS cases}} \times 100$ * Adequate investigation defined as the collection of the following data points: name and/or identifier; place of residence; sex; date of birth; date of reporting; date of investigation; date of specimen collection; history of rash illness of mother; travel history of mother; vaccination history of mother; age of mother; clinical examinations for hearing impairment, cataract, and congenital cardiac/heart defects and clinical outcome of the CRS case (alive or dead).	≥80%
Laboratory confirmation (adequate specimen rate)	Percentage of suspected cases with adequate blood specimen tested for laboratory confirmation (IgM/ IgG, PCR) in an accredited laboratory $\frac{\text{number of suspected cases from whom adequate specimens** for detecting CRS (IgM/IgG) were collected and tested}}{\text{total number of suspected CRS cases}} \times 100$ ** Adequate specimens for serology are those collected within 12 months of age of the child that consist of ≥ 0.5 ml serum	≥80%
Viral detection (adequate specimens for virus detection)	Percentage of confirmed cases with adequate specimens tested for virus detection/isolation $\frac{\text{number of lab-confirmed CRS cases for the year for whom adequate specimen was analyzed for viral detection}}{\text{total number of lab-confirmed CRS cases}} \times 100$	≥80%

Criteria	Indicator	Target
Monitoring of virus excretion	Percentage of confirmed cases with at least 2 negative tests for virus detection/isolation after 3 months of age with at least a 1 month interval between specimen collection **number of lab-confirmed CRS cases with at least two negative tests for virus detection after 3 months of age, with at least a 1-month interval between tests for the year** / **total number of lab-confirmed CRS cases** X 100	≥80%
Timeliness of detection	Percentage of confirmed CRS cases detected within 3 months of birth **number of confirmed CRS cases (clinical compatible and laboratory confirmed) detected within 3 months of birth** / **total number of lab-confirmed CRS cases** X 100	≥80%
Timeliness of specimen transport	Proportion of specimens (serologic or virology) received at the laboratory within 5 days of collection **total number of specimens (serologic or virology) received at the laboratory within 5 days of collection** / **total number of specimens (serologic or virology) received for testing in the given year.** X100	≥80%
Timeliness of reporting laboratory results	**Serology** Proportion of serologic results reported by the laboratory within 4 days of receiving the specimen **total number of serologic results reported by the laboratory within 4 days of receiving the specimen** / **total number of serology specimen received for testing in the given year** X100 **Virology** Proportion of virus detection and genotyping results (where appropriate) that are completed within 2 months of receipt of specimen **total number of virus detection and genotyping results (where appropriate) that are completed within 2 months of receipt of specimen** / **total number of virology specimen received for testing in the given year** X 100	≥80%

3.11. Feedback Mechanism

Provide feedback to stakeholders involved in the CRS surveillance system through a weekly/monthly bulletin. Feedback should include information on the status of the epidemiology of CRS including, if necessary, any updates and recommendations for improvements.

Annexure 3.1: CRS Case investigation form

Case ID: Region: District:

Date of notification: ___ /___ /___ Date of investigation: ___ /___ /___ Date of reporting: ___ /___ /___

A. Identification

Name of the child: _____ Sex: ☐Male ☐Female

Date of birth: ___ /___ /___ if not available – age in months_____
Address:_____

Place infant delivered: _____

Name of mother:_____

B. Clinical signs and symptoms

Gestational age (weeks) at birth:_____ Birth weight (grams): _____

Group A (please complete all)	**Group B** (please complete all)
Congenital heart disease: Yes ☐ No ☐ Unknown ☐	Purpura: Yes ☐ No ☐ Unknown ☐
If yes, specify defect:_____	Microcephaly: Yes ☐ No ☐ Unknown ☐
Cataracts: Yes ☐ No ☐ Unknown ☐	Meningoencephalitis Yes ☐ No ☐ Unknown ☐
Congenital glaucoma: Yes ☐ No ☐ Unknown ☐	Jaundice: Yes ☐ No ☐ Unknown ☐
Pigmentary retinopathy: Yes ☐ No ☐ Unknown ☐	Splenomegaly: Yes ☐ No ☐ Unknown ☐
Hearing impairment: Yes ☐ No ☐ Unknown ☐	Developmental delay: Yes ☐ No ☐ Unknown ☐
	Radiolucent bone disease: Yes ☐ No ☐ Unknown ☐

Other abnormalities: Yes ☐ No ☐ If yes please describe:_____

Name of physician who examined infant:_____

City/town/village:_____ Telephone:_____

Present status of infant: Alive ☐ Dead ☐

If dead, cause of death: _____

Autopsy conducted: Yes ☐ No ☐ Unknown ☐

Autopsy findings:_____

Autopsy date:_____/____/_____

C. Maternal history/Antenatal care

Number of previous pregnancies: Mother's age (years):

Vaccinated against rubella: Yes □ No □ Unknown □ If yes, give date: ___/___/__

Rubella like illness during pregnancy: Yes □ No □ Unknown □ If yes, Month of pregnancy:_____

Maculopapular rash: Yes □ No □ Unknown □ If yes, date of onset___/___/___

Lymph nodes swollen: Yes □ No □ Unknown □ If yes, date of onset___/___/__

Arthralgia/arthritis: Yes □ No □ Unknown □ If yes, date of onset___/___/___

Other complications Yes □ No □ Unknown □ If yes, date of onset___/___/___

Was rubella laboratory-confirmed in the mother Yes □ No □ Unknown □

If yes, when (date): ___/___/___

Was the mother exposed during pregnancy to person of any age with maculopapular (e.g. not vesicular) rash illness with fever Yes □ No □ Unknown □ If yes, when (date): ___/___/___

Month of pregnancy:_____

Describe where:_____

Did the mother travel during pregnancy: Yes □ No □ Unknown If yes, when (date): ___/___/___

Month of pregnancy:_____ Describe where:_____

D. Infant/child laboratory investigations

First specimen:

Specimen collected: Yes □ No □ Unknown □

Type of specimen: Serum □ Throat swab □ Urine □ Other □

Date of specimen collection: ___/___/___ Date specimen sent: ___/___/___

Date specimen received in Lab: _____/____/_____

Rubella IgM: Not tested □ Positive □ Negative □ In process □ Inconclusive □

Rubella IgG: Not required □ Not tested □ Positive □ Negative □ In process □ Inconclusive □

Second specimen:

Specimen collected: Yes □ No □ Unknown □ Not required □

Type of specimen: Serum □ Throat swab □ Urine □ Cerebrospinal fluid □ Other □

Date of specimen collection: ___/___/___ Date specimen sent: ___/___/___

Date specimen received in Lab: _____/____/_____

Rubella IgM: Not required □ Not tested □ Positive □ Negative □ In process □ Inconclusive □

Rubella IgG: Not required □ Not tested □ Positive □ Negative □ In process □ Inconclusive □

Sustained IgG level*: IgG not tested □ Yes □ No □ In process □

*(*sustained IgG level on at least 2 occasions between 6 and 12 months of age)*

Rubella virus isolation: Not tested □ Positive □ Negative □ In process □

Rubella PCR: Not done □ Positive □ Negative □ In process □

Genotype_____

Date of laboratory result (first validated result) reported: ____/____/____

E. Final classification

CRS □ Discarded □ If discarded, please specify:_____

Case classification as Laboratory-confirmed □ Clinical □

Classification by origin: Endemic □ Imported □ Import-related □ Unknown □

Date of final classification: ____/____/____

Investigator:_____

Chapter 4: Acute Flaccid Paralysis Surveillance

4.1. Introduction

Bhutan was declared as polio free country in 2014 and has remained polio-free since.

To sustain polio-free status, a sensitive quality case-based surveillance system should

be maintained. The goal of case-based surveillance is to mitigate the risk of poliovirus importation and VDPV although is risk.

The AFP surveillance is a nation-wide **case-based surveillance** whereby every health center should actively look for cases during OPD and IP service. The AFP is an immediately notifiable syndrome in the country.

4.2. Case detection and reporting

Case definition

AFP suspected case: Any child under 15 years of age with AFP (including Guillain-Barré syndrome, Transverse myelitis, Flaccid hemiplegia, traumatic neuritis, Facial palcy) or any person of any age with paralytic illness if polio is suspected.

Reporting

Every suspect case of AFP in any child under 15 years of age must be immediately reported in NEWARS information system under immediately reporting platform using either mobile SMS or web based system. If no suspected case is detected, Zero reporting should be made weekly through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform.

The health workers should make regular rehabilitation centers to search for AFP cases which may have been overlooked or misdiagnosed. Such approach is the most important strategy for AFP surveillance which can be implemented by:

Active surveillance: Designated surveillance officers should visit the health facilities to search for and investigate unreported AFP cases through a review of health facility records, interviews with health workers and/or visit to wards to review cases. Surveillance sites should be prioritized according to their probability of seeing AFP cases like referral hospitals which should be visited more frequently. Every surveillance officer should have a list of surveillance sites and a schedule of how these sites are visited. Each surveillance visit should be documented. Monitoring of active surveillance visits is a performance indicator monitored by the RCCPE.

Passive surveillance: Every health should be sent centers weekly reports even if there were no cases of AFP detected (i.e. zero reports). Monitoring of

completeness and timeliness of zero reporting are also performance indicators assessed by the RCCPE.

Active case search: To find cases, health officials should contact key persons, such as community leaders, school teachers, day care center directors, social workers, leaders of women's organizations, mothers, traditional healers and religious leaders to inquire about recently paralyzed children in the community. Active case finding should be done in districts silent for one or more years and in high-risk population and areas for any children below 15 years who have had the onset of AFP within the preceding 6 months. All cases found should be immediately investigated and two stool specimens should be collected from cases with paralysis onset within the last two months.

Retrospective record review: Retrospective record reviews should be conducted for a minimum one-year period in referral hospitals and rehabilitation centers using a limited number of international classification of diseases (ICD) codes to identify all patients under 15 years of age under these codes. Their individual records are reviewed for any sign of AFP and for every AFP case found, a standard case investigation form and summary of relevant clinical findings are completed, information collected about follow up examination results and all findings should be presented to the expert review committee for final classification.

4.3. Case investigation

Epidemiological: In the early stages, polio may be difficult to differentiate from other forms of AFP, such as Guillain-Barré Syndrome, transverse myelitis, or traumatic neuritis. As such all children with AFP should be reported and tested for poliovirus within 48 hours of onset, even if doctors are confident on clinical grounds that the child does not have polio. Using a standard case investigation form the medical and travel history, clinical features, vaccination status and other relevant information are recorded (**Annexure 4.1**).

To test for polio, faecal specimens are important to analyse for the presence of poliovirus. Because shedding of the virus is variable, two specimens – taken at least 24 hours apart are required. Speed is essential, since the highest concentrations of

poliovirus in the stools of infected individuals are found during the first two weeks after onset of paralysis.

Identification of "hot cases": For early detection of potential polio cases and their rapid investigation, AFP cases that appear likely to be polio should labeled as "hot cases". Characteristics, signs and symptoms, which are most commonly observed in polio cases, include age less than 5 years plus history of fever at onset of paralysis plus asymmetrical proximal paralysis or patchy paralysis and incomplete polio vaccination. All "hot cases" must be immediately notified to the national polio surveillance unit.

Cross notification and tracking of cases: A child presenting with AFP may first come to the attention of a clinicians/health workers in a district other than that where he/she resides, and may even come from a neighboring country. Procedures should be put in place to ensure that cases appearing in districts other than the district of residence are properly evaluated, and that health staff in the concerned districts are immediately notified about the case. For AFP cases from other countries the local and Regional WHO offices should be notified.

4.4. Unique cases identification number

Each suspected AFP case will be assigned a unique identification number. This unique identification should be assigned as follow: Country AFP surveillance code + district code + year + sequential number by order of reporting. E.g., BHU/AFP/GAS/2018/01 mean that the 1st AFP case of the country from district Gasa, reported in 2018. [Three letter codes for 20 districts are : BUM-Bumthang, CHU-Chukha, DGA-Dagana, GAS-Gasa, HAA-Haa, LHU-Lhuntse, MON-Mongar, PAR-Paro, PGA-Pemagatshel, PUN-Punakha, SAM-Samtse, SAR-Sarpang, SZK-SJongkhar, THI-Thimphu, TSI-Tsirang, TGA-Trashigang, TYZ-Trashiyangtse, TON-Trongsa, WAN-Wangdue, ZGA-Zhemgang].

4.5. Laboratory testing

Specimen collection and transportation

Two stool specimens must be collected from every suspected AFP case within 14 days of onset of paralysis to maximize the chances of isolating poliovirus. In case samples cannot be collected within 14 days, the specimens should still be collected up to 60 days from paralysis onset.

- The first specimen should ideally be collected at the time of the case investigation.
- The second sample should be collected at least 24 hours after the first specimen collection, because virus shedding may be intermittent. However, the second specimen may still be collected up to 60 days following paralysis onset if there was failure to collect it sooner.

Performance evaluation is based on adequate stools defined as two specimens collected within 14 days of paralysis onset and at least 24 hours apart; with each specimen of adequate volume (8–10 grams) and arriving at a WHO-accredited laboratory in good condition (i.e., no desiccation, no leakage, with adequate documentation and evidence that the cold chain was maintained).

In critically ill children where stool is not passed, sample should be collected with the help of rectal tubes. This method is less preferred because the volume of stools collected is inadequate to save a portion for additional testing; also the virus isolation rate may be low.

Stool specimens should be sealed in containers and stored immediately inside a refrigerator or packed between frozen ice packs at 4–8 degrees celsius in a cold box, ready for shipment to a laboratory. Specimens should shipped to EPI, MSPD, Thimphu arrive within 72 hours of collection. Otherwise they must be frozen (at -20 degrees celsius), and then shipped frozen, ideally packed with dry ice or cold packs. These procedures are known as the “reverse cold chain”.

The MSPD must maintain correct records for each sample, using the EPID number to identify each specimen. The epidemiological data from the surveillance system and the laboratory data for each case should linked by this number. All AFP case specimens should be shipped to NIH, a WHO-accredited laboratory within the Global Polio Laboratory Network (GPLN) in Bangkok.

Contact sampling

Collection of adequate stool specimens from AFP cases is the gold standard. Under certain circumstances, the ability to collect adequate stool specimens from AFP cases represents a challenge, especially in difficult to reach areas. To address this situation and to increase the sensitivity of the surveillance system, supplemental surveillance activities should be introduced such as collection of stool specimens from contacts of selected AFP cases.

A contact of an index AFP case is defined as a child less than 15 years (preferably less than 5 years) of age who had been in direct contact with the index AFP case within one week prior to the onset of paralysis and/or within two weeks after onset of paralysis. The rationale for such sampling is that polio is spread through contact; therefore contacts have a higher chance of being infected, most poliovirus infections are asymptomatic and an infected asymptomatic child may carry and excrete the virus for periods up to 2 months and sometimes longer, as in the case of immuno-deficient children. Even vaccinated children who are protected from paralysis if infected can still excrete the virus in their stools for a short time.

Contact sampling of AFP cases may apply to the following situations, especially in high risk areas:

- AFP cases with inadequate stools.
- “Hot” AFP cases.
- AFP cases from areas with limited accessibility or hard to reach districts even without reported virus isolation to increase the sensitivity of AFP surveillance and allow the programme to make use of windows of opportunity to detect any possible virus circulation in these areas.
- Any suspicion by the programme regarding the collection process or handling of the index AFP stool specimens.

Collection, storage and transportation of the stool specimens should be dealt with in the same way as for AFP cases. A specific form “Contact Stool Collection” should be filled for each contact selected. This form is sent to the laboratory along with the specimen and a copy should be maintained in the AFP surveillance file of the index case after the data is entered. Each specimen should be labeled clearly as a contact of

an AFP case with a specific ID code (EPID No.) the same as that for the case followed by contact number, e.g. C1, C2, or C3. As part of performance monitoring the timeliness of contact sampling should be assessed to ensure that the system is supporting early detection of any possible virus circulation for immediate response.

Reporting laboratory results

A “turn-around time” for testing laboratory is 28 days or less as a goal for processing specimens. Culture results are reported within less than 2 weeks. Growth on culture indicates the presence of poliovirus but does not specify the type (WPV, VDPV, or Sabin-like). Specimens from which poliovirus is isolated undergo intratypic differentiation; results are reported within 7 days and determine the type of poliovirus. Positive culture results are reported to the national programme to allow response activities / further investigation based on the preliminary information. Finally, genetic sequencing is conducted if poliovirus is isolated. While the reference polio laboratory will report to the national programme and WHO, laboratory results should also be sent to the unit/physician that reported the case.

4.6. Case Classification

60-day follow-up examination

Sixty day follow-up is done between the 60th and 90th day in certain categories of AFP cases to determine the presence/absence of residual paralysis. The presence of residual paralysis at this time is further evidence that the cause of paralysis is likely to be due to poliovirus. The 60th day follow-up should not be done before the 60th day of onset of paralysis as there is still a possibility for the paralysis to resolve, resulting in “false positive” examination outcomes.

The following categories of AFP cases should undergo 60-day follow-up:

- AFP cases with inadequate stool specimen.
- AFP cases with isolation of WPV/VDPV.
- AFP cases with isolation of vaccine-type (Sabin-type) poliovirus.

During the 60 day follow-up examination, the investigator must:

- Verify with the family the developments since the first investigation and that all the information on the case investigation form is complete and correct.

- Clinically assess the child (Look for residual weakness, Thorough CNS examination especially: Tone, Power, DTR (Deep Tendon Reflexes), If child is walking, check for any limps in the gait, Compare mid-thigh/mid-arm circumference on both sides to determine minimal wasting, Look for asymmetrical skin folds on medial side of thigh, Even minimal – limping, Wasting, Asymmetrical skin folds in young children means that residual weakness is present.
- Complete the 60 day follow-up form and send it to the national surveillance unit, according to established procedures.

Expert review committee

AFP cases are classified according to virological scheme in figure 4.1. If the case has inadequate stool samples and 60 days follow up investigation showed residual paralysis, death, and lost for follow up, the case will be classified by a national expert review committee (ERC). The ERC may request more clinical background and hospital documents and might examine the case to classify it as either compatible or discarded.

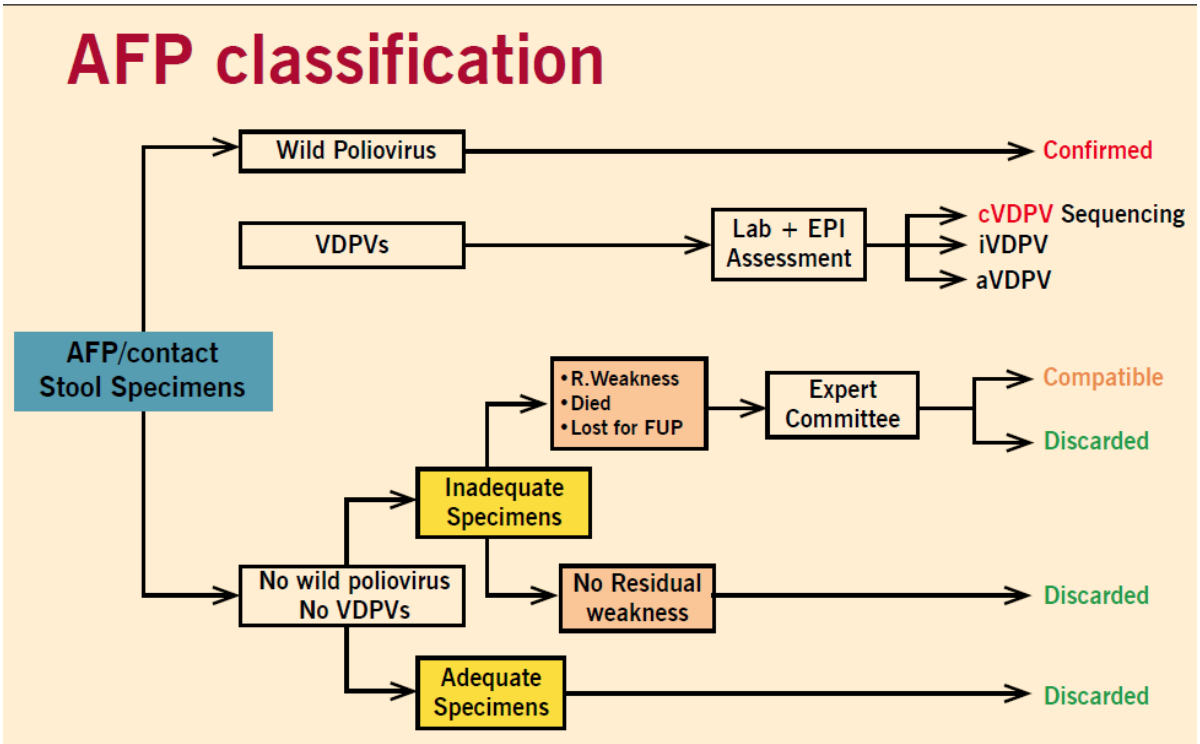


Figure 4.1: Case classification scheme of AFP cases

Confirmed polio

An AFP case is “confirmed” as polio only by the isolation of WPV or VDPV from any stool specimen. VDPVs are further classified as immune-deficient, circulating and ambiguous VDPVs. The isolation of the virus can be from the patient or from contacts.

Non polio AFP

An AFP case is classified as “non-polio AFP” if WPV or VDPV is not isolated from adequate stool specimens.

Compatible

If stool specimens are inadequate, final classification of the AFP case as either non polio AFP or compatible with polio will depend on the results of 60 day follow-up examination.

If the 60 day follow-up examination shows no residual weakness, the case is classified as non-polio AFP. If the AFP case has residual paralysis, died or is lost to follow-up, it must be reviewed and classified by the ERC. The AFP case might still be discarded as non-polio if the ERC has ruled out acute polio based on clinical and paraclinical findings. If that is not possible the ERC will do a final classification as polio-compatible.

Polio-compatible cases are indicative of a failure of surveillance, and serve as a reminder that all efforts must be made to ensure that cases are reported early enough to enable collection of adequate stool specimens from every AFP case.

4.7. Case management

There is no cure for polio. Treatment of a person with paralytic polio varies with stage of illness and the severity of paralysis. Patients with bulb spinal polio and respiratory paralysis would require hospitalization. In the acute stage, persons with isolated limb/limbs paralysis can be managed at home. They should be advised complete rest, proper positioning of the affected limb and passive range of movement at the joints. Massage and intramuscular injection should be avoided during acute phase of illness.

Public health intervention

Under the International Health Regulations (IHR), all instances of wild polio virus (WPV) isolation in a previously polio-free country, vaccine derived polio virus 2

(VDPV2) anywhere in the world, and (related to the 2016 switch) all Sabin-like 2 viruses – should be reported immediately by the national authority (country) to WHO, regardless of type of isolate or its source (clinical case, environmental sample, other). Once WPV is identified in an area (district), appropriate and timely response should follow the same as for a positive case, including: rapid and thorough investigation of the cases, strengthening of AFP surveillance in the area, and implementing immediate and appropriate immunization activities. Five strategic pillars are needed to effectively interrupt transmission in an outbreak setting: (i) a fully engaged national government, (ii) a rapid risk assessment and identification of transmission risk zones, (iii) a robust immunization response, (iv) effective communication and social mobilization, and (v) enhanced surveillance. For further polio outbreak response requirements refer to the standard operation procedures (SOP) on responding to a poliovirus event or outbreak – general SOPs and protocol for poliovirus type 2. *http://polioeradication.org/tools-and-library/resources-for-polio-eradicators/gpei-toolsprotocols-and-guidelines/*

4.8. Data Management and performance monitoring

An important aspect of a successful polio eradication programme is a well-developed information system that provides programme managers and health workers with the necessary information to take appropriate actions. The surveillance data should be reviewed on a weekly basis at the national and relevant sub-national levels to detect and quantify disease occurrence, assess changing disease patterns over time, determine risks for disease, monitor the progress of the polio eradication programme and evaluate the performance of the AFP surveillance system itself. Analysis of AFP surveillance data is required for measuring the sensitivity and consistency of the surveillance system to ensure that it is functioning at the desired level and a set of key indicators should be regularly assessed:

Timeliness of reporting	At least 80% of expected routine (weekly or monthly) AFP surveillance reports should be received on time, including zero reports where no AFP cases are seen. The distribution of reporting sites should be representative of the geography and demography of the country
Sensitivity of surveillance	At least one case of non-polio AFP should be detected annually per 100 000 population aged less than 15 years ("certification standard").To ensure even higher sensitivity, this rate should be two per 100 000 as operational target.
Completeness of case investigation	All AFP cases should have a full clinical and virological investigation with at least 80% of AFP cases having 'adequate' stool specimens collected. "Adequate" stool specimens are two stool specimens of sufficient quantity for laboratory analysis, collected at least 24 hours apart, within 14 days after the onset of paralysis, and arriving in the laboratory by reverse cold chain and with proper documentation.
Laboratory performance	All AFP case specimens must be processed in a WHO-accredited laboratory within the Global Polio Laboratory Network (GPLN).

Surveillance data is useful in the decision making process for programme actions:

- Monitor performance of surveillance using standard indicators and focus efforts in low performing areas.
- Monitor routine coverage in all geographical areas and focus efforts in low performing geographical areas.
- Identify high-risk areas for focusing greater attention during strengthening of routine immunization and supplementary immunization activities (SIA).
- Provide evidence for maintaining polio-free status.

4.9. Environmental Monitoring

Environmental surveillance involves testing sewage or other environmental samples for the presence of poliovirus. Environmental surveillance often confirms WPV and VDPV infections in the absence of cases of paralysis and as such systematic environmental

sampling provides important supplementary surveillance data. However, country being at low risk for polio reintroduction, environmental monitoring is not necessary.

Annexure 4.1: AFP Case investigation form

1. Report/Investigation information Name of investigator_____

Date Case Reported: _____ Title: _____

Date Case Investigated: _____ Name of BHU/Hospital:

2. Case Identification

Case identification no: BHU -----/-----/-----
Patient's name:_____ Sex: ☐Male ☐Female
Date of Birthday -----/-----/----- Age:Year _____Months_____
Address to find the child for follow up in 60 days:_____
Village: _____ Gewog : _____ Dzongkhag _____
Permanent Address(if different)_____ Mobile No:----------

3. Hospitalization: ☐Yes ☐No Date of Hospitalization: -----/-----/-----

Name of the hospital: _____Hospital registration number:_____

4. Immunization History: Total OPV doses received through routine EPI: _____

Total OPV doses received through NIDS: _____

Date of last does of OPV (routine):_____

Date of IPV ----------

5. Signs and Symptoms: Date of paralysis onset:_____

Number of days from onset to maximum paralysis:_____

Acute Flaccid paralysis: ☐Yes ☐No ☐Unknown

Flaccid paralysis: ☐Yes ☐No ☐Unknown

Any injections during the 30 days before paralysis onset: ☐Yes ☐No ☐Unknown

Fever on day of paralysis onset: ☐Yes ☐No ☐Unknown

Asymmetrical Paralysis: ☐Yes ☐No ☐Unknown Ascending paralysis: ☐Yes ☐No ☐Unknown

Sensation Loss: ☐Yes ☐No ☐Unknown Descending paralysis:☐Yes ☐No ☐Unknown

Site(s)of paralysis: rights arms /Left arm/Right legs/ Left legs/

6. Stool Specimen Collection:

Date Collected	Date Sent	Laboratory Result (circle)
Stool 1:_____	_____	P1 P2 P3 Wild/Vaccine Pending NPEV Negative
Stool 2:_____	_____	P1 P2 P3 Wild/Vaccine Pending NPEV Negative

7. 60 Day Follow-up Examination: ☐Yes ☐No: Date:_____ If No, why?_____ Died? (Circle): Yes/No If Yes, date: _____ if died, cause: _____ Residual paralysis present: ☐Yes ☐No Site of Paralysis: right arm/left arm/ right leg/left leg/others (describe) _____ Name of examiner:…….. Designation…… Classification……..
8. Outbreak Response: Done: Yes/No Date:_____ If No.why?_____ If yes, date begun: _____ Setting: Urban/Rural Target population of < 5 yrs: _____ Number < 5 immunized: _____
9. Final Classification a.Confirmed Polio: ☐Yes ☐No. b.Polio compatible: ☐Yes ☐No c. If discarded, why? (Tick) If discarded, what were the final diagnosis: ☐Guillian Barre Syndrome ☐Transverse Myelitis ☐ Traumatic Neuritis ☐Other------

Annexure 4.2: AFP Laboratory Request Form

(Original to accompany stool specimen to laboratory)

Case Identification Number: Case ID: BHU/____/____/____C 1, 2, 3, 4, 5*

(Matches AFP Case Investigation Form)

PART I: To be filled by Case Investigator

Report/Investigation Information:	Name of Investigator: _____
Date Case Reported: _____	Title: _____
Date Case Investigated: _____	Health Center/Hosp: _____
Case/Information:	
Patient's Name: _____	Sex: _____ Age:_____yrs_____Months
Address:	
Village_____Block_____	Dist: _____
Date of onset of paralysis: _____	
Date of last dose of OPV: _____	
Stool Specimen Collection:	

Date Collected	Date Sent to Lab
Stool 1 _____	
Stool 2 _____	

Name of person to whom laboratory result should be sent:

The Program Officer, Vaccine Preventable Disease Program (VPDP)

Department of Public Health, Communicable Disease Division, MoH,

Thimphu, Bhutan

Telephone No. 02-321328/

Fax: +975-02-326038

Fax.no. EPI, DVED: 02-323809

Date on which specimen sent to Reference Lab: _____

PART II. To be filled out by Reference Laboratory

Date specimen sent to referral lab: ____/____/_____
Date Specimen received: ____/_____/____
Date results reported to the Country's EPI Program Officer: ____/_____/_____
Results of viral Identification:
Specimen 1.

P1 No/Yes	Wild/Vaccine	P2 No/Yes	Wild/Vaccine	P3	No/Yes	Wild/Vaccine	
Specimen 2:							
P1 No/Yes	Wild/Vaccine	P2 No/Yes	Wild/Vaccine	P3	No/Yes	Wild/Vaccine	
Non-polio enterovirus: Yes/No			Pending Results: Yes/No				

Comments:……

Chapter 5: Japanese encephalitis/Acute Encephalitis Syndrome surveillance

5.1. Introduction

In Bhutan, JE vector Culex (Culex tritaeniorhynchus and Culex vishnui) mosquito is found in southern districts and few sporadic Japanese encephalitis (JE) cases have been documented. The JE surveillance is important to gather evidence and determine the need of JE vaccine introduction.

The JE or AES is a nation-wide **case-based surveillance** whereby every health center should actively look for cases during OPD and IP service. AES is an immediately

notifiable syndrome in the country. In addition, **JE sentinel surveillance** is conducted in hospitals located in south where JE vectors are prevalent to complement the case-based surveillance.

5.2. Sentinel Sites

JE sentinel sites are in Mongar Eastern Regional Referral Hospital, Gelephu Central Regional Referral Hospital, Jigme Dorji Wangchuk National Referral Hospital, SamdrupJongkhar District Hospital, Phuntsholing General Hospital and Samtse District Hospital (Figure 5.1).

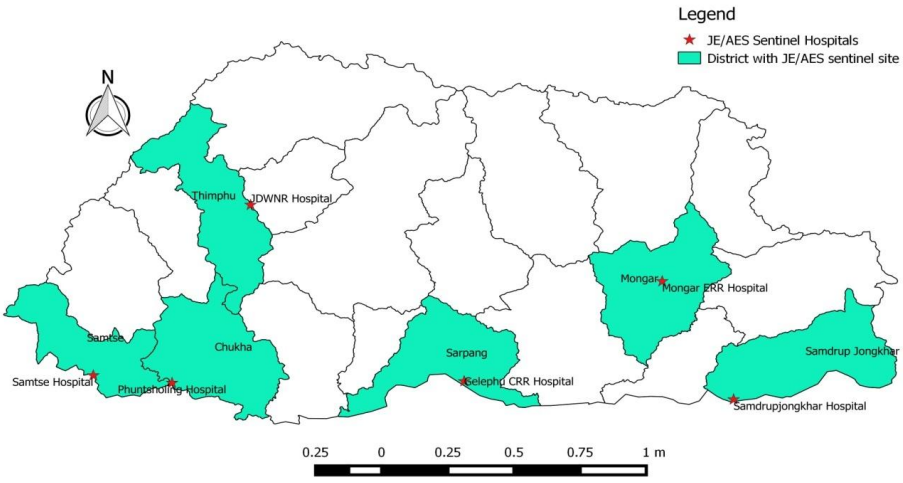


Figure 5.1: JE/AES Sentinel Sites

5.3. Case detection and reporting

Case Definition

Suspected case of AES: A person of any age, at any time of year, in known JE-affected geographic region, with acute onset of fever and after an interval of 1 to a few days of prodrome, change in mental status (including confusion, disorientation, delirium or coma) and seizures (focal or generalized).

Case reporting

A single suspected case AES should be immediately reported through NEWARS information system under immediately reporting platform using either through mobile

SMS or web-based reporting platform (refer NEWARS guideline) and AES case investigation form should be filled up the concerned health care provider.

5.4. Case investigation

A reported case should be investigated using standard Case Investigation Form (**Annexure 5.1**). Active case search should be conducted to identify other cases and determine whether other nearby areas have been exposed or are also experiencing outbreaks.

5.5. Unique case identification number

Each suspected AES case will be assigned a unique identification number. This unique identification will be assigned by five sentinel sites as follow: Country AES surveillance code + sentinel sites hospital code + year + sequential number by order of reporting (e.g.JDWNRH: BHU-AES/JDW/2018/001, MRRH: BHU-AES/MRR/2018/001, GRRH: BHU-AES/GRR/2018/001, SJongkhar:BHU-AES/SZK/2018/001, Phuntsholing: BHU-AES/PHU/2018/001, Samtse: BHU-AES/SAM/2018/001)

5.6. Specimen collection and transportation

Blood and cerebrospinal fluid (CSF) are specimens to be referred for detection of IgM antibodies to Japanese Encephalitis Virus (JEV) or other etiologic agents. However, CSF samples can be collected only at referral hospitals. These samples should be collected as soon as possible after admission of the patient and should be sent to RCDC. The samples should be stored in the hospital laboratory at 4 $^{\circ}$C for short-term storage (1 to 3 days) or at or below –20 $^{\circ}$C for longer term storage if immediately shipment is not possible. Refer blood collection and shipment under MR surveillance.

5.7. Case classification

Laboratory-confirmed JE: A suspected case that has been laboratory-confirmed as JE.

Probable JE: A suspected case that occurs in close geographic and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak.

“Acute encephalitis syndrome” – other agent: A suspected case in which diagnostic testing is performed and an etiological agent other than JE virus is identified.

"Acute encephalitis syndrome" – unknown: A suspected case in which no diagnostic testing is performed or in which testing was performed but no etiological agent was identified or in which the test results were indeterminate.

Suspected case: A case that is compatible with the surveillance case definition of acute encephalitis. [*Case Definition: An illness with an acute onset of possible encephalitis including high fever and altered mental status*.]

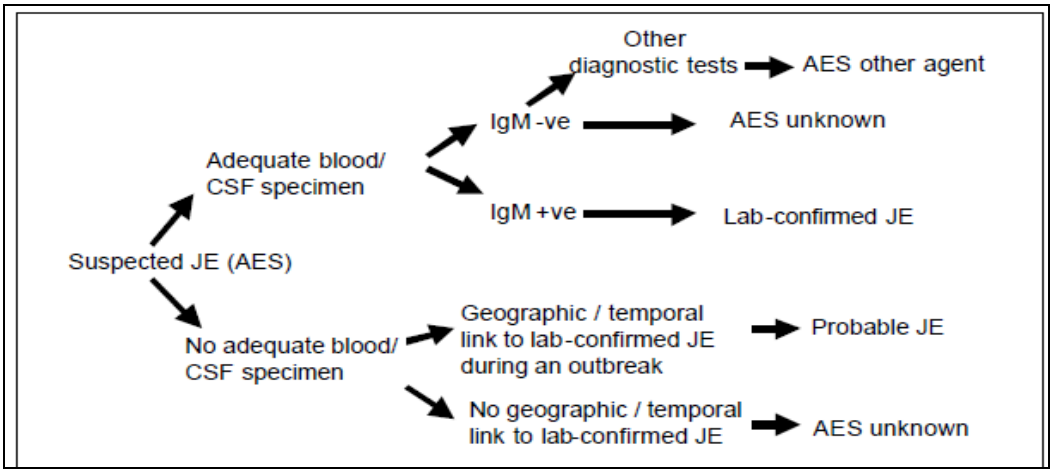


Figure 5.2: Flow chart of JE/AES diagnosis

5.8. Case Management

It is important to exclude other causes of CNS affliction, such as meningitis or cerebral malaria, which require specific treatment. Treatment depends on the condition in which patient is received in the health facility. Management of Japanese encephalitis is essentially symptomatic and requires high-quality nursing care. To reduce severe morbidity and mortality it is important to identify early warning signs and refer patient to health facility and educate the health workers about the first line of management at the grass root level. Standard national guidelines should be followed for management that would include management of airway, breathing, convulsions and circulation.

5.9. Public health intervention

(i) **Vaccination:** Immunization against JE is the single most cost-effective strategy for control and prevention of JE. However, introduction of JE vaccination will depend upon the incidence rate of JE to determine the need of vaccination.

(ii**) Health Education and Community involvement**: It has been observed that there is a direct relationship between the time lag in onset of symptoms and initiation of therapy. Immediate management of cases reduces fatality to a considerable extent. Generating awareness helps in early reporting. Further health education helps in encouraging personal protection.

(iii**) Interruption of Transmission**: Prevention of transmission is possible through vector control. For effective control of vectors in endemic areas, residual insecticidal spraying has been suggested in all animal dwellings with appropriate insecticide before the onset of transmission season.

5.10. Data management

The recommended core-variables are:

- number of suspected cases by week, month, year, age group and geographic area;
- number of confirmed cases by week, month, year, age group and geographic area;
- number of deaths due to JE;
- case fatality ratio;
- final classification of all suspect cases; and
- proportion of AES attributed to JE.

Performance indicators of surveillance quality

Indicator	Target
Completeness of monthly reporting	>90%
Timeliness of monthly reporting	>80%
Percentage of serum samples taken a minimum of 10 days after onset (when the testing methodology is IgM-capture ELISA)	>80%

Indicator	Target
Percentage of all suspect cases for which specimens were collected	>80%a
Percentage of CSF/serum samples reaching laboratory in adequateb condition	>80%
For all tests, laboratory results reported <1 month after receipt of specimen	>80%

5.11. Feedback

Provide feedback to stakeholders through a weekly/monthly bulletin. Feedback should include information on the status of the epidemiology of JE/AES, identifying geographic areas or populations at high risk.

Annexure 5.1: AES Case Investigation Form

Hospital Registration No: _____ **AES No: _____**

1. Investigation Information: Name of Investigator(s): _____

Date Case Reported: _____ /_____ /_____ Designation: _____
Date Case Investigated: ____ / ____ / ____

2. Case Identification: Patient's Name: ____ _____

Date of Birth: ____ / ____ /___ __ Age: years ___ months ___ Sex: ___

Parents Name : _____ Permanent address:
Mobile No :_____ Village:_____
Gewog:_____
Residing Address _____ Dzongkhag:_____

3. Hospitalization: Yes/No Date of Hospitalization: _____ / _____ / _____

Name of Hospital:_____

Clinical Diagnosis:_____

Outcome: Recovered completely /Recovered with disability/ Death/Unknown

4. Sign and Symptoms:

Date of onset of symptoms: _____/_____/_____

Rapid Onset: Yes / No / Unknown Change in mental status: Yes / No / Unknown

Headache: Yes / No / Unknown Seizure: Yes / No / Unknown

Neck Stiffness: Yes / No / Unknown Stupor: Yes / No / Unknown

Paresis : Yes / No / Unknown

Travel History (2 weeks before the onset): Yes / No / Unknown

If yes, where: _____

5. Specimens Collection

Specimens type	Date of sample collected	Date of sample sent to Lab (RCDC)
Serum 1		
Serum 2		
CSF		

6. Case Classification: Lab confirmed / Probable /AES-other agent /AES-unknown

7. Signature of investigator:_____Mobile No:

Case Definition of AES: Clinically, a case of Acute Encephalitis Syndrome (AES) is defined as a person of any age, in any geographical region, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) AND/OR new onset of seizures (Excluding febrile seizures).

8. To be filled by Royal center for Disease Control (RCDC)

Date of specimen received: ____/____/_____

Condition of sample */ circle it*

Serum 1 Good / poor
Serum 2 Good / Poor
CSF Good / Poor

Date test performed: _____/_____/_____
Test performed by: Name: _____Designation:_____
Type of test: _____

RCDC Laboratory results:
Serum 1 Positive / Negative / Equivocal / Pending
Serum 2 Positive / Negative / Equivocal / Pending
CSF Positive / Negative / Equivocal / Pending

Date Results sent to CEU: ____/_____/_____ other test if done and result_____
Specimens sent to reference lab: Yes / No
Date specimens sent to reference lab: ____/____/_____
Comments: _____
9. To be filled out by Reference Lab.
Name/location of laboratory: _____ Date test performed: ___/___/____
Test performed by: Name: _____ Designation: _____
Type of test: _____
Reference Laboratory results:
Serum 1 Positive / Negative / Equivocal / Pending
Serum 2 Positive / Negative / Equivocal / Pending
CSF Positive / Negative / Equivocal / Pending
Date Results sent to NHL / CEU/WHO: ____/_____/_____

Comments: _____

Chapter 6: Diphtheria surveillance

6.1. Introduction

Diphtheria is a vaccine-preventable disease that has the potential for epidemics. Recent epidemics have highlighted the need for adequate surveillance and epidemic preparedness. Surveillance data can be used to monitor levels of immunization

coverage (DPT3 target >90%) and disease as a measure of the impact of immunization programmes.

Diphtheria surveillance is a **case based surveillance** and a single suspected case is an immediately notifiable disease and should be reported immediately in NEWARS information system under immediately reporting platform.

6.2. Case Detection and Reporting

Case definition

A suspected case of diphtheria is defined as: An illness of upper respiratory tract characterized by the following by laryngitis or pharyngitis or tonsillitis; AND adherent membranes of tonsils, pharynx and/or nose.

The date of onset for diphtheria should be considered as date of onset of sore throat with fever.

Description of case definition

Pharyngitis and tonsillitis: fever with pain and redness of the throat and/or tonsils.

Laryngitis: often presents as hoarseness of voice and cough.

Membrane: initially isolated spots of grey or white exudate appear in tonsillar and pharyngeal area. These spots often coalesce within a day to form a confluent sharply demarcated pseudo membrane that becomes progressively thicker, more tightly adherent to the underlying tissue and darker grey in colour. Dislodging the membrane is likely to cause bleeding. Unlike the exudate in streptococcal pharyngitis, the diphtheritic pseudo membrane often extends beyond the margin of the tonsils onto the tonsillar pillars, palate or uvula.

The other clinical features that are associated with probability of diphtheria infections are dysphagia, difficulty in breathing, headache, change of voice (hoarseness or thick speech), nasal regurgitation and serosanguineous nasal discharge. Some patients may also present with ‘bull neck’ diphtheria where there is massive cervical lymphadenopathy with edematous swelling of the submandibular region and surrounding areas. Patients of diphtheria may also present with systemic manifestations of diphtheria toxin, such as myocarditis and polyneuritis. Bulbar

dysfunction may present as palatal, pharyngeal, facial, laryngeal, oculomotor or ciliary paralysis

Case reporting

A single suspected cases of diphtheria should be immediately reported through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform (refer NEWARS guideline). If no suspected case is detected, Zero reporting should be made weekly through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform.

6.3. Case investigation

A reported case should be investigated using standard Case Investigation Form (**Annexure 6.1**) by the concerned health care provider. Active case search should be conducted to identify other cases and determine whether other nearby areas have been exposed or are also experiencing outbreaks.

6.4. Unique case identification number

Each suspected CRS case will be assigned a unique identification number. This unique identification will be assigned by three sentinel sites as follow: Country diphtheria surveillance code + hospital center name + year + sequential number by order of reporting (E.g. Paro: BHU-DIP/Paro/2018/001).

6.5. Specimen collection and transportation

Whenever diphtheria is suspected, designated personnel should secure specimens for laboratory confirmation. A throat swab should be obtained on first contact with the patient during the case investigation.

6.6. Case classification

Laboratory confirmed: A case that meets the clinical case definition where samples are collected and laboratory results are positive for the suspected disease.

Epidemiologically linked: A case that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case.

Clinically compatible: A case that meets the clinical case definition but is neither laboratory-confirmed nor epidemiologically linked.

Discarded: A case that does not meet the clinical or epidemiological link, or does not meet.

6.7. Case management

Diphtheria case management has three main components:

Administration of diphtheria antitoxin

The mainstay of treatment is intramuscular or intravenous administration of diphtheria antitoxin (a hyper immune anti-serum produced in horses) to neutralize circulating toxin before it reaches target cells. Early administration after testing for hypersensitivity is essential as it can neutralize only free toxin.

The minimum therapeutic dose is unknown; recommendations are based on clinical experience and the assumption that duration of disease and extent of membrane formation indicate the toxin burden. As a guide, doses range from 10000 units in tonsillar diphtheria of short duration, to 40000–60000 units in pharyngeal disease, to 100000–150000 units in extensive disease of 3 or more days' duration.

Recommendations differ on the route of administration (intramuscular vs intravenous), but in severe disease at least some of the dose should be administered intravenously.

Antibiotic therapy

Antibiotics have no impact on already established toxin induced lesions but limit further bacterial growth and the duration of corynebacterial carriage that often persists even after clinical recovery. Penicillin, 0.6–1.2 g every 6 hours, or erythromycin, 0.5 g every 6 hours, is recommended. Antibiotic therapy should be continued for 14 days.

Supportive measures

Supportive management of complications, with particular attention to the airway and cardiac manifestations are an important part of case management. Patients should be nursed in strict isolation and should be attended by staff with documented immunization histories.

Early in the illness, respiratory and cardiac complications are the greatest threat. These can be minimized by close monitoring (including regular ECG) and early intervention (e.g. pacing for conduction disturbances, drugs for arrhythmias). Some experts

recommend tracheostomy or intubation at an early stage to ensure continued patency of a compromised or potentially compromised airway, and mechanical removal of any tracheobronchial membrane.

Immunization

Diphtheria infection does not always confer protective immunity. Individuals recovering from the disease should therefore complete active immunization by receiving an age appropriate booster dose of diphtheria toxoid, or a full primary series if indicated during convalescence.

6.8. Public Health Intervention

Active case search in community

Active case search (ACS) in response to identification of diphtheria cases in the community is very important as there is a probability of finding additional cases among contacts of diphtheria cases. Besides conducting active case search in households and neighbourhood, the workplace or school contacts should also be actively assessed for the illness. A thorough ACS in the community will identify any clustering of cases, and timely interventions have the potential to curtail the outbreaks and reduce case morbidity and mortality. An assessment of immunization status of the community should also be conducted during active case search in the community. Attempts should be made to conduct active case search soon after identification of a suspected case preferably within 48 hours of case confirmation.

Prophylaxis

Close contacts, especially household contacts, should receive antibiotics—benzathine penicillin G (600000 units for persons younger than 7 years old and 1200000 units for those 7 years old and older) or a 7- to 10-day course of oral erythromycin (40 mg/kg/day for children and 1 g/day for adults). Track closely and begin antitoxin at the first signs of illness. Single dose Azythromycin for 10 days was found to be equally effective with better compliance (Table 6.1)

Table 6.1: Management of close contacts with respiratory symptoms

Age	Immunization	Prophylaxis			
		Antibiotic	Dose	Route	Duration
<6 years old	DPT	Penicillin G benzathine	600 000 units	IM	Single dose
		or			
		Erythromycin	40 mg/kg in 4 divided doses	PO	7–10 days
>6 years old	DT/Td/Tdap as per availability	Penicillin G benzathine	1.2 million units	IM	Single dose
		or			
		Erythromycin	1g/day in 4 divided doses	PO	7–10 days

Note : Azithromycin (10 mg/kg body weight), a long acting oral antibiotic, is also being used as single daily dose for seven due to its better compliance , however there are no enough evidence on the duration of the use of Azithromycin.

Immunization of patient and other contacts

During convalescence, every patient with clinical diphtheria should receive an age-appropriate booster dose of diphtheria toxoid, or a full primary series if indicated.

The contacts and susceptible population identified during ACS should be given a dose of diphtheria containing vaccine appropriate to their age. All children less than 6 years of age should be immunized by a single dose of diphtheria containing vaccine, such as DPT, if they have not received such vaccine in the previous 5 years. Persons aged more than 6 years can be given DT, Td (Tetanus with low-dose diphtheria antigen) or Tdap (Tetanus with low-dose diphtheria and acellular pertussis antigens) as per availability because of the adverse effects of pertussis component in DPT.

6.9. Data management

Data analysis

Analysis should be performed at regular intervals using a standard approach. However, skillful interpretation of data is needed to determine any aberrations and to develop a focused action plan.

Time analysis: Date of onset of symptom is the most critical information on which time analysis can be based upon. Basic analysis by time can be conducted in several different ways to detect changes in disease incidence.

- comparing the number of cases occurring in the current week with the numbers in the preceding 4 weeks
- comparing the number of cases during the current period (month, quarter) with the number reported during the same period in previous years
- comparing the occurrence of disease by year to analyse long-term (secular) trends in a disease
- clustering of cases over the specified period (weeks, months) should immediately raise an alarm
- no cases reported during high transmission period should trigger an appropriate response for verification of information.

Place analysis: Place where the case was residing at the time of onset of symptoms and during incubation period must be determined for all cases. Analyse disease occurrence and pattern by time and place simultaneously. Place analysis is best displayed by plotting the location of cases on a local map over a specified period of time. Any spatial clustering of cases or silent areas will immediately become visible to guide interventions. Repeated occurrence of cases in a particular geographical area over many years helps in identifying high-risk areas for disease transmission.

Calculation of incidence of reported diphtheria cases

$$\text{Incidence of reported diphtheria cases} = \frac{\text{Total number of cases in 1 year in specified geographical area}}{\text{Total population of specified geographical area}} \times 100{,}000$$

Person analysis: Analysing surveillance data by characteristics of affected person is also helpful. Age, sex and religion are the most basic variables to be studied. Other variables, such as vaccination status, hospitalization, associated risk factors for specific disease, such as recent travel, exposure in school or work place should also be looked into for targeted interventions.

Monitoring indicators

1. **Proportion of cases with timely notification:** This indicator determines the speed and quality of a surveillance system. Timely notification of suspected cases has many advantages: sample collection during early phase of disease increases the probability of laboratory confirmation; early detection of impending outbreaks, case management and timely public health interventions can reduce the morbidity and mortality rates.

   In most cases of diphtheria, membrane appears in 2–4 days after onset and due to severity of symptoms, there is more likelihood that patients seek early medical care. The cases reported within 48 hours of disease onset should be considered as timely notified.

$$\frac{\text{Total number of suspected diphtheria cases reported within 48 hours of onset}}{\text{Total number of suspected diphtheria cases}} \times 100$$

Target of at least 80% timely notification should be achieved. The reasons for delayed notification should be analysed. These could be due to lack of awareness among health-care providers, lack of understanding of reporting protocols, reporting network not tuned to pick early cases or communication channels provided for notification are not free or updated.

2. **Proportion of cases with timely investigation:** An investigation is considered timely if it is done within 48 hours of notification. It is calculated as:

$$\frac{\text{Total number of cases investigated within 48 hours of notification}}{\text{Total number of reported cases}} \times 100$$

Target of timely investigation is at least 90%.

3. **Proportion of cases with adequate sample collection:** This indicator is calculated as:

$$\frac{\text{Total number of cases in which adequate sample is collected}}{\text{Total number of diphtheria cases}} \times 100$$

The target of collecting samples should be in at least 80% of suspected cases of diphtheria.

If large proportion of cases with no samples has been observed, the reasons could be multiple: late notification of cases outside the window period of sample collection, health-care provider not confident in sample collection procedure, lack of logistics, death, refusals and sample spoiled during storage and shipment.

4. **Proportion of timely active case search in community:** This indicator will help to monitor the preparedness of the government health system to build up a community response. It is calculated as:

$$\frac{\text{Total number of ACS conducted within 48 hours of case confirmation}}{\text{Total number of diphtheria cases}} \times 100$$

Target of at least 80% should be achieved for this indicator. Monitoring of this indicator will promote timely ACS in the community and hence early identification of impending outbreaks. This indicator will also help in identifying the areas of complacency or areas requiring support or resources from the district level.

5. **Timeliness of weekly reporting:** This indicator determines the proportion of reporting units whose weekly reports are received at the district on time as agreed by national programme. It is calculated as:

$$\frac{\text{Number of weekly reports received on time}}{\text{Total number of reporting units}} \times 100$$

Target of at least 80% timeliness of weekly reporting should be achieved. This indicator is an important tool to measure alertness of the reporting network.

6.10. Feedback

Provide feedback to stakeholders through a weekly/monthly bulletin.

Annexure 6.1: Case Investigation Form for Diphtheria/Pertussis/Neonatal tetanus

Case identification number:

1. Reporting investigation information

Date of case reported: _/_/_ Reported by:

Title/designation: Date of case investigated: _/_/_

Case investigated by: Title/designation:

Date of case verified: _/_/_ Verified by:

Title/designation: Reporting health facility:

2. Personal information:

Patient's name: Nationality:☐National ☐Non-national

Sex:☐Male ☐Female Date of birth: _/_/_ Age: Years___Month__

Father's name: Mother's name:

Present address: Village/city Gewog Dist:

Child belongs to migratory family/community: ☐Yes ☐No ☐Unknown

If yes, specify: ☐Migration ☐Nomad ☐Construction site ☐Others, specify

3. Hospitalization: ☐Yes ☐No If yes, name of hospital:

Date of admission: _/_/_ Date of discharge: _/_/_

4. Vaccination status: Any vaccine received: ☐Yes ☐No ☐Unknown

If received, encircle vaccines received irrespective of age when they were received

At birth	6 weeks	10 weeks	14 weeks	9 months	24 months	6 years
OPV0	OPV1	OPV2	OPV3	MMR1	MMR2	Td booster
BCG	Penta1	Penta2	Penta3		DT	
Hep B0 (birth dose)			IPV		OPV booster	

Source of vaccination status: by card/history_____

Date of last dose of vaccine: For diphtheria (Td, Pentavalent, DT), For Pertussis (Pentavalent): _/_/_

In case of Neonatal tetanus - mother's vaccination history TT (Td):☐1 ☐2 ☐Booster ☐Unknown

Date of last dose of Td: _/_/_

5. Clinical symptoms: Duration of illness in days:

Diphtheria

Date of onset of fever with sore throat: _/_/_ Sore throat: ☐Yes ☐No

Fever: ☐Yes ☐No Greyish white adherent membrane in throat: ☐Yes ☐No

Redness of tonsils: ☐Yes ☐No Hoarseness of voice: ☐Yes ☐No

Difficulty in swallowing: ☐Yes ☐No Bull neck: ☐Yes ☐No

Difficulty in breathing: ☐Yes ☐No

Pertussis

Cough more than 2 weeks: ☐Yes ☐No Paroxysms:☐Yes ☐No

Cough leading to vomiting: ☐Yes ☐No Whoop: ☐Yes ☐No

Cyanosis: ☐Yes ☐No History of active TB/other chronic URTI: ☐Yes ☐No

Apnoea: ☐Yes ☐No Specialist physician strongly suggest pertussis:☐Yes ☐No

Neonatal Tetanus

Child normal in 0-2 days: ☐Yes ☐No Onset 3-28 days of age: ☐Yes ☐No

Inability to suck and cry: ☐Yes ☐No Stiffness: ☐Yes ☐No

Spasm/seizure: ☐Yes ☐No If yes, precipitated by stimuli: ☐Yes ☐No

Delivery: ☐Institutional ☐home ☐others, specify:

If home delivery, birth attended by:

Any substance applied on cord: ☐Yes ☐No If yes, specify:

Encephalitic

Fever: ☐Yes ☐No Seizure: ☐Yes ☐No

Paralysis: ☐Yes ☐No Neck rigidity: ☐Yes ☐No ☐Unknown

Headache: ☐Yes ☐No ☐Unknown Unconsciousness: ☐Yes ☐No ☐Unknown

Change in mental status: ☐Yes ☐No Any other, specify:

6. Treatment history

Antibiotic started before sample collection: ☐Yes ☐No ☐Unknown

If yes, ☐Penicillin ☐Azithromycin ☐Erythromycin ☐Clarithromycin ☐Cotrimoxazole

☐Clarithromycin ☐Tetracycline ☐Doxycycline ☐Amoxicillin ☐Ampicillin ☐Cefexime

Others, specify:

Diphtheria antitoxin: ☐Yes ☐No ☐Unknown ☐Not applicable

7. Contact history

History of contact with laboratory confirmed case: ☐Yes ☐No

If yes, case ID no of laboratory confirmed case:

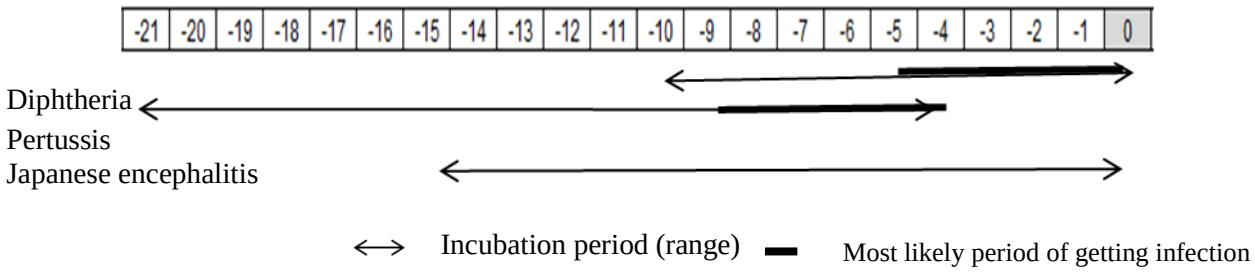
Similar symptoms in other household contacts: ☐Yes ☐No

If yes, no of cases: Details:

Similar symptoms in other neighborhood/workplace/school contacts: ☐Yes ☐No

If yes, no of cases: Details:

8. Travel history: Travel of suspected case within 21 days prior to onset (indicate date and place of date line



Place of visit:

Requires cross notification: ☐Yes ☐No If yes, date of cross notification: _/_/_

In case of neonatal tetanus, name the place of delivery:

9. History of visit to another health center after the date of onset: Yes No

If yes, date of visit: _/_/_ Name of health center:

10. Specimen collection

	Date collected	Date sent	Result date	Condition	Result
Throat swab(Diphtheria					
Serum (JE)					
CSF (JE)					
Serum (Pertussis)					

If no specimen is collected, reason of not collecting the specimen: ☐Dead ☐Not willing ☐Logistic issue ☐Late notification ☐Others, specify:

11. Active case search in the community: ☐Yes ☐No

If yes, date of search: _/_/_ Number of individuals verified:

Number of suspected cases found:

12. Final classification

☐Laboratory confirmed ☐Epi linked ☐Clinically compatible ☐Discarded

13.30 day follow-up (telephonic)

Date of follow-up: _/_/_ Outcome: ☐Death ☐Survive

14. Complications at any time during illness or follow-up

Complications of Diphtheria:☐Myocarditis ☐Bulbar palsy(palatal, pharyngeal, facial, oculomotor) ☐Peripheral neuropathy ☐Pneumonia ☐Otitis media ☐Respiratory insufficiency

Complications of Pertussis:☐Pneumonia ☐Seizures ☐Encephalopathy ☐Otitis media ☐Pressure effects (Pnemothorax, epistaxis, subdural hematomas, hernias, rectal prolapse)

Investigator name and signature
Mobile Number:
Date:

Chapter 7: Pertussis Surveillance

7.1. Introduction

The recent epidemics of pertussis in several high-income countries have indicated waning of immunity following acellular pertussis vaccine and the need for additional booster doses for better disease control. The non-availability of data on the epidemiology of pertussis in low-income countries using whole-cell pertussis vaccine has highlighted the need for better epidemiological data that can be used to make policy recommendations on the need and number of booster doses of the vaccine.

Pertussis surveillance is a **case based surveillance** and a single suspected case is an immediately notifiable disease and should be reported immediately in NEWARS information system under immediately reporting platform.

7.2. Case detection and reporting

Case definition

A suspected case of pertussis is defined as: A person with a cough lasting at least 2 weeks with at least one of the following: paroxysms (i.e. fits) of coughing, inspiratory whooping, post-tussive vomiting (i.e. vomiting immediately after coughing) without other apparent causes **OR** Apnea (with or without cyanosis) in infants (age <1-year old) with cough of any duration **OR** If a physician suspects pertussis in a patient with cough of any duration.

The date of onset for pertussis should be considered as date of onset of cough.

Description of case definition

Paroxysms of cough: cough becomes more frequent and spasmodic with repetitive bursts of 5–10 coughs, often within a single expiration. During a paroxysm, there may be a visible neck vein distension, bulging eyes, tongue protrusion and cyanosis. Frequency of paroxysmal episodes varies from several per hour to 5–10 per day. Episodes are often worse at night and interfere with sleep.

Whoop: Sound produced due to rapid inspiration against closed glottis at the end of cough paroxysm.

Post-tussive vomiting: vomiting immediately after coughing occasionally with a mucous plug expelled at the end of an episode.

Without other apparent causes: exclude other causes of chronic cough, such as tuberculosis, asthmatic episodes, chronic bronchitis, etc. The clinical features due to increased intrathoracic pressure generated due to paroxysms of cough are frequently associated with pertussis cases. These are subconjunctival and intracranial haemorrhages, rectal prolapse, hernias, pneumothorax, petechiae or rib fracture.

Case reporting

A single suspected cases of pertussis should be immediately reported through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform (refer NEWARS guideline). If no suspected case is detected, Zero reporting should be made weekly through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform.

7.3. Case investigation

A reported case should be investigated using standard Case Investigation Form (**Annexure 6.1**) by the concerned health care provider. Active case search should be conducted to identify other cases and determine whether other nearby areas have been exposed or are also experiencing outbreaks.

7.4. Unique case identification number

Each suspected pertussis should be assigned a unique identification number. This unique identification should be assigned as follow: Country pertussis (PER) surveillance code + health center name + year + sequential number by order of reporting. E.g.: BHU-PER/Samtse hospital/2018/001 if pertussis cases are detected in Samtse hospital.

7.5. Specimen collection and transportation

Whenever pertussis is suspected, designated personnel should secure specimens for laboratory confirmation. A blood should be obtained on first contact with the patient

during the case investigation and refer to RCDC (Refer blood collection under MR surveillance).

7.6. Case classification

1. **Laboratory confirmed:** A case that meets the clinical case definition, where samples are collected and laboratory results are positive for the suspected disease
2. **Epidemiologically linked:** A case that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case
3. **Clinically compatible:** A case that meets the clinical case definition but is neither laboratory-confirmed nor epidemiologically linked
4. **Discarded:** A patient that does not meet the clinical case definition on case investigation

7.7. Case management

Treatment is most effective in lessening symptoms if offered early in the disease during the first 2weeks before coughing paroxysms occur, but during this time pertussis is most difficult to diagnose. Most previously immunized adults or adolescents recover even without antibiotics because of a milder version of the illness than that seen in infants and young children.

Treatment in later stages is important to eliminate B. pertussis from the nasopharynx and prevent transmission to more vulnerable populations. Treatment is recommended at any time within 3 weeks of cough onset for those over 1year of age, and within 6 weeks of cough onset for those younger. The period of communicability is reduced to 5 days after treatment with antibiotics. Coughing (symptomatic) household members of a pertussis patient should be treated as if they have pertussis. Earlier treatment and prevention of transmission may reduce the considerable burden of adult pertussis: loss of work, prolonged symptoms and multiple provider visits.

There are no proven treatments for pertussis-induced cough; steroids and beta-agonists are not effective. Macrolide antibiotics eradicate B. pertussis within 5 days. Recommendations include azithromycin (for 5 days) and clarithromycin (7 days). These have fewer gastrointestinal side effects, easier dosing and better compliance than erythromycin (which is recommended for 14 days).Erythromycin, which is given as four doses each day for 14 days, continues to be used, but adherence to the regimen

and completion of the course are generally lower than for the other macrolides, and adverse effects (gastrointestinal distress, pyloric stenosis, etc.) occur more frequently. In infants <1 month of age, azithromycin is preferred due to concerns for infantile hypertrophic pyloric stenosis, which is associated with erythromycin.

For patients >2 months of age, Trimethoprim/sulfamethoxazole for 14 days is an alternative for patients who cannot tolerate macrolides and who are not pregnant, or nursing. Doses are standard, except for infants <6 months, for whom azithromycin is recommended at 10 mg/kg/day for 5 days. No work or school is recommended for patients with suspected pertussis until completion of at least 5 days of antimicrobial therapy.

Natural infection does not confer long-lasting protection against pertussis. Therefore, during convalescence, patients with clinical pertussis without a full primary vaccine series should receive vaccine to complete the series or age appropriate booster dose if indicated.

7.8. Public health intervention

Active case search in community: Active case search in response to identification of pertussis cases in the community is very important, as there is a probability of finding additional cases among contacts of pertussis cases. Besides conducting the active case search in the household and neighbourhood, workplace or school contacts should also be actively assessed for the illness. A thorough ACS in the community will identify any clustering of cases and allow for timely interventions. An assessment of immunization

status of the community should also be conducted during active case search in the community. Attempts should be made to conduct active case search soon after identification of a suspected case, preferably within 48 hours of case confirmation.

Prophylaxis: Extensive contact tracing and broad scale use of post-exposure antimicrobial prophylaxis (PEP) among contacts may not be an effective use of limited public health resources. However, if resources permit, administration of post-exposure therapy to an asymptomatic contact within 21 days of cough onset in the index patient can potentially prevent symptomatic infection. When pertussis is strongly suspected,

attempts to identify and provide preventative treatment to close contacts should proceed without waiting for laboratory confirmation. A course of antibiotics effective against pertussis should be administered to all close contacts of pertussis cases, regardless of age and vaccination status. When suspicion of pertussis is low, the treatment of contacts can be delayed until there is laboratory confirmation of the diagnosis. While antibiotics may prevent pertussis disease if given prior to symptom onset, there are no data to indicate that widespread use of PEP among contacts effectively controls or limits the scope of pertussis outbreaks. Therefore, antibiotic prophylaxis efforts should be mainly focused on women in their third trimester of pregnancy, infants <1 year of age and their close contacts. Preventative treatment of women in their third trimester of pregnancy, infants and their close contacts should not be delayed because pertussis can be severe and life-threatening to young infants.

Immunization: The primary DTP vaccine series is essential for reducing severe disease

in young infants. Even one dose of DTP may offer some protection against fatal pertussis disease in infants.

Immunity to pertussis from vaccine or disease wanes over times and persons who have been vaccinated or had prior infection can become infected. New data on the duration of protection from acellular pertussis vaccines suggest that significant waning of immunity occurs within 2–3 years vaccination, particularly in persons who never received any doses of whole cell vaccine.

Table 7.1: Recommended treatment and post-exposure prophylaxis for close contacts, by age group

Age group	Azithromycin	Erythromycin*	Clarithromycin	Alternate agent: TMP-SMX†
<1 month	Recommended agent for infants <1 month of age; 10 mg/kg per day in a single dose x 5 days§	Not recommended	Not recommended	Contraindicated in infants <2 months of age (risk for kernicterus).
1–5 months	10 mg/kg per day in a single dose x 5 days	40–50 mg/kg per day in 4 divided doses x 14 days	15 mg/kg per day in 2 divided doses x 7 days	Contraindicated in infants <2 months of age. For infants aged >2 months of age, TMP 8 mg/kg per day; SMX 40 mg/kg per day in 2 divided doses x 14 days
Infants aged >6 months and children	10 mg/kg as a single dose on Day 1 (maximum 500 mg); then 5 mg/kg per day as a single dose on days 2–5 (maximum 250 mg/day)	40 mg/kg per day in 4 divided doses for 7–14 days (maximum 1–2 g per day)	See above (maximum 1g/day)	See above
Adolescents and adults	500 mg as a single dose on Day 1 then 250 mg as a single dose on days 2–5	2g/day in 4 divided doses x 14 days	1g/day in 2 divided doses x 7 days	TMP 320 mg/day, SMX 1600mg/ day in 2 divided doses x 14 days

*Some experts prefer erythromycin estolate over erythromycin stearate or ethylsuccinate because it achieves higher serum levels with equal doses.

†Trimethoprim-sulfamethoxazole (TMP-SMX) can be used as an alternative agent to macrolides in patients >2 months of age who are not pregnant or nursing and are allergic to, cannot tolerate or are infected with a rare macrolide-resistant strain of Bordetella pertussis.

§Preferred macrolide for this age because of risk of idiopathic hypertrophic pyloric stenosis associated with erythromycin.

7.9. Data management

Data analysis:

Time analysis: Date of onset of symptom is the most critical information on which time analysis can be based upon. Basic analysis by time can be conducted in several different ways to detect changes in disease incidence.

- comparing the number of cases occurring in the current week with the numbers in preceding 4 weeks;
- comparing the number of cases during the current period (month, quarter) with the number reported during the same period in previous years;
- comparing the occurrence of disease by year to analyse long-term (secular) trends in a disease;
- clustering of cases over the specified period (weeks, months) should immediately raise an alarm;
- no cases during a high-transmission period should trigger an appropriate response for verification of information.

Place analysis: Place where the case was residing at the time of onset of symptoms and

during incubation period must be determined for all cases. Analyse disease occurrence by time and place simultaneously. Place analysis is best displayed by plotting the location of cases on a local map over a specified period of time. Any spatial clustering of cases or silent areas will immediately become visible to guide interventions. Repeated occurrence of cases in a particular geographical area over many years helps in identifying high-risk areas for disease transmission.

Calculation of incidence of reported pertussis cases

$$\text{Incidence of reported pertussis cases} = \frac{\text{Total number of cases in 1 year in specified geographical area}}{\text{Total population of specified geographical area}} \times 100\,000$$

Person analysis: Analysing surveillance data by characteristics of affected person is also helpful. Age, sex and religion are the most basic variables. Other variables, such as vaccination status, hospitalization, associated risk factors for specific disease, such

as recent travel, exposure in school or work place should also be looked into for targeted interventions.

Calculation of incidence of reported pertussis cases

$$\text{Incidence of reported pertussis cases} = \frac{\text{Total number of cases in 1 year in specified geographical area}}{\text{Total population of specified geographical area}} \times 100\,000$$

Monitoring indicators

2. **Proportion of cases with timely investigation:** Timely investigation of all notified cases is considered if it is done within 48 hours of notification and indicates the alertness of the surveillance system to respond to notification of cases. It is calculated as:

$$\frac{\text{Total number of cases investigated within 48 hours of notification}}{\text{Total number of reported cases}} \times 100$$

Target of at least 90% for timely investigation should be achieved.

3. **Proportion of cases with adequate sample collection:** It is calculated as:

$$\frac{\text{Total number of cases in which adequate sample is collected}}{\text{Total number of pertussis cases}} \times 100$$

Target of collecting samples in at least 80% suspected cases of pertussis should be achieved.

4. **Proportion of timely active case search in community:** Active case searches done within 7 days of case investigation should be considered timely. The indicator is calculated as:

$$\frac{\text{Total number of ACS conducted within 7 days of case investigation}}{\text{Total number of pertussis cases}} \times 100$$

Target of at least 80% should be achieved for this indicator.

1. **Proportion of cases with timely notification:** This indicator determines the speed and quality of a surveillance system. Timely notification of suspected cases leads to timely sample collection, early detection of impending outbreaks, case management and timely public health interventions.

Date of onset in suspected pertussis cases should be considered as day of onset of cough. Since the case definition of pertussis requires cough of more than 2 weeks duration and paroxysms occur late (≥2 weeks of cough onset) during the natural course of illness, early notification of pertussis cases is not expected. The cases reported within 4 weeks of disease onset should be considered as timely notified.

$$\frac{\text{Total number of suspected pertussis cases reported within 48 hours of onset}}{\text{Total number of suspected pertussis cases}} \times 100$$

Target of at least 80% timely notification should be achieved.

2. **Proportion of cases with timely investigation:** Timely investigation of all notified cases is considered if it is done within 48 hours of notification and indicates the alertness of the surveillance system to respond to notification of cases. It is calculated as:

$$\frac{\text{Total number of cases investigated within 48 hours of notification}}{\text{Total number of reported cases}} \times 100$$

Target of at least 90% for timely investigation should be achieved.

3. **Proportion of cases with adequate sample collection:** It is calculated as:

$$\frac{\text{Total number of cases in which adequate sample is collected}}{\text{Total number of pertussis cases}} \times 100$$

Target of collecting samples in at least 80% suspected cases of pertussis should be achieved.

4. **Proportion of timely active case search in community:** Active case searches done within 7 days of case investigation should be considered timely. The indicator is calculated as:

$$\frac{\text{Total number of ACS conducted within 7 days of case investigation}}{\text{Total number of pertussis cases}} \times 100$$

Target of at least 80% should be achieved for this indicator.

5. **Timeliness of weekly reporting:** This indicator determines the proportion of reporting units whose weekly reports are received on time at the district. It is calculated as:

$$\frac{\text{Number of weekly reports received on time}}{\text{Total number of reporting units}} \times 100$$

Target of at least 80% timeliness of weekly reporting should be achieved.

6. **Completeness of weekly reporting:** This indicator determines the proportion of reporting units whose weekly reports have been received at the district. It is calculated as:

$$\frac{\text{Number of weekly reports received}}{\text{Total number of reporting units}} \times 100$$

The numerator includes all weekly reports received at the district before next week irrespective of their timeliness. Target of at least 90% completeness of weekly reporting should be achieved.

7.10. Feedback mechanism

Provide feedback to stakeholders through a weekly/monthly bulletin.

Chapter 8: Neonatal Tetanus Surveillance

8.1. Introduction

All countries including Bhutan in the WHO-South East Asia Region have achieved the status of elimination of maternal and neonatal tetanus (MNT) in 2016. However, neonatal tetanus (NT) cases can still be found although rare because complete eradication of tetanus is not possible as tetanus spores are found throughout the world in soil and animal faeces; so exposure to Clostridium tetani cannot be completely prevented. However, every case of NT can be prevented. Therefore, a sensitive and reliable NT surveillance system is required to detect every suspected case and implement corrective measures to prevent further cases.

Neonatal tetanus is case based surveillance and the single suspected case immediately notifiable disease and should be reported immediately in NEWARS information system.

8.2. Case detection and reporting

Case definition

Suspected case: any neonatal death between 3 and 28 days of age in which the cause of death is unknown, or any neonate reported as having suffered from neonatal tetanus between 3 and 28 days of age and not investigated. The date of onset of NT should be considered as date of onset of inability to suck.

Confirmed case: Any neonate with normal ability to suck and cry during the first 2 days of life and who, between 3 and 28 days of age cannot suck normally and becomes stiff and/ or has spasms (i.e. jerking of the muscles).

Discarded case: A suspected NT case, which has been investigated and does not satisfy the clinical criteria for confirmation.

Explanation of case definition

Stiff and/or spasm: Initially increased tone of facial muscles (lockjaw, grimace) is seen. Inability to suck, stiffness in the neck, shoulder and back muscles appear concurrently.

Subsequent involvement of other muscles produces rigid abdomen and stiff proximal limb muscle. Muscles may go into spasms repetitively – spontaneously or when provoked by even the slightest stimuli.

Case reporting

A single suspected case of NT should be immediately reported through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform (refer NEWARS guideline).

If no suspected case is detected, Zero reporting should be made weekly through NEWARS information system under immediately reporting platform using either through mobile SMS or web-based reporting platform.

Neonatal death reported should be investigated and caused of deaths categorized to rule out NT death.

8.3. Case investigation

A reported suspected case should be investigated using standard Case Investigation Form (**Annexure 6.1**) by the concerned health care provider and confirmed. The investigation should consider finding information of gestational age, birth weight, skilled or unskilled assisted delivery, the immunization status of the mother, cord care and any local application and should also provide the history of symptoms as described by the caregiver, to allow a full understanding of the history and symptoms of the case to double check the classification.

8.4. Unique case identification number

Each suspected NT case will be assigned a unique identification number. This unique identification will be assigned as follow: Country NT surveillance code + hospital code + year + sequential number by order of reporting. E.g., BHU-NT/JDNR/2018/001 if case is detected in JDWNRH (Annexure for hospital codes).

8.5. Case management

Patient should be admitted to an intensive care unit (ICU). If the facility does not have an ICU, the patient should be transferred.

Passive immunization with human tetanus immune globulin (TIG) shortens the course of tetanus and may lessen its severity. A dose of 500 U may be as effective as larger doses. Therapeutic TIG (3,000-6,000 units as 1 dose) has also been recommended for generalized tetanus. Other treatment measures include ventilatory support, high-calorie nutritional support, and pharmacologic agents that treat reflex muscle spasms, rigidity, tetanic seizures and infections.

8.6. Public health interventions

A confirmed case should be followed by a case response. Case investigations should be used as opportunities to provide health education to the family and community around NT prevention and reporting of NT cases. In case the mother was not immunized, immediately immunize the mother with one dose of Td vaccine and provide a second dose 1 month later. Inform the mother about proper cord care.

If 90% of the mothers from the rapid community assessment are protected (clean delivery or/and TT2+), the response should be limited to the immunization of the mother of the NT case alone and promotion of hygienic cord care practices. If less than 90% of the mothers are protected, and/or if less than 90% of the children are completely immunized, determine and address the cause of non-protection and provide Periodic Intensification of Routine Immunization (PIRI). Also provide information to the community and birth attendants about proper cord care. If a source of unclean deliveries is identified, training and education may be provided to the birth attendant to prevent further NT cases

8.7. Data management

Data analysis:

Recommended data analysis includes:

- Number of cases and incidence rates month, year and geographical area,
- District-specific, sex-specific, incidence rates per 1000 live births by year.
- Case-fatality ratio among confirmed NT cases.
- Percentage of confirmed NT cases whose mother received a protective TT dose(s) subsequent to the onset of tetanus in the baby
- Completeness/timeliness of monthly and zero reporting.

Monitoring indicators

Countries that achieved MNTE should review the performance of each district annually. This annual review exercise should be a joint exercise by the Expanded Programme on Immunisation (EPI), MNCH, and Surveillance officer together with partner representatives if required.

The following indicators should be used for regular evaluation of the quality of the NT surveillance.

1. **Proportion of cases with timely notification:** Date of onset in suspected neonatal tetanus cases should be considered as day of onset of inability to suck. The disease progression in neonates is very rapid with high case fatality rate early in the course of illness therefore, cases reported within 7 days of disease onset should be considered as timely notified.

$$\frac{\text{Total number of suspected neonatal tetanus cases reported within 48 hours of onset}}{\text{Total number of suspected neonatal tetanus cases}} \times 100$$

Target of at least 80% timely notification should be achieved.

2. **Proportion of cases with timely investigation:** It is expected that the designated surveillance/medical officer should be able to investigate all notified cases within 48 hours of notification. It is calculated as:

$$\frac{\text{Total number of cases investigated within 48 hours of notification}}{\text{Total number of reported cases}} \times 100$$

Efforts should be made to achieve target of at least 90% for timely investigation.

3. **Proportion of timely case response in community:** This indicator will help to monitor the preparedness of the government health system to build up a community response. It is calculated as:

$$\frac{\text{Total number of case response conducted within 7 days of case investigation}}{\text{Total number of neonatal tetanus cases}} \times 100$$

Target of at least 80% should be achieved for this indicator. However, all cases should be followed by case response.

4. **Timeliness of weekly reporting:** This indicator determines the proportion of reporting units whose weekly reports are received on time at the district. It is calculated as:

$$\frac{\text{Number of weekly reports received on time}}{\text{Total number of reporting units}} \times 100$$

Target of at least 80% timeliness of weekly reporting should be achieved.

5. **Completeness of weekly reporting:** This indicator determines the proportion of reporting units whose weekly reports have been received at the district. It is calculated as:

$$\frac{\text{Number of weekly reports received}}{\text{Total number of reporting units}} \times 100$$

The numerator includes all weekly reports received at the district before next week irrespective of their timeliness. Target of at least 90% completeness of weekly reporting should be achieved.

8.8. Feedback mechanism

Provide feedback to stakeholders through a weekly/monthly bulletin. The feedback should cover sustaining elimination status, identify high-risk geographical areas, risk factors of NT (place of birth, assistance during delivery, cord care, immunization status, age and parity of mother) to target messages and actions appropriately.