Surveillance Guide for Vaccine-Preventable Diseases in the WHO South-East Asia Region

September 2017
# TABLE OF CONTENT

**Foreword**  
4

**Pertussis surveillance**  
7

- Introduction  
7
- Case detection and reporting  
7
- Case investigation  
8
- Allocation of unique ID  
9
- Sample collection  
9
- Case classification  
13
- Case management  
13
- Public health intervention  
14
- Data collection  
16
- Monitoring indicators  
17
- Feedback mechanism  
18

**Annexes**  
19

- ANNEX 01- Pertussis disease  
19
- ANNEX 02- Core reporting variables for Pertussis  
23

**Readings**  
24
Foreword

Today, we share a collective vision to have the South-East Asia Region free of vaccine-preventable diseases, where all countries provide equitable access to high-quality, safe, affordable vaccines and immunization services throughout the life-course.

Overwhelming evidence demonstrates the benefits of immunization as one of the most successful and cost-effective health interventions ever known. Over the past several decades, immunization has achieved many milestones, including the eradication of smallpox, an accomplishment that has been called one of humanity’s greatest triumphs. Vaccines have saved countless lives, lowered the global incidence of polio by 99% and reduced illness, disability and death from diphtheria, tetanus, whooping cough, measles, Haemophilus influenzae type b disease and epidemic meningococcal A meningitis. We have been able to make the Region free of polio for the last 6 years and eliminate maternal and neonatal tetanus.

We have vaccines against more than 25 diseases in the present day world, and this has increased the need for better surveillance against these diseases to control or eliminate them. As the essence of this subject matter, I would like to highlight that high vaccination coverage may not necessarily indicate the case-load or disease burden in a population. We need to look into the surveillance performance as the key indicators to measure progress towards disease control and/ or elimination.
A functional vaccine-preventable disease surveillance system is a key part of public health decision-making in all countries. Thus, there is an urgent need to build on the current efforts to strengthen vaccine-preventable disease surveillance with the latest state-of-the-art technologies at subnational and national levels. This will require a substantial and long-term commitment of human and material resources, usually beginning with a systematic assessment of the national vaccine preventable diseases (VPD) surveillance system by working closely in partnership with all related partners and stakeholders.

I hope that this vaccine-preventable diseases surveillance guide will be well translated into respective national programmes and add to the efforts to have a high-quality surveillance system for priority vaccine-preventable diseases and help accelerate progress towards strengthening vaccine-preventable disease surveillance in our Region.

Finally, every individual in our Region deserves our best work. We all agree that every family, no matter where residing, has the right to all immunization and health services that are provided by the respective government, in the spirit of universal health coverage contributing towards Sustainable Development Goals, especially Goal 3 on health.

Dr Poonam Khetrapal Singh

Regional Director, WHO South-East Asia Region
**LIST OF ABBREVIATIONS**

<table>
<thead>
<tr>
<th>ACS</th>
<th>active case search</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCID</td>
<td>cell culture infectious dose</td>
</tr>
<tr>
<td>CFR</td>
<td>case fatality rate</td>
</tr>
<tr>
<td>CHW</td>
<td>community health worker</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CIF</td>
<td>case investigation form</td>
</tr>
<tr>
<td>CRF</td>
<td>case report form</td>
</tr>
<tr>
<td>DPT</td>
<td>diphtheria pertussis tetanus vaccine</td>
</tr>
<tr>
<td>DTP3</td>
<td>third dose of diphtheria pertussis tetanus vaccine</td>
</tr>
<tr>
<td>EPI</td>
<td>Expanded Programme on Immunization</td>
</tr>
<tr>
<td>IU</td>
<td>international unit</td>
</tr>
<tr>
<td>ID</td>
<td>identity</td>
</tr>
<tr>
<td>IM</td>
<td>intra-muscular</td>
</tr>
<tr>
<td>NPA</td>
<td>nasopharyngeal aspirate</td>
</tr>
<tr>
<td>NPS</td>
<td>nasopharyngeal swab</td>
</tr>
<tr>
<td>NRL</td>
<td>national reference laboratory</td>
</tr>
</tbody>
</table>

**LIST OF ABBREVIATIONS**

| ORI       | outbreak response immunization |
| PEP       | postexposure prophylaxis       |
| PIRI      | periodic intensification of routine immunization |
| RRL       | Regional Reference Laboratory |
| SEAR      | South-East Asia Region (WHO)  |
| SEARO     | South-East Asia Regional Office |
| SIA       | supplementary immunization activities |
| SOP       | standard operating procedure  |
| TCID      | tissue culture infective dose |
| UNICEF    | United Nations Children’s Fund |
| URTI      | upper respiratory tract infection |
| VPD       | vaccine preventable disease   |
| WHA       | World Health Assembly        |
| WHO       | World Health Organization    |
| wP        | whole cell pertussis         |
Pertussis surveillance

1. Introduction

The recent epidemics of pertussis in several high-income countries has 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. Surveillance for pertussis will provide important information on the status of its epidemiology and control.

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.

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.

**Other associated signs and symptoms**

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.

**Date of onset**

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

**Case reporting**

The reporting network for pertussis surveillance should consist of those reporting sites that are as follows:

- medical colleges, district hospitals, subdistrict government health facilities;
- private health facilities where cases of respiratory illnesses, including pertussis, are most likely to visit and personnel should be trained to identify such cases.

All reporting sites should immediately notify a suspected case of pertussis by any available mode of communication to the concerned health authority. The minimum information required to notify a case are patient identifiers and contact details.

A mechanism of sending weekly reports containing basic information on pertussis cases should be established. When no cases are seen in a week, a weekly report has to be sent nevertheless specifying that ‘zero’ cases were seen. This is called ‘zero reporting’ or ‘nil reporting’. Nil reporting gives confidence that the surveillance system is operational even if no disease is identified.

**3. Case investigation**

Trained health-care staff should be responsible for case investigation preferably within 48-hours of case reporting. A reported suspected case should be investigated using a standard Case Investigation Form (CIF). The CIF should capture certain core variables as given in Annex 02.
4. Allocation of unique ID

A unique case identification number should be given to each suspected case. This case number should begin with one or more three-letter combinations to designate the geographic location, followed by the year and the case number. All communications and forms related to the case should cite the unique case identification number.

**Figure. Example of a unique ID**

PTS-IND-UP-BLS-16-001:
- PTS: Pertussis code
- IND: Country code
- UP: State code
- BLS: District code
- 16: Year of onset
- 001: Serial number of pertussis case of the district

5. Sample collection

The collection and transport of biological specimens is important in the isolation and identification of bacterial agents of whooping cough. The table below shows the samples collected for laboratory confirmation of pertussis.

<table>
<thead>
<tr>
<th>Sample collection for laboratory confirmation of Pertussis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Window period from onset</strong></td>
</tr>
<tr>
<td>up to 4 weeks</td>
</tr>
<tr>
<td>&gt;4 weeks–8 weeks</td>
</tr>
<tr>
<td><strong>Type of specimen</strong></td>
</tr>
<tr>
<td>Nasopharyngeal swab/aspirate and serum</td>
</tr>
<tr>
<td>Serum</td>
</tr>
<tr>
<td><strong>Number</strong></td>
</tr>
<tr>
<td>1 each</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td><strong>Transport media</strong></td>
</tr>
<tr>
<td>Regan-Lowe/Amies transport media with charcoal</td>
</tr>
<tr>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Storage and transportation</strong></td>
</tr>
<tr>
<td>2–8 ºC</td>
</tr>
<tr>
<td>2–8 ºC</td>
</tr>
</tbody>
</table>
Nasopharyngeal swab sample (NPS) collection

For identification of pertussis, nasopharyngeal swab or aspirate should be collected. Throat swab sample is not recommended for confirmation of pertussis. Universal infection prevention precautions should be taken by the person collecting the samples.

- Choose an area for NPS collection that is least used by the family. For example, a family room or kitchen may be more contaminated than other rooms.
- Obtain a thin flexible nasopharyngeal swab made up of Dacron or nylon. Cotton and calcium alginate swabs are not to be used.
- Label the specimen tube with the unique identification code, patient’s name and date of collection.
- Check the expiry date on the tube and transport media to ensure acceptability of the material to be used for sample collection.
- Place a clean paper towel on the table, which will hold the equipment.
- If the subject is a child and is to be held by the parent, the parent must be masked.
- Have patient sit with head against a wall or a support as patients have a tendency to pull away during this procedure.
- Explain the procedure to the parents or patient.
- When the subject is situated and ready for the NPS, put on gloves.
- Measure the distance between anterior nares to the lower lobe of the ear of one side.
- Mark the swab with half of the above measured distance.
- Ask the patient to blow the nose forcefully to remove any mucous plug.
- Position the head slightly upwards and insert the swab along the base of the nose up to the distance marked. Avoid insertion of swab in upward direction.
- Do not force swab if obstruction is encountered before reaching the nasopharynx. Remove swab and try the other side.
- Try to leave the swab in place for 5–10 seconds to increase sensitivity.
- Immediately place the swab in Regan-Lowe transport media/Amies transport media with charcoal and tighten the cap of specimen collection container. Best is to wrap the tape around cap to prevent any leakage.
- Ship at maintaining a temperature of 4 °C.
Nasopharyngeal aspirate (NPA)
A 15% gain in the isolation rate is obtained using NPA, compared with NPS, in neonates and infants.

- Choose an area for NPA collection that is least used by the family.
- Place a clean paper towel on the table, which will hold the equipment.
- If the subject is a child, and is to be held by the parent, the parent must be masked.
- When the subject is situated and ready for the NPA, put on gloves. Remove equipment from the bag and place on the clean paper towel.
- Loosen the cap of the sterile container but do not open until inserting the catheter tip.
- Open the syringe and remove the plastic tip.
- Secure the syringe on the end of the catheter. Test the syringe.
- Remove the catheter from the wrapper.
- Gently and slowly insert the catheter into a nostril rotating the catheter, if necessary, to proceed past the back of the nostril. Insert the catheter until the back of the throat is reached (approximately 10 cm depending on the age of the volunteer). If gagging occurs, the catheter has been inserted too far.
- Once positioned, the catheter should be withdrawn with suction by placing the thumb over the suction control on the side of the catheter, while pulling back on the syringe plunger.
- Once the catheter is removed from the nose, and without touching the tip of the catheter, open the sterile container and place the tip inside. Screw the top on with catheter and syringe still attached. This protects the part of the tubing containing the specimen.
- Label the sterile container, and place container, catheter and syringe in a plastic bag and seal. Remove gloves and place in a plastic bag for disposal.
- Transport the NPA specimen.

Serum sample collection for serological diagnosis of pertussis cases
It is recommended that one serum sample should be obtained.

- Arrange the site for serum separation and obtain a serum collection kit before going for sample collection.
- Use of standard precautions is recommended when collecting any biological specimen.
- Properly label a blood collection tube with name, identification code and collection date.
Using acceptable venepuncture technique, collect 2 to 3 mL whole blood.

Allow a minimum of 15 minutes to allow clot to form.

Centrifuge sample to separate serum from clot. This can also be accomplished by storing the whole blood sample, in an upright position, overnight in the refrigerator (2.0–6.0 °C).

Properly label a 2 mL plastic storage tube in which serum is going to be collected.

Serum samples should be stored and transported at 2–8 °C.

**KEY NOTES**

**Culture:** Culture of nasopharyngeal secretions is for the most specific diagnostic test for pertussis. *B. pertussis* is highly sensitive to drying; therefore, the specimen should be inoculated without delay onto the culture media. Regan-Lowe agar or freshly prepared Bordet-Gengou medium is generally used for culture. Fastidious growth requirement makes *B. pertussis* difficult to isolate.

**Isolation of the organism declines if**

- specimen collection has been delayed beyond the first 2 weeks of illness (catarrhal stage);
- patient has received appropriate antibiotic therapy;
- patient has been vaccinated.

Since the maximum chances of isolating the organism are during catarrhal phase, when the aetiology of the infection is not suspected, there is only a small window of opportunity for culture proven diagnosis.

**Polymerase chain reaction:** Polymerase Chain Reaction (PCR) is an important tool for timely diagnosis of pertussis. It detects DNA sequences of the bacterium and does not require presence of viable bacteria in the specimen; however, it may be more prone to false positive results. The optimal sensitivity of the test is during the first 3 weeks of cough as bacterial DNA is present in the nasopharynx during this time. After the fourth week of cough, the amount of bacterial DNA diminishes rapidly.

**Serologic testing:** It can be a useful tool for diagnosis of pertussis in cases with more than 4 weeks of cough onset. Enzyme immunoassay detecting IgA and IgG antibodies to pertussis toxin, filamentous haemagglutinin, pertactin, and fimbriae are gaining increasing importance as a diagnostic tool for *Pertussis.*
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. Case management

Treatment is most effective in lessening symptoms if offered early in the disease during the first 2 weeks 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 1 year 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.

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.
## Recommended treatment and post-exposure prophylaxis for close contacts, by age group

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

*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.
9. Data collection

Computer technology has greatly facilitated collection and analysis of surveillance data and should preferably be used in pertussis surveillance. However, even if the information system is manual, it should cover case tracking and reporting. Missing or inaccurate data may limit the usefulness of any analysis. Erroneous or incomplete data do not provide reliable information so it should be ensured that basic data are captured carefully.

**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

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

This will help in analysing disease trends over time and place; and identify high-risk areas.

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.
10. Monitoring indicators

Indicators are variables that can be measured repeatedly over time and provide measures of change in a system. The various monitoring indicators recommended for pertussis surveillance are as follows:

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.

11. **Feedback mechanism**

Feedback in the form of periodic bulletins and mails that may be combined bulletins for other vaccine-preventable diseases can be shared. Countries should notify WHO-SEARO about pertussis cases and line lists in a weekly frequency.
Annexes

ANNEX 01- Pertussis disease

Aetiology

Pertussis is a bacterial disease caused by *Bordetella pertussis*. *Bordetella spp.* is aerobic, gram negative coccobacilli. In addition to *B. pertussis*, three other *Bordetella species* can cause disease in humans: *B. parapertussis, B. holmesii* and *B. bronchiseptica*. *B. parapertussis* causes a milder pertussis-like illness. Co-infection of *B. pertussis* and *B. parapertussis* is not unusual.

Pathogenesis:

The pathogenesis of pertussis is incompletely understood. It is multifactorial. The factors filamentous haemagglutinin, pertactin and fimbriae type 2 and type 3 facilitate attachment to targeted host cells. Other factors, such as pertussis toxin, tracheal cytotoxin and adenylate cyclase toxin enable the bacterium to destroy the epithelial lining and evade the host’s immune system.

Transmission

*B. pertussis* is a human specific pathogen and is unable to survive outside its human host. It is highly infectious and spreads by aerosolized droplets. The incubation period of pertussis is commonly 9–10 days, with a range of 6–20 days.

Pertussis is highly communicable. The secondary attack rate for susceptible household contacts is 80–100%. Untreated cases are infectious for 3 weeks following symptom onset. Antibiotics can reduce the period of infectivity.

Reservoir

Pertussis is a human disease. No animal or insect source or vector is known to exist. There is no evidence of prolonged carrier state. Asymptomatic individuals have been identified during epidemics. Adolescents and adults are an important reservoir for *B. pertussis* and are significant sources of transmission of *B. pertussis* to unvaccinated infants.

Occurrence

Pertussis occurs worldwide. Outbreaks were first described in the 16th century. The disease is endemic in all countries with epidemic peaks occurring every 2 to 5 years (typically 3 to 4 years) even after the introduction of effective vaccination programmes and the achievement of high vaccination coverage. Following the introduction of vaccine in the 1940s the incidence of reported pertussis and deaths in children decreased.
Classical pertussis is most often seen in pre-school and school aged children. It is an important cause of death in infants worldwide. Pertussis may be responsible for between 12% and 32% of chronic cough in adults. Currently, pertussis remains one of the principal causes of vaccine-preventable diseases even in countries with high vaccine coverage.

Clinical features and complications

The illness begins less dramatically with non-specific symptoms and then progresses in the following three stages.

1. **Catarrhal:** Initially patients develop catarrhal symptoms, including cough. Other nonspecific symptoms are rhinorrhea, sore throat and conjunctivitis. This stage typically lasts 2 weeks. Fever is present in less than 20% cases.

2. **Spasmodic:** Later, during the course of 1–2 weeks, coughing paroxysms ending in characteristic whoop occur. In typical cases, cough is frequently followed by vomiting. Paroxysms can occur more than 30 times per 24 hours and are more common at night. They occur spontaneously or are precipitated by external stimuli, such as noise and cold air. Between coughing episodes, there are few clinical signs unless complications develop. This stage also typically lasts 2 weeks.

3. **Convalescent:** The coughing gradually subsides. Relapse can occur if another respiratory infection is acquired. This stage can last from 2 weeks to several months.
Pertussis in infants, adults and partially immunized individuals may not present with its typical clinical signs and symptoms. Other common features of pertussis are as follows:

<table>
<thead>
<tr>
<th>Infants:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>● apnoea</td>
<td>● poor feeding</td>
</tr>
<tr>
<td>● cough (no whoop)</td>
<td>● fever</td>
</tr>
<tr>
<td>● cyanotic episodes</td>
<td>● seizures</td>
</tr>
<tr>
<td>● vomiting</td>
<td>● sudden infant death syndrome.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Partially immunized:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>● duration of catarrhal phase may be reduced</td>
<td>● whoop may not occur.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adults:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>● prolonged cough</td>
<td>● post-tussive vomiting</td>
</tr>
<tr>
<td>● paroxysmal cough</td>
<td>● intracranial haemorrhage.</td>
</tr>
<tr>
<td>● whoop</td>
<td></td>
</tr>
</tbody>
</table>

The most common complication is secondary bacterial pneumonia that causes most of pertussis-related deaths. Neurologic complications, such as seizures and encephalopathy, may occur as a result of hypoxia from coughing, or possibly from toxin. Infants are at the highest risk for acquiring pertussis-related complications.

Other less serious complications of pertussis include otitis media, anorexia and dehydration. Complications resulting from pressure effects of severe paroxysms include pneumothorax, epistaxis, subdural hematomas, hernias and rectal prolapse.

**Laboratory Diagnosis**

**Culture:** Culture of nasopharyngeal secretions is considered best for diagnosis of pertussis. *B. pertussis* is highly sensitive to drying, therefore the specimen should be inoculated without delay onto the culture media. Regan-Lowe agar or freshly prepared Bordet-Gengou medium is generally used for culture.

Isolation of the organism declines if

- specimen collection has been delayed beyond the first 2 weeks of illness (catarrhal stage);
- patient has received appropriate antibiotic therapy;
- patient has been vaccinated.
Since the maximum chances of isolating the organism are during catarrhal phase, when the aetiology of the infection is not suspected, there is only a small window of opportunity for culture-proven diagnosis. Fastidious growth requirement makes *B. pertussis* difficult to isolate (success <60%). The highest rates are obtained with infants. To continue to culture is important in order to analyse the evolution and adaptation of the pathogen and to perform surveillance of the antibiotic resistance.

**Polymerase chain reaction:** Polymerase Chain Reaction (PCR) is an important tool for timely diagnosis of pertussis. It is more sensitive than bacterial culture. It detects DNA sequences of the bacterium and does not require presence of viable bacteria in the specimen. The optimal sensitivity of the test is during the first 3 weeks of cough as bacterial DNA is present in the nasopharynx during this time. After the fourth week of cough, the amount of bacterial DNA diminishes rapidly.

**Serologic testing:** It can be a useful tool for diagnosis of pertussis in cases with more than 4 weeks of cough onset. Enzyme immunoassay detecting IgA and IgG antibodies to pertussis toxin, filamentous haemagglutinin, pertactin and fimbriae are gaining increasing importance as a diagnostic tool for *B. pertussis*. However, serology should not be used in infants, as their immune system is immature and liable to interference of maternal antibodies, or in patients vaccinated within 1 year. The presence of a high level of anti-PT antibodies in the serum of a non-vaccinated individual indicates infection. Serology cannot be used as a diagnosis during the year following vaccination since it does not differentiate between antibodies due to the vaccine and natural infection.

**Immunization**

**Whole cell pertussis vaccine (wP):** It contains whole non-viable bacterial cells in various amounts. Selected *B. pertussis* strains are cultured and then killed by heat and treated with formalin to form the vaccine. The methods used for production vary among manufacturers and hence whole cell pertussis vaccines are relatively heterogeneous. Each lot of vaccine undergoes extensive testing to assess potency, toxicity, sterility and bacterial concentration. All pertussis vaccines contain aluminum salts as adjuvant and thiomersal as preservative for multi dose formulations.

Another formulation available commercially is acellular pertussis (aP) vaccine. It is based on highly purified selected components of bacterial agent. The exact components and quantity of the antigens, method of antigen production, purification and detoxification vary with the manufacturers. The aP (acellular pertussis) vaccines have lower initial efficacy, faster waning of immunity and possibly a reduced impact on transmission relative to currently internationally available wP (whole-cell pertussis) vaccines, but aP vaccines show less local and systemic side effects.
### ANNEX 02- Core reporting variables for Pertussis

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Description</th>
<th>Field Type</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>COUNTRY</td>
<td>Country of Report</td>
<td>Text (ISO3 code)</td>
<td>Must be reported</td>
</tr>
<tr>
<td>CaseID</td>
<td>Case identification number</td>
<td>Defined by country</td>
<td>Must be reported</td>
</tr>
<tr>
<td>Province</td>
<td>Province</td>
<td>Defined by country</td>
<td>Must be reported</td>
</tr>
<tr>
<td>District</td>
<td>District</td>
<td>Defined by country</td>
<td>Must be reported</td>
</tr>
<tr>
<td>Agent</td>
<td>Agent</td>
<td>Text (Option: DIP; PER; NNT; AES;</td>
<td></td>
</tr>
<tr>
<td>SEX</td>
<td>Sex</td>
<td>Text (option: F; M; U)</td>
<td>Must be reported</td>
</tr>
<tr>
<td>DOB</td>
<td>Date of birth</td>
<td>Date: (format: (DD-MM-YYYY))</td>
<td>Must be reported (if Age year/month is not provided)</td>
</tr>
<tr>
<td>AgeYear</td>
<td>Age in Year (completed)</td>
<td>Number (format: ######)</td>
<td>Must be reported (if DOB is not provided) if &lt;12 months of age, put zero 99=Unknown age</td>
</tr>
<tr>
<td>DNOT</td>
<td>Date of notification to public health system</td>
<td>Date: (format: (DD-MM-YYYY))</td>
<td>DNOT&gt; = DONSET DNOT&gt; = DOB</td>
</tr>
<tr>
<td>DOI</td>
<td>Date of investigation</td>
<td>Date: (format: (DD-MM-YYYY))</td>
<td>DOI&gt; = DONSET DOI&gt; = DOB DOI&gt; = DNOT</td>
</tr>
<tr>
<td>DosesVac</td>
<td>Number of vaccine doses received for the suspect agent</td>
<td>Number (format: #)</td>
<td>99=Unknown</td>
</tr>
<tr>
<td>DateLastVac</td>
<td>Date of last vaccination for the suspect agent</td>
<td>Date: (format: (DD-MM-YYYY))</td>
<td></td>
</tr>
<tr>
<td>DONSET</td>
<td>Date of onset symptoms</td>
<td>Date: (format: (DD-MM-YYYY))</td>
<td>Must be reported DONSET&gt; = DOB Cannot be future date</td>
</tr>
<tr>
<td>TypeTest</td>
<td>Type of laboratory method</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LabResult</td>
<td>Laboratory test result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classification</td>
<td>Final classification of case</td>
<td>Text (Option: Lab confirmed; Epi linked; Compatible; Rejected)</td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td>Follow- up</td>
<td>Text (Option: Death, Survival)</td>
<td></td>
</tr>
<tr>
<td>Comments</td>
<td>Any comments</td>
<td>Text</td>
<td></td>
</tr>
</tbody>
</table>
Readings


Acknowledgement

The document was produced under the strategic guidance of the Regional Director, Dr Poonam Khetrapal Singh; Director, Programme Management, Dr Arun Thapa, and Dr Pem Namgyal, Director FGL WHO SEARO. The entire process was overseen by Dr Nihal Abeysinghe and Dr Sunil Bahl.

Dr Sudhir Khanal, WHO SEARO, coordinated the development of the technical document in collaboration with a team of international experts, Dr Jacob T John from India, Dr Naresh Pratap KC from Nepal, Dr Sujeewa Amarasena from Sri Lanka and Dr Kumnuan Ungchusak from Thailand along with WHO Consultant Dr Sudhir Joshi who were crucial in the conceptualizing and initial drafting of the document.

This document also benefited from the dedication, support and expertise of all the participants of the regional workshop on surveillance standards for measles, rubella and priority vaccine-preventable diseases in September 2016 at Kathmandu, Nepal, which included National EPI Programme Managers from Member States as well as a number of WHO and UNICEF country office staff and external collaborators.

The IVD SEARO team wishes to thank all mentioned above, including the following contributors whose expert review and guidance made this document possible:

WHO HQ staff: Dr. Minal Patel and Mr. Antoni Sebastien reviewed the draft surveillance standard document and provided technical inputs.

WHO-SEARO: Dr. Jayantha Liyanage, Dr. Sigrun Roesel, Ms. Sirima Pattamadilok, Dr. Pushpa Ranjan Wijesinghe, Ms. Uttara Aggarwal, Mr. Tika Sedai and Dr. Aarti Garg reviewed the draft and provided necessary inputs, including drafting of selected sections.

US CDC: Dr. Jim Goodson, Dr. Heather Scobie and Dr. Susan Wang provided inputs to the various sections of the document and final draft of the surveillance standard document.

The IVD team would also like to acknowledge the support provided by the entire IVD team for the administrative work, the R-DOC team, the building management, ICT services, travel unit and all related staff who played a crucial role at the hind side in the smooth preparation of this report.