



# Pneumococcus

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## DISEASE AND VACCINE CHARACTERISTICS

The bacteria *Streptococcus pneumoniae* (pneumococcus) is the most frequent cause of severe pneumonia and pneumonia deaths worldwide. Pneumococci frequently asymptomatically colonize the human nasopharynx, particularly in children. The bacteria can spread contiguously to cause otitis media and sinusitis, be aspirated to cause pneumonia or invade normally sterile sites to cause sepsis or meningitis. Morbidity and mortality for serious pneumococcal disease is highest in children and the elderly. Case fatality rates can be high for invasive pneumococcal disease, ranging up to 20% for sepsis and 50% for meningitis in developing countries. It is estimated that in 2008, 541,000 HIV-negative children < 5 years of age died from pneumococcal disease (1). Development of pneumococcal resistance to commonly used antibiotics, such as penicillins, macrolides, cephalosporins and co-trimoxazole, is a serious problem in some parts of the world. While most pneumococcal disease is sporadic, large outbreaks of meningitis, usually serotype 1, have occurred in the African meningitis belt. Smaller outbreaks occur in crowded settings (daycare centers, homeless shelters, etc.).

There are over 90 capsular serotypes of pneumococci, although prior to introduction of pneumococcal conjugate vaccines, 6–11 serotypes accounted

for ≥ 70% of all invasive pneumococcal disease occurring in children worldwide. There are two types of pneumococcal vaccines. Currently available polysaccharide vaccines include 23 serotypes; polysaccharide vaccines are recommended in some developed countries to prevent pneumonia in older persons and persons with underlying medical conditions (2). However, these vaccines are not immunogenic in children < 2 years of age. There are two available pneumococcal conjugate vaccines (PCVs), containing 10 or 13 serotypes, which are effective in preventing pneumococcal disease in children due to vaccine serotypes. WHO recommends their use in infants worldwide. All pneumococcal vaccines include the predominant disease-causing serotypes. WHO recommends that PCV be given as a three-dose schedule, with either two doses in infancy with a booster dose or three doses in infancy without a booster dose. Serotype replacement with non-vaccine serotypes has been observed after conjugate vaccine introduction, although overall rates of invasive pneumococcal disease remain reduced after conjugate vaccine introduction.



## RATIONALE AND OBJECTIVES OF SURVEILLANCE

The objectives of surveillance pneumococcal surveillance are to:

- quantify disease burden and epidemiology to inform vaccine introduction decisions (dosing schedule, product choice)
- describe serotype distribution prior to vaccine introduction and monitor serotype replacement after vaccine introduction
- evaluate vaccine impact
- monitor antimicrobial resistance (AMR) to guide treatment choices and improve health care outcomes
- identify pneumococcal outbreaks
- identify immunization programme implementation gaps and to provide data to determine if changes in vaccine policy are needed (such as booster doses).





## TYPES OF SURVEILLANCE RECOMMENDED

### MINIMAL SURVEILLANCE

The minimal surveillance standard for pneumococcal disease is sentinel hospital surveillance for meningitis, previously referred to as Tier 1 Invasive Bacterial Vaccine Preventable Disease (IB-VPD) surveillance (3).

- Surveillance can be implemented in one or multiple hospitals that admit children with meningitis and other severe diseases. Surveillance should be active in enrolling suspected cases and implementing appropriate laboratory testing to confirm pneumococcus.
- Sentinel surveillance is case-based and prospective. It should be undertaken only in hospitals where there are sufficient numbers of cases identified to make the surveillance useful (100 cases per site per year of suspected meningitis). Smaller hospitals are not worth the resource investment and can also lead to erroneous conclusions (for example, serotype distribution) due to small numbers of cases.
- Sentinel site surveillance may not be sufficient to meet all of these objectives. Addition of other surveillance or research methods, such as case-control studies to assess vaccine effectiveness, might be needed.

### ENHANCED SURVEILLANCE

Two types of enhanced surveillance for pneumococcus are possible.

1. **Expanded sentinel hospital surveillance.**  
Meningitis sentinel surveillance can be expanded to include pneumonia and sepsis (previously referred to as Tier 2 IB-VPD surveillance). The characteristics of this surveillance are the same as meningitis sentinel surveillance – case-based, active and prospective. Pneumonia and sepsis surveillance should only be undertaken in hospitals of sufficient size to have a meaningful number of cases (500 cases per site per year for meningitis + pneumonia/sepsis). While it is difficult to identify the etiology of pneumonia, radiography can be used to identify WHO-defined endpoint pneumonia, which is more specific for bacterial disease such as that caused by pneumococcus (5).
2. **Population-based surveillance for invasive pneumococcal disease (IPD)**
  - » A defined catchment population is required in order to calculate incidence.

- » Population-based surveillance can be done around one sentinel hospital or at a regional level with multiple hospitals. Previously, this had been called Tier 3 IB-VPD surveillance.
- » If done in multiple hospitals in a defined region (district, province, etc.), most hospitals in the catchment area should collect sterile site specimens on most suspected cases as part of routine clinical practice, and these specimens should be tested for pneumococcus. This approach is often laboratory-based, where the entry point into the surveillance system is laboratory detection of an IPD case. These cases can then be followed up to gather more epidemiologic information. An example of this type of surveillance is the GERMS network in South Africa (6).
- » Population-based surveillance achieves the same objectives as sentinel site surveillance, with the addition of incidence to assess burden by age group and to monitor serotype replacement, because serotype-specific rates are preferable for following temporal trends.

### TARGET POPULATION

- Sentinel hospital surveillance should include all children aged 0–59 months of age who are admitted to a sentinel hospital and who meet the suspected case definitions.
- Population-based IPD surveillance should include children 0–59 months of age and can be expanded to include older children and adults based on the objectives and resources of the country. Including older persons in surveillance is useful to assess herd protection and serotype replacement.

### LINKAGES TO OTHER SURVEILLANCE

Where possible, surveillance for pneumococcus should be integrated with surveillance for other causes of bacterial meningitis and pneumonia, such as *Haemophilus influenzae* and meningococcus. When conducting sentinel surveillance for meningitis, pneumonia or sepsis, all three pathogens should be routinely tested for. Laboratory testing for antimicrobial resistance can be integrated with surveillance for other bacteria (such as typhoid).



## CASE DEFINITIONS AND FINAL CLASSIFICATION

### SUSPECTED MENINGITIS FOR CASE FINDING

- Any child aged 0–59 months admitted to hospital with sudden onset fever ( $> 38.5^{\circ}\text{C}$  rectal or  $38^{\circ}\text{C}$  axillary) **and** one of the following signs: neck stiffness, altered consciousness with no other alternative diagnosis, or other meningeal signs.

#### OR

- Any patient aged 0–59 months hospitalized with a clinical diagnosis of meningitis.

### PROBABLE BACTERIAL MENINGITIS

A suspected meningitis case with cerebrospinal fluid CSF examination showing at least one of the following:

- Turbid appearance
- Leucocytosis ( $> 100\text{cells/mm}^3$ )
- Leucocytosis ( $10\text{--}100\text{ cells/mm}^3$ ) AND either an elevated protein ( $> 100\text{mg/dl}$ ) or decreased glucose ( $< 40\text{mg/dl}$ ). Note: if protein and glucose results are not available, diagnose using the first two conditions (turbid appearance or leucocytosis  $> 100\text{cells/mm}^3$ )

### CONFIRMED PNEUMOCOCCAL MENINGITIS

A suspected or probable meningitis case that is lab-confirmed by culture or identification of pneumococcus (by antigen detection, immunochromatography, PCR or other methods) in the CSF or from the blood in a child with a clinical syndrome consistent with meningitis.

### SUSPECTED PNEUMONIA FOR CASE FINDING

Any child aged 0–59 months demonstrating cough or difficulty breathing and displaying fast breathing when calm, as defined by age:

- Age 0 to  $< 2$  months: 60 breaths/minute or more
- Age 2 to  $< 12$  months: 50 breaths/minute or more
- Age 12 to  $\leq 59$  months: 40 breaths/minute or more

### SUSPECTED SEVERE PNEUMONIA FOR CASE FINDING

Any child aged 0–59 months with a cough or difficulty breathing and displaying one or more of the following:

- Inability to drink or breastfeed
- Vomiting everything
- Convulsions

- Prostration/lethargy
- Chest in-drawing
- Stridor when calm.

### WHO-DEFINED ENDPOINT PNEUMONIA

Pneumonia in a patient with a chest radiograph showing an infiltrate consistent with pneumonia: dense, fluffy alveolar consolidation or pleural effusion, or both.

### CONFIRMED PNEUMOCOCCAL PNEUMONIA

Any person meeting the definition of pneumonia or severe pneumonia who has a positive culture of *S. pneumoniae* from blood or pleural fluid.

### SUSPECTED SEPSIS FOR CASE FINDING

Any child aged 0–59 months admitted to hospital with the presence of at least two of the following danger signs and without meningitis nor pneumonia clinical syndrome:

- Inability to drink or breastfeed
- Vomiting everything
- Convulsions (except in malaria endemic areas)
- Prostration/lethargy
- Severe malnutrition
- Hypothermia ( $\leq 36^{\circ}\text{C}$ ).

### CONFIRMED PNEUMOCOCCAL SEPSIS

A person meeting the definition of sepsis who has a positive culture of *S. pneumoniae* from a normally sterile site.

### CONFIRMED INVASIVE PNEUMOCOCCAL DISEASE (IPD)

- *S. pneumoniae* identified via culture from any normally sterile site (blood, CSF, pleural fluid, joint fluid) in a symptomatic person
- *S. pneumoniae* identified in the CSF or pleural fluid by antigen detection, immunochromatography or PCR. Note that for blood, only culture confirms IPD, as these other detection methods have not been shown to have enough specificity to diagnosis IPD, particularly in children.



## CASE INVESTIGATION

In sentinel hospital surveillance, all children aged 0–59 months with suspected meningitis meeting the suspected case definition should have a lumbar puncture to collect CSF unless the procedure is clinically contraindicated. CSF should be collected before antibiotic administration, otherwise the lab may be unable to culture the pathogen and therefore unable to provide information on antimicrobial susceptibility. However, a specimen should be obtained in all suspect cases as bacterial pathogens can still be detected even after antimicrobial therapy has begun. For expanded

surveillance approaches, patients with suspected pneumonia and sepsis should also have appropriate clinical specimens taken. Treatment of patient should not be delayed while awaiting collection of specimens or results from the lab. In sentinel surveillance and population-based surveillance, case report forms should be filled out on all suspected cases. In laboratory-based IPD surveillance, cases will be reported retrospectively, and likely will already have been treated. Medical record follow-up should be done to gather key data elements.



## SPECIMEN COLLECTION

Care should be taken to minimize any risk of cross-contamination during manipulation or aliquotting. For example, use sterile dispensing technique with appropriate pipettes, tips and tubes. The types of specimen that may be collected include CSF (meningitis cases), blood samples (meningitis, pneumonia and sepsis) and pleural fluid (pneumonia cases).

### VOLUME OF SPECIMENS TO COLLECT

#### ► CSF

- » 3 mL in total, 1 mL into each of three test tubes.
  - Tube 1: Chemical analysis: protein and glucose tests
  - Tube 2: Microbiological tests
  - Tube 3: Record overall appearance; perform white blood cell count
- » If only one tube of CSF is available, it should be given to the microbiological lab for culture/PCR/antigen testing. However, an aliquot of 50–100 µL should be spared from that tube for molecular testing.
- » The presence of blood in the CSF can affect cultures (antibiotics in blood can inhibit bacterial growth). If more than one tube is being collected, the first tube may contain contaminated blood from lumbar puncture and should not be the tube sent to the microbiology lab.

#### ► Blood

- » 1–3 mL is considered adequate for a child, 5–10 mL for an adult

» Collected blood should be diluted in blood culture broth in order to obtain blood cultures. It is important to use appropriate ratios of blood to culture broth for optimal bacterial growth. The recommendations of the culture broth manufacturer should be closely followed.

- Add 1–3 mL of blood from a child to 20 mL of blood culture broth.
- Add 5–10 mL of blood from an adult to 50 mL of blood culture broth.

#### ► Pleural fluid

- » Approximately 20–40 mL of aspirated fluid should be immediately placed into tubes coated with appropriate anticoagulant (EDTA or heparin) for biochemistry (5 mL), microbiology (5–10 mL), cytology (10–25 mL), PCR testing (200 µL–1 mL). Use a heparin-coated syringe for the pH measurement.

### TIMING OF COLLECTION

#### ► CSF

- » Collect CSF as soon as possible after admission, preferably before antibiotic therapy is started.
- » Inform the lab that a lumbar puncture is to be performed so the technician can be ready to process the sample as soon as possible.

#### ► Blood and pleural fluid

- » Collect prior to administration of antibiotics, whenever possible.



## STORAGE AND TRANSPORT

### ► CSF

- » Refer CSF to the lab immediately
- » If specimen cannot be processed in one to two hours, inoculate 0.5–1.0 mL into trans-isolate (T-I medium) and incubate vented at 35–37°C with 5% CO<sub>2</sub> overnight, or until transport is possible (up to four days). If transport is delayed beyond 4 days, store at room temperature (unvented) until referral.
- » CSF specimen should not be refrigerated – keep at room temperature.
- » CSF should be processed in a microbiology laboratory within two hours of collection. If there is not access to a microbiology laboratory, inoculated T-I media should be sent from the health facility to the district or reference laboratory as soon as possible. Districts should send the inoculated T-I media to the national/state reference laboratory at least twice a week.

### ► Blood and pleural fluid

- » Blood and pleural fluid should be immediately inoculated (within one minute) into a blood culture bottle and transported to a microbiology

laboratory as soon as possible for overnight incubation and growth of bacteria. All inoculated blood culture media should be protected from temperature extremes (< 18°C or > 37°C) with a transport carrier and thermal insulator (such as extruded polystyrene foam).

- » Inoculated blood culture bottles should not be placed in the refrigerator.
- » Blood cannot be transported before being placed in a blood culture bottle because the syringes do not contain any anticoagulant and the blood will coagulate within a few minutes.

## LONG-TERM STORAGE

### ► CSF, blood, and pleural fluid

- » Store isolates frozen at -20°C to allow further testing (serotyping and antimicrobial susceptibility testing) in the future, or if culture capacity does not exist in local hospitals and processing needs to occur at reference laboratory.
- » If available, storing isolates in a -70°C freezer is preferable.



## LABORATORY TESTING

### CSF

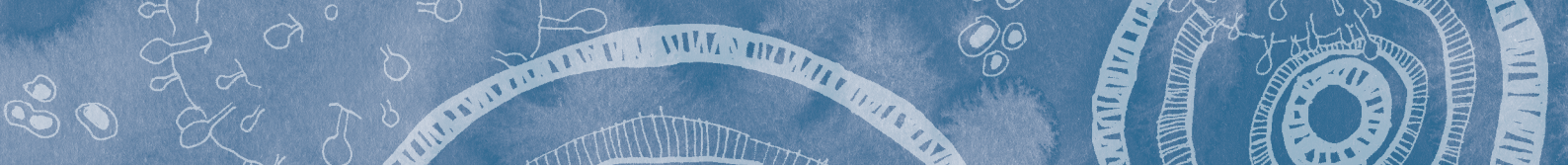
Meningitis syndrome may be caused by various pathogens; therefore, clinical syndromic surveillance must be complemented by a strong lab component. Lab confirmation of pneumococcal meningitis is done by culture, PCR or antigen detection (7). Bacterial culture is the first priority for confirmation and isolation of the pathogen. Culture is considered as a gold standard, but has low sensitivity due to potential antibiotic use by the patient before sample collection. Many local hospitals will not have adequate capacity for culture, and frozen samples will need to be sent to reference laboratories in the region.

CSF samples should be cultured on blood agar plates (BAP) and supplemented chocolate agar plates (CAP) that are prepared with 5–10% sheep or horse blood. The optimal medium for growth for pneumococcus is BAP, but it can also grow on a CAP (the optimal medium for *H. influenzae* culture).

PCR is recommended on all suspected cases because bacterial culture might be inhibited if the case has already received antibiotics. As PCR capacities are not always available at district or hospital level, the remaining volume of original non-manipulated CSF can be frozen and sent to either a national or regional reference laboratory for further testing.

Rapid diagnostic test kits (RDTs) can be used since they increase yield and provide results quickly for clinical care and outbreak identification. In general, RDTs only identify the species and not the serotype or serogroup. There are two commonly used types of RDTs. Results should be interpreted according to manufacturer's instructions.

- Immunochromatography: BinaxNOW® kit can be used on CSF and pleural fluid for detection and lower-level characterization of pneumococcus.
- Latex agglutination testing (LAT): Commercial latex kits often have a short shelf life and can be expensive.



Gram stain should not be used to confirm cases, but it is reliable and relatively inexpensive if staff are well trained and reagents are quality controlled. On Gram stain, *S. pneumoniae* is a gram-positive lance-shaped diplococcus, sometimes occurring in short chains, and may occur intracellularly or extracellularly.

#### **BLOOD**

Blood culture can be used to diagnosis pneumococcal meningitis, pneumonia and sepsis. The laboratory methods for blood culture are the same for all syndromes. However, the sensitivity of blood culture for pneumococcal pneumonia is lower than for the other syndromes because only approximately 10–15% of pneumococcal pneumonia cases are bacteremic.

- For blood culture with maximum yield of isolates, subculture all negative cultures after five days of incubation before they are discarded.
- PCR and RDTs are not used routinely on blood to diagnose pneumococcus due to low sensitivity and specificity.

Report all rapid diagnostic test results to clinical staff within one to two hours of testing. Report CSF and blood culture results to the clinicians daily if cultures are done in hospital laboratory.

#### **ANTIMICROBIAL RESISTANCE (AMR) TESTING**

To the greatest extent possible, sites should perform antimicrobial sensitivity testing for all pneumococcus isolates and evaluate these data by the following: antibiotic type and route, time of antibiotic administration before culture, volume of fluid cultured, geographic area and serotype (7). Pneumococcus should be tested for susceptibility to penicillins, sulfonamides and trimethoprim, and third-generation cephalosporins.

Recommended methods are disk diffusion (modification of the Kirby-Bauer technique) and antimicrobial gradient strip diffusion (8). It is recommended that

antimicrobial susceptibility testing be routinely done and reported to national authorities and international networks such as the Global Antimicrobial Resistance Surveillance System (GLASS) ([www.who.int/glass/en/](http://www.who.int/glass/en/)).

#### **QUALITY ASSURANCE SYSTEMS**

All of the above laboratory standards should be complemented by good quality assurance and quality control system in place to ensure that laboratory data generated for surveillance are of good quality. WHO recommends that laboratories participate in external quality assessment (EQA) programmes and send out a selection of specimens and isolates for confirmatory testing to another level of laboratory (either national, regional or global) for quality control (QC).

Most sentinel site labs will not have the necessary equipment to carry out higher level characterization (serotyping, antimicrobial susceptibility or PCR), and thus should refer isolates and specimens from suspected, probable and confirmed cases to national or regional reference laboratories that are able to provide quality assurance and higher level testing of CSF specimens. Each lab should be enrolled in an appropriate EQA/proficiency testing programme. While not an explicit objective of surveillance for pneumococcus (or other IB-VPDs), such surveillance systems can be used to build laboratory capacity globally as well as identify gaps in laboratory capacity.

#### **LABORATORY NETWORKS**

The Global Invasive Bacterial Vaccine-Preventable Diseases (IB-VPD) Laboratory Network is a global network of > 100 laboratories that supports invasive bacterial disease surveillance (9). It is coordinated by WHO and Public Health England. IB-VPD has developed standardized laboratory procedures and guidelines for data collection, and implemented quality assurance/quality control systems.





## DATA COLLECTION, REPORTING AND USE

### RECOMMENDED DATA ELEMENTS

#### ► Minimal data elements for sentinel hospital meningitis surveillance

- » Sentinel site Information – site name or code
- » Demographic
  - Name (if confidentiality is a concern the name can be omitted so long as a unique identifier exists)
  - Unique case identifier
  - Date of birth (or age if date of birth not available)
  - Sex
  - Place of residence (city, district, and province)
- » Clinical data
  - Signs and symptoms of illness (including those in case definitions)
  - Date of onset
  - Date of admission
  - Treatment
  - Patient outcome (survived without sequelae, survived with sequelae, died)
  - Discharge diagnosis
- » Vaccination history
  - Source of information (vaccination card, EPI registry, verbal report)
  - Pneumococcal vaccine received. If yes:
    - Number of doses received
    - Date(s) received
    - Type and formulation of pneumococcal vaccine (PCV13, PCV10, PPS)
  - Meningococcal vaccine received. If yes:
    - Number of doses received
    - Date(s) received
    - Type of meningococcal vaccine
  - Hib vaccine received. If yes:
    - Number of doses received
    - Date(s) received
    - Type of Hib vaccine
- » Laboratory
  - CSF collected
    - Unique ID for linkage to clinical data
    - Local laboratory ID
    - Date and time of collection
    - Specimen collected before antibiotic provision?
    - Appearance of CSF
    - Date specimens sent to laboratory
    - Date and time of CSF specimen received at laboratory
    - Condition of specimen
    - Upstream test results if referred from a lower tiered laboratory (Gram stain, white blood cells, protein, glucose, culture, rapid diagnostic test)
  - \* Results
    - ~ CSF
    - ~ Whole cell count
    - ~ Glucose level
    - ~ Protein level
    - ~ Culture done
      - › Culture results
    - ~ Gram stain done
      - › Gram stain result
    - ~ BinaxNOW® done
      - › BinaxNOW® result
    - ~ LAT done
      - › LAT result
    - ~ PCR done
      - › PCR results
    - ~ Serotyping/serogrouping
      - › *S. pneumoniae*
      - › *H. influenzae*
      - › *N. meningitidis*
- » Epidemiological
  - Date of investigation
  - Date of notification to public health
  - Final case classification

➤ **Additional minimal data elements for pneumonia/sepsis and IPD surveillance**

- » Laboratory
  - Blood collection
    - Blood specimen ID
    - Date and time of collection
    - Specimen collected before antibiotic treatment
    - Date specimens sent to laboratory
    - Date and time of blood specimen received at laboratory
    - Culture done
      - \* Culture result
    - Gram stain done
      - \* Gram stain result
  - Pleural fluid (PF) collected
    - PF specimen ID
    - Date and time of collection
    - Specimen collected before antibiotic treatment
    - Date specimens sent to laboratory
    - Date and time of PF specimen received at laboratory
    - Culture done
      - \* Culture result
    - Gram stain done
      - \* Gram stain result
    - BinaxNOW® done
      - \* BinaxNOW® result
    - PCR done
      - \* PCR results
    - Biochemistry results

➤ **Additional data elements for population-based IPD surveillance**

- » Catchment area population by age groups (0–5 months, 6–11 months, 12–23 months, and 24–59 months; children and adults aged 5–17 years, 18–64 years, > 64 years)

**REPORTING REQUIREMENTS AND RECOMMENDATIONS**

Report confirmed IPD cases to the Ministry of Health monthly. Zero reporting (no cases) should be done in sentinel surveillance sites. Aggregate reporting (numbers only) is sufficient for routine reporting, even if case-based surveillance is conducted. There are no global reporting requirements for pneumococcus (International Health Regulations or WHO/UNICEF Joint Reporting Form). Countries are encouraged to report antimicrobial resistance data to GLASS.

**RECOMMENDED DATA ANALYSES**

Sentinel hospital meningitis surveillance:

- Confirmed pneumococcal meningitis case counts, stratified by onset date (week, month, year), age group and sex.
- Probable and suspected meningitis case counts, stratified by the same groupings as confirmed cases.
- Confirmed pneumococcal meningitis death counts and case-fatality ratios.
- Probable and suspected meningitis death counts and case-fatality ratios.
- Median and range of duration of hospital stay for all suspected meningitis hospitalizations and for meningitis due to pneumococcus.
- Note: If IB-VPD surveillance is ongoing for other bacterial causes of meningitis (meningococcus and *H. influenzae*), then a similar reporting structure should be used for lab-confirmed cases of those etiologies.

**SENTINEL HOSPITAL IPD SURVEILLANCE (MENINGITIS, PNEUMONIA AND SEPSIS)**

- Confirmed IPD case counts, stratified by onset date (week, month, year), age group, sex and syndrome.
- Suspected meningitis, pneumonia and sepsis case counts, stratified by the same groupings as confirmed cases.
- Confirmed IPD death counts and case-fatality ratios.
- Suspected meningitis, pneumonia and sepsis death counts and case-fatality ratios.

## POPULATION-BASED IPD SURVEILLANCE

- Incidence of confirmed IPD, stratified by onset date (week, month, year), age group, sex and syndrome.

## USING DATA FOR DECISION-MAKING

- Determine the local disease burden (cases, deaths, disability).
- Monitor trends in disease epidemiology.
- Prioritize pneumococcal disease among other diseases of public health importance.
- Advocate for and implement proper control strategies such as immunization.
- Evaluate the impact of immunization services and identify areas with weak performance.
- Evaluate vaccine impact and effectiveness.



## SURVEILLANCE PERFORMANCE INDICATORS

### LABORATORY

EQA and QC of the laboratory should be completed annually.

There is no minimum number of cases that should test positive for pneumococcus since it varies widely among countries and depends on pneumococcal conjugate vaccine use.

TABLE  
1

Surveillance performance indicators for *S. pneumoniae*

SURVEILLANCE ATTRIBUTE	INDICATOR	TARGET	HOW TO CALCULATE (NUMERATOR / DENOMINATOR)	COMMENTS
<b>COMPLETENESS OF REPORTING</b>	Consistent reporting throughout year	At least 10 months with reporting (including zero reporting)	Number months reporting per year	Ideal is 12 months and confirmed zero reporting if no cases
<b>CASE ASCERTAINMENT</b>	Minimum number of cases reported annually	≥ 80 suspected meningitis cases per year; ≥ 400 suspected meningitis + pneumonia or sepsis cases per year	Number of cases reported per year	Ideal is ≥ 100 suspected meningitis cases per year; ≥ 500 suspected meningitis + pneumonia or sepsis cases per year
<b>SPECIMEN COLLECTION</b>	Proportion of suspected cases with specimens collected	≥ 80%	# of suspected cases with specimen collected / # of suspected cases x 100	Specimen is CSF for meningitis surveillance and CSF, blood or pleural fluid in pneumonia and sepsis surveillance; ideal is ≥ 90%
<b>LABORATORY CONFIRMATION WITH SEROTYPE DETERMINATION</b>	Proportion of laboratory-confirmed cases with serotype determined	≥ 60%	# of laboratory-confirmed cases with serotype determined / # of laboratory-confirmed cases x 100	For sentinel hospitals that do serotyping or send isolates for serotyping; ideal is ≥ 80%





## CLINICAL CASE MANAGEMENT

All cases of IPD should be hospitalized and promptly treated with intravenous (or intramuscular) antibiotics, to which the bacteria are susceptible. Supportive care, including fluids, oxygen and possibly mechanical ventilation might be necessary. Take CSF and blood

samples before antibiotic treatment, if possible. Treat patient with presumptive antibiotics without waiting for lab results.



## CONTACT TRACING AND MANAGEMENT

Contact tracing is not routinely done for pneumococcal surveillance.



## SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

Although most pneumococcal disease is sporadic, pneumococcus can cause outbreaks in crowded institutions, such as military barracks, homeless shelters and prisons. In addition, large-scale outbreaks of pneumococcal meningitis in the African meningitis belt have been reported, mostly caused by serotype 1. Sentinel site surveillance is not designed to identify all outbreaks since they will be geographically limited, so other types of surveillance with greater geographic coverage will be needed to identify outbreaks.

### DEFINITION OF AN OUTBREAK

There is no accepted definition of a pneumococcal cluster or outbreak. Some have considered a cluster of serious pneumococcal disease to be two or more temporally linked cases that occurred in a closed setting (10). If the serotype is the same among IPD cases, this strengthens the evidence for an epidemiologically linked cluster. In the African meningitis belt, there is also no established definition of a pneumococcal meningitis outbreak. Some consider a significant rise above baseline rates to be an outbreak, while others have applied the epidemic threshold of 10 suspected meningitis cases /100 000 population that was developed for meningococcal meningitis outbreak responses (11) (12).

### CHANGES TO SURVEILLANCE DURING AN OUTBREAK

Extend surveillance to all area hospitals and clinics that might see meningitis cases, and potentially cases of pneumonia and sepsis. Institute weekly reporting that includes zero reporting for all area clinics.

### PUBLIC HEALTH RESPONSE

Reactive vaccination is not an established strategy for pneumococcal outbreaks. However, some have argued that because of the high rate of sequelae with pneumococcal meningitis, it could still be considered in very large, ongoing outbreaks in Africa (13). Prompt recognition of cases and timely treatment with antibiotics is important.



## SPECIAL CONSIDERATIONS FOR PNEUMOCOCCAL SURVEILLANCE

- Neither sentinel surveillance nor most population-based invasive pneumococcal disease surveillance will have sufficient geographic representativeness to identify outbreaks. Some countries may choose to undertake national syndromic surveillance for meningitis with laboratory confirmation of cases. Some countries in the African meningitis belt, which have significant meningococcal disease burden and limited confirmation capacity, perform such meningitis syndromic surveillance. Typically, this is part of the AFRO IDSR surveillance. Meningitis surveillance is not pathogen-specific and covers the three vaccine preventable disease pathogens associated with bacterial meningitis: *N. meningitidis*, *S. pneumoniae* and *H. influenzae*. These require laboratory capacity to identify and distinguish. This surveillance can be nationwide or regional, and is typically aggregate passive surveillance. The objective of this surveillance is to detect meningitis outbreaks for a rapid public health response. For meningococcus, the public health response includes reactive vaccination; for pneumococcal outbreaks, reactive vaccination is not an accepted strategy.
- IB-VPD surveillance can be leveraged to monitor other VPDs and non-VPDs such as typhoid, diphtheria and pertussis, and can help build global bacteriology capacity, especially in a time where anti-microbial resistance is a high public health priority.
- To meet most of the objectives of pneumococcal surveillance, surveillance of children < 5 years of age is sufficient. However, there are some instances where surveillance in older children and adults may be recommended, such as when identifying and monitoring outbreaks or measuring indirect effects of the vaccine. Of note, if surveillance in adults is conducted, then urinary antigen could be included as a confirmatory lab test for pneumonia, as it has higher specificity in adults.
- Measuring the impact of pneumococcal conjugate vaccine can be challenging. The impact of pneumococcal conjugate vaccines can be measured using surveillance data and observational studies, such as case-control studies and time series analysis of secondary data sources (14). Sentinel surveillance is not adequate for measuring vaccine impact in all settings. Population-based surveillance is best for monitoring pneumococcal serotype replacement (15). The most appropriate method for measuring vaccine impact should be chosen based on the setting, and multiple methods and outcomes may need to be used to accurately measure impact.



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