Ministry of Health

STANDARD OPERATING PROCEDURE

Detection, Confirmation and Management of Meningitis Outbreak

RBC/IHDPC/ EID Division

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2 . Introduction

Meningococcal meningitis is a bacterial infection of the meninges, the thin lining that surrounds the brain and spinal cord, whose common symptoms are sudden onset of headache, high fever, stiff neck and sensitivity to light. The causative agent, *Neisseria meningitidis* (*Nm*), is transmitted from person to person through infected respiratory droplets, often from asymptomatic carriers. *Nm* is carried in the nasopharyngeal mucosa of at least 10% of the general population in endemic areas at any given time. It causes disease only when particular environmental and physical conditions overwhelm the body. If left untreated, the disease can lead to fatality rates greater than 50% and despite treatment, at least 10% of patients die within 48 hours of onset of symptoms, while 10– 20% of survivors develop severe neurological sequelae (WHO Meningitis SOP).

The aim of the standard operating procedures is to guide health care providers and public health experts from various levels of the health system in the implementation of enhanced surveillance of meningococcal meningitis.

3 Objectives

3.1 General Objective

To promptly detect, confirm, and respond appropriately to meningococcal meningitis epidemics.

3.2 Specific Objective

- To systematically collect and analyze epidemiological and laboratory data of suspected cases
- To conduct rapid laboratory confirmation of causative agent
- To respond appropriately to meningococcal meningitis.

4 Definitions

4.1 Case definition

4.1.1 Suspected meningitis case

Any person with sudden onset of fever (>38.5 C rectal or 38.0 C axillary) and presenting
One of the following signs: neck stiffness, altered consciousness or other meningeal signs.

4.1.2 Probable meningococcal meningitis case

Any suspected case with macroscopic aspect of its CSF turbid, lousy or purulent; or with microscopic test showing Gram negative diplococcus. Confirmed meningococcal meningitis case Isolation *Neisseria meningitidis* from the CSF, blood or bone marrow of a suspected/probable case by culture (Ref IDSR technical guide).

5 Epidemiological thresholds

5.1 Alert threshold

- For populations between 30 000 and 100 000 inhabitants, an attack rate of 5 cases per 100 000 inhabitants per week.
- For populations less than 30 000 inhabitants, 2 cases in 1 week or an increase in the number compared to the same time in previous non-epidemic years.

Attack rate per week = (No of cases per week / population) x 100,000

5.2 Epidemic threshold

- For populations between 30 000 and 100,000: an attack rate of 15 cases per 100 000 inhabitants per week. When the risk of an epidemic is high (no epidemic during last 3 years, alert threshold reached in dry season), epidemic threshold is 10 cases per 100 000 inhabitants per week.
- For populations less than 30 000 inhabitants: 5 cases in 1 week or the doubling of the number of cases over a 3-week period.

Enhancing Meningitis Surveillance

Early detection of meningitis outbreaks and prompt laboratory confirmation of circulating pathogens depend on effective implementation of surveillance activities at all levels. Therefore, for meningitis surveillance purposes, we will distinguish four different epidemiological phases: pre-epidemic, epidemic, post-epidemic and inter-epidemic. Specific procedures for data collection, specimen collection for laboratory confirmation will be indicated for each of these phases.

5.2.1 Pre-epidemic phase

This phase can be sub-divided into 2 phases: pre-alert and alert.

A district is in pre-alert phase, when the weekly attack rate is below the alert threshold. All suspected cases need to be investigated and laboratory confirmed as they are recruited at health facility level. For any suspected case where a lumbar puncture is performed, a case-based form should be filled and the CSF sent to the nearest reference laboratory for bacteriological tests. Treat every single meningococcal meningitis case with recommended antibiotics according to the national treatment protocols (ref). Start the presumptive antibiotic treatment without delay, as soon as the CSF is collected, and before the laboratory results are out.

For each **district in alert phase**, detailed data on the suspected cases should be recorded on a line list. CSF sample collection should be sent to the nearest satellite laboratory for identification and the National Reference Laboratory for confirmation and serotyping. It is recommend to have one(1) confirmed case of N. Meningitidis to declare an outbreak.*(Ref IDSR TG)*

This will help in making a rapid decision as to the type of vaccine to be used in case the district reaches the epidemic threshold, as well as orienting the clinicians for an effective case management.

For every district in alert phase, do the following (box 1)

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Box 1: What should be done during the pre-epidemic phase:

1. Alert immediately the health officers in the next higher level.

2. Record cases on a standard line listing form (Ref.IDSR Technical guide)

3. Collect specimens from 5 to 10 cases once the alert or epidemic threshold (see "Meningitis" in Section 8.0 IDSR TG) has been reached *and send immediately to the nearest laboratory for identification. Be sure that samplesare labelled with patient ID and have an IDSR case based form filled. Samples should be sent for culture using adequate transport media (Trans-Isolate bottles). .*

4. Confirm at least 10 positive samples for Neisseria meningitides and its antibiotic sensitivity per surveillance unit

(district or sector) for decision making about the appropriate vaccine to be used.

6. Continue data analysis

7. Treat all suspected cases with antibiotics as recommended by the national treatment protocol while waiting for the laboratory Antibiotic sensitivity).

5.2.2 Epidemic phase

- The epidemic phase occurs when the attack rate reaches the epidemic threshold.
- For populations between 30 000 and 100,000: an attack rate of 15 cases per 100 000 inhabitants per week. When the risk of an epidemic is high (no epidemic during last 3 years, alert threshold reached in dry season), epidemic threshold is 10 cases per 100 000 inhabitants per week.
- For populations less than 30 000 inhabitants: 5 cases in 1 week or the doubling of the number of cases over a 3-week period.

As soon as the epidemic threshold is reached in a district or sector, it is recommended to conduct mass immunization campaign targeting the entire district, using the appropriate polysaccharide bivalent (AC) or trivalent (ACW) vaccine, and immunize all 2-30 years old population of the district. It is also recommended to vaccinate any contiguous district in alert phase. Continue collecting CSF and sending samples to the reference laboratory to monitor the characteristics of the causative agent (serogroups, antibiotic sensitivity).

Box 2 below summarize the specific actions recommended during the epidemic phase:

Box 2. What should be done during the epidemic phase:

1. Vaccinate immediately the epidemic district with the appropriate vaccine as well as any contiguous district in alert phase.

2. Continue data collection, transmission and analysis.

3. Maintain regular collection of 5 to 10 CSF specimen per week throughout the epidemic season in the epidemic districts in order to detect any serogroup shift.

4. Treat all case with the appropriate antibiotic as recommended by the National protocols.

For longitudinal surveillance purposes, regular collection of at least 5 to 10 CSF samples will be maintained in all epidemic districts for monitoring the circulating serogroups, antibiotic susceptibility testing, as well as any serogroup shift during the epidemic period.

A Rapid Response Team (RRT) from central or district level should be sent to the affected areas to support surveillance and laboratory activities. The team should evaluate the data collection, analysis and transmission, as well as lumbar puncture practices, the use of trans-isolate medium and all laboratory procedures (eg, Gram stain, cytology, latex agglutination tests, etc).

Note that before sending a specimen to the reference laboratory, it should be adequately labelled using the IDSR case-based form.

5.2.3 Post-epidemic phase

The post epidemic phase corresponds to the first 4 weeks after the end of an epidemic. The end of a meningitis epidemic is declared when the attack rate in the last epidemic district descends below the alert threshold for two consecutive weeks. During this phase it is recommended to:

- Evaluate the response/management of the epidemic to outline the gaps, lessons learnt and make recommendations for a better control of future meningitis epidemics.

- Conduct an external evaluation (all the system, vaccine coverage survey)

These evaluations are conducted in order to draw lessons and make recommendations for a better control of future epidemics. Adequate resources should be mobilized to conduct these evaluations.

5.3 Data management

5.3.1 Data collection and transmission

For all suspected meningitis cases, some basic patient information will be collected using the IDSR Line List form (See annex 4).

The suspected cases and deaths should be recorded and transmitted weekly to the district surveillance officer. Data should be immediately compiled and transmitted telephone (call/SMS) and Internet (eIDSR) to district and national levels. Health centers District hospitals should report weekly, even when no cases are recorded ("Zero reporting").

5.3.2 Data entry

5.3.2.1 At district hospital level

The line lists sent by peripheral health facilities to the district will be entered into a computer programme (Excel and/or eIDSR) by the district surveillance officers. They will also enter the laboratory data and tests results on the same software. The completed data base will then be sent to the national level on a daily basis in case of epidemics.

5.3.2.2 At central level

The data bases received from the districts will be merged into a single national database using Excel and /or eIDSR before sending it to WHO and partners on a weekly basis during epidemics.

5.3.2.3 At the national reference laboratory

The data from the national reference laboratory will be computerized using Excel, then sent to the national surveillance/epidemiology unit, where they will be linked to the clinical data using the Epid-number. The results will then be sent to the regions and districts where the specimen came from. The data manager at the national surveillance unit should check for data entry flaws

and clean the data base on a weekly basis. He should make sure that clinical and laboratory data of each patient are linked, before any detailed data analysis.

5.3.3 Data analysis

The disease surveillance officers at each level should analyze their data. The supervisors at national levels should ensure that all districts keep an up-to-date weekly epidemic trend (curve) of meningitis cases with the alert and epidemic thresholds shown. Every week, the data manager of the national Surveillance Unit should make a standard map showing the alert and epidemic districts, as well as the laboratory results by district and for the country.

5.4 Specimen collection, storage, transportation and processing (Ref.NRL SOP's)

During an epidemic, each district hospital should:

- Avail an adequate stock of lumbar puncture kits, Rapid latex kits (Pastorex), Trans-isolate (TI) media, cryotubes, and triple packaging box for specimen transport.

Preposition these materials at district levels under the responsibility of the district disease surveillance and laboratory officers.

Note:

• TI media should be stored and used according to the manufacturer's guidelines (see Annex 5 for instructions on using TI media).

• Depending on the epidemic situation and resources available, WHO and/or other technical and financial partners, may supply the countries with TI media and other laboratory consumables on a case-by-case basis.

5.4.1 Sample collection

Health personnel or Rapid Response Teams on the field should systematically collect CSF specimens for laboratory confirmation before the commencement of antibiotics therapy. It is estimated that 5-10 CSF samples per district are sufficient to determine the circulating causal pathogens and guide the choice of the appropriate vaccine (AC or ACW). Ensure that at least 10 of the samples collected are positive for *N. meningitidis* for a better decision on the situation in a district. If not, collect more samples from that district. Perform antibiotic susceptibility testing to guide the use of appropriate antibiotic for case management. The quicker these samples are obtained at the reference laboratory the better.

Once an epidemic has been declared in a district, regular collection of CSF specimens should be maintained in that district throughout the epidemic season, in order to monitor circulating pathogens. However the systematic collect of CSF from each patient is not recommended. The number of CSF to be collected per week should be 5-10 per district.

Health personnel at health facility should be trained on lumbar puncture technique, specimen collection, TI utilization, handling and transportation to the reference laboratory. The laboratory technicians should be trained on how to perform Gram stains, rapid latex agglutination using Pastorex kits, or dipsticks.

5.4.2 Utilisation of TI bottles

The TI bottles are stored between 4°C and 8°C in the refrigerator. Before using a TI bottle, it will be sorted and kept at room temperature 30 minutes before adding the CSF. From each suspected meningitis case, 1 ml of CSF should be injected aseptically into a TI media. After the CSF has been injected, the TI medium should be vented and kept at room temperature away from direct

sunlight or dust.The inoculated TI medium should not be refrigerated (see Annex 5 for instructions on using TI media).

5.4.3 Transportation of CSF specimen

For culture:

The district hospital should send the inoculated TI media to the national reference laboratory until we reach the recommended number of samples to be collected.. Inoculated TIs are sent without venting needle and without ice packs. Once inoculated, TI media should be kept at room temperature.

5.4.4 Specimen processing

The identification of causal pathogen is essential to confirm the nature of the meningitis epidemic and institute control measures. Therefore, laboratory confirmation of suspected meningitis cases should be a standard practice during the meningitis epidemic season. The following laboratory tests should be conducted depending on the health services or organisational levels (national, district) and the technical capacity of the laboratory at that level:

- Gram stain and cell counts at district laboratory or health facility with appropriate equipment

- Rapid latex tests at district laboratory level. (Note that the use of a latex test (Pastorex®) capable of identifying *Nm* W135 is highly recommended during the initial phase of an outbreak. Pastorex can be used at field level and substantially reduce the delay for bacteriological confirmation and decision making).

- Culture and serogroup at national or regional reference laboratories.
- Antibiotic susceptibility pattern should be conducted for all specimens received at national reference laboratory.

5.4.5 Turn-around time of laboratory results

The district laboratory results should be sending to the clinician by the laboratory officer (s) within 1-2 hours:

National level: within 4 days upon reception of the sample(s)

6 Criteria for vaccine choice

The decision on the type of vaccine to be used (***See Decisional Tree in Annex 5***) should ideally be based on the results from at least 10 *Nm* positive specimens.

In order to obtain that number of *Nm* positive specimens, it is estimated that 20 to 30 CSF specimens should be collected from the affected area. Efforts should be made to collect and test CSF specimens in the field as early as possible. The proportion of *Nm* W135 required warranting the use of ACW trivalent vaccine could be defined according to the number of *Nm* positive samples available from a given affected area. The following criteria could be suggested:

> 30% of W135 out of **10-19** *Nm* positive samples

OR

> 20% of W135 out of **20 or more** *Nm* positive samples. In the total absence of laboratory evidence of *Nm* W135 the use of trivalent ACW vaccine should be strongly discouraged.

In the above-mentioned situation, vaccination with bivalent AC vaccine should be recommended (provided that some laboratory evidence of *Nm* A is available). In situations where a full blown epidemic is reported and where the minimum percentage of *Nm* W135 was not reached, the identification of one or more *Nm* W135 in the concerned area(s) and concurrent W135 epidemic in contiguous area(s) will justify the use of the trivalent vaccine.

In any other situation, decisions to use vaccine, should be evaluated on a case by- case basis and should take into account all epidemiological and laboratory information available in the country.

7 Case management (Ref. IDSR TG, find updated sensitivity data at NRL)

Treat all cases of meningitis as quickly as possible, using the adequate antibiotics and according to the national treatment protocols. If a lumbar puncture is to be performed, do so before the antibiotic treatment. Treat the patient with presumptive antibiotic without waiting for the laboratory results.

8 Communication

The following communication strategies should be implemented at all levels:

- Advocacy
- Social mobilization
- Communication for behaviour change

Key sensitization messages should be broadcast for an early treatment seeking by patients.

9 Monitoring and Supervision

9.1 District level

The District Medical Officer will ensure during supervisory activities that the personnel of health facilities have been fully briefed on the process,

Health personnel should be trained on Lumbar puncture techniques as well as how to handle and transport CSF specimens. Train also the health personnel on the proper case management, on alert and epidemic thresholds as well as data analysis and reporting using appropriate IDSR forms. The Epidemic Management Committee (EMC) of the district should be reactivated (if not functioning) for decision making and better management of the situation. Regular weekly meetings are advised.

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9.2 National Surveillance Unit

Each week, the national surveillance officer should monitor if any districts have reached the alert threshold.

The National Health Sector outbreak preparedness and response committee (HSOPRC) should be activated for situational analysis, recommendation of proper control measures and better management of the situation. Regular weekly meetings should be conducted to analyse the epidemiological and laboratory data, upon which, supervision and monitoring actions are decided to support the districts. The national ***HSOPRC*** should also advocate for resource mobilisation (funds, drugs, laboratory reagents, vaccines and logistics).

A rapid response team (RRT) should be designated at national level for field investigation and rapid implementation of control measures. For the composition of the ***HSOPRC*** and RRT refer to the IDSR guidelines, composition and terms of reference of the ***HSOPRC.***

9.3 National Reference Laboratory

The National Reference Laboratory (NRL) through the district laboratory focal officer should ensure that high-quality testing of CSF specimens in the laboratory and results are sent promptly to districts. It should provide regular feed back on samples collected and processed, in order to minimize contamination and handling/transportation problems. It should organise regular training and supervision of district laboratories, and ensure that reagents and laboratory equipment are available. It should also ensure that 10 to 20% of positive isolates are transported to WHO Collaborating Centres for QA/QC (in accordance with international standards) and for genotyping and sequence-typing.

9.4 Feed Back

Reports, bulletins, annual statistical reports, websites etc… will be used as feedback tools.

ANNEX 1: Incidence thresholds for detection and control of epidemic meningococcal meningitis (to be filed)

	Population	
Intervention	Over 30,000	Under 30,000
Alert threshold Inform authorities Investigate Confirm Strengthen surveillance Prepare		
Epidemic threshold Mass vaccination Distribute treatment to HC Treat according to epidemic protocol Inform the public		
	If there is a meningitis epidemic in a neighbouring area • The alert threshold becomes the epidemic threshold	

ANNEX 2: WHO generic Case- based reporting form including clinical and laboratory information: *Ref IDSR Technical guide*

ANNEX 3: **Line List- for Reporting from Health Facility to District and for Use during Outbreaks:** *Ref IDSR Technical guide*

ANNEX 4: Instructions on Using Trans-Isolate (TI) Bottles

How to use the Trans-Isolate (T-I) system for isolation and transport of meningococci and other agents
causing bacterial meningitis from CSF

1. Procedure for inoculating T-I medium for transporting meningcocci and other agents causing bacterial meningitis from CSF:

1.1 Remove a vial of Trans-Isolate (T-I) medium from refrigerator at least 30 minutes before inoculating it with the specimen. Allow the vial to warm to room temperature which is more favourable for growth of the organism.

1.2 Before inoculating the vial, check to see if there is any visible growth or turbidity. If there is visible growth or turbidity, discard the vial, because it may be contaminated.

1.3 Lift up the small lid in the middle of the metal cap on top of the T-I vial.

1.4 Disinfect the top of the T-I vial with 70% alcohol or iodine. Allow to dry (usually 30 to 60 seconds).

1.5 Use a sterile syringe and sterile needle preferably 21G, 0.8 mm. to aspirate 500 microliters (one-half of an ml) of cerebrospinal fluid (CSF) from the tube containing CSF.

1.6 Inject the CSF into the T-I vial through the disinfected dry stopper on the top of the T-I vial.

2. Transport and incubation of T-I vials, and inoculation of the culture media

The procedures to follow depend upon how promptly the TI vials can reach the laboratory of reference that will perform culture and isolation.

If T-I vials **cannot** reach the laboratory of reference within 24 hours:

· Label the T-I vial with the date, name of the patient, and any other necessary identifiers.

· Ventilate the T-I vial with a sterile cotton plugged needle. **The** Needle should not dip into the culture media (broth).

· Store the ventilated T-I vial in an upright position at room temperature. Make sure it is away from excessive heat, direct sunlight, and dust.

· Before transporting the vial, remove the ventilating needle from the top of the T-I vial. This will prevent leakage and contamination during shipment.

· Transport the T-I vial in a sealed plastic bag to minimize the risks of contamination and attach the case report form

If TI vials **can** reach the laboratory of reference within 24 hours:

· Label the T-I vial with the date, name of the patient, and any other necessary identifiers.

· Ship the T-I vials without ventilation.

· Transport the TI in a sealed plastic bag to minimize the risk of contamination and attach the case report form.

3. Additional recommendations about the proper use of T-I vials and ventilating the inoculated T-I vials:

· The T-I vials can be used for at least 1 year after the date of production provided that they are stored in the refrigerator.

· Freezing T-I vials destroys the T-I medium.

· Non-inoculated T-I vials should be packed in cold packs for shipment to the laboratory of reference.

· In previous studies (*Ajello et al* below), cultures on ventilated T-I vials 2 to 4 weeks after inoculation with CSF (from patients with acute bacterial meningitis), incubation and transport resulted in a loss of growth in only 20 to 25% of inoculated vials. Without ventilation the losses were much greater.

· Contamination is the single most problematic point with the system. Aseptic measures and understanding the risks are necessary to achieve good recovery of the isolates.

Reference:

Ajello GA, Feely JC, Hayes PS, Reingold AL, Bolan G, Broome CV, and Phillips CJ. *Trans-Isolate Medium: a New Medium for Primary Culturing and Transport of Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae:* J Clin Microbiol, 1984: 20
(1): 55-58.

ANNEX 5: Decisional tree for Bivalent (AC) or Trivalent (ACW) polysaccharide (PS) vaccine use