

Management of Cerebro Spinal Meningitis



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Goals

1. Updates on CSM
2. Enhance & sensitization of the surveillance of meningitis
3. Strengthen capacity building to control CSM epidemic

Acute Bacterial Meningitis



Cerebro-spinal Meningitis

- Meningitis is an infection of the meninges covering the brain and spinal cord.
- Meningococcal disease was first described in 1805 when an outbreak swept through Geneva, Switzerland. The causative agent, *Neisseria meningitidis* (the meningococcus), was identified in 1887.
- Several different bacteria can cause meningitis and *Neisseria meningitidis* is one of the most important because of its potential to cause epidemics.

- Twelve subtypes or serogroups of *N. meningitidis* have been identified
- A, B, C and W135 are recognized to cause epidemics
- The pathogenicity, immunogenicity, and epidemic capabilities differ according to the serogroup
- The identification of the serogroup responsible of a sporadic case is crucial for epidemic containment.

- *N. meningitides* has been reportedly the main cause of meningitis epidemics in the belt
- It counts for as much as 80–95% of cases of bacterial meningitis admitted in health centres
- In non-epidemic situations, only 50% of bacterial meningitis is due to *N. meningitidis* within the whole population and this percentage is lower in neonates and young children where *S. pneumoniae*, *H. influenzae* and neonato-associated organisms (*S. agalactiae*, *S. pyogenes*, Enterobacteria) are the most common

Diagnosis of CSM at peripheral level

- The prognosis of bacterial meningitis varies according to the causative agent, the age of the patient, and case management
- Identification of causative pathogen is essential if the patient is to be given the most appropriate treatment.
- Ideally, in a non-epidemic situation, lumbar puncture and laboratory identification of the bacteria in cerebrospinal fluid (CSF) should be done systematically to guide the antibiotic treatment
- In non-epidemic situations, in the absence of laboratory support, the treatment should be adapted to the most probable causative pathogen according to age of the patient

CSM

- *Neisseria meningitidis*
- serogroups: A, B, C, W135, X, Y, Z, 29E...
- Africa: 80% of the burden



Epidemiology

General occur sporadically throughout the world with seasonal variation

| | | |
|-----------------|--------|---------|
| In Africa | —————→ | N.mn A |
| In USA & Europe | —————→ | B & C . |
| In Asia | —————→ | A |

There is increase evidence of sero group W 135 associated with outbreak of considerable size e.g..

- 2000-2001 Saudi Arabia
- 2002 Burkina Faso

- The mortality and serious morbidity secondary to bacterial meningitis is greatly reduced, primarily due to the approval of the conjugate polysaccharide *Hemophilus influenzae* type b vaccine (Hib), as well as the introduction of effective antimicrobial agents to the market.

Meningitis Belt

- The highest burden of meningococcal disease occurs in sub-Saharan Africa, which is known as the “Meningitis Belt”, an area that stretches from Senegal in the west to Ethiopia in the east, with an estimated total population of 300 million people.
- This hyperendemic area is characterized by particular climate and social habits.

- During the dry season, between December and June, because of dust winds and upper respiratory tract infections due to cold nights, the local immunity of the pharynx is diminished increasing the risk of meningitis. At the same time, the transmission of N.

The African Meningitis Belt

- Meningitis belt : sub-saharan Africa
- From Senegal to Eritrea



Transmission

- Mainly by respiratory droplets & throat secretion
- Human being is the only reservoir
- No animal reservoir
- Close & prolonged contact e.g. kissing, sneezing, living in close quarters & coughing).
- 10 – 25% of population carry N.Meningitidis at any given time

Predisposing factors

- Crowding
- Poverty
- Malnutrition
- Head injury
- Immunocompromised patients
- Sickle cell disease

Features of the disease

Meningitis symptoms

- Symptoms can appear in any order
- Not everyone gets all these symptoms
- Any one who gets fever & a stiff neck should get medical attention



Severe headache



Stiff neck
Unusual in young children



Dislike of bright lights
Unusual in young children



Fever/vomiting



Drowsiness/
impaired
consciousness



Rash

➤ **Signs:**

- Neck stiffness
- Kernig's sign (pain & resistance on passive knee extension with hips fully flexed)
- Brudinisky sign (hips flex on bending head forward)

➤ **Incubation Period:**

- 2-10 days, average 4 days

➤ **Carrier State:**

- 10-15% normally in nasopharyngeal mucosa

Standard case definition

- ❖ **Suspected case** of acute meningitis: sudden onset of fever (>38.5 °C rectal or 38.0 °C) WITH stiff neck. In patients under one year of age, a suspected case of meningitis occurs when fever is accompanied by a bulging fontanelle.
- ❖ **Probable case** of meningococcal meningitis: suspected case of either acute or bacterial meningitis as defined above WITH Gram stain showing Gram-negative diplococcus OR ongoing epidemic OR petechial or purpural rash

❖ **Confirmed case:**

- suspected or probable case as defined above WITH EITHER positive CSF antigen detection for *N. meningitidis* OR positive culture of CSF

Complications

- Death : 5-10% of patients die within 24-48 hrs
- 10-20 % of the survivals end with permanent neurological deficit (Deafness, hydrcephalus, cerebral palsy, etc)
- Septicemic meningitis
 - Hypovolemic Shock (Circulatory collapse)
 - Skin Rash

Diagnosis

➤ The diagnosis of meningococcal meningitis is **Suspected by** :

1. Clinical presentation
2. L.P showing a purulent spinal fluid

Confirmed by :

1. Growing the bacteria from specimens (C/S)
2. Gram staining
3. Specialized lab test :
 - * Identification sero groups
 - * Sensitivity AB

- More specialized laboratory tests are needed for the identification of the serogroups as well as for testing susceptibility to antibiotics

Control measures & vaccination

- The current WHO recommendations for outbreak control are based on reactive mass vaccination with the meningococcal vaccine and effective case management
- Several **vaccines** are available to prevent the disease. Polysaccharide vaccines, which have been available for over 30 years, exist against serogroup A, C, Y, W135 in various combinations.
- A monovalent conjugate vaccine against serogroup C, has recently been licensed in developed countries for use in children and adolescents. This vaccine is immunogenic, particularly for children under 2 years of age whereas polysaccharide vaccines are not.

Alert threshold

Is used to:

- Sound an early warning and launch a laboratory investigation at the start of an epidemic;
- Check epidemic preparedness;
- Start a vaccination campaign if there is an epidemic in a neighbouring area; and
- Prioritize areas for vaccination campaigns in the course of an epidemic

Application of the Epidemic Threshold

- Weekly meningitis incidence should ideally be calculated for areas with population ranging between 30 000 to 100 000. Incidences calculated for areas with a larger population may delay or impede the detection of localized outbreaks.
- Therefore for surveillance and response purposes areas with more than 100 000 inhabitants should be divided in smaller sub-zones (sub-district or neighbourhood within urban areas) of approximately 30 000 to 100 000 people each

- For populations of less than 30 000, an absolute number of cases is used to define the alert and epidemic thresholds so as to avoid major incidence fluctuations due to the small population size
- The effectiveness of this approach depends on the quality of epidemiological surveillance, and especially on the completeness and timeliness of case reporting.
- Underreporting and delays in data transmission can significantly delay the detection of an epidemic

The usage of epidemic threshold

- To confirm the emergence of an epidemic so as to step up control measures, i.e. mass vaccination and appropriate case management

Epidemic threshold

- Population greater than 30 000: an incidence of 15 cases per 100 000 inhabitants per week, in 1 week,
- However, when the epidemic risk is high (no epidemic for 3 years or alert threshold crossed early in the dry season), the recommended epidemic threshold is 10 cases per 100 000 inhabitants per week, in 1 week
- Population less than 30 000: 5 cases in 1 week or doubling of the number of cases over a 3-week period (*other situations must be evaluated in a case by case basis according to the epidemic risk*).
- For operational purposes, when an epidemic is confirmed in a neighbouring area, the alert threshold also serves as the epidemic threshold.

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Collection of Cerebrospinal Fluid Specimens

- Timely identification of the pathogen (s) circulating during a meningitis epidemic is crucial for the choice of the PS vaccine to be used for outbreak control. Therefore laboratory investigation of suspected meningitis cases should be a standard practice during the meningitis epidemic season
- Basic material for collection, transport and testing of cerebrospinal fluid specimens (CSF) such as lumbar puncture kits, transport media vials (TIs), Gram stain and latex kits, should be made available at health facilities at the regional level (province) before the beginning of the epidemic season. In countries without intermediary level, the material should be kept at central level.

- During the pre-epidemic period collection of CSF samples at the periphery level should be stepped up, particularly in those areas that have crossed the alert threshold. Collected samples should be immediately transported to the national laboratory of reference for serogroup identification using TIs
- Active field investigation should be conducted in areas crossing the epidemic threshold as well as in those that remain in alert for more than three weeks. Field investigation teams (epidemiologist and lab technicians) should be sent to the epidemic areas in order to assist data collection and analysis, as well as CSF specimens collection and laboratory confirmation (Gram stain, latex tests).

- Local health staff and field investigation teams should systematically collect and test CSF specimens within two weeks after the epidemic threshold was crossed. We estimate that 20 to 30 CSFs suffice to support the choice of the adequate PS vaccine and limit the number of invasive medical practices. The quicker these samples are obtained the better
- Once the epidemic has been confirmed, regular collection of CSF specimens should be maintained in selected districts⁵ throughout the epidemic season, in order to monitor circulating *Nm* serogroups. Systematic collection of samples from all suspected cases is not recommended. The number of CSF specimens to be collected weekly may vary according to local circumstances and human resources available.

Laboratory Confirmation of CSF Samples

- The identification of *Nm* as the main causative pathogen is essential to confirm a meningococcal meningitis epidemic. All CSF specimens collected should undergo a Gram stain at the nearest laboratory for germ determination

- The identification of the *Nm* serogroup is crucial for deciding on the most appropriate PS vaccine to be used for outbreak control. *Nm* should therefore be confirmed from CSF specimens by either:
 - rapid latex tests that can be used at the peripheral laboratories and allow the identification of most common pathogens/serogroups; or
 - Culture and serogrouping at national or regional laboratories of reference.

- The use of a latex test for identification of *Nm* W135 (Pastorex®) is highly recommended as they can be used at field level and substantially reduce the delay for bacteriological confirmation and decision making
- The field performance of this test has not been properly evaluated and its use should be limited to laboratories fulfilling the following criteria:
 - trained staff;
 - availability of an appropriate infrastructure (cold chain, centrifuge)

- TIs are necessary to transport CSF specimens to laboratories that have the capacity to perform culture and serogroup determination. SOPs procedures for the appropriate use of the TIs should be made available to the countries before the beginning of the epidemic season
- If TIs are not available for the transport of CSF specimens to laboratories, CSF specimens should be stored in sterile tubes preferably in a freezer (-20°C) or in the refrigerator (+4°C for few weeks), and shipped in a cool box for PCR assays in national or regional reference laboratories for the determination of serogroup and genotype.

- Given the need to monitor epidemiological trends of serogroups and genotypes and better understand the spreading patterns of *Nm* epidemic complexes in the region, it is recommended to split a proportion of samples being processed at national level and to ship aliquots to WHO collaborating centres⁶ for genotype characterization

Laboratory Criteria for PS Vaccine Choice

- The decision on the type of PS vaccine to be used should ideally be based on the results from at least 10 *Nm* positive specimens. In order to obtain that number of *Nm* positive specimens, we estimate 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 in the epidemic so as to support the appropriate choice of the PS vaccine.

- The proportion of *Nm* W135 required to warrant the use of ACW trivalent PS vaccine could be defined according to the number of *Nm* positive samples available from a given affected area.

The following 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 PS trivalent ACW vaccine should be strongly discouraged.

- In the above mentioned situation, vaccination with the PS 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 on which PS vaccine should be used, should be evaluated in a case-by-case basis and should take into account all epidemiological and lab information available

Prevention

- ❖ Polysaccharide vaccine
- ❖ Monovalent conjugate vaccine

➤ Vaccine protection

1. It is not routinely recommended
2. Not very effective
3. Not protect children less than 2 years
4. Protect only against a few groups
5. Its usually takes 2 wk to develop immunity
6. It protect for only 2-3 years

- All these vaccines have been proven to be safe and effective with infrequent and mild side effects. The vaccines may not provide adequate protection for 10 to 14 days following injection.
- Group (AC) vaccine (bivalent) is commonly used to vaccinate areas of cases.
- There is a plan to vaccinate one third of school children and displaced people (yearly) in some States.

❖ **Vaccination is used in:**

- Routine vaccination
- Protection of close contact
- Vaccination for epidemic control
- Emergence of W135
- Travelers

- Meningococcal disease is potentially fatal and should always be viewed as a medical emergency. Admission to a hospital or health centre is necessary. Isolation of the patient is not necessary. Antimicrobial therapy must be commenced as soon as possible after the lumbar puncture has been carried out (if started before, it may be difficult to grow the bacteria from the spinal fluid and thus confirm the diagnosis).

- A range of antibiotics may be used for treatment including penicillin, *ampicillin*, *chloramphenicol*, and *ceftriaxone*. Under epidemic conditions in Africa, oily chloramphenicol is the drug of choice in areas with limited health facilities because a single dose of this long-acting formulation has been shown to be effective

Doses of Chloramphenicol

In adult:

- ✓ Three gram single dose Chloramphenicol / IM

In children:

- ✓ 100 mg/kg/IM single dose (max 3/gram)

Advantages

- Drug of choice for most of meningococcal diseases
- Cross the brain barrier and CSF
- Very effective with less side effects
- Single dose is enough and can be repeated after 48 hours
- Stable and can be save in normal room temperature
- Cheap and available
- Easy to use at district level (one intramuscular injection)
- Low risk of misuse due to its limited indication

Alternative to OC as presumptive treatment for meningitis

- Ceftriaxone is the recommended treatment for bacterial meningitis because it presents a wide spectrum of action and a long half-life (8 hours in the blood, 14 hours in CSF)
- Considered as a second-line treatment for bacterial meningitis in all age groups due to the high cost of the 5 patented molecule
- Ceftriaxone has been used with success in the treatment of bacterial meningitis in a 4-day treatment (a single injection daily) (100 mg/kg)

❖ Benzyl Penicillin

In adult:

✓ 3-4 million unit/4-6 hourly / 4days

In children:

✓ **400,000 unit / Kg/4-6 hourly/4 days**

- **Emergence of W135:** Bivalent AC vaccine is commonly used in Africa but the emergence of *N. meningitidis* W135 as an epidemic strain involves revising this control strategy.
- A tetravalent ACYW135 polysaccharide vaccine exists but its high price and limited availability restricts its use in the African context.

- In 2003, WHO reached an agreement with a manufacturer to produce an affordable polysaccharide vaccine for Africa which would protect against A, C and W135 strains.

Health Education

- **Health education using National and States TVs, Radio, Newspapers and health education sessions in schools and houses is a continuous activities during meningitis season.**

REMEMBER

Surprises are always greater for the unprepared.

Common disease outbreaks occur more frequently.

The quality of response is directly proportional to the level of preparedness.

“The future is not some place we are going to, but one we are creating.

The paths to it are not found, but made; and the activity of making them changes both the maker and the destination.”

Peter Ellyard