



Epidemiological Alert: Meningococcal Meningitis (Cerebrospinal fever)

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Given the increasingly frequent occurrence of meningococcal meningitis clusters in different countries of the Region and the need for information to characterize the situation and direct public health actions, the Pan American Health Organization / World Health Organization (PAHO/WHO) encourages Member States to strengthen surveillance and laboratory capacity to enable the detection of outbreaks and to implement an appropriate response in a timely manner.

Meningococcal meningitis is a variable proportion of endemic bacterial meningitis and is usually present in small clusters with seasonal variations in the number of reported cases. In temperate regions, the number of cases increases in winter and spring.

In the Americas, in 2011 and early 2012, Argentina, Bolivia, Brazil,² Chile,³ Colombia,⁴ the United States, Mexico,⁵ Uruguay⁶ and Venezuela⁷ reported cases of meningococcal meningitis, most in the form of small clusters that could be controlled. Some situations, such as that of Bolivia, drew attention due to the detection of cases in areas where they had not been reported in 10 years.

The largest proportion of cases was due to serogroups B and C although those due to serogroups Y and W-135 are increasing. In Brazil, vaccination against serogroup C was incorporated into the routine vaccination system after an outbreak of this serogroup in 2009.⁸

The lack of historical information regarding the number of cases, lethality, concerned serogroup and other epidemiologic data have prevented a better characterization and evaluation of the regional situation.

Meningococcal meningitis (ICD-10 A39.0)

It is an acute bacterial disease caused by the meningococcus (*Neisseria meningitidis*). The capsular polysaccharide of *N. meningitidis* distinguishes at least 13 serogroups, of which 6 are most frequently associated with disease: A, B, C, Y, W-135 and X. Serogroups A and C has the most epidemic potential.

Meningococcal meningitis primarily affects children and adolescents and is spread from person to person by droplets.

It is characterized by the sudden onset of fever, intense headache, nausea and often vomiting, stiff neck and photophobia.

It has an incubation period of four days (ranging from 2 to 10 days). Communicability persists up to 24h after initiation of antibiotic treatment.¹

There are three main clinical presentations: meningeal syndrome, septic form and pneumonia. The fatality rate can reach 50% in untreated cases.

Of surviving patients, 10- 20% may experience sequellae, the most frequent being necrosis of extremities, neurological deficits and varying degrees of hearing loss (especially in children).

¹ Meningococci usually disappear from the nasopharynx within 24 hours after commencement of treatment with efficient antimicrobials.

² http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto.cfm?idtxt=37810

³ http://epi.minsal.cl/epi/html/AtlasInteractivos/AB_101/Menin.htm

⁴ <http://www.ins.gov.co/?idcategoria=94853#>

⁵ http://www.dgepi.salud.gob.mx/2010/plantilla/intd_boletin.html

⁶ http://www.msp.gub.uy/ucepidemiologia_5428_1.html

⁷ http://issuu.com/sotero/docs/bolet_n_50/26

⁸ http://portal.saude.gov.br/portal/saude/profissional/area.cfm?id_area=1563

Recommendations

1. Laboratory diagnostic

Laboratory diagnostic tests to confirm the detection of a *Neisseria meningitidis* infection are culture, antigenic tests or polymerase chain reaction (PCR).

The reference etiological diagnosis is by blood or cerebrospinal fluid culture. However, the sensitivity is poor in patients who have received antibiotics prior to the sample being taken. Antimicrobial susceptibility testing should be performed routinely to confirm the decisive start of antimicrobial treatment and to provide epidemiological data to guide the decisive treatment in successive cases.

The latex agglutination reaction and counterimmunoelectrophoresis are found among antigen tests. The latex agglutination test tends to give false negative results particularly in serogroup B cases.

The polymerase chain reaction is based on the detection of meningococcal DNA in cerebrospinal fluid or plasma, for which specific primers are used. It has a greater sensitivity than cultivation in patients previously treated with antimicrobials.

Microscopic examination of a smear Gram stained material obtained from petechiae can prove the presence of *N. meningitidis* in lesions, but the results should be interpreted with caution due to the high proportion of false negative results.

Serogroup confirmation

Serogroup confirmation is achieved through serum agglutination with specific antibodies. When an isolate is untypable through this technique, the polymerase chain reaction (PCR) is the recommended technique to determine the serogroup.

2. Case management and chemoprophylaxis

Early diagnosis and treatment are critical as meningococcal meningitis can reach 50% lethality, as described in classical works,⁹ if not treated with antimicrobials in a timely manner.

To suspect this diagnosis is vital for immediate initiation of appropriate antimicrobial therapy, assessment of chemoprophylaxis for contacts and to take appropriate action in case of an outbreak. Always when possible, perform a lumbar puncture and collect blood cultures before starting antibiotic therapy, while not delaying the start of treatment to microbiological samples.

Treatment of cases:

Antibiotic therapy must be started decisively, as soon as possible. In addition to antibiotic treatment, necessary support measures to address problems of disseminated intravascular coagulation, shock, heart failure, lethargy, pericarditis and pneumonia should be implemented as they can complicate an infection and their correct application has a clear and positive impact on prognosis. In Table 1, it is included the antimicrobial treatment options in case of suspected acute

⁹ Norton JF, Gordon JE. Meningococcus meningitis in Detroit in 1928-1929. *J Epidemiology J Prev Med.* 1930; 4:207.

bacterial meningitis community acquired. In table 2, it is included the antimicrobial treatment when *N meningitidis* is confirmed.

Table 1. Antimicrobial treatment options in cases of suspected acute bacterial meningitis community acquired¹⁰

Age group	First option	Other options
< 1 month	Cefotaxime 200 mg/kg/iv/d divided into 4 doses + ampicillin 400 mg/kg/iv divided into 4 doses for 14 to 21 d. In case of enterobacterial infections, a minimum of 21 d, according to progress, and 28 d in cases of ventriculitis.	Ampicillin 300 mg/kg/iv/d divided into 4 doses + gentamicin 5-7.5 mg/kg/iv or amikacin 15-20 mg/kg/iv, both in 1 dose, for 14 to 21 d. In case of enterobacterial infections, a minimum of 21 d, according to progress, and 28 d in cases of ventriculitis.
1 to 3 months	Cefotaxime 300 mg/kg/iv/d divided into 4 doses or ceftriaxone 80-100 mg/kg/iv/d in 1 dose or divided into 2 doses + ampicillin 200-400 mg/kg/iv/d divided into 4 doses, for 10 to 14 d. Enterobacterial infections, minimum of 21 d, according to progress, and 28 d in cases of ventriculitis.	Ampicillin 400 mg/kg/iv/d divided into 4 doses + chloramphenicol 75-100 mg/kg/iv divided into 4 doses, for 10 to 14 d. Enterobacterial infections: minimum of 21 d, according to progress, and 28 d in cases of ventriculitis.
> 3 months to 5 years ^{11, 13}	Cefotaxime 300 mg/kg/iv/d divided into 4 doses or ceftriaxone 80-100 mg/kg/iv/d in 1 dose or divided into 2 doses, for 7 to 10 d. ¹²	Ampicillin 400 mg/kg/iv/d divided into 4 doses + chloramphenicol 75-100 mg/kg/iv divided into 4 doses, for 10 to 14 d.
> 5 to 18 years ^{11, 13}	Cefotaxime 300 mg/kg/iv divided into 4 doses or ceftriaxone 80-100 mg/kg/iv in 1 dose or divided into 2 doses for 7 to 10 d ¹² . In the presence of resistant strains of <i>Streptococcus pneumoniae</i> , add vancomycin 60 mg/kg/iv divided into 4 doses.	Ampicillin 400 mg/kg/iv divided into 4 doses or crystalline penicillin G 400,000 IU/kg/iv divided into 4 to 6 doses for 7 to 10 d.

When *N meningitidis* is microbiologically confirmed, the following treatment can be provided:

¹⁰ PAHO/WHO. Treatment of Infectious Diseases, 2011-2012, 5th Edition. Washington DC 2011.

¹¹ Where the resistance of strains of *Streptococcus pneumoniae* to penicillin (MIC > 0.1 µg/ml) is higher than 5%: use cefotaxime 300/mg/kg or ceftriaxone 100/mg/kg. When there may be resistance to cefotaxime (MIC > 0.5 µg/ml), empirically add vancomycin 60 mg/kg/iv/d divided into 4 doses until sensitivity is documented. A controlled cerebrospinal fluid study is recommended within a period of 24 h to 48 h. Rifampicin or iv should be added to the antibiotic treatment when dealing with strains of pneumococcus with MIC of cefotaxime ≥ 4 µg/ml in culture of the cerebrospinal fluid or when there is no clinical response within 48 h after initiating the treatment.

¹² Children infected by *N. meningitidis* and good clinical progress: 5 days of treatment.

¹³ Allergy to β-lactams in children under 5 years of age: initiate treatment with vancomycin 60 mg/kg/iv/d divided into 4 doses, plus rifampicin 20 mg/kg/po or iv/d divided into 4 doses for 7 to 10 days, provided that gastrointestinal absorption can be guaranteed. In children older than 5, initiate empiric treatment with vancomycin 60 mg/kg/iv/d divided into 4 doses + rifampicin 20 mg/kg/iv or per os.

Table 2. Antimicrobial treatment for meningococcal meningitis¹⁴

First choice	Other choices
<p>Ceftriaxone 2 g/iv c/12h for 7 days or cefotaxima 2 g/iv c/4 hours for 7 days.</p> <p>Change to crystalline penicillin G 4,000,000 UI/iv c/4 hours to complete 7 days if you know this antibiotic sensitivity (MIC= 0.1 to 1 microgram/mil)</p>	<p>If β-lactam allergy: chloramphenicol 1g/iv c/6 hours for 7 days.</p>

G: grams; IV: intravenous; MIC (Minimum Inhibitory Concentration).

National authorities' recommendations and current full prescribing information available in the package insert of each drug should be consulted before prescribing any product. Recommendations on treatment schemes can change at the light of new evidences or because the emerging of resistance to specific antimicrobials.

3. Measures of prevention and infection control

Transmission is through respiratory droplets, for which close contact at least 4 hours a day within a radius of 1 meter in the 7 days preceding illness onset, is necessary; or close contact with respiratory secretions such as in kissing, mouth to mouth resuscitation, tracheal intubation or aspirate nasopharyngeal secretions in the case of health personnel.

All cases should be hospitalized, using standard precautions and droplet transmission precautions. Use of masks is recommended for contacts less than or equal to one meter for at least 24 hours after the initiation of effective treatment.

It is recommended to isolate cases in single rooms. If not possible, patients should be admitted in cohorts. Isolation precautions should be maintained until 24 hours after initiation of antibiotic therapy¹⁵.

The use of masks for health personal that perform a lumbar puncture is recommended.

4. Prevention

Chemoprophylaxis

Chemoprophylaxis is to prevent secondary infection after the index case, and is therefore indicated on an individual basis by a treating physician, according to the risk of contracting the infection.

People most at risk for infection include:

- household contacts;
- other close contacts, especially children (school contacts, people who have eaten or slept with the patient at least 4 hours a day within a radius of 1 meter in the 7 days preceding illness onset);
- health workers in contact with the patient's oral secretions (e.g. mouth to mouth resuscitation).

¹⁴ PAHO/WHO. Treatment of Infectious Diseases, 2011-2012, 5th Edition. Washington DC 2011.

¹⁵ <http://www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf>

Chemoprophylaxis for close contacts is administered with one of the following options:

- Rifampicin:
 - Adults: 600 mg orally, every 12 hours, for 4 doses
 - Children > 1 month: 10 mg/kg weight every 12 hours, for 4 doses
 - Children < 1 month: 5 mg/kg weight every 12 hours, for 4 doses or
- Ceftriaxone:
 - Adults: 250 mg IM, one dose. Preferred during pregnancy
 - Children < 15 years: 125 mg IM, one dose or
- Ciprofloxacin¹⁶:
 - Adults: 500 mg orally, one dose

Immunoprophylaxis

There are three types of vaccinations.

- The polysaccharide-based vaccines have been available for over 30 years. These vaccines can be bivalent (groups A and C), trivalent (groups A, C and W) or tetravalent (groups A, C, Y and W135).
- Vaccines against group B based on polysaccharides by antigenic mimicry of polysaccharide human nervous tissue cannot be developed. Therefore, vaccines against meningococcal group B developed in Cuba, Norway and the Netherlands are based on outer membrane proteins.
- Since 1999, conjugate vaccines against meningococcal serogroup C have been available and widely used. Since 2005, a quadrivalent conjugate vaccine (groups A, C, Y and W135) for children and adults has been authorized for use in the United States, Canada and Europe.

These vaccines have been shown to be safe and effective and side effects mild and infrequent. The vaccines may not provide protection until 10 to 14 days after administration.

The decision of which vaccine is the most appropriate per country should be based on the circulating serogroup, or serosubtype in the case of serogroup B.

Meningococcal vaccination is recommended for defined risk groups, such as children and young adults residing in closed communities, e.g. boarding schools or military camps. Laboratory workers at risk of exposure to meningococci should also be vaccinated. Travelers to high-endemic areas should be vaccinated against the prevalent serogroup(s). In addition, meningococcal vaccination should be offered to all individuals suffering from immunodeficiency, including asplenia, terminal complement deficiencies, or advanced HIV infection.

¹⁶ Ciprofloxacin is contraindicated in pregnant women and children.

5. Outbreak response

Outbreak response must include early and appropriate treatment of cases, chemoprophylaxis of close contacts and vaccination of the group considered at high risk (boarding schools or military camps).

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