

CDAlert

Monthly Newsletter of National Institute of Communicable Diseases,
Directorate General of Health Services, Government of India

April 2005

Special issue

Vol.9 : No.4

MENINGOCOCCAL DISEASE

Meningococcal disease is an acute bacterial disease caused by the meningococcus (*Neisseria meningitidis*) and manifested by sudden onset of fever, severe headache, nausea and vomiting, stiff neck and frequently a petechial rash with pink macules and very rarely vesicles often accompanied by delirium and coma. Occasionally fulminating cases exhibit severe sudden prostration, ecchymoses and shock at onset. Thirteen subtypes of sero groups of *N.meningitidis* have been identified and four sero groups (namely A, B, C and W135) are recognized to cause epidemics. The pathogenicity, Immunogenicity and epidemic capabilities differ according to serogroup and its identification is crucial for containment of epidemic. Other serogroups to name a few X,Y,Z etc. are less virulent. However, fatal infections and secondary cases are known to occur with all.

A small proportion of cases progress to invasive disease characterized by one or more clinical syndromes including bacteraemia. Many with septicaemia develop petechial rash. Joints may also be involved. Meningococcaemia may occur without meningitis.

Epidemics of meningococcal disease can occur in any part of the world. However, the largest epidemics occur mainly in the semi-arid areas of sub-Saharan Africa, designated the African "meningitis belt".

Epidemic meningococcal disease

Meningococcal meningitis occurs globally. The disease is endemic in temperate climates with sporadic cases or a small cluster of cases and having a seasonal increase in winter and spring. A different pattern, with periodic epidemics covering large geographic area, has been observed in countries in sub-Saharan Africa. This area has experienced epidemic cycles every 8 to 12 years in the past, and the intervals between major epidemics have become shorter and more irregular since the beginning of the 1980s. During 1970-2000, a large number of epidemics of meningococcal disease has been reported from Africa, Asia, South and Central America & Europe.

Recent Outbreaks of Meningococcal disease in the world

- An outbreak has been reported from two districts of Ethiopia. Between 30th January and 12th March 2000, 81 cases with 3 deaths were reported from Kobo district, while 48 cases and 6 deaths were reported from the Alameter district.
- In Central African Republic, between October 1999 and January 2000 a total of 86 cases and 14 deaths were reported from Vakaza, Bamingui-Bangaron, Haute Katto and Ouham pend areas.
- In early December 1999, 30 cases and 4 deaths were reported from Bacs-Kiskum area of Hungary.

- During August-September 1999, an outbreak was reported from Yambala area of Angola. Reports refer to 253 cases with 147 deaths
- Between 1st September and 6th October 1999, an outbreak was reported from Rwanda, affecting areas of Kayenze, Nyabikenke and Rutobwe.
- Until May 12, 1999, a total of 22,000 cases of meningococcal disease with 1,600 deaths were notified from 19 states of Sudan. A total of 10.7 million doses of meningococcal vaccine were distributed to the affected states.
- In 2002, the Great Lake region (U.S.A.) was affected by outbreaks in villages and refugee camps which caused more than 2200 cases including 200 deaths.
- In 2000 and 2001, several hundred pilgrims attending the Haj in Saudi Arabia were infected with N.meningitides W135.
- In 2002, W135 emerged in Burkina Faso where 130,000 people got affected and 1500 died.

Indian scenario

The historical background of the meningococcal meningitis disease in India is as follows:

1883	Earliest record of an outbreak of meningococcal meningitis in Shikarpur Jail.
1886	Recorded in Alipore Jail
1932	Outbreak in Borstal Institute in Lahore
1935	Delhi and Indore
1933-39	Calcutta
1966-67	Delhi
1985	Delhi, Haryana, Rajasthan, Maharashtra, Bihar, West Bengal

1986-89	Delhi, Gujarat, Maharashtra, Madhya Pradesh, Orissa, Bihar, Rajasthan, Andhra Pradesh, Haryana
1989-99	Sporadic cases from different parts of the country

Major outbreaks in the country

Outbreak in 1966

During March 1966, an increased number of pyogenic meningitis cases were admitted in 5 major hospitals of Delhi. A total of 616 cases were recorded. The proportion of laboratory confirmed cases increased from 4.8% in January to 10.6% in February to reach a peak of 44.9% in May 1966. The outbreak was due to meningococcus serogroup A. The percentage of meningococcal meningitis cases followed the pattern of the incidence of pyogenic meningitis cases. Overall in 18.8% of the cases, meningococci were proved to be the causative agent. Two peaks were noticed - one in May and the other in December 1966.

Outbreak in 1985-86

After a gap of about 20 years, Delhi and adjoining areas experienced another outbreak of meningococcal meningitis. The causative agent was again meningococcus serogroup A. During the year 1985, a total number of 6133 pyogenic meningitis cases with 799 deaths were recorded, with an overall case-fatality of 13% as compared to 1731 cases and 569 deaths in the year 1984.

Epidemiology

The meningococci most often inhabit the human nasopharyngeal area without causing any symptoms or with only local symptoms. The disease may become invasive with involvement of meninges and presenting as acute purulent meningitis. The main epidemiological features of meningococcal disease are given in the box.

EPIDEMIOLOGICAL FEATURES OF MENINGOCOCCAL DISEASE

Reservoir	: Man, no extrahuman reservoir
Transmission	: Direct contact with droplets and discharges from nose and throat of patients and carriers. Infection usually causes only a subclinical mucosal infection. Invasion sufficient to cause systemic disease is comparatively rare. Carrier prevalence rate upto 25% or more may exist without a case of meningitis.
Incubation period	: 2-10 days (average 3-4 days)
Seasonal variation	: More in winter months or spring
Age group affected	: Primarily a disease of small children; occurs commonly in children or young adults. However no age is exempt.
Male:Female ratio	: 2:1 in clinical cases
Case fatality rate	: More in meningococcaemia and in delayed treatment case.
Period of communicability	: Until meningococci are no longer present in discharges from nose and mouth
Cyclic trend	: Epidemics occur every 8-12 years or more

Considering the cyclic trend of meningococcal disease and recent occurrence of outbreaks in many parts of the world, which due to rapid travel can spread to any country, makes it mandatory to augment surveillance and observe strictest vigil for this disease and remain alert through continuing medical education.

LABORATORY DIAGNOSIS

For meningitis	For meningococcaemia
<ul style="list-style-type: none"> ▪ CSF cytology shows increased WBC count with increased polymorphs ▪ CSF sugar decreased, protein increased ▪ CSF Gram stained smear shows gram-negative intracellular & extra cellular diplococci. ▪ CSF & blood culture may show growth of meningococcus ▪ Meningococcal antigen in CSF detected by latex agglutination confirms diagnosis ▪ Petechial fluid may show presence of meningococci 	<ul style="list-style-type: none"> ▪ Blood culture is the single most important investigation ▪ Smears and culture from petechiae may reveal meningococci

Note: Samples for culture should be collected before administration of antibiotics and sent to laboratory at room temperature and should not be refrigerated.

STANDARD CASE DEFINITION OF MENINGOCOCCAL MENINGITIS

1. Suspected case of acute meningitis

- sudden onset of fever (>38.5°C rectal or 38.0°C axillary), **WITH**
- stiff neck

In patients under one year of age, a suspected case of meningitis occurs when fever is accompanied by a bulging fontanelle

2. Probable case of bacterial meningitis

- suspected case of acute meningitis as defined above, **WITH**
- turbid CSF

3. 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 purpurial rash

4. Confirmed case

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

1. This case definition allows the detection of cases of meningococcal septicaemia.
2. Often the only diagnosis can be made in the dispensaries (peripheral level of health care)
3. Diagnose in health centre where lumbar puncture and CSF examination are feasible (Intermediate level)
4. Diagnose in well equipped hospital (State or Central level)

Standard case definition of Meningococemia

Probable: Sudden onset of fever (>38.5°C rectal or 38.0°C axillary) with or without shock, and one of the following

- i. Petechial or purpurial rash
- ii. Gram stain showing Gram negative diplococcus

Confirmed: Probable case, and

Demonstration of *N.meningitidis* or antigen in blood and/or CSF

Note: All probable or confirmed cases of Meningococcal meningitis or Meningococemia should be reported to the (i) DHA (MCD), Tel: 23936101; Fax: 23942056, 23832314, (ii) Director (EMR), Tel: 23017302; Fax: 23017457, and (iii) Director, NICD, Tel:23971272, 23971060,23912836; Fax: 23922677

How to recognize and confirm meningococcal disease?

Symptoms and signs

- Sudden onset of intense headache
- High fever
- Stiff neck
- Nausea and vomiting
- Photophobia

- Neurological signs like confusion, lethargy, delirium, coma, and/or convulsions
- Infants may have illness without any stiff neck and onset could be slow

Meningococcal septicaemia (meningococcaemia) – It is difficult to recognize. Main symptoms/signs are:

- Abrupt onset
- Fever

- Shock
- Petechial rash or purpura may not be obvious initially and meningeal symptoms are usually absent.
- Rapid circulatory collapse.

Physical examination should include an examination for

- Meningeal rigidity, stiff neck, Kernig's or Brudzinski's signs
- Neurological signs such as decreased awareness; localizing neurological symptoms are unusual
- Purpura, sometimes extensive and necrotic, usually localized to the extremities, or generalized, cutaneous or mucosal (conjunctival) are often associated with meningococcal disease; purpura is a basic symptom of meningococcaemia
- Lowered blood pressure and symptoms of shock
- shock associated with purpura indicates fulminating meningococcaemia, the most severe form of meningococcal disease
- Focal infection such as arthritis, pleuritis or pneumonia, pericarditis, episcleritis

In infants (under one year of age), the clinical features of meningitis are often atypical and may be difficult to recognize. The onset is not always rapid. In addition to fever, inconsolable irritability and screaming, failure to feed, vomiting, lethargy, convulsions or hypotonia may be presenting features. Stiff neck may be absent, bulging fontanelle may be observed.

The bacterial meningitis may result in brain damage, hearing loss or learning disability in 10-20% of survivors.

How to manage patients with meningococcal disease?

Meningococcal disease (either meningitis or septicaemia) is potentially fatal and should always be viewed as a medical emergency.

- Admission to a hospital or health centre is necessary for diagnosis (lumbar puncture and CSF examination) and for treatment
- Antimicrobial therapy is essential and should be combined with supportive treatment
- As contagiousness of patients is moderate and disappears quickly following antimicrobial treatment, isolation of the patient is not necessary

Antimicrobial therapy

Antimicrobial treatment must be instituted as soon as possible after the lumbar puncture has been carried out. Many antimicrobials are active against meningococci *in vitro*, but only those that penetrate sufficiently the cerebrospinal space and are affordable should be used. A range of antibiotics used for treatment are Penicillin, Ampicillin, Chloramphenicol and Ceftriaxone. Chloramphenicol is a good and inexpensive alternative. The third generation cephalosporins, ceftriaxone and cefotaxime, are also very effective.

Oily Chloramphenicol is the drug of choice in area with limited health infrastructure as a single dose of this long acting formulation is found to be very effective.

The antimicrobials useful in the treatment of meningococcal disease are listed in the box.

ANTIBACTERIALS TO TREAT BACTERIAL MENINGITIS					
Agent (generic name)	Route	Dose adults	Dose children	Duration days	Cost
Penicillin G	IV	3-4 MU . 4-6 h	400,000 U/kg	≥ 4	low
Ampicillin or Amoxicillin	IV	2-3 g . 6 h	250 mg/kg	≥ 4	moderate
Chloramphenicol	IV	1 g . 6 h	100 mg/kg	≥ 4	moderate
Cefotaxime	IV	2 g . 6 h	250 mg/kg	≥ 4	Expensive
Ceftriaxone	IV	1-2 g q. 12-24 h	50-80 mg/kg	≥ 4	high

Supportive therapy

Fluid and electrolyte balance should be monitored and fluid replaced accordingly. When required, anticonvulsants or antiemetics may be administered. Severe forms of the disease including coma, shock, purpura should be treated in an intensive care unit by well trained physicians.

How to prevent meningococcal disease?

Meningococcal disease is potentially preventable through vaccination and/or chemoprophylaxis in special circumstances.

Prevention of transmission

Transmission of *N.meningitidis* occurs from person to person, usually from a nasopharyngeal carrier rather than from a patient, through contact with respiratory droplets or oral secretions. The prevalence of nasopharyngeal carriage is variable, and does not correlate with the risk of an outbreak. Contagiousness rapidly disappears in patients after starting antibiotic therapy.

Vaccination

Vaccines against four specific antigens related to serogroups A, C, Y and W135 are currently available. They are distributed in freeze-dried form. Vaccine contains 50 ug of each antigen. The dose of vaccine is 0.5 ml given subcutaneously.

These polysaccharide vaccines are generally very well tolerated but may induce some mild adverse reaction (local pain and swelling, fever and malaise) in 10-20 percent of recipients, for 2-3 days following the vaccination. Duration of immunity is 1-3 yrs. Vaccine needs to be stored at +2 to 8°C. The shelf life of vaccine is 2 years and after reconstitution the vaccine has to be used same day. It is available as monovalent, bivalent (A+C) and tetravalent forms (A+C+Y+W135).

Meningococcal polysaccharide vaccines are not routinely used in early childhood because of their general lack of efficacy in infants and young children below 2 years.

In some countries, recruits are routinely vaccinated with A+C vaccine, at the beginning of military service.

Vaccination policy

Vaccine should be given to:

- Haj pilgrims
- High risk groups

Mass vaccination is not recommended

Chemoprophylaxis

The aim of chemoprophylaxis is to prevent secondary cases by eliminating nasopharyngeal carriage.

Chemoprophylaxis has been considered for control of meningococcal disease but it has several limitations, and its use should be limited to special circumstances. **To be effective in preventing secondary cases, chemoprophylaxis must be initiated as soon as possible (i.e. not later than 48 hours after diagnosis of the case).**

Special circumstances for which chemoprophylaxis are appropriate:

In non-epidemic settings, chemoprophylaxis should be restricted to close contacts of a case, which are defined as:

- Household members (i.e. persons sleeping in the dwelling as the case); institutional contacts who shared sleeping quarters (i.e. for boarding school pupils, room-mates; for military camps, persons sharing a barrack); nursery school or childcare centre contacts (i.e. children and teachers who share a classroom with the case)
- Others who have had contact with the patient's oral secretions through kissing or sharing of food and beverages.

In addition, in areas where household contacts routinely receive prophylaxis, chemoprophylaxis should also be given to the patient with meningococcal disease upon discharge from the hospital provided the patient's illness was treated with antibiotics (e.g. penicillin) which do not eliminate the organism from the nasopharynx.

THE RECOMMENDED DRUGS FOR CHEMOPROPHYLAXIS ARE

Generic name	Dose Adults	Dose children	Route	Duration
Rifampicin	600 mg/12h	10 mg/kg/12h	Oral	2 days
Spiramycin	1 gm/12h	25 mg/kg/12h	Oral	5 days
Ciprofloxacin	500 mg	Not given	Oral	Single dose
Ofloxacin	400 mg	Not given	Oral	Single dose
Ceftriaxone	250 mg	<15 yr – 125 mg	IM	Single dose

Mass chemoprophylaxis to prevent/control epidemics is not recommended.

Meningococcal Disease and Haj Pilgrims

Visitors from all over the world arriving for the purpose of pilgrimage are required to produce a certificate of vaccination against meningitis issued not more than 3 years and not less than 10 days before arrival in Saudi Arabia.

- Adults and children over the age of two years must be given one dose of quadrivalent vaccine (A+C+Y+W135).
- Children between three months and two years must be given two doses of A polysaccharide vaccine with a three month interval between the two doses.

In case of a documented outbreak at the Haj site, all the Hajjis returning to the country should receive chemoprophylaxis irrespective of their vaccination status.

Can one predict an epidemic?

Nasopharyngeal carrier studies in healthy population have not been found to predict an epidemic. However some of the early warning signals are:

- An attack rate of at least 5 fold higher than that observed during previous years in the same area, or if data for the same are not available, an attack rate of at least 5 fold higher than rates in the similar areas of the country.
- An attack rate of probable and confirmed meningococcal disease surpassing 5 cases per one lac population (while working out the attack rate, the preceding three months could be considered. Attack rate should be

applied to the populations of a district, estimation of attack rates in an entire country will usually fail to detect local/focal epidemics).

- Rising incidence of the disease (probable or confirmed) for three consecutive weeks in the same area also calls for immediate attention.

Occurrence of even a single case in epidemiological settings such as nursery, hostels, military barracks and jails need immediate attention.

Control of epidemics

Management of patients

Provision for prompt and proper management of patients to prevent morbidity and mortality is of utmost importance. The hospitals should be well stocked with the required medicines as per the recommended guidelines for management of the patients.

Augmentation of surveillance should be done so that cases could be detected early.

Epidemiological investigation to identify various factors involved in outbreak should be instituted.

Immunoprophylaxis

It has been documented that a mass vaccination campaign if appropriately carried out is able to halt the epidemic of meningococcal diseases due to serogroups A&C within weeks. However, such a decision depends on many other issues e.g. geographical distribution of cases, age specific attack rates and the resources

DO'S	DON'TS
<ul style="list-style-type: none"> ➤ Wash hands properly after coming in contact with patient. ➤ Cover your nose, mouth while coughing and sneezing ➤ Keep a watch for the symptoms of disease ➤ In the event of noticing any symptoms of disease immediately contact the doctor 	<ul style="list-style-type: none"> ➤ Avoid going to crowded places ➤ Don't share food, drinks, smoking, clothing and bedding with a person having illness ➤ Don't panic, it is curable

available. If the number of cases is below the epidemic threshold, mass vaccination is not recommended.

Chemoprophylaxis

During an epidemic, a large number of people are already affected & therefore application of mass chemoprophylaxis will require large deployment of resources. The chemoprophylactic drugs being recommended are also not without side effects. In addition from epidemiological point of view, reinfection of asymptomatic persons is also quite frequent and therefore application of **mass chemoprophylaxis during an outbreak is not considered epidemiologically appropriate and cost effective.**

In a focal outbreak (small cluster) chemoprophylaxis to close contacts should be given, particularly so in boarding schools, hostels, institutions, jail-inmates etc. Chemoprophylaxis is also indicated in close contacts of sporadic cases.

Use of media

The media can help to increase awareness among health workers and educate the community about early symptoms that may be related to disease in the outbreak. Local

beliefs about the disease transmission should be explored and any misconceptions addressed. A close collaboration between the media and health authorities is necessary throughout an epidemic.

Diagnostic and epidemiological support for any suspected meningococcal disease outbreak can be provided by NICD, Delhi, if requested.

General measures

Although some uncertainty remains about the circumstances in which transmission of meningococci occurs, it has been suggested that transmission may be enhanced when people are together in crowded situations which should be avoided.

Prevention & Control of outbreak

- Early diagnosis and management.
- Chemoprophylaxis to close contacts in household and health care workers.
- Vaccination of high-risk group.
- Health education to allay fear and improve knowledge of signs and symptoms to seek early treatment.
- Inform neighboring districts
- Respiratory isolation of all patients for 72 hours.

...about CDAlert

CDAlert is a monthly newsletter of the National Institute of Communicable Diseases (NICD), Directorate General of Health Services, to disseminate information on various aspects of communicable diseases to medical fraternity and health administrators. The newsletter may be reproduced, in part or whole, for educational purposes.

Chief Editor: Dr. S.P. Agarwal

Editorial Board: Dr. Shiv Lal, Dr. Usha K. Baveja, Dr. R. L. Ichhpujani, Dr. Shashi Khare, Dr. Jagvir Singh

Guest Editor: Dr. Sunil Gupta

Publisher: Director, National Institute of Communicable Diseases, 22 Shamnath Marg, Delhi 110 054

Tel: 011-23971272, 23971060 Fax : 011-23922677

E-mail: dirnicd@bol.net.in and dirnicd@del3.vsnl.net.in

Acknowledgement: Financial assistance by WHO/USAID is duly acknowledged.