Meningococcal Meningitis

The most important pathogen for meningitis is *Neisseria meningitides*

***because of its* potential to cause epidemics**

Problem Statement

- Occurs worldwide in both endemic and epidemic forms.
- It is estimated to be responsible for over 500,000 cases and about 135,000 deaths annually
- ‘African meningitis belt’, stretches across sub – Saharan Africa from Senegal in the west, to Ethiopia in the east.
- During epidemics this region has a disease incidence rate of >1,000 cases per 10,000 population.
- The largest recorded outbreak occurred in Africa in 1996
- Major epidemics reported from Asia over the past 35 years. China, Vietnam, Mongolia, Bhutan, and Nepal

Problem Statement

- Indian states reporting epidemics - Haryana, U.
  P., Rajasthan, Sikkim, Gujarat, Jammu & Kashmir, W. B., Chandigarh, Kerala and Orissa.
- Several outbreaks have been reported from Delhi in 1966, 1985 and 2005.

Problem Statement

- Isolated in 1887, *N. meningitides is an exclusive human* pathogen
- Natural habitat and reservoir - The mucosal surfaces of the human nasopharynx
- In most cases colonization of the human nasopharynx is asymptomatic.
- However, blood stream invasion *can* lead to meningitis and septicaemia with serious consequences.
- Even with adequate chemotherapy, meningococcal meningitis has a fatality rate of about 10% and about 15% of the survivors have residual Central Nervous System (CNS) damage

Agent: *Neisseria meningitides*

- ***Bean shaped gram*** negative, aerobic diplococci.
- The bacteria are surrounded by an outer membrane of lipids, membrane proteins and lipopolysaccharides.
- At least 13 serogroups have been described : A, B, C, D, E, H, I, K, L, W - 135, X, Y and Z.
- Almost all meningococcal infections are caused by five serogroups A, B, C, 29 E or W – 135
- Worldwide serogroups A, B and C account for most cases of meningococcal disease
- The predominant serogroups in Asia and Africa are A & C
- Recent outbreaks among Haj pilgrims have been

Host

- Maternal antibodies offer protection against invasive disease till the age of six months.
- Susceptibility peaks at age 6 - 12 months and decreases again after colonization of closely related nonpathogenic bacteria.
- Subsequent colonization with *Neisseria meningitides induces antibodies to the infecting* strain, thus reinforcing natural immunity.
- Invasive disease occurs if no protective bactericidal antibodies are mounted against the infecting strain.
- Those infected with the Human Immunodeficiency Virus are probably also at increased risk for sporadic meningococcal

Host and Environment

- Highest incidence – 6 months to 2 yrs
- Rarely reported over 50 years of age.
- No gender predilection, though males account for slightly more than half the reported cases.
- Increased Risk with smoking (both active and passive), antecedent upper respiratory tract infection, underlying chronic illnesses are all associated with increased risk of meningococcal disease.
- Low socioeconomic status - poor housing, overcrowding, and inadequate ventilation consistently associated with higher risk for meningococcal disease
- The risk of invasive disease is higher in the first few days after exposure to a new strain.

Transmission & Communicability

- The main modes of transmission are direct contact and respiratory droplets.
- Close contact like living in close quarters (like military dormitories) and sharing of utensils enhance the risk of transmission
- The average incubation period is 3 - 4 days with a range of 2 to 10 days.
- This is also the period of communicability.
- The bacteria are rapidly eliminated from the nasopharynx after starting antibiotics, usually within 24 hours.

Reservoir

- Humans are the only reservoir.
- Both cases and carriers serve as the source of infection.
- 5 - 10% adults are asymptomatic nasopharyngeal carriers during inter - epidemic periods.
- This figure can, however, rise to 60 - 80% in closed populations like military recruits in camps

Pathogenic Strain

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Susceptible Host

Colonized on naso - oropharyngeal mucosa

Overcome host defense & attach to the microvillous surfa
of nonciliated columnar mucosal cells of the nasopharynx,

mucosal penetration followed by invasion of blood stream a
finally, invasion of meninges

meningococcemia leading to systemic disease, usually precedes meningitis by 24 to 48 hours

Meningococcemia leads to diffuse vascular injury with circulatory collapse and disseminated intravascular coagulation.

Clinical Features

- Acute onset (within several hrs to 2 days) of intense headache, high fever, nausea, vomiting, photophobia, and stiff neck, altered mental state
- Less commonly reported symptoms include stupor or coma, which carries a poorer prognosis.
- A more severe form of disease is meningococcal septicaemia, characterized by a haemorrhagic rash which usually indicates disease progression and rapid circulatory collapse

Clinical features

- In infants and young children there is a slower onset of signs and symptoms with nonspecific symptoms and neck stiffness may be absent.
- Irritability and projectile vomiting may be the presenting features.
- Seizures occur in 40% of children with meningitis.
- The Waterhouse - Friderichsen syndrome may develop in 10 - 20% of children with meningococcal infection, characterized by large petechial haemorrhages in the skin & mucous membranes, fever, septic shock
- Even when the disease is diagnosed early and adequate therapy instituted, 5% to 10% of patients die, typically within 24 - 48 hours of onset of symptoms.
- Bacterial meningitis may result in brain

Diagnosis

- Suspected by the clinical presentation and a L.P. showing a purulent spinal fluid
- CSF - increased pressure (>180 mm water), WBC counts between10 and 10,000 cells/μL, (predominantly neutrophils), decreased glucose concentration (<45 mg/dL) and increased protein concentration (>45 mg/dL)

Diagnosis

- Bacteriological diagnosis by Gram staining of CSF,
- Direct antigen detection using latex agglutination, or
- Culture- only CSF samples are generally positive.
- Kits to detect polysaccharide antigen in CSF are rapid and specific and can provide a serogroup - specific diagnosis, but false negatives!

Management

- Since its potentially fatal, should always be viewed as a medical emergency
- Early recognition of the disease, prompt initial parentral antibiotic therapy and close monitoring with frequent repeated prognostic evaluations
- Several antibiotics can be used for treatment including penicillin, ampicillin, chloramphenicol and ceftriaxone
- Isolation of the patient is not necessary

- A single intramuscular dose of an oily suspension of chloramphenicol has been shown to be as effective as a five - day course of crystalline penicillin in the treatment of meningococcal meningitis.
- During epidemics, this may offer a practical alternative to penicillin or ceftriaxone which require multiple injections

Antibiotic	Adult Dose	Pediatric Dose
Penicillin	4 million units IV X 4 a day	250,000 Units/Kg/day I.V. in devided doses
Ceftriaxone	4 gram IV per day divided into two doses	50 mg/Kg IV divided into two doses (not to exceed 4 g/d).

Prevention and Control

- **Chemoprophylaxis :** as soon as possible (ideally within 24 hours), limited or no benefit if given more than 14 days after the onset of disease
- Adults -
  - Ciprofloxacin single oral dose of 500 mg,
  - Rifampicin 600 mg 12 hourly for two days,
  - or ceftriaxone 250 mg IM single dose
  - Rifampicin should be avoided during pregnancy.
- Children - rifampicin 10 mg/Kg 12 hourly for two days (5mg/Kg for infants) or injection ceftriaxone 125 mg IM single dose.

Prevention & Control

- Chemoprophylaxis is not recommended during epidemics because of multiple and prolonged sources of exposure
- Logistic problems and high cost
- Secondary cases comprise less than 2% of all meningococcal disease
- Immunization using safe and effective vaccines is the only rational approach to the control of meningococcal disease

Meningococcal Vaccines

- Of the five common serotypes responsible for more than 90% of meningococcal disease, vaccines are available for group
- A, C, Y and W - 135.
- At present two types of meningococcal vaccines are licensed;
  - meningococcal polysaccharide vaccines (bivalent and quadrivalent) and
  - meningococcal conjugated polysaccharide vaccine.

Polysaccharide Vaccines

purified, heat - stable, lyophilized capsular polysachrides

- Bilvalent- against serogroups A and C,
- Quadrivalent against serogroups A, C, Y and W - 135.
- Single dose - of the reconstituted vaccine contains 50 µg of each of the individual polysaccharides.
- The dose for primary vaccination for both adults and children older than two years

is a single 0 .5 - ml subcutaneous

Polysaccharide Vaccines

purified, heat - stable, lyophilized capsular polysachrides

- Protective levels of antibody are usually achieved within 7 - 10 days
- The serogroup A and C vaccines have good immunogenicity, with clinical efficacy rates of 85% to 100% among children five years of age or older and adults.
- Serogroup Y and W - 135 polysaccharides are safe and immunogenic in older children and adults.
- Vaccination has been highly effective in the control of community outbreaks and epidemics in military centers.
- Carrier status is unaffected by vaccination
- Extremely safe, major drawback is the absence of activity against group B meningococci

Conjugated polysaccharide vaccine

- A quadrivalent A, C, Y and W - 135 conjugate vaccine has been licensed since January 2005.
- Contains 4 µg each of A, C, Y and W - 135 polysaccharide conjugated to 48 µg of diphtheria toxoid.
- Induce a T - cell - dependent response, resulting in an improved immune response in infants, priming immunologic memory and leading to a booster response to subsequent doses.
- These vaccines provide long - lasting immunity
- Nasopharnygeal carriage rates may also be decreased, reducing bacterial transmission.

Recommendations for use of meningococcal vaccine

- Routine vaccination is recommended for certain high - risk groups, including persons who have terminal complement component deficiencies and those who have anatomic or functional asplenia.
- Travelers above 18 months of age going to an area experiencing an epidemic or to areas with a high rate of endemic disease.
- Revaccination may be indicated for persons at high risk for infection particularly for children who were first vaccinated when they were less than four years of age; such children should be considered for revaccination after 2 - 3 years if they remain at high risk.