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Mahnoor Khan [a] Maham Jahangir [b] Khadija Ahmadi [c]

Risk Factors and Management of Bacterial Meningitis

Abstract *Meningitis is the infection of the spinal cord and brain. Bacterial meningitis is a great public health concern, especially in immunocompromised patients and children, particularly in underdeveloped counties. There are various types of bacterial meningitis (pneumococcal, meningococcal, listeria monocytogenes, neonatal, Hemophilus) having different rates of incidences and etiological agents. It occurs when bacteria get into the bloodstream from the nose, sinuses and ear. s. Infants and children are more susceptible to bacterial meningitis; similarly, alcoholics, smokers, malnutrient people, people with HIV and TB are at higher risks of this infection; all these factors must be taken into account to determine its severity. The diagnosis has critical importance and is considered one of the most urgent microbial medical emergencies. The use of vaccines is essential to eradicate this disease from the globe. This article highlights the risk factors, current diagnosis, treatment options and management plans in terms of bacterial meningitis.*

Key Words: Meningitis, S. Pneumoniae, HIV, Serotype

Introduction

Meningitis is a severe illness of meninges, which are the coverings of the brain and the spinal cord such as pia, arachnoid and subarachnoid space. Infection to these meninges is called meningitis. (Tonjum T. &.-N., 2013) The various causative agents of meningitis are viruses, bacteria, fungi or parasites and can affect adults, children and even infants. It can be hazardous and can cause severe impairments, especially when the diagnosis of bacterial meningitis is delayed; however, it can be treated if diagnosed earlier. (Runde TJ, 2021)

Bacterial Meningitis

It is an infection of meninges caused by bacteria. It can be life-threatening and needed quick diagnosis and treatment; it can be fatal and can damage brain as well if not treated on time. In most the cases, bacterial meningitis starts when bacteria enter the bloodstream from various routes like sinuses, throats and ears and then eventually (Runde TJ, 2021)

Types of Bacterial Meningitis

Pneumococcal Meningitis

It is because of *Streptococcus pneumoniae* and is the most general kind of bacterial meningitis, particularly in adults. (Torpy JM, 2007)

[a] Department of Pharmacy, Faculty of Biological Sciences, Quaid-e-Azam University Islamabad, Pakistan.

[b] Department of Pharmacy, Faculty of Biological Sciences, Quaid-e-Azam University Islamabad, Pakistan.

[c] Department of Pharmacy, Faculty of Biological Sciences, Quaid-e-Azam University Islamabad, Pakistan.

Meningococcal Meningitis

It is caused by the bacteria *Neisseria meningitidis;* it is commonly affecting children under the age of 5 and teenagers. It is mainly caused by three strains of *Neisseria meningitidis* (B, C & Y). However, strain B is more common among teenagers. (Torpy JM, 2007)

Listeria Monocytogenes Meningitis

The bacteria listeria monocytogenes resides in food, particularly in processed meats, pre-cooked meats in raw milk, hot dogs and cheese.

Pregnant women, infants and immunocompromised people are more susceptible to this form of meningitis. Expecting women can transfer this strain to their newborns resulting in neonatal meningitis. (Torpy JM, 2007)

Neonatal Meningitis

Newborns can acquire meningitis from bacteria like Group B streptococcus (GBS), E. coli.

- **GBS:** Infection from this strain is the main cause of neonatal meningitis. Infants get it from their mothers. Pregnant women have their test around 36-37 weeks of pregnancy and will be treated with antibiotics at the time of labor to prevent infection to babies.
- **E. Coli:** Pre-mature newborns are also at a higher risk of getting bacterial meningitis by E. coli. This bacterium is becoming resistant to antibiotics and it's hard to assess as well as hard to treat it. (Torpy JM, 2007)

Hemophilus (Hib) Meningitis

Hib was once a popular causative agent of bacterial meningitis particularly in children and infants but now due to the availability of Hib vaccine the incidences is much reduced. 48% of the cases were of bacterial meningitis. (Runde TJ, 2021)

Epidemiology of Bacterial Meningitis

Frequency of meningitis caused by bacteria is about 5–7 per 1,00,000 inhabitants. In advanced nations, *Neisseria meningitidis* and *Streptococcus pneumoniae* cause acute bacterial meningitis in children. (Tonjum T. &.-N., 2013)

Streptococcus Pneumoniae

This strain of bacteria is a popular reason of meningitis caused by bacteria globally. A survey was conducted, and it was assessed that 1.5 to 2 million people became victim of this infection per year and die Immunocompromised children are the major target of this disease. 156 studies were conducted, and it was issued in 2000. This assessed worldwide drain of disease resulted from pneumococcus in kids over the age of 5 years. There were 826,000 deaths and among these deaths 91,000 were HIV positive patients. Among them most of the 60% deaths took place in 10 different Asian and African countries. 6 per 100,000 was the lowest rate that was observed in Europe. The highest rate was observed in Africa which was 38 per 100,000. Vaccination against this disease is introduced and due to this vaccine, the occurrence of this disease reduced 1.09 per 100,000 in 1998–1999 to 0.81 in 2006–2007.

Neisseria Meningitidis

Six serogroups of *Neisseria meningitides* are there that can cause severe and life-threatening meningitis. *Neisseria meningitidis* can cause either an epidemic form of infection or endemic infection. There were around about 170,000 deaths due to this strain in 2010. In industrialized countries, the fatality rate is approximately 5-10%. These strains cause disease at the incidence of 1–3/100,000, which are endemic. Major cases of this disease were caused by Serogroup A and C in China and in the Middle East. 'Meningitis belt', which is present in Africa, can cause major sporadic epidemics because of the serogroup A that occurs after every 6–12 years, with attack rates of 5000/100,000 inhabitants. There is an increase in Serogroup Y strains in the USA and Sweden that is responsible for the majority of deaths there. (Tonjum T. &.-N., 2013)

Haemophilus Influenzae Type b

48% of all bacterial meningitis is caused by *Hemophilus influenzae type B* (Hib), but when the vaccination program of Hib was introduced, there was an extreme reduction in the cases of this meningitis. This now remains limited to the US and is observed in patients who are not vaccinated. However, the Hib in developing countries is still there because most of the people didn't have access to the vaccine causing a rise in the numbers of the patient suffering from this disease. Only 42% of children globally by 2007 had the facility of Hib immunization program.

Etiology of Bacterial Meningitis

Patients who are suffering from bacterial meningitis are more susceptible to high death and morbidity

chances which include newborns who are living in under-developed countries. (Tonjum T. &.-N., 2013)

Neisseria Meningitidis

It causes both endemic and epidemic meningitis. These bacteria have an outer membrane made up of protein, lipid, and polysaccharide. These bacteria have total 6 serogroups of Neisseria meningitides which can cause severe meningitis. (E. Umaru, 2013)

Streptococcus Pneumoniae

It is the popular reason of bacterial meningitis in European countries and the US. Along with a healthy kid it can be seen in children with asplenium or HIV infection. It is also common in patients having a cochlear implant. There is 30 times more risk of meningitis in patients having cochlear implants as compared to the normal ones. This bacterium will cross the barrier between blood and brain either transcellularly, paracellularly, or with the help of phagocytes that are infected as live bacteria.

Other Causative Agents

Table 1

Organism	Description
Haemophilus influenzae type B	It is a member of family pasteurellaceae. After vaccination program was introduced into the population, there were reduced incidences of this infection.
Group B streptococcus	Not a common pathogen but many cases were reported in neonates having meningitis by this strain in Europe.
Non typeable H. influenzae	This bacterium may cause infection in children under age 5. These pathogens are not the common cause of meningitis, but they were found to be the main leading cause of meningitis before the vaccination was introduced in children.
Escherichia coli	These infectious agents also cause meningitis in children below age 5. (E. Umaru, 2013)
Listeria monocytogenes	It is the gram-positive bacilli and is third most popular reason of bacterial meningitis.
Listeria monocytogenes	They cause infection in neonates and people over the age 60.
Staphylococcal species	Staphylococcal meningitis is caused by this species and this infection is severe and is life-threatening and can even cause death (Flower, 2012)

Routes of Infection

Meningitis is a serious infection that occurs when bacteria get into your bloodstream from your ears, sinuses, and throat. This bacterium will then travel from your blood to your brain, surpassing the blood-brain barrier causing the inflammation of meninges. Transmission of meningococcal usually occurs through the respiratory droplets that can take place. (Tonjum T. &.-N., 2013)

Risk Factors of Meningitis

Following are the major risk factors that are associated with meningitis. (Flower, 2012)

Age

The major factor that is associated with meningitis is age. Meningitis is more common in neonates, children, and adults above the age of 60. Neonates who usually include pre-mature or term babies up to 3 months of their birth, it has been seen that group B streptococci (subtype III strain) are the major cause of meningitis in them. When different studies were considered, it was noted that meningococcal meningitis or Neisseria meningitidis were more common in the age group between 1-19.

Social Behavior Related Risk Factors

Smoking

One of the major risk factors of meningitis is smoking. The type of meningitis associated with this social behavior is meningococcal disease, or we can say or Neisseria meningitidis. Some studies were carried out in Britain, which shows that meningitis in young children has some relationship with smoking. The more people smoke, the more they have the chance of developing meningitis. Tobacco smoke can carry bacteria which means that people have greater chances of pathogens entering their bodies. Tobacco smoke is a risk factor as it decreases the resistance ability of nasopharyngeal mucosa against the attack of meningococcal disease.

Alcoholism

A study was conducted on alcoholic and non-alcoholic patients, and it was concluded that alcoholic patients were more susceptible to meningitis. The bacteria that was responsible for meningitis in the alcoholic patient were S. pneumoniae and L.

monocytogenes. The cause of bacterial meningitis in alcoholic patients was due to the fact that alcoholic patients are more likely to suffer from cardiorespiratory failure; also, the alcoholic patients have low leucocytic count, due to which they can't show their full ability to fight with these bacteria and protect the body. (Tonjum T. &-N., 2013)

Lifestyle-Related Risk Factors

Travelling

Frequent travelling to the areas where meningitis infection is common can really cause an increase in chances of getting this infection. Avoid travelling to the most susceptible regions where the infection is most common in order to avoid this meningitis.

Working with Animals

Among humans, the zoologists were the common people who were infected by this meningitis. Meningitis is common in animals, and it can be transferred from humans to animals.

Poor Living Conditions

Meningitis can be triggered by poor living conditions. A lot of studies have shown that meningitis is directly related to poor housing conditions and household overcrowding People living in crowded areas or children in daycare are more susceptible to this meningitis. As more cases of meningitis, specifically meningococcal disease, occurs when transmitted from patient to person from nasopharyngeal so this transmission from person to person is easy in overcrowded areas. (Flower, 2012)

Health-Related Risk Factors

Malnutrition

In under-developed countries, malnutrition is common among people, especially children. Children suffering from malnutrition are more prone to infections and mortality. The immune system of these children is also impaired, so when a pathogen enters their bodies, their immune system does not defend the body against that pathogen and cause meningitis.

HIV

A study was conducted in Indonesia where it was concluded that this infection was very usual among HIV positive people and was the major reason for death among patients. These HIV patients are immunocompromised. In HIV positive patients, tuberculosis is the major cause of meningitis. The immune system of meningitis is also weak, making the body more prone to bacteria causing meningitis.

Tuberculosis

Tuberculosis is an airborne and contagious disease that specifically lungs. The bacteria causing tuberculosis mycobacterium tuberculosis can quickly travel to the blood-brain barrier and cause the inflammation of meninges, and became a reason of meningitis, a condition known as meningeal tuberculosis. (Flower, 2012)

Septic Shock

Neisseria meningitidis can cause septicemia. This condition is called meningococcal septicemia. In this condition, the bacteria usually enter the bloodstream, and there it multiplies, causing damage to blood vessels. Due to this damage, there will be a capillary leakage causing the blood to go to different organs. This bacterium will cross the blood-brain barrier, causing meningitis.

Diabetes Mellitus

Diabetic patients are double the risk for meningitis. Diabetes can cause an immune-compromised state which will lead to a decreased efficacy of cell-mediated immunity. There will also be a decrease in the level of leucocytes and monocytes, ultimately leading to impaired immunity.

Respiratory Tract/Viral Infections

Several studies were carried on risk factors of meningococcal meningitis, which indicates that respiratory tract infection or viral infections, particularly influenza is a major one.

Asplenia

Asplenia is a condition in which the spleen is absent, and this spleen is removed from the patient through Splenectomy. Sometimes after this splenectomy, infection occurs, which become a major reason for meningitis. The bacteria causing this infection, particularly in these patients, is pneumococcus. (Flower, 2012)

Climate Conditions

In seasonal rise of meningococcal disease, climate conditions play an important role. (Tonjum T. &-N., 2013)

Geographical Area

Meningitis belt is defined as it is where meningitis incidences are common and occur frequently within a year. This area is between latitudes 4° and 16° north and is present in sub-Saharan Africa. In this belt, there is a low temperature at night, which is maybe 10C during the dry season, which will cause a strong impact of harmattan on nasopharyngeal on person's mucosa, which will then cause meningococcus to attack the person.

Pathogenesis of Meningeal Pathogens

Meningeal pathogens have the potential to traverse blood brain barrier and invade the meninges and contract the disease. The means of access for these pathogens into the body is the nasopharynx in the non-existence of any neurosurgery, craniotomy, or cerebrospinal fluid leak. These pathogens can inhabit and colonize the nasopharynx resulting in the asymptomatic phase of the disease. 4 days can be the average incubation period for this disease. The disease is progressed further by the passage of bacteria into the blood. After surviving the host's lines of defenses, the bacteria can successfully pervade the blood-brain barrier. Traversing into meninges, it strongly reproduces in the subarachnoid space, causing meningitis with the induction of inflammation by pro-inflammatory cytokines. (Tonjum, 2013)

Pathophysiology of Bacterial Meningitis

Inflammatory host response in meningitis is mainly induced by numerous virulence factors or cellular structures of meningeal pathogens such as polysaccharides or teichoic acid. The attachment of lipoteichoic acid to CD14 receptors causes immune activation, which expresses itself with TLR-2 receptors. It brings about the leukocyte infiltration into the subarachnoid space. MAPK pathway is activated by these inflammatory stimuli, resulting in signal transduction and the activation of a variety of transcription factors. Several pro-inflammatory mediators are produced, such as TNF-alpha, IL-6 and IL-beta, which are involved in the inflammation process. The expression of chemokines and adhesion molecules is also stimulated by Tumor necrosis factor-alpha & Interleukin -1 beta, which causes the traversal of leukocytes from the bloodstream into subarachnoid space by a multistage process via adhesion receptors. This multistage process has 4 concomitant steps, which include tethering, triggering, firm adhesion & emigration entailing selectins & integrin molecules. Their activation is triggered by IL-1beta and IL-8. All this process sequentially increases the penetrability of the B-B barrier and the outflow of plasma proteins within the subarachnoid space, which causes the eradication of bacteria but can also have damaging effects on the CNS and lead to permanent brain damage & neuronal death. (Tonjum T. &.-N., 2013)

Clinical Features

Some can show minute symptoms, and others can have no symptoms at all. Some infants might experience pyrexia, exhaustion, poor feeding, hypothermia, irritability, diarrhoea, seizures, vomiting, respiratory distress, or bulging fontanelles. Some infants may also develop nuchal rigidity at a certain stage. Clinical symptoms in young children are photophobia, fever, nausea, headaches, vomiting, lethargy, irritability & confusion.

When the physical examination was done, other indications of bacterial meningitis were discovered, which includes, Kernig's signs and Brudzinski's neurological focal findings. 75% of children may experience irritation in the meninges. The assemblage of bradycardia increased blood pressure, and Cushing's triad is a late sign of increased intracranial pressure.

The Disease

usually begins abruptly with headache, meningeal signs include-ing stiffness of the neck, and fever. However, classic signs of meningitis (i.e., confusion, headache, fever, and nuchal rigidity) are seen in only about one-half of infected patients.

This disease starts with a sudden attack of severe headache and some meningeal signs, which include nuchal rigidity, and pyrexia whereas, the old and typical symptoms of meningitis are confusion, headache, pyrexia, and nuchal rigidity.

Ecchymotic skin lesions can cause advanced infections that can cause necrosis. However, skin lesions can be in the form of dysplastic nevi, evanescent, or overall absent in the person who has meningococcal sepsis that ultimately causes tissue death which further causes coagulopathy, decreased blood pressure, and Waterhouse–Frederiksen syndrome. Gangrene can be caused in the extremities due to thrombosis, and cardiovascular collapse can also take place, leading to death. (Scheld, 2013)

Diagnosis

Pleocytosis, Gram staining both with and without Cerebrospinal fluid cultural identity, or blood or skin lesions are used to identify meningococcal meningitis and pleocytosis; Gram stain with any kind of culture is used to make a diagnosis. When there are no rash or meningeal symptoms, it is difficult to diagnose meningococcemia early. In individuals with severe meningococcemia, primarily, general signs of sepsis-like leg ache appear (Tonjum T. &., january,1984) . Meningococcal and pneumococcal infections, however, do not cause these symptoms. Parents and relatives should examine a feverish child or adult for rash. The doctors, along with nurses, must take parents' or relatives' worries seriously if they describe a patient's abrupt or rapid deterioration.

Laboratory Diagnosis of Meningitis

In order to accurately identify all kinds of meningitis, it is necessary to evaluate the CSF. Skin biopsies, blood, Cerebrospinal Fluid, aspirates, and nasopharyngeal swabs are utilized as a specimen for the detection of this disease if it is clinically indicated. Because pneumococci and meningococci are prone to desiccation and severe temperatures, after collection, samples must be cultured as fast as possible. **Gram and acridine orange stain** are used to analyze material for **preliminary diagnosis**. If the Cerebrospinal Fluid is hazy, acridine orange-and gram-stained samples are prepared straight from the Cerebrospinal fluid or after centrifugation if the Cerebrospinal Fluid is clear. Gram-negative diplococci and polymorphonuclear cells can be seen in the smears when Cerebrospinal Fluid bacterial count is >105/ milliliter. Almost 25% of the total sample will taint when the bacterial density in the CSF is less than 103 milliliters. 60–90 percent of the surveyed Cerebrospinal fluid sample must stain positive that are also cultured positive. 62% of the total patients identify meningococci in them by the method containing **gram stain smears** with the culture from the petechial skin lesion which is related to the disease (Stephens DS, 2007 Jun) we can do latex agglutination and conglutination with for serogroups identified meningococcal capsular polysaccharides directly in Cerebrospinal Fluid (Javid)These approaches are highly sensitive and used for direct identification of meningococci in blood and Cerebrospinal Fluid by Nucleic acid amplification tests or Polymerase chain reaction (Chanteau, 2007),they can be used to confirm a diagnosis in individuals who have been treated with antibiotics before taking a sample or who have tested negative in all previous tests like antigen test, culture and Gram stain.

Gram-positive stains were present in 90% of the children having pneumococcal meningitis. Among this, almost 80% of patients have meningococcal meningitis, which is particularly present in children; approximately half of the patients were identified with Gram-negative bacillary meningitis, and almost one-third of patients have been affected from Listeria meningitis (Flower, 2012). The percent of samples that stain favorably rises when Cerebrospinal fluid is elucidated by Cytospin centrifugation (La Scolea LJ Jr, 1984). A differential diagnosis of various kinds of meningitis is typically aided by Cerebrospinal Fluid cell counts and differentials, as well as glucose and protein concentrations.

The clinical materials should be infused on both nonselective and selective mediums of growth in order to isolate *Neisseria meningitidis* (Olson MM, 1994 Jun). Pneumococci and meningococci are cultivated on medium containing at 35–37°C (95–98.6°F) in a carbon dioxide-enriched, somewhat humid atmosphere. Translucent, greyish-brown 1–3 mm clusters of *S. pneumoniae* or *N. meningitidis* emerge after almost 18–24 hours that can be studied with Gram staining procedures (Olson MM, 1994 Jun). The presence of catalase- and oxidase-positive Gram-negative bacteria is enough to establish a meningococcal illness diagnosis. Opochin-sensitive bacteria with a distinctive central umbilicus recognize *S.pneumoniae.* To validate the separation of *S. pneumoniae* and *N.meningitidis*, methods like an amplification of nucleic acids such as (NAATs/PCR), MALDI/TOF analysis, sequencing of DNA can all be utilized.

Non-Culture Methods

These tests are basically used for fast pathogen identification Examples of such testing include PCR, latex agglutination, biochip or microarray, loop-mediated isothermal amplification, and immunochromatography.

Latex Agglutination

It involves the use of latex beads that have been coated with microbe-definite antibodies; the antibody-coated latex beads agglutinate visibly because of homologous antigen. Surveillance study of pneumococcal meningitis shows that latex agglutination was tested positive in 50 (67 percent) of 74 cerebrospinal fluids.

Multiplex Polymerase Chain Reaction

Also, conventional proves is effective in detecting invading germs in a person who already has taken antibiotics (Runde TJ, 2021). Pathogen detection in Cerebrospinal fluid may benefit from complex Polymerase chain reaction or broad-range PCR. In those individuals who had received antibiotics previously, the detection frequency with Polymerase Chain Reaction was greater than with that cultures (Runde TJ, 2021). However, the detection limit varies amongst tests. Cerebrospinal fluid, Polymerase chain reaction has shown to recognize even the 2 copies of *S. pneumoniae*, *E. coli and* N. *meningitidis*, (Runde TJ, 2021),

Furthermore, utilizing serotype-specific primers, PCR-based serotyping of *S. pneumoniae* should enhance the determination of pneumococcal serotype distribution in circumstances where prior antibiotic usage is significant. The results can be seen with naked eyes using color or turbidity development by SYBR green, and also, it does not require a thermocycling device, so it is popular.

Nucleic Acid Amplification Test

A newly discovered isothermal amplification test, which is involved in the amplification of DNA under constant temperature settings (63 C), it is a potential technique, mainly in source-limited situations. The assay detected 10 transcripts of *S. pneumoniae* in oral mucosa swab specimens.

Biochip or Microarray

Pathogen detection utilizing a biochip or microarray involves the withdrawal of DNA of the genome from Cerebrospinal fluid, hybridization of labeled DNA and amplification of targeted DNA, having oligonucleotide probes halted on a microarray. In 122 children suffering from pneumococcal meningitis, a quick immunochromatographic test was carried out in which *S. pneumoniae* was evaluated (Runde TJ, 2021).

Immunochromatography

This test was used for the diagnosis of pneumococcal meningitis as it was 100 percent sensitive to detection of pneumococcal meningitis, compared to latex agglutination (86% sensitivity) and Cerebrospinal fluid culture (71% sensitivity), which suggest that immunochromatography may be suitable for the diagnosis of pneumococcal meningitis.

World Health Organization assessments may have underestimated the true illness burden. Further, it might be owing to a lack of resources to make a diagnosis. At least one laboratory for meningococcal disease surveillance is accessible in many poor countries, but not all, although there are some restrictions in the availability of typing and diagnostic procedures that can cause underestimating of disease burden. (Runde TJ, 2021)

Prognosis

Mortality increases exclusively in bacterial meningitis.57% in meningococcal sepsis, 7% of meningococcal meningitis and 30% of pneumococcal. In bacterial meningitis, morbidity is more common. Studies reported 50% cases of focal neurological deficits, 14% cases of moderate to severe disability and 14% of hearing impairment. The mortality rate for bacterial meningitis is 10-15%. Early recognition of bacterial meningitis is essential for survival, which is followed by appropriate antibiotic therapy. It can cause increased intracranial pressure due to delay in treatment and ultimately lead to death. (Michael J Griffiths, 2018)

Management

The administration of antibiotics is essential. If there is a delay in the administration, e.g., 3 to 6 hours, the chances of mortality will increase. The selection of antibiotics depends upon the type of bacteria identified. If the diagnosis is delayed, treatment with ceftriaxone should be considered. Patients should receive ampicillin who are immunocompromised or older than 50. Patients with bacterial meningitis need to be covered for aerobic gram-negative organisms and *Staphylococcus aureus*. Patients should receive ceftazidime or cefepime and vancomycin. For HSV coverage Acyclovir should be administered. Decadron may increase survival if it is given for *S. pneumoniae* infections. Patients having bacterial meningitis should be monitored carefully and should be kept in observation until they have taken 24 hours of antibiotics. People who were in close contact with the patient should also be monitored and treated accordingly. Cephalosporin, including Ciprofloxacin and ceftriaxone can be used. Close contacts mean those people who were at a distance of 3 feet from the patient for more than 8 hours during a week before and after taking antibiotics for 24 hours. (Runde TJ, 2021)

Treatment

Antibiotic therapy is important in immediate

treatment. Before treatment, a blood culture should be taken, and the following factors should be considered like patient age, antibiotic resistance rates, resources and predisposing conditions. (Runde TJ, 2021)

Table 2

	Pathogens	Antibiotics
Neonates	Gram-negative (*E. coli*, *Klebsiella*, *Enterobacter, Proteus*)	Cephalosporin, ampicillin
Children and Infants	*N. meningitides, S. pneumoniae*	Cephalosporin or rifampin
Adults	*N. meningitidis, L. monocyte genes*, *(H. influenzae)*	Cephalosporin, ampicillin
Nosocomial, trauma, ventriculitis,	Staphylococci, Gram-negative, *P. aeruginosa*	vancomycin, rifampicin or Fosfomycin
Immunocompromised patients	*Enterobacteriaceae, S. pneumoniae, P. aeruginosa*	Cephalosporin, ampicillin, vancomycin

No bacterial infection worldwide has undergone a more spec-tacular evolution in epidemiology than acute meningitis since 1990.

Prevention

Prevention of meningococcal and pneumococcal disease is based on chemoprophylaxis and vaccination (Rosenstein et al. 2001). The advancement of vaccine design in enhancing immunoge-nicity has been shown to be important in preventing meningitis caused by Nmeningitidis and Spneumoniae. Protein-conjugated capsular polysaccharide vaccines have almost completely eliminated meningitis caused by vaccine serotypes. Meningococcal Capsular Vaccines. Meningococcal polysac-charide vaccines reduce the incidence of infection among mili-tary recruits, reduce the progress of epidemics of serogroup A disease, and protect susceptible complement-factor-deficient individuals (Stephens et al. 2007). Capsule polysaccharide vac-cines are available for the pathogenic meningococcal serogroups A, C, Y, and W-135. These vaccines are safe with mild local adverse events and have good efficacy (>85 %) in older children and adults. However, due to lack of a T-helper response, the vaccines are poorly immunogenic below 2 years of age, fail to induce immunological memory, and provide protection for only 3–5 years. Polysaccharide vaccines are used by travelers visiting countries with a high incidence of meningococcal disease Since 1990 bacterial meningitis has undergone tremendous evolution as compare to other bacterial infection (Scheld WM, 2002). Meningitis is caused by three types of bacteria: *N. meningitis, S. pneumonia* and Haemophilus influenza type b. This disease can be prevented through chemoprophylaxis and vaccination. (Rosenstein NE, 2001)

Vaccination

It has been seen that meningitis caused by *N-meningitides* and *S. pneumoniae* can be prevented through advancement in vaccine design that enhances immunogenicity. Studies show that polysaccharide vaccine against Meningococcal disease decreases the frequency of infection in military recruits. (DS., 2007). Vaccines such as capsule polysaccharides are accessible only for the 4 meningococcal serogroups in children and adults; such vaccines have been found to be effective with efficacy more than 85% and mild adverse events. However, this vaccine is not effective in children under 2 years of age because of lack of T-helper response. Polysaccharide vaccine can provide immunity up to 3–5 years. There is an advancement of vaccine development against meningitis disease characterized by the development of meningococcal polysaccharide and protein conjugates that has been introduced in several parts of the world, such as USA, Canada, UK, and several other parts of Europe. (Snape M, 2005) These vaccines are found to be safe and cause immunogenicity in children and induce immunological memory. Recently, second-generation conjugated vaccines have been launched such as PCV10 and PCV13. Vaccine development against serogroup B is still challenge (R., 2012)because the capsule of serogroup B has structure similar to polysialic structures. Developed outer membrane vesicle (OMV) vaccines have efficacy to almost 50–80 % but it is not efficient in children and these vaccines work against specific strain. (R., 2000)

Chemoprophylaxis

It helps in order to prevent the outbreak of the

disease. People belonging to different age groups and communities who are at a higher risk of having bacterial meningitis are treated with different antibiotics such as ceftriaxone, azithromycin, rifampicin and quinolones but can't be used for complete eradication of the disease. The risk of infection in household members is 150-1000 times that general population. (Deghmane A-E, 2009)

Different Challenges and Future Opportunities

Bacterial meningitis continues to be an important cause of mor-tality and morbidity throughout the world, with differential risk for disease among small children, individuals living in low-income countries, and due to infection with antimicrobial- or multidrug-resistant pathogen. Vaccination with protein-conjugated H. influenzae type b, S. pneumococcus PCV, and N. meningitidis Mencevax ACWY has successfully reduced worldwide incidence of meningitis; this raises the hope that other conserved bactericidal epitopes exist and can be identified and exploited in a similar manner. Unfortunately, conjugated vaccines have so far been introduced only in the developed world, even though the highest incidence of meningococcal and pneumococcal invasive diseases occurs in less affluent countries. Host receptors and signal transduction pathways involved in the microbial invasion of the BBB might represent potential targets for novel therapeutic approaches for meningococcal and pneumococcal disease (Huang and Jong 2009). Using a model system that analyzed penetration of the BBB by E. coli, a proof-of-concept study suggested that the HBMEC receptor for CNF1 (RPSA) and cytosolic phospholipase A2a might represent such ''druggable'' targets, at least for E. coli, but potentially also for meningococci and pneumococc Meningitis caused by bacteria is a fast-evolving microbe as compared to other microbes therefor it is the major reason of high death rate among children and people living in low-income countries. Bacterial meningitis has gained multidrug resistance because of its fast-evolving capabilities. Although protein conjugated vaccine against Hib, *S. pnemoniae* and *N. meningitidis* has reduced the world-wide incidence of this disease and have raised hopes among people but unfortunately the developed countries have this privilege of getting the conjugated vaccines. Another challenge faced by the researchers are the lack of information of molecular mechanism of action of meningococcal and pneumococcal infections which is needed for the advance and novel therapeutics and preventive approaches. This knowledge will help the researchers to enhance the knowledge of bacterial emergence, genome structure, pathogenesis, gene transfer and immune responses. Studies of pathogenicity and genetics of *bacteria* reveals the evolving, spreading and disease-causing ability of these pathogens in humans. (Rosenberg E, 2013)

Conclusion

Meningitis-associated brain injury and neuronal death is not mediated simply by the presence of viable bacteria but occurs as a consequence of the host reaction to bacterial components. A wide variety of inflammatory host factors involved in the complex pathophysiologic cascade of bacterial meningitis have been identified during the past decade, largely with experimen-tal studies, but have also been confirmed in limited studies of human material. The crucial role of the caspase 1–IL-1b path-way in the induction and amplification of the host inflammatory response during pneumococcal meningitis may lead to the iden-tification of new potential therapeutic adjunctive agents. Sim-ilarly, peroxynitrite and other important effector molecules con-tributing to BBB disruption and neuronal injury may be susceptible to adjunctive treatments. Lipid peroxidation and the activation of PARP-1 are also Meningitis is a disease associated with neuronal death and brain injury. The mode of this disease is not only through the bacteria but also occur through host reaction to certain components of bacteria. Multiple inflammatory host factors against this disease have been identified through experimental studies in past decades, such as, caspase 1–Interleukin -1b pathway that induces and amplifies the inflammatory response of host during pneumococcal meningitis. This can help in identification of new effective therapeutically strong adjunctive agents. The most promising adjunctive therapeutic strategy is through interference with the lipid peroxidation and the activation of Poly [ADP-ribose] polymerase 1. Further studies of these pathways can help developing therapeutically effective adjunctive strategies in bacterial meningitis and different inflammatory conditions of CNS such as, ischemia, hemorrhage, meningo-encephalitis etc.

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