# MENINGITIS CAUSED BY STREPTOCOCCUS PNEUMONIAE, CAUSES, SYMPTOMS AND TREATMENT: A REVIEW

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**Abstract:** Meningitis is a serious infection of the meninges, the thin layers of tissue that surround and protect the brain and spinal cord. Although most cases of meningitis are caused by viruses, bacteria can also cause this potentially life-threatening condition. Streptococcus pneumonia is a type of bacteria that is a common cause of meningitis, particularly in young children and adults over age 65. This bacterium can also cause other serious infections, such as pneumonia and blood poisoning (sepsis). Symptoms of meningitis can include headache, stiff neck, fever, confusion, and seizures. Meningitis is most often caused by infections with viruses or bacteria, but can also be caused by other things like cancer or certain drugs. Treatment for meningitis generally includes antibiotics or antiviral drugs, depending on the cause.

**Keywords**: Meningitis, Meningitis Causes, Meningitis Symptoms, Streptococcus Pneumonia

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## INTRODUCTION

Meningitis history is long and complicated. It is believed to have originated in Africa during 1905-1908. Meningitis is still a serious public health problem in many parts of the world [1]. Each year, approximately 1.2 million cases of Meningitis worldwide which may lead to approximately 250,000 deaths [2]. The most common form of Meningitis is bacterial, which several different bacteria can cause. Viral Meningitis is also common but less severe than bacterial Meningitis and usually resolves independently without treatment [3].

Meningitis is a severe infection of the meninges, which are the protective membranes that surround the brain and spinal cord. Inflammation in Meningitis is the body's reaction to an infection or injury [4]. It is a normal immune system response, but in Meningitis, it can become life-threatening. The inflammation begins when white blood cells and other chemicals are released into the bloodstream to fight an infection or repair damaged tissue. This release of substances causes blood vessels to widen and leak fluid into nearby tissues [5]. The leaked fluid accumulates and puts pressure on the brain, which can cause serious problems [6].

Although several different organisms can cause Meningitis, bacteria are the most common cause in developed countries [7]. Meningitis is severe and can lead to death or permanent disability if not treated promptly and adequately. Meningitis is caused by an infection of the meninges, the protective membranes surrounding the brain and spinal cord. The most common cause of Meningitis in developed countries is bacteria, but viruses, fungi, or parasites can also cause it [8]. Meningitis is a severe illness that can be fatal or cause permanent disability if not treated promptly and properly [9].

**Symptoms**

The early signs and symptoms of meningitis can develop over several hours or even 2 to 3 days. They include fever, headache, stiff neck, vomiting, confusion or sleepiness and sometimes a rash [10]. A stiff neck is often more prominent in young children with meningitis. In newborns and infants, the classic signs and symptoms are often subtle [11]. The infant may only appear fussy or lethargic. A bulging fontanel — the soft spot on top of a baby's head — is another common sign of meningitis in infants younger than 2 months old [12].

Symptoms of strep throat may include fever, headache, sore throat, difficulty swallowing, and neck stiffness [10]. Symptoms of meningitis may include nausea or vomiting, high fever, stiff neck, seizures (fits) and sensitivity to light. Laboratory results may be normal or return with a high fever [11]. There are many products designed to help prevent the spread of disease. For example, one product called Fluconazole treats both strep throat

and meningococcal infections and has been shown to reduce the need for hospitalization in children with these infections [13].

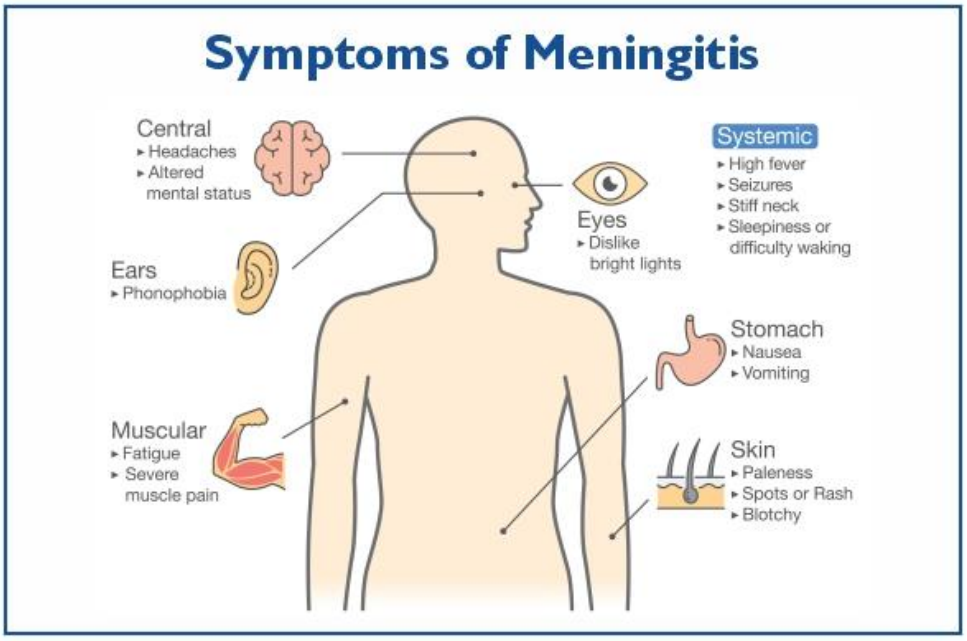


**Fig.-1: Symptoms of Meningitis [14]**

## Types of Meningitis

There are four types of meningitis: aseptic, bacterial, viral, and fungal. Aseptic meningitis is the most common type and is usually caused by a virus or infection. Bacterial meningitis is more serious and can be life-threatening [15]. It is often caused by bacteria such as Streptococcus pneumoniae *or Haemophilus influenzae* type b [16]. Viral meningitis is usually less severe than bacterial meningitis but can still be serious. It is often caused by viruses such as herpes simplex virus, Enterovirus, or West Nile virus. Fungal meningitis is the least common type but can be very serious if not treated promptly. It is usually caused by fungi such as Cryptococcus neoformans or *Candida albicans* [17].

## Anatomy of the Brain

The brain is a complex and fascinating organ. It is the centre of the nervous system, controlling all thoughts, feelings, and movement. The brain has three main parts: the cerebrum, the cerebellum, and the brainstem [18]. The cerebrum is responsible for consciousness, voluntary movement, and higher cognitive function.

It consists of two hemispheres (left and right) connected by a bridge of nerve fibers called the corpus callosum [19].

The surface of the cerebrum is covered in a layer of tissue called grey matter, which contains most of the brain's neurons (nerve cells). The cerebellum controls balance and coordination. It consists of two halves connected by a bridge of nerve fibers called the pons [20]. The surface of the cerebellum is covered with a thin layer of grey matter called the cerebellar cortex. Underneath the cortex is white matter, made up of nerve fibers that connect the different parts of the cerebellum. The largest part of the cerebellum is made up of the two hemispheres, which are separated by a deep groove. The hemispheres are connected by a bridge of tissue called the vermis [18-20].

**Diagnosis**

Meningitis is diagnosed through a spinal tap to look for increased white blood cells and inflammation in the cerebrospinal fluid [22]. A lumbar puncture is performed by numbing the lower back and inserting a needle between the vertebrae into the spinal canal. A small amount of cerebrospinal fluid is removed and sent to a laboratory for analysis. The procedure is also called a spinal tap [23].

A lumbar puncture, also known as a spinal tap, is a diagnostic procedure used to collect cerebrospinal fluid (CSF) for testing. CSF surrounds and cushions the brain and spinal cord and helps to remove waste products from these organs [24]. During a lumbar puncture, a thin needle is inserted into the lower back, between the spine's bones, and into the CSF-filled space around the brain and spinal cord. A small amount of CSF is then withdrawn for testing [25].

**Pathogenesis of Meningitis**

Streptococcus pneumoniae is spread through contact with respiratory secretions, such as saliva, mucus, or cough droplets from an infected person [26]. The bacteria can also be spread through contact with objects or surfaces contaminated with respiratory secretions. Once inside the body, Streptococcus pneumoniae colonizes the upper respiratory tract and begins to multiply. In some cases, the bacteria invade more profound into the lungs, where they can cause pneumococcal pneumonia, a severe lung infection [27].

In other cases, *S. pneumoniae* invades the bloodstream and spreads to other body

parts, including the meninges (the protective membranes covering the brain and spinal cord) [28]. This invasion of Meningitis is an infection of the meninges, the protective layer surrounding the brain and spinal cord. Meningitis caused by *Streptococcus pneumoniae* is the most common type of meningitis [26].

Streptococcus pneumoniae is a bacterium that can cause several different infections, including meningitis [29]. When *Streptococcus pneumoniae* infects someone's lungs, it can spread to their bloodstream and other body parts. This is how *Streptococcus pneumoniae* can cause meningitis in people with other health conditions, such as diabetes or HIV/AIDs. People usually get strep throat (a throat infection caused by *Streptococcus pneumoniae*) around the time they are exposed to other people [30].

**Etiology of Meningitis**

Meningitis etiology is typically divided into several categories, which include: bacterial, viral, fungal, parasitic, and non-infectious. The most common cause of meningitis is a virus, with bacteria causing about 20% of cases and fungi causing about 1% of cases [31]. Meningitis can also be caused by physical injury (trauma) or cancer. The most common types of meningitis are bacterial and viral [32].

Bacterial meningitis is usually caused by one of three types of bacteria: *Streptococcus pneumoniae, Neisseria meningitides, or Haemophilus influenza* [33]. All three of these bacteria can also cause other diseases such as pneumonia or sepsis (blood infection). Viral meningitis is most commonly caused by enteroviruses, which are a group of viruses that includes polioviruses, *Coxsackieviruses*, echoviruses, and others. These viruses are spread through contact with respiratory secretions or stool (feces) from an infected person [34].

Meningitis is a serious infection of the meninges, the protective membranes covering the brain and spinal cord [35]. It can be caused by bacteria, viruses, or other microorganisms. Pro-inflammatory cytokines and chemokine play an important role in the development of meningitis. These substances are released by cells in response to infection or injury and cause inflammation [36].

The pro-inflammatory cytokines and chemokine’s involved in meningitis include interleukin-1 (IL-1), interleukin-6 (IL-6),

tumor necrosis factor alpha (TNFα), and monocyte chemotactic protein 1 (MCP-1) [37]. These molecules cause increased production of white blood cells and fluids, which results in swelling and pressure on the brain. Treatment of meningitis typically involves antibiotics to kill the causative agent, as well as supportive care to reduce symptoms [38].

**Phases of Meningitis**

**Adhesion**

Pneumococcal meningitis is the presence of S. pneumoniae bacteria in the nasopharynx. These bacteria can colonize the nasopharynx by binding to epithelial cells via adhesion [39]. Once these bacteria have colonized the nasopharynx, they can invade the bloodstream and cause meningitis. The symptoms of pneumococcal meningitis include headache, stiff neck, and fever. If left untreated, this disease can lead to death [40].

**Invasion**

The second step in initiating pneumococcal meningitis is the invasion of bacteria into the bloodstream [41]. This step is facilitated by several virulence factors possessed by the bacteria. Pneumococci can attach to and invade various host cells, including endothelial and epithelial cells. The interaction between the bacterial surface proteins and receptors on host cells allows for the entry of the bacteria into the host cell. Once inside the host cell, Streptococcus pneumoniae can multiply and spread to other nearby cells [42].

**CNS invasion**

CNS invasion by tumour cells is a hallmark of high-grade brain tumour and the main reason these tumour are so difficult to treat. The blood-brain barrier (BBB) protects the CNS from foreign invaders, but cancer cells can exploit this barrier and invade the brain. Once inside the brain, tumour cells can grow and spread quickly, leading to serious neurological problems and death [43]. There are currently no effective treatments for CNS invasion by tumour cells, which is why preventing this tumour from developing in the first place is essential.

CNS invasion in meningitis can lead to cerebral abscesses, and pus-filled lesions that form in the brain. These abscesses can cause a range of symptoms, including headaches, seizures, and changes in mental status. If not treated promptly, cerebral abscesses can be fatal [44].

**Neuronal Injury**

Neuronal injury in meningitis results from the release of pro-inflammatory cytokines and chemokine, which recruit and activate leukocytes, resulting in direct injury to neurons. Cytotoxic T cells are also activated in meningitis and can damage neurons directly. The death of neurons leads to cerebral edema and increased intracranial pressure, which can further damage brain tissue [45].

**Treatment**

Meningitis is a serious, life-threatening illness. Early diagnosis and treatment is essential. Treatment usually involves hospitalization and antibiotics [46]. In some cases, corticosteroids may also be used to reduce inflammation. If meningitis is caused by a bacterial infection, the patient will usually be given intravenous (IV) antibiotics [47].

If the patient has a viral infection, they will usually be treated with supportive care to help relieve symptoms [48]. Meningitis is a serious condition that can lead to death if not treated early. The mainstay of treatment for meningitis is antibiotics, which must be given intravenously if the patient has a bacterial infection. Corticosteroids may also be used in some cases to reduce inflammation around the brain and spinal cord. Patients with meningitis caused by a viral infection will typically receive supportive care to help manage their symptoms [49].

Bactericidal therapy targeting Gram-positive bacteria is the mainstay of treatment for serious S. aureus infections, with Vancomycin being the agent most commonly used. However, the emergence of Vancomycin-resistant strains of *S. aureus* (VRSA) has limited the usefulness of this drug [50]. Linezolid is an alternative bactericidal therapy with activity against Gram-positive bacteria, including VRSA. This agent inhibits protein synthesis by binding to bacterial ribosomes. Clinical studies have demonstrated that linezolid is effective in the treatment of various types of infections caused by Gram-positive bacteria, including VRSA infections [51].

**Ampicillin plus Broad-spectrum Cephalosporin**

Ampicillin and cephalosporin mechanism of action are very similar and used in the

treatment of *S. agalactiae, E. coli, or L. monocytogenes* [52]. Both drugs are beta-lactam antibiotics that work by inhibiting bacterial cell wall synthesis. This ultimately leads to cell death. Both bind to and inhibit bacterial penicillin-binding proteins (PBPs) [53].

PBPs are enzymes involved in the final stages of peptidoglycan synthesis, which is an important component of the bacterial cell wall. By inhibiting PBPs, ampicillin and Cephalosporins prevent the cross-linking of peptidoglycans, leading to cell lysis [54]. The main difference between the two drugs is their spectrum of activity. Ampicillin has a narrower spectrum of activity than cephalosporin and is effective against gram-positive bacteria while cephalosporin has a broader spectrum of activity and is effective against both gram-positive and gram-negative bacteria [54].

**Ampicillin plus Broad-spectrum Cephalosporin**

Ceftazidime is a third generation cephalosporin antibiotic. It is active against most gram-negative bacteria including *Pseudomonas aeruginosa, S. pneumoniae, L. monocytogenes*, or Gram-negative bacilli [51]. Ceftazidime has good activity against many Gram-positive bacteria, with the exception of methicillin-resistant Staphylococcus aureus (MRSA). The bactericidal action of Ceftazidime results from interference with bacterial cell wall synthesis [55].

**Vancomycin plus Ceftazidime**

Vancomycin inhibits bacterial cell-wall synthesis by binding to one or more of the components (peptidoglycan precursors) required for peptidoglycan assembly [55]. This action leads to lethal wall distortion and eventual osmotic lysis of the bacteria. Vancomycin has little activity against Gram-positive bacteria (*Staphylococci*, gram-negative bacilli, *or S. pneumoniae*) that have already acquired a thick peptidoglycan layer [56].

Both Vancomycin and Ceftazidime work by inhibiting bacterial cell wall synthesis. Vancomycin does this by binding to the peptidoglycan component of the cell wall, while Ceftazidime inhibits the activity of enzymes involved in cell wall synthesis. This action leads to the death of the bacteria [57].

**Broad-spectrum Cephalosporin**

Cephalosporin mechanism of action is similar to that of penicillin and work against *N. meningitidis, S. pneumoniae, or H. influenzae*. They are bactericidal agents that work by inhibiting bacterial cell wall synthesis [58]. More specifically, they bind to and inhibit enzymes (penicillin-binding proteins) required for the cross-linking of peptidoglycans in the bacterial cell wall. This leads to the weakening of the cell wall, which causes it to rupture and lyse [59].

Cephalosporins are classified into four generations based on their spectrum of activity. The first-generation Cephalosporins have a limited spectrum of activity and are mostly active against Gram-positive bacteria, with some activity against Gram-negative bacteria [57]. The second-generation Cephalosporins have a broader spectrum of activity and are more active against Gram-negative bacteria than first-generation Cephalosporins. The third-generation Cephalosporins have an even broader spectrum of activity and are also active against some species of *Enterobacteriaceae* [60].

## Conclusion

Meningitis is a severe infection of the brain and spinal cord. It can occur in people of any age but is most common in infants and young children. Early diagnosis and treatment are essential to avoid permanent damage or death. Meningitis can be caused by several different bacteria, viruses, and other organisms. The most common cause in the developed world is viral meningitis, which usually resolves without lasting effects. Bacterial meningitis is much more severe, often resulting in death or permanent disability if not treated promptly with antibiotics.

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