



A STUDY ON PATHOLOGICAL AND MANGEMENT OF MENINGOENCEPHALITIS

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Article Received on 26/07/2023

Article Revised on 14/08/2023

Article Accepted on 04/09/2023

ABSTRACT

Meninges are 3 thin layers that cover and protect the brain and spinal cord. They are the dura matter, arachnoid matter and pia matter. These meninges provide a support system for blood vessels, nerves, lymphatics and the cerebrospinal fluid that surrounds your central nervous system. Meningoencephalitis is a medical emergency. Meningoencephalitis refers to the inflammation of meninges and brain and is considered as a neurological emergency. Meningoencephalitis can be caused by various types of organisms (including viruses, bacteria, and protozoa). Treatment include Corticosteroids, antivirals, antibiotic, antifungal, anti-convulsant, immunoglobulin therapy.

KEYWORDS: Meninges, cerebrospinal fluid, central nervous system, organisms, neurological emergency, treatment, corticosteroids, immunoglobulin therapy.

INTRODUCTION

Anatomy of Meninges- Meninges are 3 thin layers that cover and protect the brain and spinal cord. They are the dura matter, arachnoid matter and pia matter. These meninges provide a support system for blood vessels, nerves, lymphatics and the cerebrospinal fluid that

surrounds your central nervous system.^[1] Meningoencephalitis is a neurological condition resembling both meningitis, which is the inflammation of the meninges, and encephalitis, which is the inflammation of the brain tissue.^[2] [Fig:1]

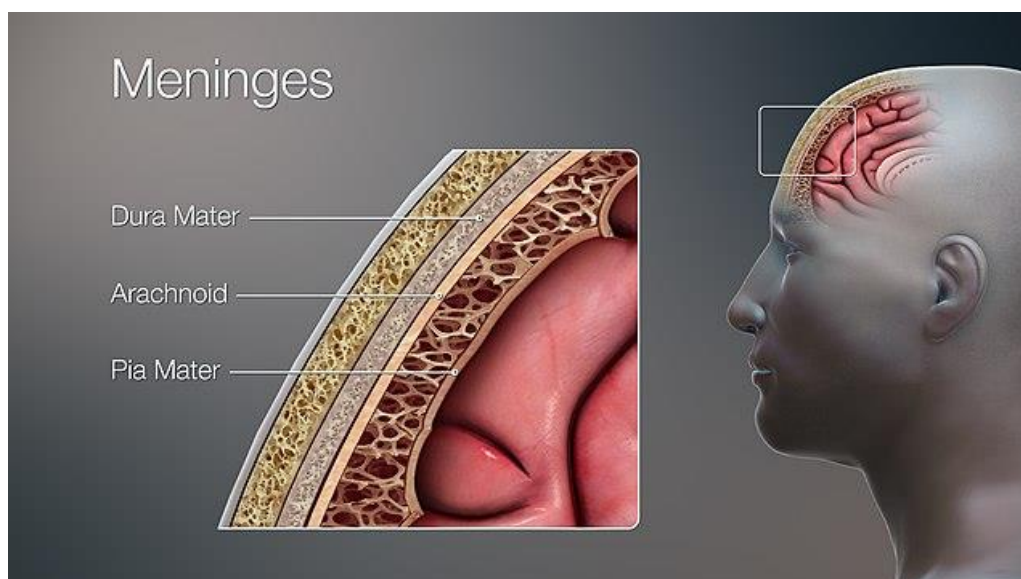


Fig 1: Layers of brain.

What is Meningoencephalitis:

➤ Meningoencephalitis is a combination of encephalitis (inflammation or infection of the brain tissue) and meningitis (inflammation or infection of

the protective membranes around the brain). It is also referred to as encephalomeningitis [3]. It represents in [Fig:2]

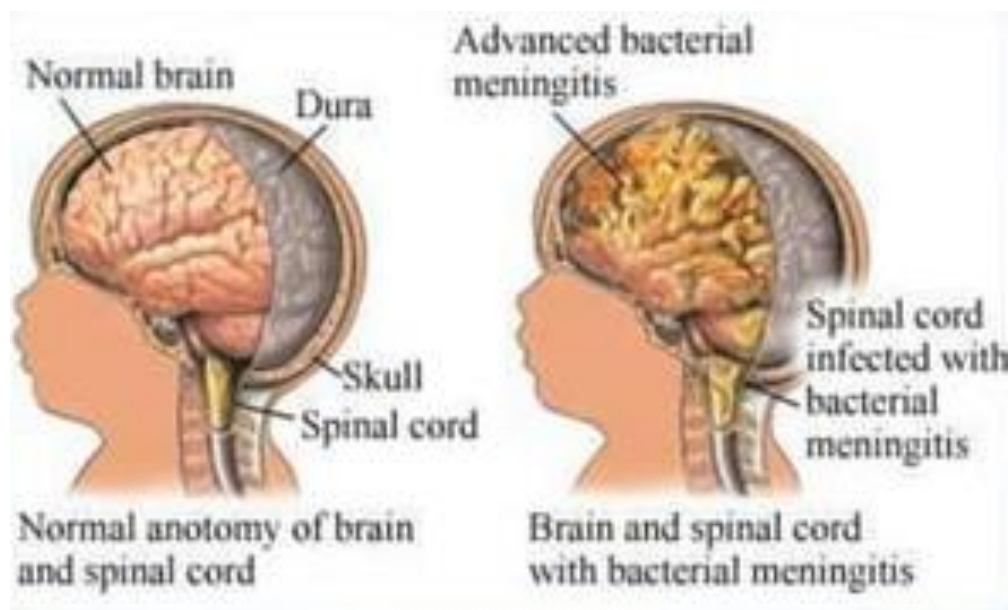


Fig 2: Difference between normal brain and meningoencephalitis brain.

Meningoencephalitis is a medical emergency.

- Meningitis is a serious infection of the meninges that surround the brain and spinal cord.
- Encephalitis is a serious form of neurological disease with inflammation of the brain parenchyma.
- Meningoencephalitis refers to the inflammation of meninges and brain and is considered as a neurological emergency. The infection may be caused by bacteria such as *Streptococcus pneumoniae*, *Hemophilus influenza* and *Mycobacterium tuberculosis* etc; viruses like Herpes simplex virus, fungi like *Cryptococcus neoformans* or parasites like plasmodium.
- Bacterial meningitis is an acute purulent infection within subarachnoid space that is followed by a central nervous system inflammatory reaction that causes coma, seizure, raised intracranial pressure and stroke. The meninges, subarachnoid space and the brain parenchyma are all involved in the inflammatory reaction; hence meningoencephalitis is a more accurate descriptive term. In encephalitis a degree of leptomeningeal inflammation is invariably present.
- Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae,

requiring rapid diagnosis and treatment. Death may occur as a result of missed diagnosis and delayed treatment. Meningoencephalitis is a severe neurological condition that results in significant morbidity and mortality.

- Early diagnosis and treatment can have major impact on the ultimate outcome for a patient with meningoencephalitis.
- Correct early diagnosis and administration of symptomatic and specific treatment will lead to increased influence upon survival and also decreases the extent of neurological consequences. Distinguishing the aetiologies and identification of specific agent helps in terms of both reducing antibiotic usage, prognosis, hospital bed occupancy and reassuring contacts of cases and healthcare staff.
- So, present study focuses on mortality and morbidity of admitted patients with meningoencephalitis in a tertiary care centre. The objective of the present study was to observe the clinical profile and aetiological causes of meningoencephalitis and to analyse the mortality and morbidity due to meningoencephalitis in a tertiary care centre. [Fig:3]

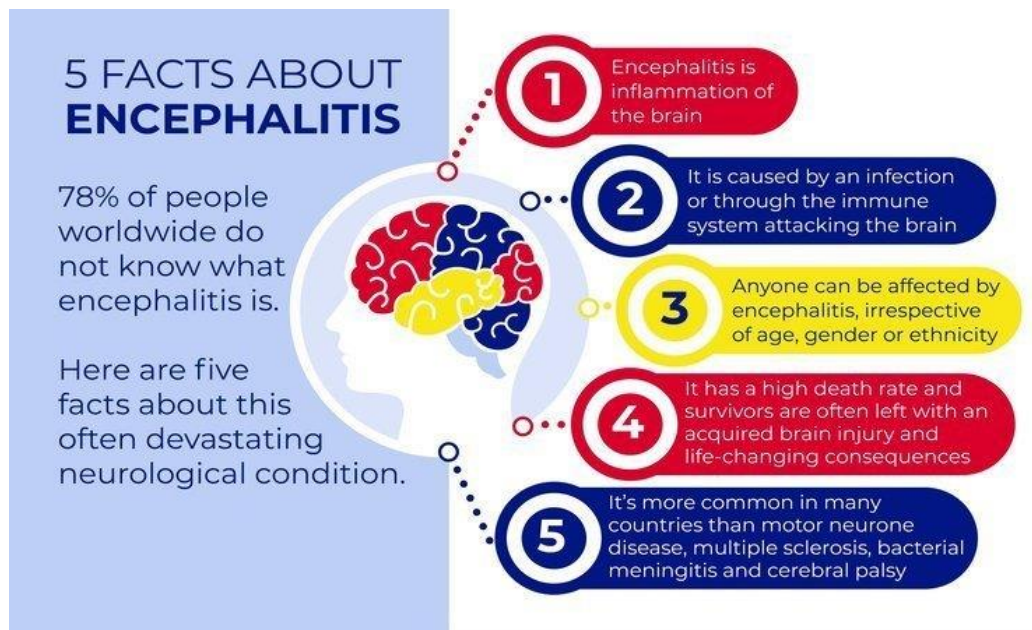


Fig 3: Facts about encephalitis.

EPIDEMIOLOGY

The median age was 43 years; 53% were female. The most common etiology was enterovirus (13463 [51.6%]), followed by unknown (4944 [21.4%]), bacterial meningitis (3692 [14.1%]), herpes simplex virus (2184 [8.3%]), non-infectious (921 [3.5%]), fungal (720 [2.7%]), arboviruses (291 [1.1%]), and other viruses (214 [0.8%]).^[4]

TYPES^[5]

Viral meningitis

Viral meningitis is the most common type of meningitis. Viruses in the Enterovirus category cause about 52 percent of cases in adults and 58 percent of cases in infants. These are more common during the summer and fall [5], and they include.

- Coxsackievirus A.
- Coxsackievirus B.
- Echoviruses.

Viruses in the Enterovirus category cause about 10 to 15 million infections trusted Source per year, but only a small percentage of people who get infected will develop meningitis.

Other viruses can cause meningitis. These include.

- West Nile virus.
- Influenza.
- Mumps.
- HIV.
- Measles.
- Herpes viruses.
- Coltivirus, which causes Colorado tick fever.

Viral meningitis typically goes away without treatment. However, some causes do need to be treated.

Bacterial meningitis

- Bacterial meningitis is contagious and caused by infection from certain bacteria. It can be fatal if left

untreated. About 1 in 10 people Trusted Source who get bacterial meningitis die, and 1 in 5 Trusted Source have serious complications. This can be true even with proper treatment.

- The most common types of bacteria that cause bacterial meningitis are:
- *Streptococcus pneumoniae*, which is typically found in the respiratory tract, sinuses, and nasal cavity and can cause what's called "pneumococcal meningitis".
- *Neisseria meningitidis*, which is spread through saliva and other respiratory fluids and causes what's called "meningococcal meningitis".
- *Listeria monocytogenes*, which are foodborne bacteria.
- *Staphylococcus aureus*, which is typically found all over the skin and in the nasal passages, and causes "staphylococcal meningitis".

Fungal meningitis

- Fungal meningitis is a rare type of meningitis. It's caused by a fungus that infects your body and then spreads from your bloodstream to your brain or spinal cord.

- People with a weakened immune system are more likely to develop fungal meningitis. This includes people with cancer or HIV.

The most common fungi related to fungal meningitis include:

- *Cryptococcus*, which is inhaled from dirt or soil that is contaminated with bird droppings, especially pigeons and chickens, or rotting vegetation.
- *Blastomyces*, another type of fungus found in soil, particularly in the Midwestern United States.
- *Histoplasma*, which is found in environments that are heavily contaminated with bat and bird droppings, especially in the Midwestern States near the Ohio and Mississippi Rivers.

- Coccidioides, which is found in soil in specific areas of the U.S. Southwest and South and Central America.

Parasitic Meningitis

- This type of meningitis is less common than viral or bacterial meningitis, and it's caused by parasites that are found in dirt, feces, and on some animals and food, like snails, raw fish, poultry, or produce. One type of parasitic meningitis is rarer than others. It's called eosinophilic meningitis (EM). Three main parasites are responsible for EM. These include:
 - *Angiostrongylus cantonensis*.
 - *Baylisascaris procyonis*.
 - *Gnathostoma spinigerum*.

Parasitic meningitis is not passed from person to person. Instead, these parasites infect an animal or hide out on food that a human then eats. If the parasite or parasite eggs are infectious when they're ingested, an infection may occur.

One very rare type of parasitic meningitis, amoebic meningitis, is a life-threatening type of infection. This type is caused when one of several types of amoebae enters the body through the nose while you swim in contaminated lakes, rivers, or ponds. The parasite can destroy brain tissue and may eventually cause hallucinations, seizures, and other serious symptoms. The most commonly recognized species is *Naegleria fowleri*.

Non-infectious meningitis

Non-infectious meningitis is not an infection. Instead, it is a type of meningitis that's caused by other medical conditions or treatments. These include.

- Lupus.
- A head injury.
- Brain surgery.
- Cancer.
- Certain medications.

Chronic Meningitis

- This classification is given to cases of meningitis that last longer than 4 weeks. The causes of chronic meningitis can be fungi, rheumatological conditions, and cancer, among others. Treatment for chronic meningitis is directed at treating the cause (i.e., managing rheumatoid arthritis).

CAUSES

- Meningoencephalitis can be caused by various types of organisms (including viruses, bacteria, and protozoa) or it can occur as a secondary development caused by other types of inflammation (such as HIV).
- Aseptic meningoencephalitis describes viral and non-infectious causes, and it is usually diagnosed when the cerebrospinal fluid (CSF) that surrounds

the brain and spinal column tests negative for bacteria.

Viral Causes^[6]

- Herpes meningoencephalitis (HME) is the most common form of meningoencephalitis, caused by the herpes simplex virus. Most cases of viral meningoencephalitis are caused by this virus.

There are two types of herpes simplex virus.

- Herpes simplex virus type 1 (HSV1): The virus that causes cold sores and the most common type of herpes that causes meningoencephalitis. HSV1 is also known to be sexually transmitted to the genital area.
- Herpes virus type 2 (HSV2): Can be spread through sexual contact or from a mother who is infected with HSV2 to her unborn child during birth.
- The herpes viruses stay in the body for a person's entire life. They can be dormant, not causing any signs or symptoms of infection, and then can reactivate. Sometimes meningoencephalitis is contracted during the initial herpes infection, but it usually occurs during reactivation of the virus from a previous infection.

Other causes of viral meningoencephalitis may include.

- Varicella-zoster viruses: A type of herpes virus that causes chickenpox and shingles measles virus.
- Enteroviruses: Includes several viruses responsible for a wide variety of diseases, from the common cold to polio and hand foot and mouth disease.
- HIV: The human immunodeficiency virus (HIV) can infect the brain and meninges within weeks or months of HIV diagnosis.
- Japanese encephalitis (JE): This is the primary type of meningoencephalitis in Asia, caused by the Japanese encephalitis virus. It is preventable by vaccine.^[7]

Bacterial Causes^[8]

- Bacterial meningoencephalitis is a very serious life-threatening infection with a high risk of mortality (death) and complications, such as disability.⁴ It is sometimes also referred to as pyogenic meningoencephalitis.
- There are several organisms that can cause bacterial meningoencephalitis. Most bacterial sources of meningoencephalitis are spread from person to person, and they are spread differently, depending on the type.

The most common causes of bacterial meningoencephalitis include.

- *Streptococcus pneumoniae*: A bacteria commonly found in the nose and throat.
- *Haemophilus influenzae* (HIB): A type of bacteria that commonly causes respiratory infections, and which is preventable by vaccine.

- *Neisseria meningitidis*: A type of bacteria that commonly lives in the back of the nose and mouth without causing any adverse symptoms. Severe infection is preventable by vaccine.

Fungal Causes.

- Fungal meningoencephalitis results from the spread of fungus through the bloodstream. It tends to affect people who have a suppressed immune system due to medication, cancer, or HIV.

Parasitic Causes

- Parasitic meningoencephalitis is caused by a reaction to a parasite, usually transmitted by eating contaminated food.

Secondary Causes

- Secondary meningoencephalitis occurs when an infection starts somewhere else in the body, then travels to the brain.

Pathophysiology of meningoencephalitis^[9 and 10]

Bacterial invasion

- Bacteria invade from blood stream to central nervous system.

- Anatomical site of bacterial invasion some blood stream remains unidentified. Experimental evidence suggest choroid plexus may be the site of the invasion.
- Streptococcal proteins such as CBPA interact with glycol conjugate receptors of phosphoryl choline with platelet activation factor on eukaryotic cells and promotes endocytosis and crossing blood brain barrier.
- Inflammatory response.
- Adhesion of molecules as ICAM1.
- Subsequently these molecules promote multistep process of leukocyte invasion and shows the presence of granulocytes.
- Early inflammatory response and the bacterial invasion shows activation of leukocytes, MMPS and NO and shows early damage of blood brain barrier and blood CSF barrier.
- Once bacteria have entered the sub arachnoidal space they replicate and undergo autolysis and cause further inflammation.
- Cells involved endothelial cells, macrophages and mast cells will play a crucial role for showing the inflammatory response.

Neuronal damage: [Fig:4]

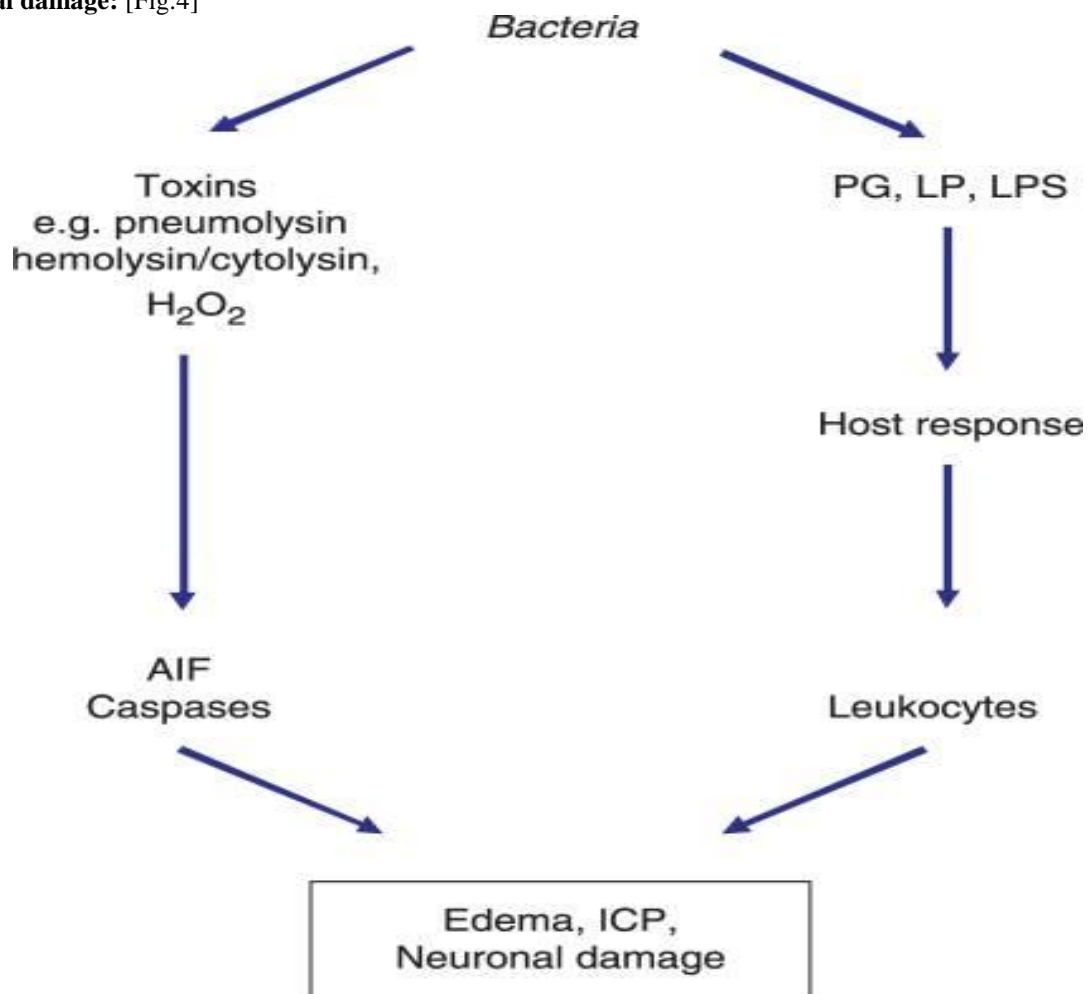


Fig 4: Neuronal damage.

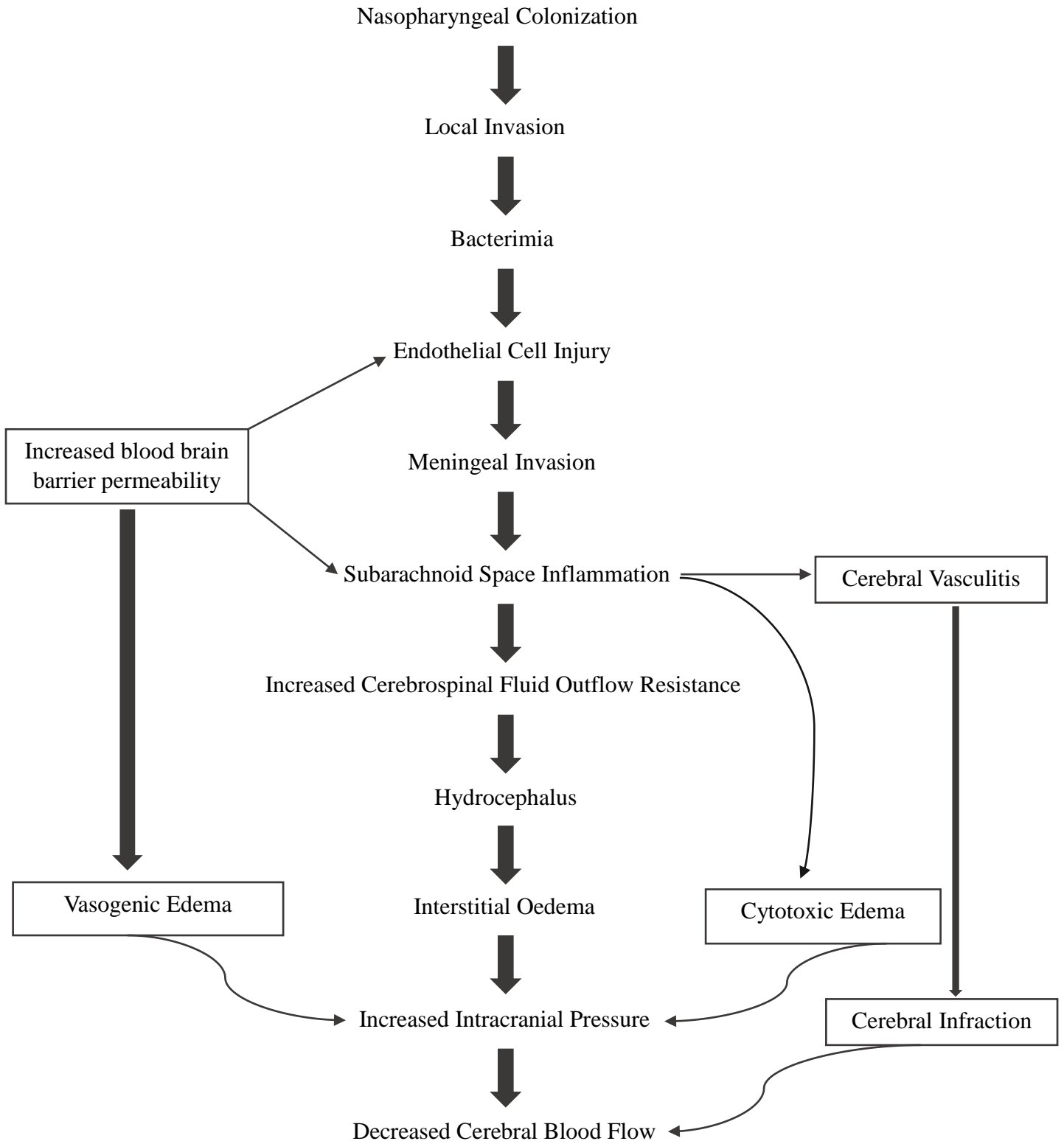


Fig 5: Detailed pathophysiology of meningococcal meningitis.

Symptoms^[11]: [Fig:6 & 7]

In Children and Infants just as in adults, the symptoms of meningococcal meningitis in children and newborns usually begin like symptoms of the common flu.

Early symptoms in children may include.

- Fever.
- Headaches.
- Speech problems.
- Purple rashes (indicative of viral meningococcal meningitis).

- Disorientation.

Later symptoms in children may include

- Vomiting.
- Drowsiness.
- Seizures.
- Behavioural changes.
- Unconsciousness.

In infants, the primary symptoms of herpes simplex type 2, which occurs from transmission at birth usually include.

- High fever.
- Bulging of the forehead.
- Poor appetite/feeding.
- Continual sleepiness.

- Fever.
- Light sensitivity.
- Headache.
- A stiff neck
- Confusion.
- Difficulty thinking clearly.
- Hallucinations (seeing or hearing things that aren't actually there).
- Unusual behaviours.
- Personality changes.
- Fatigue or sleepiness.
- Seizures.
- Focal neural deficit (a problem with nerve function in a specific area of the body).
- Unconsciousness.

Common symptoms include.

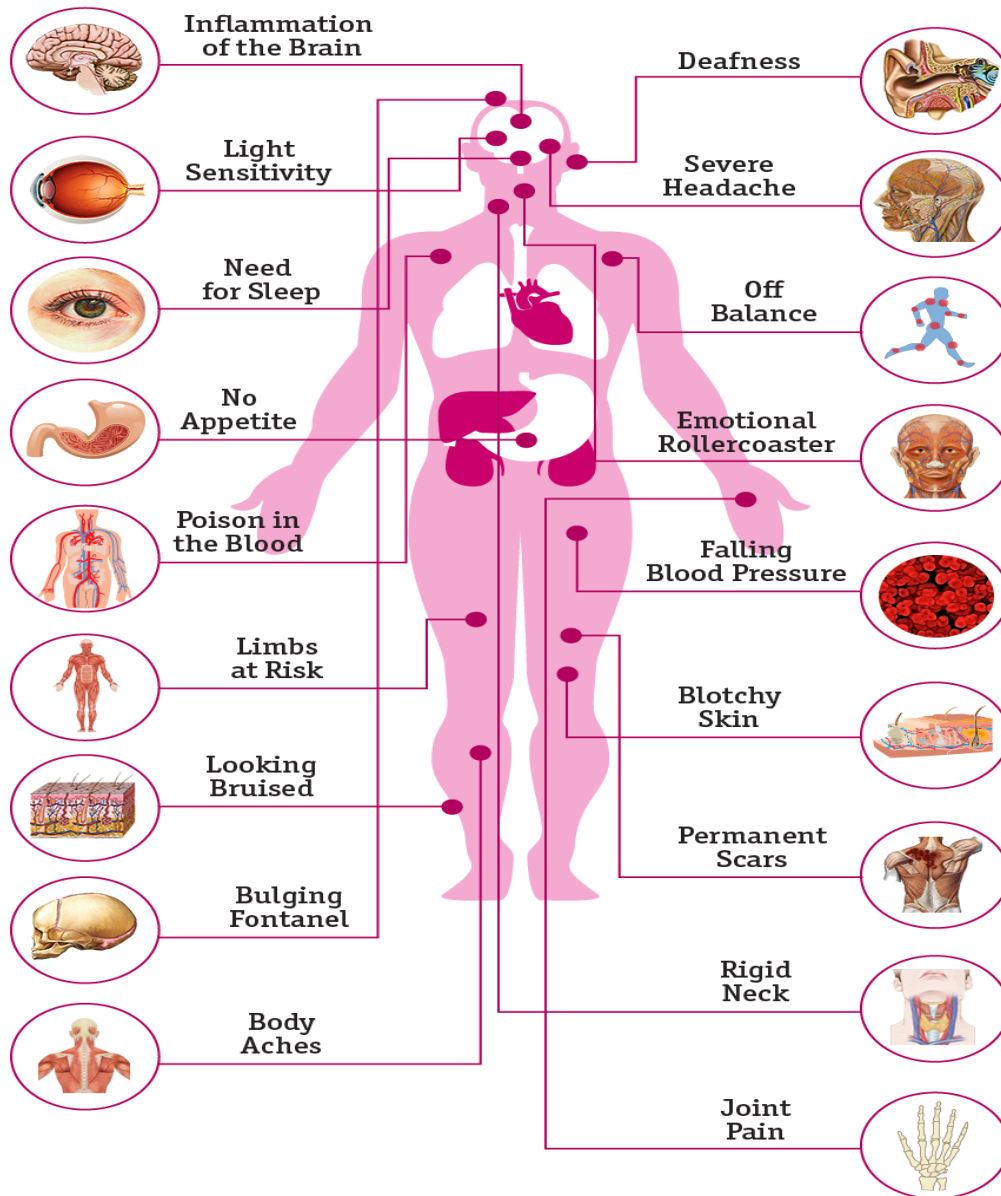


Fig 6: Symptoms of meningoencephalitis.

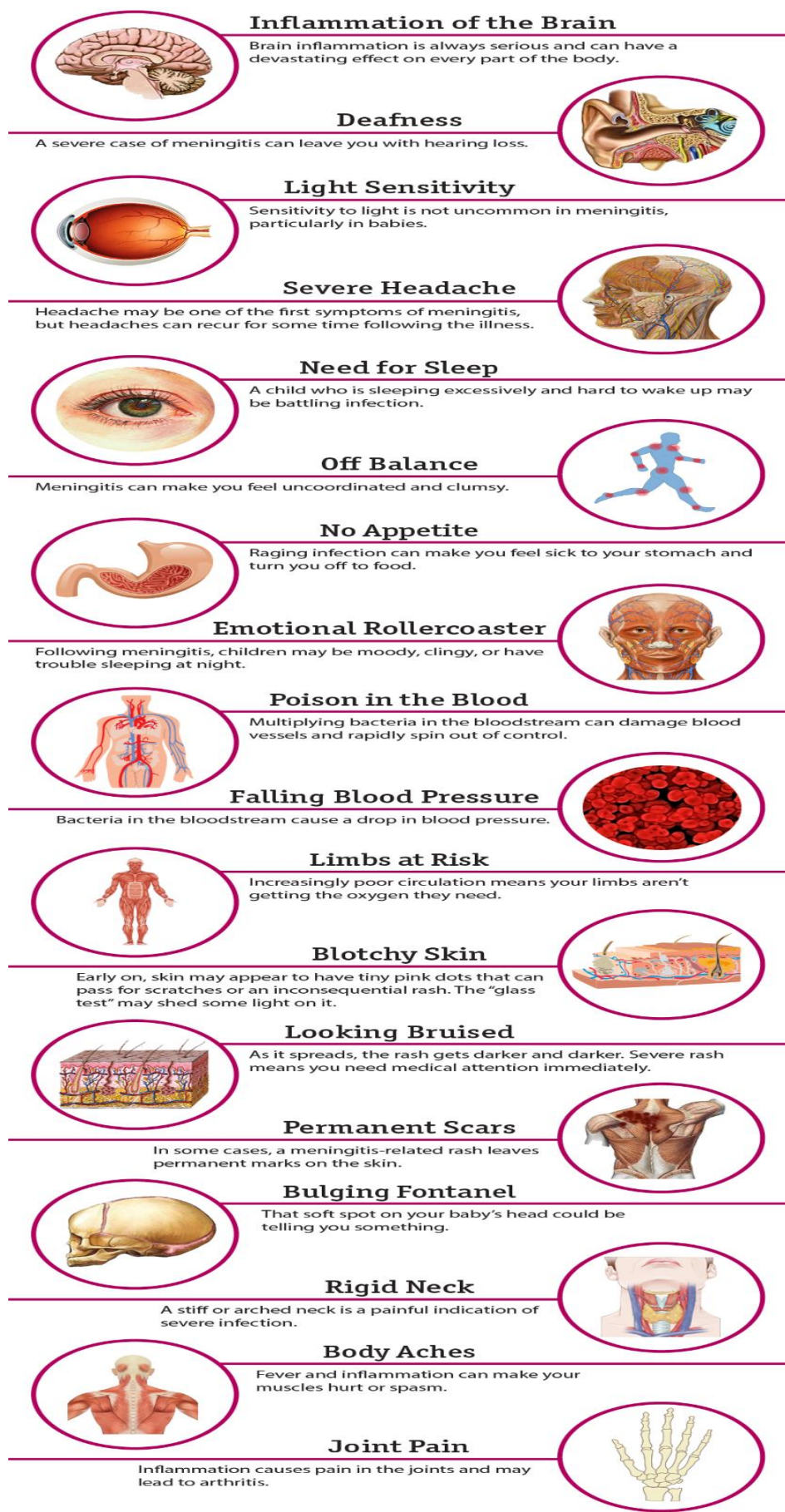


Fig 7: Symptoms of meningoencephalitis.

How Meningoencephalitis is Transmitted

Common modes of transmission (spread of the disease) for the bacteria that can cause meningoencephalitis include:

- Coughing or sneezing (HIB and *S. Pneumoniae*).
 - Kissing or close contact in which saliva is shared (*N. Meningitidis*).
- Viral meningoencephalitis caused by the herpes simplex type 1 and the herpes virus type 2 is often transmitted by:
- Droplet spread (such as from coughing or sneezing).
 - Water or food transmission.
 - Sexual intercourse.
 - Oral to oral contact (via sores and saliva as well as other surfaces in or around the mouth).^[12]
 - Transmission from mother to child during childbirth.^[13]

The following are some of the risk factors for meningitis.

- Compromised immunity
- People with an immune deficiency are more vulnerable to infections. This includes the infections that cause meningitis. Certain disorders and treatments can weaken your immune system. These include.
- HIV/AIDS.
 - Autoimmune disorders.
 - Chemotherapy.
 - Organ or bone marrow transplants.
 - Cancer.
 - Immunosuppressive medication.
 - Cryptococcal meningitis, which is caused by a fungus, is the most common form of meningitis in people with HIV.
 - Community living.

Meningitis is easily spread when people live in close quarters. Being in small spaces increases the chance of exposure. Examples include.

- College dormitories.
- Barracks.
- Boarding schools.
- Daycare centres.
- Assisted living facilities.

Pregnancy

- Pregnant women have an increased risk of listeriosis, which is an infection caused by the listeria bacteria. Infection can spread to the unborn child.

Age

- All ages are at risk for meningitis. However, certain age groups have a higher risk. Children under the age of 5 are at increased risk of viral meningitis. Infants are at higher risk of bacterial meningitis. Older adults can also be at risk for certain infections that can lead to meningitis.

Working with animals.

- Farm workers and others who work with animals have an increased risk of infection with listeria.

Complications may include

- Loss of memory, especially among those who had HSV encephalitis.
- Behavioural or personality changes, such as mood swings, bouts of frustration and anger, and anxiety.
- Epilepsy.
- Aphasia, language, and speech problems.
- Seizures.^[15]
- Hearing loss.
- Vision loss.
- Memory problems.
- Migraine headaches.
- Brain damage.
- Hydrocephalus.
- A subdural empyema, or a buildup of fluid between the brain and the skull.^[15]
- Impairment in intelligence.^[14]
- Mood and behaviour changes.
- Residual neurological deficits.
- Extrapyramidal symptoms (JE).
- Hyponatremia (esp. St. Louis encephalitis).
- Encephalopathy.
- Mononeuropathy.
- Flaccid paralysis.
- SIADH (St louis' encephalitis).^[14]

Diagnosis

A physical and neurological examination is performed to evaluate for abnormalities in motor and sensory function, coordination, balance, and altered mental status. If the healthcare provider suspects meningoencephalitis, some lab tests will be performed, including.

1. **Blood tests**^[19]: These will evaluate the presence of an infection in the body.
2. **Lumbar puncture**: This procedure involves needle aspiration of a sample of cerebrospinal fluid (CSF), to check for inflammatory cells, proteins, and organisms.
3. **CSF culture**^[18]: The CSF sample is examined microscopically for bacteria, fungi, and red and white blood cells. A sample is incubated in culture media to identify whether there's growth of causative bacteria such as *N. meningitidis*, *S. pneumoniae*, and *H. influenzae*.
4. **Electroencephalogram (EEG)**^[17]: The test is performed by placing electrodes on the scalp that provide a reading on a person's brain wave activity to identify certain brain function disturbances.
5. **Imaging**^[16]
 - **Computerized tomography (CT) scan**: This is an imaging test that takes many different pictures from various angles inside of the body. An injected dye may help delineate the images.
 - **Magnetic resonance imaging (MRI) scan**: This imaging test uses radio waves and very strong

magnetic fields to create a series of detailed images of the brain.

- **Ultrasound or sonography:** This test uses sound waves to make an image of the structure and fluid flow in the brain. Brain changes such as swelling, lesions, or inflammation can sometimes be detected using ultrasound technology.

Treatment

Treatment for encephalitis focuses on treating underlying causes and alleviating symptoms.

Treatment options include.

- **Corticosteroids:** Doctors may recommend steroid injections to reduce inflammation in the brain.
- **Antiviral medication:** In cases of viral encephalitis, antiviral medications can treat the root cause of the condition.

- **Antibiotics:** Antibiotics can treat bacterial infections that may cause encephalitis.
- **Antifungal medications:** In cases of fungal encephalitis, antifungal medications can help.
- **Anticonvulsants:** If encephalitis is causing seizures, these medications can reduce convulsions.
- **Surgery:** If doctors determine that a tumour or other growth caused encephalitis, they may perform surgery to remove it.
- **Immunoglobulin therapy:** During immunoglobulin therapy, a doctor will administer a solution containing a large number of antibodies from donated blood. This is often an IV administration.
- **Therapeutic plasma exchange:** This process removes Trusted Source blood from the body and filters out antibodies to help prevent them from attacking the body. A doctor then replaces the person's blood with albumin or donated blood. Albumin is a protein the liver creates.^[20]

Table 1: Treatment of meningoenephalitis.^[21]

Empiric antimicrobial therapy in acute bacterial meningitis

Age group	Causative pathogens	Empirical therapy
Infants and children	<i>S. pneumoniae</i> , <i>N. meningitidis</i> , <i>H. influenzae</i> , <i>S. agalactiae</i>	Ceftriaxone 50 mg/kg iv, plus Vancomycin 15 mg/kg iv
Adults	<i>S. pneumoniae</i> , <i>N. meningitidis</i>	Ceftriaxone 2 g IV q 12 hrs, plus Vancomycin 15 mg/kg q 12 h
Neonates and elderly	<i>S. pneumoniae</i> , <i>N. meningitidis</i> , <i>L. monocytogenes</i>	Ampicillin 2g iv q 6h, plus Ceftriaxone 2 g IV q 12 hrs, plus Vancomycin 15 mg/kg q 12 h
Immunocompromised	<i>S. pneumoniae</i> , <i>N. meningitidis</i> , <i>H. influenzae</i> , aerobic Gram-negative bacilli	Ampicillin 2g iv q 6h, plus Ceftriaxone 2 g iv q8h or Cefipime 2g iv q8h, plus Vancomycin 15 mg/kg q 12h
Nosocomial	<i>S. aureus</i> , <i>S. epidermidis</i> , aerobic Gram-negative Bacilli	Ceftazidime 2 g iv q8h or Cefipime 2g iv q8h or Meropenem 40 mg/kg iv q8h, plus Vancomycin 15 mg/kg q 12h

Medical Management^[22]

Treatment for mild encephalitis usually consists of.

- Bed rest.
- Plenty of fluids.
- **Anti-inflammatory drugs:** such as acetaminophen (Tylenol, others), ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve) — to relieve headaches and fevers.
- **Antiviral drugs** Encephalitis caused by certain viruses usually requires antiviral treatment.

Supportive care.

People who are hospitalized with severe encephalitis might need.

- Breathing assistance, as well as careful monitoring of breathing and heart function.

- Intravenous fluids to ensure proper hydration and levels of essential minerals.
- Anti-inflammatory drugs, such as corticosteroids, to reduce swelling and pressure within the skull.
- Anticonvulsant medications, such as phenytoin (Dilantin), to stop or prevent seizures.

Rehabilitation

Lokomat-Pro-Robotic-Gait-Training.jpg Good rehabilitation is a holistic approach. It recognises the complex cognitive, behavioural, social, emotional and medical problems faced by people affected by encephalitis and their families. Complications of encephalitis may require the following services.

- Physical therapy to improve strength, flexibility, balance, motor coordination and mobility eg

Exercise therapy; Gait rehabilitation; Otago Balance training.

- Occupational therapy to develop everyday skills and to use adaptive products that help with everyday activities.
- Speech therapy to relearn muscle control and coordination to produce speech.
- Psychotherapy to learn coping strategies and new behavioural skills to improve mood disorders or address personality change.

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