WHY IS THIS IMPORTANT?

- Infections that affect the central nervous system (CNS) can be catastrophic and potentially lethal.
OVERVIEW

- In some cases, the CNS is the main target.
- In others, the CNS is a secondary target.
- Infections of CNS can be caused by:
  - Bacteria, viruses, fungi, and parasites, like other body systems
  - Infectious proteins, called prions, that only infect the CNS

ANATOMY OF THE CNS

- CNS has two major parts
  - Brain
  - Spinal cord
- Both surrounded by three layers of connective tissue – meninges.
- Cerebrospinal fluid is found in the subarachnoid space.
- The brain and spinal cord are protected from the body by the blood-brain barrier.
  - Protects against infectious disease
  - Some pathogens can pass through the blood-brain barrier

- No room for swelling in the CNS.
- Inflammation is one of the first and most formidable responses.
  - Always causes swelling
- Vasogenic edema – swelling caused by inflammatory response in the subarachnoid space
- Cytotoxic edema – swelling from toxic substances produced by bacteria and neutrophil invasion
ANATOMY OF THE CNS

- Infection can also affect proper brain function through:
  - Acidosis
  - Hypoxia
  - Destruction of neurons
- Effects of infection can be profound and irreversible.
- Blood-brain barrier can make it difficult to treat CNS infections.

COMMON PATHOGENS AND ROUTES FOR CNS INFECTIONS

- Organisms reach the brain and spinal cord in a variety of ways.
- Organisms in blood can enter the cerebrospinal fluid and cause meningitis.
- Infections in the sinuses and mastoid air spaces eventually cause erosion of the skull bone.
  - Pathogens can then enter the brain and cause abscesses.
- Most CNS infections result from the passage of pathogens across the blood-brain barrier.

COMMON PATHOGENS AND ROUTES FOR CNS INFECTIONS

- CNS infections can be caused by:
  - Normal bacterial flora
  - Pathogens acquired through ingestion
  - Pathogens acquired during the birthing process
  - Contamination of shunts
COMMON PATHOGENS AND ROUTES FOR CNS INFECTIONS

- Initial source of a CNS infection is either:
  - Occult – infection of mononuclear phagocytic system cells
  - Overt – from complications of other infections
    - Pneumonia
    - Pharyngitis
    - Skin abscesses
    - Infectious endocarditis

The infection site can be close to or in direct contact with the CNS.
- Pathogens can enter the CNS through:
  - Defects in the structures that encase the CNS
  - Opening left by surgical, traumatic, or congenital developmental abnormalities

Intraneural pathways are the least common route to the CNS.
- Exceptions are:
  - Rabies virus – uses peripheral sensory nerves
  - Herpesvirus – uses trigeminal nerve
COMMON PATHOGENS AND Routes FOR CNS INFECTIONS

- Brain abscesses are relatively rare, but present a special problem.
- They can be found in:
  - Subdural space
  - Epidural space
  - Directly in the brain tissue
- Commonly formed by bacteria or fungi from a distant site
- Also result from:
  - Extensions of pathogens located at the site of mastoiditis or sinusitis
  - Surgical complications

PURULENT MENINGITIS

- Infection of the meninges associated with:
  - Acute inflammatory exudates
  - Usually caused by a bacterial infection
  - Characterized by fever, irritability, and various degrees of neurological dysfunction

CHRONIC MENINGITIS

- More insidious onset than purulent meningitis
  - Signs and symptoms develop over weeks.
  - Usually caused by *Mycobacterium tuberculosis*, fungi, or protozoan parasites
ASEPTIC MENINGITIS

- Infection of the meninges associated with:
  - Meningeal inflammation
  - Increased lymphocytes and mononuclear cells in cerebrospinal fluid
  - Absence of bacteria or fungi
- Most often attributed to viral infection.
- Usually self-limiting
- No clinical involvement of neural tissue
- Characterized by fever, headache, stiff neck and back, nausea, and vomiting

ENCEPHALITIS

- Describes signs of CNS dysfunction with no symptoms of aseptic meningitis.
- Involves seizures, paralysis, or defective mental faculties.
- Problem is not with the meninges, but the actual nervous tissue.

POLIOMYELITIS

- Infection which destroys cells associated with the anterior horn of the spinal cord, and brain stem.
- Causes weakness or paralysis of muscle groups
  - Can cause respiratory difficulties
- Characterized by asymmetrical paralysis
ACUTE POLYNEURITIS

- Inflammatory infection of the peripheral nervous system
- Characterized by symmetrical paralysis
- Can be caused by diphtheria toxin, enteric pathogens, cytomegalovirus, and Epstein-Barr virus

COMMON PATHOGENS OF THE CNS

- Acute purulent meningitis usually caused by:
  - *H. influenzae*
  - *N. meningitidis*
  - *S. pneumoniae*
  - A vaccine is available to protect against *H. influenzae*.
  - Group B streptococci and *E. coli* often involved in meningitis in newborns
    - Acquired through the birthing process

- Most common viral causes of acute CNS infections:
  - Enterovirus
  - Herpes simplex virus
  - HIV
  - Epstein-Barr virus
  - Also several arthropod-borne viruses
  - Viral infections manifest as aseptic meningitis, encephalitis, and poliomyelitis.
COMMON PATHOGENS OF THE CNS

- Sub-acute sclerosing panencephalitis results from measles or rubella infections.
- *M. tuberculosis* can cause CNS infections.
- Deep fungal mycoses *Cryptococcus neoformans* and *Coccidioides immitis*.

GENERAL TREATMENT OF CNS INFECTIONS

- Bacterial and fungal infections require prompt and aggressive treatment.
- Treatment periods vary depending on the type of infection.
  - 10 days to 12 months for uncomplicated cases
  - Longer if the infection is caused by *M. tuberculosis*
- Treatment of fungal infections can last for years.
- Treatment of viral infections is mostly supportive.

MENINGITIS

- Broad category of infections of the fluid surrounding spinal cord and brain.
- Usually caused by virus or bacteria – important to know which
  - Severity of illness differs
  - Treatments differ
**MENINGITIS:**

**Bacterial**

- Bacterial meningitis can be severe and cause:
  - Brain damage
  - Hearing loss
  - Learning disability
- Important to know type of bacterium
  - Antibiotic therapy can prevent its spread.

**MENINGITIS:**

**Bacterial**

- Some forms of bacterial meningitis are contagious
  - Spread by exchange of respiratory and throat secretions
  - Not as contagious as the common cold
- *N. meningitidis* can spread to other people via close or prolonged contact.
  - Bacterial meningitis concern for daycare centers and schools.

**MENINGITIS:**

**Viral**

- Viral meningitis is generally less severe:
  - Usually resolves without treatment.
- Caused by several types of virus:
  - 90% of cases by enterovirus
  - Also herpesvirus and mumps virus.
- Viral meningitis rarely fatal if there is a competent immune system:
  - Patient usually recovers completely.
Patients with any symptoms of meningitis should see a doctor immediately.

Diagnosis of the bacterial strain is usually made by growing bacteria from spinal fluid.

Identification helps in selecting the most effective antibiotic therapy.

Early antibiotic therapy limits risk of death to 15%.

Viral meningitis is also diagnosed using spinal fluid.

No antibiotic therapy.

Bed rest, plenty of fluids, medicines to relieve fever and headache.

Many bacteria cause meningitis.

Increased cranial pressure and inflammation

Tetanus and botulism infections affect the CNS in different ways.

Produce exotoxins with an affinity for CNS tissue.

Antibiotic therapy is ineffective once the exotoxin has been produced.

Tetanus is caused by Clostridium tetani.

Gram-positive

Anaerobic

Rod shaped

Produces a terminal spore
TETANUS (CLOSTRIDIUM TETANI)

- \textit{C. tetani} is a strict anaerobe.
- Cannot survive in the presence of oxygen
- Commonly found in the soil
  - Spores can survive there for years.
  - Gets into wounds via contaminated soil
- Spores are very resistant to disinfectants and can withstand boiling.

TETANUS (CLOSTRIDIUM TETANI)

- Toxin produced by \textit{C. tetani} is neurogenic.
  - Affinity for and targets nervous tissue
  - Called tetanospasmin or tetanus toxin
  - Acts by enzymatically degrading proteins required for normal physiology
TETANUS: Pathogenesis

- Tetanus spores require areas of low oxygen to germinate.
  - Area of necrosis around tissue injury is perfect
  - Spores germinate and *Clostridium* begins to grow
- Bacteria do not cause damage to the tissue where they reside.
  - Produce their neurogenic toxin
  - Toxin enters the presynaptic terminals of the lower motor neurons.
  - From there, it gets into the CNS.

- Tetanus toxin is systemic for muscles.
  - Masseter muscle of the jaw usually first to be affected
    - Mouth cannot be opened (sometimes called lockjaw)
  - Muscles for respiration and swallowing can eventually be compromised.
  - Severe cases can suffer from opisthotonos
    - Head and heels move toward each other

- Incubation period can vary between 4 days and several weeks.
  - The shorter the incubation period, the more severe the infection.

- Toxin acts at the anterior horn cells in the spinal cord.
  - Blocks postsynaptic inhibition of the spinal motor reflexes
  - Produces spasmodic contraction of the muscles
    - Occur locally at first
    - May extend up and down the spinal cord

- The shorter the incubation period, the more severe the infection.

- Head and heels move toward each other
TETANUS: Pathogenesis

- Death results from exhaustion and respiratory failure.
  - Mortality for untreated tetanus is 15 - 60%.
- Several factors affect mortality:
  - Location of lesion
  - Incubation period
  - Age
    - Mortality is highest in infants and the elderly.

TETANUS: Treatment

- Antibiotics are not effective once toxin is produced.
- Neutralization of the toxin with human tetanus immunoglobulin is important.
- Additional supportive measures are:
  - Maintenance of a dark, quiet environment
  - Sedation
  - Provision of an adequate airway for breathing
**BOTULISM**

**(CLOSTRIDIUM BOTULINUM)**

- Etiologic agent is *Clostridium botulinum*.
  - Gram-positive
  - Anaerobic
  - Spore-forming
  - Rod-shaped
- Found naturally in soil and sediments of ponds and lakes.

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**BOTULISM**

**(CLOSTRIDIUM BOTULINUM)**

- Spores contaminate food under anaerobic conditions.
  - Spores convert to the vegetative state and begin to produce toxin.
- Contamination of food with botulinum toxin does not affect the smell, taste, or color.
  - Commonly seen in cases of home canning
- Botulinum toxin is among the most poisonous toxins in the world.

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**BOTULISM: Pathogenesis**

- Begins with cranial nerve palsy
  - Develops into a descending symmetrical motor paralysis
  - May involve the respiratory muscles
- No fever or inflammation
- No obvious sign of infection
**BOTULISM: Pathogenesis**

- Time course of the infection depends on:
  - Amount of toxin
  - Whether toxin was ingested in a preformed state, or produced in the intestinal tract

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**BOTULISM: Pathogenesis**

- Foodborne botulism is classified as intoxication not infection.
- Toxin is absorbed directly through the intestinal tract.
  - Reaches a neuromuscular junction via bloodstream
  - Binds and inhibits the release of acetylcholine
    - Causes muscular paralysis

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**BOTULISM: Pathogenesis**

- Symptoms depend on which nerves are damaged.
  - Damage is permanent.
- Foodborne botulism usually starts 12-36 hours after ingestion of toxin.
  - First symptoms are nausea, dry mouth, and sometimes diarrhea.
- Nervous system dysfunction starts later.
  - Includes blurred vision, pupillary dilation, and rapid eye movements
BOTULISM: Pathogenesis

- Symmetrical paralysis begins with ocular, laryngeal, and respiratory muscles.
  - Spreads to trunk and extremities
  - Most serious complication is complete respiratory paralysis.
  - Mortality rates are 10 - 20%.

Two other forms of botulism:

- Infant form
- Wound form
- Infant botulism is the most commonly diagnosed form.

Infant botulism occurs between 3 weeks and 8 months.

- Organism introduced on weaning or through dietary supplements, particularly honey
- Multiplies in colon
- Toxin is absorbed into the blood
- Symptoms are constipation, poor muscle tone, lethargy, and feeding problems.
- Severe cases can cause vision problems and paralysis
BOTULISM: Pathogenesis

- Wound botulism is very rare.
  - Usually seen in intravenous drug users
- Symptoms are similar to those of food poisoning.
  - Usually begin with muscle weakness in extremities used for injection

BOTULISM: Treatment

- Single most important determinant in survival is availability of intensive support measures, particularly mechanical ventilation.
  - Mortality is less than 10% with proper ventilation.
- Antibiotic therapy is only given to patients with the wound form.

VIRAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

- Viruses can cause meningitis.
  - Increased intracranial pressure and inflammation
- Viruses can also cause other symptoms.
- Such viral CNS infections can be split into:
  - Acute
  - Persistent
RABIES

- Rabies is an acute and fatal viral CNS infection.
- Can affect all mammals
- Transmitted by infected secretions (usually through a bite)
- Virus is large and bullet-shaped
  - Glycoproteins cover the entire virion

RABIES: Pathogenesis

- Rabies involves severe neurological symptoms.
- CNS abnormalities include:
  - Relentless progression of excess motor activity
  - Agitation
  - Hallucinations
- Also overproduction of saliva
  - Can be an inability to swallow

RABIES: Pathogenesis

- Rabies exists in two forms:
  - Urban
  - Sylvatic
- Urban form is associated with unimmunized dogs and cats.
- Sylvatic form is seen in wild animals.
- Infection in humans incidental.
  - Does not contribute to maintenance or transmission of infection

Rabies is an acute and fatal viral CNS infection. It can affect all mammals and is typically transmitted by infected secretions, usually through a bite. The virus is large and bullet-shaped, with glycoproteins covering the entire virion.

Rabies involves severe neurological symptoms. CNS abnormalities include relentless progression of excess motor activity, agitation, hallucinations, and overproduction of saliva, which can result in an inability to swallow.

Rabies exists in two forms: urban and sylvatic. The urban form is associated with unimmunized dogs and cats, while the sylvatic form is seen in wild animals. Infection in humans is incidental and does not contribute to the maintenance or transmission of the infection.
RABIES: Pathogenesis

First event of rabies infection is introduction of the virus.
- Usually through the epidermis via an animal bite
- Also through inhalation of heavily contaminated material such as bat droppings.

Virus replicates at the site of infection.
- Immunization immediately after infection keeps virus from migrating into the nervous tissue.
- Without intervention, virus moves into peripheral nervous system.
  - Spreads into the CNS
  - Replicates exclusively in gray matter

After replication, virus moves into other tissues.
- Adrenal medulla, kidneys, lungs, and salivary glands
- Lymphocytes and plasma cells infiltrate into the CNS.
  - Destroy nerve cells
  - Primary lesion is the Negri body
RABIES: Pathogenesis

- Incubation period varies from 10 days to as long as a year depending on:
  - Amount of virus initially introduced
  - Amount of tissue infected
  - Host’s immune response
  - Innervation at the site
  - Distance virus must travel to reach CNS

- Rabies presents as acute, fatal encephalitis.
  - Once symptoms appear the infection is irreversibly fatal.
  - Illness begins with nonspecific fever, headache, malaise, nausea, and vomiting.
  - Onset of encephalitis is marked by:
    - Periods of excessive motor activity
    - Agitation accompanied by hallucinations
    - Combativeness
    - Muscle spasms
    - Seizures followed by coma

- There can also be:
  - Excessive salivation
  - Dysfunction of brain and cranial nerves
  - Double vision, facial palsy, and difficulty in swallowing
  - Involvement of respiratory centers causes respiratory paralysis.
  - Major cause of death
  - Median survival after the onset of symptoms is 20 days.
**Rabies:**

**Treatment**

- Prevention is the best cure.
- Treatment consists of a course of injections.
  - Only beneficial if administered before the onset of symptoms
- Mortality for rabies is 90%.

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**Polio**

- Condition first known as infantile paralysis
  - Risk of paralysis actually increases with age.
- Essentially nonexistent in most modern countries
  - There is an effective vaccine.
- Still a major problem in underdeveloped countries

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**Polio:**

**Pathogenesis**

- Virus is an enterovirus with an affinity for the CNS.
  - Normally crosses the blood-brain barrier
  - Can also use axons or the perineural sheath of the peripheral nervous system
- Motor neurons are particularly vulnerable.
POLIO: Pathogenesis

- Various levels of neuronal destruction cause:
  - Necrosis of neural tissue
  - Infiltration by mononuclear cells, primarily lymphocytes
  - 90% of poliomyelitis infections are very mild and subclinical.
  - Incubation time varies from 4 to 35 days.
    - Average is about 10 days.

POLIO: Pathogenesis

- Three types of polio infection:
  - Abortive poliomyelitis
  - Nonparalytic poliomyelitis (aseptic meningitis)
  - Paralytic poliomyelitis

POLIO: Pathogenesis

- Abortive poliomyelitis:
  - Nonspecific febrile illness
  - Lasts two to three days
  - No signs or symptoms
**POLIO: Pathogenesis**

- Nonparalytic poliomyelitis (aseptic meningitis):
  - Characterized by meningeal irritation, stiff neck, back pain, and back stiffness
  - Rapid and complete recovery

**POLIO: Pathogenesis**

- Paralytic poliomyelitis:
  - Occurs in 2% of persons infected
  - Characterized by asymmetric flaccid paralysis
    - Extent varies from case to case
  - Temporarily damaged neurons can regain function
    - Recovery can take six months
  - Paralysis persisting after this period is permanent

**POLIO: Prevention**

- Polio vaccine essentially wiped out this infection.
- Two types of vaccine:
  - Inactive form – developed by Jonas Salk
  - Live attenuated form – developed by Albert Sabin
VIRAL ENCEPHALITIS

- Neurological infections classified as viral encephalitis are caused by arboviruses.
  - Not a microbial taxonomic group
  - There is a variety of clinical types.
  - These viruses are common in U.S.
    - Increased occurrence of infections in summer months due to increased number of mosquitoes

Infections range in severity from subclinical symptoms to rapid death.
- Infections are all characterized by chills, headache, and fever.
  - Can lead to mental confusion and coma
- Survivors can subsequently develop permanent neurological disease.

Both horses and people are affected by arboviruses:
- Eastern equine encephalitis (EEE)
- Western equine encephalitis (WEE)
  - Cause severe infection in humans
- St. Louis encephalitis is the most common form of arbovirus encephalitis.
  - Less than 1% show clinical symptoms
**VIRAL ENCEPHALITIS**

- West Nile virus is an emerging encephalitis infection.
  - Mostly affects birds
  - Can also infect humans and horses
    - Most human cases are subclinical.
    - Some can be a severe infection with rapid death in elderly

**PERSISTENT VIRAL CNS INFECTIONS**

- Progressive neurological diseases in both humans and animals are caused by viruses or other filterable agents.
  - Termed slow viral disease
  - Better term is persistent viral infection
    - Long period between infection and illness
    - Prolonged period of illness

**CONVENTIONAL VIRAL AGENTS**

- Several major persistent viral CNS infections are caused by viruses (conventional agents).
- Subacute sclerosing panencephalitis:
  - Rare chronic measles infection
  - Occurs in children
  - Produces progressive neurological disease
  - Insidious onset of personality change, progressive intellectual deterioration, and dysfunction of the autonomic nervous system
CONVENTIONAL VIRAL AGENTS

- Several major persistent viral CNS infections are caused by viruses (conventional agents).
- Persistent enterovirus infection:
  - Seen in patients with congenital or acquired immunodeficiency
  - Chronic CNS infection
  - Characterized by headache, confusion, lethargy, seizures, and increased numbers of mononuclear cells in CNS
  - Caused by both echoviruses and enteroviruses.

AIDS dementia complex:
- Presents as a persistent CNS infection
- Seen in asymptomatic AIDS patients
- Clinical course varies from mild to very severe progressive dementia.

UNCONVENTIONAL AGENTS

- Prions (unconventional agents) cause five fatal CNS infections in mammals.
- Prions do not elicit inflammatory or immune responses in a host.
- Pathogenesis of these infections is not well understood but they have similar features.
  - Loss of neurons
  - Proliferation of astrocytes
  - Vacuoles seen in the brain cortex and cerebellum
UNCONVENTIONAL AGENTS

- Incubation period can be from months to years.
- Course of infection is protracted and always fatal.
- Prions are very hard to destroy:
  - Remain viable in brain tissue after years of being immersed in formalin
  - Resistant to ionizing radiation and many common disinfectants

UNCONVENTIONAL AGENTS: Kuru

- Subacute progressive neurological disease
  - Discovered 1957 in the Fore people of New Guinea
  - Symptoms are failure of muscular coordination, hyperactive reflexes, and muscular spasms
  - Leads to progressive dementia and death
  - Causes diffuse neuronal degeneration and spongiform change of the cerebral cortex and basal ganglia

UNCONVENTIONAL AGENTS: Creutzfeld-Jacob disease

- Progressive fatal infection often seen in patients aged 60-70 years
- Initially presents as a change in cerebral function
  - Often mistaken for a psychiatric disorder
  - Patient exhibits forgetfulness and disorientation
  - Progresses to overt dementia
UNCONVENTIONAL AGENTS: Creutzfeld-Jacob disease

- Progression can last 4 – 7 months and involve changes in gait, involuntary movements, and seizures.
- There is eventual paralysis, wasting, pneumonia, and death.
- Infection seen throughout the world
  - One case per million people is reported each year.

Mode of transmission is essentially unknown but could include:
- Contaminated dura mater grafts and corneal transplants
- Contact with contaminated instruments used in neurosurgical procedures
- Transmission has also been linked to contaminated growth hormone.
- No evidence of transmission by direct contact or airborne spread.

Incubation period is anywhere from 3-20 years.
- Pathology identical to that seen in kuru
  - High levels of prions are found in the brain
- Examination of brain tissue is the only way to confirm the disease.
- There is no treatment.
UNCONVENTIONAL AGENTS:
Fatal Familial Insomnia

- Presents as a difficulty in sleeping followed by increasingly progressive dementia.
- Occurs in people between 35-61 years.
- Always fatal
  - Death occurs between 13-25 months after diagnosis.

UNCONVENTIONAL AGENTS:
Bovine Spongiform Encephalopathy

- BSE (mad cow disease) was first identified in the UK in 1986.
  - Source of prions traced to cattle feed containing bone meal from sheep that had scrapie.
  - Cows ate the feed and became infected.
  - The infection passed to humans who ate infected beef.
- Infection in humans is known as variant Creutzfeld-Jacob disease (vCJD).
  - Cases frequently present in young adults.
  - Presents as psychiatric problems progressing to dementia.
  - Average life expectancy after diagnosis is 14 months.

FUNGAL INFECTIONS OF THE CNS

- Primarily opportunistic
- Usually seen in immunocompromised patients
CRYPTOCOCCOSIS

- Cryptococcosis is the most important fungal CNS infection.
- Caused by *Cryptococcus neoformans*
  - Encapsulated form of yeast
  - Capsule production varies with the strain and environmental conditions.
  - Found throughout the world, especially in soil contaminated with bird droppings
    - Birds are not infected.

CRYPTOCOCCOSIS: Pathogenesis

- Causes a chronic form of meningitis
  - Slow, insidious onset
  - Symptoms include low-grade fever and headache
  - Progresses to altered mental status and seizures

CRYPTOCOCCOSIS: Pathogenesis

- Infection usually seen in patients immunocompromised.
  - Common in AIDS patients
  - Infection begins with inhalation of the yeast cells.
  - Each yeast cell begins to overproduce its capsule.
    - Capsule is anti-phagocytic.
    - Can bind to complement components
      - Reduces opsonization
    - Can interfere with the presentation of antigens to T cells
      - Inhibits the adaptive immune response
CRYPTOCOCCOSIS: Pathogenesis

- After inhalation, yeast cells multiply outside the lungs and move into the nervous system.
- Initial symptoms can continue for weeks or months.
  - Intermittent headache, dizziness, and difficulty with complex cerebral function
- Later stages of the infection show:
  - Seizures, cranial nerve damage, and papilledema (edema of the optic nerve)
  - Dementia and decreased levels of consciousness
- Progression of disease is accelerated in patients with AIDS.

CRYPTOCOCCOSIS: Treatment

- Amphotericin B and fluconazole are effective.
- 75% patients with cryptococcal meningitis initially respond to treatment.
  - Significant portion relapse when therapy is stopped
- Patients with chronic infection require repeated courses.
- Residual neurological damage occurs in more than half of cured patients.

PARASITIC INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

- Free living amebas can infect the CNS.
  - Cause parasitic amebic meningoencephalitis
- Infections are rare and usually fatal.
PARASITIC AMEBIC MENINGOENCEPHALITIS

- Caused by free-living amebas of two genera
  - *Naegleria*
  - *Acanthamoeba*
- *Naegleria* is found in large numbers in shallow freshwater ponds, especially in warm weather.
  - Acquired by swimming in fresh water
  - Infection seen in children and young adults
- *Naegleria* infection is infrequent and almost always fatal.

PARASITIC AMEBIC MENINGOENCEPHALITIS

- *Acanthamoeba* causes a sub-acute or chronic illness.
  - Almost always fatal
  - *Acanthamoeba* found in soil and fresh brackish water.
    - Most occur in the southeastern US
    - Patients typically fall ill during the summer after swimming or water skiing in small shallow freshwater lakes.
- *Acanthamoeba* is also found in the oropharynx of asymptomatic humans.

AMEBIC MENINGOENCEPHALITIS: Pathogenesis

- *Naegleria* enters the CNS by traversing the nasal mucosa and cribriform plate.
- In the CNS produces a purulent, hemorrhagic inflammatory reaction.
  - Extends from the olfactory bulb to other regions of the brain
- Characterized by rapid onset of severe bifrontal headache and seizures
  - Occasionally abnormal sense of taste and smell
- Progresses to coma and death within days.
- Wet mounts of cerebrospinal fluid reveal trophozoite forms of the parasite.
AMEBIC MENINGOENCEPHALITIS:
Pathogenesis

- Epidemiology of *Acanthamoeba* encephalitis is not clearly defined.
  - Known to involve the elderly and immunocompromised
- Thought that the ameba reaches the brain by hematogenous dissemination
  - Site of infection is unknown, possibly respiratory, eye, or skin.
- Infection produces diffuse necrotizing granulomatous encephalitis

AMEBIC MENINGOENCEPHALITIS:
Pathogenesis

- Both cysts and trophozoites can be found in lesions.
- AIDS patients can have:
  - Cutaneous ulcers and hard nodules containing amebas
  - Amebas in the cerebrospinal fluid.
- Clinical course of *Acanthamoeba* infection is more prolonged than that of *Naegleria*.
- *Acanthamoeba* occasionally ends in spontaneous recovery.
  - It is invariably fatal in the immunocompromised.
AMEBIC MENINGOENCEPHALITIS: Treatment

- Only four patients have ever survived infection with *Naegleria*.
  - All were diagnosed early
  - Treated with high doses of amphotericin B with rifampin