NERVOUS SYSTEM
Neurons - highly specialized.
Not much capacity to regenerate
Specialized chemicals for nerves to talk to each other- nervous system must be isolated.
no normal flora.
Barrier for isolation - in a "plastic" bag

Brain and spinal cord
meninges : dura matter, arachnoid matter, pia matter (outside to inside).
bag filled with fluid. Fluid mostly between arachnoid and pia matter = cerebral spinal fluid. Nutrients and oxygen enter via blood to brain. Vessels must reach deep into brain.
CSF -- shock absorber, mechanical + chemical barrier. Not a molecular barrier.

Molecular Barrier at Blood Vessels
Lining cells of capillaries - very densely packed, forms blood/brain barrier. Oxygen nutrients pass. Stops MOST microbial infection.
Brain has no lymphatic circulation instead menigial fluid takes over the hydrodynamic functions of the lymph.
CSF tested by lumbar puncture.
Normal--very little protein, few antibodies, very few white cells.
Inflammatory Process or Blood/Brain Breach: abundant protein and antibodies, cells, WBC, lymph, + macrophages.
BRAIN - generally organized with nerves inside and cell bodies outside.
SPINAL CORD - Nerves out, cell bodies inside
NEURONS - sensory, signals in; motor, signal out.

Infections of PERIPERAL NERVES

BACTERIAL:
LEPROSY - (Hansen’s disease)
– 2 types Caused by Mycobacterium leprae. Schwann cells. Picked up by nasal secretions. Causes nerve damage by inflamed granuloma near those nerves.
1. Tuberculoid leprosy -
The outcome is much like Mtb. Occurs if the immune response activates macrophages. A strong delayed hypersensitivity reaction but a weak antibody response. lymphocytes forming granulomas. Relatively few bacilli are seen in tissues because production of cytokines mediates macrophage activation, phagocytosis and bacillary clearance.
2. Lepromatous leprosy -
occurs if the immune response activates antibodies. This is the most infectious form of leprosy. Damage is due to nerve destruction.

culture difficult: grows in........

Also remember Clostridium Botulinum and Tetanus
VIRAL
HSV -
Initiated by direct contact, dependant on infected tissue.
Causes direct cytopathology. Avoids antibody by cell-cell spread.
Latency occurs in neurons. Reactivated by stress or host compromised.
Cell mediated immunity is necessary to rid the infection. Both NK cells and T cells

POLIOMYELITIS -
caused by polio virus, enterovirus; picorna. Enters through the gut, the virus spreads from the blood to anterior horn cells of spinal cord + motor cortex of the brain. Severity of the paralysis depends on neurons affected.
fecal-oral route.
Vaccination:
Salk - killed virus in suspension
Sabin - live virus, only infects gut cells. Colonizes the gut, this causes generation of antibodies which protect neurons from infection of the wild type.

RABIES -
rhabdovirus; transmitted by animal bites. Virus multiplies at site of inoculation remains localized for days to months, before infecting the peripheral nerves. Once virus reaches spinal cord rapid infection of brain follows. Virus then disseminates from the CNS via afferent neurons to highly innervated sites. Antibody can block the spread of the virus to CNS and brain, if present during incubation. Hydrophobia - stemming from pain associated with attempts to swallow water, due to spasms in the throat ="foaming at the mouth".

MENINGEAL INFECTIONS
Bacterial Meningitis
Strep. pneumonia - common inhabitant of throat and nasopharynx.
Haemophilus
E. coli - causes neonatal meningitis.

Neisseria meningitis - Encapsulated, G negative, diplococci.
Can asymptotically colonize the nasopharynx of healthy people or cause meningitis.
Pathogenesis by three factors:
– 1) ability to colonize nasopharynx
– 2) systemic spread [ if no antibody-mediated phagocytosis] (capsule)
– 3) expression of toxic effects.
Attaches selectively to specific receptors for menigoccocal pili. Binds to nonciliated columnar cells of the nasopharynx. The anti-phagocytic characteristic of the polysaccharide capsule protects it from phagocytosis. The diffuse vascular damage is in large part because of the lipopolysaccaride endotoxin. Serum bactericidal antibodies are important for preventing systemic disease.
Transmission is by respiratory droplets. Humans are only natural carriers.

Listeria monocytogenes
facultative intracellular pathogen, motile, capable of growth in macrophages, epithelial cells and fibroblasts.
listeriolysin O, necessary for release of bacterium after phagocytosis made by all virulent strains
intracellular growth--breaks the phagolysozome which releases the bug. The bug then takes up actin and uses it to push through host cells. [spread!]

FUNGAL
Cryptococcus neoformans - fungus -yeast form. Capsular polysaccharide (acidic), critical for pathogenicity.
Lung -primary site of infection but spreads to the brain and meninges. --pigeon habitats.
Can produce symptomatic pneumonia, also localize to bone infection.

PROTOZOA

Toxoplasma gondii - causes meningo-encephalitis=infests meninges and brain. Most common reservoir is cats. Intracellular parasite. Humans become infected by 2 sources:
1) improperly cooked meats
2) infective oocysts from cat feces.
Illness is affected by immune status of the person
reactivation of previously latent infection common. Can be benign and asymptomatic with symptoms only occurring as the parasite moves in the blood to tissues where it becomes an intracellular parasite. Avoids phagosome fuse with lysosome --covers itself with the host's protein called laminin.

VIRAL
Encephalitis - arboviruses, host in arthropods; alphavirus and flavivirus. Attach to specific receptors.
The flavivirus attaches to Fc receptors on macrophages, monocytes, and other cells when they are coated with antibodies. The antibody enhances the infectivity of the virus by providing new receptors for the virus, promotes uptake into cells. The difference between alphavirus and flavivirus: the organization of their genomes and the mechanisms of protein synthesis. Both cause lytic or persistent infections. They make a nucleotide triphosphatase that degrades DNA. The virus infects the epithelial cells of the midgut of the mosquito and spreads through the basal lamina of the midgut to the circulation, then infects salivary glands. The virus sets up persistent infection and replicates to high titers. The mosquito inserts virus containing saliva into the victim’s bloodstream. The virus circulates free in the plasma and comes in contact with the target cells.

These viruses may cause mild systemic infections because of the inflammation due to induction of interferon. (like rhinoviruses)

SLEEPING SICKNESS
-caused by Trepanosoma brucei, a flagellated protozoan
- transmitted by bite of tsetse fly.
- infected state is trypomastigote, these enter the wound by bite and get into blood and lymph eventually invading CNS.
- Produces chronic and progressive disease.
- early sign of disease may be an occasional ulcer at site of bite
- ability to undergo rapid genetic modifications and change the antigen present on their surface
this means protective antibody resistance is limited.

SLOW VIRUSES (or PRIONS)
- are modified host proteins that leads to proteinaceous aggregates in the brain, which leads to progressive neuronal damage
- no immune response then no inflammation
Creutsfelt-Jacobs disease - a genetic predisposition. Transferred by contaminated tissue, medical devices, and injection.
Kuru - found in New Guinea highlands. Transmitted by ritual cannibalism.
Causes shivering and trembling.
NOTE: No treatment for CJD or Kuru exists.