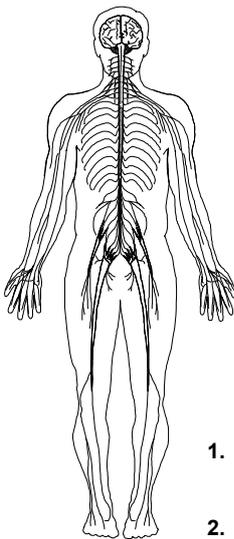


BBS2711

Virology

Central Nervous System (CNS) Viruses

*Dr Paul Young, Department of Microbiology & Parasitology.
p.young@mailbox.uq.edu.au*



Viruses of the CNS

Many human pathogenic viruses are capable of spreading to the CNS

Neurological disease however is exceptional rather than normal consequence of infection
e.g. alpha, flavi, entero and herpes viruses
most commonly implicated but still rare

Access to the CNS:

- 1. direct spread through blood vessels (of brain and spinal chord) eg alpha, flavi, polio, mumps.**
- 2. by neural route from peripheral nerves (eg rabies, herpes)**

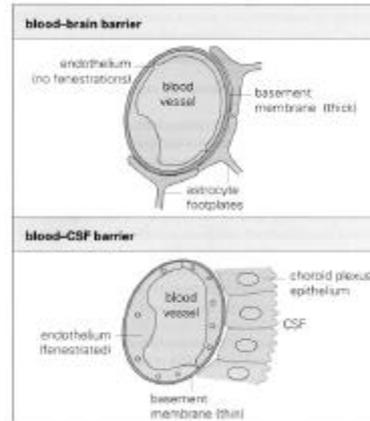
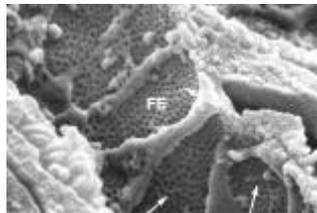
Blood-borne invasion of the CNS

In most regions of the CNS

- capillary endothelial cells joined by tight junctions
- underlying dense basement membrane

Exception is the choroid plexus

- capillary endothelium is fenestrated
- underlying basement membrane is sparse



it is here that many viruses invade the CNS

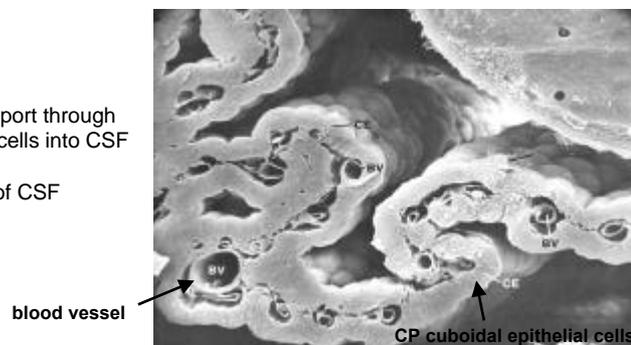
CNS invasion proceeds via a number of steps

1. Viruses may enter stroma of choroid plexus by

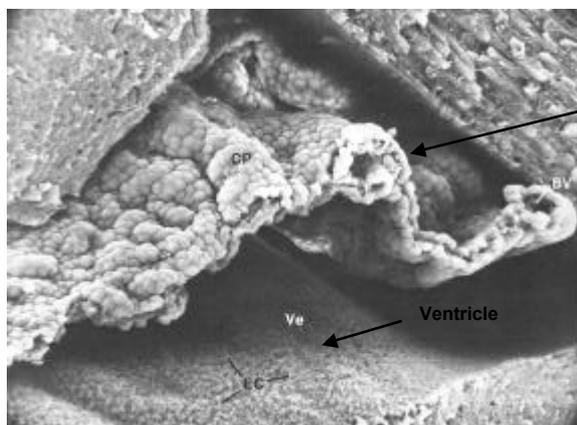
- growth through endothelium (enteros, alphas)
- leakage through or passive transfer (via fenestrations)
- transport within migrating infected monocytes or lymphocytes (measles, mumps, HIV)

2. Infection or passive transport through choroid plexus epithelial cells into CSF

- spread in CNS by flow of CSF



3. Infection of ependymal cells lining ventricles leads to invasion of underlying brain tissue (mumps, alphas)



Choroid plexus

Ventricle

Some viruses localize in small blood vessels of brain & spinal cord
- direct invasion of neural tissue

Neural spread to the CNS

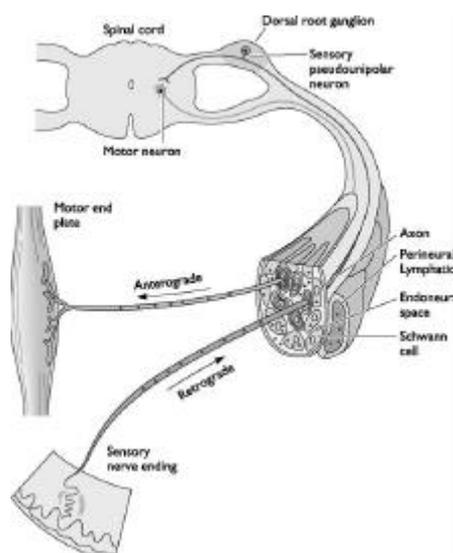
Pasteur was first to demonstrate virus transmission along nerves (rabies)
transport slow - ~10mm/hour

- herpes, polio and some arboviruses also known to travel along peripheral nerves

May enter sensory or motor neuron endings

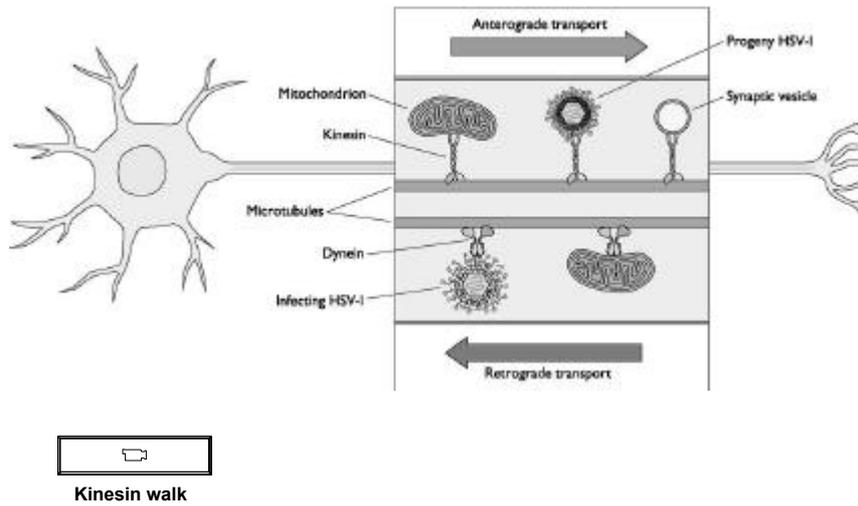
Various routes are available:

1. within axons
- MUST be transported to cell body
2. endoneural space
3. perineural lymphatics
4. endoneural cells, eg Schwann cells



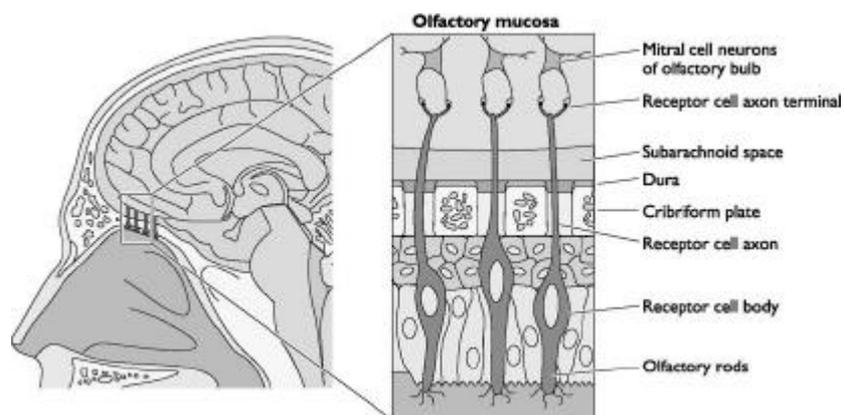
Rabies and herpes transported across axon terminals at neuromuscular junction

- viruses hitch a ride on microtubule network



Nerve fibres of olfactory bulb offer potential direct path from olfactory mucosa

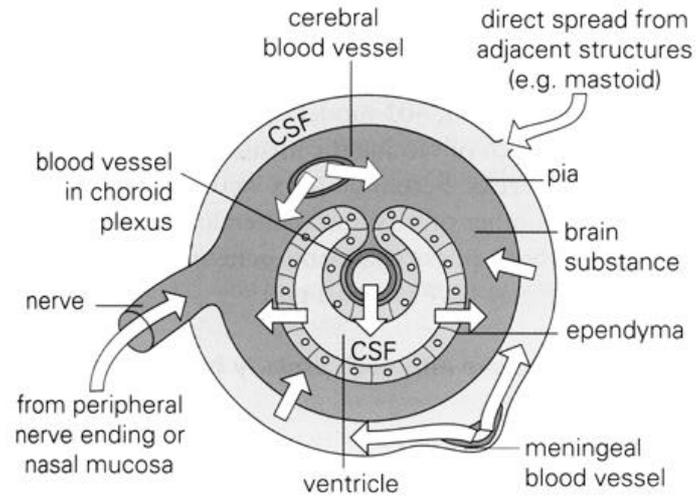
- rabies virus in speleologists!



Some flaviviruses via bloodstream to neurones of olfactory bulb

- then retrograde neural spread to CNS

Summary of available routes of entry for viruses into the CNS



Outcome of invasion of CNS by viral infection

- some viruses cause meningitis (coxsackie and echo)
- others cause meningitis and encephalitis as a result of invasion of brain tissue (mumps, polio, herpes)

Cytocidal infections of neuronal cells characterized by:

- cell necrosis
- phagocytosis by glial cells
- perivascular infiltration by inflammatory cells

hallmarks of encephalitis whether caused by polio, arbo or herpes

Viral neurological diseases fall into two clinical categories

Acute neurological disease

There are four main syndromes:

1. *Encephalitis*

- Viral replication occurs in brain tissue itself causing destructive lesions in grey matter.
- Symptoms are fever, drowsiness, mental confusion, convulsions, focal neurological signs
- Morbidity and mortality high

- herpes simplex, arbo, rabies, AIDS dementia complex

2. *Paralysis*

- Direct infection of motor neurones.
- Fever and flaccid paralysis of lower limbs – meningitis often associated

- polio, enteros

3. *Aseptic meningitis*

- Inflammation of the meninges – cells in CSF (lymphocytes).
- Relatively mild disease – fever, headache, neck stiffness

- enteros, mumps

4. *Post-infectious encephalomyelitis*

- Symptoms similar to encephalitis, brain and spinal cord involved – virus not found in either.
- Demyelating lesions and lymphocytic infiltration
- Believed to be auto-immune response
 - triggered by exposure to foreign proteins - molecular mimicry
- Guillan-Barre syndrome – peripheral nerve roots rather than substance of the brain or spinal cord
 - post flu vaccine

Chronic neurological disease

- Rare, long incubation, slow progression but invariably fatal
- Symptoms are varied: neurological & often affect intellectual capacity as well as both motor and sensory functions
 - *Subacute sclerosing panencephalitis (SSPE)*
 - measles persistence
 - *Spongiform encephalopathies*
 - Prion diseases
 - *Retrovirus* – HIV1 and 2 - dementia

Learning objectives

- ***Mechanisms, pathways and examples of blood-borne and neural invasion of the CNS***
- ***Clinical outcome and details of selected CNS viruses***