Neuroinfections

- Diseases of the NS caused by:
- Viruses
- Bacterias
- Candides
- Parasites

- sometimes fulminant course of disease and fatal complications

Neuroinfections - etiological classification

- 1. Bacterial
- 2. Viral
- 3. Fungal
- 4. Specific (e.g. TBC)

Neuroinfections

1. Meningitis
2. Encefalitis
3. Meningo-encefalitis
4. Myelitis
5. Neuritis, polyneuritis
6. Radiculitis, polyradiculoneuritis

Etiopatogenesis

- Spread of viruses to the CNS by the hematogeneous or neural route

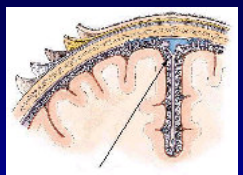
A) Hematogeneous route - the viruses gain the CNS through perivascular spaces, entrance in the CSF is through the epithelial cells of the choroid plexus

B) Neural - (Herpes simplex vírus - HSV, Varicella zoster vírus - VZV)

C) Direct spreading from ear, nose, injury

Meningitis

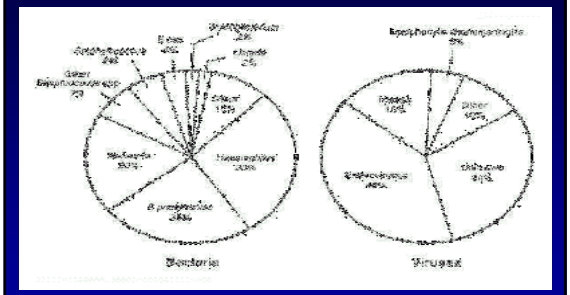
- **Meningitis** is the inflammation of the meninges, (the membranes around the brain and spinal cord)
- **Pachymeningitis -** involves the outermost membrane
- is generally caused by trauma, such as a skull fracture, or by extension of an infection.
- **Leptomeningitis-** involves the inner membranes, and may be caused by invading bacteria from other organisms



Meningitis

- The germs that cause **bacterial meningitis** are very common and live naturaly in the back of the nose and throat
- People of any age can carry these germs without becoming ill

Meningitis:
1. Bacterial
2. Viral
3. Mycotic



Meningitis

- **Etiological agents**
- **Streptococcus pneumoniae**
- **Neisseria meningitidis**

Meningitis

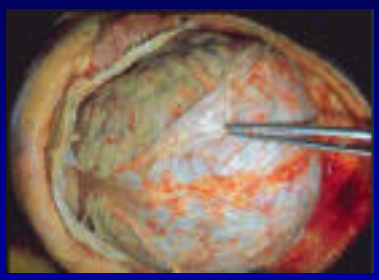
- **Etiological agents (G-)**

- **E. colli**
- **Klebsiella pneumonie**
- **H. influenzae**
- **Pseudomonas**
- **Enterobacter species**
- **Listeria monocytogenes**

Meningitis

- **Enteroviruses: Echovirus, Coxackie**
- **Mumps (late winter and spring)**
- **Herpes simplex, typ 2, Epstein-Barr**
- **Lymfocytic choriomeningitis (winter)**
- **Adenovirus infections**
- **HIV**

Pneumococcal meningitis



Pathogenesis - bacterial, purulent meningitis

- Bacteria from the place of primary infection → to blood → CSF through chorioid plexus of the lateral ventricles, or other areas of altered BBB permeability
- Germs multiply rapidly in the subarachnoid space
- Recruitment of inflammatory cytokines (IL-1, TNF) and polymorphonuclear leukocytes

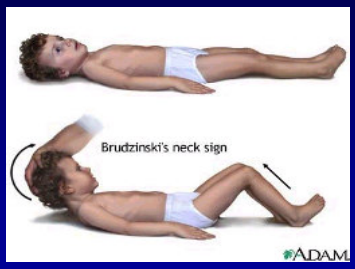
Pathogenesis - bacterial, purulent meningitis

- Result – purulent exudate in subarachnoid space, which is the basis of the neurological complications
- Obstruction of flow of CSF
- Adherence of leukocytes to the cerebral capillary endothelial surface increase the permeability of cerebral vessels → allowing for leakage of plasma proteins through open intercellular junctions → vasogenic brain edema

Clinical features

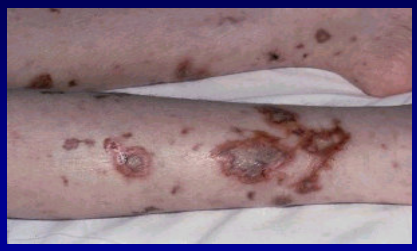
- Headache
- Fever ↑ (↓ - sepsis)
- Neck stiffness (not present in sepsis !)
- Fotophobia
- Vomitus
- Intracranial hypertension
- Altered level of consciousness
- Seizures

Meningeal syndrome



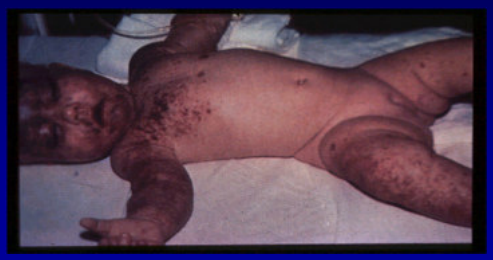
Kernig – flexion of passive extended LE

Petechial rash in meningococcemia (Neisseria meningitidis) – develops in few hours



(trunk, LE, mucous membranes, conjuctiva, palms, soles

Meningococcal meningitis



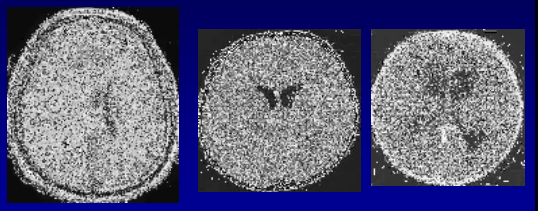
Clinical features – neonates !

- Fever or hypothermia
- Lethargy
- Seizures
- Irritability
- Bulging fontanel
- Poor feeding
- Vomitus
- Respiratory distress
- Absence of meningeal syndrom – can be

CSF

- Increased CSF pressure
- Blood - ↑ Leu, FW, CRP
- Viral meningitis
  - Pleocytosis : ↑ lymphocytes, proteins +/-, sugar is normal
- Bacterial meningitis
  - Pleocytosis: ↑ polymorfonuclear leukocytes
  - ↑ proteins, ↓ sugar

Brain CT



Therapy

- The 3rd.generation Cephalosporins
- Ampicilin
- Dexamethason – inhibits the syntesis of inflammatory citokines – IL-1, TNF
- Antiedematous treatment – Manitol
- Symptomatic therapy

TBC, tuberculous meningitis

- **TBC – frequent in 20th century**
- **Chopin, Keats, Paganini, Modigliani, Thomas Wolf – died because of TBC**
- **90-ties of 20th century – again increased number of TBC**

TBC meningitis

- **Etiology - Mycobacterium tuberculosis**
- During dissemination from caverna - exudate, which is located predominantly in **basilar cysterns,** surrounds the cranial nerves and major blood vessels at the base of the brain

TBC meningitis

- Headache
- Meningeal syndrome
- Cranial nerves lesions - VI, III, IV, VII
- Changes in behaviour, confusion
- Hydrocephalus
- Brain edema

CSF

- Increased CSF pressure
- Pleocytosis – Ly
- ↓↓ sugar
- ↑ proteins
- positive cultivation
- Positive PCR test

Therapy

- **INH + Rifampicin + Pyrazinamid**
- Corticosteroids
- Manitol

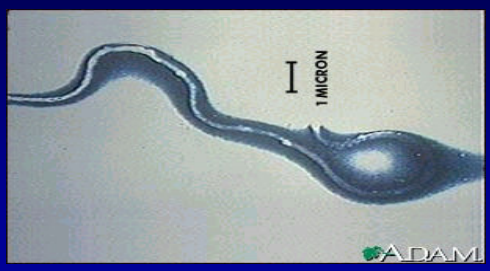
- **Symptomatic therapy**

Spirochetal infections

- **Borreliosis (Lyme disease)**
  Etiology: Borrelia Burgdorferi

- **Syphylis (Lues)**
  Etiology: Treponema pallidum

Borrelia burgdorferi

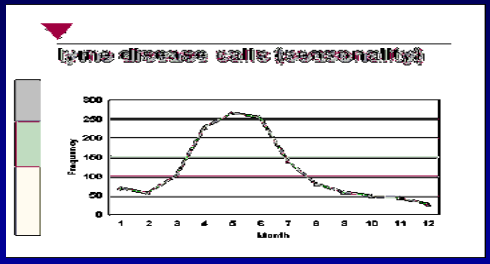


Lyme disease

After tick bite

Skin lesion

Lyme disease



Lyme disease - pathogenesis

- **Spreading –** by spirochetemia, spreading in all the body
- CNS and PNS clinical feature

- **Early symptoms:** meningitis, facial nerve palsy (less other cranial nerves), radiculoneuritis
- **Late symptoms:** encephalopathy senzorimotor polyradiculoneuropathy

Lyme disease - meningitis

- Within 12 weeks of infection
- **Headache, fatigue, myalgia, arthralgia**

- **CSF:**
  - pleocytosis – Ly
  - ↑ proteins
  - sugar – normal
  - intrathecal production of BB antibodies -IgG, IgA
- PCR

Lyme disease – facial palsy

- In 4 weeks from erythema migrans
- Unilateral or bilateral facial palsy
- Other cranial nerves - rarely

- Dg: ELISA test (antibodies)
- CSF: pleocytosis – Ly, intrathecal production of antibodies (about 10 %)
- Treatment:
- CSF negat.- Doxycycline (2x100 mg/D, 2W) i.v.
- CSF pozit.- Ceftriaxone

Lyme disease - radiculoneuritis

- **Severe, sharp, jobbing or deep and boring pain, in a radicular nerve distribution**

- **Within days, weeks: sensory loss, weakness, hyporeflexia, if there is myelitis – sphincter dysfunction, + Babinski**

- **CSF: Ly, ↑ proteins, intrathecal production of antibodies**
- **EMG: axonal lesion**

Lyme disease - encephalopathy

- In patients with systemic manifestation and arthritis
- **Confusional state, memory and cognitive slowing**

- **CSF –** only in 5 % pozit. Ly
  less than in 50 % pozit. antibodies

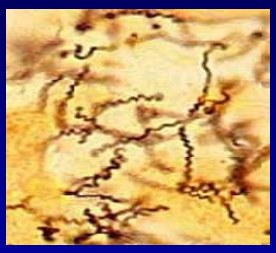
Lyme disease– senzorimotoric polyradiculoneuropathy

- **Chronic radiculoneuropathy –** sensory symptoms, particularly distal paresthesias in a stocking and glove distribution, less severe than in acute polyradiculoneuritis Guillain Barre syndrome
- EMG – axonal lesion
- CSF – frequently negat.

Syphilis (Lues)

•**1/3 nontreated patients – neurovascular complications of syphilis**

•Etiology: spirochetal inf. Treponema pallidum



Neurosyphilis

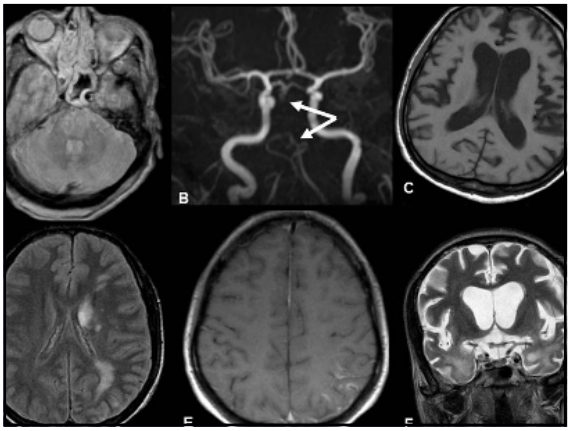
- **Pathogenesis**
- Perivascular infiltration of the meninges
- focal meningeal inflammation – hypertrophic meninges or gumma
- Inflammatory cells invide blood vessel wall – arteritis (luminal occlusion, stroke like epizodes)
- Parenchymal involvement – gliosis in late stages
- Lymphocytic infiltration of preganglionic portion of dorsal roots and posterior columns atrophy of posterior columns

Neurosyfilis – meningitis

- **CSF Ly, ↓ Glu, ↑ proteins**
- **Pozit. VDRL test**

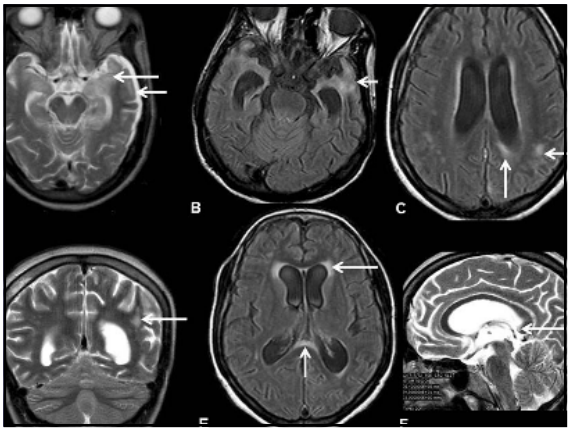
Neurosyphilis – meningovascular

- **Endarteritis –** small and medium vessels (MCA) – can be stroke etiology in young people !!!
- **Focal signs**
- **AG: narrowing of arteries**
- **MRI: multiple infarcts**
- **Spinal artery – transversal myelitis**

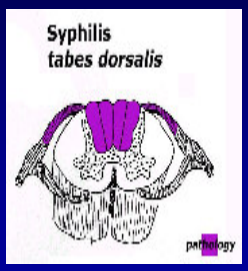


Dementia paralytica Progressive paralysis

- **Decreased cognitive functions**
- **memory problems**
- **pupilary abnormality- Argyll-Roberts pupils**
-



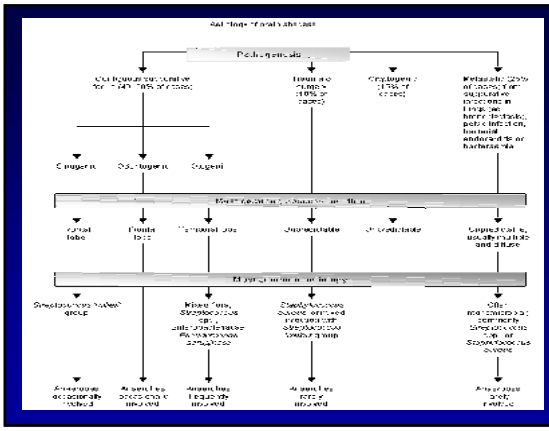
Tabes dorsalis



- Paresthesias in root distribution
- Decreased proprioception
- Spinal ataxia
- Argyll-Roberts pupils

Brain abscess

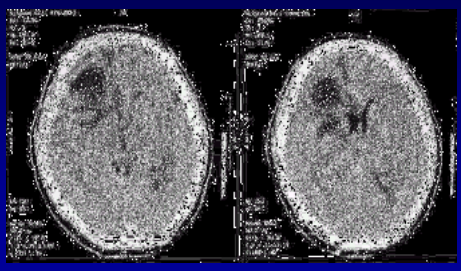
- A rare complication in immunocompetent individuals:
  - AIDS
  - Chronic corticosteroid therapy
  - Immunosupression after bone marrow transplantation



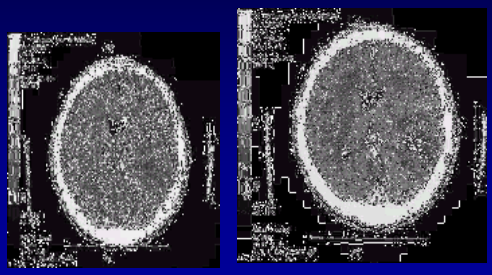
Clinical feature

- Headache
- Fever
- Vomitus
- Focal neurological deficit
- Focal or generalized seizures
- Syndrome ICH – letargy,confusion, coma
- Papilledema
- Palsy of cranial nerves III, VI., or both

Brain abscess - CT

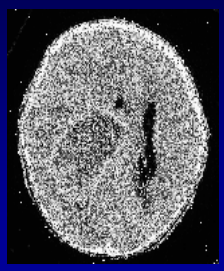


Brain abscess - CT

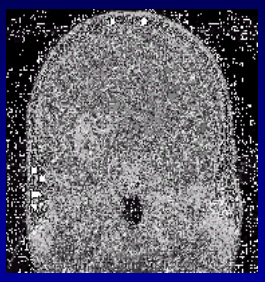


Brain abscess - CT

- Brain abscess in 2 years old child
- Ptosis, fever, papilloedema
- 60 ml of pus Gram + and Gram – bacteria



Brain abscess - CT



Diagnosis and therapy

- **Brain CT** (enhancing lesion)
- **CSF – lumbar puncture – contraindicated!!! in brain abscess**
- **Therapy: aspiration or extirpation abscess + antibiotics**

Encephalitis

- Inflammation od brain tissue
- Frequently with meningitis (meningo-encephalitis)
- Disease course and symptoms:
- impairment of consciousness – confusion, stupor, coma, seizures, aphasia, hemiparesis, involuntary movements, cerebellar ataxia, polymyoclonus, cranial nerves lesions
- Except herpetical - seasonal, epidemic form

Encephalitis

- **VIRAL:**
  - Herpetic
  - Epstein-Barr virus
  - Tick-born
  - CMV
  - Varicella zoster

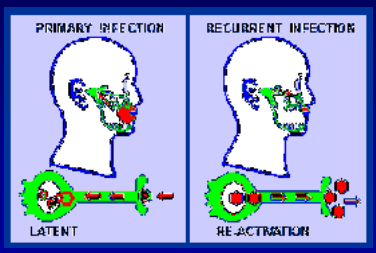
Herpes simplex encephalitis

- **Herpes simplex virus 1**
- Incidence – 4/ 1 million people/year
- Most severe, most frequent
- Without therapy – mortality 70%

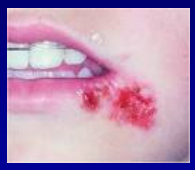
Herpes simplex encephalitis

- After primoinfection – most often oropharyngeal – virus is trasported to *ganglion Gasseri*
- virus survives latent for all life
- In the case of **reactivation** - there is retrograde transport of the virus by rought of n.V.

Herpes simplex encephalitis



Herpes simplex encefalitis



Herpes simplex encephalitis

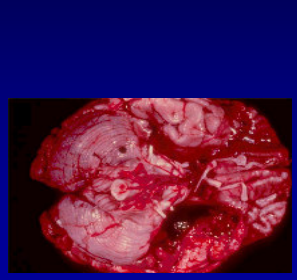
- Clinical feature
  - High fever
  - Headache
  - Vomitus
  - Dezorientation, confusion, memory problems
  - Focal neurological symptoms
  - Seizures

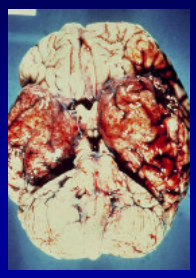
Herpes simplex encephalitis

- Signs from **temporal lobe** – changes in personality and behaviour, aphasia, seizures
- Brain edema – can lead to temporal herniation
- Inflammation, bleeding and pannecrosis of nearly all tissue elements

Herpetic encephalitis

necrosis of temporal lobe

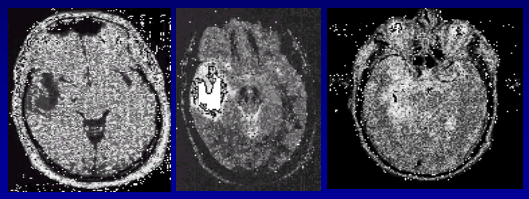




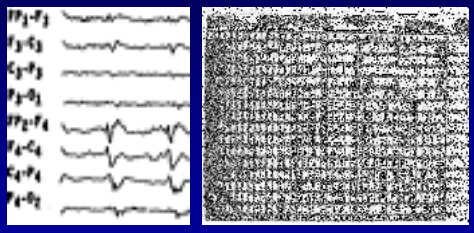
Herpes simplex encephalitis - diagnosis

- **CSF – ↑ Ly, ↑ proteins**
- **CT, MRI**
- **EEG –** high, periodical waves in temporal regio and complex of slow waves in interval 2-3 sec.
- **½ of patients do not survive**
- **Th: Acyclovir 30 mg/kg/D 14 days –** the better prognosis after earlier beginning

Herpetic encephalitis



EEG



Tick-born encephalitis

- TBE is caused by tick-borne encephalitis virus (TBEV), a member of the family Flaviviridae
- Transmitted by Ixodes ricinus
- Initially isolated in 1937
- Clinical course – non-specific with symptoms that may include fever, malaise, anorexia, muscle aches, headache, nausea, and/or vomiting

Tick-born encephalitis

- The CNS symptoms of **meningitis** (e.g., fever, headache, and a stiff neck) or
- **encephalitis** (e.g., drowsiness, confusion, sensory disturbances, and/or
- motor abnormalities such as paralysis) **or meningoencephalitis**
- Myelitis
- Consequences – 10% patients

Tick-born encephalitis

- CSF - an increase in the number of white blood cells
- Low white blood cell count (leukopenia) and a low platelet count (thrombocytopenia)

- There is no specific drug therapy for TBE
- Anti-inflammatory drugs, such as corticosteroids, may be considered

Encephalitis

- Varicella zoster encephalitis (VZV)
- through n.V.

- Epstein-Barr virus (EBV)
- EBV in 90% people
- Manifestation – mononukleosis, with meningitis, encephalitis

- CMV encephalitis
- Imunodeficient people - AIDS

Encephalitis CMV

- Encephalitis cytomegaloviral (CMV)
- After reactivation CMV in immunodeficient persons, AIDS
- Slow disease course (weeks)

- Therapy: antivirotics

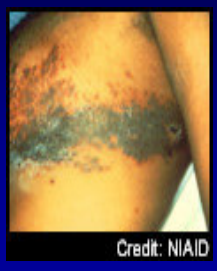
Herpes zoster (shingles)

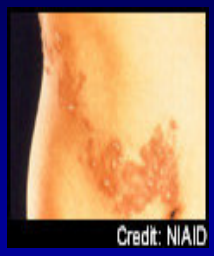
- Varicella zoster virus
- Incidence 3-5 /1000/ year
- old people, with malignancies, mainly lymphoma and M. Hodgkin
- Reactivation of varicella virus – latent in senzoric ganglia after the primary infection with chicken post

Herpes zoster

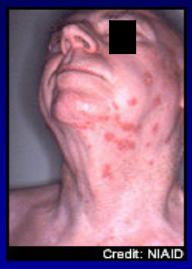
- Radicular pain – sometimes before erruption
- Vesicular cutaneous erruptions spread ower two or three dermatomas on one side
- Most often - thoracal part
- Cranial ganglia – oftalmic paresis
  Ramsay Hunt - n. VII. palsy, vertigo, deafness

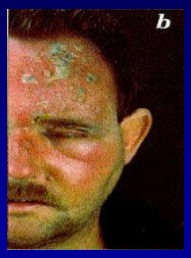
Herpes zoster





Herpes zoster





Herpes zoster

- **CSF –↑Ly and proteins**
- **Pain 1 – 4 weeks**
- **Later complication= postherpetic neuralgia**
- **Treatment: Acyclovir 800 mg 5x /day, 7 days**
  reality – 5 x 200 mg

Herpes zoster

- **Postherpetic neuralgia**
- **Pain in territory of herpes zoster, lasting minimally 3 months after skin erruptions**
- **10 -15% patients**
- **Treatment – Gabapentin 3 x 300 mg– 3 x 1200 mg , pregabalin**
  Common analgetics are not effective!

Prion diseases or transmissible spongiform encephalopathies (TSEs)

- rare progressive neurodegenerative disorders that affect both humans and animals
- They are distinguished by long incubation periods, characteristic spongiform changes associated with neuronal loss, and a failure to induce inflammatory response.

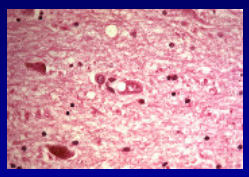
Prion diseases

- Normal prion protein PrP^{c} – encoded by the prion gene (PRNP) on human chromosome 20
- The function of PrP^{c} - role in anti-oxidant systems cellular coper metabolism

Prion diseases

- Prion disease – normal gene produces normal PrP^{c}, post-translational confirmational change to a disease related form – PrP^{sc}
- PrP^{sc} - insoluble and protease resistant protein → accumulates in tissues forming amyloid structures

Prion diseases



- PrP^{sc} deposition →neuronal loss, astrocytic gliosis, spongiform change

Prion diseases

- In human prion diseases – common polymorphism at codon 129 → important effects on susceptibility to disease
- At codon 129 of PRNP an individual may encode for methionin or valin
- 80% of UK sporadic JCD – MM

Prion diseases

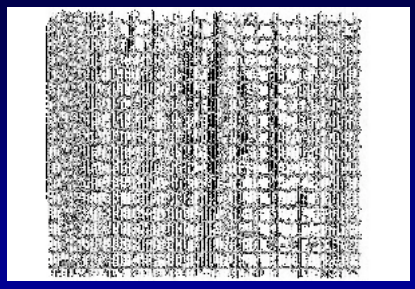
- Creutzfeldt - Jakob Disease (CJD)
- Variant Creutzfeldt-Jakob Disease (vCJD)
- Gerstmann-Straussler-Scheinker Syndrome
- Fatal Familial Insomnia

Creutzfeldt – Jakob sporadic form

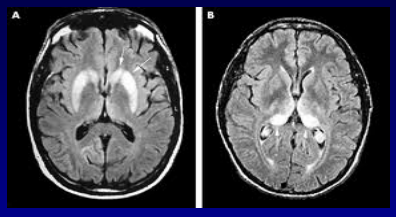
- **90%**
- **Annual frequency – 1/milion/ per year**
- **Middle age (55-70 years)**

Creutzfeldt – Jakob sporadic form

- **Mental deterioration**
- **Speech disorders**
- **Memory loss**
- **Cerebellar signs**
- **Visual –**
- **Pyramidal , extrapyramidal signs**
- **Involuntary movements (myoklonus)**
- **Mutism, global dementia – death (6M-2R)**
- **Lost ability to walk**

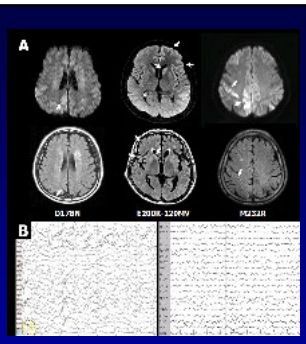


The typical periodic EEG seen in many cases of sporadic CJD.



(A) sCJD: axial FLAIR image at the level of the basal ganglia showing symmetrical high signal in the caudate head and anterior putamen (arrows).

(B) vCJD: axial FLAIR image at the level of the basal ganglia showing symmetrical high signal in the pulvinar and dorsomedial nuclei of the thalamus (arrows).



(A) Brain MRIs - PRNP polymorphisms. The top three are DWI images and the bottom three are T2-FLAIR images. The white arrow indicates a lesion with a high signal.

Creutzfeldt – Jakob disease

- CSF – protein 14-3-3
- Normal protein being released to CSF following neuronal damage
- Not specific for JCD
- Sensitivity – 94%
- Genetic testing – most common mutation – E200K

Gerstmann-Sträussler-Scheinker sy (GSS)

- **Begins between the ages of 45 and 50**
- **Slowly evolving ataxia**
- **Mental deterioration**
- **Dementia, myoclonus, duration 5-10 years**
- **Point mutation at codon 102, 105 (spastic paraparesis), 117 (pseudobulbar signs), 145, 198, 217 (GSS + AD)**

Fatal familial insomnia (FFI)

- Autonomic and endocrine dysfunction
- Insomnia (during day - somnolence)
- Unexplained disorders of temperature, cardiovascular and respiratory regulation
- Later – pyramidal, extrapyramidal signs, cerebellar ataxia, myoclonus
- Duration: 1 –2 years
- Mutation at codon 178

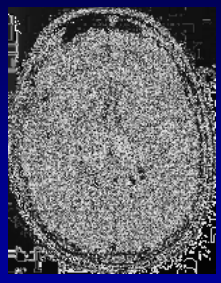
Creutzfeldt – Jakob iatrogenic –accidentally trasmitted

- **Accidentally** introduced into the body
- Length of incubation – 2 years in cases when infection introduced directly into the brain, 15 years – after s.c. inoculation
- Now - rare
- Corneal graft, stereotactic EEG

Creutzfeldt – Jakob new variant (vCJD)

- Due to consumption of beef contamined by the agent of bovine spongiform encephalopathy (BSE)
- Young age at onset of illness (27-50)
- Psychiatric or sensory disturbance
- Long duration of illness (14 months)
- Clinical feature – like sporadic form (dementia, myoclonus, multisystem neurological deficits)

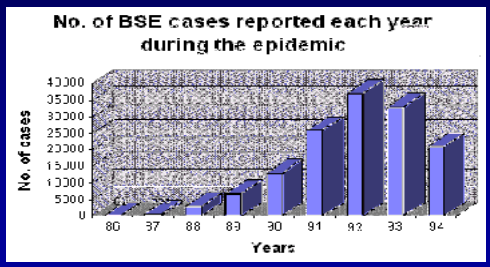
MRI – pulvinar sign



Creutzfeldt – Jacob variant (vCJD)

- **There are no changes on EEG**
- **There is no protein 14-3-3 in CSF**
- **MRI –** abnormally high symmetrical signal in pulvinar talami – strong diagnostic clue
- **Neuropathological examination –** diffuse spongiform changes, especially in BG, posterior thalamus and cerebellum

Bovine spongiform encephalopathy



Acquired immunodeficiency syndrom (AIDS) Human immunodeficiency virus (HIV)

- **Neurological complications**
- **Aseptic meningitis**
- **Cognitive disturbances –** adults
- **Progressive encephalopathy –** children
- **Myelopathy**
- **Neuropathy (inflammatory demyelinizating polyneuropathy, brachial plexopathy, mononeuritis)**
- **Myopathies – myopathy, myositis**

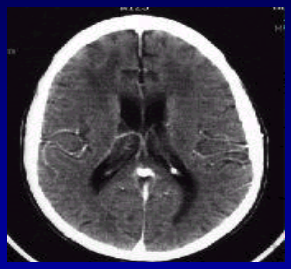
AIDS

- **tumors**
- **Primary lymfoma of CNS (PCNSL) most frequent, children, adult – 5% clinical feature – headache, confusion, impaired memory , seizures, cran. nn.) Dg.: MRI**
- **MTS non-Hodgkin lymfoma into CNS**
- **Kaposi sarcoma**

AIDS

- **Oportune infections**
- **Bacterial –** (Mycobacterium tuberculosis, Treponema pallidum, Nocardia, ...)
- **Viral –** (Cytomegalovirus, Herpes simplex, Varicella zoster, JC, ...)
- **Fungal –** (Cryptococcus neoformans, candida, ...)
- **Protozoal –** (Toxoplazma gondii, ...)

AIDS dementia complex (ADC)
brain atrophy, wide ventricles and subarachnoid space



AIDS dementia complex (ADC)

- **T2- MRI:**
- Enlargement of ventricles, hyperintensity in subcortical white matter of both frontal lobes