Prion diseases or transmissible spongiform encephalopathies (TSEs)

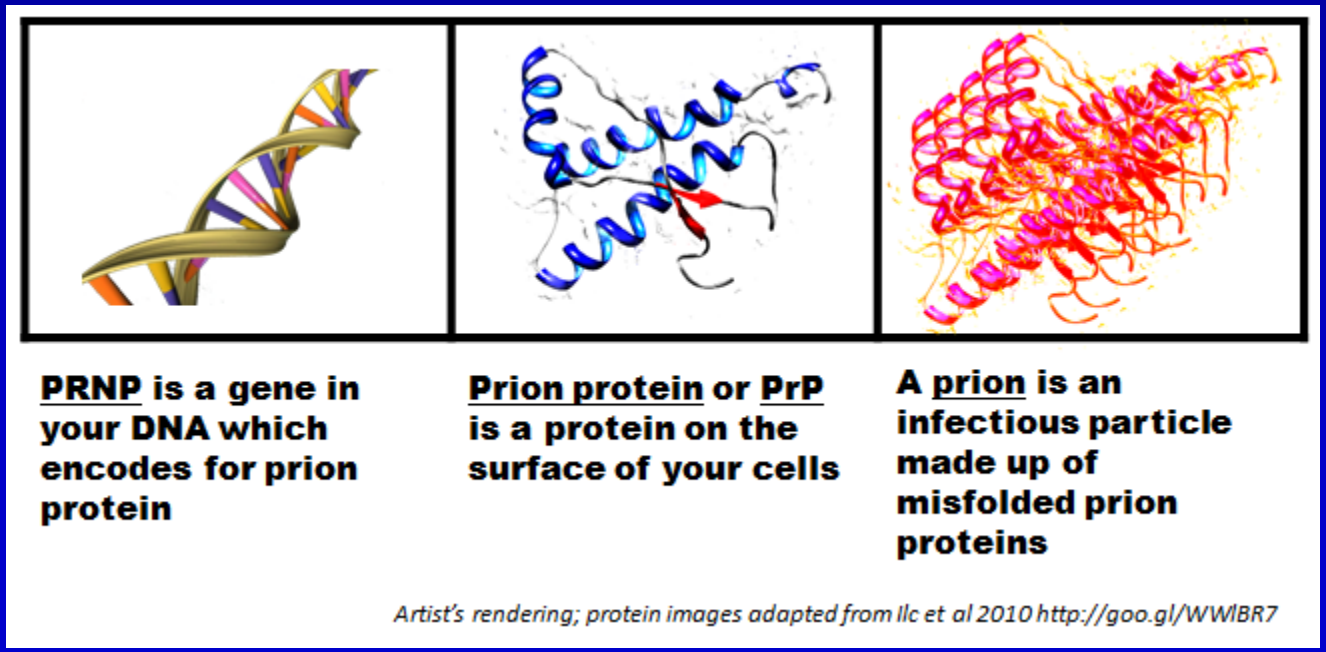
- rare progressive neurodegenerative disorders that affect both humans and animals.
- They are distinguished by long incubation periods, characteristic spongiform changes associated with neuronal loss, and a failure to induce inflammatory response.

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

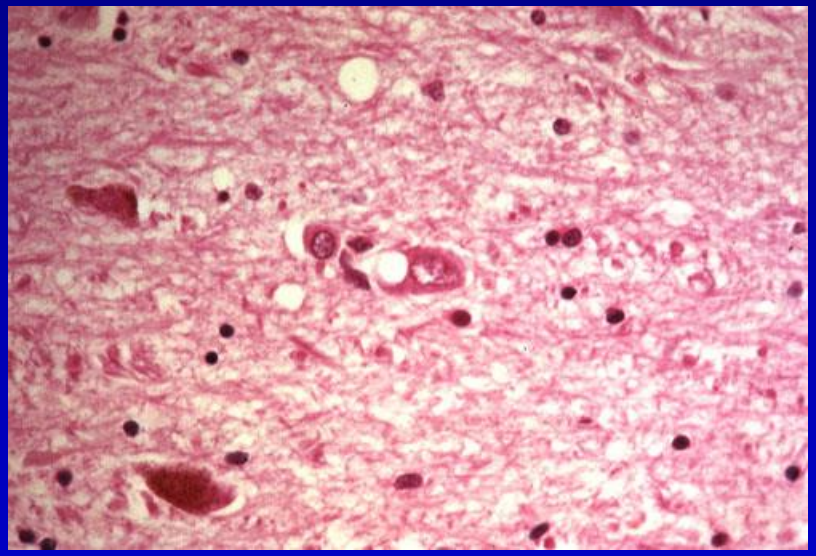
  cellular coper metabolism



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

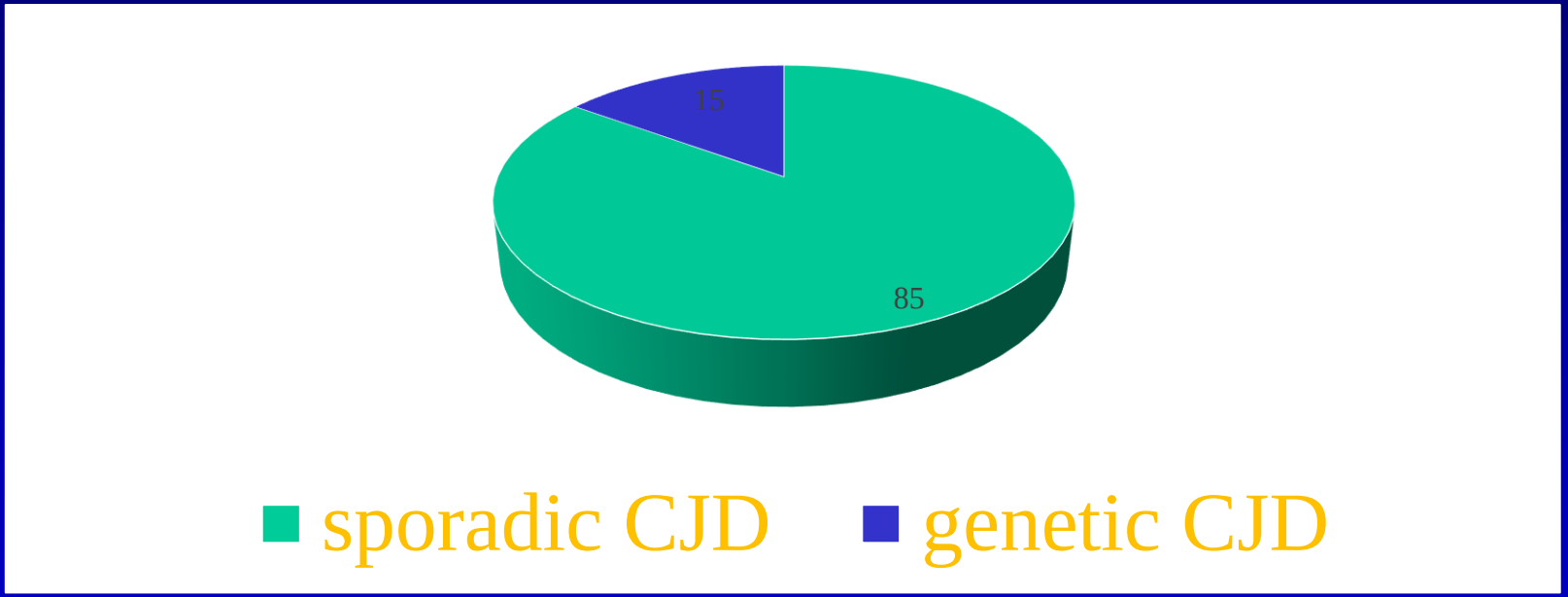
Prion diseases

- 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)
  - Sporadic CJD
  - Genetic CJD
  - Variant Creutzfeldt-Jakob Disease
- Gerstmann-Straussler-Scheinker Syndrome
- Fatal Familial Insomnia

Creutzfeldt – Jakob Disease
sporadic form



- **Mortality rate – 1- 1.5 /milion/ per year**
- **Middle age (55-70 years)**

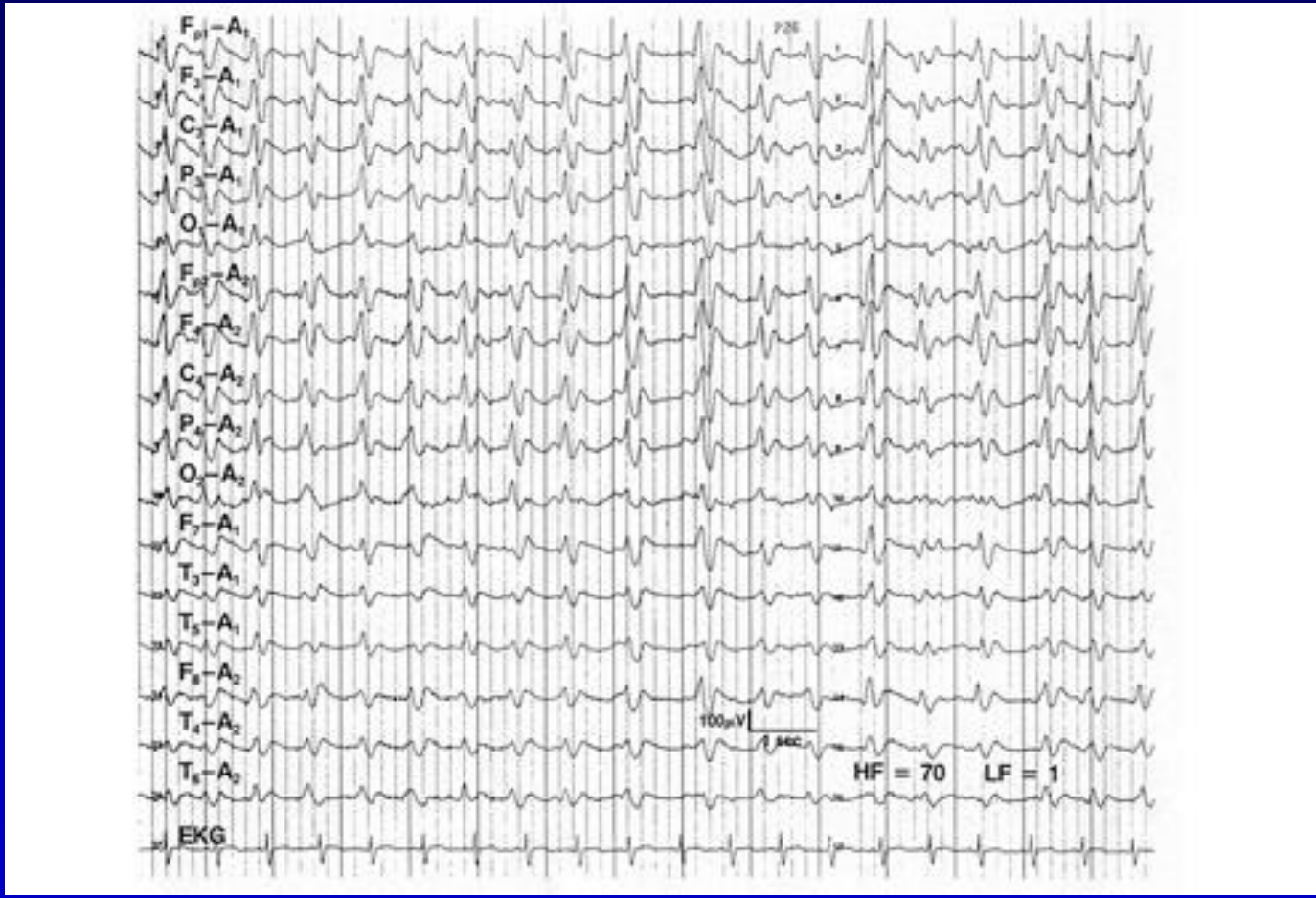
Creutzfeldt – Jakob Disease
sporadic form (sCJD)

- **Probable sCJD**
  - rapidly evolving dementia (<2 years)
  - EEG: periodic sharp wave complexes (PSWC) with triphasic morphology
  - and/or CSF: 14-3-3 protein

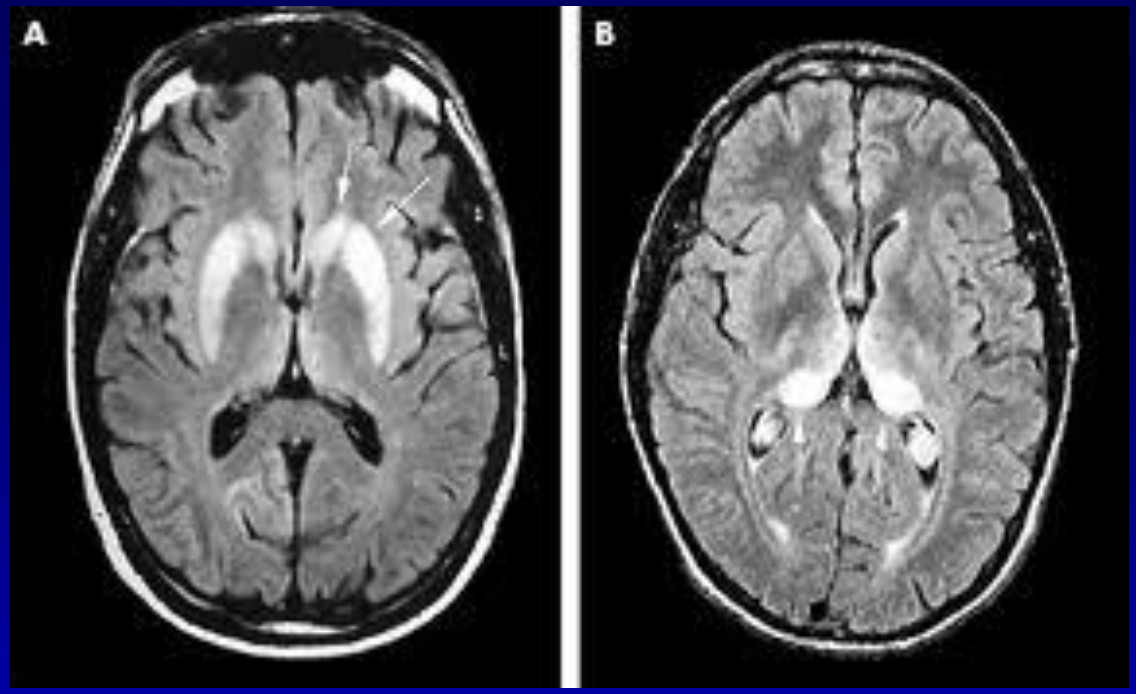
  and

  + (at least two of the following 4) clinical signs:
    - myoclonus
    - ataxia
    - visual signs and symptoms
    - extrapyramidal and/or pyramidal signs and symptoms
    - akinetic mutism
- **Definite sCJD**

  histopathologic the presence of spongiform degeneration and gliosis and/or Western blot presence of protease-resistant PrP.

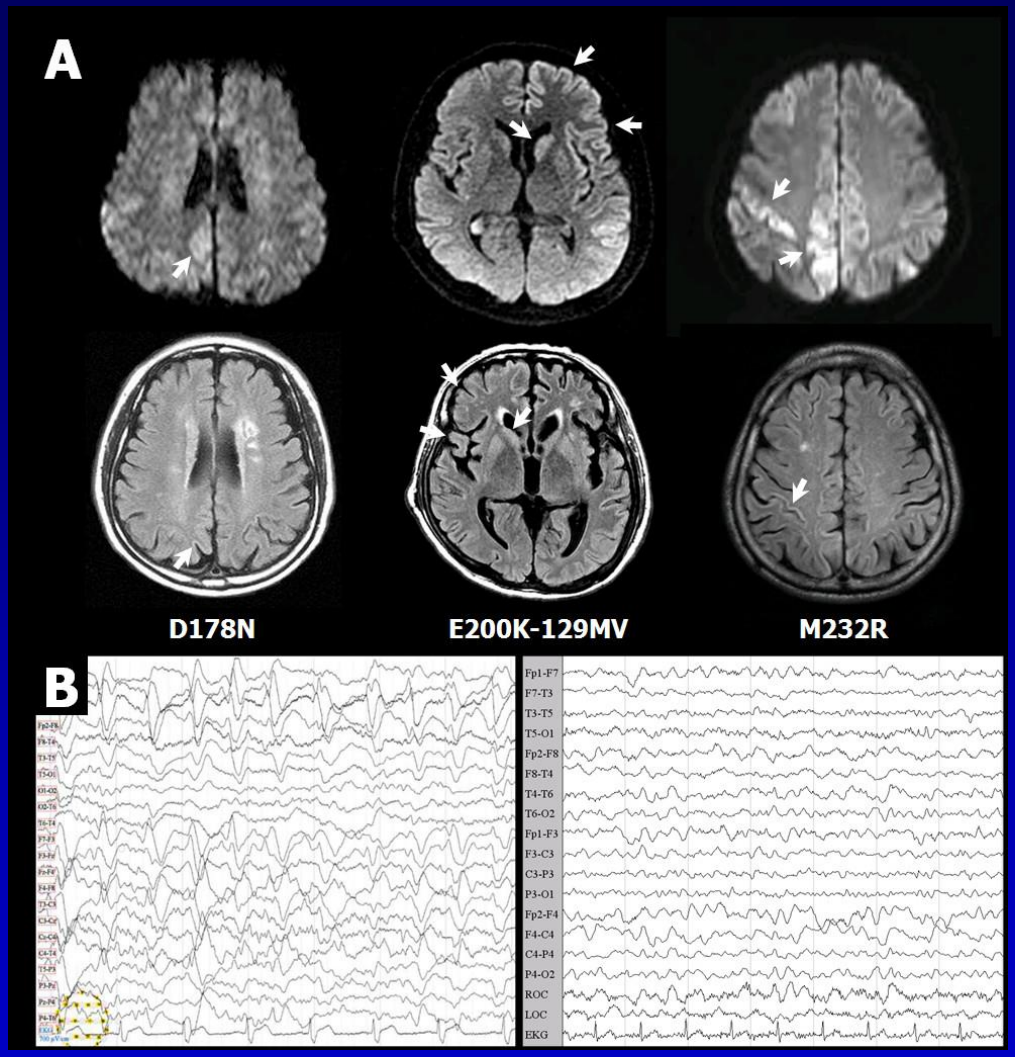


The typical periodic EEG seen in many cases of sporadic CJD.



(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).



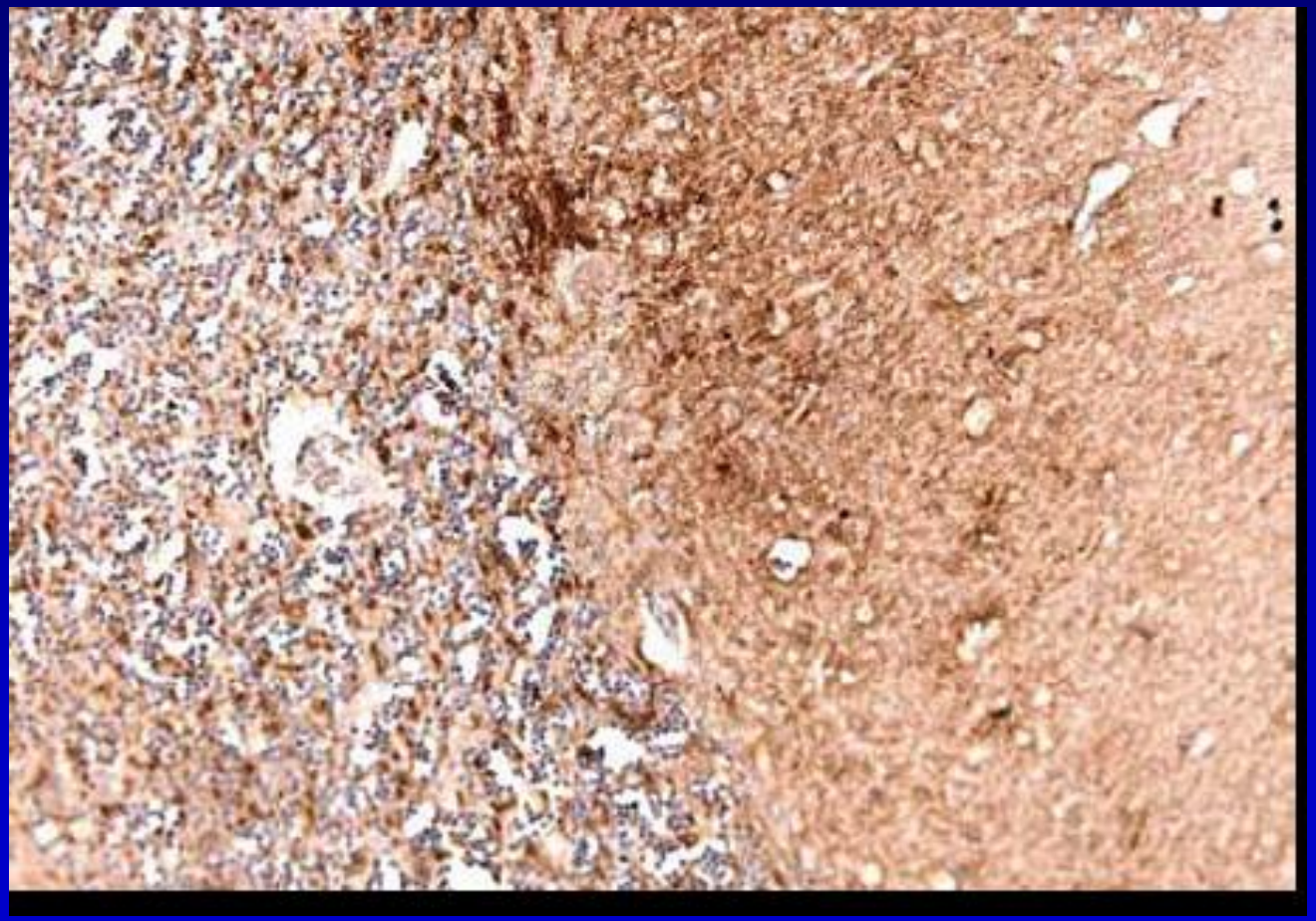
(A) Brain MRIs - PRNP polymorphisms. The top three are DWI images and the bottom three are T2-FLAIR images. The white arrow indicates a lesion with a high signal.

Creutzfeldt – Jakob

- 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 present in genetic CJD

Definite sCJD

histopathologic the presence of spongiform degeneration and gliosis and/or Western blot presence of protease-resistant PrP.



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

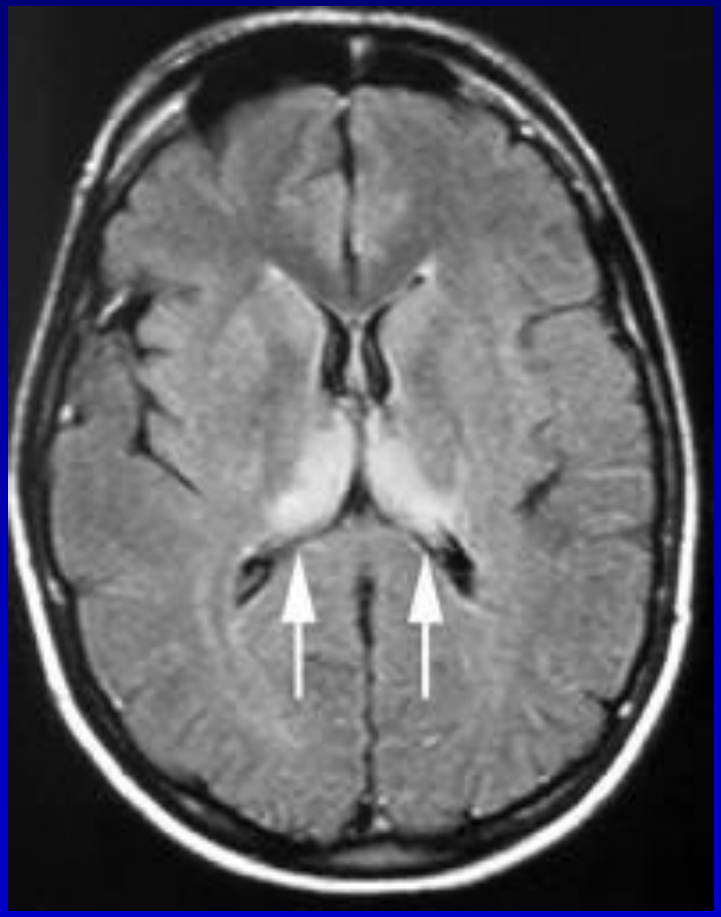
Creutzfeldt – Jakob iatrogenic –accidentally trasmitted

- 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 ilness (27-50)
- Psychiatric or sensory disturbance
- Long duration of illness (14 months)
- Clinical feature – like sporadic form (dementia, myoclonus, multisystem neurological deficits)

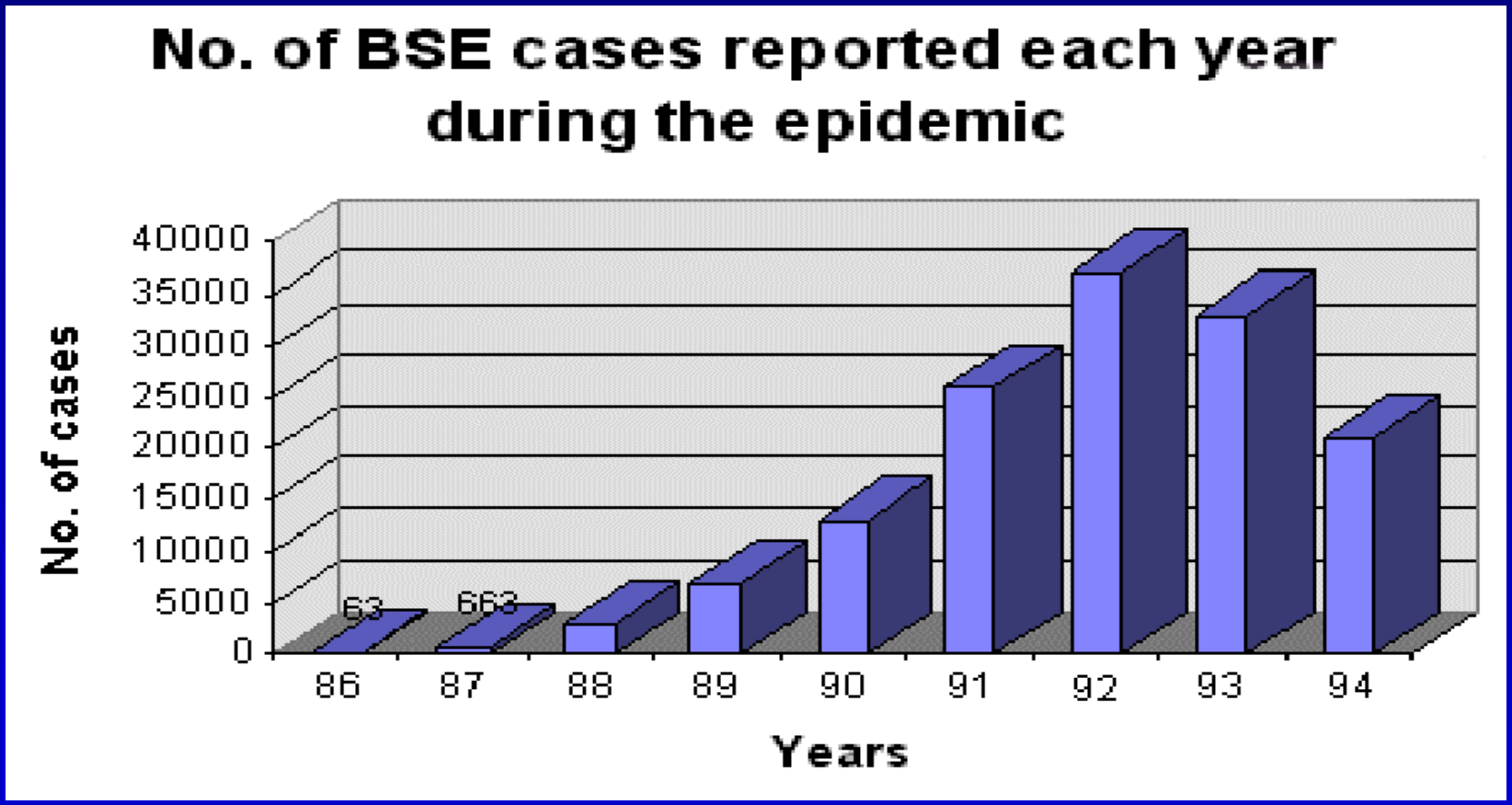
MRI – pulvinar sign



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 – difuse 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**

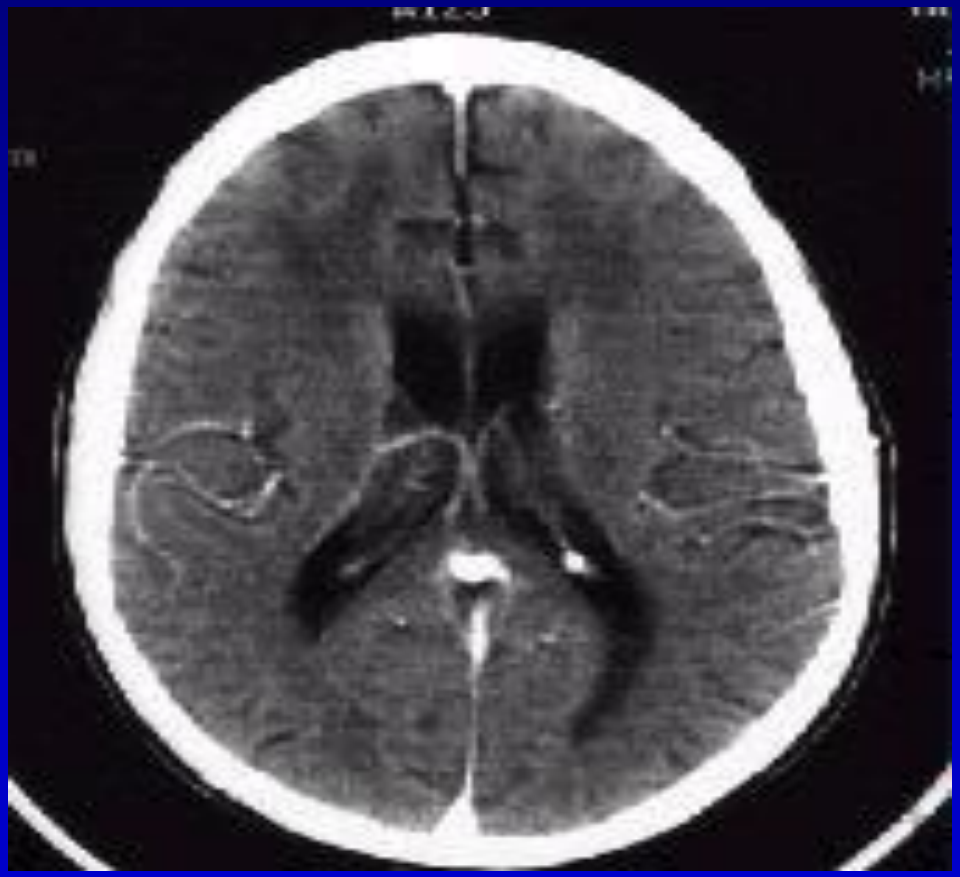
AIDS

- **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, ...)**
- **Protozoa – (Toxoplazma gondii, ...)**

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



AIDS dementia complex (ADC)

- **T2- MRI:**
- **Enlargement of ventricles,**

  hyperintenzity in subcortical white matter of both frontal lobes