# NURS 821 Neurological Disorders

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Lecture 11

Part 4 Disorders of the Central Nervous System:Infections and Inflammation and Neurodegenerative Diseases

## Prion Disease

Prions (a protein) act as an infectious pathogen that can cause degeneration of the CNS

- Reproduce by recruiting normal cellular prion protein and stimulating its conversion to the disease causing isoform
- Can be infectious and genetic (inherited or spontaneous mutation)

## Prion Disease Pathophysiology

Microscopically, the outstanding features are widespread neuronal loss and gliosis

- A striking spongy state of the affected regions
  - Cerebral
  - Cerebellar cortices
  - And/or occipitoparietal regions

## Prion Disease Clinical Features

- Prodromal symptoms:
  - Fatigue, depression, weight loss, disorders of sleep and appetite lasting for several weeks
- Early phase:
  - Confusion, hallucinations, delusions, agitation, cerebellar ataxia, and visual disturbances, HA, vertigo

## Prion Disease

- Progresses rapidly, see changes day to day, week to week
- Soon myoclonic contraction appear associated with a striking startle response, mainly to loud noise
- Ataxia, dysarthria, mute state, stupor, coma and death

## Mad Cow Disease

Recently has received a great deal of attention

- Epidemic among cows in the British Isles
- Began 1985 with putative transmission of the disease to approx. two dozen humans
- Interestingly, and for unknown reasons, these patients are younger than those affected by other prion diseases. Average age of onset is 27 years

Source: Prusiner, 2001, NEJM

## Mad Cow Disease

- Prion strain in patients with “mad cow disease” is identical to the one from affected cattle
- Mode of transmission is presumed to be the ingestion of infected meat
- As of 2000, 100 cases recorded
- No dietary habits distinguish patients with this disease from apparently health persons

Source: Prusiner, S.B. (May 17, 2001)

## Mad Cow Disease

- Manifestations of “mad cow disease” differ slightly from CJD
  - Psychiatric and sensory symptoms as the 1st sign of illness
  - Do not have the usual EEG findings that CJD patients have
  - As a result this disease has been called “new variant CJD”

## Neurodegenerative Diseases

- Etiology: abnormalities in protein processing
- Defective processing causes accumulation of one or more specific neuronal proteins
- Misprocessed proteins often accumulate because the cellular mechanisms for removing them are ineffective
- The particular protein improperly processed determines the neuron malfunction and thus the clinical manifestation of the disease

## Neurodegenerative Diseases

- Begin insidiously, after a long period of normal nervous system function
- Often is a familial occurrence
  - (may be due to an inherited gene or because more than one member may be exposed to the same infectious or toxic agent)
- Pursue a gradual yet ceaselessly progressive clinical coarse

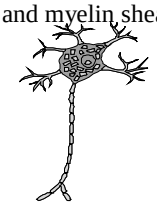
## Neurodegenerative Diseases

- May continue for many years, > decade
- May have long periods of stability
- With few exceptions (such as Parkinson's Disease), the course of these diseases are uninfluenced by medical or surgical measures
- Clinical symptoms are usually symmetric, distinguishing them from many other diseases of the nervous system
  - Note: Parkinson Disease and ALS may start unilaterally; however, will become symmetrical as the disease process progresses.

## Neurodegenerative Diseases

General Pathological Features:

- A slow wasting and loss of neurons, dendrites, axons, and myelin sheaths



## Neurodegenerative Diseases

General Pathological Features:

- This process is unaccompanied by an intense tissue reaction or cellular response
- The cerebrospinal fluid (CSF) shows little if any change – at most a slight increase in protein content
- Radiologic exam shows either no change or a volumetric reduction (atrophy)

## Prevalence of Neurodegenerative Diseases in the US in 2000

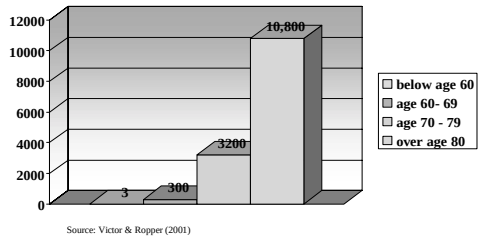
| Disease | No. of Cases | per 100,000 pop. |
|---|---|---|
| Prion | 400 | <1 |
| Alzheimer's | 4,000,000 | 1450 |
| Parkinson's | 1,000,000 | 360 |
| ALS | 20,000 | 7 |
| Huntington's | 30,000 | 11 |

Source: Prusiner, S.B. (May 17, 2001)

## Alzheimer Disease

- Most common degenerative disease of the brain
- In 2000, there were an estimated 4 million persons with Alzheimer disease (AD) in the United States
- Prevalence is three times higher in women
- Survival of patients with AD is reduced to half of the expected rate
- Most deaths from AD occur ultimately from respiratory or cardiac causes.

## Incidence of Alzheimer Disease – New Cases Yearly Per 100,000 Persons




Source: Victor & Ropper (2001)

## Alzheimer Disease

- Etiology: unknown
- Current theories include:
  - Loss of neurotransmitter stimulation by choline acetyltransferase
  - Mutation for encoding amyloid precursor protein
  - Alteration in apolipoprotein E which binds beta amyloid

## Alzheimer Disease Pathophysiology

Radiographically:

- Most prominent finding is the extremely atrophied hippocampus
- Frontal, temporal, and parietal lobes are also atrophied
- In advanced stages, brain is diffusely atrophied with it's weight reduced by 20%

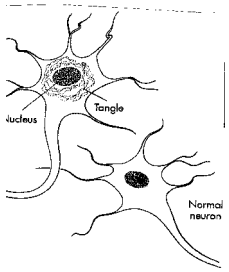
## Alzheimer Disease Pathophysiology

Microscopically, 3 changes in brain tissue have been found:

- Neurons become distorted and twisted forming a neurofibrillary tangle
- Amyloid plaques scattered in the cerebral cortex
- Granulovacuolar degeneration of neurons, most evident in the hippocampus

Lost cells are replaced by fibrous astrocytes – a process called gliosis

## Neurofibrillary tangle




## Alzheimer Disease Clinical Features

- **Gradual development of forgetfulness**
  - Small day to day happenings are not remembered
  - Seldom-used names are particularly elusive
  - Appointments are forgotten and possessions misplaced
  - Questions are repeated again and again, forgetting what was just discussed
- Gradually, speech becomes halting because of failure to recall the needed word (the same difficulty affects writing)
- Progression to repeating a question before answering it, and later echolalia.
- Arithmetic suffers a similar deterioration

## Alzheimer Disease Clinical Features

- Visuospatial orientation becomes defective
  - Car cannot be parked
  - Arms do not find the correct sleeves of the shirt
  - Turns in the wrong direction or becomes lost. Directions from one place to another are not understood
- As this state worsens, the simplest of geometric forms and patterns cannot be copied
- Forgets how to use common objects
- Dressing, shaving, and bathing are neglected

## Alzheimer Disease Clinical Features:

- Paranoia and other personality changes may occur
  - May be convinced that relatives are stealing his possessions
  - May hide belongings
  - May spy on family members

## Alzheimer Disease Clinical Features:

- Paranoia and other personality changes may occur
  - Constantly worried, tense and agitated
  - Social indiscretions such as rejection of an old friend, embarking on an imprudent financial venture, or an amorous pursuit that is out of character are examples of these types of behavioral changes