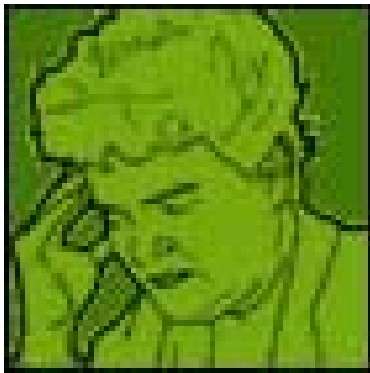


What is dementia?

A chronic and usually progressive decline of intellect and/or comportment which causes a gradual restriction of customary daily living activities unrelated to changes of alertness, mobility, or sensory function.



*Symptoms more severe than the usual losses in RT, **memory**, cognitive flexibility and visuo-spatial skills of normal aging.*

Some specific characteristics:

- reduced effectiveness at work
- difficulty dealing with social pressure
- tendency towards withdrawal
- changes in personal habits
- superficiality
- increased intensity of emotionality
- irritability, paranoia

What causes dementia?

Damage to neural networks that underlie cognitive functions like memory, language, etc.

Multiple causes:

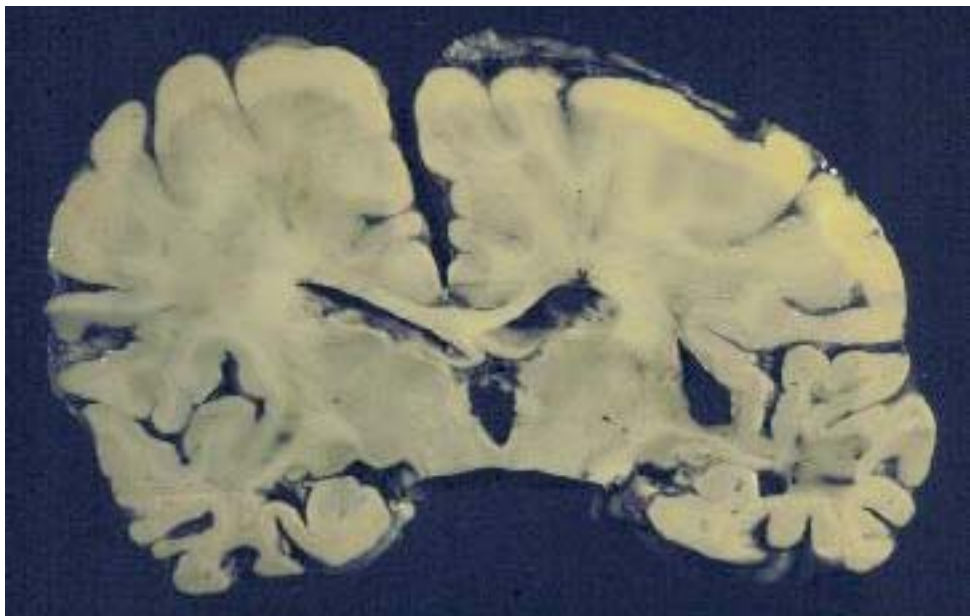
1. Degenerative diseases
(Alzheimer's, Pick's, Huntington's)
2. Neoplasia (tumors)
3. Bacterial/viral infections
(e.g., syphilis, meningitis)
4. Vascular disease (e.g., stroke, MID)
5. Vitamin deficiency (e.g., Pellagra)
6. Endocrine disorders (e.g., Cushing's)
7. Cerebral trauma
8. Korsakoff's syndrome
9. Hydrocephalus
10. Prions (e.g., mad cow disease)

Pick's disease

Selective progressive deterioration of the frontal and temporal lobes.



Note wider sulci, smaller gyri in those regions



Most common forms of dementia

1. Degenerative

(mostly Alzheimer's)

2. Vascular

(multi-infarct dementia)

3. Alcohol-induced

(Korsakoff's syndrome)

Dementia generalizations

Rate of dementia doubles
every five years after age 60;
then declines after age 90.

Alzheimer's disease is more
common in women than in men.

Multi-infarct disease is more
common in men than in women.

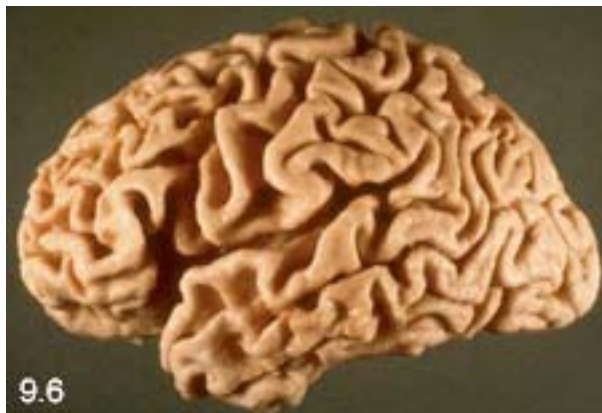
Alzheimer's disease

Insidious declarative memory loss.

Severe damage to hippocampus, PFC.

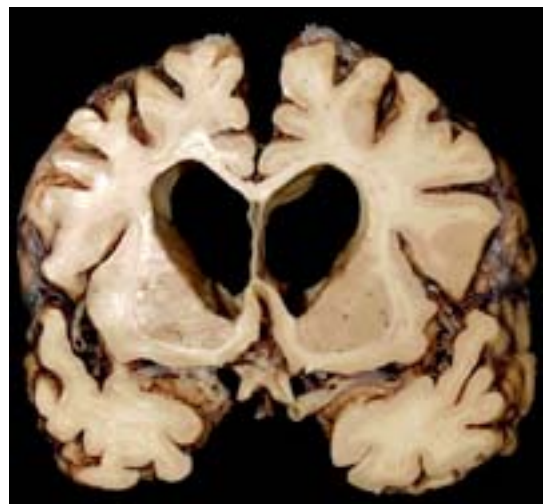
Some sparing of procedural memory.

Other progressive cognitive losses.



Wide sulci, thin gyri
in many brain areas

Enlarged ventricles

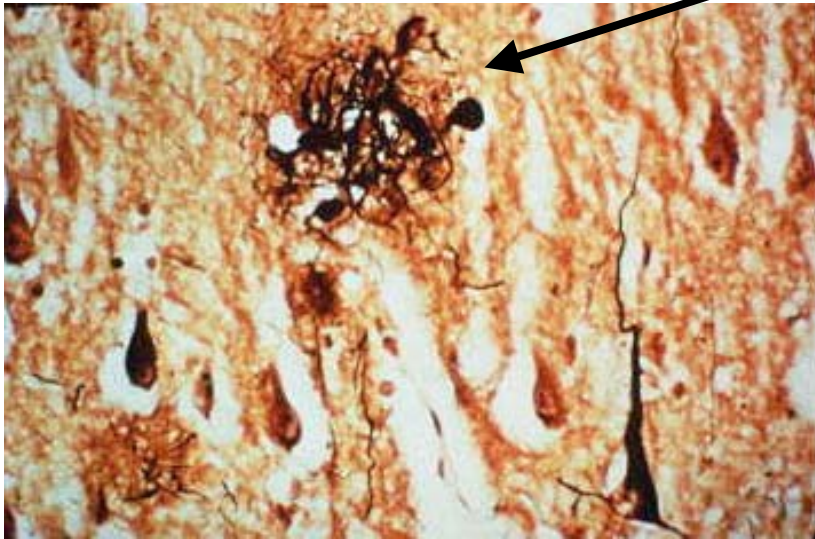


Diagnosis based on typical dementing course
and exclusion of alternative diagnoses. Definitive
diagnosis requires **post-mortem examination...**

Post-mortem diagnosis of Alzheimer's disease

Neurofibrillary tangles

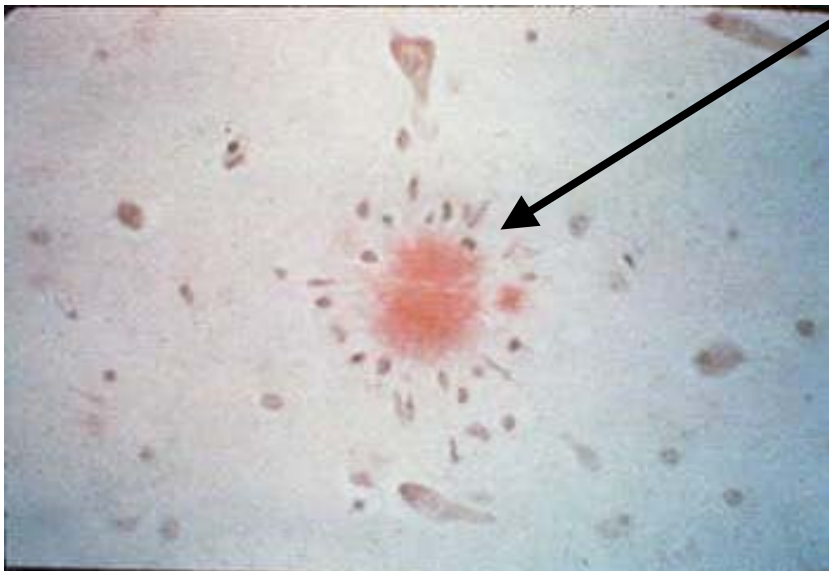
Tangle
in cortex



Dense bundles of paired helical fibers in neurons; Interfere with cell function and lead to degeneration.

Beta amyloid plaques

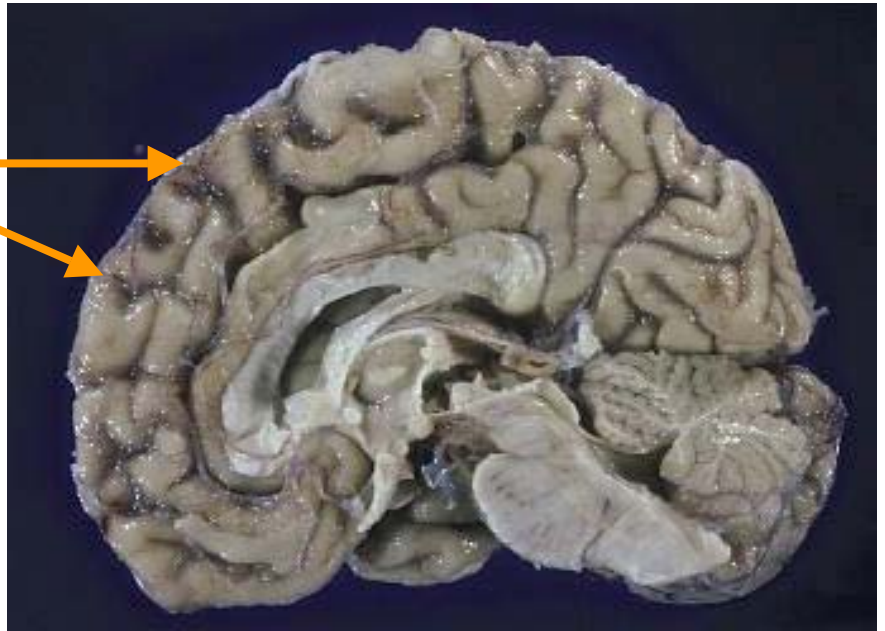
Plaque in cortex



Abnormal Accumulations of CNS protein; Forms plaques, especially near pre-synaptic terminals

Alzheimer's: Two forms

Widened
sulci due to
diffuse atrophy
of cortical cells



1. Late onset form of Alzheimer's

Most common form of Alzheimer's disease
Generally detected after age 60; Progresses
over a 5-15 year period.

2. Early onset form of Alzheimer's

Also known as **presenile form** of AD

Usually detected in 40's or 50's; Progresses
rapidly, leading to death in only 2-3 years.

Alzheimer's and Genes



There is **no clear genetic contribution in 95% of Alzheimer's disease cases.** *But in 5%...*

Three genes confer a predisposition for the early onset (pre-senile) form of AD:

1. Amyloid precursor protein (APP)
2. Presenilin 1
3. Presenilin 2

One gene increases risk for late onset AD:

1. ApoE4: E4 allele associated with more risk; E2 allele may reduce risk.

*** ALL GENES AFFECT BETA AMYLOID**

Alzheimer's and the environment

Tangles (but not plaques) can be produced by exposure to high levels of aluminum.

Plaques often cluster around blood vessels (suggests a toxic factor carried by blood).

At least 20 risk factors proposed

(including sex, race, social class, free radical exposure, etcetera)



The Nun Study

School Sisters of Notre Dame

David Snowden, Ph.D., University of KY

Nuns with grammatically complex entrance exam essays were less likely to develop AD