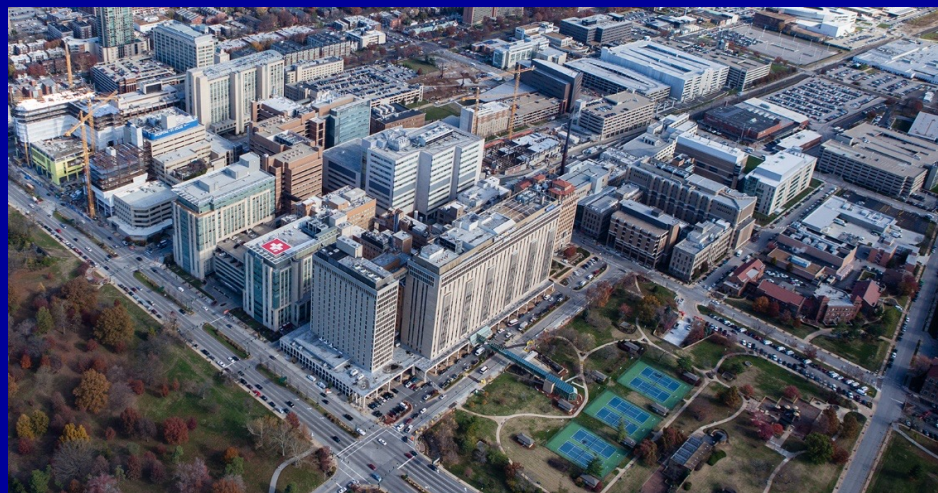


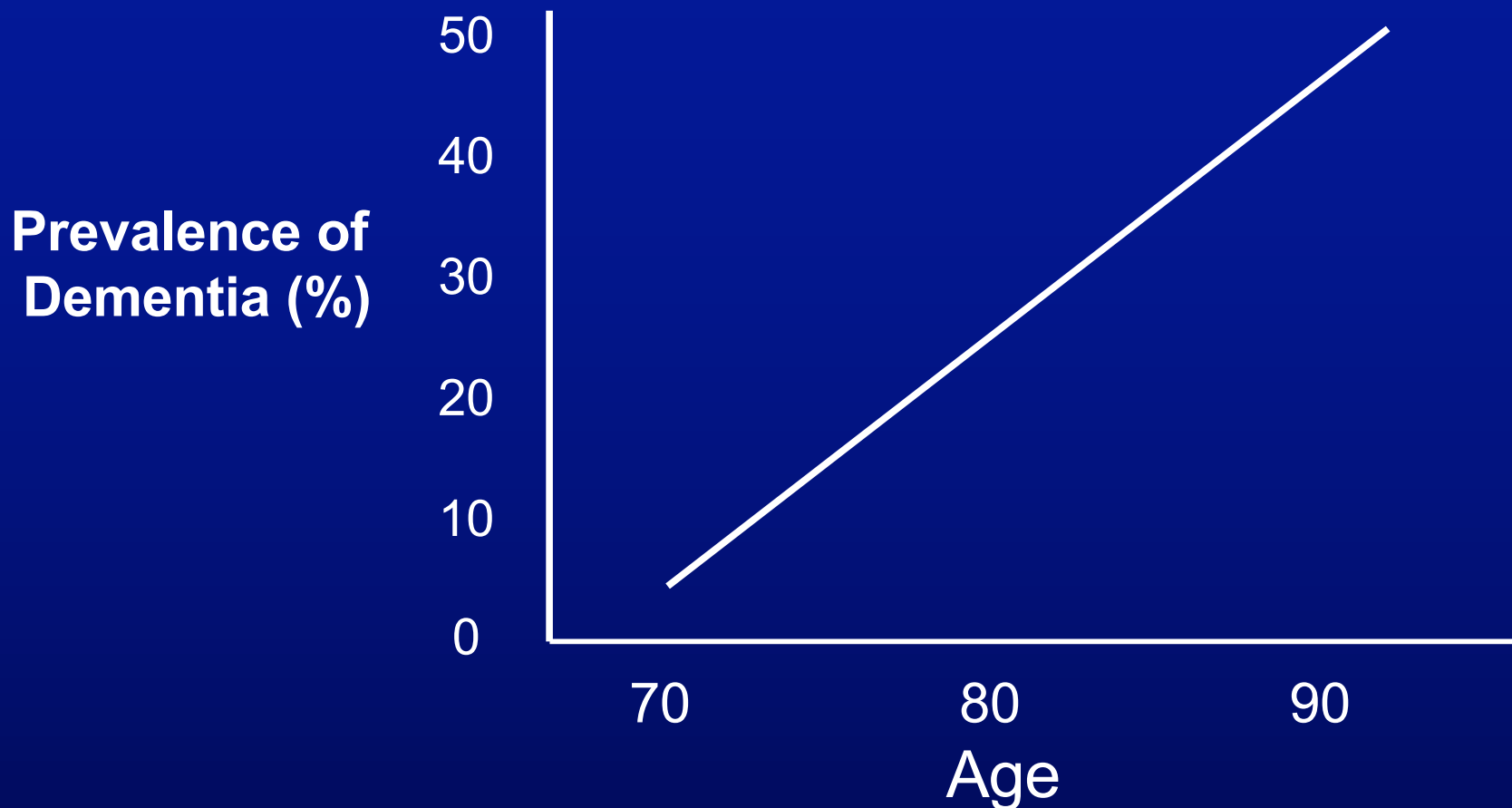
# Pathological and clinical considerations in Alzheimer's Disease

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**Dementia: Decline in memory and other cognitive abilities sufficient to impair social and occupational functioning**

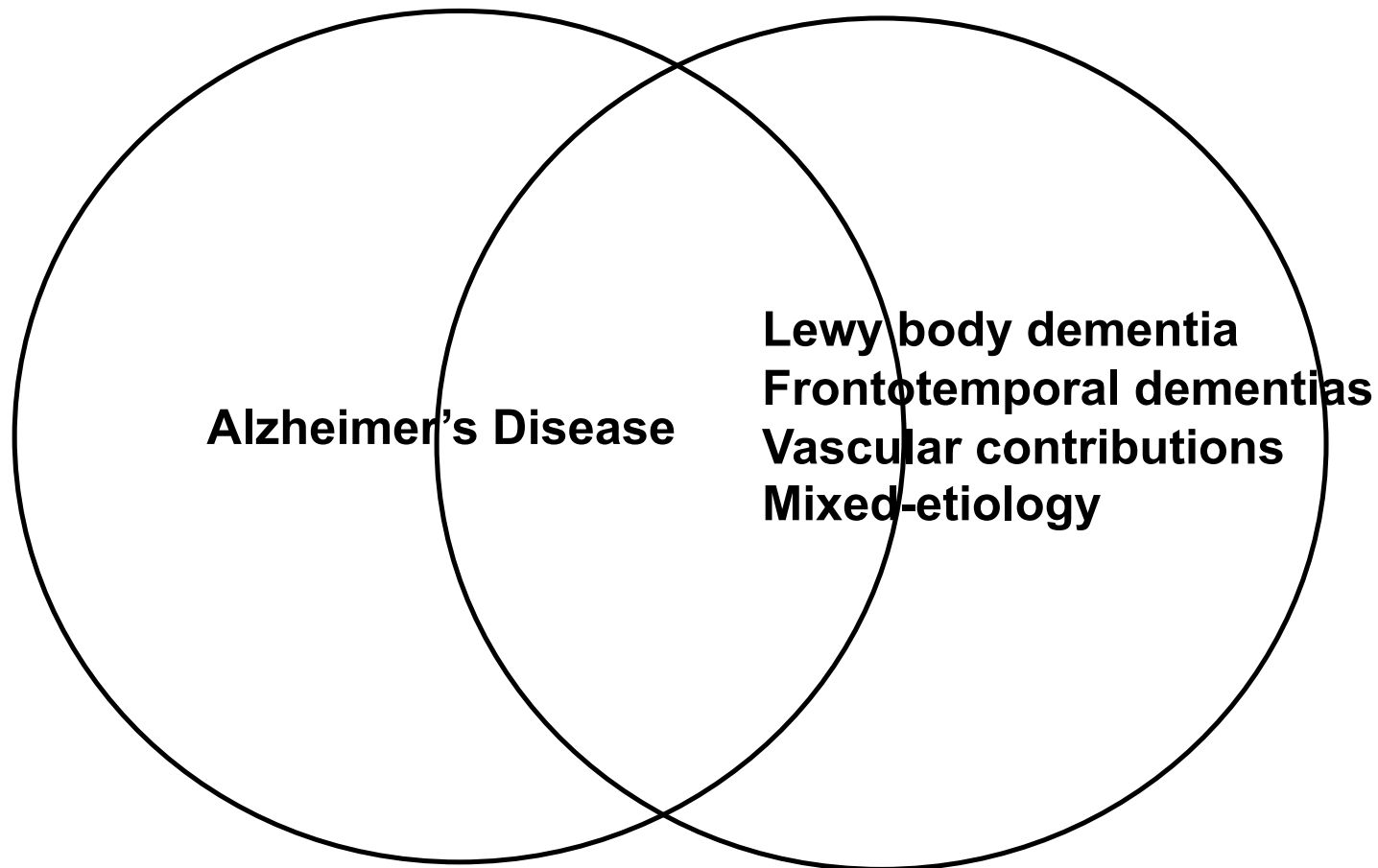


**Dementia is very common with increasing age and Alzheimer's disease (AD) contributes to ~70-75% of cases of dementia. Estimated 6.5 million Americans are living with AD dementia in 2022. Expected doubling by 2050**

## Types of AD and Risk

### Three Major Types of AD

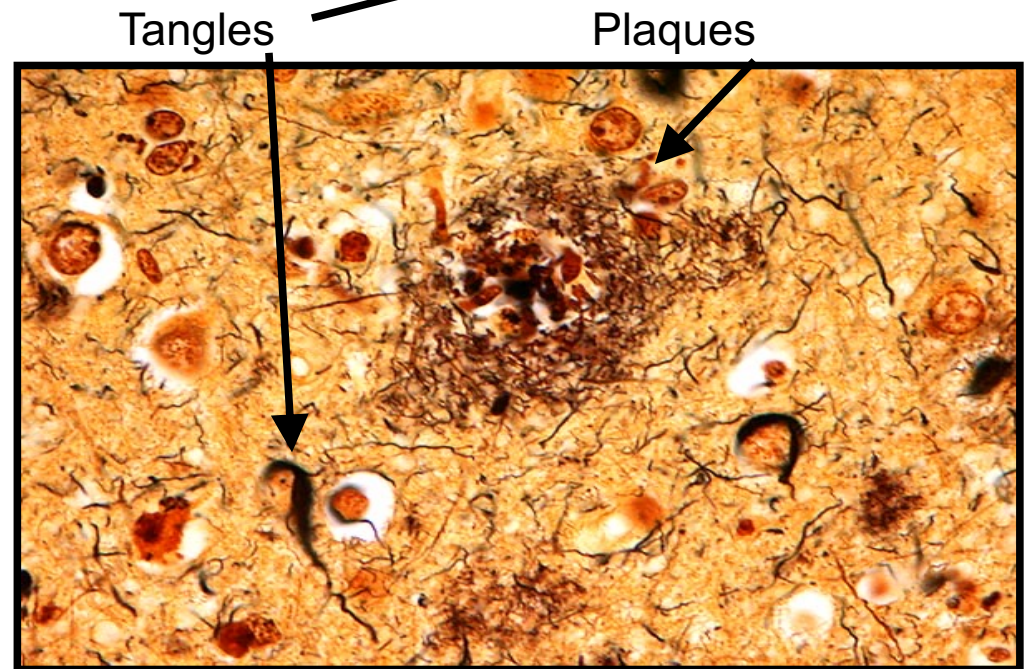
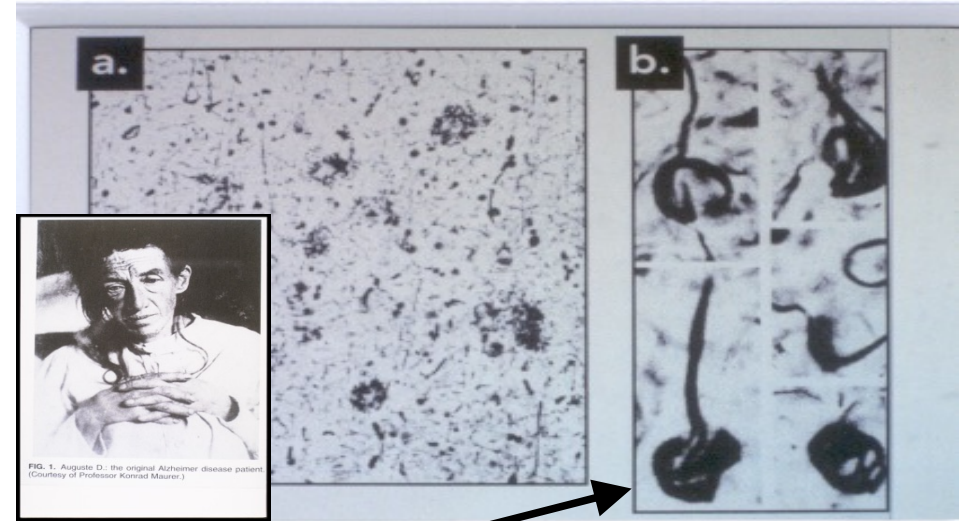
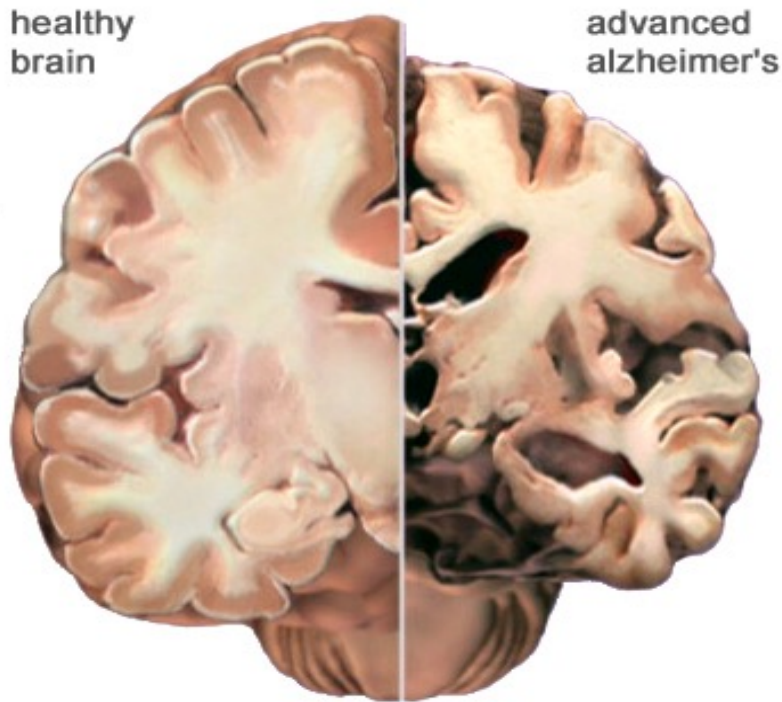
- 1) Early-onset dominantly inherited AD
  - <1% of cases
- 2) Early-onset AD
  - non-autosomal dominant
- 3) Late-onset AD
  - age > 65, most cases
  - Strongly influenced by genetics



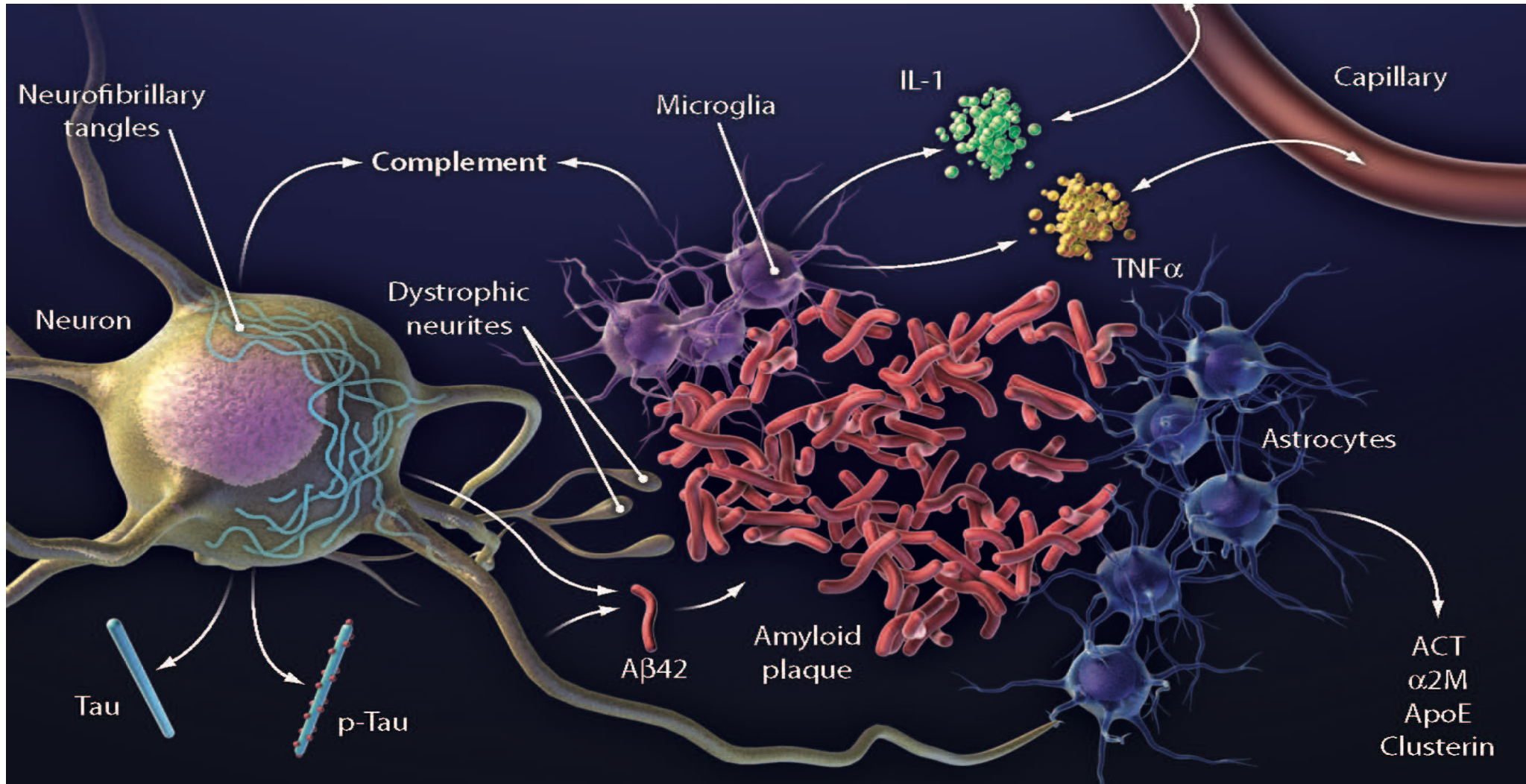
**Alzheimer's disease causes or contributes to ~70% of dementia. A variety of other disorders cause the other 30%. The most common contributors are vascular contributions (stroke), Lewy body dementia, and frontotemporal dementia. A fairly large percentage of people with AD over 70 also have pathologies of these other disorders, especially vascular related.**

## Neuropathology of AD

- Plaques (Amyloid- $\beta$ )
- Neurofibrillary tangles (NFT) (tau)
- Nerve cell and synapse dysfunction, loss of connections, cell death, brain shrinkage
- Inflammation

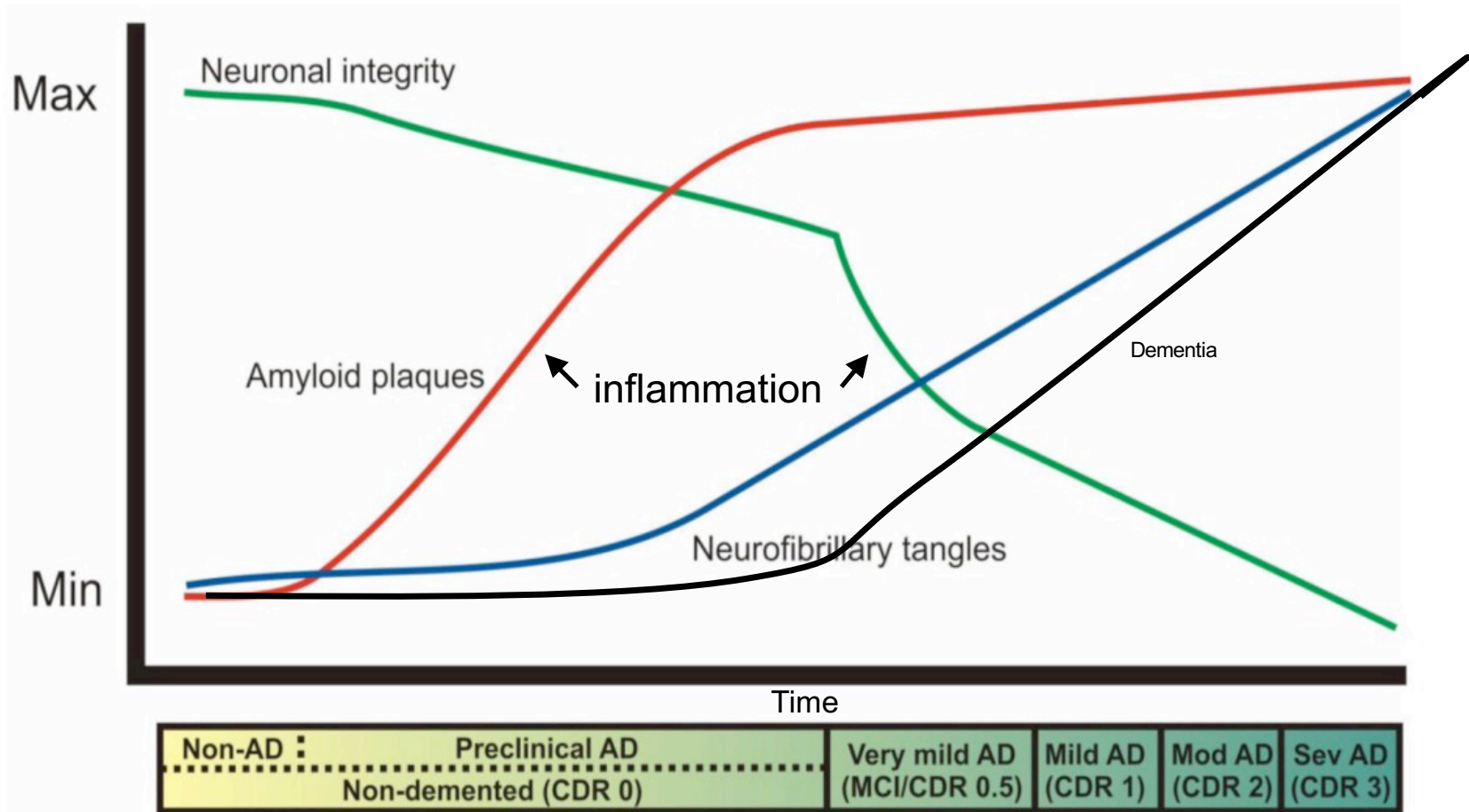


# Model of Alzheimer's brain pathology



Holtzman DM, Morris JC, Goate AM (2011) Science Translational Medicine Vol 3, Issue 77

Time course of the pathology of Alzheimer's disease:  
 Pathology begins and accumulates many years prior to symptom onset



Perrin R, Fagan A, Holtzman DM. Nature 2009