

Pre-clinical (asymptomatic) AD

AD-mutations
(APP, PS1, PS2 genes)

Risk-genes
(apolipoprotein E)

Overproduction of A β
Abnormal APP metabolism
Reduced A β clearance

Aging

Unknown factors

Amyloid- β
accumulation

Pre-dementia

Activation of neurotoxic cascades
Decreased neurotrophic support

Fibrillary A β
A β oligomers

Hyperphosphorylation of TAU

Clinical dementia

Glia activation
Inflammation
Oxidative stress
Mitochondrial dysfunction

Amyloid plaques

Synaptic dysfunction
Axonal dysfunction
Collapse of cytoskeleton

Neuritic plaques

Neurofibrillary
tangles

Dementia