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### **Chronic mild cerebrovascular dysfunction as a cause for Alzheimer's disease?**

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Alzheimer's disease (AD) is a progressive chronic disorder and is characterized by  $\beta$ -amyloid plaques and angiopathy, tau pathology, neuronal cell death, and inflammatory responses. The reasons for this disease are not known. This review proposes the hypothesis that a chronic mild longlasting cerebrovascular dysfunction could initiate a cascade of events leading to AD. It is suggested that (vascular) risk factors (e.g. hypercholesterolemia, type 2 diabetes, hyperhomocysteinemia) causes either damage of the cerebrovascular system including silent strokes or causes dysregulation of beta-amyloid clearance at the blood-brain barrier resulting in increased brain beta-amyloid. A cascade of subsequent downstream events may lead to disturbed metabolic changes, and neuroinflammation and tau pathology. The role of NGF on the cell death of cholinergic neurons is discussed. Additional risk factors (e.g. acidosis, metals) contribute to plaque development.