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What occurs in the brain of an Alzheimer's patient?

About 30 years before symptoms appear, amyloid-Aß starts to aggregate and to form amyloid plaques in the brain. Aß is a small protein breakdown product of the large amyloid precursor protein made in nerve cells. The process of amyloid deposition starts in the brain's default network. The default mode network is active when we are not focused on the outside world and while we are awake, thinking about others, thinking about ourselves, remembering the past, and planning for the future. In this default mode, the "brain talks to itself," which demands a very significant amount of energy. Once started, the amyloid pathology spreads to nerve cells connected with the default network. As a result, nerve cell contacts become destroyed and as a consequence, nerve cells begin to suffer from the formation of neurofibrillary tangles, aggregates of the tau protein. One of the likely scenarios is that amyloid-Aß aggregation destroys nerve cell contacts and as soon as enough contacts are destroyed, neurons form neurofibrillary tangles, become dysfunctional, and commit suicide – a process called apoptosis. Thus, as a consequence, people with low numbers of nerve cell contacts progress much faster with Alzheimer's disease than those with high numbers of nerve cell contacts.

How is Alzheimer's disease diagnosed and how important is early diagnosis?

According to NIA's new criteria and guidelines for Alzheimer's disease diagnosis, published April 2011, there are three stages of the disease. These three stages are (1) preclinical Alzheimer's disease, (2) mild cognitive impairment (MCI) due to Alzheimer's disease, and (3) dementia due to Alzheimer's disease. Preclinical Alzheimer's disease is the time before symptoms, such as memory loss and confusion about time or place, are noticeable and indicated by changes in biomarkers measurable perhaps two to three decades before symptoms occur. The new guidelines, however, do not establish diagnostic criteria that doctors can use now. They propose additional biomarker research to find out which biomarker results confirm that a person has preclinical Alzheimer's disease. MCI due to Alzheimer's disease is noticeable by mild changes in memory and thinking abilities recognized by the person, family members, and friends, which can be measured by an expert. MCI does not affect a person's ability to carry out everyday activities. Not all people with MCI will develop dementia due to Alzheimer's disease. The new

guidelines define criteria for ruling out other causes of MCI and making sure that the diagnosis of MCI is due to Alzheimer's disease. Dementia due to Alzheimer's disease is diagnosed when memory, thinking, and behavioral symptoms impair a person's ability to function in daily life. Two biomarker categories are identified in the new guidelines: (1) biomarkers showing the level of amyloid-Aß accumulation in the brain and (2) biomarkers showing that nerve cells in the brain are injured or degenerating. Although the use of biomarkers is proposed for all three stages of the disease, it is only intended for research at this time.

Regarding the importance of early diagnosis, consensus exists that treating the disease before symptoms occur is the best way to enable people to live healthy lives free of disability caused by Alzheimer's disease. At present, early diagnosis of dementia can help those affected to get the right treatment, find the best sources of support, and make decisions about their futures.

In your opinion, how far are we from a cure?

Given that the development of disease pathology and massive loss of nerve cell contacts occur decades before symptom onset, and that data suggest that intervention might be beneficial if started earlier in the disease process, primary and secondary prevention during the early clinical and preclinical stages are recommended in order to provide the most effective approach towards "Aging Without Alzheimer's Disease." According to a groundbreaking study that looked at how diet, exercise, and other non-drug interventions affect cognitive decline as well as promising research on amyloid-ß-directed immunotherapy, "Aging Without Alzheimer's Disease" remains a realistic "principle of hope," which may be achieved before 2050.