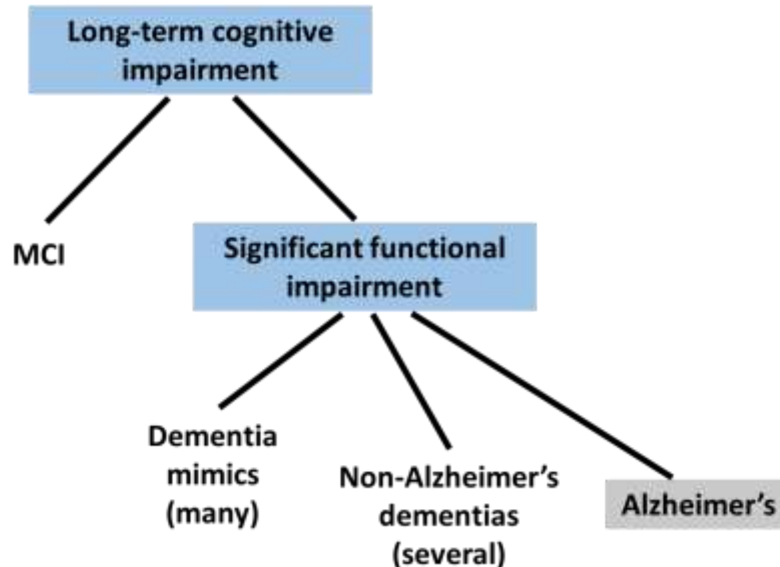
Adjourning Alzheimer's

Alzheimer's (Day 50)



Finally, we arrive at **Alzheimer's**; we discuss Alzheimer's at the end, for good reason.

The pathological process that is Alzheimer's has no hallmark clinical features. The most common symptom, memory loss, may also be prominent in mild cognitive impairment (MCI), dementia mimics, and the non-Alzheimer's dementias. Moreover, since no test or scan can conclusively identify the Alzheimer's pathological process, **we can never be 100% confident that a person has Alzheimer's**; the best we can do is make a diagnosis of "probable" Alzheimer's (currently, the gold standard for diagnosing Alzheimer's is at autopsy - not so helpful to the living).

In 1984, United States neurologist **Guy McKhann** attempted to improve the accuracy of the diagnosis by publishing diagnostic criteria for **probable Alzheimer's**. In 2011, McKhann published a revised version that attempted to improve the diagnostic accuracy of probable Alzheimer's even more. In both cases, it was stipulated that after excluding MCI, dementia mimics, and the non-Alzheimer's dementias, a person can be diagnosed with probable Alzheimer's as long as they satisfy two additional sets of clinical criteria:

(1) Criteria for **all-cause dementia** (effectively excluding MCI).

(2) Criteria for **probable Alzheimer's-related dementia** (effectively excluding a dementia mimic or non-Alzheimer's dementia).

The revised criteria for **all-cause dementia** state that a person with long-term cognitive impairment must have symptoms that:

(1) Interfere with the ability to work or usual activities.

(2) Represent a decline from previous functioning and performance.

(3) Are not explained by delirium or a major psychiatric disorder.

(4) Are confirmed by a corroborated history and cognitive testing.

(5) Involve decline in at least two of memory, language, visuospatial skills, executive function, or behaviour.

McKhann criteria for all-cause dementia.

The revised criteria for **probable Alzheimer's-related dementia** state that the dementia has features that are consistent with the Alzheimer's pathological process:

(1) Gradual onset (over months to years).

(2) Clear-cut worsening of cognition by report or observation.

(3) The initial and most prominent symptoms involve memory or one of language, visuospatial skills, or executive function.

(4) There should be no features of a non-Alzheimer's dementia.

Revised McKhann criteria for probable Alzheimer's-related dementia.

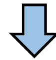
Sticking to McKhann's revised criteria, the probable Alzheimer's diagnosis is thought to correctly identify the presence of the Alzheimer's pathological process **80-90% of the time**, depending on the experience of the doctor.

Alzheimer's can also be graded by **severity**. In **mild Alzheimer's**, a person's cognitive and functional difficulties are noticed by close relatives, but the person appears normal to the casual observer. In **moderate Alzheimer's**, a person's cognitive and functional difficulties make it difficult for them to operate in the community, and their difficulties are apparent to the casual observer. In **severe Alzheimer's**, a person is dependent upon a caregiver for their daily needs.

By combining the McKhann criteria with the **5-step approach**, a diagnosis of probable Alzheimer's can be made as follows:

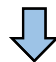
(1) Corroborated history

The person describes a progressive deterioration in cognition, usually memory loss, but the complaint may also relate to deficits in attention, concentration, language, visuospatial skills, or executive function. There will also be a decline in normal daily function. The decreases in cognition and function should be corroborated by an informant.



(2) Focused examination

The examination is usually normal, with no compelling evidence of a neurological abnormality.

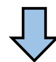


(3) Cognitive and functional scales

Cognitive scales will be well below normal; for example, the Montreal Cognitive Assessment (MoCA) score will usually range from 12 to 21 (out of a total of 30 points), although the range can be even broader than this. Functional scales will be below normal. If done, the Geriatric Depression (short form) score will be 8 or less, and the Hachinksi Ischemia score will be 4 or less.

(4) Laboratory tests

Blood tests will be normal. Lumbar punctures are only done in exceptional circumstances and will be normal, unless cerebrospinal biomarkers are ordered which may reveal the presence of amyloid beta (Aβ) and tau proteins in the brain.



(5) Brain imaging

CT and MRI imaging may be normal, or they may reveal atrophy of the hippocampus or certain regions of cerebral cortex. PET scans, which measure brain glucose uptake and metabolism, are only done in exceptional circumstances and will reveal areas of substantially impaired brain glucose uptake and metabolism.

Epidemiologically, Alzheimer's is by far the most common dementia syndrome, comprising **60-70% of all dementia cases**. To put this in perspective, Alzheimer's is about twice as common as all the dementia mimics and non-Alzheimer's dementias - combined.

Despite the revised McKhann criteria being 80-90% accurate for identifying Alzheimer's, **there remain a number of people with mild Alzheimer's who remain undiagnosed**. The reasons for this vary. Some people are simply unaware that there may be a problem. Others are aware that there is a problem, but believe (or are told) that it is part of "normal aging," or attribute it to something else, such as a stressful or traumatic life situation. Still others are aware that there is a problem, but choose not to acknowledge it, perhaps out of fear that they might have a disorder such as Alzheimer's; some people would rather not know.

To sum up, the Alzheimer's pathological process has no hallmark clinical features, nor can we use any test or scan to identify it; therefore, **the best we can do is diagnose a person with probable Alzheimer's**. Using the revised McKhann criteria, Alzheimer's can be accurately diagnosed 80-90% of the time. Moreover, a number of people with mild Alzheimer's remain undiagnosed - some may be unaware that something is amiss, others are aware but explain it away (or have it explained away), and still others are aware yet prefer not to acknowledge a possible diagnosis of Alzheimer's.

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References

(1) McKhann et al. 1984. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 34, 939-944.

(2) McKhann et al. 2011. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 7(3), 263-269.

(3) Holtzman et al. 2011. Alzheimer's Disease: The Challenge of the Second Century. Sci Transl Med 3(77), 1-35.