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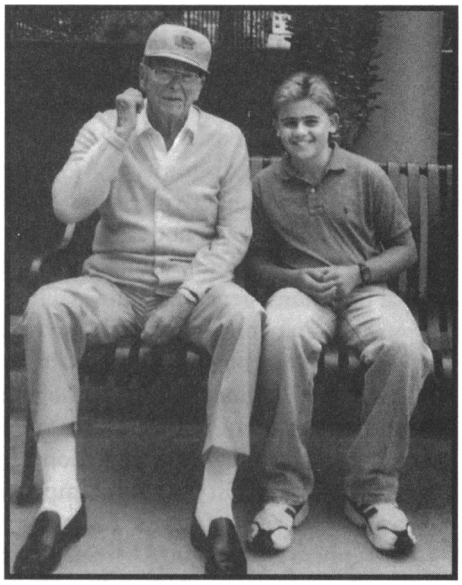
Alzheimer's Disease: The Evolution of a Diagnosis

Those of us who entered the medical profession near mid-century have witnessed a remarkable evolution in how we think about disease and how the society we live in responds to and influences medical thinking. Our concepts concerning the diseases of aging are especially interesting examples. When we began our medical educations, Alzheimer's disease was a rare "presenile dementia" and the word "senility" or the term "senile dementia" were used to describe the state of mental deterioration that occurred commonly (albeit not inevitably) with aging. Cognitive impairment that began gradually after age 65 was generally not designated as due to a disease unless it had a clear cause in a pathological condition such as strokes.

Today "senility" has become an anachronism while "senile dementia of the Alzheimer type" has largely been replaced with the simpler "Alzheimer's disease." In current medical thinking, substantial impairments in cognitive functioning at any age deserve designation as a disease. In the future, any degree of cognitive decline may become unacceptable as a normal consequence of aging.

Diseases and causes of death used to be relatively unambiguous: myocardial infarction, stroke, and cancer were easy to identify and name as our most important enemies. With such enemies our goals were clear: to organize and expand medical knowledge and practice so as to minimize premature mortality and suffering, with everyone ultimately dying a "natural" death.

Today, however, the line between what is natural and what is disease has been made ambiguous by improvements in medical diagnosis and our growing sophistication regarding aging and the pathogenesis of disease. We understand that while myocardial infarction is an acute event, it is truly the end result of an insidious atherogenic process beginning commonly in childhood but advancing differentially in different individuals. Stroke, an equally sudden and catastrophic event, is now commonly viewed as the result of years of accumulated microscopic and submicroscopic injury to cerebral vessels resulting in structural changes that make them more likely to tear or be occluded—the cerebrovasculature of a person who develops a stroke has been distorted by a lifetime of pulse poundings, making the vessels narrow, inelastic, tortuous, and vulnerable to a clot or embolus. Cancer involves stochastic processes, entropic decay of genetic information, and a declining effectiveness of the normal housekeeping mechanisms that get rid of maverick cells.



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While we recognize the pathogenicity of the underlying processes, we conventionally reserve disease names for the final, unambiguous conditions. This generally works for the most common causes of death because the final event or condition tends to appear precipitously. In Alzheimer's disease (AD), however, the process turns gradually into the disease. In fact, the criteria for diagnosis include insidious onset and more or less continuous progression. This makes AD quite different from the other common causes of death.

Because it develops gradually, AD often goes unrecognized for weeks, months, or years.[1] Even when the family recognizes that a problem exists, the person may not receive a medical evaluation, and a specific diagnosis may or may not be made before death. If no one expresses concern, a medical evaluation is unlikely; if no evaluation is done, a formal diagnosis and specific treatment are unlikely. Although family members are less able to ignore or deny the presence of a problem as the dementia progresses, even people with moderate or severe impairments may never receive a medical evaluation for dementia. The likelihood that a person who has AD will actually receive that diagnosis is strongly dependent on the quality and severity of his or her functional and behavioral changes and on the social, cultural, and educational characteristics of family members. The medical sophistication of the community and its health

care providers also undoubtedly influence recognition and formal diagnosis. Medical fashion, a rarely discussed but undeniable phenomenon closely related to the education and composition of medical communities, also influences diagnosis.

Even if the diagnosis of AD is made, identifying the disease as an underlying cause of death is problematic. Severe dementia is not easily missed and clearly predisposes to aspiration pneumonia, decubitus ulcers, bacterial infections, general debility, falls, and fractures. Mechanisms that might link mild or moderate dementia to death are less obvious and may be uncommon. Finally, research illuminating the pathogenesis of the disease and comorbidity phenomena is moving so rapidly that our understanding of the relationships between dementia and mortality—while improving—may remain somewhat out of focus for some time. Hoyert and Rosenberg's paper on Alzheimer's disease as a cause of death must be understood against this complex and evolving background.[2]

How reliable and complete are current death certificate data on AD? The prevalence of dementia among people ages 65 years and older in the United States has been reported as being between 6% and 12%, with 7%–8% being a figure most would accept. About one-quarter or one-fifth of those with dementia are severely affected. Half to three-quarters of aging-related dementia is attributed to AD. We can turn these percentages into numbers by applying them to national Census data. Conservative estimates place the number of cases of AD in the United States among people ages 65 and older between one and two million, including at least 200,000 to 400,000 who are severely demented. One might reasonably expect half of the severely or profoundly afflicted people—100,000 conservatively—to die within one year.

Hoyert and Rosenberg note that AD was reported as the underlying cause on about 20,000 death certificates in 1995.[2] They found that AD was mentioned as another (not underlying) cause on an approximately equal number, bringing the total to about 40,000 death certificates in which AD (all levels of severity) was mentioned as a multiple or underlying cause of death. Although there had been more than a tenfold increase in AD as the underlying cause of death between 1979 and 1995, this figure of 40,000 remains substantially below our reasonable prediction of at least 100,000. Whether this represents underrecognition of the disease or a failure to attribute to AD even a contributing role in a large number of deaths is uncertain.

Given these considerations, what is the public health and research utility of death certificate data on AD? Recent dramatic increases in the frequency with which AD appears on death certificates clearly reflect the change in the way we perceive AD—transformed by a conceptual and taxonomic revolution from a rare "presenile" illness to the single most common, expensive, and tragic disease of late life. If the burgeoning numbers of cases of AD being diagnosed were partly due to some sort of environmental exposure layered atop developments such as the demographic "graying of America," changing medical taxonomy, and a growing sophistication with regard to diagnostic methods, we would not know this to be true and could not meaningfully investigate it using death certificate statistics. There are just too many possible explanations for secular variations in rates to attribute any to specific factors at this time.

The complex pathogenesis of aging-related cognitive decline could well include occupational and industrial exposures, nutritional factors, hormone and drug exposures, air and water contaminants, and other factors. Their identification will require both reliable data measuring the candidate exposures and reasonable accuracy in defining the endpoint, be it AD or another type of dementia. Standardized coding of the dementing illnesses together with improvements in recognition and diagnosis are carrying us in the right direction.

In their report, Hoyert and Rosenberg present data drawn from death certificates on AD as the underlying cause of death for the 50 states. The rather dramatic differences seen between states are undoubtedly multicausal, and the low or high rates of any specific region could reflect social, educational, medical, or biological differences. When we are able to understand those interacting factors, or when some stability has been achieved with standardized recognition and reporting, we will have developed an enormously valuable surveillance system. That should be our goal.

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