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Recognition of Alzheimer's disease as a major public health problem: An historical account of the American experience

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As late as the early 1970s, most US physicians considered Alzheimer's disease to be an esoteric neurological disorder. The American public was essentially totally unaware of its existence. Elderly individuals with cognitive impairment or senility were thought to have 'hardening of the arteries' or 'little strokes.' This view was shared by many specialists in the aging field. Fewer than a half a dozen laboratories were involved in research on Alzheimer's disease. By 1990, the situation has changed dramatically. Today, it is recognized that up to four million Americans have Alzheimer's disease and that 35-45% of those of the age of 85 are afflicted, a figure of special importance because the over-85 age group is the fastest-growing segment of the US population. The National Institutes of Health, during 1991, spent more than 230 million US dollars to fund biomedical research addressed to Alzheimer's disease. The lay organization, the Alzheimer's Association, now has over 100 chapters and many hundreds of 'support' groups. The national Alzheimer's Association itself has raised more than \$18 million in 1991 to support education, care, and research in Alzheimer's disease, and a similar amount will be raised by the individual chapters. How has this remarkable change in recognition of the importance of Alzheimer's disease occurred in the United States?

Following Alzheimer's description in 1907¹ of the typical pathological changes—the brain atrophy, the neuritic plaque, the neurofibrillary tangle—in the case of a woman who died in her fifties following a several-year

course of progressive memory loss, difficulty in naming, and delusions, the existence of this disorder as a presenile dementia was immediately recognized and the eponym was widely accepted. A number of cases of elderly individuals with so-called senility who had the same pathologic changes as described by Alzheimer in his presenile case were reported. But there was not unanimous agreement about the relationship of Alzheimer pathology and 'senile dementia.' In particular, other authors emphasized the occurrence of multiple strokes, particularly small strokes, in brains of older individuals who died at state hospitals in a senile condition², although as early as 1948, Newton³ had noted that the clinical course of Alzheimer's disease and that of senile dementia was quite similar, but not much attention was paid to this prescient report. When I was an intern and resident in the early 1950s, the general medical teaching was that elderly demented individuals had 'hardening of the arteries', 'cerebral arteriosclerosis' and that this hardening was inevitable and that nothing could be done about it. On the other hand, Alzheimer's disease as a presenile condition was considered to be a markedly uncommon but interesting disorder that I, a neurology resident, observed from time to time on the neurology wards of my teaching hospital. This state of affairs was further abetted by the nomenclature that had been adopted by the American Psychiatric Association in 1952 in the first addition of its *Diagnostic and Statistical Manual*⁴, in which dementia in the elderly was subsumed under the title of Organic

Brain Syndrome and with a subtitle of Senile Psychosis. Patients with 'organic brain syndrome' and 'senile psychosis' would certainly not have been of interest to a young neurologist or internist at the time.

The modern scientific approaches to Alzheimer's disease can be dated to the early 1960s when two laboratories^{5,6} first described the ultrastructure of the plaques and tangles that Alzheimer observed using silver stains. Both Terry⁵ and Kidd⁶ noted the unusual twisted fibrils within the neurofibrillary tangles which are now termed 'paired helical filaments' and the amyloid structure of the protein that accumulated in the center of the neuritic plaque. The periodic structure of the paired helical filament in the neurofibrillary tangle and presence of degenerating swollen neurites surrounding an amyloid core within the neuritic plaque was found in both 'presenile' and 'senile' cases. In 1968, Blessed *et al.*⁷ carried out a prospective study in a group of very elderly in a nursing home and a chronic disease hospital, measuring cognition and function during life and comparing the scores obtained with the number of plaques and tangles and the volume of cerebrovascular infarcts present in the brains at postmortem examination. This seminal work established that, in the elderly population, the majority of cases showing dementia during life had pathological changes characteristic of Alzheimer's disease, with the number of neuritic plaques showing a reasonable correlation with mental status and functional scores during life. Among those with major cerebral infarcts caused by cerebrovascular disease, the volume of the cerebral infarcts appeared related to the presence of dementia. It thus became recognized that on a pathological basis, a majority of individuals in late life with dementia did, in fact, have essentially identical pathology to that of a typical presenile Alzheimer brain. It became apparent that the separation on the basis of age of onset was quite arbitrary and that, in fact, most patients with 'senility' or 'senile dementia' were not suffering from normal aging, but instead, had Alzheimer's disease⁸. When one looked at the actual number of individuals in nursing homes with the so-called organic brain syndrome, and in the few community studies then available of the prevalence of dementia, one could see there were indeed very many elderly who were demented, and the data of Blessed *et al.*⁷ as well as our own data indicated that the significant majority had Alzheimer's disease. Indeed, when one began to calculate the prevalence of dementia, with the assumption that 60% of those with dementia had Alzheimer's disease, the total number of individuals with Alzheimer's disease in the population based on the figures then available could be estimated at more than one million individuals in the United States. Furthermore, the sparse, but consistent data in the literature indicated that once one developed Alzheimer's disease, life expectancy was cut

in half, a figure leading to the estimate of at least 100,000 deaths annually of Alzheimer victims in the United States, making it the fourth or fifth most common cause of death. I had the opportunity of publishing these estimates in an editorial in the *Archives of Neurology*⁹ in 1976.

In 1976 and 1977, the interest in Alzheimer's disease was intensified by a major research breakthrough when three laboratories in Great Britain reported a major loss of choline acetyltransferase, the marker of cholinergic terminals, in neocortex of the brains of Alzheimer patients¹⁰⁻¹². This intrigued clinicians because it was initially hoped that replacement therapy for acetylcholine would have the same usefulness in Alzheimer's disease as replacement therapy with L-DOPA had in Parkinson's disease.

These advances in understanding the importance of Alzheimer's disease and that it might be approached through biomedical research led to the convening of a workshop conference on Alzheimer's disease that was sponsored jointly by three of the National Institutes of Health—the National Institute on Neurological Diseases, the National Institute of Mental Health, and the newly formed National Institute on Aging—a workshop that was most successful in its attempt to interest a variety of neuroscientists and others in the problem of Alzheimer's disease¹³.

This heightened, although still quite isolated, medical interest in the disorder was matched by the increasing number of individuals with dementia who were beginning to be correctly diagnosed as having Alzheimer's disease by sophisticated neurologists and psychiatrists, leading to the development of useful clinical definitions and criteria for the diagnosis of dementia and Alzheimer's disease^{14,15}. In several locales, the spouses of these victims became interested in helping other caregivers and started to develop small local organizations. The concept of the support group evolved: biweekly or monthly meetings of caregivers of Alzheimer or other dementia patients, for the exchange of information and for mutual practical and emotional support. Some of the support groups met with a health professional, such as a social worker, nurse, or physician, but many consisted only of lay persons trying to cope with the difficulty of caring for a demented spouse or parent in the context of a modern industrialized society. This lay interest led family members and physicians to develop small nonprofit organizations devoted to Alzheimer's disease. In late 1979, Dr Robert Butler, then director of the National Institute on Aging, brought these fledgling organizations together in Washington DC, with the expressed purpose of promoting the formation of a single organization rather than having the many competing organizations. At that meeting, the Alzheimer's Disease and Related Disorders Association was formed. Jerome

Stone, the leader of a major corporation and himself a family member, provided the financial support for the beginning of this national organization. Once this organization, now renamed the Alzheimer Association, began to develop, a number of individuals with Washington connections, who were family members, were attracted to it. Of particular help to the organization was the family of the former movie star, Rita Hayworth, who were willing to publicize that she did have Alzheimer's disease, making the disease socially acceptable. The impact was almost immediate¹⁶. In 1976, the federal outlay for Alzheimer's disease research was approximately four million dollars. By 1984, there had been enough expansion of research, for the first announcement of the development of Alzheimer's Disease Research Centers to be made, and the progress has continued since then. Alzheimer's disease has become of major interest to Congress, in part because care of Alzheimer victims represents a major expenditure of public health dollars (estimated to be over 88 billion dollars last year), and the discovery of cause, prevention, and treatment would be extremely cost effective, but in part because the older members of Congress often have a family member or a close friend with the disorder. Following a report by the Office of Technology Assessment¹⁷, the United States Congress legislated the formation of an Advisory Panel on Alzheimer's disease. In 1989 the panel recommended that research support be increased to 350 million dollars¹⁸, the research budget for research in Alzheimer's disease will approach 300 million dollars in the fiscal year that began 1 October 1991. Research support thus will have increased 75-fold in 15 years! The research advances now being made are often headlined in United States newspapers, and indeed, they are remarkable as will be attested to in this issue of *Current Science*. With this, there are growing resources to help caregivers such as informational materials, both

pamphlets and videotapes, day-care centers, respite centers, and a wide network of support groups. Thus the growth of the Alzheimer's disease movement in the United States represents a success story both for the families of Alzheimer's disease victims and the investigators intent on understanding the disorder.

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