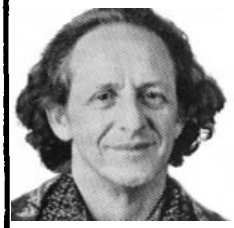
Essays of an Information Scientist, Vol:5, p.138-142, 1981-82 Current Contents, #24, p.5-9, June 15, 1981



Current Comments

Senility: A Major Health Problem in Need of a Solution

Number 24 June 15, 1981

None of us is getting any younger. Many of us consider old age with some trepidation. We fear the loss of our mental and physical faculties as much as or more than death itself. Many people don't seem to realize that most of us have a good chance of living long lives and showing few signs of mental decline. Some psychiatrists even believe that leading an active life, mentally and physically, can prevent or slow the declines associated with old age.[1]

However, those who worry about aging have grounds for concern. Perhaps ten percent of the over-65 population of Northern Europe and the US has some form of intellectual impairment that could be classified as senility. And about four percent may be incapacitated by senility.[2] (p. 484) Victims of senility, or senile dementia, as it's sometimes called, exhibit some disturbing behavioral symptoms. The minor forgetfulness that often accompanies normal aging may be the first sign. Patients' friends and family, and sometimes the patients themselves, notice other problems as the condition worsens. Signs of increasing senility include memory loss, failing attention, declining linguistic or mathematical ability, loss of sense of humor, disorientation and confusion, irritability, restlessness, and loss of judgment. In severe cases, victims may be incapable of caring for themselves.[3]

In the worst stages of dementia, victims' behavior can be very erratic. For example, an Australian study of 200 dementia victims turned up one who was referred for treatment after being arrested for indecent exposure.[4] And a friend of mine has a senile grandmother who shoplifts. When her family takes her out they have to follow her around and let her pick up a few things she thinks are too expensive to buy. Such extreme cases of dementia obviously take a great emotional toll on the family. The burden has been compared to the burden of untreatable cancer. Sometimes the family must admit the relative to a nursing home, which can increase the family's guilt and anxiety. But sometimes professional care is necessary, if only because senility victims may be at increased risk of pneumonia and other diseases, as well as accidents.[5]

Unfortunately, only about ten percent or 20 percent of all cases of senile dementia are reversible. Such cases are caused by treatable or curable disorders, such as metabolic disturbances, tumors, infections, chronic pain, sensory deprivation, vitamin deficiencies, or the side effects of medication.[3] Most cases of senile dementia are not reversible, however. About 20 percent of them are caused by a series of minor strokes. This form of senility is called multi-infarct dementia (MID). Hypertension may be a major factor in causing it, so controlling high blood pressure probably helps stave off MID. It can also help prevent further "mini-strokes" when MID is already present.[6] To pinpoint the risk factors in MID, a five-year study of about 500 elderly people has

been underway for about eight months. This project is directed by neurologist Robert Katzman, Albert Einstein Medical College, Bronx, New York.[7]

About half the cases of senile dementia are caused by Alzheimer's disease. This disorder is named after Alois Alzheimer, the German physician who in 1907 first observed some of the odd brain changes that characterize it. Later, the electron microscope made it possible for researchers to study these brain abnormalities in more detail. One sign of Alzheimer's disease is senile plaque, composed of distorted axon endings surrounding a substance called amyloid. Another sign is the appearance in nerve cells of neurofibrillary tangles, which are made of abnormal filaments.[2] (p. 485) These tangles may originate in neurotubules, the long parallel tubes found in neurons.[8] The number of tangles has been correlated with the severity of senility.[2]

Alzheimer's disease can be diagnosed after a thorough medical exam, which is usually intended to rule out other causes of dementia, such as hormonal problems. Computed tomography (CT) scans, sophisticated computerized x-rays, can also be valuable, since they can help rule out problems like brain tumors. The diagnosis can be confirmed by microscopic examination of brain tissue samples.[9]

The disease is incurable at present. Research on the causes could lead to a cure, though. There's no shortage of possible causes. In fact, the disease may have many causes.

Perhaps one of the most promising findings is that Alzheimer's patients have lower than normal levels of a brain chemical called choline acetyltransferase. The brain needs this enzyme to manufacture an important neurotransmitter, acetylcholine. The discovery raises the possibility that a chemical cure will be found. Just as L-dopa helps with Parkinson's disease, an enzyme might make up for the neurochemical deficiency in Alzheimer's disease.[10] Choline-rich foods such as egg yolks, meat, and fish might also be helpful. But studies have not been conclusive.[11]

Some researchers think Alzheimer's disease may be inherited. Leonard L. Heston and Angeline R. Mastri, University of Minnesota, report on some interesting clues from autopsy studies of Alzheimer's victims. They found that relatives of people who died from Alzheimer's disease also had a high incidence of the disease. Also common in this group were blood malignancies and Down's syndrome, a congenital condition characterized by mental retardation and distortion of the face, skull, and digits. The researchers note that Down's syndrome victims, if they survive to adulthood, almost always display the neurofibrillary tangles and senile plaque of Alzheimer's disease. Not only that, but Down's victims have a 20-fold risk of contracting leukemia. So it's possible that these problems are tied together genetically, in a way not yet fully understood.[12]

An as-yet-unpublished study by Donna Cohen and Carl Eisdorfer, University of Washington, seems to strengthen the genetic connection. A *Science 81* report of their work says that Alzheimer's disease seems to be more common among the firstborn offspring of older parents. The study of 80 Alzheimer's victims showed the median age of their mothers at the time of birth was 35.5; of their fathers, 38. This is about ten years older than new parents generally are.[13]

Scientists working with Alzheimer's disease have other clues to work with. One of them is aluminum. In 1965, Igor Klatzo[14] and co-workers, National Institute of Neurological Diseases and Blindness, reported that rabbits exposed to aluminum salts showed neurofibrillary changes in the brain. D.R. Crapper[15] and colleagues, University of Toronto, later showed that the brains of Alzheimer's victims contained relatively large quantities of aluminum. However, the role of aluminum is ambiguous. One study, by John R. McDermott, Medical Research Council, England, and colleagues showed that nine non-demented

elderly people had roughly the same brain aluminum concentrations as ten Alzheimer's victims.[16]

Yet another hypothesis is that Alzheimer's disease is caused by a slow-acting virus. The idea is plausible, because a neurological disease called kuru, which causes senility-like symptoms, has been shown to be virus-caused. However, no Alzheimer's virus has yet been identified.[17]

Since there's no cure for senility, whatever its cause, many people commonly assume that nothing can be done. However, patients' families can ease the stress of dementia. Probably the best thing families can do is to involve the patient in family activities as much as possible.[18] Private, nonprofit organizations called "support groups" can help families of dementia victims. They provide information on research programs, public facilities for the aged, and emotional support for victims and families. One organization acts as a clearinghouse for such information. The Alzheimer's Disease & Related Disorders Association, 292 Madison Avenue, New York, New York 10017, can direct families to whatever services are available near their homes. The group publishes the monthly *ADRDA Newsletter*. This periodical covers meetings and conferences about senility. The March 1981 issue, the first, includes an informal review of the topic by David Drachman, University of Massachusetts. Drachman notes, " 'It has been pointed out that just the nursing home costs are over $10 billion per year and the research funds available are approximately one-thousandth of that, or $10 million.' "[19] The issue also includes practical suggestions for living with an Alzheimer's patient. For example, to prevent patients from accidentally scalding themselves, water temperature in private homes should be lowered.[20]

We have recently added to *Current Contents®/Life Sciences* (*CC®/LS*) a journal called *Neurobiology of Aging*, which is obviously relevant to senility. Papers on the topic also frequently appear in neuroscience journals, such as *Neurology* and *Annals of Neurology*, which are covered in *CC/LS* and *CC/Clinical Practice* (*CC/CP*), and in journals on aging, such as the *Journal of the American Geriatrics Society*, covered in *CC/Social & Behavioral Sciences* and *CC/CP*.

To get a better idea of how much research activity on senile dementia is conducted we consulted ISI/BIOMED™.[21] This online service uses co-citation analysis to identify the most active topics in biomedicine. As a matter of fact, at the threshold used to identify 3,000 other highly active biomedical research specialties, only one turned up directly related to dementia. A pair of co-cited papers by B.E. Tomlinson *et al.*, Newcastle General Hospital, Newcastle upon Tyne, England, proved to be the basis for the cluster of papers in Table 1. The 1968 Tomlinson paper is a study of the neurological features of 28 *non*-demented old people.[22] The second Tomlinson paper, published in 1970, used the same techniques to analyze the brains of 50 senility victims.[23]

Eleven current papers citing the Tomlinson pair were retrieved. The list of articles in Table 1 needs no lengthy comment. As it turns out, Tomlinson is the author of the one review article on the aging brain. A few of the articles indicate how CT technology has penetrated the field. The paper by C.E. Wells, Vanderbilt University Medical School, Nashville, in the *American Journal of Psychiatry*, discusses the mimicry of dementia by psychiatric disorders. It reports ten cases of this "pseudodementia."

While traditional neurology seems to dominate studies of senile dementia, we would have to do a more detailed analysis of the important but still less active areas of research. An interdisciplinary problem, senile dementia is only an aspect of interrelated areas of aging research. Table 2 provides the names of five other aging related fronts we identified in ISI/BIOMED. For each of these highly active fields we've indi-

Table 1: Citing papers related to senile dementia, retrieved by a research front specialty search in ISI/BIOMED™. The papers cited the core papers of Tomlinson *et al.*

Anderson F H, Richardson E P, Okazaki H & Brody J A. Neurofibrillary degeneration on Guam. *Brain* 102:65-77, 1979.

Braak H. Spindle-shaped appendages of IIIab-pyramids filled with lipofuscin. A striking pathological change of the senescent human isocortex. *Acta Neuropathol.* 46:197-202, 1979.

DeLeon M J, Ferris S H, Blau I, George A E, Reisberg B, Kricheff I I & Gershon S. Correlations between computerized tomographic changes and behavioural deficits in senile dementia. *Lancet* 2:859-60, 1979.

Earnest M P, Heaton R K, Wilkinson W E & Manke W F. Cortical atrophy, ventricular enlargement and intellectual impairment in the aged. *Neurology* 29:1138-43, 1979.

Kaszniak A W, Garron D C, Fox J H, Bergen D & Huckman M. Cerebral atrophy, EEG slowing, age, education, and cognitive functioning in suspected dementia. *Neurology* 29:1273-9, 1979.

Pellissier J F, Labrecque R & Salamon G. Lésions cérébrales séniles. (Lesions in senile brain.) *Neuroradiology* 16:181-2, 1978.

Ropper A H. A rational approach to dementia. *Can. Med. Ass. J.* 121:1175-90, 1979.

Tomlinson B E. The ageing brain. *Rec. Advan. Neuropathol.* 1:129-59, 1979.

Uemura E & Hartmann H A. Quantitative studies of neuronal RNA on the subiculum of demented old individuals. *Brain Res. Bull.* 4:301-5, 1979.

Uemura E & Hartmann H A. RNA content and volume of nerve cell bodies in human brain. *Exp. Neurol.* 65:107-17, 1979.

Wells C E. Pseudodementia. *Amer. J. Psychiat.* 136:895-900, 1979.

cated the number of core papers (those co-cited) and the number of current citing papers. The core papers in four of these fields are listed in Table 3. We excluded the large "cell senescence and aging" cluster for lack of space.

Senility imposes an enormous financial drain on society. It also drains the family involved, financially and emotionally. No one can measure the emotional cost, but I've witnessed the impact senile dementia can have on a family. To watch the deterioration, in

Table 2: Aging-related research fronts from ISI/BIOMED™.

	Core papers in cluster	1980 citing papers in research front
Aging and hepatic drug metabolism	2	35
Aging and pharmacokinetics	2	41
Cell biology of aging and senescence	3	45
Neuroendocrine mechanisms and aging	2	41
Cell senescence and aging	28	248

Table 3: Core papers to aging-related research front specialties in ISI/BIOMED™.

Aging and Hepatic Drug Metabolism

Hurwitz N. Predisposing factors in adverse reactions to drugs. *Brit. Med. J.* 1:536-9, 1969.

O'Malley K, Crooks J, Duke E & Stevenson I H. Effect of age and sex on human drug metabolism. *Brit. Med. J.* 3:607-9, 1971.

Aging and Pharmacokinetics

Crooks J, O'Malley K & Stevenson I H. Pharmacokinetics in the elderly. *Clin. Pharmacokinet.* 1:280-96, 1976.

Triggs E J & Nation R L. Pharmacokinetics in the aged: a review. *J. Pharmacok. Biopharm.* 3:387-418, 1975.

Cell Biology of Aging and Senescence

Holliday R, Huschtscha L I, Tarrant G M & Kirkwood T B L. Testing the commitment theory of cellular aging. *Science* 198:366-72, 1977.

Martin G M, Sprague C A, Norwood T H & Pendergrass W R. Clonal selection attenuation and differentiation in an *in vitro* model of hyperplasia. *Amer. J. Pathol.* 74:137-50, 1974.

Smith J R & Hayflick L. Variation in the life-span of clones derived from human diploid cell strains. *J. Cell Biol.* 62:48-53, 1974.

Neuroendocrine Mechanisms and Aging

Finch C E. Catecholamine metabolism in the brains of ageing male mice. *Brain Res.* 52:261-76, 1973.

Simpkins J W, Mueller G P, Huang H H & Meites J. Evidence for depressed catecholamine and enhanced serotonin metabolism in aging male rats: possible relation to gondotropin secretion. *Endocrinology* 100:1672-83, 1977.

the form of senility, of a loved one, is particularly painful. It is unlike any other disorder where patients lose touch with their surroundings.

To eliminate senile dementia only prepares us to die, hopefully with dignity, from some other cause. But it would seem reasonable to give research in this field a high priority. Henryk M. Wisniewski and Khalid Iqbal, New York State Institute for Basic Research in Mental Retardation, Staten Island, New York, point out that the over-75 population is growing at 2.5 times the rate of the general population. They state that if further dramatic extensions of the lifespan become possible, "the problem of ageing control probably will become more vital than the problem of birth control."[24] For as medical advances improve our chances for longer lives, the probability of falling victim to senility also increases. Resources for the care of the elderly are already limited, and even today older people who can't care for themselves are all too often subject to neglect or abuse. An increase in the population of the needy elderly could make society less charitable and responsive than it often already is. The bioethical question of who gets treatment, and who doesn't, could become even more crucial. To prevent these problems from occurring, it seems wise for us to invest in basic research now, rather than to count on being able to treat every case in the near future.

* * * * *

My thanks to Lynn Davis, Patricia Heller, and Tom Marcinko for their help in the preparation of this essay.

REFERENCES

1. **Leo J.** Fighting off old age. *Time* 117(7):54, 16 February 1981.
2. **Katzman R.** Degenerative and heredodegenerative diseases. (Harter D F & Merritt H H, eds.) *A textbook of neurology.* Philadelphia: Lea & Febiger, 1979. p. 484-9.
3. **Task Force Sponsored by the National Institute on Aging.** Senility reconsidered. *J. Amer. Med. Assn.* 244:259-63, 1980.
4. **Smith J S & Kiloh L G.** The investigation of dementia: results in 200 consecutive admissions. *Lancet* 1(8224):824-7, 11 April 1981.
5. **National Institutes of Health.** *Q & A: Alzheimer's disease.* NIH publication no. 80-1646, June 1980. Brochure.
6. Senility. *Harvard Medical School Health Letter* 6(7):1-2;5, May 1981.
7. **Manber M M.** Senility. *Med. World News* 22(7):24-30, 30 March 1981.
8. **Grundke-Iqbal I, Wisniewski H M, Johnzon A B, Terry R D & Iqbal K.** Evidence that Alzheimer neurofibrillary tangles originate from neurotubules. *Lancet* 1:578-80, 1979.
9. Alzheimer's disease. *Brit. Med. J.* 281:1374-5, 1980.
10. **Kolata G B.** Clues to the cause of senile dementia. *Science* 211(4486):1032-3, 6 March 1981.
11. **Ferris S H, Sathananthan G, Reisberg B & Gershon S.** Long-term choline treatment of memory-impaired elderly patients. *Science* 205:1039-40, 1979.
12. **Heston L L & Mastri A R.** The genetics of Alzheimer's disease. *Arch. Gen. Psychiat.* 34:976-81, 1977.
13. Senility linked to parental age. *Science 81* 2(3):7, April 1981.
14. **Klatzo I, Wisniewski H & Streicher E.** Experimental production of neurofibrillary degeneration. I. Light microscopic observations. *J. Neuropathol. Exp. Neurol.* 24:187-99, 1965.
15. **Crapper D R, Krishnan S S & Quittkat S.** Aluminum, neurofibrillary degeneration and Alzheimer's disease. *Brain* 99:67-80, 1976.
16. **McDermott J R, Smith A I, Iqbal K & Wisniewski H M.** Brain aluminum in aging and Alzheimer disease. *Neurology* 29:809-14, 1979.
17. **Gajdusek D C.** Unconventional viruses and the origin and disappearance of kuru. *Science* 197:943-60, 1977.
18. **Kennie D C & Moore J T.** Management of senile dementia. *Amer. Fam. Physician* 22:105-11, 1980.
19. **Alzheimer's Disease & Related Disorders Association.** Drachman summarizes mini-White House proceedings. *ADRDA Newsletter* 1(1):4-6, March 1981.
20. ----------. Helpful hints for everyday living. *ADRDA Newsletter* 1(1):2, March 1981.
21. **Garfield E.** ISI's on-line system makes searching so easy even a scientist can do it: introducing METADEX automatic indexing and ISI/BIOMED SEARCH. *Current Contents* (4):5-8, 26 January 1981.
22. **Tomlinson B E, Blessed G & Roth M.** Observations on the brains of non-demented old people. *J. Neurol. Sci.* 7:331-56, 1968.
23. ----------. Observations on the brains of demented old people. *J. Neurol. Sci.* 11:205-42, 1970.
24. **Wisniewski H M & Iqbal K.** Ageing of the brain and dementia. *Trends Neurosci.* 3:226-8, 1980.