6 December 1985, Volume 230, Number 4730 **SCIENCE**

Alzheimer's Disease: A Biologist's Perspectives

Public concerns about Alzheimer's disease are rising. With the increasing survival to advanced ages, it is predicted that Alzheimer's disease will afflict about 2 million people in the United States by the year 2000. Funding for basic and clinical studies on this disease has been increased and now includes $9 million a year that Congress added to the budget of the National Institute on Aging for ten Alzheimer's disease research centers, about $40 million from other National Institutes of Health programs, and $2 million from private foundations. Biologists may ask how the emphasis on Alzheimer's disease could influence support and opportunities for basic research.

My view is that little recognized but implicit aspects of these programs will greatly benefit the neurosciences and biogerontology. An important resource will be the greater availability of brain tissues from normal subjects. To delineate Alzheimer's disease from other common age-related changes requires at least as many (probably several times more) normal controls as individuals with Alzheimer's and other age-related dementias. Postmortem specimens from normal individuals with detailed personal and medical histories are usually scarce. However, healthier relatives and friends of victims of Alzheimer's disease are often willing to donate their own tissues. The Alzheimer's disease research centers could provide the complex logistical support for the short postmortem intervals (4 hours or less) needed to preserve many macromolecules and microscopic structures.

The tissue resources will permit new approaches concerning the impact of heredity and environment on the cellular structure and chemistry of the healthy human brain. The correlation of detailed pre- and postmortem data promises to support major growth of research on human neurobiology and could reveal long-lasting effects of drugs, diet, stress, or even subtler experiences. Pursuit of these far-reaching and difficult questions will also build on the spectacular advances from brain imaging in vivo. Other topics so far studied much less in humans than in animals include mechanisms of nonischemic neuronal death; cytoskeletal organization; sex differences; receptors; membrane transport; tissue factors that influence neurite outgrowth; and messenger RNA. The brain messenger RNA's examined at my laboratory and that of M. Morrison have a remarkable postmortem stability; this invites aggressive use of molecular genetic technology.

Screening for hereditary influences on Alzheimer's disease could also reveal genetic markers linked to depression and other common late-onset neurological disorders. Moreover, even without knowing the base sequence of an Alzheimer's locus, linked genetic markers could reveal environmental factors as well as other genes that influence the age of onset and progress of neurological diseases in high-risk individuals.

Studies on Alzheimer's disease also probe basic mechanisms of synaptogenesis. Recently, evidence of neuronal plasticity and sprouting in the human brain was found in the hippocampus of victims of Alzheimer's; these synaptic reorganizations are similar to the changes induced in the rat hippocampus by lesions of the entorhinal cortex.* Intriguing results are being obtained by C. Cotman, F. Gage, D. Gash, and others in the use of embryonic cell transplants to correct experimental or congenital brain lesions that may yield therapies for victims of Alzheimer's. Moreover, research leading to the prevention or effective treatment of Alzheimer's disease seems likely to illuminate one of the great mysteries in biology—the nature of memory and cognition. I would be surprised if the major new resources required for a serious attack on Alzheimer's do not also benefit the basic neurosciences on the same scale as funding for cancer research has done for many areas of molecular, cell, and developmental biology.—

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*J. W. Geddes, D. T. Monaghan, C. W. Cotman, I. T. Lott, R. C. Kim, H. C. Chui, *Science*, this issue, page 1179.