

Commentary

Ageing: a Cause or a Risk for AD?

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Although Alzheimer's disease (AD) as a distinct clinical entity was described nearly one hundred years ago, until recently it was considered an inevitable consequence of aging and dismissed as an untreatable condition. Since the mid-1970s, the progress of research rapidly moved this disease from obscurity to a position of prominence. In the last few years the numbers of theories about the underlying mechanisms have increased, scientific knowledge and attitudes about the disease have change dramatically.

The article by Ming Chen and Hugo L. Fernandez entitled "Revisiting Alzheimer's disease from the new perspective: Can 'risk factors' play a key role?" is another important attempt to develop a new theory on this disease. The authors assert that "natural aging plays a more important role in neurodegeneration than is currently recognized. Does this model over-simplify the disease origin?" The short answer to this rhetorical question is a simple yes! This answer is based on the following reasoning.

The results of several epidemiological studies of risk factors have confirmed a correlation between age and the prevalence of the disease. The relationship between age, prevalence of dementia and presence of different alleles of APO E has added further credence to the assertion (hypothesis) that everyone over 65, if they live long enough, will eventually get "it", Alzheimer's dis-

ease. Presently the evidence to support this proposition is not sufficient or compelling.

Alzheimer's disease or some form of dementia has probably always been part of the human condition. The ancient physicians knew some of the clinical features of dementia. However, these late-life disorders of the "mind" were infrequent occurrences in the repertoire of diseases they treated, because people very rarely survived beyond the age of 40. William Shakespeare, 1564–1616, an astute observer of human behavior, knew some things about aging and dementia. In *As You Like It*, 1595–1600, Act II Scene VII, speaking through 'Jaques', Shakespeare describes the human aging process as, "... All the world's a stage, and all the men and women merely players; they have their exits and their entrances; and one man in his time plays many parts, his acts being seven ages. At first the infant, mewling and puking in the nurse's arms... Last scene of all, is the second childishness and mere oblivion; sans teeth, sans taste, sans every-thing."

Although one might grant Shakespeare poetic license for a loose description of the clinical features of dementia in the seventh stage of life, he mistakenly attributed the losses of independence, cognition and sensory functions, merely to the state of being old or the aging process. Contrary to the widely shared misconception, many older individuals remain healthy, continue to be creative and productive, can function well and live independently into late life. There are many examples of individuals who have lived well beyond the tenth decade, with their brain operating in perfect order. The complex operations of the brain can be carried out with great efficiency throughout the full life span of the person, as long as a disease process, toxins or trauma do not

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cause damage to the neurons.

The fallacy of assigning a causal relationship between aging and dementia, two independent processes that appear to be correlated, has persisted from Elizabethan times to the present. The term "senile" was used to connote the combination of being old and "not totally with it". Until recently the concept of "senility" was used as a convenient pseudo-medical term to explain away our ignorance of how to diagnose, treat or manage dementia patients or how to distinguish the functions of the normal aged from that of the sick degenerating brain. Although recent studies have consistently found a correlation between "age" and the presence of dementia, "aging" as a continuous process of biological development has not been shown to cause dementia. Dementia is the result of a specific cascade of aberrant biological events (yet to be discovered), which lead to *disease* processes.

The two phenomena, which have had the most profound influence on the emergence of AD as a modern public health problem are: a) the steady increases in the life-expectancy of the oldest-old since the early 1900s, and b) the relationships between age, prevalence and selective risk factors. As a greater proportion of the population survives beyond the age of 85 years, the number of individuals at risk for some form of cognitive

dysfunction will increase because of the higher prevalence rates in this group. The prevalence of dementia increases nearly exponentially beyond age 65, the rates double every five years after age 65.

The concept of a risk factor and the role it plays in the expression of a complex disease such as AD, which may have many causative determinants interacting, is important in developing interventions to alter the course of the disease or to prevent it. Some of the other key risk factors that have been associated with AD include: age, genetic predisposition (family history), gender, head trauma, education/occupation, and exposure to toxins. These observations of potential risk factors have begun to provide new clues to the mechanisms of the disease by linking genetic and non-genetic risk factors to changes in the brain.

The cognitive losses and behavioral changes in dementia are the direct result of the destructive processes of the disease, which ultimately leads to breakdown of communication between some nerve cells and the loss of increasing numbers of neurons. The heart of the scientific quest to discover the cause(s) of AD revolves around the questions of how and why some nerve cells lose their ability to communicate and why some neurons die.