Etiology and pathogenesis of alzheimer’s disease

Health & Medicine, Disease

Alzheimer’s disease is a degenerative brain disorder and is the main cause ofdementia. The major clinical manifestations of Alzheimer’s disease include gradual loss of memory and language. Other major symptoms and signs of this disease are psychiatric and behavioral abnormalities and disabilities in the routine or daily living activities.

The etiology and Pathogenesis of Alzheimer’s disease include various factors. Biological Factors Even though the etiology and pathogenesis of Alzheimer’s disease is still not known fully, it is discovered to involve a complex mix of genetic as well as environmental factors.

Among genetic and environmental factors, genetic factor is proved to be playing a major role in the etiology and pathogenesis of Alzheimer’s disease. The most important cause of Alzheimer’s disease is found to be the mutations in chromosomes 21, 14 and 1 which are spread or moved in a typical autosomal dominant mode. These mutations make protein overproduction in neuritic plaques, B amyloid. Even though the beginning of the familial form is often early, the nature and route of the disorder is found to be influenced by few environmental factors.

But it is found out that familial form is responsible for only a negligible proportion of cases of Alzheimer’s disease (even less than five percent) (Cummings et al. , 1998b). Nearly fifty percent of the people who are having ancestors with Alzheimer’s disease are found to be getting this disorder once they enter their 80s and 90s (Mohs et al. , 1987). Few genotypes (the model of genetic inheritance in a person’s body) are found to give risk for the late-onset Alzheimer’s disease (which is very common).

Taking an example, the ApoE-e4 allele on chromosome 19, that encourages the deposition of B amyloid, is proved to increase the risk for developing Alzheimer’s disease (Corder et al. , 1993). All other genes that are doubted to be responsible for the development of Alzheimer’s disorder are being studied (Kang et al. , 1997). Apart from this particular reason, there are various other biological risk factors that contribute to the development of Alzheimer’s disorder Cummings et al. , 1998b).

Cognitive capabilities and aging are among the biological factors. The manner in which these traits contribute to the increased risk is not still proved, however, it is proved in the medical field that the numerous neurobiologic changes that are associated with the normal aging of the brain of a person also contribute to the major risk factors of Alzheimer’s disorder. As people get into the later part of their life, this age related neurobiologic changes make then more liable for Alzheimer’s disorder.

These neurobiologic changes include neuron and synaptic loss, lessened dendritic p, reduced size and density of neurons present in the nucleus basalis of Meynert, and poor cortical acetylcholine levels (Cummings et al. , 1998b). Based on these factors and the frequency and occurrence curve of this disorder, medical researchers have come to the conclusion that people are very much liable to Alzheimer’s disorder if their life p is extended (beyond the normal age) beyond eighties and nineties (up to 100 and 150). People above 90 years are highly susceptible to Alzheimer’s disorder.

Among this, those who have Alzheimer’s history in theirfamilyare 90 % prone to this disorder. Protective Factors Apart from the biological factors there are various other factors that influence the onset of Alzheimer’s disease. Various

protective factors that are powerful enough to delay the commencement of Alzheimer’s disorder have been discovered. For example, Genetic endowment with the ApoE-e2 allele is capable of reducing the risk of Alzheimer’s disorder (Duara et al. , 1996). The exact role and the original mechanism of action of ApoE-e2 allele, however, are not completely understood.

Deep thinking, higher educational level and wisdom are also proved to be associated with the delay in the commencement of Alzheimer’s disease (Stern et al. , 1994; Callahan et al. , 1996a). Few medication and drugs are also found to be good for delaying the onset of Alzheimer’s disorder. For example, medications, like nonsteroidal anti-inflammatory drugs (Andersen et al. , 1995; McGeer et al. , 1996) and estrogen replacement therapy (Paganini-Hill & Henderson, 1994), are found to be effectively delaying the commencement of Alzheimer’s disease.

Apart from this, Vitamin E and the drug selegiline (otherwise known as deprenyl) are also proved to holdup the crucial stages of the course of Alzheimer’s disorder, for example thenursinghome placement, serious functional impairments or disorders as the disease progresses and lead to death (Sano et al. , 1997). According to Behl et al. , 1995, the course of action of the protective agents in a person is not completely known; however, these agents are proved to check the toxic action of oxidativestress(through antioxidants like vitamin E or estrogen).

These agents also counter the work of inflammatory mediators related to plaque formation (through anti-inflammatories) (Mark et al. , 1995). Histopathology The pathophysiology of Alzheimer’s disorder is also proved to

be associated with the histopathologic variations in Alzheimer’s disease. These histopathologic changes include neuritic plaques, synaptic loss, neurofibrillary tangles, hippocampal granulovacuolar degeneration, and B amyloid angiopathy (Cummings et al. , 1998b).

Majority of the genetic and epigenetic risk factors are some or the other way linked with B amyloid. This has helped the medical researchers to conclude that the formation of B amyloid peptide is the most crucial pathological event or step in the course of spread of Alzheimer’s disorder in a person (Cummings et al. , 1998b; Hardy & Higgins, 1992). A successful intervention in the course of Alzheimer’s disease spreading may include get in the way of any of the numerous steps included in the slow progress of Alzheimer’s disease pathogenetic cascade.

Few of the intervention modes include intervening to reduce B amyloid generation from the amyloid precursor protein, intervening to decrease the B amyloid aggregation as well as the generation of beta-pleated sheets, and intervening in the amyloid-related neurotoxicity process. Successful interference in these steps may help interrupt Alzheimer’s spread. Apart from this, few therapies can successfully block the neuronal cell death and can slow down the inflammatory response occurring in neurotic plaques.

Therapies are also proved to inhibit the work of certain growth factors and hormones and also delay the replenishment of deficient neurotransmitters. As the complete obstruction of the processes within the B amyloid cascade may affect the usual cerebral metabolic processes, successful interruptions may bring about partial interruptions (Cummings & Jeste, 1999). Studies

about the molecular neuroscience of Alzheimer’s disease have researched several crucial aspects of pathophysiology and etiology.

Researchers are working to thoroughly understand the entire processes and reasons behind cell death, neuronal degeneration and subsequent memory degradation. Medical world is expecting new revelations from these studies and are on the way to lay a new therapeutic path for eliminating Alzheimer’s disease from the world (National Institute on Aging, 1996). Medical world is expecting researchers to come out with the real physiological factor that makes a human body prone to Alzheimer’s syndrome. Role of Acetylcholine

Acetylcholine is also suspected to play a part in encouraging Alzheimer’s disorder in a person. Loss or decrease of the neurotransmitter acetylcholine also is proved to be responsible for the pathogenesis of Alzheimer’s disease. Postmortem researches in Alzheimer’s disease infected people have explained the loss or reduction of basal forebrain and cortical cholinergic neurons and the exhaustion of choline acetyltransferase, which is the enzyme that carry out acetylcholine synthesis (Mesulam, 1996). Several post mortem reports have come out with the same reason.

The scale of this central cholinergic deficit is associated with the severity of dementia that results in the ‘ cholinergic’ hypotheses of cognitive deficits in Alzheimer’s disorder (Mesulam, 1996). This hypothesis and the clinical researches have proved that Acetylcholine play a major role in Alzheimer’s disease. However, acetylcholine is not the only neurotransmitter that encourages the growth of Alzheimer’s disorder in a patient. Researchers are still working to find out the role of other substances in the pathogenesis of the Alzheimer’s disorder.

The researches related to the pharmacological treatment of this syndrome are coming out with new results. It has been proved that a delay or break in the spread of Alzheimer’s disease is proved to reduce its prevalence in the body of a patient even by half (Breitner, 1991). In order to inhibit the spread of this syndrome in a person it is necessary to delay the onset of the disease to such an extent where mortality from other resources surpasses the frequency of the steps of the disease.

So the most crucial step in inhibiting Alzheimer’s disease is the identification of the factors that stop the onset or slow down the progress of the disease in the patient. Working on these agents would help reduce the spread of the disease. References Aarts, P. , & Op den Velde W. (1996). Prior traumatization and the process of aging. In B. A. van der Kolk, A. C. McFarlane, & L. Weisath (Eds.), Traumatic stress: The effects of overwhelming experience on mind, body and society (pp. 359–377). New York: Guilford Press. Abrams, R. C. , Rosendahl, E. , Card, C. , & Alexopoulos, G. S. (1994).

Personalitydisorder correlates of late and early onsetdepression. Journal of the American Geriatrics Society, 42, 727–731. Adams, W. L. , Garry, P. J. , Rhyne, R. , Hunt, W. C. , & Goodwin, J. S. (1990). Alcohol intake in the healthy elderly. Changes with age in a cross-sectional and longitudinal study. Journal of the American Geriatrics Society, 38, 211–216. Aevarsson, O. , & Skoog, I. (1996). A population-based study on the incidence of dementia disorders between 85 and 88 years of age. Journal of the American Geriatrics Society, 44, 1455–1460. Aiken, L. (1990). Chronic mental illness. In B. S. Fogel, A. Furino, & G.

Gottlieb (Eds.), Mentalhealthpolicy for older Americans: Protecting minds at risk. Washington, DC: American Psychiatric Press. Albert, M. S. , Jones, K. , Savage, C. R. , Berkman, L. , Seeman, T. , Blazer, D. , & Rowe, J. W. (1995). Predictors of cognitive change in older persons: MacArthur studies of successful aging. Psychologyand Aging, 10, 578–589. Alexopoulos, G. S. (1997, November 6). Epidemiology, nosology and treatment of geriatric depression. Paper presented at Exploring Opportunities to Advance Mental Health Care for an Aging Population, meeting sponsored by the John A. Hartford Foundation, Rockville, MD.