ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is the most common form of dementia in North America and currently afflicts more than four million people. Studies estimate that as many as five to ten percent of adults over the age of 65 will be affected. Over age 80 this figure can rise to one in three. Given the change in our population demographics towards longer life spans, this represents an enormous future burden. Alzheimer's disease follows heart disease, cancer and stroke as the fourth most common cause of death.

Alzheimer's is a Neurodegenerative disease with progressive deterioration of memory, comprehension, intellectual function and behavior. It may have a subtle onset with a slow progression over twenty years or the patient may deteriorate rapidly with a devastating decline in mental capacity over a short period of time. The average duration is about seven years.

Not to be confused with the simple forgetfulness of normal aging, Alzheimer's leads to significant memory lapses, dramatic mood changes, emotional outbursts, childish behavior, inability to retain new information and general confusion or disorientation, particularly at night. Health and abilities decline until one is unable to care for oneself and eventually dies.

CAUSES

Alzheimer's disease is characterized by a degeneration of brain nerve cells and a shrinkage of brain mass. Although its exact cause has yet to be determined, certain changes in the brain have been well identified. Patients have decreased or altered levels of certain neurotransmitters such as ACh and GABA, which relay messages from neuron to neuron. Two other striking features or neurofibrillary tangles and neural plaque formation.

Several theories attempt to explain these changes. Alzheimer's was once thought to be a variant of the normal aging process. It used to be called 'senile dementia'. It is now clear that Alzheimer's is an abnormal condition but that a number of factors may at least delay or slow its progression. Recent research has identified a blood protein called ApoE which appears to be altered in Alzheimer's patients and leads to nerve cell damage. Other studies point towards the interaction of this protein with heavy metals such as aluminum and mercury, and other elements such as iron, zinc and calcium, leading to plaque formation. A strong argument has been made for the role of oxidative stress and free radical formation in promoting the damage in these tissues.

GSH AND ALZHEIMER'S DISEASE

How and where does GSH fit into this picture? If heavy metals are involved in the progression of Alzheimer's, GSH can play a critical role in their elimination and detoxification. Certain studies have demonstrated that when aluminum is 'pulled' out of the cells using chelators, the symptoms of Alzheimer's can be reduced or delayed. As we outlined in Chapter 2 one of our primary defenses against these toxins is an adequate GSH enzyme system. And as researchers further define how free radicals contribute to

brain cell destruction, the role of GSH as the primary intracellular antioxidant will come to the forefront.

Much research has been focused on the role of antioxidants in alleviating Alzheimer's symptoms and its progression, especially vitamin E because of its availability and low price. But as we saw in Chapter 1 the interaction of these antioxidants is complex. Many are dependent on adequate GSH levels for their proper functioning. A large number of post-mortem studies have compared normal with diseased brain tissue. They reveal significant changes in GSH and GSH peroxidase levels as well as elevated levels of the powerful oxidant lipid peroxide, against which GSH is a primary defense. Fibroblast cells cultured from brain tissue affected by Alzheimer's disease are more sensitive to damage by free radicals than normal tissue. The sites of this increased vulnerability likely occur at the mitochondrial level. Adams and his research team found GSH levels diminished in the area of the brain involved in short-term memory (hippocampus). Jenner and his co-workers found a similar decrease in the areas of the brain involved in higher intellectual functioning (the cerebral cortex).

Although Alzheimer's disease is certainly a multifactorial problem, certain aspects must be emphasized. It is unclear whether oxidative damage is the cause or just an effect of Alzheimer's. However, there is no doubt that diminished oxidative stress can retard or diminish disease progression. In addition, the part apparently played by toxins such as heavy metal needs to be addressed. In either case, elevated GSH levels can be a critical strategy against both of these dangers.

CASE STUDY

Despite excellent care at home, Max eventually had to be institutionalized for his Alzheimer's disease. His 78 year-old wife's arthritis and heart disease left her unable to give him the high-maintenance care he needed. Previously a gregarious salesman who loved to tell a joke, in his present condition he was even unaware of who was in the room. His previous history of smoking one to two packs a day left him with chronic bronchitis, requiring frequent inhalation therapy. To treat his ever-thickening secretions, the respiratory therapist started using Mucomyst (N-acetylcysteine – a GSH-promoting drug). After several weeks on the Mucomyst, Max began to smile when his wife entered his room and was visibly pleased by her visits.

CONCLUSION

In Alzheimer's disease certain proteins seem to react with heavy metals and other elements, leading to plaque formation. Oxidative stress and free radical formation definitely play a role in promoting this damage. When heavy metals are removed by chelators, the symptoms of Alzheimer's can be reduced or delayed.

It is unclear whether oxidative damage is the cause or just an effect of Alzheimer's. Nevertheless, antioxidants such as vitamin E may be useful. Their antioxidant function is maximized by maintaining adequate GSH levels. By diminishing oxidative stress disease the progression of this disease can be retarded or diminished.

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