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BIOLOGICAL, SOCIOLOGICAL, AND ECONOMIC PROBLEMS OF ALZHEIMER'S DISEASE

An Interactive Qualifying Project Report

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by

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ABSTRACT

The purpose of this Interactive Qualifying Project was to investigate the social, economic, and psychological impact of an important human disease on society. Alzheimer's disease was chosen for the investigation due to its costly impact on affected individuals and their families, and because of the devastation caused by slowly and helplessly watching a family member lose ones memory, and eventually one's entire mind. We conclude from our report that new modes of treatment and the design of special Alzheimer's day care centers can greatly reduce the psychological and economic cost of this disease.

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EXECUTIVE SUMMARY

Alzheimer's Disease (AD) is an ever-present problem in today's society among people above the age of sixty-five. Approximately four million people in the United States have developed the disease, and the number is continually growing. Alzheimer's has drastic effects on the people who suffer from it, ranging from forgetfulness to incapacitation. The disease also places significant stress on the patient's families, including serious financial and time constraints. As a result of its' impact on society, researchers are investigating causes and potential cures for this problematic disease.

The biological aspects of AD are very significant because they provide information on how the disease works. Hallmarks of the disease include amyloid plaques, neurofibrillary tangles and mutations in certain genes including apolipoprotein E4, presenilin1, presenilin 2 and amyloid prescursor protein. Knowledge of these hallmarks provides scientists with targets for a cure in order to help the millions of people that are now suffering from Alzheimer's disease.

Two important areas of research that are currently of interest to scientists are the production of plaques and tangles, and the role of enzymes in the disease. If scientists can minimize plaques and tangles in some way, a lessening of their effects on the human brain or a cure for the disease may result. Scientists are also looking for an enzyme that may cause the disease or that may play an important role in the development of amyloid plaques and neurofibrillary tangles. These two areas of research may lead to a cure of the disease.

The treatment of Alzheimer's Disease in the United States today costs about $100 billion dollars per year. Therefore, economists are searching for ways to alleviate the costs of caring for AD patients. One possibility is the use of new drugs to delay the onset of later stages of the illness. This, in turn, can delay placement of the patient in a nursing home, reducing annual costs. Another possibility is to use assisted living facilities instead of nursing homes. This also reduces the annual cost of caring for AD patients.

Special care units play an important role in caring for patients with Alzheimer's Disease. These units, when designed properly, can alleviate many of the problems that Alzheimer's patients face. They affect the safety, comfort and mental stimulation of patients, therefore providing the patients with optimal care. Landmarks, lighting, and floors must be carefully planned when designing such a special care unit.

This Interactive Qualifying Project investigated the biological, economic, and psychological impact of AD on society. Through research, many current and innovative ideas were found that will improve the devastating burden of the disease. Conclusions came about as a result of this research. These conclusions include preventative measures, treatments, and specialized care options that we believe are most beneficial to patients, caregivers and society.

PROJECT OBJECTIVE

The purpose of this Interactive Qualifying Project was to investigate the social, economic, and psychological impact of an important human disease on society. Alzheimer's disease was chosen for the investigation due to it's costly impact on affected individuals and their families, and because of the devastation caused by slowly and helplessly watching a family member lose ones memory, and eventually one's entire mind.

Initial research focused on the biology of the disease, explaining in layman's terms our current understanding of the role of amyloid plaques and neurofibillary tangles in causing this neurodegenerative disorder. Current treatments, as well as treatments on the biological research frontier were also discussed. Economic, social, and psychological impacts of the disease on society were topics of individual sections of the report. Then, in view of those negative impacts on society, the design of a new type of treatment center was discussed. Finally, based on all of the above information, conclusions and recommendations were provided.

INTRODUCTION

Alzheimer's Disease (AD) is an ever-present problem in today's society among people above the age of sixty-five. Approximately four million people in the United States have developed the disease, making it the fourth leading cause of death among adults. A typical life expectancy for a person with Alzheimer's Disease is about eight to ten years after symptoms appear.

Alzheimer's has drastic effects on the people who suffer from it, ranging from forgetfulness to incapacitation. It is a degenerative disease so the symptoms become far more serious over time. Biological aspects of AD provide scientists with targets for a cure in order to help the millions of people that are now suffering from the disease. Two important areas of research that are of interest to scientists are – the production of plaques and tangles, and the role of enzymes in the disease.

Alzheimer's Disease also places significant stress on the patient's families, including serious financial and time constraints. The treatment of Alzheimer's Disease in the United States today costs about $100 billion dollars per year. As a result, economists are searching for ways to alleviate the costs of caring for AD patients.

This project seeks to discuss new ways to minimize the devastating social and economic burden of this disease.

CHAPTER 1: ALZHEIMER'S DISEASE – BIOLOGY

Alzheimer's Disease is an ever-present problem in today's society among people above the age of sixty-five. Approximately four million people in the United States have developed the disease, and the number is continually growing. Alzheimer's has drastic effects on the people who suffer from it, ranging from forgetfulness to incapacitation. The disease also places significant stress on the patient's families, including serious financial and time constraints. As a result of its' impact on society, researchers are investigating causes and potential cures for this problematic disease.

The term Alzheimer's Disease originated from a German neurologist named Alois Alzheimer [1864-1915]. In 1906, Dr. Alzheimer performed an autopsy on Auguste D., who died several years after she possessed signs of mental deterioration. Upon completion of his autopsy, Dr. Alzheimer found an unusual clustering of nerve cells in the brain that he termed neurofibrillary tangles. He also saw accumulation of cellular debris around the neurofibrillary tangles that he termed senile plaques. These plaques later became known as amyloid plaques. The findings of Dr. Alzheimer led to today's intensive research concerning the causes, effects and potential cures of the disease.

Nearly one in ten people over the age of sixty-five suffer from AD, affecting approximately four million people in the United States alone. AD is also the fourth leading cause of death among adults, with a typical life expectancy of about eight to ten years after symptoms appear. The beginning stages of AD are responsible for a person's loss of short-term memory and slight disorientation. Alzheimer's Disease is degenerative so the symptoms become far more serious over time. AD patients in the latter years

possess symptoms that may include total disorientation, the inability to remember immediate family, incapacitation, and finally death.

In the past ten to fifteen years there have been remarkable advancements in our understanding of Alzheimer's Disease. Today there is a far greater understanding of the biology of AD and the consequences the disease has on human beings. These biological aspects are very significant because they provide information on how the disease works. This knowledge provides scientists with targets for a cure in order to help the millions of people that are now suffering from Alzheimer's disease.

1.1 The Brain

The biology of the human brain has been extensively studied in order to attain a greater understanding of the processes that it performs and how it performs them. "We now know that Alzheimer's begins in the entorhinal cortex (See Figure 1) and proceeds to the *hippocampus* (C), a waystation important in memory formation. It then gradually spreads to other regions, particularly the *cerebral cortex*"(A) (McNeil, 1998). The cerebral cortex is directly involved with the functions of language and reason; the hippocampus is essential to

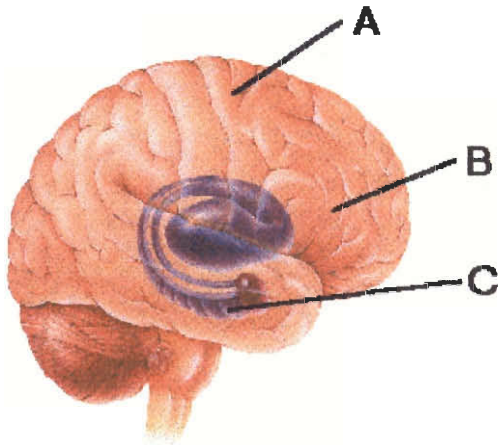

Figure 1: The nerve cells attacked by AD include the cerebral cortex (A), the basal forebrain (B), and the hippocampus (C), all very important in cognitive functions. This figure is from (National Institute on Aging, 1998).

memory storage. All of these processes are altered drastically upon latter stages of Alzheimer's disease, which is why researchers are extensively investigating these areas.

In patients suffering from Alzheimer's Disease the nerve cells or *neurons* within the brain begin to degenerate and lose their connections or *synapses* with other neurons. Neurons then begin to die; thus, there are far less healthy, living neurons in the brain (See Figure 2). This leads to the symptoms that have been described above, ranging from forgetfulness to complete incapacitation. Scientists are performing critical research on the neurons of the brain in order to find a cure for this devastating disease.

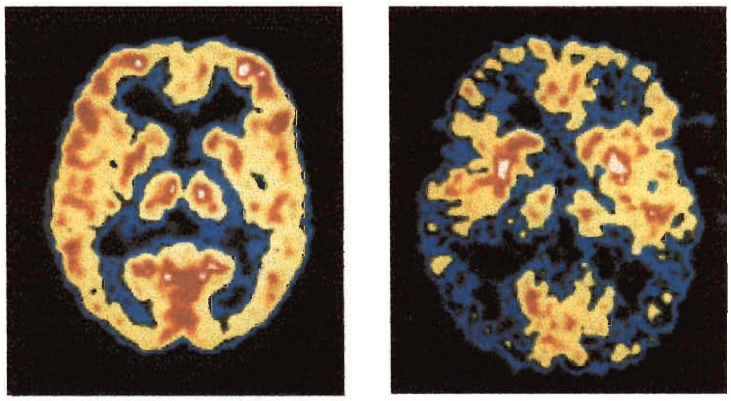

Figure 2: The PET of a normal brain (left) versus that of a brain affected by Alzheimer's (right). The significant decrease in brain activity is clearly depicted by the larger dark area of the affected brain. This figure is from (National Institute on Aging, 1998).

The brain contains billions of neurons or nerve cells, which have a vast number of connections with other neurons. Among these connections there exist chemical messengers, such as neurotransmitters, which establish the communication linkage that is required for one neuron to pass information to another. Neurotransmitters reside at the very end of the branch of the neuron called the axon. The neurotransmitter's function is

to relay the messages between neurons through the minute space called the synapses. In the 1970's, scientists discovered depleted levels of acetylcholine, a key neurotransmitter in Alzheimer's patients. This neurotransmitter is commonly used in memory formation and it is generally found in the hippocampus and cerebral cortex. As a result, research on acetylcholine has become an important part of Alzheimer's Disease research. Scientists have been performing research in order to determine the cause of the drastic decline of acetylcholine in patients suffering from AD, and figure out ways to increase the depleted levels of acetylcholine. There have been two different drugs approved in order to help control the depletion of the acetylcholine, by inhibiting acetylcholinesterase, the enzyme which breaks down acetylcholine. The first medication approved by the Food and Drug Administration was that of tacrine (Cognex), approved in 1993. The second was that of donepezil approved in 1996. Both of these drugs inhibit acetylcholinesterase and will be discussed in more depth in chapter two.

Another important area of research being performed is that of the acetylcholine receptor that binds to the neurotransmitter carrying the message. The receptors are coil-shaped proteins embedded in the neuron, and contain chemical bonds with fats, or phospholipids. In many Alzheimer's cases there exist abnormalities with these fats in the neuron. This is very critical for a couple of reasons. First, the impact that the abnormal fats have on the message being passed; second, there are many different types of receptors for acetylcholine.

1.1.1 *Amyloid Plaques*

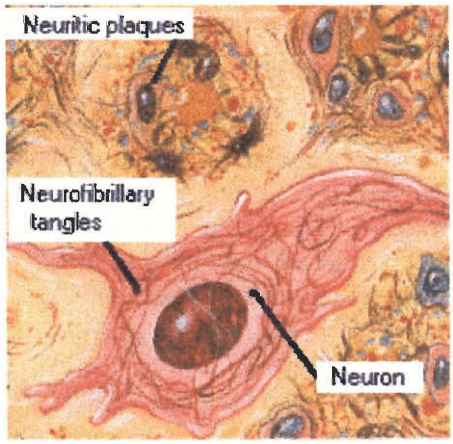

Figure 3: An example of plaques and tangles. This figure is from (National Institute on Aging, 1998).

Since the discovery of Alzheimer's Disease in 1906, beta-amyloid plaques (See Figure 3) have been associated with the disease. To this day it still not understood whether they are a side effect of AD or if they are the cause of AD. Plaques are composed of a protein called beta-amyloid, which is cleaved from a precursor that is normally involved in a cell's metabolism. The precursor is cleaved by gamma secretase during metabolism and the beta-amyloid is produced. The protein forms insoluble aggregates, which bind with the dying neurons and form dense plaques. Researchers have shown that injection of beta-amyloid into a mouse brain caused neurodegeneration. This finding indicates that plaque formation creates the most likely mechanism for losses in memory and other cognitive functions during AD.

Scientists are trying to determine how plaques affect the neurons of the brain. The plaques have been shown to increase transport of a molecule called choline across nerve cells, which is critical in synthesizing acetylcholine. "Many scientists believe that beta-amyloid is toxic to neurons by causing inflammation in the brain or by generating free radicals" (National Institute on Aging, 1998). Although research is constantly being done, beta-amyloid's actual role in Alzheimer's Disease is still not fully understood.

1.1.2 *Neurofibrillary Tangles*

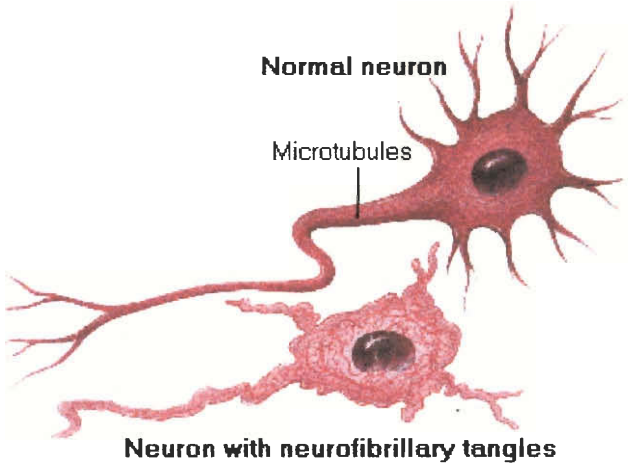

Figure 4: A normal neuron (upper) versus a neuron containing neurofibrillary tangles. The support system for the neuron is gone and the neuron loses its shape and then its activity, leading to its death. This figure is from (National Institute on Aging, 1998).

Neurofibrillary tangles are another hallmark of Alzheimer's Disease. The tangles are abnormal collections of twisted threads found inside cells. They are mainly composed of the protein tau (See Figure 4). In healthy neurons there are *microtubules* that are responsible for guiding nutrients and molecules through the neuron to the axon, and for giving the cell its shape. The tau protein is used to connect the microtubules. In Alzheimer's patients, the tau protein is chemically altered (phosphorylated) and it no longer holds the microtubules together. The collapse of the transport system results in communication loss between nerve cells and eventually neuron death. There is continual research of the neurofibrillary tangles, but today there is a far greater understanding of their makeup and their effect in the brain.

1.2 Alzheimer's Genes

Every healthy person possesses 23 pairs of chromosomes that are found in the nucleus of a cell. Chromosomes are made of genes, which contain all the information needed to carry out life's processes. Genes form the basis of every organism by

controlling the production of proteins in the body. Every human cell contains thousands of genes, which are made of four bases arranged in different sequences. Each of these sequences encodes a different protein. If an error is found within the sequence, it can result in the production of a faulty protein, which can lead to cell malfunction. These mutations have been found to play an important role in Alzheimer's Disease.

There are two types of Alzheimer's Disease - Familial Alzheimer's Disease and Sporadic Alzheimer's Disease. Sporadic AD has no inheritance pattern and progresses slowly. This type of AD is termed late-onset because it generally affects people 65 years of age and older. The gene "Apolipoprotein E epsilon-4" increases the risk of late-onset AD. Familial AD (FAD) is inherited and progresses faster than sporadic AD. This rare form of AD is classified as early-onset because it affects people between the ages of thirty and sixty (The National Institute on Aging, 1998). Many cases of FAD are caused by defects located in three genes—chromosome 21, chromosome 14 and chromosome 1. If a person inherits any of these genes, he or she is seventy to eighty percent likely to develop FAD (Das and Lal, 1997). As a result of these findings, researchers believe genes play a very important role in AD. One significant finding is that all of the Alzheimer's genes discovered to date increase the rate of beta amyloid formation, each by a separate mechanism.

1.2.1 Amyloid Precursor Protein

For example, for those Alzheimer's mutations mapped to chromosome 21 all are found in the amyloid gene, some to the left (Swedish) and others to the right (Indiana, London, Baltimore pedigrees) of the secretase cleavage sites, accelerating its formation. Perhaps these mutations alter the sequence of the amyloid protein to accelerate its processing, or to allow gamma secretase to now nick it.

1.2.2 Presenilin 1

The defected gene located on chromosome 14 that causes early-onset AD is called Presenilin 1 (PS1). The PS1 gene codes for a protein that is found in the membrane of a cell (See Figure 5). Therefore, PS1 interacts with other proteins, including amyloid precursor protein, apolipoprotein epsilon4, and tau (Das and Lal, 1997).

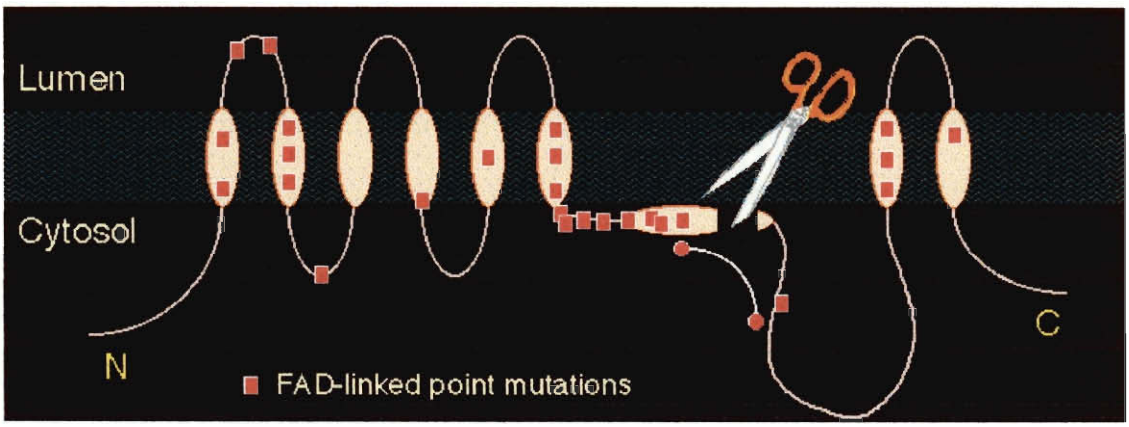

Figure 5: The Familial Alzheimer's Disease mutations can be clearly seen throughout the Presenilin 1 protein. This figure is from (Thinakaran, 1996).

There are a few theorized functions of Presenilin 1. One states that PS1 plays a role in the packing and moving of amyloid precursor protein (APP) through the cell. Mutations in PS1 change the way cells handle APP. Usually, when APP folds inappropriately, it is destroyed by the cell. However, mutated PS1 is hypothesized to allow accumulation of the misfolded APP, keeping it in a spot where it can be cleaved to beta amyloid (BA) fragments. These BA fragments are of varying lengths, the most important one being BA4 because it plays a very important role in the formation of plaques that are crucial in AD (Das and Lal, 1997).

Scientists also found that Presenilin 1 binds two proteins that are part of the *cytoskeleton*, or skeletal support for cells. The mutated PS1 protein causes alterations in the proteins of the cytoskeleton, which results in abnormality of the neuron. AD patients possess these two-cytoskeletal proteins in their plaques and tangles (McNeil, 1998).

1.2.3 Presenilin 2

The gene irregularity on chromosome 1 that causes early-onset AD is called presenilin 2. This PS2 gene codes for a membrane protein of a cell. PS1 and PS2 are sixty-seven percent similar, so they are believed to

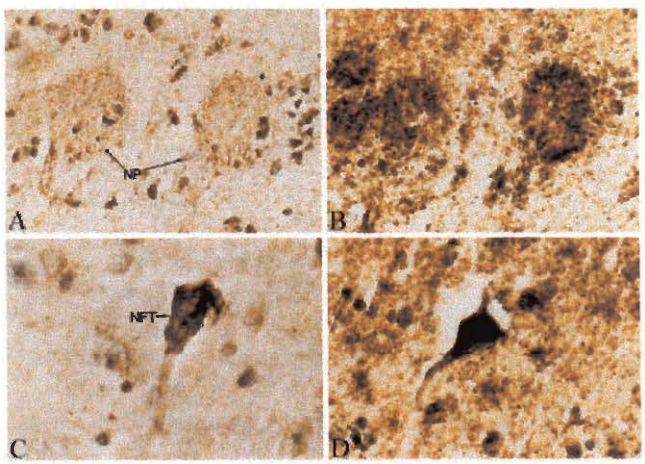

Figure 6: Presenilin 1 and Presenilin 2 seem to help in the formation of plaques and tangles. Both PS1 and PS2 are found in plaques (A and B) and tangles (C and D). This figure is from (Roses, 1997).

have resembling functions. The mutant PS2 gene, like the mutated PS1 gene, increases generation of beta amyloid 4. The defected PS2 protein also cleaves at a different area than the normal PS2 protein, which seems to kill cells. This process is called programmed cell death and results in the onset of Alzheimer's Disease (Das and Lal, 1997).

1.2.4 Apolipoprotein E4

Researchers noticed that several members of the same family developed late-onset Alzheimer's Disease. Therefore, they searched for a common mutant gene in all the family members. They found the common link to be apolipoprotein E, which is a gene found on chromosome 19. As a result of more research, it is now known that ApoE has three *alleles* – apoE2, apoE3, and apoE4. An *allele* is two or more forms of the same gene. ApoE3 is the most common allele of apolipoprotein E, followed by apoE4 and apoE2. Patients who have two apoE4 genes increase the risk of late-onset AD by at least eight fold. People who inherit two apoE3 genes are less likely to develop late-onset AD, while people with two apoE2 genes are much less likely to develop the disease. As a result, apoE4 has been termed a risk factor gene for Alzheimer's Disease.

There are a few hypothetical functions for apoE4, one being its interaction with beta amyloid and tau (See Figure 7). According to this hypothesis, ApoE4 binds very quickly and firmly to beta amyloid. When it secures itself to the amyloid, it becomes insoluble. This results in the production of amyloid plaques. ApoE has also been shown to interact with the tau protein. Because tau steadies the microtubule structure of the

brain, if apoE4 interacts with the structure, the structure may disintegrate causing neurofibrillary tangles.

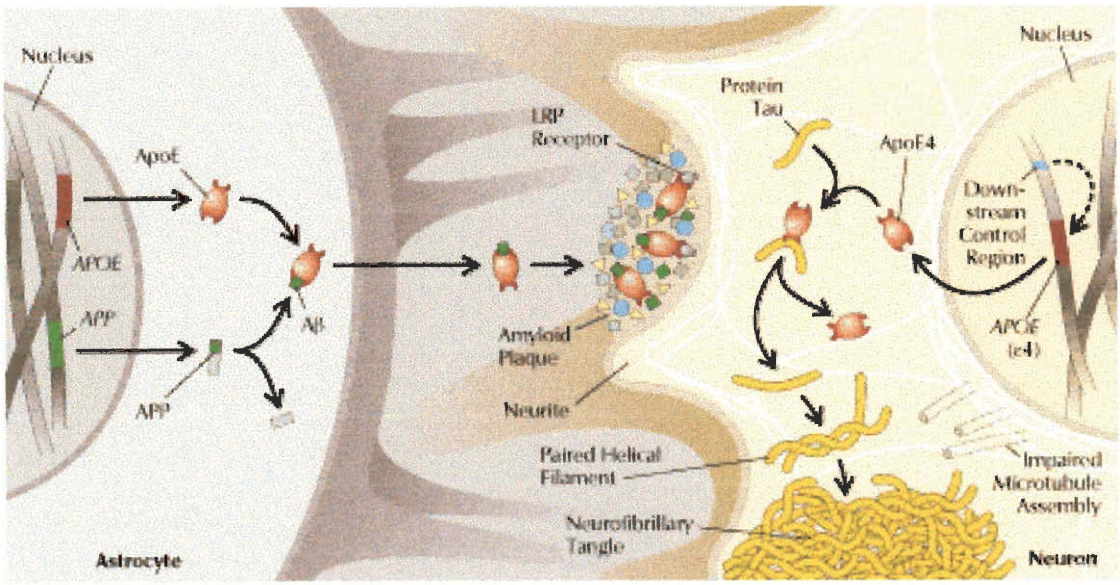

Figure 7: Apolipoprotein e4 seems to interact with beta amyloid and tau, causing plaques and tangles to develop. This process is shown here. This figure is from (Roses, 1997).

Another function of apoE4 is its effect on *dendrites* – neuron branches that receive messages from other neurons. Some researchers presume that the dendrites are shorter in AD patients as a result of some interaction with ApoE4 (McNeil, 1998).

1.2.5 Other Genes

Currently, scientists are searching for other genes that may play a role in the onset of early-onset or late on-set Alzheimer's Disease. One possible gene lies on chromosome 12 (Roses, 1997). As of yet, the gene has not been identified but researchers are narrowing down its location. Gene research is a continuing importance to our

understanding of Alzheimer's Disease. Without knowledge of the causes of Alzheimer's disease, there is little hope in finding a cure.

CHAPTER 2: ALZHEIMER'S DISEASE – CURRENT AREAS OF RESEARCH

A significant amount of research includes finding what causes the plaques and tangles in the brain, and in turn what effects these plaques and tangles have on the body. This has provided a great deal of interest to many researchers because these plaques and tangles have been a trademark of the disease from its earliest discoveries.

The beta-amyloid plaques and neurofibrillary tangles can be seen in every Alzheimer's patient. Today there is a fairly good understanding of what causes both the plaques and tangles. However, why they form and the mechanism in which it happens is unknown. With a more intimate knowledge of these two aspects, a solution to end the production of the plaques and tangles will be much more feasible and practical. With this knowledge scientists are much more likely to be able to remove or decrease the aggregation of the beta-amyloid plaques, which may in turn have a cascade effect on the rest of the disease. In many cases the altering of one step in a multi-step process can alter the way in which all the other processes work. If the scientists can alter beta-amyloid plaques in some way, a lessening of their effects on the human brain or a cure for the disease may result. This has been a highly favorable area of research due to the significant knowledge that is already present and the ability to understand and control the genetic factors that contribute to these plaques.

Another area that has been under scrupulous research is that of the enzymes, and enzymatic reactions that take place within the brain. Many of these enzymatic reactions involve that of proteins, which have been determined to play significant roles in the brain

and Alzheimer's Disease. Scientists are looking for either a particular enzyme(s) that may cause the disease, or an enzyme that plays an important role in the development of amyloid plaques and neurofibrillary tangles. With knowledge of the particular enzyme scientists can then begin working on finding an inhibitor for that enzyme. These two areas are of research are of great interest to researchers and as of this past summer the most significant accomplishment with Alzheimer's Disease yet was uncovered.

2.1 Transgenic AD Mice

Transgenic mice have recently proved useful in AD research. Mouse models have provided a great deal of information on brain inflammation, called activated microglia, and the possibilities of potential therapy with anti-inflammatory drugs. Transgenic mice have provided researchers with nearly all the knowledge known about AD today, and have allowed them to concentrate on specific areas to find a cure or vaccine.

Once specific genes related to AD had been identified, a race was on to insert those human genes into mice to try to create transgenic mouse models for the disease. If successful, such models would mimic portions of the disease enabling new experimental therapies to be tested on the mice that could not be tried in humans. Such mice would also enable us to understand more about the mechanisms of the disease.

Scientists first focused on using the human APP gene for insertion. Several such mice were initially made, but disappointingly none of them displayed any hallmark of the disease. These mice showed that merely giving mice (who already have their own amyloid) additional human amyloid does not initiate the disease. But in 1995 the world's

first partially successful model was created by a team of scientists that included WPI's Professor Adams (Games et al., 1995). This animal was given a mutated version of the APP gene (Indiana mutation) that causes an early onset in AD in humans. Unlike the previous models, this model not only showed signs of the neurodegeneration, it also showed signs of learning deficits (Nalbantoglu et al., 1997). Although this mouse was not a perfect model, and did not show full signs of the disease, it did prove that amyloid deposition was necessary and sufficient for initiating the disease.

This past summer the first Alzheimer's vaccine was synthesized (Schenck et al., 1999). The vaccine is a beta-amyloid vaccine, which has been found to have astonishing results with mice. Mice were injected with beta amyloid conjugated to an adjuvant. Over several weeks, this process induced the formation of beta amyloid antibodies in the blood. These antibodies bond to the protein fragments that form the plaques in the brain preventing plaque formation and no neural damage was found in the mice previously genetically modified to develop an Alzheimer's-like condition (Games et al., 1995). The vaccine worked to either clear out pre-formed plaques, or to prevent their appearance in the first place. There are still a great deal of questions concerning the vaccine's mechanism of action. It is not understood whether the vaccine just prevents plaque formation or whether it actually cures the disease and prevents the deaths of the neurons within the brain. The results may not be completely applicable to humans since unlike humans, these mice do not develop tangles within the brain and they also do not show significant neurodegeneration. Nevertheless, this development has provided many people with feeling of hope and exhilaration of what is to come in the future for the treatment of Alzheimer's Disease.

2.2 Current Alzheimer's Disease Therapies

There are a significant number of proposed and active therapies that are being investigated and used with patients today. These therapies have been found to alleviate the degenerative effects of the disease for short periods of time, and prolong the patient's normal brain activity longer than untreated patients do. Many of these therapies are not effective for periods longer than two years, and also possess a wide array of side effects.

2.2.1 Proposed Therapies-Calcium Regulators

There have been many studies done that indicate that a significant rise in the level of calcium within neurons is the final contributor to neuron death in Alzheimer's Patients. Calcium is critical within the body and within the neuron; it is involved in muscle contraction and transmittance of signals. Neurons and other cells within the body possess mechanisms of regulating the amounts of intracellular calcium through calcium channels, which is critical to cellular life. It has been shown that in AD patients there exists an excess amount of calcium within the cells, which is a key candidate as to what is actually causing the death of the neurons.

This information had led scientists to come up with two therapeutic approaches. One area is that of decreasing the number of active calcium import channels, with calcium channel blockers. This goal has proven to be a very complex task because calcium exchange within the cells occurs through various channels. In order for researchers to lower the levels of calcium they must first determine the correct channels

to block in order to block calcium from entering the cell rather than exiting the cell. Several channel blockers are currently being tested on Alzheimer's patients including Tacrine and Donepezil. The other area of research is that of determining if the calcium pumps within the cells are defective, and if so to rehabilitate or synthesize artificial calcium pumps.

2.2.2 Nonsteroidal Anti-inflammatory Drugs

Several studies have shown the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with a lower incidence of onset of Alzheimer's Disease. NSAIDs have also been demonstrated to reduce the rate of cognitive decline in patients who already suffer from the disease. Anti-inflammatory drugs target cytooxygenases (COX) I and II. Cox II is present in neurons and is significantly decreased in AD, presumably due to neuron loss. The NSAIDs have been found to increase COX II and may also help to regenerate the dead neurons. There is one particular NSAID being used today, prednisone, which is being tested to see if it can slow the progress of Alzheimer's Disease while it is still in its early stages (National Institute on Aging, 1999).

2.2.3 Neurotrophic Factors

Neurotrophic Factors are essential in the maintenance and development of neurons. One of the most common neurotrophic factor is nerve growth factor (NGF). NGFs have the ability to regenerate injured neurons and they also promote the growth of

both axons and dendrites, responsible for communication. Many researchers have investigated NGFs with mice and have had compelling results with the treatments. After the injections of the nerve growth factors, older mice were found to be able to navigate a maze quicker (National Institute on Aging, 1999). Scientists now believe that since NGFs (and others) have the ability to regenerate injured neurons, then by simply increasing the NGFs in the brain there should be an increase in the functional neurons and thus an increase in cognitive function.

There have been a few problems with this idea; the main problem is that the NGFs are site sensitive, meaning they have to be sent to the exact area of nerodegeneration. Another problem researcher's encountered is getting the NGFs into the brain itself. The brain possesses what is called a blood-brain barrier, which is the brain's defense against possible toxins. The barrier will not allow any unfamiliar chemicals or substances (including therapeutics) to enter the brain. Enzymes have been found that bind only to particular substances and shuttle them to the brain. Researchers are working on a finding a safe and effective way to use these enzymes as carriers to deliver the NGFs to the brain. This difficult endeavor may eventually be a very practical way to treat Alzheimer's patients.

2.2.4 Hormone Replacement

Studies have also been conducted on women after menopause that have taken estrogen replacement, with significant findings. Women who have taken estrogen replacement after menopause are nearly fifty percent less likely to acquire Alzheimer's

Disease (McBee, 1997). Estrogen receptors and nerve growth factors have been found on cholinergic neurons, which are the neurons most affected by the disease. It has been proposed that in AD the interaction between the NGF and estrogen receptors is somehow being disrupted and thus causing the neuron death, but researchers are not sure what the significance of taking estrogen replacement after menopause is. There are a great number of studies presently underway to determine if estrogen replacement reduces the risk of attaining AD in women.

2.2.5 Cholinergic Replacement

Cholinergic Replacement Therapy is based on the knowledge that Alzheimer's Disease is marked by the loss of cholinergic neurons that produce acetylcholine, which is very important in cognitive functioning. Many researchers have taken that idea and have developed chemicals that inhibit acetylcholinesterase, the enzyme that breaks down acetylcholine. The hope is that this will slow the breakdown of acetylcholine and the effects of AD would not be felt as strongly or as quickly. This is one such area of research that has produced numerous drugs that are currently on the market. Examples of these drugs are tacrine and donepezil. They both slow the rate of cognitive decline and are used to treat patients with mild and moderate AD. The problem to date with these drugs is that they have not been found to be effective longer than two years, and the side effects though not great can be very uncomfortable.

2.2.6 Therapy- Most Promising

The area of neurotrophic factors is one of the most promising areas of research concerning a cure for this disease. Many of the therapies described above have been, and will probably continue to alleviate symptoms of Alzheimer's Disease. Nerve growth factor and other NTFs have shown remarkable results within mice. Upon attaining a greater understanding of exactly how NTFs work and their ability to regenerate neurons, axons and dendrites, one can only see this as being the most promising area for treatment.

Alzheimer's Disease affects our entire society in one-way or another. Nearly seventy percent of Alzheimer's Disease patients live at home even though to be highly dependent of care from others. The remaining thirty percent live in nursing homes, or government funded housing. This dependence on others is extremely time consuming, stressful and financially demanding on their caretakers. The average lifetime cost per patient is about one hundred seventy-four thousand dollars. This is one reason why it is so devastating to the families of the loved one's who are suffering from the disease. Alzheimer's is one of the most expensive, destructive and devastating diseases, and until a cure is found, humanity has got to determine a better way to care for these patients.

CHAPTER 3: ALZHEIMER'S DISEASE – ECONOMICS

Approximately four million people in the United States suffer from Alzheimer's Disease today with this number increasing to nine million by 2040. As this number increases, so will the cost of caring for AD patients. The treatment of Alzheimer's Disease in the United States today costs about $100 billion dollars per year. This amount includes direct costs and indirect costs. Table 1 lists these costs.

Direct Medical Costs	Direct Nonmedical Costs	Indirect Costs
Medications, monitoring, diagnostic tests, physician visits, nursing homes, hospitalization, mental health, respite care	Daycare, social services, ancillary equipment, home health services	Loss of productivity

Table 1: Direct and Indirect Costs for Patients with Alzheimer's Disease. This table was taken from Schumock, 1998.

Economists are searching for ways to alleviate the costs of caring for AD patients. One possibility is the use of new drugs to delay the onset of later stages of the illness. This, in turn, can delay placement of the patient in a nursing home, reducing annual costs.

Another possibility is to use assisted living facilities instead of nursing homes. This also reduces the annual cost of caring for AD patients.

3.1 The Cost of Care

Patients who are diagnosed with AD live in the community for an average of 2.58 years before their condition deteriorates enough for them to enter a nursing home. 69% enter a nursing home, while 31% remain in the community. Both groups live an additional average of 2.72 years. An important economic factor is the patient's stage of AD. In the mild stage, patients can be cared for at home and most of the costs are indirect. In later stages, patients are institutionalized and most costs are direct. Table 2 shows the cost of various care routes for patients in different stages of the disease.

Care Setting, Cost ($)	Alzheimer's Disease Stage			
	Mild	Moderate	Severe	All
Community Care				
Managed Care	4,836	6,444	16,020	7,284
Academic medical center	7,008	11,064	11,520	8,868
Residential Care				
Assisted living facility	31,344	29,172	33,216	31,308
Nursing home	41,832	41,964	42,684	42,336

Table 2: The annual cost of care (in 1996 dollars) by AD stage and care setting. This table was taken from Fillit, 1999.

3.1.1 The Medicare Alzheimer's Disease Study

Medicare is the nation's largest health insurance program for people over the age of 65. This program covers about 39 million Americans. Many middle class families

turn to Medicare for support in paying the costly nursing home bills. The rate of enrollment in Medicare is increasing rapidly – about 13% of the Medicare population is enrolled in managed care. Studies have shown that the cost of caring for demented patients is about twice as high as the cost of caring for an average Medicare patient. Each Alzheimer's patient costs Medicare about $6208 per year, which is about $517 per month.

In the Medicare study, there were two case management models - Model A and Model B. Model A had a manager-to-client ratio of 1:100, and reimbursements from $290 to $489 per month per patient. Model B had a client-to-manager ratio of 1:30, and reimbursements from $430 to $699 per month per patient. Enrollment in the study was voluntary. Applicants had to be diagnosed with irreversible dementia, had to be eligible for enrollment in both parts A and B of Medicare, and had to live in the area where the study was being held (Newcomer et al., 1999).

The study began in December of 1989 and ran until November 31, 1994. The applicants were randomly placed in the demonstration group or in the control group. Applicants in the demonstration group could use case management and service coverage, while applicants in the control group continued to use their usual care. Community services that the control group could choose from were chore, personal care, companion and adult day care.

The economists performing the study had three hypotheses. 1) Treatment participants would be more inclined to use more services relative to those in the control group; 2) use of services would be higher in the demonstration group than in the control group; and 3) participants in the Model B program would use more services than those in the Model A group (Newcomer, 1999).

The results of the study support Medicare's hypotheses. At the time the study began, one fifth of the clients in the demonstration and control groups were using core services. During the first twelve months, the amount of clients in both the demonstration and control groups who used core services increased rapidly. The demonstration group's use more than doubled (200%), while the control group's use increased by 50%. Prior to the study, similar amounts of people used day care services. The same increase in use was found in the core services and daycare services. This pattern shows that the demonstration group was 1.7 to 2.3 times more likely than the control group to use one of the services provided by the study. The demonstration group was also 2.8 times more likely than the control group to use adult day care (Newcomer et al., 1999).

In conclusion, both the control group and the demonstration group used different levels of services. The demonstration group used fund reimbursement instead of private payments for care, instead of using fund reimbursement as a supplement to private payments. Also, the demonstration group in Model B seemed to have no advantage over the demonstration group in Model A, even though Model B received greater reimbursements. This showed that the same level of care could be achieved with less reimbursements (Newcomer et al., 1999).

3.2 Costs of Drugs

Drugs, such as Donepezil and Tacrine, improve cognitive function while providing economic relief for patients suffering from Alzheimer's Disease. Both Donepezil and Tacrine are acetylcholinesterase inhibitors used to treat patients with mild

and moderate Alzheimer's Disease. They have similarities and differences which can be seen in Table 3.

Feature	Donepezil	Tacrine
Drug Class	Piperidine	Aminoacridine
Mechanism of action	AchE inhibitor	AchE inhibitor
Pharmcokinetics		
t_{max} (hours)	~ 4	1.3 – 2.0
$T_{1/2}\beta$ (hours)	70-80	2.9-3.6
Dosage and Interaction		
Recommended dosage (mg/day)	5 or 10	40-160
Route of adminisistration	Oral	Oral
Frequency	Once Daily	Four times daily

$T_{1/2}\beta$=elimination half-life
AchE=acetylcholinesterase
t_{max}=time to reach peak plasma concentration

Table 3: Similarities and differences between donepezil and tacrine. This table was taken from Drug and Therapy Perspectives, 1998.

Both drugs slow the rate of cognitive decline, which delays placement of the AD patient in a nursing home. This delay saves thousands of dollars in care-giving costs.

3.2.1 Donepezil

Donepezil is an acetylcholinesterase inhibitor used to treat Alzheimer's Disease. It has a half-life of 70 to 80 hours; therefore, one daily dose is effective. Donepezil improves cognitive function in AD patients with mild or moderate diagnosis. However, it does not prevent degeneration of the brain. A cost-effectiveness analysis (CEA) was performed to justify the cost of this drug in relation to treating mild and moderate AD

patients (Donepezil: A Step Forward Compared with Tacrine for Alzheimer's Disease, 1998). In the study, patients were classified to be within three stages of the disease: mild, moderate or severe. They were also divided by where they lived, either in the community or in a nursing home. Patients were divided into their respective groups and were checked on periodically to see if they needed to be moved to a disease stage and setting combination (Neumann et al., 1999).

The effects of donepezil were measured by analyzing data from a 24-week study that examined the results of five and ten milligram doses of donepezil versus a *placebo* (a pill with no effect given to control patients) on mild and moderate AD patients. It was found that the drug delayed cognitive degeneration for an average of 17.8 months. The costs of using the drug include direct and indirect medical costs plus costs for unpaid caregiving. QALYs, which rank life as quality-weighted health states, were also considered when analyzing the data of the dopenezil study. A QALY of zero usually stands for death, while one stands for good health. The results of the study are summarized in the table below (Neumann et al., 1999).

Severity of AD, duration of treatment	Treatment			
	With Donepezil		Without Donepezil	
	Cost ($)	QALYs	Cost ($)	QALYs
Mild				
6 months	22,310	0.310	21,774	0.306
12 months	50,239	0.678	49,750	0.663
18 months	72,487	0.950	72,227	0.923
Threshold analyses (at 24 months)	94,809	1.207	94,883	1.165
Moderate				
6 months	26,849	0.242	26,246	0.241
12 months	59,497	0.518	58,678	0.512
18 months	84,427	0.717	83,585	0.706
Threshold analyses (at 24 months)	108,473	0.900	107,699	0.883

Table 4: This table shows the cost effectiveness of using donepezil to treat patients with mild and moderate AD. This table was taken from Neumann et al., 1999.

3.2.2 Tacrine

Tacrine, like Donepezil, is an acetylcholinesterase inhibitor that is used to treat Alzheimer's Disease. Tacrine has a half-life of 2.9 to 3.6 hours; therefore the drug must be administered 4 times a day. Tacrine improves cognitive function in AD patients with mild or moderate diagnosis. However, it does not prevent degeneration of the brain. A cost analysis of tacrine was performed in caring for patients with AD.

The study began by following the trial of tacrine versus a placebo for 30 weeks in mild and moderate AD patients. The tacrine dose began at 40 mg/day and increased every 4 weeks in 40 mg increments up to a maximum of 160 mg/day.

After two years, patients who took part in the trial were contacted in order to determine if they continued using tacrine, entered a nursing home or died. The patients

who continued use of tacrine were broken into three groups: doses of >120 to ≤160 mg/day, doses of >80 to ≤120 mg/day and doses of ≤80 mg/day. It was found that nursing home placement was much lower for patients in the two higher dose groups than those in the lower dose group. Also, there is a higher probability of death in AD patients in the lower dose group than in the higher dose groups.

Patients who began taking tacrine have several different courses. The 38% of patients that reach a dosage of >120 to ≤160 mg/day delay nursing home placement for an average of 439 days (See Figure 8). The 30% of patients that reach a dosage of >80 to ≤120 mg/day delay nursing home placement for an average of 444 days. The 32% of patients that reach a dosage of ≤80/mg/day receive no benefit in delaying nursing home placement (Henke and Burchmore, 1997).

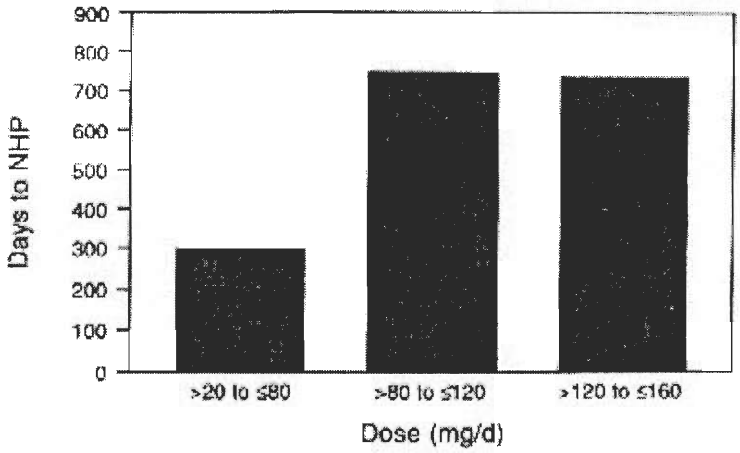

Figure 8: The amount of days from the beginning dose of tacrine to time of nursing home placement. This figure was taken from Henke and Burchmore, 1997.

The total cost for all patients who begin tacrine is $114,548 while the total cost for those who do not take tacrine is $123,798. The use of tacrine saves $9250 per person. These savings come primarily from fewer nursing home costs due to the delay of

placement. Those patients who are able to take a dosage of >120 to ≤160 mg/day or a dosage of >80 to ≤120 mg/day and enter nursing homes have 25% lower lifetime costs. Those patients who take a dosage of ≤80 mg/day have the highest expense of all because they do not save any money on nursing home costs and they have to pay for drug treatment (Henke and Burchmore, 1997).

The economic effects of tacrine on patients with AD can be seen in the following two tables:

Component of Cost	**Patients Starting Tacrine Therapy**	**Patients not Starting Tacrine Therapy**
Total Cost	$114,548*	$123,798
Community Care	$47,411	$45,909
Nursing home care	$64,160	$77,889
Tacrine Acquisition	$2655	-
Tacrine–related doctor visits, monitoring tests, and side-effect treatment	$321	-

* Sum of components does not equal total cost because of rounding.

Table 5: Average cost of caring for Alzheimer's Disease from diagnosis to death. This table was taken from Henke and Burchmore, 1997.

Branch	Cost
Continue tacrine, > 120 to ≤ 160 mg/d, NHP	$108,917
Continue tacrine, > 120 to ≤ 160 mg/d, no NHP	$70,989
Continue tacrine, > 80 to ≤ 120 mg/d, NHP	$108,467
Continue tacrine, > 80 to ≤ 120 mg/d, no NHP	$70,899
Continue tacrine, > 0 to ≤ 80 mg/d, NHP	$149,231
Continue tacrine, > 0 to ≤ 80 mg/d, no NHP	$79,109
Discontinued tacrine, NHP	$146,270
Discontinued tacrine, no NHP	$76,148
No tacrine, NHP	$145,536
No tacrine, no NHP	$75,414

NHP = nursing home placement

Table 6: Shows the lifetime costs of the different options of treatment for AD patients. This table was taken from Henke and Burchmore, 1997.

3.3 The Cost of Caregiving

Most AD patients live in the community and are cared for by a close family member. Caregivers who care for AD patients often experience depression, anger, anxiety and experience a negative attitude towards the patient and other family members. They are forced to give up social time and, in some cases, even their job. All of these effects are referred to as caregiver burden (Newcomer et al., 1999).

3.3.1 The Medicare Study on Caregiver Burden and Depression

The Medicare Alzheimer's Disease Demonstration evaluation provided case management and community care for AD patients and their caregivers. Taking part in the program was voluntary, and the applicants were randomly chosen to be in either the

control group or treatment group. The control group received their usual care while the treatment group was eligible for case management and support services. The study ran from December 1989 to November 31, 1994.

There were two case management models – Model A and Model B. Model A had a case manager to client ratio of 1:100 and had a monthly reimbursement from $290 to $489 per client. Model B had a case manager to client ratio of 1:30 and had a monthly reimbursement from $430 to $699 per client.

Caregivers in the treatment group were given training and education classes on AD through case mangers and support services. The case managers told caregivers about formal services available, coordinated formal help and monitored the quality of service contributed by the formal care providers. The support services contained support groups and caregiver and family counseling. Case management and support services were not included in the monthly expenses of the client. They were included in the administrative budget of the program (Newcomer et al., 1999).

The study monitored both caregiver burden and caregiver depression over a 36-month period. The following conclusions were found. First, the treatment group was six times more likely to have case management exposure and was twenty percent more likely to use community services. These differences did not substantially reduce caregiver burden and depression for the treatment group versus the control group. This can be seen in Table 7.

Mean Scores on the Caregiver Well-Being Outcomes at Each Reassessment Interval				
	Treatment Group		*Control Group*	
Outcome Measure	*N*	*Mean*	*N*	*Mean*
Caregiver Burden*				
Baseline	2728	14.3	2576	14.3
6 months	2268	14.4	2138	14.9
12 months	1702	14.1	1597	14.4
18 months	1437	13.7	1283	14.3
24 months	1528	13.8	1354	14.2
36 months	986	13.7	920	14.2
Caregiver Depression**				
Baseline	2731	4.24	2576	4.21
6 months	2269	4.29	2139	4.48
12 months	1705	4.28	1597	4.42
18 months	1439	4.17	1288	4.53
24 months	1531	4.06	1356	4.36
36 months	988	4.20	922	4.49

* Scores can range from 0 to 32. Higher scores indicate greater caregiver burden
** Scores can range from 0 to 15. Higher scores indicate greater caregiver depression.

Table 7: Mean scores of caregiver burden and depression at baseline and at each reassessment interval. This table was taken from Newcomer et al., 1999.

Second, the monthly reimbursement caps were too low to increase the amount of formal care used by the treatment group compared with the services purchased by the control group. Third, the treatment group and control group used the same types of services throughout the study. If more unique services were made available to the treatment group, there may have been more of a difference in caregiver outcomes. Fourth, all but one of the program sites were staffed by social workers. The one site staffed mostly by nurses had a much greater decrease in caregiver burden and depression probably because nurses were more able to see changes in heath and respond to the changes. From these conclusions, it is clear that more work needs to be done in order to reduce caregiver burden and depression (Newcomer et al., 1999).

CHAPTER 4: ALZHEIMER'S DISEASE - SPECIAL CARE UNITS

Alzheimer's Disease affects the lives of not only the person suffering from the disease but also their families, caregivers, and society. There have been many attempts to alleviate the problems that the disease places on society. These attempts include special care units designed specifically for Alzheimer's patients. Special care units provide a far superior environment for the patients and the patient's family. And such units specializing in day care are less expensive than full time nursing homes.

4.1 Purpose and Goal of Special Care Units

Special care units within nursing homes, group homes, and assisted living facilities, are designed for a wide array of reasons. Some are designed to keep potentially problematic patients away from the rest of the group while others are designed to suit the best interest of the patients suffering from dementia. As a result of research, such facilities have knowledge of the behavior of Alzheimer's Disease patients and work toward a common goal. "The goal of care for people with Alzheimer's disease is to maximize functional independence, effectiveness, freedom and human dignity" (Calkins, 1987). Many great things are lost in patients suffering from AD, but a few of the largest are competence, ability of self-control, and control of the immediate environment.

4.2 Designing Special Care Units

The designing of special care units is directly correlated with Alzheimer's research. The biological understanding of the disease and its symptoms of cognitive memory loss, are what have to be considered when trying to design the ideal environment for people suffering from AD. The special care units have to establish a safe, comfortable, and mentally stimulating environment in order to best suit a patient suffering from dementia. There are a vast number of ways in which these three areas can be fully accounted for.

4.2.1 Safety

The safety of patients suffering from Alzheimer's disease must be thoroughly considered when designing a special care unit. Patients are more susceptible to falling injuries resulting from disorientation or loss of motor skills. They frequently get lost from wandering and are unable to direct themselves back to their proper location. These factors that patients with dementia suffer from have to be carefully considered during the designing process. When designing a safe special care unit appearance, lighting, floors, landmarks and many other features must be carefully planned out.

Appearance is a very big issue that can significantly help a patient move around and alleviate disorientation. "Outlines, contours, shapes, color, contrast and movement must be carefully considered" (Brawley, 1992). Familiar shapes become very important to an Alzheimer's patient when trying to maneuver about. Objects that are familiar to a

patient such as lamps, tables or chairs become markers for movement and allow a patient to move safely. Curves and rounded surfaces are also very critical for maneuvering and preventing injury upon falling. Eliminating all sharp edges and hard objects helps prevent injury in case a patient falls.

Appropriate lighting is another very critical safety issue. Most adult care centers use very bright lighting, even though this is not appropriate for AD patients. The best means of lighting for special care units is that of consistent light sources to eliminate shadows, and task lighting. The lighting should be shielded and provide no glare on any objects. Glare and unshielded lights may disorient people suffering from AD and cause them to loose their balance or even become lost. Patients have been shown to be more comfortable and have a longer attention span with focused lighting and glare reduction. Proper lighting can compensate in many ways for poor vision and disorientation.

The air quality of a facility is very important in that stale air may become poisonous or toxic to elderly, demented patients. The circulation of fresh air and the addition of plants will help provide a safer environment for breathing and may also help the patient's condition. Increased oxygen supply has been found to increase activity and mental function in elderly patients. The addition of proper plants to an environment helps eliminate poisonous toxins and provides better air quality, which is beneficial to the patients of special care units.

AD patients suffer from impaired depth perception, which leads them to see many false illusions. Contrasting floor or wall color must be subtle, in order to alleviate the impression of a depth change. Sharp colorations on a floor may lead to patients thinking there is a step or hole in the floor causing them to fall and injure themselves. There

should also be a sharp color change between the floors and walls of a special care unit to allow the patient to distinguish them. This sharp contrast helps prevent patients from walking into walls. Solid, plush carpeting is one of the best flooring covers that can be used. It completely covers the floor and is soft in case a patient should fall. There are many different considerations when planning a safe special care unit and all must be thought out and planned carefully.

4.2.2 Comfort

Comfort is a critical issue with special care units for a variety of reasons. Patients of special care units are much more likely to be happy and responsive if they are content with their surroundings. Comfort also invokes many other responses that are beneficial for the patients. It will allow them to interact more with other people and thus increase mental stimulations. Patients that are comfortable also tend to be significantly less depressed, which is a major problem in special care units. There are many different issues and control measures that can be applied to special care units in order to attain the most comfortable and safe environment possible.

Hearing loss is a major change associated with increase in age. Background noise of all sorts can be extremely distracting and can inhibit a person with hearing loss from hearing important information. Good acoustics can be a very big issue in a special care unit, in that it creates an environment much more residential-like. It inhibits many sources of noise pollution including the noises from traffic and cleaning equipment. The

decrease in background noise helps reduce agitation with the patients and provides a much more comfortable living environment overall.

There are many texture differences between living in an industrial environment and living in a residential environment. These differences are what make many patients uncomfortable and are almost always overlooked when designing a special care unit. Textures within an environment can provide a patient with a feeling of warmth and can invoke past memories causing patients to feel wanted and happy. "There is some evidence to indicate that textures may stimulate thinking and responsiveness as well as reinforce memories" (Brawley, 1992). There are many different textures that can be applied to a patient's personal space including wall coverings, throw rugs and draperies. Textures such as seat and pillow covers can be mentally stimulating to a patient, and in turn make a significant difference with their outlook on their surroundings.

Comfort is very important in an Alzheimer's patient's living environment. There are an assorted number of contributions that can be made to special care units to invoke that feeling of living at home, and the associated feelings of comfort and satisfaction. These factors have unfortunately been mostly trial and error and therefore there are many special care units that have not incorporated them into special care units. Good acoustics, textures and independent temperature controls for each person's room are things that have been shown to positively influence the mind set of Alzheimer's patients.

4.2.3 Mentally Stimulating

Alzheimer's disease is a degenerative disorder, causing the patient to lose cognitive memory and brain function. This nature of the disease leads to a very serious problem when trying to create a mentally stimulating environment. There are many different approaches to stimulate the mind and invoke brain function. This can be done through patient-to-patient, patient-to-family, and even patient-to-pet interactions. All of these interactions increase brain activity and stimulate a person in a very positive manner. Activities are another great way to stimulate a patient mentally. Whether they are indoor or outdoor, many activities that require thought, movement, and interaction have been shown to be very positive.

Social interaction is also a very important part of the design of a special care unit. Interaction between patients is a key element to a mentally stimulating environment, yet too much interaction may be detrimental. Patients should be allowed private space, whether it be in their own room or rooms in which a patient can sit down in solitude. This becomes a very important aspect of designing a special care unit; because it must be incorporated in bedroom layouts, quiet rooms, social rooms, and even hallway design. The special care unit has to allow and create social interaction, but it also has to allow for a patient's privacy and solitude.

4.3 Complete Special Care Unit

The process of designing the special care units is an ever-changing one. Today's technology has allowed researchers to consistently learn more and more about Alzheimer's disease and the effects it has on the patients. The addition of the newly found knowledge of Alzheimer's helps designers make corrections and additions to the special care units in order to best suit the patients. There are a great deal of factors that contribute to the design of the special care units, including the few mentioned above. There are other factors that contribute to having the best living environment possible; one of the largest is having the medical staff trained according to the needs of demented patients. These patients possess a totally different type of care than many other patients in adult care centers. Alzheimer's patients require a great deal more patience and understanding, due to their inability to perform normal activities.

The correlation of safety, comfort and mental stimulation need to be considered when designing a special care unit. Special care units when designed properly can alleviate and/or terminate many of the problems that have been mentioned with each group. Special care units help caregivers save money and time and help patients live in an environment that is comfortable and safe while they receive the best care possible.

CHAPTER 5: ALZHEIMER'S DISEASE - CONCLUSION

This Interactive Qualifying Project investigated the biological, economic, and psychological impact of AD on society. Many current and innovative ideas were discussed to improve these impacts of the disease. The following conclusions came about as a result of this research.

Nearly one in ten people over the age of sixty-five suffer from AD, affecting four million people in the United States alone. AD is also the fourth leading cause of death among adults, with a typical life expectancy of about eight to ten years. These reasons alone are enough to warrant research on the biology of the disease. In the past ten to fifteen years there have been remarkable advancements in our understanding of AD. We now know that amyloid plaques and neurofibrillary tangles play an important role in the disease. Plaque formation creates the most likely mechanism for losses in memory and other cognitive functions while the chemically altered tau protein of neurofibrillary tangles can no longer hold microtubules together so such tangles affect cell shape and connections. We also know that gene mutations can play an important role in the development of early onset forms of AD. One significant finding is that all of the Alzheimer's genes discovered to date increase the rate of beta-amyloid formation, each by a separate mechanism.

Even though there is a fairly good understanding of what causes plaques and tangles, why they form and the mechanism in which it happens is unknown. These two areas of research should be carefully investigated in the future. With a more intimate knowledge of these two aspects, scientists are more likely to be able to remove or

decrease the aggregation of beta-amyloid plaques, which may in turn have a cascade effect on the rest of the disease. Another area of research that should be watched closely is that of enzymes and enzymatic reactions that take place within the brain. Scientists are looking for enzyme(s) that may cause the disease, or an enzyme that plays a role in the development of amyloid plaques and neurofibrillary tangles. If one is found, scientists can then begin to design an inhibitor for that enzyme.

There are many treatments that are currently on the market or are being tested to help AD patients. These include calcium regulators, nonsteroidal anti-inflammatory drugs, neurotropic factors, hormone replacement and cholinergic replacement (Donepezil and Tacrine).

Many studies indicate that a significant rise in the level of calcium in neurons is the final contribution to neuron death in AD patients. This information has led scientists to come up with two therapeutic approaches. One area is that of decreasing the number of active calcium import channels, with calcium channel blockers. Several of these blockers are currently being tested on patients suffering from AD. The other area of research is that of determining if the calcium pumps within the cells are defective and, if so, rehabilitate or synthesize artificial calcium pumps.

Several studies have shown that the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with a lower incidence of onset of AD. NSAIDs have also been demonstrated to reduce the rate of cognitive decline in patients who already suffer from the disease. One NSAID, prednisone, is currently being tested to see if it can slow the progress of AD.

Neurotrophic factors are newly discovered brain proteins that are essential in the maintenance and development of neurons. Nerve growth factor, a common neurotrophic factor, has the ability to regenerate injured neurons. Scientists believe that since NGFs can regenerate injured neurons, then by simply increasing the NGFs in the brain there should be an increase in functional neurons and thus an increase in cognitive function.

Hormone replacement has also been found to be an important therapy of Alzheimer's Disease. Women who take estrogen replacement after menopause are nearly fifty percent less likely to acquire AD.

Cholinergic Replacement Therapy is based on the knowledge that Alzheimer's Disease is marked by the loss of cholinergic neurons that produce acetylcholine, which plays an important role in cognitive function. This is one area of research that has produced numerous drugs that are currently on the market. Tacrine and Donepezil are just two of them.

From the research performed on drug therapies for AD, we recommend that AD patients take a cholinergic drug because they seem to provide the most widespread effective therapy. We also recommend that women that have experienced menopause take estrogen supplements as a preventative measure against AD. The most promising future therapies being tested are the NSAIDs and the neurotropic factors.

The economic role of Alzheimer's Disease has great effects on society. The treatment of this disease costs about $100 billion dollars annually in the United States alone. We found two ways to alleviate the costs of caring for AD patients. One possibility is the use of new drugs to delay the onset of later stages of the illness. This, in turn, can delay placement of the patient in a nursing home, reducing annual costs.

Another possibility is to use assisted living facilities instead of nursing homes. This also reduces the annual cost of caring for AD patients.

Drugs, such as donepezil and tacrine, can improve cognitive function while providing economic relief for patients suffering from Alzheimer's Disease. Both drugs slow the rate of cognitive decline, which delays placement of the AD patient in a nursing home. This delay saves thousands of dollars in care-giving costs. For example, the total cost for all patients who begin tacrine is $114, 548 while the total cost for those who do not take tacrine is $123,798. Thus on average the use of tacrine saves $9250 per person.

Special care units play an important role in caring for patients with Alzheimer's Disease. These units, when designed properly, can alleviate many of the problems that Alzheimer's patients face. They affect the safety, comfort and mental stimulation of patients, therefore providing the patients with optimal care.

Comfort is a critical issue with special care units for a variety of reasons. Patients of special care units are much more likely to be happy and responsive if they are content with their surroundings. Comfort invokes many other responses that are beneficial for the patients. There is an increase in mental stimulation and a decrease in depression. As a result, we believe landmarks, lighting, sight, floors, must be carefully planned out when designing a special care unit.

Familiar landmarks are very important to an Alzheimer's patient when trying to maneuver about. Using objects that have no sharp edges and are familiar to a patient allows them to move about more easily and prevents injury.

Proper lighting is also important in a special care unit. The best means of lighting is consistent light sources to eliminate shadows. Glare and unshielded lights may

disorient people suffering from AD and cause them to loose their balance or even become lost. Patients have been shown to be more comfortable and have a longer attention span with focused lighting and glare reduction.

AD patients suffer from impaired depth perception. As a result, contrasting floor colors must be subtle, in order to alleviate the impression of a depth change. There should also be a sharp color change between the floor and walls of a special care unit to allow the patient to distinguish the two. This sharp contrast helps eliminate patients from harming themselves.

Texture also has an effect on AD patients. Textures within an environment can provide a patient with a feeling of warmth and can invoke past memories causing patients to feel wanted and happy. There are many different textures that can be applied to a patient's personal space including wall coverings, throw rugs and draperies. These can be mentally stimulating to a patient, making a significant impact on their outlook of their surroundings.

In conclusion, this Interactive Qualifying Project investigated the biological, economic, and psychological impact of AD on society. Through research, many current and innovative ideas were found to improve these areas of disease. We hope that our conclusions provide preventive measures, treatment and care options for Alzheimer's patients.

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