Introduction.

Two elderly gentlemen with Alzheimer's disease lived together in a nice little flat. One of the men heard the sound of an ice cream van. He turned and said to the other man, "would you like anything from the ice cream van ".
The other man replied "oh I'll have and ice cream cone thanks but you better write that down cos I know what you're like you'll forget".
"No, no I won't forget" said the first man and left to go to the ice cream van.
Whilst he was leaving the second man shouted from the window
"Hey get me a chocolate flake as well, and write it down before you forget".
"I won't I won't" replied the first man.
The second man then shouted again "oh yeah and some 100 and 1000's and monkeys blood now you better write that down as I know you will forget that"
Yet again the first man promised he would not forget and made his way to the ice cream van. Three hours passed and the first man eventually returned and gave the other man a mince pie in which he questioned "Where's my chips"?

Although it is very easy to make fun and make up jokes about a disorder or disease as I have done here, but the actual truth and the real nature of suffering with Alzheimer's disease is no joke at all. In this essay I am going to discuss the aetiology, pathology, and physiological response to a sufferer of this disease.

History of a world of forgetfulness.

The case of a 51 year old woman who was suffering severe memory problems, confusion, unexplained paranoia and eventually profound dementia was presented by German psychiatrist Dr. Alois Alzheimer, (Mera S L 1997). After her death Alzheimer carried out an autopsy on her brain. He described degenerated nerve cells in the cortical areas of the brain; the dead neurons produced a number of neuritic plaques. The inside of the nerve cell were twisted bands of fibres known as neurofibrillary tangles. Although the symptoms were first described by Emil Kraepelin the professor Alzheimer was working with, it was Alzheimer that first observed and described the characteristic neuropathology. It was then Kraepelin made the decision to name the disease after Alzheimer. Most of the last century Alzheimer's disease was only referred to middle aged people whom presented symptoms of pre-senile dementia; this was considered to be a normal outcome of ageing. However research throughout the 70's and 80's studies of the elderly showed that the lesions of a 50 year old sufferer were identical and in correlation with senile dementia in aged patients. It was the result of these studies that age has become the greatest risk factor of the development of the disease and a significant rise in the disease beginning at the age of 65 and above, (Smith and Perry 1998). Though there are other causes of dementia the diagnosis can still not defined without an autopsy.

If they forget how do we know?

Though there are many different causes of dementia for example strokes, Parkinson's disease, severe head trauma, and other causes such as drug use tumours and infection. Though shown in fig 1 Alzheimer's disease actually accounts for 50% of all reported cases of dementia, (Mera S L 1997).

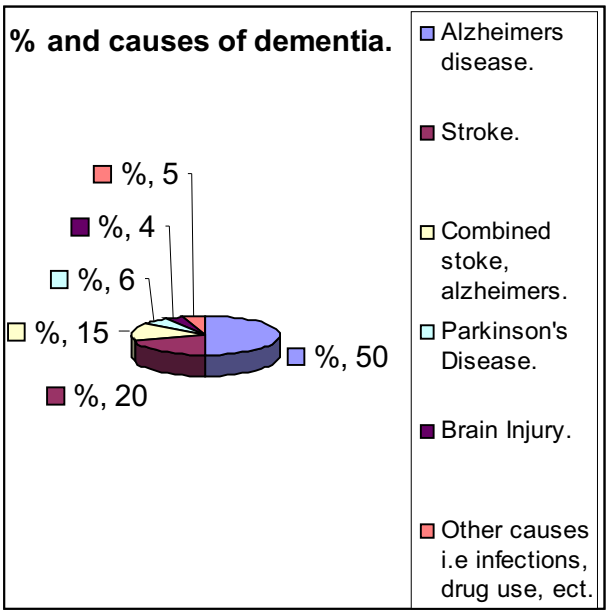


Figure 1. Shows the percentage of causes of dementia.

Patients suffering with Alzheimer's disease have the main symptoms of loss of recent memory (**progressive amnesia**), they begin to develop a difficulty in using and understanding words (**aphasia**), suffer with problems in carrying out normal movement tasks (**apraxia**) and then the development of problems recognising people's face's and objects (**agnosia**). As well as these main symptoms patients will also be likely to suffer from depression and become poor at time keeping and seem emotionless.

The long term memory of the patient seems intact and as a result sufferer's spend there time dwelling on past memories. My Grand mother was a sufferer of Alzheimer's and it was this that I found the hardest to deal with, when visiting her she never new who I was until I told her my name a hundred times. She would then turn around and ask why I was not at school. It was very difficult for her to comprehend that the little boy she was looking at was actually her 27 year old grandson. My Mother who cared for her until her death recalled she would always remember the dead people in her life and past events could be described vividly, but when it came to the daughter who was caring for her day after day my Grandmother couldn't recognise her and always forget my Mothers name. Even with symptoms like this patients are allowed to stay at home to prevent any distress that may be brought on by unfamiliar surroundings. However as there conditions deteriorate and there safety becomes an issue they are eventually institutionalised. After this the rate of progression of the disease will vary and it is normally a decade after diagnosis that the patient will die, (Mera S L 1997).

Aetiology, Genetic or Infiltrated.

It's in your genes.

The early onset Alzheimer's disease has been shown to be an autosomal dominant inheritance. The result of this is a genetic mutation on chromosomes 1, 14 or 21 . It is believed that the chromosomes 1 and 14 change the amyloid to an insoluble fibrillar formation deposited extracellularly in the brain. There mutations either cause the increase of amyloid – β or the amino acid form. Together these cause amyloid – β fibre formation by increasing the concentration or decreasing the solubility. In the case of chromosome 21 downs syndrome sufferers have an extra copy of chromosome 21 and this gene contains the amyloid precursor which is present across all membranes. Its role is believed to maintain the stability of the membrane or act as a membrane receptor. Therefore extra copies excess production of the protein. A result of this may cause the amyloid to become deposited as the insoluble amyloid – β in the brain. Research and evidence have put the suggestion that chromosome 19 apolipoprotein E mutations play a part in the development of late onset of the disease. It is this that is involved in the regeneration of the nervous system and is involved in the metabolism of lipids in the brain. It is possible that apolipoprotein E plays a part in the wrong deposition of the amyloid – β plaques. Apolipoprotein E has been associated with the neurofibrillary tangles and plaques in patients especially those containing amyloid, (Smith and Perry 1998). It was recently demonstrated somatostatin expression in the brain decreases with ageing in mammals which causes an increase in amyloid – β therefore proposing that age was the predominant factor in the onset and development of the disease, (Hamo & Saido 2005)

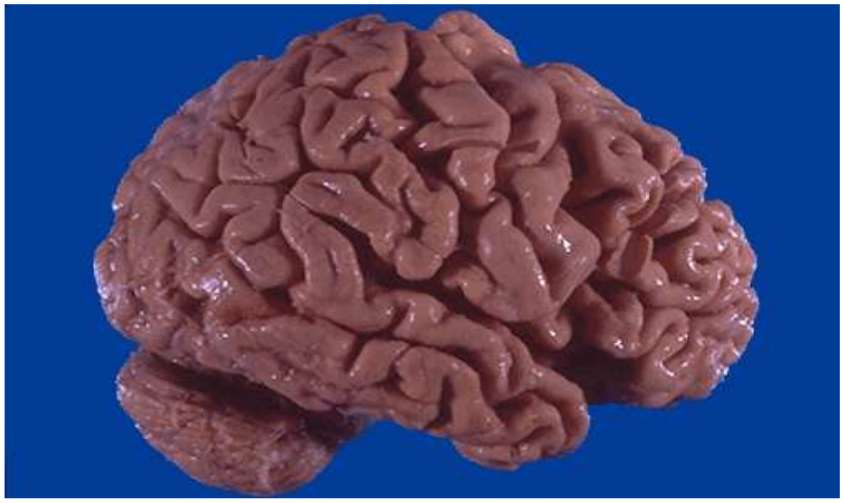
Is The Answer in The Water?

Some studies have suggested that aluminium is a causative factor to the onset of Alzheimer's disease. Most of these studies have focused on exposure to aluminium through drinking water and the link between Alzheimer's. This is believed as the toxicity of aluminium was first discovered in patients with renal failure, which was known as dialysis encephalopathy the first human disorder related to exposure to aluminium, (Trond Peder Flaten 2001). It is known that aluminium causes neurofibrillary changes in the neurons. This is most likely by interfering with the transport along the axons of the neurofiliments. An experiment using mice was carried out in 1956 in which the mice where inoculated with aluminium it resulted in the neurofibrillary degeneration and had a striking resemblance to the lesions in Alzheimer's disease. Recent studies showed that in Norway the mortality of Alzheimer's disease was significantly higher in areas where there was aluminium in the drinking water, (Trond Peder Flaten 2001) and studies in the USA reported that areas with high fluoride concentration in the water showed a lower rate of Alzheimer's in relation to areas with low fluoride concentration. This was put down to the fluoride possibly decreasing the aluminium's bioavailability. Although Flaten (2001) provides evidence that links aluminium to the disease, studies have shown that the aluminium is more likely to be just simply a marker of the alteration of metal metabolism in iron accumulation. In contrast to the aluminium irons biological functions are altered with the onset of Alzheimer's disease, (Smith and Perry 1998).

The pathology.

The major signs and pathology of this disease are the neuritic plaques, the neurofibrillary tangles and granolovacuolar degeneration.
In a sufferer of this disease the anatomy of the brain is altered and it leads to cerebral atrophy. There is an increase in the size of the fluid canal and a widening of the sulci. As shown in fig 2

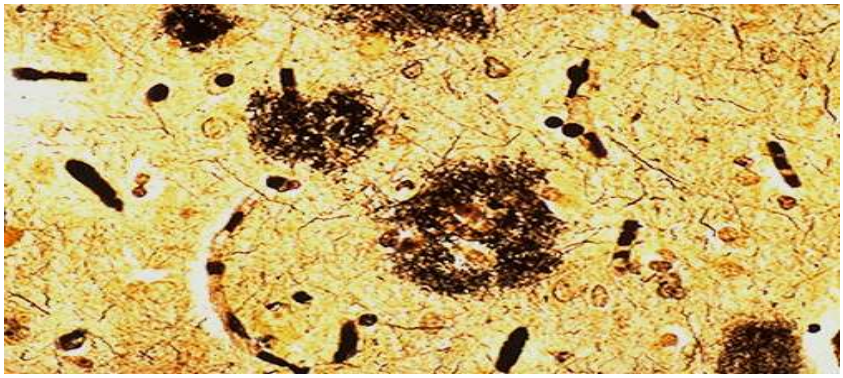
Figure 2. This picture shows the brain of a patient who died as a result of Alzheimer's disease. The widening of the sulci can be easily seen as well as the increase in size of the fluid canal.



http://medlib.med.utah.edu/WebPath/TUTORIAL/CNS/CNSDG001.html

The location of the plaques and tangles are usually found in the area of the hippocampus with the tangles on the inside of the neurons and the plaques on the outside of the neurons. Some of these plaques will be made of debris from the neurons which have died. Although the plaques and tangles are not particularly unique to this disease and are also found in people without the disease. There difference is there quantity in which there are far more found in sufferers of Alzheimer's.

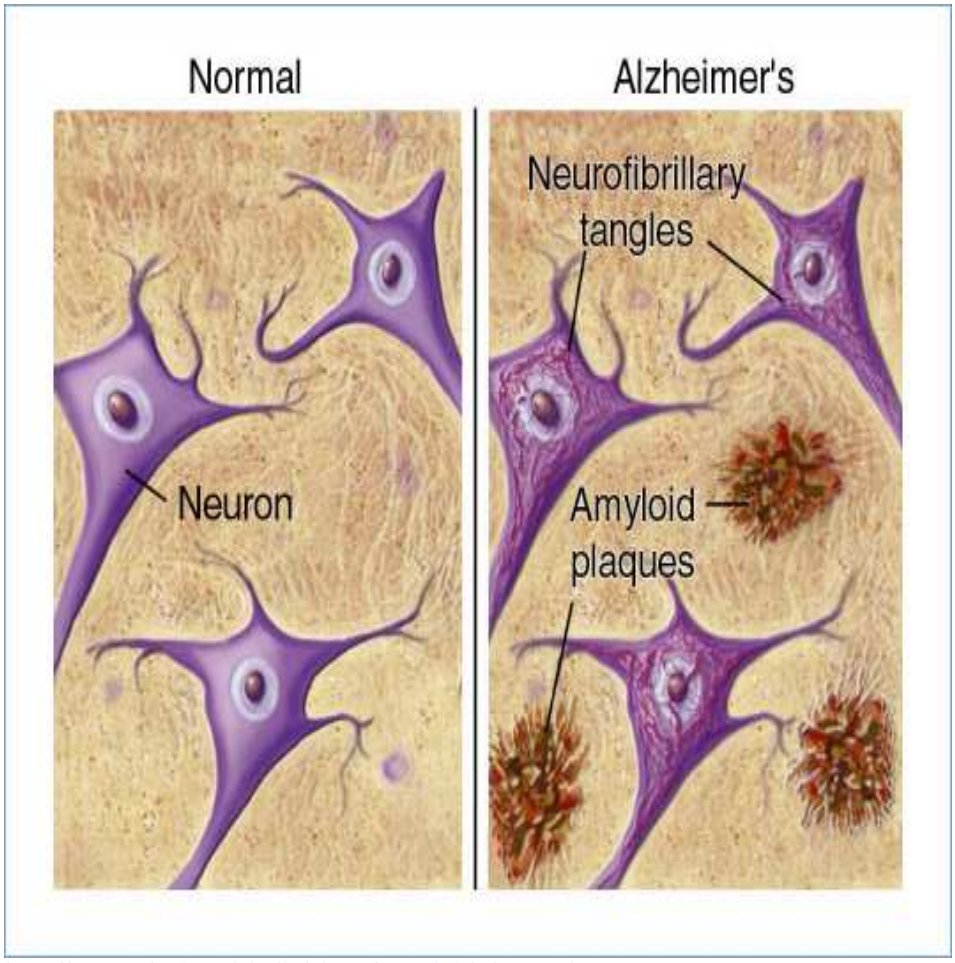
Figure 3. An example of a neuritic plaque within the brain of a sufferer of the disease.



http://bb.westernu.edu/web/Pathology/webpath60/webpath/labs/cnslab/cns007.htm

The structures of the plaques come in a number of different forms. There are some that contain material which derived from the neurons and others that contain amyloid. The tangles are fibrillar in there structure and there appearance and composition differ from that of the normal structure of the neurofiliments.

Figure 4. This picture shows the difference of a normal brain to the brain and neurons of a sufferer of Alzheimer's.



http://www.ahaf.org/alzdis/about/AmyloidPlaques.htm

There is some biochemical evidence that suggest a loss of the choline acetyltransferase and acetylcholine in the cerebral cortex of patients with Alzheimer's disease. However, the significance of this finding is not clear. Alzheimer's eventually leads to severe profound dementia as a result of the loss of higher brain functions. The course is usually over 5 to 7 years. The immediate cause of death for most persons with Alzheimer's disease is pneumonia, typically aspiration pneumonia, (Mera S L 1997).

How does the body cope?

The physiological response to Alzheimer's disease is neuronal sprouting in which some of the neurons attempt to repair themselves. This can be described as a meshwork of curly fibres known as neuropil threads. Another response is to fill the spaces caused by the proliferation of neuroglia carried out by brain cells called microglia. However this process can lead to further damage as there is an uncontrolled release of proteolytic enzymes (Mera S L 1997). As a result of these responses and the loss of neurons the transmission of neurotransmitters is disrupted and the onset of depression and anxiety can be a result. At present there is no cure for the disease and treatment of it is just slowing down its development. Patients receive anti-depressants to counter act and relieve the depression and anxiety. Drug free interventions are a way to educate the caregiver's strategies to reduce behavioural abnormality and problems in patients with Alzheimer's disease. Though there is a list of different drug therapies which include cholinesterase inhibitors (tacrine, donepezil), psychotropic medications, mood stabilizing medications (anti-agitation), anti-anxiety medications and anti-depressants

Conclusion.

Though there has been extensive research into this disease the aetiology still remains in doubt of which factors actually cause it. Even though Alzheimer's have single cellular pathogenesis its aetiology is heterogeneous. As well as discuss the history of the disease I have also discussed in this paper the different theories whether they follow the genetic path in which there is evidence to support this or the path of environmental causes such as the connection to aluminium. Though treatment today is only a way of slowing the progression research is still being carried out to find a possible cure. I have shown the major pathological signs of the disease and also shown a few examples of the physiological response to the disease. Although I started this paper with a joke about this disease and the way it affects people I believe I have shown here that there is a very serious side of the infliction we call Alzheimer's disease.

Barry Hollinshead.

WORD COUNT

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