**Alzheimer’s Disease**

**Alzheimer’s Disease** **(AD)** is a progressive neurodegenerative disease that affects about 6% of the world’s population. AD presents itself in a wide range of symptoms which fall under three main categories- cognitive dysfunction, executive dysfunction, and deterioration of everyday life. AD is the most common form of dementia and accounts for about 70% of all dementia cases worldwide. There is an estimated 35 million people living with AD, and as the population collectively ages an increase in the number of diagnoses is expected to rise accordingly.

**History**

The term ‘Alzheimer’s Disease’ is named after Dr. Alois Alzheimer, a psychiatrist from Germany. In 1901, Dr. Alzheimer was working at a psychiatric hospital in Frankfurt when he was introduced to a new patient named Auguste Deter. Mrs. Deter was a mere 50 years old, but her husband had noticed her memory was slipping quite often, which then turned into aggressive mood swings, panic attacks, and episodes of delirium. She was an inpatient at the psychiatric hospital for 5 years until she died. It was then that Dr. Alzheimer asked permission and microscopically analyzed her brain tissue. He discovered neurofibrillary tangles and patches of amyloid-beta plaque. Dr. Alzheimer took his findings and found similar results in other patients. His former boss from the psychiatric hospital, Dr. Kraepelin published Dr. Alzheimer’s finding his highly respected psychiatry textbook. It was also Dr. Kraepelin who named the disease after his former junior colleague.

 Since Mrs. Deter was only 50 years old, it was assumed that her condition stemmed from an ageing-related vascular disease, rather than being considered as any form of dementia. Because of this, Alzheimer’s Disease was first thought of as a ‘presenile dementia’. In the 1970s, an American neurologist named Robert Katzman analyzed studies from Dr. Alzheimer and other colleagues to find that there was not a distinct difference in the ‘presenile’ and ‘senile’ forms of Alzheimer’s Disease, and therefore redefined Alzheimer’s Disease into what we know it to be today.

**Neuropathology**

Alzheimer’s Disease is categorized as a protein misfolding disease. This means that one or more proteins naturally occurring in the brain undergo a conformational change that changes the function of the protein or creates a byproduct associated with the disease. The Amyloid Precursor Protein (APP) has been identified as a contributing factor to AD. APP itself is naturally occurring in the brain and plays a role in neuronal development. However, when APP undergoes proteolysis (the breakdown of proteins into smaller peptides and amino acids) in the body of someone with AD, an unwarranted byproduct called Amyloid-Beta protein is formed. In high concentrations, this protein deposits outside and around the neuron as dense, insoluble senile plaque.

 Another protein associated with AD is the Tau protein. Like APP, Tau proteins are natural and play a role in stabilizing the axons in the nervous system. In AD patients, the Tau protein isn’t properly regulated. This creates entangled bundles of the Tau protein inside the cell body. This unregulated Tau protein also forms small nodes on a neuron (they can be present on the body, dendrite and/or axon) called neurites. Tau neurites are locally associated with the Amyloid-Beta plaque previously mentioned.

 These plaques and other biochemical factors result in the degeneration of neurons in affected areas on the brain which include the temporal and parietal lobes, the cerebral cortex, and the cingulate gyrus. The degeneration of neurons in the brain can be thought of like unplugging something from an outlet. The result is that whatever pathway was “plugged in” now doesn’t have its power source.

**Symptoms**

The range of symptoms exhibited by those affected by Alzheimer’s Disease is very wide. As mentioned earlier, these symptoms can be grouped into three primary categories. Cognitive dysfunction is characterized by memory loss and language degeneration. Executive dysfunction is referring to the inability to make decisions, think critically, and process emotions rationally. Some behaviors that display executive dysfunction are throwing ‘temper tantrums’, unprovoked crying, and hallucinations. The third category of symptoms is the deterioration of everyday life. This includes daily activities that an unaffected person wouldn’t consciously think about, such as driving, getting dressed, eating, and unlocking a door.

 Alzheimer’s Disease does not affect all parts of memory equally. The short-term memory is almost always affected. This creates a severe impairment in the ability to learn new things. The semantic and episodic memory are less commonly affected, and if they are it typically doesn’t occur until the final stages of the disease. The semantic memory is responsible for retaining facts and figures learned, while the episodic memory stores a person’s early life memories. The implicit memory, which is responsible for knowing how to perform routine tasks, is often affected in the later stages of AD.

**Stages of Alzheimer’s Disease**

 The symptoms that typically appear during the earliest stages of dementia are mild cognitive impairment and some memory loss. In the early stage of AD, a person is typically able to operate independently, and are aware of symptoms when they occur. As the disease progresses and these early symptoms become more frequent, a diagnosis is usually assigned.

 As the disease progresses into a moderate condition, a person affected will start to display more symptoms that are detrimental to their daily lives. Language and vocabulary will begin to dwindle, and the person might use incompetent word substitutions or communicate with repetitive words and short phrases. Many of those affected in the moderate stages of AD will display some behavioral issues, such as unwarranted aggression or excessive crying. By the time a person reaches the moderate stages, they are less aware of their condition and often they won’t understand their actions or the actions occurring in the world around them. Many affected experience long-term memory loss in this stage. Persons affected in these stages often experience sundowning. “Sundowning” or “sundown syndrome” is when a person displays more behavioral inconsistencies or a state of confusion or delirium at sunset. They might also hallucinate or have an unexplained sense of urgency. Doctors are unsure of the cause, but nearly 20% of those with AD experience sundowning. It should be noted that sundowning is not exclusive to those with AD, and affects many of the older population.

 Once the disease reaches the severe stages, the person affected will have become totally dependent on others for care and will begin to lose the ability to verbally communicate. This doesn’t mean that they aren’t thinking or experiencing emotion, they have only lost the ability to verbalize it. Many will still show emotion with facial expressions. The ability to ambulate is lost, which consequently leads to rapid loss of muscle mass and the person becomes bedridden. Some people in these stages are still able to use a straw on their own to drink, but most cannot feed themselves and are incontinent. If a person lives long enough to experience these stages, they typically die from an external cause, like infection, pneumonia, or cardiovascular disease, rather than Alzheimer’s Disease itself.

 There is no true time frame for when the disease will progress through the stages, but a person who is diagnosed with AD is expected to live anywhere for 3-15 years past the onset.

 **Test your knowledge:** A condition that causes one to experience extreme confusion in the late afternoon is called\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

**Causes**

 The exact cause of Alzheimer’s Disease is unknown. There are many risk factors that have been assessed and grounded in evidence. Studies have linked factors including age, head trauma, family history, vascular diseases and conditions, depression, and low physically or cognitively challenging activity to AD. Those who have a first degree relative that is affected by AD is considered to have a 3.5-fold increase in risk.

**Familial Alzheimer’s Disease**

 A genetic predisposition for a specific form of Alzheimer’s Disease has been identified. Mutations in a few different genes are identified as hallmarks for the development of AD. The genes are the amyloid precursor protein, presenilin 1, and presenilin 2. The mutation of these genes allows for the development of Early Onset Familial Alzheimer’s Disease (fAD). While fAD is characteristically the same as late onset AD, those affected will begin to see symptoms in their 40s and 50s rather than late 60s and 70s. There is only one genetic risk factor associated with late onset Alzheimer’s Disease- APoE. APoE has three gene forms APoE e2, APoE e3 and APoE e4. Those who carry APoE e3 are considered to be at a threefold increased risk for the disease, though environmental factors are still contributors.

**Test your knowledge:**

The protein that naturally occurs in the brain and is known to cause plaque buildup in the brain is \_\_\_\_\_\_\_\_\_\_\_\_.

Those who have a first degree relative that is affected by AD is considered to have a ­­­\_\_\_\_\_-fold increase in risk factor.

**Diagnosis**

Alzheimer’s Disease can be difficult to diagnose, as many who display the early symptoms like mild memory loss or inaccurate word retrieval attribute them to normal ageing. When symptoms worsen to a point that dementia or AD is suspected, there are some simple cognitive tests administered to the patient. A common test is to simply have the patient draw a clock with the numbers and hands on it. This is something we can all easily visualize, but the visualization to translation into a drawing can prove challenging for those with developing AD. Since these are subjective tests, the diagnosing is heavily based off of the physician’s judgment after assessing their test results, symptoms, medical history, input from credible source (often a spouse or child of the patient) on the patient’s daily activities.

**Treatment and Care**

As a person enters the moderate stages of Alzheimer’s Disease, they become dependent on others to maintain a good quality of life. In the United States, it is typical for a person at this stage to seek care in an assisted living home. Approximately 50% of all residents in assisted living facilities in the US have some form of dementia, including AD. In an assisted living home facility, the resident has an apartment that is decorated to their preference to help a seamless transition and make the facility feel more like home. The residents are monitored closely by a nursing staff, and an activity director who designs activities based around the residents’ hobbies and interests. As for those who do not seek care in a facility, they require at-home care from either a loved one or a home health provider. This can be good for those who feel like a transition to a new home might be too difficult; however, if the patient lives alone, this does not add much for cognitive stimulation. In-home care can also be dangerous if the resident is a fall risk or an elopement risk. In the recent years, memory care facilities solely dedicated to the care of those with dementia and AD have opened. The memory care facilities focus on engaging the residents in social interaction and cognitively challenging activities daily to combat the symptoms of AD.

 When it comes to treating AD, there is no known cure. There are only a few pharmaceuticals that can be prescribed to help combat some of the symptoms though. Before taking a pharmaceutical approach, clinicians will begin with non-drug interventions. Therapeutic interventions are important to the treatment of AD, because it is designed to make the patient comfortable with their clinician and understand the authority the clinician has on the subject. These therapeutic sessions are mean to be continuous, to ensure a genuine relationship with the patient. This mutual respect helps the patient recognize changes in their own cognitive function from session to session. Without a complex relationship, the patient may feel closed off and be dishonest in their condition. Patients with AD might also report inconsistent feedback regarding their assessment of their condition, which is a sign that a new dimension of treatment might be needed.

 There are currently two types of medications approved by the Food and Drug Administration to combat cognitive decline in AD patients. The first is cholinesterase inhibitors. This is prescribed to help treat symptoms related to memory, thinking, decision making, and language. Cholinesterase inhibitors stop the breakdown of Acetylcholine, a neurotransmitter that is crucial to thinking and learning. Consequently, these inhibitors promote communication between neurons. Cholinesterase inhibitors are prescribed to those with mild to moderate symptoms of AD. The second type of medication that can be prescribed for patients who exhibit more severe symptoms of AD is Memantine. Memantine regulates glutamate activity, which is important for information processing, storage, and retrieval. These two types of drugs can be prescribed together if needed. For patients who display severe symptoms of aggressiveness and agitation, antipsychotics may be prescribed. This practice is becoming controversial as the effects of antipsychotics on the aging brain are being heavily researched.

 The environment in which a person with AD lives in largely impacts the symptoms displayed. For example, if the person is socially isolated most of the day, and the interaction they do have isn’t stimulating and positive, that person is more likely to display signs of agitation and depression when compared to another person with AD, who has constant cognitive stimulation and is consistently surrounded by loved ones.

**Test your knowledge:** The type of medication that can be prescribed for AD patients that regulates glutamate activity ­­­\_\_\_\_\_\_\_\_\_\_\_\_\_.

**Society and Alzheimer’s Disease**

When considering direct medical treatment and the cost of caretaking, Alzheimer’s Disease has significant social and economic implications. An estimated $18 Billion (USD) is spent every year on AD, which is equivalent to about 1.1% of global gross domestic product (GDP).

Alzheimer’s Disease is portrayed in many movies, such as Stephen King’s *The Notebook*, where a husband attempts to rekindle his wife’s (who has AD) memories by reading to her from his notebook. Another well known movie to portray AD is *Still Alice.* This movie tells the story of a woman named Alice who develops early onset fAD, and her adult children who are working to maintain their mother’s quality of life. Some criticized *Still Alice* for not including bits that explain the probable genetic predispositions to fAD that Alice’s children have.

**Prevention**

 While there is no known cure to Alzheimer’s Disease, there are some preventative measures recommended. One of they key risk factors to AD is vascular disease. To combat vascular disease, regular physical activity and a heart-healthy diet is strongly recommended. Another preventative measure is to reduce risks for head trauma. Some examples of this would be to wear a seat belt when in a car, reduce fall risks, and wearing a helmet when playing contact sports. Social interaction has been shown to combat cognitive decline in older individuals. This is likely due to the upkeep of social mechanisms and the cognitive stimulation that comes from a conversation or activity. As for the Familial Alzheimer’s Disease, the same preventative measure should be taken, but frequent check ups with a physician are recommended to monitor the plaque building up in the brain tissue.

**Review**

1. What is the name of the first patient to have been named to have Alzheimer’s Disease?

2. Which two proteins in the brain are associated with Alzheimer’s Disease?

3. How long is a patient diagnosed with Alzheimer’s Disease expected to live after onset occurs?

4. Explain why a heart-healthy diet would be recommended in combatting Alzheimer’s Disease.

5. Name one book, movie, or TV show not mentioned in this chapter that portrays some form of dementia or Alzheimer’s Disease.

6. At what age range would you expect a person with familial Alzheimer’s Disease to start displaying symptoms?

7. Why is the study and research of Alzheimer’s Disease relevant in the world today?

8. Do you know someone with Alzheimer’s Disease or dementia? If so, list some of the symptoms you see them exhibit.

9. Consider the pros and cons to each of the forms of care for patients with Alzheimer’s Disease. Which would you prefer for a loved one? Why?

10. Under which of the three broad symptom categories would you classify the inability to perform simple math calculations?

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