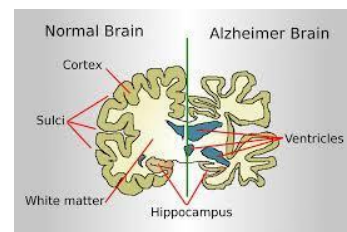


Alzheimer's

Introduction

Definition & Overview

Alzheimer's disease is the most common type of dementia. It is a progressive disease beginning with mild memory loss and possibly leading to loss of the ability to carry on a conversation and respond to the environment. Alzheimer's disease involves brain parts that control thought, memory, and language. It can seriously affect a person's ability to carry out daily activities.



Alzheimer's History

In the late 1890s, a German woman named Auguste Deter began having acute memory loss and behavioral changes at the age 50 years. Her deteriorating condition led to her admission into an institution in 1901, where Dr. Alois Alzheimer attended to her. He noted her disorientation and loss of thinking and, following his death in 1906, the abnormal plaques and tangles in her brain. These findings were associated with what became known as Alzheimer's disease. What had been considered to be a rare disease was brought into the mainstream as a major public health problem by neurologist Robert Katzman in 1976. This brought to the world the realization that further research is needed on this menace. Today, although there still is no cure, treatments are much more effective at managing the symptoms, and there has been far greater emphasis on person-centered care. Making a proper diagnosis today means that Auguste will receive support and resources much more adequately than she did all those years ago, which reflects a significant movement from the time of Dr. Alzheimer.

Epidemiology

In 1984, the NINCDS-ADRDA criteria standardized the diagnosis of AD by recommending medical history, clinical examination, neuropsychological testing, and laboratory assessments. These criteria have been reliable over the past three decades by correlating clinical symptoms with post-mortem findings and are the first to introduce levels of certainty for the diagnosis of

AD. In 2011, revisions took into account progress in neuropsychological testing, brain imaging, and knowledge of AD pathology that changes could precede dementia by years and the role of cerebrovascular disease. In 2005, estimates pointed to 24.2 million people worldwide to have dementia, with 4.6 million new cases annually and the highest prevalence in North America and Western Europe. The prevalence of AD increases significantly after age 65, with a huge increase between ages 60 and 85. Geographic variations reported are many; some of these may be related to different ascertainment methods or, in the US, higher rates in African-American and Hispanic populations. Improved diagnostic methods have strengthened worldwide comparisons of AD prevalence.

Etiology

Causes & Risk Factors

Alzheimer's disease is a disorder caused by the abnormal accumulation of two proteins: amyloid and tau, which eventually lead to the death of brain cells. The brain relies on over 100 billion nerve cells to control functions such as thinking, learning, and memory, all of which are compromised since these proteins form plaques and tangles that block the line of communication between nerve cells. This progressive cell death starts in the hippocampus and spreads to other brain areas. Although much research has been done on this protein accumulation, its exact cause is still unknown. Genetic mutations may lead to early-onset Alzheimer's disease, while late-onset Alzheimer's probably results from a complex interplay of genetics with environmental and lifestyle factors. The largest risk factor is age. The risk-reducing strategies include avoiding smoking, moderate alcohol consumption, a balanced diet, remaining physically, cognitively, and socially active, and management of medical conditions such as diabetes, heart issues, and hypertension.

Genetic & Environmental influences

The genetic factors for Alzheimer's include risk genes and deterministic genes. The risk genes, like APOE-e4, increase the risk of developing late-onset Alzheimer's but do not determine it. The first identified risk gene, APOE-e4, affects 40-65% of

the diagnosed, though the effects may vary across populations. On the other hand, the deterministic genes virtually guarantee the development of the disease and are responsible for early-onset Alzheimer's, occurring in a minority of cases. The environmental factors in the development of Alzheimer's involve aluminum exposure, which has always been controversial, with some studies showing both positive and negative results pointing to its link with the disease. Zinc levels have been implicated in both deficiency, affecting the formation of amyloid plaque, and excess. Food-borne toxins, like the amino acids from certain legumes and the domoic acid from contaminated mussels, have been associated with similar neurological damage. Beyond that, even viruses have been implicated, but with no firm evidence. Thus, the most likely scenario is that Alzheimer's is the result of complex interactions between genetic and environmental factors. Further well-designed studies are required to understand these influences.

Clinical Features

Signs & Symptoms

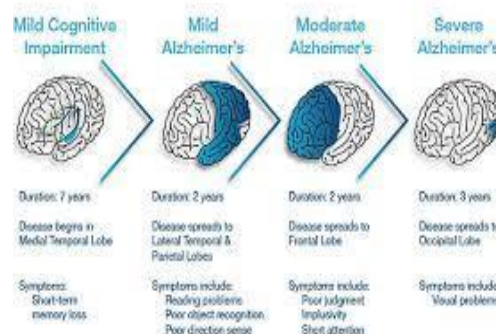
There are three basic stages during AD. Preclinical Alzheimer's is a time when changes in the brain—amyloid plaques and tau tangles—occur years before symptoms appear. In mild Alzheimer's, memory loss increases, judgment worsens, and problems with daily tasks gradually become evident to the affected person and his or her family. Moderate Alzheimer's exacerbates these problems, resulting in increased confusion, social withdrawal, and problems with language and familiar tasks. Other behavioral changes, such as hallucinations and agitation, become more common. In severe Alzheimer's, patients can no longer communicate, their physical decline becomes severe, and care becomes full-time; this can lead to such complications as aspiration pneumonia. Preserved skills throughout the disease, like reading and singing, may last much longer because they reflect the areas of the brain that are affected later.

Stages & Progression

There are five progressive stages of Alzheimer's disease in terms of the effects it has on different cognitive and physical functions over time. Preclinical Alzheimer's is early brain changes, like amyloid plaques and tau tangles, which are detectable only by advanced imaging; no symptoms have manifested at this stage.

Mild Cognitive Impairment (MCI) exhibits subtle memory lapses, trouble planning, or problems with

decision-making; however, it does not significantly impact daily life. Mild dementia: A more significant decline in memory, problem-solving, and personality, causing noticeable problems in daily activities. In moderate dementia, confusion increases, memory loss is greater, and needs increasing assistance with self-care and daily tasks. They may also develop behavioral changes like paranoia and agitation. Severe dementia is the last stage, whereby one loses communication abilities and now requires complete assistance to live through the day. The physical abilities drop drastically; most patients become unable to walk, sit, or swallow without support. The speed of progression also highly varies, but the average patient can survive for approximately three to eleven years post-diagnosis, though some live longer. Complications such as pneumonia, malnutrition, and infections often contribute to death.



Complications

People with AD often become restless and agitated as a result of declining cognitive abilities that prevent them from understanding their environment, leading to confusion and fear. It is addressed by creating a quiet environment with minimal stimulation and reduced stressors and by providing physical comfort. Incontinence and constipation are frequent changes with AD; the person may not be aware of the urge to urinate or have a bowel movement or may not have the ability to act on these urges. These would include reminders, easy access to bathrooms, and aids such as commodes or incontinence products. Depression is also quite common and can have symptoms that resemble AD, such as sleep patterns disrupted and mood changes; it may require a geriatric psychiatrist to differentiate between the two. Safety is also an issue as balance is impaired, and some precautions which would help to decrease falls include clear pathways and

walking aids such as walkers. Choking is a serious risk due to difficulties in swallowing; this can be prevented by proper eating posture and food preparation. Medical alert bracelets and home security can deal with wandering, while adequate nutrition and hydration is very important to prevent dehydration and malnutrition.

Diagnosis

Diagnostic Criteria

Diagnosis of Alzheimer's dementia includes a full examination by the treating doctor, whereby he will review symptoms, case history, and even contributions from family members. Early symptoms present with memory impairment, problems in daily activities, and changeable mood or behavior. Diagnosis usually consists of neuropsychological testing, imaging, and laboratory tests that identify or rule out other causes. Imaging brain scans like MRI and PET assess brain degeneration but are not in themselves diagnostic for Alzheimer's. New tests, like blood-based biomarkers, hold some promise for early detection. Early diagnosis enables management of symptoms, access to treatments, and planning of the future—from care to financial decisions.

Diagnostic Tests & Procedures

The diagnosis of Alzheimer's disease is made based on a comprehensive clinical assessment by health professionals that includes a review of medical and psychiatric history, current medications, and physical and neurological examinations. Some of the main tests used in diagnosis include monitoring vital signs, testing cognitive and behavioral function, and ruling out other causes of dementia such as depression or sleep apnea. These may include blood and urine samples, imaging of the brain by MRI or CT, and analysis of cerebrospinal fluid for tau and beta-amyloid biomarkers. Investigated newer blood tests and digital cognitive tools could provide a more timely and accurate diagnosis. While these current tests are helpful in some capacity, future research looks to standardize

and validate newer methods for the better diagnosis and tracking of Alzheimer's disease.

Differential Diagnosis

It's often the differential diagnosis for AD from similar disorders that share common symptoms. Key conditions to consider are vascular dementia, caused by stroke-related damage to the brain and affecting also the motor component; Lewy body dementia, characterized by visual hallucinations and motor symptoms resembling Parkinson's disease; and frontotemporal dementia, presenting at a younger age than AD and having predominantly affected personality or language, at times even preceding the onset of Alzheimer's. Parkinson's disease dementia features cognitive decline combined with motor difficulties. Moreover, depression may also present as dementia syndrome, termed pseudodementia, and needs to be differentiated from true dementia. Normal pressure hydrocephalus is the accumulation of fluid in the brain, associated with gait disorder and progressive mental deterioration. Thyroid disorders and deficiency of vitamins—especially B12 deficiency—also trigger reversible dementia. Traumatic brain injury and infections, which include meningitis or encephalitis, are other causes that manifest with dementia-like cognitive symptoms. Accurate diagnosis requires a comprehensive evaluation that includes a history, physical examination, neuroimaging, neuropsychological testing, and, in some cases, laboratory examinations.

Pathophysiology

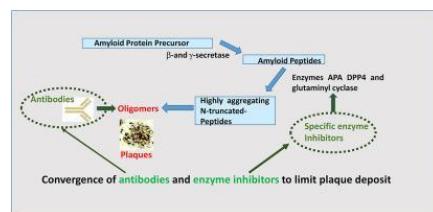
Mechanism & Development

Alzheimer's dramatically interferes with the functionality of the brain by disabling its communication, metabolic, and repair operations, which are conducted through the neurons in the brain. The very basic working units of the brain communicate by electrical and chemical signals; however, the hippocampal and entorhinal cortex are the very first brain places to get destroyed in the memory responsible for the brain. After these initial stages, the disease extends to the

cerebral cortex, which weakens the functions of language and behavioral reasoning. Key features of Alzheimer's are the accumulation of beta-amyloid plaques between neurons and tau tangles in the cytoplasm of neurons, both of which impede normal cell function and connectivity. This causes substantial brain atrophy, a reduction in neuronal connections, and chronic inflammation brought about by poorly functioning glia cells. Other vascular problems, like insufficient blood flow and glucose metabolism, also advance the disease because of intensified damage and inflammation of neurons. It advances gradually over time, and the later stages show signs of serious cognitive decline, where a person cannot communicate or take care of themselves. Understanding such changes facilitates the creation of targeted interventions to manage, and possibly retard, the progression of Alzheimer's.

Cellular & Molecular changes

New and important information about the disease process of Alzheimer's has been found in recent studies through examinations of brain tissue from living patients and molecular processes. One group, led by the Broad Institute, examined brain tissue from 52 patients where 17 were diagnosed with Alzheimer's at later stages of their lives, identifying early cellular changes such as neuronal hyperactivity and microglial inflammatory changes. They found that oligodendrocytes also participate in plaque formation—this together with the known production of amyloid beta by neurons. On the basis of these findings, this study links data from single-nucleus RNA sequencing with clinical data, putting a line under unique cell alterations at the beginning of this disease, which may turn into early intervention strategies. In a related development, researchers from Cambridge have thrown more light on molecular mechanisms driving Alzheimer's, focused on protein misfolding and the creation of toxic amyloid fibrils. Their work has illustrated the malfunctions of proteins that initiate chain reactions, whereupon toxic oligomers will then accumulate and hence be poisonous to neurons. Understanding such processes may help scientists in the development of directed therapies and improvement of the accuracy of early diagnosis. Indeed, this is one gigantic step toward the cure of Alzheimer's, through cellular and molecular approaches.



Impacts on body systems

The effects of the progression of Alzheimer's disease extend to various other body systems outside the brain. For example, gut microbiota dysbiosis in the gastrointestinal tract may induce the production of amyloids and lipopolysaccharides that enter into the circulation and contribute to Alzheimer's pathology. Dietary interventions such as a plant-based diet or Mediterranean diet may therefore offset these effects. Respiratory complications mostly arise in an older patient who suffers from Alzheimer's disease, brought about by conditions such as asthma, infection, or COPD. Preventive measures are aimed at keeping off such irritants and performing breathing exercises. This disease mostly affects the nervous system, hence leading to a decline in cognitive abilities, loss of memory, and problems related to daily activities. It also leads to enormous brain damage, which disrupts the normal way of neuronal communication, widespread cell death, and impairment of cognitive and functional abilities.

Management & Treatment

Medical & Surgical treatments

Although now, there is no cure for AD, several treatments can relieve its symptoms. Acetylcholinesterase inhibitors, such as donepezil, galantamine, and rivastigmine, and memantine are medications that achieve beneficial effects by either improving communication among brain cells or by blocking toxic chemicals temporarily. Later on in the advanced stage, antipsychotics like risperidone or haloperidol may be prescribed for heavy behavioral symptoms, but they are very cautiously prescribed as they have several side effects. Cognitive function and well-being targeted treatments comprise cognitive stimulation therapy, cognitive rehabilitation, and reminiscence therapy. Some surgical options, such as deep brain stimulation, seem to have some effect on neurological disorders and thus may probably hold a role in Alzheimer's. Deep brain stimulation involves the implantation of a device that sends electrical impulses into the brain, altering brain activity to ameliorate the symptoms.

Lifestyle & Dietary modification

Living well with Alzheimer's disease means attending to one's physical, emotional, social, and spiritual welfare. The importance of physical health needs to be stressed with regular checkups, a good diet, and exercise. In this respect, brisk walking or cycling combined with a heart-healthy Mediterranean diet might have benefits to brain function and general health. Keeping the mind active with mentally stimulating activities may enhance activity in the brain, and many such activities provide social contact. Feelings are supported through talking, joining support groups, and intimate relationships. Spiritual health can be fostered by introspection, community involvement, or spiritual activities. Dietary changes, especially easily chewable and swallowable food, and hydration are extremely important in the advanced stages of the condition. Eating habits and food preparation modifications are required in the advanced stages of the condition for appetite and dysphagia-related problems.

Rehabilitation & supportive care

The rehabilitation program for Alzheimer's patients has to be individualized concerning symptoms and course of illness. The basic components are physical activity, social activity, good nutrition, and good health care. The activities ought to be structured, familiar, and matched to the person's capability with cues from the caregivers for preferred behaviors to be performed. Safety is a significant factor to be watched out for. Palliative care concentrates on the enhancement of quality of life for patients and families, dealing with such symptoms as depression and anxiety, overlooking health in general. That is to say, it provides a multidisciplinary support team for facilitating the management of symptoms and guiding the future of care decisions with access to services available in hospitals, outpatient clinics, or at home.

Prevention & Control

Prevention Strategies

Healthy lifestyle habits, such as diet, exercise, not smoking, and cognitive activities: There is very limited evidence that these may have a risk-reducing effect on AD and dementia, and further research in this area is needed. Adherence to the

Mediterranean diet, characterized by a high intake of fruits, vegetables, legumes, cereals, and fish and a high use of olive oil, is associated with a lower risk of AD and better cognitive function. In addition, it lowers the risk of high blood pressure, high cholesterol, and type 2 diabetes—these are risks for dementia. Preventive measures to ensure good brain health include not smoking, controlling vascular risk factors, adhering to a balanced diet, keeping physically active socially, maintaining a good weight, taking care of one's mental health, engaging in mental exercises that challenge one's cognitive skills, protecting oneself from head injuries, managing one's hearing loss by seeking treatment, not consuming much alcohol, and getting enough sleep.

Public health Interventions

The three-tiered comprehensive Dementia Prevention Action Plan at the levels of primary, secondary, and tertiary prevention was developed by the NNIDR Dementia Prevention Special Interest Group. It identifies strategies that involve creating public health and clinical practice guidelines related to dementia prevention, educating primary care providers, and increasing the focus of the Medicare Benefits Schedule on dementia prevention. Research funding in evidence-based interventions, health promotion activities, expansion of diversity in public health campaigns, and multi-sectoral coordination are some of the significant elements of the plan. Some public health approaches include population-based data mobilization, education campaigns, and competency development among health professionals. The National Alzheimer's Project Act along with Healthy Brain Initiative concentrates on prevention and cure of Alzheimer's disease through research, public education, and evidence-based practices.

Vaccination & Screening programs

Vaccination against tetanus, diphtheria, pertussis, shingles, and pneumococcus is associated with a reduced risk for Alzheimer's disease, according to UTHealth Houston research published in the Journal of Alzheimer's Disease. It concluded that vaccinated subjects had a very statistically significant decreased risk of developing Alzheimer's, possibly because vaccines modulate toxic proteins and decrease neuroinflammation. This is also in line with previous research showing flu vaccination lowers Alzheimer's risk. Alzheimer's screening is commonly done using the tools like Montreal Cognitive Assessment and Saint Louis University

Mental Status Exam. Other tests include the AD8 Informant Interview and the Clock-Drawing Test. Further testing after screening may be done including a physical exam, blood testing or brain imaging so as to rule in or rule out dementia.

Prognosis

Outcomes & survival rates

Gradual but continuous, Alzheimer's takes place through five successive steps of progressive decline in brain functions. The preclinical stage does not yet show symptoms, but through imaging, the authors note the early changes with amyloid plaques and neurofibrillary tangles. Mild cognitive impairment (MCI) consists of subtle memory difficulties and problems with thinking that are not severe enough to affect everyday life. Mild dementia is more of a problem with memory loss, problem-solving difficulty, and personality changes that make everyday functions different. Moderate dementia refers to important confusion and memory loss and an increasing need for help with daily activities; there is also marked behavioral change. In severe dementia, a serious decline in the capability of communication and motor functions would ensue, thereby requiring absolute help on daily care, often leading to loss of motor functions. The speed at which the disease takes its course varies; average life expectancy post-diagnosis ranges from three to 11 years, influenced by factors such as untreated vascular risk and complications like pneumonia.

Prognosis affecting factors

This study aimed at pointing out factors that are prognostic for very old patients suffering from Alzheimer's disease, vascular dementia, and other dementias, based on follow-up examinations 3 and 7 years later. Carried out in Stockholm, Sweden, based on 133 AD, 52 VaD, and 38 OD cases, the outcome was that older age, male gender, low education, comorbidity, and functional disability were significant predictors of poor survival. In 81 subjects with mild to moderate dementia, who survived 3 years, cognitive decline averaged 2.4 MMSE points per year. The rate of decline was influenced by dementia type, higher baseline

cognitive function, and by functional disability, with differential effects based on dementia type, and for AD, by female sex. This study identifies the use of clinical and demographic data in predicting poorer outcomes and calls for detailed clinical assessments, more so in patients with extra chronic conditions.

Quality of life

Dementia reduces the quality of life, as patients become dependent on their caregivers to execute day-to-day activities. The patient seems to lose control over his or her life with the progressing illness and is in much emotional distress and mental decline. This can be managed through medication and therapy, but a good attitude and acceptance help work wonders in improving attitudes. Most cases, however, result in increased anxiety and depression with a decline in independence. The worse dementia is, the harder it becomes to be optimistic, and this moves back again to affect their quality of life.

Current research & Future directions

Recent advances & discoveries

Recently, families with late-onset Alzheimer's disease have been identified in which the illness had a purely genetic origin; these individuals all carried two copies of the APOE4 gene, which delayed the age of symptom onset by 7 to 10 years compared with other causes of late-onset illness. This discovery implicates APOE4 as a cause, not just a risk factor, in some 15% of all Alzheimer's patients. Studies have shown that carriers of two copies of APOE4 start building up more amyloid in the brain at an earlier age and begin to show initial symptoms of the disease sooner. The findings point to a strong need for targeted treatments and further research into APOE4, but not everyone who has this pair of genes develops Alzheimer's, and the way they interact in diverse populations needs further study. Genetic tests are currently used mostly for research purposes and for making treatment plans, but they cannot be recommended yet for general screening.

Ongoing Clinical Trials

Current Alzheimer's treatments, such as cholinesterase inhibitors and memantine, improve symptoms but don't stop disease progression. New approaches are exploring targeted therapies to address the disease's underlying causes, including drugs that reduce beta-amyloid plaques, prevent tau tangles, and reduce inflammation. Additionally, researchers are investigating connections between heart health and Alzheimer's and testing new medications like saracatinib. Despite some experimental drugs showing limited success, the Critical Path for Alzheimer's Disease (CPAD) consortium is working to accelerate treatment development through data sharing and standardized trials.

Future research needed

Knowing the drugs for Alzheimer's will help make informed treatment decisions. The two main categories of approved drugs by the FDA today are those that alter the disease progression and those that alleviate symptoms temporarily. An example is anti-amyloid treatments, such as those targeting beta-amyloid plaques, that intend to slow cognitive and functional decline; they are especially beneficial for those patients in their early phases. Such medications offer meaningful changes in the progress of the disease but on the other hand, they also may have possible side effects including ARIA and infusion-related reactions. The anti-amyloid drug Aducanumab, approved for early Alzheimer's, is being discontinued. Current users can retain access until late 2024.

Case study

A 68-year-old engineer, Mr. A, was evaluated for progressive verbal communication difficulties noted by his wife during the past four years. Although he had slight problems in daily life and at work, he experienced specific language malfunction manifested by word-finding difficulty, anomia, and inability to recall recent conversations. The neurological examination revealed important language disorders, together with prominent disturbances of memory, with some preserved cognitive functions. Though an MRI and cerebrospinal fluid tests did not show anything, neuropsychological testing proved severe disturbances in memory and language. An autopsy was done later, which confirmed the diagnosis of AD based

on the presence of amyloid plaques, neurofibrillary tangles, and other classical pathology. Although the initial symptoms and family history suggested an AD diagnosis, the appearance of parkinsonism-like symptoms and a pattern of progression of the cognitive decline were typical for AD but less usual for Parkinson's disease and other dementias.