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Causes of Dementia

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Dementia is characterized by a decline in cognitive abilities that impairs everyday activities. The dementias are diverse syndromes, often thought of as syndromes of isolated memory loss, they also include a diverse array of cognitive symptoms including: language impairment, mood disorders, impaired control of skilled movements, mis-perception or impaired recognition, and difficulties with planning and organization. The varied causes of dementia are characterized by distinct abnormalities of brain structure and function that lead to these diverse symptoms.

Most of the dementias are considered to be neurodegenerative diseases. That is, they reflect a fundamental loss of neuronal structure and function that is not attributable to any other recognized condition. These disorders are often associated with the accumulation of abnormal proteins, or normal proteins in abnormal forms. These proteinopathic etiologies trigger a diverse array of inflammatory, vascular, and neurotoxic effects that may play varying roles in the pathophysiology of these disorders.

Alzheimer's Disease is the most common neurodegenerative dementia, accounting for more than half of all cases of dementia in the US. Other common neurodegenerative dementias include: Fronto-temporal lobar degeneration, Parkinson's disease, Lewy Body disease, and less commonly, Huntington's disease (What's Causing your Memory Loss?)

The neurodegenerative dementias are generally considered irreversible; at this time, there is no therapy that can reverse the loss of brain cells (Table 1). In others cases, patients may develop the late-life cognitive decline of a dementia that is secondary to some other disorder. This commonly include endocrine, metabolic, cardiovascular, and infectious causes (Table 2). In these cases, the dementia may be reversed by the effective treatment of the underlying disease. Finally, a substantial number of dementias are attributable to abnormalities in the blood vessels of the brain (Table 3). These vascular dementias may lead to irreversible symptoms, but may be well-controlled by appropriate treatments that limit the rate of further

Table 1: Causes and Characteristics of Irreversible Dementia.

Cause	Characteristics
Alzheimer's Disease	<ul style="list-style-type: none"> ● Most common cause of dementia; accounts for an estimated 60 percent to 80 percent of cases. About half of these cases involve solely Alzheimer's pathology; many have evidence of pathologic changes related to other dementias (see mixed vascular dementia). ● Difficulty remembering recent conversations, names or events is often an early clinical symptom; apathy and depression are also often early symptoms. Later symptoms include impaired communication, disorientation, confusion, poor judgment, behavior changes and, ultimately, difficulty speaking, swallowing and walking. ● Revised criteria and guidelines for diagnosing Alzheimer's were proposed and published in 2011. They recommend that Alzheimer's be considered a slowly progressive brain disease that begins well before clinical symptoms emerge. ● The hallmark pathologies of Alzheimer's are the progressive accumulation of the protein fragment beta-amyloid (plaques) outside neurons in the brain and twisted strands of the protein tau (tangles) inside neurons. These changes are eventually accompanied by the damage and death of neurons.
Dementia with Lewy Bodies (DLB)	<ul style="list-style-type: none"> ● People with DLB have some of the symptoms common in Alzheimer's, but are more likely to have initial or early symptoms of sleep disturbances, well-formed visual hallucinations and slowness, gait imbalance or other parkinsonian movement features. These features, as well as early visuospatial impairment, may occur in the absence of significant memory impairment. ● Lewy bodies are abnormal aggregations (or clumps) of the protein alpha-synuclein that accumulate in neurons. When they develop in a part of the brain called the cortex, dementia can result. Alpha-synuclein also aggregates in the brains of people with Parkinson's disease (PD), in which it is accompanied by severe neuronal loss in a part of the brain called the substantia nigra. While people with DLB and PD both have Lewy bodies, the onset of the disease is marked by motor impairment in PD and cognitive impairment in DLB. ● The brain changes of DLB alone can cause dementia. But very commonly brains with DLB have coexisting Alzheimer's pathology. In people with both DLB and Alzheimer's pathology, symptoms of both diseases may emerge and lead to some confusion in diagnosis. Vascular dementia can also coexist and contribute to the dementia

<p>Fronto-temporal lobar degeneration (FTD)</p>	<ul style="list-style-type: none"> • Includes dementias such as behavioral-variant FTLD, primary progressive aphasia, Pick's disease, corticobasal degeneration and progressive supranuclear palsy. • Typical early symptoms include changes in personality and behavior and difficulty with producing or comprehending language. Unlike Alzheimer's, memory is typically spared in the early stages of disease. • Nerve cells in the front (frontal lobe) and side regions (temporal lobes) of the brain are especially affected, and these regions become markedly atrophied (shrunken). In addition, the upper layers of the cortex typically become soft and spongy and have protein inclusions (usually tau protein or the transactive response DNA-binding protein). • The brain changes of behavioral-variant FTLD may in patients age 65 years and older, as in Alzheimer's disease. Most people with this form of dementia develop symptoms at a younger age (~60). In this younger age group, FTLD is the second most common degenerative dementia
<p>Parkinson's Disease (PD)</p>	<ul style="list-style-type: none"> • Problems with movement (slowness, rigidity, tremor and changes in gait) are common symptoms of PD. • In PD, alpha-synuclein aggregates appear in an area deep in the brain called the substantia nigra. The aggregates are thought to cause degeneration of the nerve cells that produce dopamine. • The incidence of PD is about one-tenth that of Alzheimer's. • PD is often accompanied by dementia secondary to the accumulation of Lewy bodies in the cortex (as in DLB) or the accumulation of beta-amyloid clumps and tau tangles (as in Alzheimer's disease)
<p>Creutzfeldt-Jakob Disease</p>	<ul style="list-style-type: none"> • This very rare and rapidly fatal disorder impairs memory and coordination and causes behavior changes. Results from a misfolded protein (prion) that causes other proteins throughout the brain to misfold and malfunction. • May be hereditary (caused by a gene that runs in one's family), sporadic (unknown cause) or caused by a known prion infection. • A specific form called variant Creutzfeldt-Jakob disease is traced to the consumption of products from cattle affected by mad cow disease.
<p>Huntington's</p>	<ul style="list-style-type: none"> • Huntington's disease is a progressive brain disorder caused by a single defective gene on chromosome 4. • Symptoms: Include abnormal involuntary movements, a severe decline in thinking and reasoning, irritability, and mood changes. • Brain changes: The gene defect causes abnormalities in a brain protein that, over time, lead to worsening symptoms.

Table 2: Types of Reversible Dementias, Descriptions, and Possible Treatments

Reversible Dementia	Description	Treatment
Normal Pressure Hydrocephalus	Abnormal buildup of CSF in the brain. Swelling and pressure over time can damage the brain.	implantation of a shunt to divert fluid from the brain
Drug side effects	Drugs can build up in the system or interact with one another and cause memory symptoms	Cessation of drug administration
Depression	Regions of the brain responsible for memory, thinking, mood, sleep, and appetite are impaired (psuedodementia)	Treatment of depression
Delirium	Mental changes that mimic dementia but develop quickly, in a matter of hours or days. May occur because of a life-threatening illness, after surgery, or because of drug or alcohol withdrawal.	Treatment of cause
Vitamin B-12 deficiency	Pernicious anemia: the bone marrow produces RBC that are larger and less numerous, usually caused by an inability to absorb the vitamin from food.	B12 injections
Tumors	Can interfere with cognitive functioning and trigger other symptoms	Treatment of tumor, removal
Subdural Hematomas	Blood clots caused by bruising between the brain surface and the thin membrane that covers it. Caused by head trauma	Removal of the clot
Thyroid Disease	Hyperthyroidism (overproduction of thyroid hormones) and hypothyroidism (underproduction of thyroid hormones)	Hyperthyroidism: removal of thyroid Hypothyroidism: hormone replacement
Wernicke-	severe deficiency of thiamine (vitamin	B1 supplements

Toxic exposure	damage to brain cells caused by exposure to solvents or heavy metal dust and fumes (especially lead)	Exposure treatment, avoiding further exposure (Davis, 2015)
Sleep Disorders	Sleep apnea, cognition becomes slower	Treat sleep disorder, CPAP (Span, 2014)

Table 2: **Types of Reversible Dementias, Descriptions, and Possible Treatments.** Created using data from What’s Causing Your Memory Loss? (n.d.), Harvard Health Publications, from <http://www.helpguide.org/harvard/whats-causing-your-memory-loss.html>

Table 3: *Types of Reversible Dementias, Descriptions, and Possible Treatments*

Reversible Dementia	Description	Treatment
Vascular Dementia	<ul style="list-style-type: none"> Previously known as multi-infarct or post-stroke dementia, vascular dementia is less common as a sole cause of dementia than Alzheimer’s, accounting for about 10 percent of dementia cases. However, it is very common in older individuals with dementia, with about 50 percent having pathologic evidence of vascular dementia (infarcts). In most cases, the infarcts coexist with Alzheimer’s pathology (see mixed dementia in this table). Impaired judgment or impaired ability to make decisions, plan or organize is more likely to be the initial symptom, as opposed to the memory loss often associated with the initial symptoms of Alzheimer’s. Vascular dementia occurs most commonly from blood vessel blockage or damage leading to infarcts (strokes) or bleeding in the brain. The location, number and size of the brain injuries determine whether dementia will result and how the individual’s thinking and physical functioning will be affected. In the past, evidence of vascular dementia was used to exclude a diagnosis of Alzheimer’s (and vice versa). That practice is no longer 	<ul style="list-style-type: none"> Anti-platelet, anti-coagulant, anti-arrhythmic therapies

	coexist. When evidence of two or more causes of dementia are present at the same time, the individual is considered to have mixed dementia (see mixed dementia in this table).	
Mixed Dementia	<ul style="list-style-type: none"> • Characterized by the hallmark abnormalities of more than one cause of dementia — most commonly Alzheimer’s combined with vascular dementia, followed by Alzheimer’s with DLB, and Alzheimer’s with vascular dementia and DLB. Vascular dementia with DLB is much less common. • Recent studies suggest that mixed dementia is more common than previously recognized, with about half of those with dementia having pathologic evidence of more than one cause of dementia. 	<ul style="list-style-type: none"> • Anti-platelet, anti-coagulant, anti-arrhythmic therapies
Cerebral Vasculitis	Inflammation and necrosis of blood vessel walls	Immuno-suppressive therapies

Table 3: **Vascular Dementias**. Adapted from Alzheimer's Disease Facts and Figures. Gaugler, J., James, B., Johnson, T., Scholz, K., & Weuve, J. (2015). Alz.org.

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