Dementia with Lewy bodies

Dementia with Lewy bodies is a nervous system disorder characterized by a decline in intellectual function (dementia), a group of movement problems known as parkinsonism, visual hallucinations, sudden changes (fluctuations) in behavior and intellectual ability, and acting out dreams while asleep (REM sleep behavior disorder). This condition typically affects older adults, most often developing between ages 50 and 85. The life expectancy of individuals with dementia with Lewy bodies varies; people typically survive about 5 to 7 years after they are diagnosed.

REM sleep behavior disorder is usually the first sign of dementia with Lewy bodies. It can occur years before other symptoms appear. Individuals with REM sleep behavior disorder act out their dreams, talking and moving in their sleep. This behavior becomes less pronounced as dementia with Lewy bodies worsens and additional features develop.

Dementia is often the second major feature to develop in dementia with Lewy bodies. This intellectual decline often leads to impaired ability to perform visual-spatial tasks such as puzzles. Affected individuals may also have poor problem-solving skills (executive functioning), speech difficulties, and reduced inhibitions. Problems with memory typically do not occur until later.

In people with dementia with Lewy bodies, visual hallucinations typically involve people or animals. Fluctuations in behavior and intellectual ability include sudden changes in attention, thought processes, and mood. Affected individuals might have inconsistent behaviors, unintelligible speech, and brief episodes of altered consciousness that may appear as staring spells.

Parkinsonism is usually the last major feature to develop in people with dementia with Lewy bodies. In affected individuals, the movement problems typically include tremors, rigidity, unusually slow movement (bradykinesia), and impaired balance and coordination (postural instability). Affected individuals often require walking aids or wheelchair assistance.

Individuals with dementia with Lewy bodies may also experience a sharp drop in blood pressure upon standing (orthostatic hypotension), fainting episodes (syncope), difficulty controlling the flow of urine (incontinence), or constipation.

Frequency

Dementia with Lewy bodies is estimated to affect 1.4 million people in the United States. It accounts for about 5 percent of all dementia cases in older individuals and is the second most common dementia after Alzheimer disease.
Causes
Mutations in the \textit{SNCA} or \textit{SNCB} gene cause dementia with Lewy bodies. \textit{GBA} gene mutations increase the risk of developing the condition, but are not a direct cause. The \textit{SNCA} and \textit{SNCB} genes provide instructions for making proteins that are found primarily in the brain, called alpha-synuclein and beta-synuclein, respectively. Alpha-synuclein plays a role in communication between nerve cells (neurons), helping to regulate the release of chemical messengers (neurotransmitters). Beta-synuclein is likely involved in a process that allows neurons to change and adapt over time, which is necessary for learning and memory. Beta-synuclein may also prevent harmful accumulation of alpha-synuclein in neurons. The enzyme produced from the \textit{GBA} gene is found throughout the body in cell structures called lysosomes that digest and recycle proteins and other materials that are no longer needed.

Mutations in these three genes result in the formation of Lewy bodies, which are clusters of alpha-synuclein protein. \textit{SNCA} gene mutations result in misshapen alpha-synuclein proteins that cluster together (aggregate). \textit{SNCB} gene mutations lead to the production of an altered beta-synuclein protein that allows accumulation of alpha-synuclein. \textit{GBA} gene mutations are thought to disrupt the normal function of lysosomes. Research suggests that malfunctioning lysosomes impair the breakdown of alpha-synuclein, increasing the risk of its accumulation and the formation of Lewy bodies.

In dementia with Lewy bodies, these clusters accumulate in neurons throughout the brain where they impair cell function and ultimately cause cell death. Neurons that produce the neurotransmitter dopamine seem to be particularly sensitive to the presence of Lewy bodies. Dopamine has many important functions, including playing complex roles in thought (cognition), motivation, behavior, and control of movement. Over time, the loss of dopamine-producing neurons increasingly impairs intellectual and motor function and the regulation of emotions, resulting in the signs and symptoms of dementia with Lewy bodies.

Inheritance Pattern
When dementia with Lewy bodies is caused by \textit{SNCA} or \textit{SNCB} gene mutations, it is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In these cases, an affected person usually has one parent with the condition.

People with a mutation in one copy of the \textit{GBA} gene inherit an increased risk of developing dementia with Lewy bodies, not the condition itself. Some people with a mutation in the \textit{GBA} gene never develop dementia with Lewy bodies. This increased risk is inherited in an autosomal dominant pattern.

Other Names for This Condition
- dementia of the Lewy body type
- dementia, Lewy body
• diffuse Lewy body disease
• DLB
• LBD
• Lewy body dementia
• Lewy body disease

Diagnosis & Management

Formal Diagnostic Criteria


Formal Treatment/Management Guidelines

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting

- Genetic Testing Registry: Lewy body dementia

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22dementia+with+Lewy+odies%22+OR+%22Lewy+Body+Disease%22+OR+%22Lewy+body+dementia%22

Other Diagnosis and Management Resources

- Johns Hopkins Medicine
  https://www.hopkinsmedicine.org/healthlibrary/conditions/adult/nervous_system_disorders/dementia_with_lewy_bodies_134,76

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Dementia
  https://medlineplus.gov/dementia.html

- Health Topic: Lewy Body Disease
  https://medlineplus.gov/lewybodydisease.html

Genetic and Rare Diseases Information Center

- Lewy body dementia
  https://rarediseases.info.nih.gov/diseases/3243/lewy-body-dementia

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Dementia-Lewy-Bodies-Information-Page

- National Institute on Aging
  https://www.nia.nih.gov/health/what-lewy-body-dementia

- National Institutes of Health
Educational Resources

• Johns Hopkins Medicine
  https://www.hopkinsmedicine.org/healthlibrary/conditions/adult/nervous_system_disorders/dementia_with_lewy_bodies_134,76

• Merck Manual Consumer Version

Patient Support and Advocacy Resources

• Alzheimer’s Association
  https://www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/dementia-with-lewy-bodies

• Brain Foundation (Australia)

• Caregiver Action Network
  http://caregiveraction.org/

• Dementia Society of America
  https://www.dementiasociety.org/lewy-body-dementia

• Family Caregiver Alliance
  https://www.caregiver.org/

• Lewy Body Dementia Association
  https://www.lbda.org/

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28dementia+with+Lewy+bodies%5BTI%5D%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• DEMENTIA, LEWY BODY
  http://omim.org/entry/127750

Medical Genetics Database from MedGen

• Lewy body dementia
Sources for This Summary

  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3162640/


  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5496518/


  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3841974/

  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5079284/

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